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TURKISH JOURNAL OF OBSTETRICS AND GYNECOLOGY

CONTENTS

TURKISH JOURNAL OF OBSTETRICS AND GYNECOLOGY

LETTER FROM THE PRESIDENT

Dear Turkish Society of Gynecology and Obstetrics Family,

I am greatly honored to be before you once again with the June issue of our scientific journal. As a result of intensive work and effort, we take justified pride in presenting another scientifically strong issue to you, our esteemed colleagues. When our June issue is reviewed, it will be seen that we have included the works of respected national and international scientists. I would also like to share the good news that the current impact factor of our journal, which has gained great momentum, is 1.4.

Dear colleagues, as you all know, we held the 23rd National Turkish Gynecology and Obstetrics Congress at Limak Hotel in Cyprus between 13 and 17 May, with 1,400 participants, 56 scientific sessions, 7 satellite symposia, 13 oral presentation sessions, and the support of 95 sponsoring companies, in a manner befitting the largest umbrella association of our country, both in scientific terms and in terms of the richness of its social content.

With the pride of serving as the president of the Turkish Society of Gynecology and Obstetrics, the largest obstetrics and gynecology association in our country, and with an understanding of scientific and social association work that embraces all our colleagues, I extend my warm regards and best wishes until we meet again in the next issue of our scientific journal.

Best Regards
Ismail Mete Itil, Prof. MD
President of TJOD

TURKISH JOURNAL OF OBSTETRICS AND GYNECOLOGY

EDITORIAL

Dear Colleagues,

We are once again before you with the June issue of the Turkish Journal of Obstetrics and Gynecology, the scientific journal of the Turkish Society of Gynecology and Obstetrics. During the preparation of this issue, we went through a demanding three-month period together with our editorial board, section editors, and reviewers. Our journal receives significant interest from both national and international platforms. This clearly demonstrates the distinguished position of our journal and indicates that, in the coming years, it will become an indispensable cornerstone of prestigious scientific indexes.

In our June issue, in addition to our scientifically high-quality publications, we have also included the poster and oral presentations presented at the congress organized by the Turkish Gynecologic Cancer Foundation in Ankara on 3-5 April 2026.

We would like to share with our esteemed colleagues that our dedicated efforts will continue, and we look forward to meeting you again in the September issue, the third issue of 2026.

Best Regards
Ercan Yilmaz, Prof. MD

Clinical Investigation / Araştırma

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Long non-coding RNA maternally expressed gene 3 (*MEG3*) rs4081134 gene polymorphism and preeclampsia risk

Uzun kodlayıcı olmayan bir RNA olan maternal eksprese edilen gen 3'teki (MEG3) rs4081134 gen polimorfizmi ve preeklampsi riski

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Abstract

Objective: Preeclampsia (PE), a significant challenge for health systems, is a hypertensive disorder of pregnancy. Some studies have suggested that long non-coding ribonucleic acids play a major role in the pathogenesis of PE by regulating the biological behaviors of maternal vascular smooth muscle cells and trophoblasts. In this study, the impact of the maternally expressed gene 3 (*MEG3*) rs4081134 gene polymorphism on susceptibility to PE has been evaluated.

Materials and Methods: We conducted a case-control study comprising 130 PE patients and 140 normotensive pregnant women with normal gestational outcomes genotype analysis was performed using the polymerase chain reaction-restriction fragment length polymorphism method.

Results: A significant association was evident between the AA genotype and PE risk under the recessive model, indicating that these may serve as protective factors against the development of PE. No significant relationships were detected between other genotypes, genetic models, or allelic distributions and PE risk. Additionally, among pregnant women with PE, a notable correlation was observed between newborn birth weight and the rs4081134 polymorphism in the *MEG3* gene.

Conclusion: We found a significant association between the AA genotype, as well as the recessive model of the *MEG3* rs4081134 gene polymorphism, and PE deployment. Among women diagnosed with PE, *MEG3* rs4081134 gene polymorphism was significantly associated with newborn's birth weight.

Keywords: Maternally expressed gene 3, preeclampsia, gene, polymorphism

Öz

Amaç: Sağlık sistemleri için önemli bir sorun olan preeklampsi (PE), gebeliğin hipertansif bir bozukluğudur. Bazı çalışmalar, uzun kodlayıcı olmayan ribonükleik asitlerin maternal vasküler düz kas hücrelerinin ve trofoblastların biyolojik davranışlarını düzenleyerek PE patogenezinde önemli bir rol oynadığını öne sürmüştür. Bu çalışmada, maternal eksprese edilen gen 3 (*MEG3*) rs4081134 gen polimorfizminin PE'ye yatkınlık üzerindeki etkisi değerlendirilmiştir.

Gereç ve Yöntemler: Yüz otuz PE hastası ve normal gebelik sonuçlarına sahip 140 normotansif hamile kadından oluşan bir olgu-kontrol çalışması yürütüldü ve genotip analizi polimeraz zincir reaksiyonu-restriksiyon fragment uzunluk polimorfizmi yöntemi kullanılarak gerçekleştirildi.

PRECIS: Based on our results, AA genotype and recessive model may be act as a protective factor on preeclampsia development. Furthermore, the maternally expressed gene 3 rs4081134 gene polymorphism had a significant impact on newborns' birth weight.

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Bulgular: Resesif model altında AA genotipi ile PE riski arasında bunların preeklampsi gelişimine karşı koruyucu faktörler olarak işlev görebileceğini gösteren anlamlı bir ilişki saptandı. Diğer genotipler, genetik modeller veya alel dağılımları ile preeklampsi riski arasında anlamlı bir ilişki saptanmadı. Ek olarak, preeklampsi tanısı konmuş hamile kadınlarda, yenidoğan doğum ağırlığı ile *MEG3* genindeki rs4081134 polimorfizmi arasında dikkat çekici bir korelasyon gözlemlendi.

Sonuç: AA genotipi ve *MEG3* rs4081134 gen polimorfizminin resesif modeli ile preeklampsi gelişimi arasında anlamlı bir ilişki bulduk. Preeklampsi tanısı konmuş kadınlarda, *MEG3* rs4081134 gen polimorfizmi yenidoğan doğum ağırlığı ile anlamlı bir şekilde ilişkiliydi.

Anahtar Kelimeler: Maternal eksprese edilen gen 3, preeklampsi, gen, polimorfizm

Introduction

Preeclampsia (PE), as a significant risk for mother and fetus, is specified by unprecedented hypertension (>140/90 mmHG) and proteinuria (>300 mg/24 hours) after 20 weeks of gestation, which occurs in about 3% of all pregnancies[1]. PE is divided into two main categories based on the time of diagnosis: early-onset PE (occurring before 34 weeks) and late-onset PE (occurring after 34 weeks)[2]. The increased frequency of certain maternal and fetal adverse outcomes in early-onset PE suggests that this type represents a more severe manifestation of the condition compared to late-onset PE, thus requiring particular attention[3,4]. Impacts of PE on the fetus include intrauterine growth restriction, lower birth weight, stillbirth, preterm birth, and its associated complications[5]. Maternal complications vary among individuals because of variability in organ involvement during PE. Hypertension, liver failure, renal failure, cardiomyopathy, coronary artery disease, pulmonary edema, diabetes mellitus, and stroke are some maternal outcomes of PE. Despite the advancement of our knowledge in the field of PE, Considerable progress has still not been made in the clinical context to address our challenges in exposure to PE[6,7].

Findings including the predisposition to PE in certain molar pregnancies (where no fetus is present), along with the resolution of PE-related symptoms after childbirth, indicate that the placenta has a central role in the PE pathogenesis[8]. In contrast to late-onset PE, the underlying pathophysiology of early-onset PE is more closely related to abnormalities during placental development[9]. In normal placentation, the remodeling of maternal myometrial and decidual spiral arteries plays a pivotal role in providing sufficient uteroplacental blood flow[10]. Interstitial and endovascular extravillous trophoblasts invasion and migration to decidua of the uterus, drive spiral artery remodeling by influencing vascular smooth muscle cells (VSMCs) and endothelial cells, respectively[11]. Shallow invasion of the spiral arteries following defective placentation causes poor placental perfusion. In response to hypoxic conditions, an imbalance of angiogenic factors occurs, and proinflammatory cytokines and reactive oxygen species are released into the maternal bloodstream. These substances are key contributors to the pathogenesis of PE[12].

Non-coding ribonucleic acids (ncRNAs) are functional RNA transcripts that lack protein-coding capacity. They are divided into two subgroups: structural and regulatory. Regulatory noncoding RNAs consisting of <200 nucleotide (nt) are considered small non-coding RNAs (sncRNAs), and those with more than 200 nt are called long ncRNAs (lncRNAs) [13]. LncRNAs influence numerous biological and pathological processes within cells by modulating gene expression at various levels, including transcription and chromatin remodeling. multiple studies have demonstrated the key role of lncRNAs in the development of PE by modifying trophoblast biological behaviors, including proliferation, migration, invasion, and apoptosis[14,15]. Furthermore, using microarray and RNA-seq approaches has revealed dysregulation of lncRNAs within placental and decidual tissues from preeclamptic individuals compared to healthy controls[16,17].

Maternally expressed gene 3 (*MEG3*) is a tumor suppressor lncRNA from chromosome 14q32.2[18]. Yu et al.[19] have demonstrated lower expression of *MEG3* in placental tissue of PE compared to standard controls. In addition to, lower expression of *MEG3* decreased the migratory and invasive properties of human trophoblasts *in vitro* by attenuating the epithelial-mesenchymal transition (EMT) process. Although *MEG3* regulatory mechanism on EMT remains to be elucidated, a negative relationship between EMT and the transforming growth factor β (TGF-β)/Smad pathway has been documented upon *MEG3* dysregulation. On the other hand, it has been suggested that downregulating *MEG3* by inhibiting the Notch1 signaling pathway diminishes EMT process in trophoblasts and subsequently leads to PE as a possible mechanism of action[20]. The effects of *MEG3* in placentation are not limited to trophoblasts. On the maternal side, initiation of spiral artery remodeling requires proliferation arrest of VSMCs, induction of apoptosis, and enhanced migration of these cells. Upregulation of *MEG3* induced by factors released from uterine natural killer cells facilitates these essential alterations of VSMCs in the maternal spiral arteries of the uterus[21,22].

Regarding the significance of *MEG3* in healthy placentation, this study aimed to evaluate the involvement of the *MEG3* rs4081134 gene polymorphism in PE susceptibility.

Materials and Methods

Participants Data

We conducted a case-control study comprising 130 PE patients and 140 healthy pregnant women. All participants were recruited from among pregnant women seeking prenatal

care at the obstetrics clinic of Ali-ebn Abitaleb Hospital, which is affiliated with Zahedan University of Medical Sciences in Iran. Patients in the case group were determined to have PE according to diagnostic criteria which was defined as unprecedented systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg measured twice separately. Additionally, protein excretion in urine higher than 300 mg in a 24-hour urine specimen was present in all patients after 20 weeks of pregnancy. All participants with diabetes, gestational diabetes, chronic hypertension, chronic kidney disease, cardiovascular disease, hyperthyroidism, or who smoked were excluded from the study. All participants provided written informed consent, and the study protocol received approval from the Ethics Committee of Zahedan University of Medical Sciences (approval number: IR.ZAUMS.REC.1399.239, date: 09.08.2020).

Genotyping

After drawing blood samples from all participants, the samples were stored in K2-EDTA-containing tubes. Peripheral leukocyte deoxyribonucleic acid (DNA) was extracted from 500 µL of blood using the salting-out method and stored at -20 °C until further use. The forward primer (5ı-TTTCTTGTAGCTGCCTCCTCC-3ı) and the reverse primer (5ı-CGTCTGTTGGCTGTGAGTGAATGA-3ı) were used to amplify the desired gene fragment by polymerase chain reaction (PCR). The PCR mixture consisted of 7.5 µL master mix Red 2x, 0.82 forward primers, 0.82 reverse primer, 4.86 µL H_2O, and one µL of DNA. The PCR program was set for 40 cycles, with denaturation at 95 °C for 30 seconds, annealing at 65 °C for 40 seconds, and extension at 72 °C for 35 seconds. 2.7 µL H_2O, 0.3 µL Ndel enzyme, and one µL H_2O were added to 6 µL of PCR product for *MEG3* rs4081134 genotypic determination[23]. After overnight incubation at 37 °C, the microtube contents were separated by gel electrophoresis.

Statistical Analysis

Statistical analysis was performed using SPSS Statistics version 26.0 (SPSS Inc., Chicago, IL, USA). The independent-samples t-test was used to compare demographic and clinical characteristics between the two groups. For women with PE versus healthy controls, odds ratios with 95% confidence intervals were computed for various genotypes, genetic models, and alleles. furthermore, chi-square test and one-way analysis of variance were used to compare PE clinical characteristics in different genotypes of case group. Results with p-values were defined as statistically significant.

Results

Demographic and Clinical Characteristics of PE Patients and Controls

Table 1 demonstrates the demographic and clinical characteristics of the two groups. All precipitants were matched respect to the maternal age (26.7±5.6 and 27.75±6.65 in the control and PE groups, respectively, p=0.164). Significant differences were found between the two groups in birth weight, systolic blood pressure, and diastolic blood pressure. The frequencies of mild and severe PE were 52.3% and 47.7%, respectively. Moreover, 55.4% of participants had early-onset PE, while 44.6% had late-onset PE.

The Correlation Between *MEG3* rs4081134 Gene Polymorphism and PE Susceptibility

As shown in Table 2, the genotype frequencies for GG, GA, and AA were 61.6%, 36.9%, and 1.5% in the PE group and 57.1%, 35.8%, and 7.1% in the control group. A significant association with PE risk was found for both the AA genotype and the recessive model, indicating that they may be protective against the development of PE. Other genotypes, genetic models, and allelic distributions were not significantly associated with PE risk.

Relationship of The Clinical and Demographic Characteristics of PE Patients with *MEG3* rs4081134 Gene Polymorphism

The average maternal age [mean ± standard deviation (SD), years] for the GG, GA and AA genotypes was 28.53±6.78, 26.64±6.4 and 23±5.65, sequentially, which was not statistically significant (p=0.180). The average gestation age (mean ± SD, weeks) for GG, GA and AA genotypes was 36.10±3.61, 35.48±3.91 and 36±2.82, respectively, which was not statistically significant (p=0.66). A significant relationship was found between birth weight (mean ± SD, grams) and the *MEG3* rs4081134 gene polymorphism (p=0.043). The average birth weight for GG, GA and AA genotypes was 2879.38±628.18, 2576.04±817.15 and 3225±318.19, respectively. Moreover, there was no significant correlation between the *MEG3* rs4081134 polymorphism and other clinical characteristics in patients with PE (Table 3).

Discussion

Prior research has supported the involvement of lncRNAs such as *MEG3* in the pathogenesis of PE. Through alternative splicing, various isoforms of *MEG3* are generated. To date, 12 isoforms of *MEG3* have been described. Among them, *MEG3* has been well-reputed[24]. Based on information extracted from GenBank, this isoform contains exons 1-4 and 8-10. The studies have not identified any functional open reading frame (ORF) in the *MEG3* isoforms. The functional studies of ORFs revealed that one ORF does not mediate the functions of *MEG3* . In other words, the whole-length sequence of *MEG3* is needed for essential functions of this ncRNA[25]. Gene expression profiling of *MEG3*-knockdown mice revealed increased expression of genes that contribute to angiogenesis, including vascular endothelial growth factor alpha and its receptor. Angiogenesis is a pivotal step in tumor growth. Therefore, it seems that *MEG3* is involved in procedures that contribute to tumor suppression[24]. *MEG3* interacts with

some targets, through which multiple genes involved in the TGF-β pathway are regulated[26]. The decreased or lost level of *MEG3* was associated with some cancers including pituitary adenomas and meningioma[27,28]. The studies showed that *MEG3* is likely to regulate the p53 protein in different ways. For example, the *MEG3* could block MDM2 transcription, leading to inhibiting the degradation of p53[29]. While many studies confirmed the tumor suppressor role of *MEG3*, primarily through activation and accumulation of p53, there is evidence of an association between knockdown *MEG3* and activation of p53 and metastasis[30].

MEG3 is a key participant in several cancer-related signaling pathways, including Wnt, PI3k/Akt/mTOR, WT1, and TGF-β. Additionally, the serum level of *MEG3*, as well as several single-nucleotide polymorphisms in this ncRNA, serves as a biomarker for specific cancers[31,32]. *MEG3* contributes to the response of cancer cells to chemotherapy agents. An expression study on non-small cell lung carcinoma demonstrated an association between reduced *MEG3* levels and unfavorable responses to cisplatin treatment. In addition, *MEG3* improved the sensitivity of chemotherapy drug response in correlation with miR-21-5p[33].

Bone morphogenetic protein (BMP) and its receptors, *BMPR1* and *BMPR2*, form a tetrameric structure that triggers specific signal cascades. BMP signals through *BMPRs* induce several alterations that are assumed to result in cell proliferation, differentiation, and metastasis[34]. The evidence shows that *BMPR2* is involved in embryonic development and angiogenesis and appears to be correlated with hypertension. The study by Andruska et al.[35] showed a link between *BMPR2* gene mutations and pulmonary hypertension. The expression profile of the placental tissue of PE women showed an increase in miR-21 expression[36,37]. Overexpression of miR-21 inhibitors induced proliferation and invasion of trophoblast cells. These results are consistent with the findings from in silico analysis, which confirmed *BMPR2* as a key direct target of miR-21. Furthermore, *MEG3* has decreased in the placentas of PE participants. Based on bioinformatics results, *MEG3* acts as a molecular sponge that regulates miR-21. Therefore, it is not surprising that the downregulation of *MEG3* led to increased miR-21 expression in women with PE. Conclusively, *MEG3* , acting as a sponge for miR-21, regulates the expression of *BMPR2* and thereby improves trophoblast proliferation. Therefore, *MEG3* is involved in a regulatory mechanism that prevents premature ejaculation (PE)[38]. These do not bear on the *MEG3* effects in the pathogenesis of PE. It is suggested that *MEG3* is involved in metastasis by expression regulation of elements that contribute to the metastasis process, including nuclear factor kappa B, caspase, and Bax[39]. The documents showed that *MEG3* blocked cell proliferation by targeting Notch1 in endometrial carcinoma cells. In addition, Notch1 downregulation in PE promotes

Table 1. Demographic and clinical characteristics of preeclampsia patients and controls

Variable	Controls	PE	p-value
Maternal age (mean ± SD, years)	26.7±5.6	27.75±6.6	0.164
Gestation age (mean ± SD, weeks)	38.56±1.4	35.87±3.7	<0.0001
Birth weight (mean ± SD, g)	3131.93±396.4	2772.69±714.5	<0.0001
SBP (mean ± SD, mmHg)	108.31±8	152.91±16.3	<0.0001
DBP (mean ± SD, mmHg)	69.82±8	88.62±22.7	<0.0001
Proteinuria (n, %)			
Trace	-	11 (8.5%)	
1+	-	43 (33.1%)	
2+	-	35 (26.9%)	
3+	-	35 (26.9%)	
4+	-	6 (4.6%)	
Severity			
Mild		68 (52.3%)	
Severe		62 (47.7%)	
Onset			
Early-onset		72 (55.4%)	
Late-onset		58 (44.6%)	

PE: Preeclampsia, SD: Standard deviation, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

trophoblast cell apoptosis. Consistent with these findings, the evaluation of the expression of *MEG3* and Notch1 showed decreased levels in PE subjects compared with their regular counterparts, promoting apoptotic processes. On the other hand, *MEG3* enhancement showed the opposite effect and promotes cell proliferation and inhibits cell apoptosis[20].

In the present study, we evaluated the association between the *MEG3* rs4081134 variant and PE risk in an Iranian population. according to the results, we did not observe a statistically significant correlation between the allelic frequency of rs4081134 and the risk of PE in our sample, likely due to the small sample size.

Table 2. The genotypic and allelic distribution of *MEG3* rs4081134 gene polymorphism in PE and control

	PE, n (%)	Control, n (%)	p-value	OR (95% CI)
***MEG3* rs4081134**				
GG	80 (61.6)	80 (57.1)		1
GA	48 (36.9)	50 (35.8)	0. 874	0.96 (0.58-1.58)
AA	2 (1.5)	10 (7.1)	0.026	0.2 (0.04-0.94)
Dominant (GA + AA vs. GG)	50 (38.4) 80 (61.6)	60 (42.9) 80 (57.1)	0.463	0.83 (0.51-1.36)
Recessive (AA vs. GG + GA)	2 (1.5) 128 (98.5)	10 (7.1) 130 (92.9)	0.026	0.2 (0.44-0.94)
Over dominant (GA vs. GG+AA)	48 (36.9) 82 (63.1)	50 (35.8) 90 (64.2)	0.836	1.05 (0.64-1.73)
Allele				
G	208 (80%)	210 (75%)		1
A	52 (20%)	70 (25%)	0.181	0.75 (0.49-1.12)

PE: Preeclampsia, OR: Odds ratio, CI: Confidence interval, *MEG3*: Maternally expressed gene 3

Table 3. Association between clinical characteristics of PE patients and *MEG3* rs4081134 gene polymorphism

Variable	GG	GA	AA	p-value
Maternal age (mean ± SD, years)	28.53±6.78	26.64±6.4	23±5.65	0.180
Gestation age (mean ± SD, weeks)	36.10±3.61	35.48± 3.91	36±2.82	0.660
Birth weight (mean ± SD, g)	2879.38±628.18	2576.04±817.15	3225±318.19	0.043
SBP (mean ± SD, mmHg)	152.56±16.05	152.98±17.15	165±7.07	0.572
DBP (mean ± SD, mmHg)	87.40±24.87	89.97±19.12	105±7.07	0.491
Proteinuria (n, %)				
Trace	8 (10%)	3 (6.3%)	0	0.249
1+	26 (32.5%)	17 (35.4%)	0	
2+	20 (25%)	15 (31.3%)	0	
3+	20 (25%)	13 (27%)	2 (100%)	
4+	6 (7.5%)	0	0	
Severity				
Mild (n, %)	42 (52.5%)	26 (54.2%)	0	0.323
Severe (n, %)	38 (47.5%)	22 (45.8%)	2 (100%)	
Onset				
Early-onset (n, %)	42 (52.5%)	29 (60.4%)	1 (50%)	0.675
Late-onset (n, %)	38 (47.5%)	19 (39.6%)	1 (50%)	

SD: Standard deviation, PE: Preeclampsia, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, *MEG3*: Maternally expressed gene 3

To our knowledge, this study is the first to investigate whether *MEG3* rs4081134 is associated with the risk of PE. previous studies have evaluated the association of *MEG3* rs4081134 and the risk of some tumors, including papillary thyroid carcinoma[40], neuroblastom[41], and lung cancer[42].

Study Limitations

In the current study, we faced several challenges, including the small size of the study population and technical limitations. It is recommended that future work evaluate the expression levels of *MEG3* and its downstream targets, such as miR-21 or *FOXM1*, as key participants in the proliferation of placental cells.

Conclusion

We found a significant relationship between the AA genotype of the *MEG3* rs4081134 polymorphism and the risk of PE development. Furthermore, there *MEG3* rs4081134 gene polymorphism showed a significant relationship with newborn's birth weight in patients with PE.

Ethics

Ethics Committee Approval: The study protocol received approval from the Ethics Committee of Zahedan University of Medical Sciences (approval number: IR.ZAUMS.REC.1399.239, date: 09.08.2020).
Informed Consent: All participants provided written informed consent.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.S., H.D., M.N., H.S.G., M.G., M.Z., M.S., Concept: S.S., H.D., M.N., H.S.G., M.G., M.Z., M.S., Design: S.S., H.D., M.N., H.S.G., M.G., M.Z., M.S., Data Collection or Processing: S.S., H.D., M.N., H.S.G., M.G., M.Z., M.S., Analysis or Interpretation: Literature Search: S.S., H.D., M.N., H.S.G., M.G., M.Z., M.S., Writing: S.S., H.D., M.N., H.S.G., M.G., M.Z., M.S.
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Depression and anxiety among women with unwanted pregnancies seeking termination

İstenmeyen gebeliği sonlandırmak isteyen kadınlarda depresyon ve anksiyete

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Abstract

Objective: To compare depressive and anxiety symptoms in women with unwanted and planned pregnancies.

Materials and Methods: In this cross-sectional comparative study, we enrolled 220 pregnant women who presented to the Obstetrics and Gynecology Department of Yozgat Bozok University between January 2023 and June 2025. The study group comprised 120 women with unwanted pregnancies seeking elective termination before 10 weeks of gestation. The control group included 100 women with planned pregnancies. Socio-demographic and obstetric data were collected. Depressive and anxiety symptoms were assessed using the Beck Depression Inventory and Beck Anxiety Inventory, respectively.

Results: Women with unwanted pregnancies had a significantly higher prevalence of depressive symptoms than women with planned pregnancies (46.7% vs. 28.0%; p=0.004). In contrast, there was no statistically significant difference in the prevalence or severity of anxiety symptoms between the groups (p=0.450). Women in the unwanted pregnancy group were significantly older, had higher parity and lower educational attainment, and were more likely to be unmarried (all p<0.001). Following termination, 20.8% of women had no future contraceptive plans, whereas 40% intended to use an intrauterine device.

Conclusion: Unwanted pregnancy culminating in a request for termination is a potent risk factor for depressive symptoms, particularly among socioeconomically vulnerable women, but not necessarily for anxiety. These findings underscore the critical need to integrate mental health screening, especially for depression, and comprehensive, patient-centered contraceptive counseling into routine antenatal and post-abortion care services. Addressing the psychosocial needs of this population is essential for mitigating adverse mental health outcomes.

Keywords: Unwanted pregnancy, unintended pregnancy, depression, anxiety, pregnancy termination, abortion, contraception, mental health

Öz

Amaç: İstenmeyen ve planlı gebelik yaşayan kadınlar arasında depresyon ve anksiyete belirtilerini karşılaştırmak.

Gereç ve Yöntemler: Bu kesitsel karşılaştırmalı çalışmada, Ocak 2023 ile Haziran 2025 tarihleri arasında Yozgat Bozok Üniversitesi Kadın Hastalıkları ve Doğum Anabilim Dalı'na başvuran 220 gebe kadın dahil edilmiştir. Çalışma grubunu, 10 gebelik haftasından önce isteğe bağlı gebelik sonlandırma talebinde bulunan 120 istenmeyen gebelikli kadın oluşturmuştur. Kontrol grubunda ise planlı gebeliği olan 100 kadın yer almıştır. Sosyo-demografik ve obstetrik veriler toplanmıştır. Depresyon ve anksiyete belirtileri sırasıyla Beck Depresyon Envanteri ve Beck Anksiyete Envanteri kullanılarak değerlendirilmiştir.

PRECIS: Women with unwanted pregnancies seeking termination show higher depressive symptoms but similar anxiety levels compared to women with planned pregnancies, highlighting the need for integrated mental health screening.

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Bulgular: İstenmeyen gebeliğe sahip kadınlarda depresif belirtilerin prevalansı, planlı gebeliği olan kadınlara göre anlamlı derecede daha yüksekti (%46,7'ye karşı %28,0; p=0,004). Buna karşın, gruplar arasında anksiyete belirtilerinin yaygınlığı veya şiddeti açısından istatistiksel olarak anlamlı bir fark bulunmadı (p=0,450). İstenmeyen gebelik grubundaki kadınlar anlamlı şekilde daha ileri yaşta, daha yüksek pariteye sahip, daha düşük eğitim düzeyine sahip ve bekar olma olasılığı daha yüksekti (tüm p<0,001). Gebelik sonlandırma sonrasında kadınların %20,8'inin geleceğe yönelik herhangi bir kontraseptif planı bulunmazken, %40'ı rahim içi araç kullanmayı planladığını belirtmiştir.

Sonuç: Sonlandırma talebiyle sonuçlanan istenmeyen gebelik, özellikle sosyoekonomik açıdan dezavantajlı kadınlarda depresif belirtiler için güçlü bir risk faktörüdür; ancak anksiyete için aynı durum geçerli değildir. Bu bulgular, rutin doğum öncesi ve gebelik sonlandırma hizmetlerine, özellikle depresyon açısından ruh sağlığı taramasının ve hasta merkezli kapsamlı kontraseptif danışmanlığın entegre edilmesinin önemini vurgulamaktadır. Bu grubun psikososyal ihtiyaçlarının karşılanması, olumsuz ruh sağlığı sonuçlarının azaltılması açısından kritik öneme sahiptir.

Anahtar Kelimeler: İstenmeyen gebelik, planlanmamış gebelik, depresyon, anksiyete, gebelik sonlandırma, kürtaj, kontrasepsiyon, ruh sağlığı

Introduction

Family planning is a cornerstone of public health, essential for social stability and sustainable population dynamics. Despite global efforts, unintended pregnancies—defined as pregnancies that are either mistimed or unwanted—remain a pervasive challenge, affecting millions of women annually and representing a significant medical and societal issue[1,2]. A substantial proportion of these pregnancies result in elective termination (abortion), a decision often influenced by a complex interplay of personal, social, and economic factors[3]. The antecedents of unintended pregnancy are multifactorial and disproportionately concentrated among vulnerable populations. Key risk factors include low socioeconomic status (SES), low educational attainment, unmarried status, and high parity[4,5]. Studies have consistently shown that even when financial barriers to contraception are removed, women with low SES remain at a significantly higher risk of unintended pregnancy[4]. This highlights the deep-rooted social determinants that shape reproductive health outcomes. Beyond the immediate decision-making process, an unintended pregnancy can have profound and lasting implications for a woman's mental health. The experience is often associated with heightened psychological distress, including symptoms of depression and anxiety[6,7]. Seminal longitudinal research, such as the Wisconsin Longitudinal Study, has demonstrated a strong and persistent association between experiencing an unwanted pregnancy carried to term and poorer mental health outcomes, including higher depressive scores, later in life[8]. This association holds even after controlling for pre-existing personality traits and a range of early life confounders, suggesting that the pregnancy experience itself is a significant stressor.

While the link between unintended pregnancy and depression is well-established, the psychological impact on women who choose to terminate is more complex. Some research indicates that the decision to terminate can be accompanied by feelings of guilt, shame, and regret, which may precipitate or exacerbate depressive symptoms[9,10]. Conversely, other studies suggest that being denied an abortion is associated with worse mental health outcomes than those associated with receiving one, and that most women who have an abortion do not experience long-term psychological harm[11]. This complex landscape highlights a critical gap in the literature: the need to differentiate the psychological profiles of women based on their pregnancy intentions and decisions. Specifically, there is a need for a clearer understanding of the mental health status of women who identify their pregnancies as unwanted and actively seek termination. This study focuses specifically on this subgroup. Our primary objective was to assess the impact of unwanted pregnancies on maternal mental health by comparing levels of depression and anxiety in women seeking elective termination with levels in women with planned pregnancies. A secondary aim was to identify the socio-demographic and obstetric factors associated with vulnerable mental health in this context.

Materials and Methods

Study Design and Population

This comparative cross-sectional study was conducted at the Obstetrics and Gynecology Outpatient Clinic of Yozgat Bozok University, a tertiary care center in our country. The study protocol was approved by the Clinical Research Ethics Committee of Yozgat Bozok University (approval number: 2017-KAEK-189_2023.10.26_02, date: 26.10.2023), and all participants provided written informed consent prior to enrollment. Data were collected between January 2023 and June 2025.

The study population consisted of 220 pregnant women, divided into two groups. The study group included 120 women who presented with an unwanted pregnancy and voluntarily requested elective termination (curettage) within the first 10 weeks of gestation, as permitted by Turkish law. The control group consisted of 100 women with a planned, desired, and healthy ongoing pregnancy who were the clinic for routine antenatal care.

The exclusion criteria for both groups were: history of major psychiatric disorders (e.g., schizophrenia, bipolar disorder); current use of psychotropic medications (antidepressants or antipsychotics); cognitive impairment that would preclude understanding the questionnaires; or pregnancy complicated by severe obstetric conditions.

Data Collection and Measures

Data were collected by trained research personnel through structured face-to-face interviews. A standardized

questionnaire was used to gather information on sociodemographic characteristics (age, marital status, educational level, employment) and obstetric history (gravida, parity, number of living children, previous deliveries, and terminations).

Mental Health Assessment

Depressive and anxiety symptoms were assessed using the Turkish-validated versions of the Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI).

BDI: The BDI is a 21-item self-report inventory measuring the severity of depressive symptoms. Each item is scored on a 4-point scale from 0 to 3. The total score ranges from 0 to 63, with higher scores indicating more severe depression. Standard cut-off scores were used: 0-9 (minimal), 10-16 (mild), 17-29 (moderate), and 30-63 (severe)[12].

BAI: The BAI is a 21-item self-report scale designed to measure the severity of anxiety symptoms. Similar to the BDI, each item is rated on a 4-point scale, yielding a total between 0 and 63. The scores were categorized as follows: 0-7 (minimal), 8-15 (mild), 16-25 (moderate), and 26-63 (severe) [13]. Both the BDI and the BAI are widely used, well-validated instruments for assessing mood and anxiety symptoms in diverse populations, including perinatal women[14].

Other Variables

Regarding marital problems and violence, participants were asked about their relationship satisfaction. Marital problems were defined as self-reported, ongoing significant conflict with a spouse or partner. Exposure to intimate partner violence (verbal, physical, or sexual) within the past year was also recorded.

Contraceptive Plans: Women in the study group who underwent termination were asked about contraception following the procedure.

Statistical Analysis

Statistical analyses were performed using SPSS for Windows, version 27.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Kolmogorov-Smirnov test and visual inspection of histograms. Normally distributed continuous variables were presented as mean ± standard deviation, while categorical variables were reported as frequencies and percentages (%).

Differences between the unwanted-pregnancy and control groups were analyzed using an independent-samples t-test for continuous variables and the chi-square (χ^2) test for categorical variables. Fisher's exact test was used when the expected cell count was fewer than five. Statistical significance was set at $p<0.05$. A subgroup analysis within the unwanted pregnancy group was performed to compare primigravida and multiparous women.

Results

Participant Characteristics

A total of 220 women were enrolled in the study, with 120 in the unwanted pregnancy group and 100 in the planned pregnancy (control) group. The socio-demographic and obstetric characteristics of the participants are presented in Table 1.

Women in the unwanted pregnancy group were, on average, significantly older than those in the control group (31.20±6.17 vs. 27.91±5.92 years; $p<0.001$). Significant differences were also observed in marital status and education. The unwanted pregnancy group had a higher proportion of unmarried women (14.2% vs. 0%; $p<0.001$) and a lower proportion of with a university education (15.0% vs. 39.0%; $p<0.001$).

Regarding obstetric history, women seeking pregnancy termination had significantly higher mean gravida (3.7 vs. 2.36), mean parity (2.14 vs. 0.96), and mean number of living children (2.13 vs. 0.93) than those in the control group (all $p<0.001$). The smoking rate was also substantially higher in the unwanted pregnancy group (37.5% vs. 16.0%; $p<0.001$).

Mental Health Outcomes: Depression and Anxiety

The primary mental health outcomes are presented in Table 2. A key finding of this study is the significant difference in the prevalence of depressive symptoms between the two groups. Nearly half of the women in the unwanted pregnancy group (46.7%) screened positive for depressive symptoms (BDI score ≥10), compared to 28.0% in the control group. This difference was statistically significant ($p=0.004$). Specifically, moderate-to-severe depressive symptoms were more than three times as common in the unwanted-pregnancy group (15.8% vs. 6.0%).

By contrast, no statistically significant difference in anxiety levels was observed between the groups ($p=0.450$). The distribution of anxiety severity—from minimal to severe—was comparable across both the unwanted-pregnancy and control groups.

Subgroup and Other Analyses

Within the unwanted pregnancy group, a subgroup analysis was conducted to determine whether mental health outcomes differed between primigravida women (n=12) and multiparous women (n=108) (Table 3). No significant differences were found in the prevalence or severity of anxiety ($p=0.334$) or depression ($p=0.385$) based on parity within this group.

Rates of self-reported marital problems and verbal violence were low in the overall sample and did not differ significantly between the groups ($p>0.05$ for all comparisons). No participants reported physical or sexual violence.

Contraceptive Planning Post-termination

Among the 120 women who underwent pregnancy termination, clinicians assessed their future contraceptive plans (Figure 1). A significant proportion (40.0%) planned to

Table 1. Demographic and obstetric characteristics of women with unwanted pregnancies and the control group

Variables	Unwanted pregnancy group (n=120)	Control (n=100)	Total (n=220)	p-value
Age (mean ± SD)	31.20±6.17	27.91±5.92	29.7±6.27	<0.001
Occupation, n (%)				
Employed	34 (28.3%)	19 (19%)	53 (24.1%)	0.108
Unemployed	86 (71.7%)	81 (81%)	167 (75.9%)	
Marital status, n (%)				
Married	103 (85.83%)	100 (100%)	203 (92.3%)	<0.001
Single	14 (11.66%)	0	14 (6.4%)	
Cohabiting	3 (2.5%)	0	3 (1.4%)	
Chronic illness, n (%)	21 (17.5%)	17 (17%)	38 (17.3%)	0.923
Educational level, n (%)				
Illiterate	6 (5%)	3 (3%)	9 (4.1%)	<0.001
Primary School	49 (40.8%)	26 (26%)	75 (34.1%)	
High School	47 (39.2%)	32 (32%)	79 (35.9%)	
University	18 (15%)	39 (39%)	57 (25.9%)	
Gestational age (weeks)				
By LMP (mean, min-max)	6.94 (5-9)	7.41 (5-10)	7.15 (5-10)	0.002
By ultrasound (mean, min-max)	6.86 (5-9)	7.37 (5-10)	7.09 (5-10)	<0.001
Gravida (mean, min-max)	3.7 (1-8)	2.36 (1-7)	3.09 (1-8)	<0.001
Parity (mean, min-max)	2.14 (0-7)	0.96 (0-6)	1.60 (0-7)	<0.001
Living children (mean)	2.13 (0-7)	0.93 (0-6)	1.58 (0-7)	<0.001
Curettage (mean)	0.29 (0-3)	0.06 (0-2)	0.19 (0-3)	<0.001
Abortion (mean, min-max)	0.31 (0-3)	0.33 (0-3)	0.32 (0-3)	0.811
Normal vaginal delivery (mean, min-max)	1.37 (0-7)	0.6 (0-6)	1.02 (0-4)	<0.001
Cesarean section (mean, min-max)	0.77 (0-5)	0.36 (0-3)	0.58 (0-4)	0.008
Smoking, n (%)	45 (37.5%)	16 (16%)	61 (27%)	<0.001

LMP: Last menstrual period, SD: Standard deviation

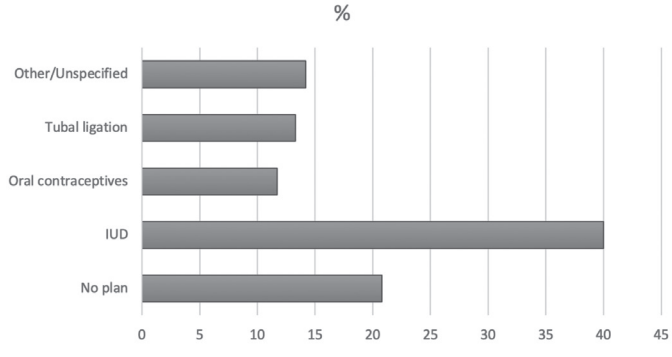

Figure 1. Distribution of planned contraception methods reported by women following an unwanted pregnancy

use an intrauterine device (IUD), a highly effective long-acting reversible contraceptive (LARC). However, a concerning 20.8% of women reported having no contraceptive plan for the future. Tubal ligation (13.3%) and oral contraceptives (11.7%) were other planned methods.

Discussion

This study provides a focused analysis of the mental health of women seeking termination of an unwanted pregnancy, revealing a significant burden of depressive symptoms, but no corresponding increase in anxiety. Our findings highlight that women in this situation are demographically distinct and psychologically vulnerable, underscoring the need for targeted clinical and public health interventions.

The central finding of our research is a markedly higher prevalence of depression among women with unwanted pregnancies compared with those with planned pregnancies. This is consistent with a large body of evidence linking unintended pregnancy to adverse mental health outcomes[7,15]. A systematic review by Nelson et al.[15] similarly found that unintended pregnancy was significantly associated with higher odds of maternal depression both during pregnancy and postpartum. Our study adds to this literature by demonstrating that this risk is particularly pronounced in a subgroup of women who have decided to terminate their pregnancy. Confronting an unwanted pregnancy, navigating the decision-making process, and dealing with potential social stigma and internal conflict can precipitate psychological distress, manifesting as depression[9,10].

Perhaps the most intriguing finding is the absence of a significant difference in anxiety levels between the two groups. This contrasts with the common assumption that the period preceding an abortion would be fraught with anxiety[10]. One possible explanation, which warrants further investigation, is related to the psychological construct of decision-making and resolution. For the women in our study group, the decision to terminate the pregnancy had already been made. This resolution of uncertainty may have had a mitigating effect on anxiety symptoms, which are often tied to anticipation of a future threat. While the decision itself may be emotionally painful and lead to feelings of loss, sadness, or guilt, the state of anxious uncertainty may already have passed. In contrast, the depressive symptoms may reflect the emotional aftermath of the decision and the circumstances leading to it. This dissociation between anxiety and depression in this specific clinical context represents a critical focus for future research and underscores the importance of avoiding bundling these conditions together in clinical screening.

Our socio-demographic findings paint a clear picture of vulnerability. Women with unwanted pregnancies were more

Table 2. Anxiety and depression levels among women with unwanted pregnancy and control group.

Variable	Unwanted pregnancy (n=120)	Control group (n=100)	Total (n=220)	p-value†
Anxiety, n (%)				
None	72 (60.0%)	52 (52.0%)	124 (56.4%)	0.450
Mild	35 (29.2%)	30 (30.0%)	65 (29.5%)	
Moderate	9 (7.5%)	12 (12.0%)	21 (9.5%)	
Severe	4 (3.3%)	6 (6.0%)	10 (4.5%)	
Depression, n (%)				
None	64 (53.3%)	72 (72.0%)	136 (61.8%)	0.004
Mild	37 (30.8%)	22 (22.0%)	59 (26.8%)	
Moderate	15 (12.5%)	4 (4.0%)	19 (8.6%)	
Severe	4 (3.3%)	2 (2.0%)	6 (2.7%)	

† Chi-square test

Table 3. Association between anxiety and depression levels and first pregnancy among women with unwanted pregnancies

Variable	First pregnancy (n=12)	Has living child(ren) (n=108)	Total (n=120)	p-value†
Anxiety, n (%)				
None	5 (41.7%)	67 (62.0%)	72 (60.0%)	0.334
Mild	5 (41.7%)	30 (27.8%)	35 (29.2%)	
Moderate	2 (16.7%)	7 (6.5%)	9 (7.5%)	
Severe	0 (0.0%)	4 (3.7%)	4 (3.3%)	
Depression, n (%)				
None	7 (58.3%)	57 (52.8%)	64 (53.3%)	0.385
Mild	2 (16.7%)	35 (32.4%)	37 (30.8%)	
Moderate	3 (25.0%)	12 (11.1%)	15 (12.5%)	
Severe	0 (0.0%)	4 (3.7%)	4 (3.3%)	

† Chi-square test

likely to be older, to have more children, to be unmarried, and to have lower educational attainment. These findings align with previous research indicating that high parity and lower SES are significant risk factors for unintended pregnancy[4,5]. The finding that women in the unwanted pregnancy group were older and had higher parity suggests that for many, the decision to terminate may be driven by the desire to limit family size because of limited economic or personal resources, which is also supported by previous studies[14,16]. The higher proportion of unmarried individuals in the unwanted pregnancy group underscores the profound influence of social context and support systems on reproductive decisions[17].

The data on post-termination contraceptive planning reveal both a challenge and an opportunity. It is encouraging that 40% of women plan to use an IUD, a highly effective LARC method. This aligns with recommendations from major health organizations, such as ACOG, which advocate offering LARC at the time of abortion to reduce subsequent unintended pregnancies[18,19]. However, the absence of a contraceptive plan in over 20% of women is alarming and highlights a critical gap in care. This highlights the necessity of integrating comprehensive, non-coercive, and patient-centered contraceptive counseling into all abortion-care services. The goal should be to empower women with the knowledge and access to choose a method that best fits their needs and life circumstances, thereby reducing the risk of repeat unintended pregnancies[20].

The extremely low rate of reported violence within our sample (<1%) is noteworthy and likely reflects significant underreporting due to social stigma, which is common in studies relying on self-report for sensitive topics[21]. International studies have shown a strong link between exposure to violence and both unintended pregnancy and adverse mental health outcomes, including PTSD, anxiety, and depression[22]. Obstetric care providers must be trained to create a safe and confidential environment for screening for intimate partner violence as part of a comprehensive psychosocial assessment.

Study Limitations

Several limitations of this study should be acknowledged. First, its cross-sectional design precludes causal inference. The study has a relatively small sample size for a retrospective design. We can report only an association between unwanted pregnancy and depression and cannot conclude that the former causes the latter. Second, the study was conducted at a single tertiary center in Türkiye, which may limit the generalizability of our findings to other geographic regions or healthcare settings. Third, our reliance on self-report measures (BDI and BAI) introduces the possibility of response bias, particularly for sensitive topics such as mental health symptoms and intimate partner violence. The low reported rate of violence strongly suggests underreporting. Fourth, while our study highlights the importance of sociodemographic factors, the sample size did not permit robust multivariable regression analysis to fully the independent effects of these variables from pregnancy intention. Finally, our control group consisted of women with planned pregnancies. Future research could benefit from including a third group of women with unintended (mistimed or unwanted) pregnancies who decide to carry their pregnancies to term, which would allow for a more nuanced understanding of the role of the final decision in mental health outcomes.

Conclusion

This study demonstrates that women seeking termination of an unwanted pregnancy constitute a population with a significantly elevated burden of depressive symptoms, but not of anxiety. These mental health outcomes are closely linked to a profile of socioeconomic vulnerability characterized by lower educational attainment, unmarried status, and higher parity. The findings strongly support the integration of routine mental health screening—with a particular focus on depression—into standard obstetric and abortion care. Furthermore, the significant proportion of women lacking a post-termination contraceptive plan highlights a critical gap in care. Providing patient-centered, comprehensive contraceptive counseling is a crucial, actionable step toward empowering women, preventing repeat unintended pregnancies, and ultimately improving maternal mental health.

Ethics

Ethics Committee Approval: The study protocol was approved by the Clinical Research Ethics Committee of Yozgat Bozok University (approval number: 2017-KAEK-189_2023.10.26_02, date: 26.10.2023).

Informed Consent: All participants provided written informed consent for the use of their clinical data for research purposes.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.B., Ç.A., E.S.Y., Concept: M.B., Ç.A., Design: Ç.A., E.S.Y., Data Collection or Processing: M.B., Ç.A., E.D.G., E.S.Y., Analysis or Interpretation: Ç.A., E.D.G., Literature Search: M.B., Ç.A., E.D.G., Writing: Ç.A., E.D.G., E.S.Y.

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Flexible progestin-primed ovarian stimulation is a safe and effective alternative to GnRH antagonist protocol in PGT-A cycles

Esnek oral progestin destekli over stimülasyonu protokolü PGT-A sikluslarında gonadotropin salgılatıcı hormon antagonisti protokolüne güvenli ve etkili bir alternatiftir

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Abstract

Objective: To test the hypothesis that flexible progestin-primed ovarian stimulation (fPPOS) is non-inferior to the gonadotropin-releasing hormone (GnRH) antagonist protocol in terms of safety and efficacy for patients undergoing controlled ovarian hyperstimulation and preimplantation genetic testing for aneuploidy (PGT-A).

Materials and Methods: This retrospective analysis included data from 548 cycles involving 367 women aged 35 to 45 years. The fPPOS and GnRH antagonist groups comprised 307 cycles (56%) and 241 cycles (44%), respectively. All participants underwent absolute blastocyst culture, trophectoderm biopsy, and PGT-A, with advanced maternal age as the sole indication. The primary outcomes were incidence of premature luteinizing hormone (LH) rise (>10 mIU/mL), cycle cancellation due to premature ovulation, and euploid blastocyst rate per injected metaphase II oocyte. Spearman's rho correlation and the generalized linear model (logit) were applied for statistical analysis.

Results: The incidence of premature LH rise (8.2% versus 6.6%; p=0.302) and cycle cancellation due to premature ovulation (2% versus 0.4%; p=0.112) did not differ significantly between the fPPOS and GnRH antagonist groups. Maturation, fertilization, and blastulation rates were also similar (p>0.05). The euploid blastocyst rates per biopsy (50.12% versus 53.06%; p=0.317) and per injected metaphase II oocyte (23.84% versus 23.34%; p=0.231) were comparable between groups. Secondary outcomes, including rates of positive pregnancy tests, implantation, ongoing pregnancy, biochemical pregnancy losses, and early miscarriages, were also similar (p>0.05).

Conclusion: The fPPOS protocol represents a viable alternative to the GnRH antagonist protocol for patients aged 35 years or older undergoing PGT-A.

Keywords: Progestin-primed ovarian stimulation, gonadotropin-releasing hormone antagonist, controlled ovarian hyperstimulation, preimplantation genetic testing for aneuploidy

PRECIS: The flexible administration of medroxyprogesterone acetate effectively prevents the luteinizing hormone rise during ovarian hyperstimulation when compared to gonadotropin-releasing hormone antagonists. Furthermore, it does not have an adverse effect on euploidy rates.

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Öz

Amaç: Çalışmanın amacı, kontrollü over hiperstimülasyonunda esnek oral progestin destekli (eOPD) protokolün güvenliğini ve etkinliğini değerlendirmek ve aneuploidi için preimplantasyon genetik testi (PGT-A) dahil olmak üzere embriyolojik süreçler üzerindeki etkisini araştırmaktır.

Gereç ve Yöntemler: Bu çalışma, 35-45 yaş aralığındaki 367 kadına ait 548 tedavi siklusundan elde edilen verilerin retrospektif analizini içermektedir. eOPD grubunda 307 siklus (%56) ve gonadotropin salgılayıcı hormon (GnRH) antagonisti grubunda 241 siklus (%44) yer almaktaydı. Mutlak blastokist kültürü uygulandı. İleri anne yaşı endikasyonu ile trofektoderm biyopsisi ve PGT-A yapıldı. Birincil sonuçlar arasında erken luteinize edici hormon (LH) yükselme oranları (>10 mIU/mL), erken ovülasyona bağlı siklus iptalleri ve enjekte edilen metastaz II (MII) oosit başına öploid blastokist oranı yer alıyordu. Spearman'ın rho korelasyonu ve genelleştirilmiş doğrusal model (logit) kullanıldı.

Bulgular: eOPD grubundaki erken LH yükselişinin (%8,2-6,6; p=0,302) ve erken ovulasyona bağlı siklus iptalinin (%2-0,4; p=0,112) insidansı GnRH antagonisti grubundakine benzerdi. Olgunlaşma, döllenme ve blastülasyon oranları benzerdi (p>0,05). Biyopsi yapılan blastokist başına (%50,12-53,06; p=0,317) ve enjekte edilen MII oosit başına (%23,84-23,34; p=0,231) elde edilen öploid blastokist oranı eOPD ve GnRH antagonisti grupları arasında benzerdi. Pozitif gebelik testi oranları, implantasyon, devam eden gebelik, biyokimyasal gebelik kayıpları ve erken düşükler gibi ikincil sonuçlar gruplar arasında benzerdi (p>0,05).

Sonuç: eOPD protokolü, PGT-A uygulanan 35 yaş üstü hastalarda GnRH antagonist protokolüne uygulanabilir bir alternatif sunmaktadır.

Anahtar Kelimeler: Oral progestin destekli protokol, gonadotropin salgılatıcı hormon antagonisti, kontrollü overyan hiperstimülasyon, preimplantasyon genetik tanı

Introduction

Controlled ovarian hyperstimulation (COH) aims to enhance the quantity of oocytes retrieved and, consequently, the number of embryos generated. Follicles that would typically undergo atresia under natural circumstances are stimulated to grow by administration of gonadotropins, thereby increasing the couple's probability of achieving conception. It is important to note that not every oocyte collected has the same potential for developing into a viable embryo[1].

A fundamental aspect of COH is preventing premature luteinizing hormone (LH) surges[2]. The primary pharmacological agents employed for this purpose have long been gonadotropin-releasing hormone (GnRH) agonists and antagonists. In the literature, a reported incidence of premature LH surge ranges from 0.34% to 8% in the context of treatments involving GnRH antagonists[3]. The incidence is comparable in the short agonist protocol[4] but significantly lower in the long GnRH agonist protocol[5,6]. The primary disadvantages of these agents include their mode of administration, which requires injection, and the resulting high treatment costs[7].

Since the beginning of the last decade, progestin-primed ovarian stimulation (PPOS) has become one of the most frequently used alternatives to prevent a premature LH surge in in vitro fertilization (IVF) treatments. Research suggests that elevated serum endogenous progesterone levels during the luteal phase of COH can sufficiently inhibit pituitary function, indicating that additional GnRH antagonist administration may not be necessary[8]. This concept served as the foundation for the PPOS strategy. A landmark randomized controlled trial (RCT) published in 2015 demonstrated that, among normoresponder patients, the rates of premature LH surges, the developmental potential of the embryos, and pregnancy outcomes in the medroxyprogesterone acetate (MPA) group were similar to those in the GnRH antagonist group[9]. The primary drawback of this protocol is that fresh embryo transfer (ET) cannot be executed, as the endometrium is exposed to exogenous progesterone prematurely during the follicular phase, unlike with GnRH preparations[10]. Considering this perspective, it would be prudent to analyze its impact on embryological outcomes and pregnancy rates in protocols involving freeze-all strategies, such as oocyte cryopreservation, preimplantation genetic testing, embryo cryobanking, and prevention of ovarian hyperstimulation syndrome[11].

Research has consistently demonstrated that the aneuploidy risk in embryos increases with advancing maternal age (AMA)[12]. This relationship has been validated through both preimplantation genetic testing for aneuploidy (PGT-A)[13] and analyses of products of conception[14]. Utilizing next-generation sequencing (NGS) to evaluate trophectoderm (TE) biopsy samples during the PGT-A process can provide significant benefits for patients in this demographic, owing to its high negative predictive value[15]. Today, the predominant practice for PGT-A cycles globally involves TE biopsy followed by the vitrification of blastocysts. The increased embryo survival rates resulting from the vitrification method have led to a considerable increase in the utilization of frozen ET applications in recent years[16].

Promising outcomes for various oral progestin regimens have been demonstrated in IVF/intracytoplasmic sperm injection (ICSI) treatments during the past decade[17]. However, studies evaluating flexible protocols in which exogenous progesterone is introduced later in the stimulation course remain limited compared with conventional approaches. This disparity may indicate ongoing clinical caution regarding flexible protocols for LH surge management. Therefore, this study compared the effects of the flexible PPOS (fPPOS) protocol, which used MPA as the oral progestin, with those of the GnRH antagonist protocol, focusing on the stimulation period and embryological outcomes in PGT-A cycles. This study is the first extensive analysis directly comparing these

protocols, using a dataset comprising more than 500 cycles in this specific context.

Materials and Methods

Study Design

The medical records of participants who underwent ICSI with PGT-A from June 1, 2020, to December 31, 2024, were retrieved from the internal medical database. Due to the retrospective design of the study, ethics committee approval was deemed not required by Acıbadem Fulya Hospital. Institutional permission was granted for the analysis of the data. In this study, informed consent was not considered necessary because the data used were entirely anonymized. All patient identifiers were diligently removed prior to analysis to ensure that confidentiality standards were maintained. This study was conducted in accordance with the ethical guidelines set forth in the revised Declaration of Helsinki (2020). The fourth author, H.B., served as the embryologist for patients involved in this study.

A total of 894 treatment cycles involving 590 women were included in this analysis. From this cohort, a specific subset of 346 treatment cycles involving 223 women was excluded based on the following criteria: i) presence of monogenic disorders in either the maternal or paternal lineage and identification of structural chromosomal abnormalities; ii) history of recurrent miscarriages or repeated implantation failures; iii) body mass index (BMI) below 18 kg/m² or above 35 kg/m²; iv) male participants with a sperm concentration of less than 2 million or those requiring testicular sperm aspiration or percutaneous epididymal sperm aspiration. In accordance with the legal regulations in our country, the use of donor gametes is not permitted. Additionally, all procedures were carried out exclusively with fresh gamete cells and embryos.

The study included PGT-A procedures that were performed solely on couples classified as AMA. The definition of AMA aligns with the most recent recommendations set forth by the European Society of Human Reproduction and Embryology PGT Consortium, which establishes an age threshold of 35 years or older[18]. The upper age limit was established at 45 years.

A total of 548 treatment cycles involving 367 women were included in the final analysis. Of these, 307 cycles (56%) were assigned to the fPPOS group and 241 cycles (44%) to the GnRH antagonist group. Absolute blastocyst culture was performed as a standard procedure for all patients scheduled for PGT-A.

Controlled Ovarian Hyperstimulation

COH was initiated using either the fPPOS or GnRH antagonist protocol. The initial dosage was tailored by considering the woman's age, BMI, initial follicle sizes, and prior treatment response. Recombinant follitropin alpha follicle-stimulating hormone (r-FSH) (Gonal F; Merck Serono S.p.A., Modugno, Italy) or menotropin (HP-hMG) (Meriofert; IBSA, Switzerland) were administered either individually or in combination. The analysis did not encompass mild stimulation protocols that exclusively employed clomiphene citrate or letrozole. The ovarian response was assessed through a series of transvaginal scans and hormonal monitoring. Serum LH levels were monitored systematically in both groups from the initiation of LH suppression until the day of ovulation triggering. Any necessary dosage adjustments were made at the attending clinicians' discretion based on the observed ovarian response. In the fPPOS protocol, 5 mg of MPA (Tarlusal; Deva, Türkiye) was administered twice daily, once the follicles reached 12 mm in size, and the treatment continued until the ovulation trigger day. In the GnRH antagonist protocol, 0.25 mg/day cetrorelix acetate (Cetrotide; Merck Serono, Darmstadt, Germany) was initiated once the leading follicle reached 13-14 mm in size. The final injection was administered on the day of the ovulation trigger. Oocyte maturation was induced by 250 µg of human chorionic gonadotropin (hCG) (Ovitrelle; Merck Serono, Germany) and 0.1 mg of triptorelin (Gonapeptyl; Ferring, Switzerland), and oocyte retrieval was scheduled 35 hours thereafter.

Laboratory Procedures and PGT-A

Metaphase II (MII) oocytes were fertilized by ICSI in G-MOPS™ fertilization medium (Vitrolife, Göteborg, Sweden) supplemented with 10% human serum albumin (HSA, Vitrolife). The embryos were cultured in one-step continuous single-culture media (Global® Total® LP, LifeGlobal™). The evaluation of embryo quality involved grading fresh cleavage-stage embryos produced by ICSI according to rigorous criteria[19]. Accordingly, embryos were categorized as top-quality (TQ) if they had reached the 7-10-cell stage on day 3 (64-66 hours) of *in vitro* culture, had exhibited symmetrical blastomeres free of multinucleation, and had demonstrated no more than 20% cytoplasmic fragmentation. Blastocyst morphology was assessed at two time points: days 5 (114 hours after ICSI) and 6 (138 hours after ICSI). This assessment encompassed an evaluation of three parameters, namely, the degree of blastocoel expansion, inner cell mass score, and TE score, utilizing the grading methodology established by Gardner and Schoolcraft[20]. Per standard protocol, biopsy and vitrification were not performed on blastocysts with CB or CC scores and a degree of expansion below 3. Assisted hatching via a laser pulse (RI Saturn 5, Cooper Surgical) was conducted on day 5 or 6 once the blastocyst reached a degree of expansion of 3 or higher. After re-expansion, TE biopsy was performed using the pulling method[21]. As a standard procedure, 3-5 cells were removed from the TE layer. The vitrification process for blastocysts adhered to standard protocols and used the Irvine Scientific Freeze Kit in conjunction with a custom-made straw carrier system.

PGT-A was performed using the Ion ReproSeq PGS Kit NGS platform (Thermo Fisher Scientific, USA) to screen for aneuploidy across all 24 chromosomes. The assay was performed using the Ion Chef and Ion S5 systems (Thermo Fisher Scientific, Inc., MA, USA), and the data were analyzed via Ion Reporter software (version 5.4). Embryos were systematically categorized as either euploid or aneuploid. Embryos exhibiting single-chromosome mosaicism, whether trisomy or monosomy, at frequencies below 50% were designated as euploid. This threshold is routinely accepted in our practice based on previously reported outcomes, which indicate that clinical pregnancy, implantation, and live-birth rates associated with ETs of blastocysts exhibiting low-level mosaicism (less than 50%) are comparable to those of euploid blastocysts[22]. Conversely, those with mosaic rates exceeding this threshold were classified as aneuploids. Furthermore, embryos characterized by two-chromosome mosaics or complex mosaic patterns were also classified as aneuploids.

Frozen Single-euploid Blastocyst Transfer and Luteal Phase Support

This study included only the first frozen ET cycle for each patient. In the context of endometrial preparation, a true natural-cycle follow-up approach was preferred for patients with regular menstrual cycles of 24 to 35 days over the preceding three months. In contrast, hormone replacement therapy (HRT) was the method of choice for individuals with irregular menstrual cycles or those unable to undergo serial ultrasound and serum hormone monitoring.

During true natural follow-up, serum estradiol and LH levels were monitored daily or every other day once the dominant follicle reached 16 mm. Ovulation was confirmed by a drop in serum estradiol together with a surge in LH. Subcutaneous progesterone (Prolutex; IBSA Institut Biochimique SA) was administered once daily between 4:00 pm and 7:00 pm on the same day as the estradiol decline, with the ET procedure scheduled for the sixth day after progesterone initiation.

The HRT protocol was performed as described elsewhere[23]. Progesterone support was continued through the eighth week of gestation for both transfer methods.

Outcome Measures

The primary outcome measures were organized into two main categories to enhance clarity and analytical hierarchy. Safety endpoints included the rates of premature LH rise (>10 mIU/mL) and cycle cancellations due to premature ovulation. We evaluated the euploidy rate per injected MII oocyte as the primary measure of effectiveness.

The secondary outcomes included the maturation and fertilization rates, the formation rate of day-3 TQ embryos, the blastulation rate, the euploid blastocyst rate per biopsy, and the proportion of cycles yielding a euploid blastocyst. Other secondary outcomes included rates of positive pregnancy tests, biochemical pregnancy losses, implantation, early miscarriages, and ongoing pregnancies.

Pregnancy was confirmed by a serum β-HCG concentration exceeding 5 IU/mL, measured 11 days after the frozen ET. Successful implantation was confirmed by the detection of a gestational sac on transvaginal ultrasound (TV-USG) at 6 weeks' gestation. An ongoing pregnancy was defined as the detection of a viable embryo with a fetal heartbeat at 12 weeks of gestation. Biochemical pregnancy loss is characterized by a temporary rise in hCG levels without the confirmation of a gestational sac via TV-USG. An early miscarriage is defined as a pregnancy loss that occurs before the 12th week of gestation after confirmation of successful implantation.

Statistical Analysis

The research methodology used frequency distributions to describe nominal and ordinal parameters, while scale parameters were characterized by means and standard deviations. To analyze differences in nominal and ordinal parameters, we employed the chi-square test, the likelihood ratio test, and Fisher's exact test. Additionally, the Kolmogorov-Smirnov test was conducted to assess the normality of the scale parameters. Since all parameter differences were non-normally distributed, the Mann-Whitney U test was used to evaluate differences among the scale parameters.

For the relational analysis, due to observed deviations from linearity, we applied Spearman's rho and the generalized linear model (logit) to investigate the association between the euploid blastocyst rate per injected MII oocyte and several pertinent variables[24]. All analyses were performed using the SPSS 25.0 platform for Windows, with a 95% confidence interval and a significance level of 0.05.

Results

The distribution of the entire cohort (n=548) based on age groups is as follows: 35-37 years, n=87 (16%); 38-40 years, n=156 (28%); 41-42 years, n=119 (22%); and >42 years, n=186 (34%). Regarding serum anti-Müllerian hormone (AMH) (ng/mL) levels, the distribution is as follows: 0.01-0.49, n=197 (36%); 0.50-1.19, n=188 (34%); and ≥1.20, n=163 (30%).

Table 1 presents the baseline characteristics and clinical parameters of the patient groups. Among these characteristics, mean female age, BMI, duration of infertility, number of previous failed attempts, type of infertility (primary or secondary), number of previous miscarriages, and AMH levels were comparable across groups (p>0.05). A premature LH rise was observed in 25 cycles (8.2%) within the fPPOS group and in 16 cycles (6.6%) in the GnRH antagonist group. No statistically significant difference was observed between the groups (p=0.302). Furthermore, the incidence of cycle cancellations due to premature ovulation was comparable between the groups, with 6 cancellations (2%) in the fPPOS group and 1 cancellation (0.4%) in the GnRH antagonist group (p=0.112).

Table 1. Baseline and clinical parameters of study groups

mean ± SD	fPPOS (n=307)	GnRH-ant (n=241)	p-value
Female age, years	40.91±2.92	40.54±2.82	0.092[a]
BMI (kg/m²)	23.57±4.29	23.39±4.16	0.676[a]
Duration of infertility, years	4.64±3.49	4.86±3.94	0.805[a]
No of previous failed attempts, n	2.49±1.81	2.35±1.94	0.289[a]
Type of infertility, n (%)			
Primary	116 (37.8)	98 (40.7)	0.275[b]
Secondary	191 (62.2)	143 (59.3)	
Previous miscarriages, n	1.07±1.34	0.86±1.16	0.057[a]
Previous live birth, n	0.16±0.43	0.23±0.50	*0.045[a]
AMH, ng/mL	1.09±1.07	1.08±1.30	0.590[a]
Antral follicle count, n	8.18±5.63	6.91±5.05	*0.001[a]
Sperm concentration, 10^6/mL	42.71±31.36	37.20±30.32	*0.026[a]
Duration of COH, days	10.51±1.83	9.83±1.97	*0.000[a]
Duration of LH suppression, days	5.57±1.29	4.59±1.12	*0.000[a]
Total gonadotropin dosage, IU	2669.17±901.97	2286.61±911.82	*0.000[a]
LH level on the trigger day, mIU/mL	5.96±4.95	4.65±4.17	*0.001[a]
Premature LH rise, >10 mIU/mL, n (%)	25 (8.2)	16 (6.6)	0.302[b]
Cancellation due to premature ovulation, n (%)	6 (2.0)	1 (0.4)	0.112[b]

[a]: Mann-Whitney U test, [b]: Fisher's exact test, GnRH: Gonadotropin-releasing hormone, fPPOS: Flexible progestin-primed ovarian stimulation, SD: Standard deviation, COH: Controlled ovarian hyperstimulation, BMI: Body mass index, LH: Luteinizing hormone, AMH: Anti-Müllerian hormone, *: A statistically significant difference was identified by p<0.05

In contrast, the fPPOS group demonstrated significantly higher antral follicle counts (AFC), sperm concentrations, and mean number of previous live births (p<0.05). This group also experienced significantly longer durations of COH (p<0.001) and LH suppression (p<0.001). Additionally, the fPPOS group required a higher total gonadotropin dosage (p<0.001) and exhibited elevated LH levels on the trigger day (p<0.005) compared with the GnRH antagonist group.

The embryological and genetic outcomes of the patient cohort are displayed in Table 2. The fPPOS group demonstrated significantly higher mean numbers of oocytes retrieved, MII oocytes, 2PN zygotes, and day 3-TQ embryos (p<0.05). However, the maturation rate, the fertilization rate, the blastulation rate, and other metrics such as the number of cycles resulting in zero blastocysts and zero euploid blastocysts, the number of cycles yielding at least one euploid blastocyst, the euploid blastocyst rate per biopsy, and the euploid blastocyst rate per injected MII were comparable between the groups (p>0.05).

The Spearman's rho correlation analysis, as presented in Table 3, indicated that the euploid blastocyst rate per injected MII oocyte was significantly correlated with female age, AMH levels, AFC, the number of oocytes retrieved, the number of MII oocytes, and the number of 2PN zygotes in both groups. BMI showed a negative correlation in the GnRH antagonist group (r=-0.166; p<0.05). Previous live birth, sperm concentration, durations of COH and LH suppression, and total gonadotropin dosage were not correlated with euploid blastocyst rate per injected MII oocyte in either group.

The Generalized Linear Model analysis demonstrated that both the maturation rate [odds ratio (OR)=0.114; p<0.05] and the blastulation rate (OR=0.194; p<0.01) were significant independent predictors of the euploid blastocyst rate per injected MII oocyte within the fPPOS group. Conversely, in the GnRH antagonist group, the blastulation rate (OR=0.132; p<0.01) was identified as the only significant independent variable influencing the outcome (Table 4).

Table 5 presents the outcomes associated with frozen ET cycles. The numbers of cycles in which at least one euploid blastocyst was obtained and frozen ET was performed in the fPPOS and GnRH antagonist groups were 98 (84.5%) and 65 (83.3%), respectively. The parameters compared, including the day embryos were transferred, endometrial thickness, and the rates of positive pregnancy tests, implantation, and ongoing pregnancy, did not reach statistical significance (p>0.05). In addition, the biochemical pregnancy loss rate and the early miscarriage rate were comparable (p=0.912).

Table 2. Embryological outcomes of study groups

mean ± SD	fPPOS (n=307)	GnRH-ant (n=241)	p-value
No. of oocytes retrieved, n	6.95±5.18	6.29±5.68	*0.025[a]
No. of MII, n	5.67±4.47	5.12±4.89	*0.026[a]
No. of 2PN, n	4.81±3.96	4.08±3.86	*0.005[a]
Maturation rate, %	0.81±0.21	0.80±0.24	0.917[a]
Fertilization rate, %	0.85±0.20	0.82±0.24	0.487[a]
No. of day 3 TQ embryos, n	2.85±2.78	2.18±2.25	*0.005[a]
Blastulation rate, %	0.47±0.31	0.53±0.35	0.059[a]
No. of cycles with zero blastocyst, n (%)	65 (21.17)	57 (23.65)	0.278[b]
No. of cycles with zero euploid blastocyst, n (%)	126 (52.07)	106 (57.61)	
No. of cycles with at least one euploid blastocyst, n (%)	116 (47.93)	78 (42.39)	0.291[c]
Embryo biopsy day			
D5	1.87±2.03	1.59±2.04	0.098[a]
D6	0.44±0.81	0.50±0.96	0.647[a]
Euploid blastocyst rate per biopsy, %	206/411 (50.12)	156/294 (53.06)	0.317[a]
Euploid blastocyst rate per injected MII, %	206/864 (23.84)	156/641 (23.34)	0.231[a]

[a]: Mann-Whitney U test, [b]: Fisher's exact test, [c]: Chi-square likelihood ratio, GnRH: Gonadotropin-releasing hormone, fPPOS: Flexible progestin-primed ovarian stimulation, SD: Standard deviation, MII: Metaphase II, TQ: Top-quality, *: A statistically significant difference was identified by p<0.05

Table 3. Spearman's rho correlation for effects of baseline and clinical parameters on euploid blastocyst rate per injected MII oocyte

Euploid blastocyst rate per injected MII oocyte	fPPOS		GnRH-ant	
	r	p	r	p
Women's age	-0.548**	0.000	-0.487**	0.000
BMI	-0.017	0.769	-0.166*	0.012
Previous live birth	-0.045	0.438	-0.052	0.428
AMH	0.161**	0.005	0.350**	0.000
Antral follicle count	0.231**	0.000	0.366**	0.000
Sperm concentration	0.041	0.481	0.047	0.478
Duration of COH	0.011	0.854	0.036	0.589
Duration of LH suppression	0.060	0.303	0.106	0.107
Total gonadotropin dosage	0.009	0.881	-0.030	0.646
No. of oocytes retrieved	0.233**	0.000	0.365**	0.000
No. of MII	0.264**	0.000	0.380**	0.000
No. of 2PN	0.289**	0.000	0.412**	0.000

*p<0.05, **p<0.01, COH: Controlled ovarian hyperstimulation, BMI: Body mass index, LH: Luteinizing hormone, GnRH: Gonadotropin-releasing hormone, fPPOS: Flexible progestin-primed ovarian stimulation, MII: Metaphase II, AMH: Anti-Müllerian hormone

Table 4. Generalized linear model (logit) for effects of clinical parameters on euploid blastocyst rate per injected MII for patient groups

Parameter	OR	Standard error	95% wald confidence interval		Hypothesis test		
			Lower	Upper	Wald X^2	df	p-value
fPPOS group							
(Intercept)	-0.345	0.2787	-0.891	0.201	1.534	1	0.216
Duration of COH	-0.007	0.0090	-0.024	0.011	0.534	1	0.465
Duration of LH suppression	0.001	0.0085	-0.016	0.017	0.004	1	0.947
Total gonadotropin dosage	0.033	0.0418	-0.049	0.115	0.605	1	0.437
LH level on the trigger day	-0.002	0.0023	-0.006	0.003	0.524	1	0.469
Maturation rate	0.114	0.0542	0.008	0.220	4.432	1	0.035*
Fertilization rate	0.095	0.0595	-0.022	0.212	2.546	1	0.111
No of day 3-TQ embryos	-0.007	0.0067	-0.020	0.006	1.111	1	0.292
Blastulation rate	0.194	0.0382	0.119	0.269	25.814	1	0.000*
Embryo biopsy day 5	0.016	0.0097	-0.003	0.035	2.782	1	0.095
Embryo biopsy day 6	0.001	0.0139	-0.027	0.028	0.001	1	0.971
(Scale)	0.025	0.0021	0.022	0.030			
GnRH-Ant group							
(Intercept)	0.460	0.2987	-0.126	1.045	2.367	1	0.124
Duration of COH	0.001	0.0110	-0.021	0.022	0.002	1	0.964
Duration of LH suppression	0.010	0.0140	-0.017	0.038	0.541	1	0.462
Total gonadotropin dosage	-0.061	0.0460	-0.151	0.029	1.770	1	0.183
LH level on the trigger day	0.002	0.0034	-0.005	0.008	0.219	1	0.640
Maturation rate	-0.103	0.0597	-0.220	0.014	2.990	1	0.084
Fertilization rate	0.014	0.0571	-0.098	0.126	0.063	1	0.802
No of day 3-TQ embryos	0.014	0.0088	-0.003	0.031	2.616	1	0.106
Blastulation rate	0.132	0.0369	0.060	0.205	12.862	1	0.000*
Embryo biopsy day 5	0.015	0.0097	-0.004	0.034	2.421	1	0.120
Embryo biopsy day 6	-0.003	0.0143	-0.030	0.025	0.031	1	0.860
(Scale)	0.027	0.0026	0.023	0.033			

*: A statistically significant difference was identified by p<0.05, COH: Controlled ovarian hyperstimulation, LH: Luteinizing hormone, TQ: Top-quality, GnRH: Gonadotropin-releasing hormone, fPPOS: Flexible progestin-primed ovarian stimulation, OR: Odds ratio, MII: Metaphase

Table 5. Frozen embryo transfer outcomes

Parameter	fPPOS	GnRH-ant	p-value
Day of embryos transferred			
D5	85 (27.7)	55 (22.8)	0.422[a]
D6	13 (4.2)	10 (4.1)	
Endometrial thickness, mm	9.75±6.81	9.35±1.84	0.483[b]
Positive pregnancy test rate, n (%) (per transfer)	78/101 (77.23)	49/65 (75.38)	0.314[a]
Implantation rate, n (%) (per transfer)	67/101 (66.34)	45/65 (69.23)	0.415[c]
Ongoing pregnancy rate, n (%) (per transfer)	55/101 (54.45)	35/65 (53.84)	0.538[d]
Pregnancy loss rate, % (per transfer)			
Biochemical pregnancy loss, n (%)	11/101 (10.89)	5/65 (7.69)	0.912[c]
Early miscarriage, n (%)	12/67 (17.91)	9/45 (20.00)	

[a]: Pearson's chi-square test, [b]: Mann-Whitney U test, [c]: Chi-square likelihood ratio, [d]: Fisher's exact test, SD: Standard deviation, *: A statistically significant difference was identified by p<0.05, GnRH: Gonadotropin-releasing hormone, fPPOS: Flexible progestin-primed ovarian stimulation

Discussion

This research is the first comprehensive study to present detailed data on embryological processes and embryo ploidy in the fPPOS group. We analyzed the outcomes associated with the fPPOS and GnRH antagonist protocols, focusing on clinical, embryological, and PGT-A results. The number of cycles in which a premature LH rise occurred and the number of cycles cancelled due to premature ovulation were similar across both groups. Although the fPPOS group produced greater numbers of retrieved oocytes, 2PN zygotes, and day 3-TQ embryos, we did not find significant differences in maturation, fertilization, and blastulation rates, or in euploid blastocyst rates per biopsy and per injected MII oocyte.

Univariate correlation analysis indicated that several demographic, embryological, and clinical parameters showed similar associations with the euploid blastocyst rate per injected MII oocyte in both groups, except for increased BMI, which showed a negative correlation in the GnRH antagonist group. The multivariate regression analysis revealed that factors such as the duration of COH and LH suppression, total gonadotropin dosage, LH levels on the trigger day, the number of day 3-TQ embryos, and the embryo biopsy day (D5 or D6) did not significantly influence the euploid blastocyst rate per injected MII oocyte in either group. Additionally, the pregnancy outcomes were comparable between the two groups.

The flexible approach was first introduced for hyperresponder donor patients and compared with the GnRH antagonist protocol[25]. A similar comparison was conducted in a distinct population of patients with diminished ovarian reserve who underwent oocyte freezing[2,26]. In both the previously mentioned studies and a recently published randomized non-inferiority trial[27], no significant differences were observed between the fPPOS and GnRH antagonist groups regarding total gonadotropin dosage requirements and early embryological parameters. Despite the limited use of MPA in our study, the fPPOS group demonstrated a prolonged duration of COH and a higher total gonadotropin dose requirement, which contrasts with the existing literature. The intentional delay of at least one day in triggering maturation for the fPPOS group, aimed at optimizing the number of retrieved oocytes, may have contributed to these outcomes. Furthermore, we observed significantly higher numbers of retrieved oocytes, MII oocytes, 2PN zygotes, and D3-TQ embryos in the fPPOS group. However, the maturation, fertilization, and blastulation rates were comparable between the groups, which is consistent with the literature[17]. This finding can primarily be attributed to the higher baseline AFC in the fPPOS group compared to the GnRH antagonist group (8.18±5.63 vs. 6.91±5.05; p<0.01). Additionally, the mild pituitary suppression theory proposed by Vidal et al.[28] may have contributed to this outcome. This theory was validated in this study, and the observed significance was attributable to higher serum LH levels measured on the maturation trigger day in the fPPOS group than in the GnRH antagonist group (5.96±4.95 versus 4.65±4.17; p<0.01). A similar phenomenon was documented in an RCT conducted by Chen et al.[3], which employed the conventional PPOS protocol (3.17±4.84 versus 2.59±1.77; p=0.023). Moreover, a recently published RCT by Cai et al.[27] utilizing the fPPOS protocol corroborated these findings [2.9 (1.9-4.4) versus 2.5 (1.4-3.7); p=0.017].

The euploidy rate is a robust indicator of embryo quality. The transfer of euploid embryos notably enhances live birth rates per transfer, particularly in cases involving women aged over 35 years[29]. The identification of similar or elevated euploidy rates in the fPPOS group compared with those in the GnRH antagonist or agonist groups would significantly substantiate the treatment's reliability. In a recent review, the topic was assessed under the subtitle "Does PPOS Affect Developmental Potential of Oocytes"[17]. The collective findings of one prospective[30] and three retrospective studies[31-33] suggest that the euploidy rate per biopsy was similar in both the conventional PPOS and GnRH antagonist groups. However, one study in which the euploidy rate was claimed to be lower in the PPOS group (5.4% versus 26.7%; p=0.006) was criticized because of its small sample size[34]. Conversely, a current retrospective cohort study reported significantly high rates of both euploid blastocysts per biopsy (54.94% versus 40.88%; p=0.015) and euploid blastocysts per MII oocyte (15.48% versus 10.47%; p=0.013) in the conventional PPOS group compared to GnRH antagonist group; however, these findings may also be questioned due to the small sample size involved[35]. Apart from these, a recent prospective study reported a comparable mean number of biopsied blastocysts, a mean number of euploid blastocysts, and a euploidy rate per biopsied blastocyst across treatment protocols[28]. Consistent with these findings, our study did not identify any significant differences between treatment groups in the euploid blastocyst rate per biopsy (50.1% vs. 53.1%; p>0.05) or per injected MII oocyte (23.8% vs. 23.3%; p>0.05).

The pregnancy outcomes noted in this study are consistent with those found in a previously published review[17] and a meta-analysis[36]. Moreover, recent findings from a retrospective study[35] and an RCT[27] lend further support to these conclusions. The fPPOS protocol yielded results comparable to the widely used GnRH antagonist protocol in terms of implantation rates (66.34% vs. 69.23%; p=0.415) and ongoing pregnancy rates (54.45% vs. 53.84%; p=0.538) per transfer. In light of these findings, we can conclude that ETs utilizing euploid blastocysts obtained through the fPPOS protocol are not inferior to those achieved with the GnRH antagonist protocol.

This study demonstrates its strength through a targeted focus on a patient group that faces significant challenges in treatment management and often has suboptimal outcomes.

Additionally, it provides a thorough, first-time evaluation of the fPPOS protocol, particularly with respect to embryological and PGT-A outcomes.

Study Limitations

This study provides a snapshot of daily practice. Although maturation, fertilization, blastulation, and euploidy rates per biopsy and per injected MII oocyte were similar across groups according to a comprehensive multivariate analysis, the higher AFC, prolonged duration of COH, and higher total gonadotropin dose in the fPPOS group may still influence embryological yield. Another limitation of this study is its retrospective design, which necessitates a cautious interpretation of the findings. To substantiate these results, future large-scale randomized trials with adequate sample sizes will be essential. Furthermore, research calculating cumulative live birth rates using robust statistical methods will yield more valuable insights into comparing pregnancy outcomes between the two groups.

Conclusion

The fPPOS protocol, utilizing MPA, offers a straightforward, convenient, and effective treatment that requires fewer pills and is more patient-friendly. Flexible application does not adversely affect embryological outcomes or PGT-A results, nor does it increase the risk of cycle cancellations due to premature ovulation. Furthermore, no negative effects on pregnancy outcomes were observed. Therefore, fPPOS may be recommended as the preferred option in cases where fresh ET does not immediately follow ovarian stimulation.

Ethics

Ethics Committee Approval: Due to the retrospective design of the study, ethics committee approval was deemed not required by Acıbadem Fulya Hospital. Institutional permission was granted for the analysis of the data.
Informed Consent: In this study, informed consent was not considered necessary because the data used were entirely anonymized.

Footnotes

Authorship Contributions

Surgical and Medical Practices: N.E.T., Concept: N.E.T., Design: N.E.T., E.B., Data Collection or Processing: N.E.T., H.B., Analysis or Interpretation: E.K., Literature Search: N.E.T., S.Ö., Writing: N.E.T.
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Mutation analysis of the *FOXL2* and *BMP15* genes in patients with premature ovarian insufficiency

Prematür over yetersizliği olan hastalarda FOXL2 ve BMP15 genlerinin mutasyon analizi

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Abstract

Objective: Premature ovarian insufficiency (POI) is defined by irregular menstrual cycles or amenorrhea before age 40 with elevated follicle-stimulating hormone (FSH) levels. We evaluated *FOXL2* and *BMP15* variants in Turkish women with POI and assessed the distribution of the *BMP15* promoter variant c.-9C>G in a case-control setting.

Materials and Methods: Seventy-five women younger than 40 years with hypergonadotropic hypogonadism, primary/secondary amenorrhea, serum FSH ≥25 mIU/mL on two occasions at least four weeks apart, a normal 46,XX karyotype, and negative *FMR1* CGG repeat testing were included. Women with prior ovarian surgery, pelvic chemotherapy/radiotherapy, or endocrine or autoimmune disease were excluded. *FOXL2* and *BMP15* coding regions and intron-exon junctions were analyzed by Sanger sequencing. *BMP15* c.-9C>G genotype frequencies were compared with 80 ethnically matched controls with normal ovarian function. Genotype-specific analyses compared CG versus CC + GG using Fisher's exact test, with odds ratios (ORs) and 95% confidence intervals (CIs).

Results: No pathogenic POI-associated variants were detected in *FOXL2* or *BMP15*. The heterozygous *BMP15* c.-9C>G variant was identified in 34/75 patients; it occurred alone in 21, with c.308A>G in 12, and with c.352G>A in 1 patient. In the case-control comparison, the CG genotype was more frequent in POI than in controls (34/75, 45.3% vs. 15/80, 18.8%) and was associated with increased POI risk (OR=3.59, 95% CI: 1.74-7.40; p=0.0005).

Conclusion: No pathogenic *BMP15* or *FOXL2* variant was identified. The *BMP15* c.-9C>G variant may be associated with susceptibility to POI in this Turkish cohort, but this finding requires confirmation in larger, unrelated, well-matched populations and functional studies.

Keywords: *BMP15*, *FOXL2*, premature ovarian insufficiency

Öz

Amaç: Prematür over yetersizliği (POY), 40 yaşından önce düzensiz menstrüel sikluslar veya amenore ile birlikte yüksek folikül stimülan hormon (FSH) düzeyleri ile tanımlanır. Bu çalışmada, POY tanılı Türk kadınlarda *FOXL2* ve *BMP15* varyantları değerlendirildi ve *BMP15* promotör varyantı c.-9C>G'nin dağılımı olgu-kontrol düzeninde araştırıldı.

PRECIS: *FOXL2* and *BMP15* sequencing in 75 Turkish women with premature ovarian insufficiency (POI) revealed no pathogenic variants; the *BMP15* c.-9C>G CG genotype was common and associated with increased POI risk.

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Gereç ve Yöntemler: Hipergonadotropik hipogonadizm, primer/sekonder amenore, en az dört hafta arayla yapılan iki ölçümde serum FSH düzeyinin ≥25 mIU/mL olması, normal 46,XX karyotip ve negatif *FMR1* CGG tekrar testi bulunan 40 yaş altındaki 75 kadın çalışmaya dahil edildi. Daha önce over cerrahisi geçirmiş, pelvik kemoterapi/radyoterapi almış veya endokrin ya da otoimmün hastalığı bulunan kadınlar dışlandı. *FOXL2* ve *BMP15* genlerinin kodlayan bölgeleri ile intron-ekzon sınırları Sanger dizileme yöntemiyle analiz edildi. *BMP15* c.-9C>G genotip frekansları, normal over fonksiyonuna sahip etnik olarak eşleştirilmiş 80 kontrol ile karşılaştırıldı. Genotipe özgü analizlerde CG genotipi, CC + GG genotipi ile Fisher'in kesin testi kullanılarak karşılaştırıldı; olasılık oranları (OR) ve %95 güven aralıkları (GA) hesaplandı.

Bulgular: *FOXL2* veya *BMP15* genlerinde POY ile ilişkili patojenik varyant saptanmadı. Heterozigot *BMP15* c.-9C>G varyantı 34/75 hastada belirlendi; bu varyant 21 hastada tek başına, 12 hastada c.308A>G ile birlikte ve 1 hastada c.352G>A ile birlikte bulundu. Olgu-kontrol karşılaştırmasında, CG genotipi POY grubunda kontrollere göre daha sık bulundu (34/75, %45,3; 15/80, %18,8) ve artmış POY riski ile ilişkiliydi (OR=3,59; %95 GA: 1,74-7,40; p=0,0005).

Sonuç: *BMP15* veya *FOXL2* genlerinde patojenik varyant saptanmadı. *BMP15* c.-9C>G varyantı bu Türk kohortunda POY yatkınlığı ile ilişkili olabilir; ancak bu bulgunun daha büyük, akraba olmayan, iyi eşleştirilmiş popülasyonlarda ve fonksiyonel çalışmalarla doğrulanması gerekmektedir.

Anahtar Kelimeler: *BMP15*, *FOXL2*, prematür over yetersizliği

Introduction

Premature ovarian insufficiency (POI) is defined as irregular menstrual cycles or amenorrhea for at least four months occurring before the age of 40. This diagnosis is established when two or more follicle-stimulating hormone (FSH) measurements obtained at least four weeks apart demonstrate levels ≥25 mIU/mL[1]. POI affects approximately 1% of women and commonly presents with infertility and hypoestrogenic symptoms[1,2]. In addition to infertility, women with POI are at an increased risk of developing osteoporosis, cardio-cerebrovascular, neurodegenerative, and metabolic diseases[3]. The pathogenesis is heterogeneous and may involve a reduced primordial follicle pool, accelerated follicular atresia, or impaired follicular growth, with genetic, autoimmune, metabolic, infectious, iatrogenic (e.g., gonadotoxic cancer treatments), and environmental contributors[4,5]. Genetic factors account for 25-30% of cases of POI and up to ~50% in familial POI, and more than 100 genes have been implicated[6,7]. In this context, we focused on *FOXL2* and *BMP15*, key regulators of oocyte-granulosa cell communication. *FOXL2* is critical for granulosa-cell differentiation and identity, and loss-of-function variants cause blepharophimosis-ptosis-epicanthus inversus syndrome, which may be associated with POI[8,9]. *BMP15* is an oocyte-derived transforming growth factor β superfamily ligand that modulates granulosa-cell proliferation, steroidogenesis, and FSH responsiveness; pathogenic *BMP15* variants have been linked to ovarian dysgenesis/POI through a dosage-sensitive mechanism[10-12]. This study aimed to investigate *FOXL2* and *BMP15* variants in Turkish women with POI and to assess the association of the *BMP15* c.-9C>G promoter variant with POI in a case-control setting.

Materials and Methods

A total of 75 unrelated patients were included in the study: 50 who presented to the Ankara University Faculty of Medicine, Department of Medical Genetics clinic with a preliminary diagnosis of POI and 25 who presented to the Zekai Tahir Burak Women's Health Education and Research Hospital, Clinic of Medical Genetics. The Ankara University Clinical Research Ethics Committee approved the study (approval number: 05-187-13, date: 25.03.2013), and 75 patients were included after obtaining their informed consent. The inclusion criteria of the study were being under 40 years of age, serum FSH ≥25 mIU/mL on two occasions at least four weeks apart, presence of primary or secondary amenorrhea, normal karyotype: 46,XX, and negative *FMR1* CGG repeat testing. The exclusion criteria were a history of ovarian surgery, pelvic chemotherapy, pelvic radiation exposure, or endocrine or autoimmune disease. Eighty women who presented to our clinic and were assessed as having normal ovarian function were recruited as the control group. Controls were ethnically matched women who had regular menstrual cycles, no history of primary or secondary amenorrhea, and no prior diagnosis of POI. Women with a personal history suggestive of POI or amenorrhea were excluded. Genotype distributions of *BMP15* c.-9C>G were compared in POI cases and controls using Fisher's exact test. In addition, exploratory inheritance-model analyses were performed, and effect sizes were reported as odds ratios (ORs) with 95% confidence intervals (CIs). Departure from Hardy-Weinberg equilibrium for *BMP15* c.-9C>G was assessed in the control group using an exact test. All statistical analyses were performed using SPSS Statistics, version 31.0.1.0.

Lymphocyte Cell Culture from Peripheral Blood

Peripheral blood lymphocytes were cultured using standard cytogenetic procedures. Heparinized peripheral blood was incubated in culture medium at 37 °C for 72 hours. Colchicine treatment, hypotonic incubation, and fixation were subsequently performed, and metaphase chromosome analysis was carried out on the prepared samples.

Fragment Analysis

Genomic deoxyribonucleic acid was isolated from peripheral blood collected in ethylenediamine tetraacetic acid tubes, using the Magna Pure LC Instrument (Roche Applied Science). Fragment analysis was performed using fluorescently labeled polymerase chain reaction (PCR) primers and capillary electrophoresis with the ROX 1000 size standard. Fragment sizes were analyzed using GeneMapper software (Applied Biosystems).

Sanger Sequencing

FOXL2 and *BMP15* were analyzed by bidirectional Sanger sequencing. The single exon of *FOXL2* and the two exons of *BMP15*, including exon-intron junctions, were amplified by PCR using gene-specific primers. Amplification was verified by agarose gel electrophoresis, purified, and then sequenced on a 3130 Genetic Analyzer (Applied Biosystems). Sequence data were analyzed using SeqScape version 2.7 and Sequencing Analysis version 5.1 software. NM_023067.4 and NM_005448.2 were used as the reference transcripts for *FOXL2* and *BMP15*, respectively. Variants were described and classified according to American College of Medical Genetics and Genomics (ACMG) guidelines[13]. Further details of the laboratory protocols are available from the corresponding author upon reasonable request.

Results

The ages at diagnosis ranged from 11 to 39 years, with a mean of 29.93±6.86 years. Of the 75 patients included in the study, 11 (14.67%) were diagnosed with primary amenorrhea and 64 (85.33%) with secondary amenorrhea. Hormonal analysis revealed a mean FSH level of 70.69±29.58 mIU/mL and a mean luteinizing hormone level of 29.76±15.54 mIU/mL. In the patients, chromosomal analysis and *FMR1* CGG repeat testing were normal. The clinical and laboratory characteristics of the patients are summarized in Table 1.

FOXL2 sequencing was performed in three fragments in 67 of the 75 patients; in the remaining eight patients, only the first two fragments could be analyzed because of technical difficulties. Variants in the *FOXL2* gene were detected in four of the 75 patients. Three patients carried both the c.501C>T (rs61750361) and c.536C>G (rs7432551) variants, and one patient carried the c.672A>T variant. The *FOXL2* variants c.501C>T and c.536C>G were classified as benign, whereas the c.672A>T variant was classified as likely benign. *BMP15* variants were detected in 36 of the 75 patients. The c.-9C>G variant was homozygous in two patients (cases 6 and 20) and heterozygous in 34 patients. In this heterozygous group, the c.-9C>G (rs3810682) promoter variant was present alone in 21 patients, in combination with c.308A>G (rs41308602) in 12 patients, and in combination with c.352G>A (rs142156356) in one patient. The *BMP15* variants c.-9C>G and c.308A>G were classified as benign, whereas the c.352G>A variant was classified as likely benign. Detailed information on *FOXL2* and *BMP15* variants is presented in Table 2.

A control group of 80 women (ethnically matched women with normal ovarian function) was analyzed to determine the frequency of the *BMP15* c.-9C>G variant in the Turkish population. In the control group, 15 women were heterozygous, and 9 were homozygous for this variant. The distribution of *BMP15* c.-9C>G genotypes in the patient and control groups is shown in Table 3.

In the control group, the *BMP15* c.-9C>G genotype distribution deviated from the Hardy-Weinberg equilibrium (exact $p<0.01$). Formal haplotype analysis was not performed in our study. In the patient group, the c.308A>G variant was observed only in individuals carrying the c.-9G allele (CG or GG genotypes), which may suggest linkage between these two variants. However, the same pattern was observed in the control group, and the distribution of c.308A>G among c.-9C>G carriers was similar in patients and controls. Therefore, our current data do not support a clear disease-specific effect attributable to a c.-9C>G/c.308A>G haplotype. The observed association appears more likely attributable to c.-9C>G heterozygosity, although this interpretation remains preliminary in the absence of formal haplotype-based analysis.

In the case-control comparison, the genotype distribution for *BMP15* c.-9C>G differed significantly between POI cases and controls (2×3 Fisher's exact test, $p=0.0006$). The association signal was mainly driven by enrichment of the heterozygous CG genotype in POI cases (34/75, 45.3%) compared with controls (15/80, 18.8%). In exploratory inheritance-model analyses, the overdominant model (CG vs. CC + GG) provided the best fit, and showed that heterozygous carriage was associated with increased risk of POI (OR=3.59, 95% CI 1.74-7.40; Fisher's exact test, $p=0.0005$). By contrast, the GG genotype was not significantly associated with case status. The distribution of the c.-9C>G and c.308A>G variants in the patient and control groups is shown in Table 4.

Discussion

The etiology of POI is the result of the interplay of several genes, and *FOXL2* and *BMP15* represent functionally important genes that have a role in this process[3]. In the present study, we analyzed *FOXL2* and *BMP15* in patients with POI to determine the spectrum and frequency of variants and to assess their pathogenicity.

We did not identify any *FOXL2* or *BMP15* pathogenic variants in the analyzed regions of our cohort. Because *FOXL2* sequencing was incomplete in eight patients, rare variants in the unanalyzed *FOXL2* region cannot be fully excluded. Although the *BMP15* promoter variant c.-9C>G is classified as benign according to ACMG criteria, its relatively high frequency in our cohort and the case-control comparison suggested a possible association between the CG genotype at position -9 and POI susceptibility. This finding should not be interpreted as evidence of pathogenicity, but rather as a preliminary association signal that requires cautious interpretation and confirmation in larger independent cohorts.

Functional *in vitro* studies have demonstrated that the *BMP15* c.-9C>G promoter variant results in a significant increase in *BMP15* expression and has been proposed to contribute to the pathogenesis of POI[14]. In the study by Fonseca et al.[14],

Table 1. The clinical and laboratory characteristics of the patients

No	Age	Diagnosis	FSH	LH	E2
Case 1	24	SA	54	12	-
Case 2	24	SA	115	66	<20
Case 3	32	SA	75	25	62
Case 4	38	SA	60	32	<20
Case 5	35	SA	48	-	-
Case 6	29	SA	95	74	11
Case 7	38	SA	182	50	<20
Case 8	18	PA	68	16	<20
Case 9	39	SA	49	18	<20
Case 10	33	SA	45	16	22
Case 11	31	SA	42	22	<20
Case 12	29	SA	48	20	<20
Case 13	33	SA	121	49	34
Case 14	32	SA	48	11	<20
Case 15	39	SA	66	27	32
Case 16	32	SA	177	13	10
Case 17	39	SA	63	37	<20
Case 18	28	SA	60	17	25
Case 19	11	PA	68	14	<20
Case 20	24	SA	75	17	<11
Case 21	35	SA	106	37	-
Case 22	25	SA	53	15	28
Case 23	34	PA	48	25	6
Case 24	29	SA	52	19	5
Case 25	29	PA	83	29	<20
Case 26	33	SA	90	28	21
Case 27	39	SA	54	21	<20
Case 28	26	PA	57	16	<20
Case 29	36	SA	73	29	48
Case 30	22	SA	94	48	<20
Case 31	28	SA	103	34	33
Case 32	32	SA	88	49	<20
Case 33	38	SA	102	51	<20
Case 34	27	SA	99	46	34
Case 35	37	SA	42	13	<20
Case 36	28	SA	111	49	21
Case 37	38	SA	66	-	35
Case 38	30	SA	41	15	<20
Case 39	39	SA	45	7	<20
Case 40	39	SA	44	31	<20
Case 41	38	SA	130	56	<20
Case 42	19	SA	52	45	42
Case 43	26	SA	41	5	35
Case 44	25	SA	88	37	21
Case 45	29	SA	62	55	128
Case 46	31	SA	40	17	<20
Case 47	29	PA	40	23	25
Case 48	39	SA	116	41	<20
Case 49	25	SA	40	11	<20
Case 50	30	SA	46	13	<20
Case 51	26	SA	40	12	<11.8
Case 52	32	SA	71	28	<20
Case 53	18	PA	61	15	<11.8
Case 54	15	SA	94	48	17
Case 55	22	PA	57	35	60
Case 56	38	SA	48	21	64
Case 57	39	SA	74	55	42
Case 58	20	SA	75	30	26
Case 59	23	SA	87	29	<20
Case 60	19	SA	67	41	<20
Case 61	26	SA	45	25	31
Case 62	37	SA	40	-	-
Case 63	38	SA	45	-	-
Case 64	17	PA	101	30	16
Case 65	39	PA	46	38	<20
Case 66	33	SA	81	36	<20
Case 67	28	SA	100	55	33
Case 68	29	SA	85	10	19
Case 69	21	SA	70	47	12
Case 70	28	SA	47	19	19
Case 71	39	PA	81	39	<20
Case 72	33	SA	46	27	<20
Case 73	28	SA	49	32	87
Case 74	29	SA	65	8	10
Case 75	25	SA	62	32	48

FSH and LH values in the table are presented in mIU/mL, and E2 values are presented in pg/mL. PA: Primary amenorrhea, SA: Secondary amenorrhea, FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, E2: Estradiol

Table 2. Pathogenicity and other characteristics of the identified variants

Gene variants	Protein position	Variant type	GnomAD AF	TGP AF	ACMG criteria	ACMG classification
FOXL2 c.501C>T	p.Phe167=	S	0.040	0.039	BA1, BS2, BP7, BP6	Benign
FOXL2 c.536C>G	p.Ala179Gly	M	0.042	0.039	PP2, BA1, BS2, BP6	Benign
FOXL2 c.672A>T	p.Ala224=	S	-	-	PM2, BP4, BP7	Likely benign
BMP15 c.-9C>G	-	-	0.210	-	BA1, BS2, BP7, BP6	Benign
BMP15 c.308A>G	p.Asn103Ser	M	0.071	-	BA1, BS2, BP4, BP6	Benign
BMP15 c.352G>A	p.Gly118Ser	M	0.000020	-	PM2, BP4	Likely benign

M: Missense, S: Synonymous, AF: Allele frequency, GnomAD: Genome aggregation database, TGP: Turkish Genome Project, ACMG: American College of Medical Genetics and Genomics

Table 3. Genotype distribution of the *BMP15* c.-9C>G variant in patient and control groups

	CC	CG	GG	Total
Patients	39	34	2	75
Controls	56	15	9	80
Total	95	49	12	155

the *BMP15* c.-9G allele was associated with POI. It has been established that *BMP15* is co-expressed with the transcription factor *PITX1* (pituitary homeobox 1), which binds to the *BMP15* promoter between positions -14 and -8. *PITX1* can transactivate the *BMP15* promoter carrying either the C or the G allele at position -9; however, the c.-9C>G substitution modifies the *PITX1*-binding site and results in enhanced *BMP15* transcription, which has been implicated in POI[14]. It has been reported that *BMP15* expression increases significantly in the presence of the c.-9G allele, leading to altered granulosa cell proliferation. Moreover, high ovarian *BMP15* levels have been shown to further reduce *FSHR* messenger RNA expression. Consistent with these findings, a transgenic mouse model with high *BMP15* expression exhibited an increased number of primary follicles but a reduced number of secondary follicles, and increased granulosa-cell mitosis was associated with accumulation of primary follicles and atresia of secondary follicles[15]. Collectively, these data provide biological plausibility for a possible contributory role of the *BMP15* c.-9G allele in ovarian dysfunction; however, they do not establish this common variant as a pathogenic cause of POI.

Several studies have shown that the *BMP15* c.-9C>G variant is associated with POI[16-18]. In a study of 202 Indian patients with POI, Dixit et al.[16] demonstrated that the *BMP15* c.-9G allele forms part of a haplotype associated with the disease. They performed haplotype analysis of three variants that are commonly observed in POI patients (c.-9C>G, c.308A>G, and c.852C>T) and found a significant association between the G-G-C haplotype (c.-9G, c.308G, c.852C) and POI[16]. Although c.308A>G was observed only in carriers of the c.-9G allele in our cohort, a similar pattern was present in controls, and formal haplotype analysis was not performed. Therefore, our data do not allow firm conclusions regarding a disease-specific *BMP15* haplotype. Morón et al.[17] investigated the association between *BMP15* alleles and ovarian hyperstimulation syndrome. The study included 307 women undergoing in vitro fertilization treatment, of whom 35 had a high ovarian response to stimulation. A significant association was found between carriage of the *BMP15* c.-9G allele and a high ovarian response to ovarian stimulation in this cohort[17]. In another study, Hanevik et al.[18] examined the association between *BMP15* variants and the ovarian response to stimulation. They found a significant association

Table 4. Genotype distribution of *BMP15* c.-9C>G genotypes (CC, CG, GG) and carriage of c.308A>G (AG) in POI patients and controls

Patient (n=75)						Control (n=80)					
CC (n=39)		CG (n=34)		GG (n=2)		CC (n=56)		CG (n=15)		GG (n=9)	
CC	CC + AG	CG	CG + AG	GG	GG + AG	CC	CC + AG	CG	CG + AG	GG	GG + AG
39	0	22*	12	1	1	56	0	10	5	5	4

* One POI patient carrying c.-9C>G together with c.352G>A (rs142156356), without c.308A>G, was included in the CG (without AG) cell. POI: Premature ovarian insufficiency

between a high ovarian response and carriage of the *BMP15* c.-9G allele. Taken together, these studies suggest that the *BMP15* c.-9G allele is associated with an increased ovarian response to stimulation, perhaps by increasing the number of primary follicles at the early stages of folliculogenesis[18].

Although functional and association studies support a potential link between the *BMP15* promoter variant c.-9C>G and reproductive phenotypes, the published evidence remains inconsistent across populations. Peluso et al.[19] analyzed 186 infertile Brazilian women undergoing their first assisted reproduction cycle and reported higher serum AMH levels among women homozygous for c.-9C>G; however, they found no significant association with ovarian stimulation parameters or assisted reproduction outcomes. Mehdizadeh et al.[20] screened *BMP15* exon 1 in 70 Iranian women with polycystic ovary syndrome and detected c.-9C>G in 31.4% of patients (28.6% heterozygous and 2.9% homozygous), suggesting a possible contributory role in disease susceptibility rather than a primary causal effect. In contrast, several case-control studies in POI reported no significant association between c.-9C>G and POI risk, including cohorts from Brazil (74 women with POI and 88 controls)[21] and the Chinese Hui population (63 women with POI and 58 controls)[22]; similarly, no significant difference for *BMP15* rs3810682 was observed in a Korean recurrent implantation failure cohort (133 patients and 317 controls)[23]. In a single-case report of POI coexisting with blepharophimosis-ptosis-epicanthus inversus syndrome, Settas et al.[24] identified a *de novo FOXL2* mutation alongside *BMP15* variants and did not consider c.-9C>G to be causally related to the POI phenotype in that patient.

Study Limitations

An important limitation of this study is incomplete sequencing of *FOXL2* in eight patients. Although *FOXL2* sequencing was successfully completed for all three fragments in 67 of the 75 patients, only the first two fragments could be analyzed in the remaining eight patients because of technical difficulties. Therefore, rare *FOXL2* variants located in the unanalyzed region cannot be excluded from this subset. This limitation is important for the interpretation of our negative *FOXL2* findings, which should therefore be interpreted with caution, particularly in these partially analyzed cases.

A significant limitation of this study is the deviation from the Hardy-Weinberg equilibrium observed for the *BMP15* c.-9C>G variant in the control group. This pattern, characterized by a deficit of heterozygotes and an excess of homozygotes, may be attributable to sampling variation related to the modest sample size, subtle population stratification, or, less likely, technical/genotyping issues. Although genotyping was performed by bidirectional Sanger sequencing, which reduces the likelihood of systematic misclassification, systematic misclassification, this possibility cannot be completely excluded. Because deviation from Hardy-Weinberg equilibrium may bias estimates of genotype-specific associations, particularly for the CG genotype, the observed association between *BMP15* c.-9C>G and POI should be interpreted with caution. Therefore, our findings should be considered preliminary and require validation in larger, independent, well-matched cohorts. Because *BMP15* c.-9C>G is classified as a benign variant under ACMG criteria, the observed case-control association should be interpreted not as evidence of pathogenicity but as a hypothesis-generating finding.

Formal haplotype analysis of *BMP15* variants was not performed. Therefore, the possible combined contribution of c.-9C>G and c.308A>G to POI susceptibility could not be fully assessed in this cohort.

Conclusion

In our study, no pathogenic variant associated with POI was detected in *BMP15* or in the analyzed regions of *FOXL2*. Because *FOXL2* sequencing was incomplete in eight patients, rare variants in the unanalyzed region cannot be entirely excluded. Although the *BMP15* c.-9C>G variant was relatively frequent in our Turkish POI cohort and showed a genotype-based association in the case-control comparison, it is classified as benign according to ACMG criteria and should not be interpreted as a pathogenic cause of POI. Rather, it may represent a common variant associated with disease susceptibility in this cohort. These findings should be interpreted cautiously and confirmed in larger, unrelated, well-matched populations, ideally supported by functional and haplotype-based analyses.

Ethics

Ethics Committee Approval: The Ankara University Clinical Research Ethics Committee approved the study (approval number: 05-187-13, date: 25.03.2013).

Informed Consent: Written informed consent was obtained from all participants.

Footnotes

Authorship Contributions

Concept: M.B.M., H.G.K., Design: M.B.M., H.G.K., Data Collection or Processing: M.B.M., V.T., Ş.E.Ç., Y.Ü., A.B., C.S.A., H.I.R., H.G.K., Analysis or Interpretation: M.B.M., V.T., A.B., H.I.R., H.G.K., Literature Search: M.B.M., H.I.R., H.G.K., Writing: M.B.M., H.G.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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Follicular fluid cytokine and homocysteine profiles in poor ovarian responders with and without sonographic endometrioma: A comparative study

Sonografik endometrioması olan ve olmayan düşük over rezervli kadınlarda foliküler sıvı sitokin ve homosistein profilleri: Karşılaştırmalı çalışma

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Abstract

Objective: To compare follicular fluid (FF) cytokine and homocysteine profiles in women with poor ovarian response (POR) undergoing in vitro fertilization (IVF), with and without sonographic endometrioma, and to explore potential inflammatory alterations associated with endometrioma in this population.

Materials and Methods: This prospective comparative study was conducted among 60 women diagnosed with POR who were undergoing IVF treatment. Participants were divided into two groups according to the presence of sonographic endometrioma: Group I included women without sonographic endometrioma (n=30) and Group II included women with sonographic endometrioma (n=30). FF samples were collected during oocyte retrieval and analyzed for inflammatory biomarkers. Concentrations of interleukin-1β (IL-1β), IL-6, IL-8, IL-10, IL-12p70, IL-17A, IL-18, IL-23, IL-33, interferon-α2 (IFN-α2), IFN-γ, tumor necrosis factor-α (TNF-α), monocyte chemoattractant protein-1 (MCP-1), and homocysteine were measured using LEGENDplex multiplex assays and flow cytometry. Cytokine and homocysteine levels were compared between groups.

Results: Most inflammatory cytokines, including IL-1β, IL-6, IL-8, IFN-γ, and MCP-1, showed lower levels in women with sonographic endometrioma compared with women without sonographic endometrioma. In contrast, TNF-α and IL-33 levels tended to be higher in the endometrioma group. Homocysteine levels were also lower in women with sonographic endometriomas. However, none of the observed differences reached statistical significance. Overall, the findings suggested distinct, albeit non-significant, inflammatory trends in the FF microenvironment of women with POR and sonographic endometrioma.

Conclusion: Women with POR and sonographic endometrioma showed altered trends in FF inflammatory-marker profiles compared with women without sonographic endometrioma; however, these differences were not statistically significant. Since the absence of sonographic endometrioma does not exclude endometriosis, the findings should be interpreted cautiously. Larger prospective studies that include IVF and assess embryological and reproductive outcomes are required to clarify the clinical significance of FF biomarkers in women with POR and endometrioma.

Keywords: Endometrioma, poor ovarian response, follicular fluid, cytokines, homocysteine, IVF

PRECIS: Women with poor ovarian response and sonographic endometrioma showed directional but non-significant differences in selected follicular fluid cytokines. The findings are exploratory and require validation using in vitro fertilization outcomes.

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Öz

Amaç: Bu çalışmanın amacı, in vitro fertilizasyon (IVF) tedavisi gören düşük over rezerv (DOR) tanılı kadınlarda, sonografik endometrioma varlığına göre follikül sıvısı (FS) sitokin ve homosistein profillerini karşılaştırmak ve endometrioma ile ilişkili olası enflamatuvar değişiklikleri araştırmaktır.

Gereç ve Yöntemler: Bu prospektif karşılaştırmalı çalışmaya IVF tedavisi gören ve DOR tanısı bulunan toplam 60 kadın dahil edildi. Katılımcılar sonografik endometrioma varlığına göre iki gruba ayrıldı: Grup I, sonografik endometrioması olmayan kadınlardan (n=30); Grup II ise sonografik endometrioması bulunan kadınlardan (n=30) oluştu. FS örnekleri oosit toplama işlemi sırasında elde edildi ve inflamatuvar biyobelirteçler açısından analiz edildi. İnterlökin-1β (IL-1β), IL-6, IL-8, IL-10, IL-12p70, IL-17A, IL-18, IL-23, IL-33, interferon-α2 (IFN-α2), IFN-γ, tümör nekroz faktörü-α (TNF-α), monosit kemoatraktan protein-1 (MCP-1) ve homosistein düzeyleri LEGENDplex multipleks analiz yöntemi ve akım sitometrisi kullanılarak ölçüldü. Sitokin ve homosistein düzeyleri gruplar arasında karşılaştırıldı.

Bulgular: IL-1β, IL-6, IL-8, IFN-γ ve MCP-1 dahil olmak üzere çoğu enflamatuvar sitokin düzeyi, sonografik endometrioması bulunan kadınlarda, sonografik endometrioması olmayan kadınlara kıyasla daha düşük bulundu. Buna karşılık TNF-α ve IL-33 düzeyleri endometrioma grubunda daha yüksek eğilim gösterdi. Homosistein düzeyleri de sonografik endometrioması bulunan kadınlarda daha düşük saptandı. Ancak gözlenen farklılıkların hiçbiri istatistiksel anlamlılığa ulaşmadı. Genel olarak bulgular, DOR ve sonografik endometrioması bulunan kadınların FS mikroçevresinde belirgin ancak istatistiksel olarak anlamlı olmayan inflamatuvar eğilimler olduğunu düşündürdü.

Sonuç: DOR ve sonografik endometrioması bulunan kadınlarda, sonografik endometrioması olmayan kadınlara kıyasla FS enflamatuvar belirteç profillerinde değişmiş eğilimler gözlenmiş, ancak istatistiksel olarak anlamlı farklılık saptanmamıştır. Sonografik endometrioma yokluğunun endometriozisi dışlamadığı göz önünde bulundurularak bulgular dikkatli yorumlanmalıdır. IVF, embriyolojik ve üreme sonuçlarını içeren daha geniş prospektif çalışmalara, DOR ve endometriomalı kadınlarda FS biyobelirteçlerinin klinik önemini daha iyi açıklığa kavuşturmak için ihtiyaç vardır.

Anahtar Kelimeler: Endometrioma, düşük over rezervi, foliküler sıvı, sitokinler, homosistein, IVF

Introduction

Endometriosis is a chronic inflammatory condition characterized by the presence of endometrial-like tissue outside the uterus, affecting approximately 10-15% of women of reproductive age and up to 40% of infertile women[1,2]. Despite significant advances in diagnostic imaging and surgical treatment, the pathophysiology of endometriosis remains complex and multifactorial, involving hormonal, immunological, and genetic factors[3-5].

Several immunological abnormalities have been implicated in the development and progression of endometriosis, including altered macrophage activity, cytokine imbalance, and impaired natural killer cell function[6-8]. The local peritoneal and follicular environment in affected individuals is often enriched with pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), IL-8, and monocyte chemoattractant protein-1 (MCP-1), which may contribute to abnormal folliculogenesis, impaired oocyte quality, and reduced implantation potential[9-13].

The follicular fluid (FF) is a key microenvironment supporting oocyte development and maturation. It contains a wide array of soluble factors—cytokines, growth factors, metabolites—that mediate paracrine signaling and reflect both systemic and local ovarian conditions[14]. In women with endometriosis, the FF may exhibit a disrupted immunological milieu, potentially compromising oocyte competence and embryo development during in vitro fertilization (IVF)[15].

Poor ovarian response (POR) to controlled ovarian stimulation, defined by the Bologna criteria or more recently the POSEIDON classification, presents an additional challenge in assisted reproductive technologies[16,17]. Women with POR often show altered inflammatory and metabolic signaling in FF, with higher levels of oxidative stress markers and reduced concentrations of growth-promoting cytokines[18]. The coexistence of POR and endometriosis may further exacerbate this unfavorable follicular environment, although few studies have examined this specific subgroup in detail.

Recent studies suggest that evaluating FF cytokines and metabolic markers such as homocysteine may offer insight into the pathophysiology of oocyte competence, particularly in complex infertility cases[19,20]. Homocysteine, a sulfur-containing amino acid involved in methylation pathways, has been linked to impaired follicular angiogenesis, mitochondrial dysfunction, and increased oxidative stress, all of which may affect oocyte and embryo quality[21].

The present study aims to compare the cytokine and homocysteine profiles in FF from women with POR, both with and without sonographically confirmed endometrioma. By focusing on this underexplored intersection, we hope to identify immunological or metabolic differences that may contribute to reduced fertility outcomes and may help generate hypotheses for individualized strategies in IVF.

Materials and Methods

Study Design and Participants

This prospective comparative study was conducted at the Assisted Reproductive Technologies Unit of Acıbadem Maslak Hospital, İstanbul, Türkiye, as an exploratory biomarker analysis in women with POR comparing patients with and without sonographic endometrioma. No single primary biomarker was predefined; a predefined inflammatory marker panel and homocysteine levels were evaluated to generate hypotheses. A total of 60 infertile women diagnosed with POR were recruited and divided into two groups: those

with a sonographically confirmed diagnosis of endometrioma (n=30) and those without (n=30) (Figure 1). This was a pilot exploratory study. No a priori sample size calculation was performed. The target sample size of 30 per group was determined based on feasibility within the study period. All participants had a history of infertility of at least one year and at least one functional ovary.

Inclusion criteria followed the POSEIDON classification [Groups 3 and 4: antral follicle count (AFC) <5 and anti-Müllerian hormone (AMH) <1.2 ng/mL, stratified by age] [17] . Exclusion criteria included severe male factor infertility (azoospermia, cryptozoospermia), congenital or acquired uterine anomalies, polycystic ovary syndrome, recurrent pregnancy loss, and recurrent implantation failure.

Endometriosis Characterization: In the endometrioma group, endometriomas were identified using standard transvaginal ultrasound criteria (thick-walled, homogeneous, low-level internal echoes). Where available, endometrioma size (maximum diameter, mm) and laterality (unilateral/bilateral) were abstracted from clinical records. Deep infiltrating endometriosis was not systematically assessed. Prior endometriosis surgery and medical/hormonal treatments were recorded where available. The duration of infertility (months) was recorded at enrollment. All assessments were performed by experienced clinicians at the beginning of the ovarian stimulation cycle.

Ovarian Stimulation Protocol and Oocyte Retrieval

All participants underwent a controlled ovarian hyperstimulation protocol. Stimulation was initiated on days 2-4 of the menstrual cycle using recombinant follicle-stimulating hormone (FSH; 150-300 IU daily), with or without the addition of human menopausal gonadotropin, based on clinical judgment. Serial transvaginal ultrasonography and serum estradiol (E2) measurements guided dose adjustments. Final oocyte maturation was triggered with 6500 IU human chorionic gonadotropin in combination with 0.2 mg gonadotropin-releasing hormone agonist when at least one follicle reached ≥18 mm or three follicles were ≥17 mm in diameter. Oocyte retrieval was performed 36 hours post-trigger under sedation.

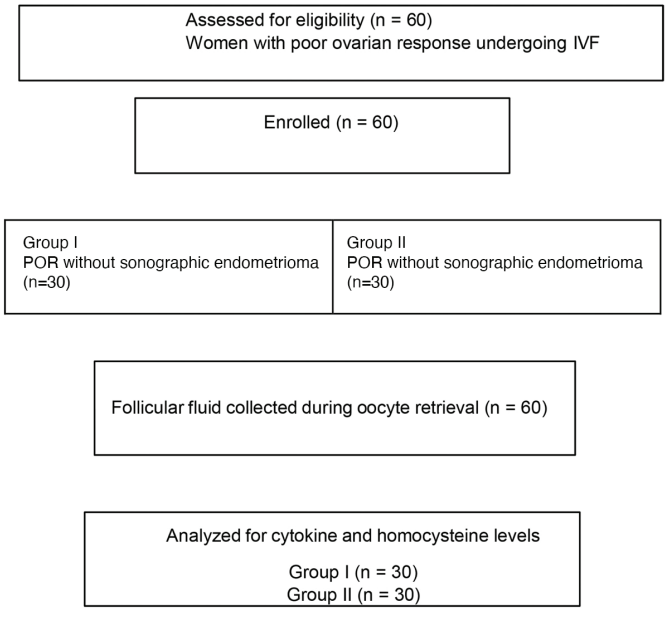

Figure 1. The flowchart of the study

IVF: In vitro fertilization, POR: Poor ovarian response

FF Collection and Analysis

Immediately following oocyte retrieval, FF was aspirated from the first accessible ≥18 mm follicle prior to any flushing. When multiple mature follicles were present, only the first aspirated follicle was used; follicles were not pooled. Tubes were inspected immediately; samples with visible blood contamination (reddish discoloration, hemolysis) were discarded. Cumulus-oocyte complexes were separated, and the remaining FF was centrifuged at 450 g for 5 minutes at room temperature. The supernatant was aliquoted and stored at -20 °C within 60 minutes of retrieval; a single freeze-thaw cycle was permitted for analysis, and no aliquot underwent more than one cycle. Assays were performed at the Acıbadem Labmed Clinical Laboratory using the LEGENDplex Human Inflammation Panel 1 (BioLegend, Germany), a bead-based multiplex flow cytometry assay, on a BD FACSCanto II flow cytometer. Standard curves and controls were run on each plate. Analysts and laboratory personnel were blinded to clinical data and group assignment. Concentrations of IL-1β, IL-6, IL-8, IL-10, IL-12p70, IL-17A, IL-18, IL-23, IL-33, IFN-α2, IFN-γ, TNF-α, MCP-1, and homocysteine were measured and analyzed with LEGENDplex Data Analysis Software.

Ethical Approval

The study protocol was approved by the Institutional Review Board and the Ethics Committee of Acıbadem University (approval number: 2023-03/59, date: 24.02.2023). Written informed consent was obtained from all participants prior to enrollment. This study was conducted in accordance with the principles of the "Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Participants".

Statistical Analysis

Cytokine and homocysteine distributions were assessed using the Shapiro-Wilk test and visual inspection (histograms and Q-Q plots). Given the typical right skewness of the data, we also analyzed log10-transformed values. Continuous variables are presented as mean±SD and, where appropriate, median interquartile range (IQR). Between-group comparisons used independent-samples t-tests when assumptions were met, and Mann-Whitney U tests otherwise. Potential outliers were screened visually using box plots and the IQR rule;

sensitivity checks did not change the inference. Alongside p-values, we interpret the direction of effects using two-sided 95% confidence intervals where applicable. Given multiple biomarkers, analyses were treated as exploratory; we did not claim statistical significance after adjustment for multiplicity, and we interpreted findings in light of the increased risk of false positives.

Results

A total of 60 women with POR undergoing IVF were included in the study (Figure 1). The mean age of patients in the POR with sonographic endometrioma group was slightly higher than the POR without sonographic endometrioma group (37.9±5.8 vs. 35.1±5.1 years, respectively; p=0.06), although the difference was not statistically significant. Partner age, body mass index, and baseline ovarian reserve markers, including FSH, AMH, and AFC were comparable between groups. A higher number of previous IVF cycles was observed among patients with POR with sonographic endometrioma, but again, this did not reach statistical significance (3.0±3.1 vs. 1.8±2.1; p=0.07). Demographic and baseline characteristics are summarized in Table 1.

Regarding the FF analysis, homocysteine levels were lower in the POR with sonographic endometrioma group compared to the POR without sonographic endometrioma (1.65±1.53 vs. 4.85±4.14 µmol/L), although the difference was not statistically significant (p=0.277).

Among the 13 inflammatory markers analyzed, most cytokine levels—including IL-1β, IFN-α2, IFN-γ, MCP-1, IL-6, IL-8, IL-10, IL-12p70, IL-17A, IL-18, and IL-23—were lower in the POR group with sonographic endometrioma than in women without sonographic endometrioma. None of these differences reached statistical significance (p>0.05 for all comparisons). Interestingly, two markers—TNF-α and IL-33—were slightly elevated in the POR with sonographic endometrioma group, though again without statistical significance (TNF-α: 10.19±17.38 vs. 6.54±8.72 pg/mL, p=0.761; IL-33: 47.43±72.82 vs. 40.97±61.62 pg/mL, p=0.912).

Across all 14 biomarkers, no between-group differences reached conventional statistical significance. Given right-skewed distributions and multiple comparisons, we conducted complementary nonparametric tests and log10-transformed analyses; both approaches yielded the same inference. Accordingly, we interpret all observed patterns as directional and exploratory rather than definitive. Consistent with this approach, we did not claim statistical significance for any isolated trend after accounting for multiplicity. Despite numerically large mean differences for some biomarkers (e.g., MCP-1, IL-6, IL-18, and homocysteine), wide variances, skewed distributions, and the modest sample size likely reduced statistical power, yielding non-significant p-values; non-parametric and log-transformed analyses led to the same inference.

A full comparison of cytokine and homocysteine levels in FF between the two groups is presented in Table 2.

Although none of the measured biomarkers showed statistically significant differences, the trend toward elevated TNF-α and IL-33 in the POR with sonographic endometrioma group may be consistent with localized inflammatory signaling; however, given the non-significant and imprecise estimates, these observations are exploratory. Conversely, the lower levels of most other cytokines, including IL-6 and MCP-1, suggest a potentially suppressed or dysregulated immune response in the follicular environment of these patients.

Discussion

This exploratory study compared FF cytokines and homocysteine between women with POR who had sonographic endometrioma and those who did not. Across 14 biomarkers, no between-group differences reached conventional statistical significance. Observed patterns were directional: TNF-α and IL-33 tended to be higher, while several cytokines tended to be lower in the endometrioma group, and should be regarded as hypothesis-generating.

TNF-α and IL-33 trends align with proposed inflammatory mechanisms in endometriosis; however, the estimates

Table 1. Socio-demographic parameters (values are mean ± SD unless otherwise specified)

	POR without sonographic endometrioma (n=30)	POR with sonographic endometrioma (n=30)	p-value
Age (years)	35.1±5.1	37.9±5.8	0.06
Partner's age (years)	38.3±6.3	38.1±6.4	0.90
BMI (kg/m^2)	24.7±5.3	25.6±4.8	0.50
FSH (mIU/mL)	17.7±14.3	14.6±9.9	0.32
AMH (ng/mL)	0.47±0.27	0.35±0.31	0.12
AFC (n)	3.1±1.5	2.9±1.5	0.66
Number of previous IVF trials (n)	1.8±2.1	3.0±3.1	0.07

Values are mean ± SD. Units: years (age, partner's age); kg/m^2 (BMI); mIU/mL (FSH); ng/mL (AMH); count (AFC, previous IVF trials)
POR: Poor ovarian response, BMI: Body mass index, FSH: Follicle-stimulating hormone, AMH: Anti-Müllerian hormone, AFC: Antral follicle count, SD: Standard deviation, IVF: In vitro fertilization

Table 2. Comparison of follicular fluid cytokine and homocysteine levels between groups

	POR without sonographic endometrioma (n=30) mean ± SD	POR with sonographic endometrioma (n=30) mean ± SD	p-value
Homocysteine (µmol/L)	4.85±4.14	1.65±1.53	0.277
IL-1β (pg/mL)	34.70±32.12	4.37±4.59	0.181
IFN-α2 (pg/mL)	1.44±1.16	0.72±1.25	0.509
IFN-γ (pg/mL)	34.58±31.64	11.10±12.45	0.298
TNF-α (pg/mL)	6.54±8.72	10.19±17.38	0.761
MCP-1 (pg/mL)	895.87±625.14	195.37±193.56	0.137
IL-6 (pg/mL)	26.86±7.54	8.57±13.91	0.116
IL-8 (pg/mL)	1477.26±694.62	756.85±1310.90	0.448
IL-10 (pg/mL)	4.67±3.79	1.34±2.32	0.264
IL-12p70 (pg/mL)	1.10±0.69	0.23±0.03	0.095
IL-17A (pg/mL)	3.41±5.36	0.21±0.22	0.360
IL-18 (pg/mL)	326.61±141.34	94.07±124.85	0.100
IL-23 (pg/mL)	1.80±2.11	0.58±0.00	0.374
IL-33 (pg/mL)	40.97±61.62	47.43±72.82	0.912

Cytokine symbols are standardized as IL-1β, IFN-γ, TNF-α, and MCP-1. Values are mean ± SD. Units are pg/mL for cytokines and µmol/L for homocysteine. Analyses were treated as exploratory given multiple biomarker comparisons. Complementary non-parametric tests and log10-transformed analyses yielded consistent inferences
POR: Poor ovarian response, IL: Interleukin, IFN: Interferon, TNF: Tumor necrosis factor, MCP: Monocyte chemoattractant protein, SD: Standard deviation

were imprecise and not statistically significant; therefore, they should not be interpreted as evidence of a distinct inflammatory profile in POR with endometrioma.

TNF-α has been widely implicated in the inflammatory cascade associated with endometriosis and has been shown to impair oocyte maturation and granulosa cell function[8,12,19]. IL-33, a member of the IL-1 cytokine family, has gained increasing attention for its role in tissue remodeling and immune activation in chronic inflammatory diseases[20]. Our findings align with these observations and suggest a potentially heightened inflammatory state within the follicles of women with both POR and endometriomas.

In contrast, levels of IL-6, IL-1β, IL-8, and MCP-1 were generally lower in the endometrioma group. This counterintuitive finding may indicate an immunological adaptation or exhaustion resulting from chronic local inflammation[20]. Previous studies have suggested that the follicular immune microenvironment in endometriosis may vary depending on disease stage, ovarian reserve, or previous treatment history, all of which could influence cytokine expression profiles[11,18].

Importantly, none of the between-group differences reached conventional statistical significance, and the estimates were imprecise, with wide confidence intervals. Given skewed distributions and multiple biomarker comparisons, these analyses are best considered exploratory. Accordingly, we refrain from inferring a distinct inflammatory profile and instead interpret the observed patterns as directional signals requiring confirmation in larger, outcome-linked cohorts. We note that several large numerical differences were accompanied by wide standard deviations and skewness, which, together with the modest sample size, limit statistical power. The concordance of non-parametric and log-transformed analyses supports the inference that these are directional, non-significant trends.

FF homocysteine levels were also lower in the POR with endometrioma group. Elevated homocysteine is typically considered a negative factor in IVF due to its association with oxidative stress, mitochondrial dysfunction, and impaired methylation capacity[21,22]. The reduced levels in our cohort may reflect an altered metabolic phenotype associated with endometriosis or differences in folate metabolism, although the clinical significance remains unclear.

In addition to cytokine imbalance, alterations in FF composition—including amino acids, lipids, and oxidative stress markers—have been shown to significantly affect oocyte competence and embryo development[14]. Recent approaches using metabolomics support the notion that FF is a dynamic, integrative reflection of both local ovarian physiology and systemic health, making it a promising focus for personalized IVF strategies[14].

Our results are partially consistent with those of Yland et al.[22], who reported differential cytokine patterns in the FF of endometriosis patients, including increased IL-15 and IL-13 and decreased IFN-γ and TNF-α. However, discrepancies may be due to population differences, as their study included

women with normal ovarian reserve, whereas our cohort consisted exclusively of POR patients. The coexistence of endometrioma and poor ovarian reserve likely contributes to a unique immunometabolic profile that warrants further investigation.

Importantly, none of the between-group differences reached conventional statistical significance, and estimates were imprecise with wide confidence intervals. Given skewed distributions and multiple biomarker comparisons, these analyses are best considered exploratory. Accordingly, we refrain from inferring a distinct inflammatory profile and instead interpret the observed patterns as directional signals that require confirmation in larger, outcome-linked cohorts. We note that several numerically large differences were accompanied by wide standard deviations and skewness, which, together with the modest sample size, limit statistical power. The concordance of non-parametric and log-transformed analyses supports the inference that these are directional but non-significant trends.

We did not collect embryological or clinical IVF outcomes (e.g., MII rate, fertilization, blastulation, clinical pregnancy), which precludes correlating FF markers with treatment success in this cohort.

Potential confounders merit consideration. The endometrioma group was slightly older and had undergone more prior IVF cycles, which may influence ovarian response and FF composition. Protocol-related factors (e.g., total gonadotropin dose, trigger-day E2, and follicle counts) can also modulate biomarker levels. In this exploratory dataset, robust multivariable adjustment was not feasible; therefore, we interpret directional patterns with these potential confounders in mind and recommend adjusted analyses in larger cohorts.

Taken together, these non-significant directional findings warrant confirmation in larger, well-phenotyped cohorts that incorporate standardized IVF and pregnancy outcomes and, where possible, detailed endometriosis staging.

Study Limitations

This study has several limitations. First, group allocation relied on the presence of a sonographic endometrioma; the absence of endometrioma does not exclude endometriosis, and occult disease may be present in controls. We did not systematically stage endometriosis or quantify lesion burden beyond the presence of a sonographic endometrioma. Data on endometrioma size, laterality, and prior surgical or medical therapy were incomplete, which may have introduced heterogeneity.

Second, the sample size is modest, increasing imprecision and the risk of type II error, particularly across multiple biomarker comparisons. The modest sample size, in the absence of an a priori power calculation, likely limited our ability to detect small-to-moderate effects.

Third, cytokine distributions are typically skewed. Although we used complementary non-parametric and log-transformed analyses, residual distributional issues cannot be fully excluded.

Moreover, multiple biomarker comparisons increase the risk of false-positive findings; therefore, we treated the analyses as exploratory and claims of statistical significance without adjustment for multiplicity. Residual pre-analytical variability (e.g., subtle blood contamination, storage time, and freeze-thaw effects)cannot be fully excluded despite standardized handling. In addition, residual confounding by age, prior IVF exposure, and stimulation variables cannot be excluded.

Fourth, IVF outcome parameters (e.g., MII rate, fertilization, blastulation, clinical pregnancy) were not collected or reported, which limits clinical interpretability of the findings. Future larger studies should integrate standardized assay performance metrics, correlate FF markers with oocyte, embryo, and pregnancy outcomes, and, where possible, include surgical staging or lesion burden to refine phenotype definitions.

Despite these limitations, our findings underscore the importance of considering both immunological and metabolic markers when evaluating the follicular microenvironment in complex infertility cases. Future research with larger cohorts and functional assays may help elucidate the mechanisms linking endometriosis, ovarian reserve, and follicular health.

Conclusion

In this exploratory study of women with POR undergoing IVF, FF cytokine and homocysteine levels did not differ significantly between patients with and without sonographic endometrioma. Non-significant trends toward higher TNF-α and IL-33 levels and lower homocysteine levels in the endometrioma group should be considered hypothesis-generating. Confirmation in larger, well-phenotyped cohorts incorporating standardized embryological and pregnancy outcomes is needed before clinical inferences can be drawn.

Ethics

Ethics Committee Approval: The study protocol was approved by the Institutional Review Board and the Ethics Committee of Acıbadem University (approval number: 2023-03/59, date: 24.02.2023).

Informed Consent: Written informed consent was obtained from all participants prior to enrollment.

Footnotes

Authorship Contributions

Surgical and Medical Practices: B.E.Ş., Concept: B.E.Ş., E.T., N.Y.S., Y.Ç., B.T., Design: B.E.Ş., Y.Ç., B.T., Data Collection or Processing: B.E.Ş., E.T., İ.Ö.A., N.Y.S., Analysis or Interpretation: B.E.Ş., E.T., N.Y.S., Y.Ç., Literature Search: B.E.Ş., İ.Ö.A., Y.Ç., Writing: B.E.Ş., İ.Ö.A., Y.Ç., B.T.

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Comparative outcomes of abdominal, laparoscopic, and vaginal sacral colpopexy: A national analysis of apical suspension procedures (2014-2022)

Abdominal, laparoskopik ve vajinal sakral kolpopeksinin karşılaştırmalı sonuçları: Apikal süspansiyon prosedürlerinin ulusal analizi (2014-2022)

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Abstract

Objective: Sacral colpopexy is a well-established procedure for apical suspension, but the relative outcomes of abdominal, laparoscopic, and vaginal approaches remain debated. This study compared perioperative outcomes across these surgical routes using a national database and evaluated trends in robotic assistance.

Materials and Methods: We analyzed sacral colpopexy cases from the American College of Surgeons National Surgical Quality Improvement Program between 2014 and 2022. Patient demographics, complication rates, and surgical outcomes were compared among abdominal, laparoscopic, and vaginal procedures. Relative risks (RR) were adjusted for confounders. The utilization of robotic systems in laparoscopic procedures was examined.

Results: Among 61,524 cases, 3,497 (5.7%) were abdominal, 22,752 (37.0%) laparoscopic, and 35,275 (57.3%) vaginal. Vaginal procedures were more common in older patients, while laparoscopic approaches predominated among younger and higher-body mass index patients. Non-Hispanic White patients most often underwent vaginal surgery (60.5%), whereas African American patients most frequently underwent laparoscopic procedures (6.4%). Laparoscopic sacral colpopexy had the lowest complication rate (7.8%), with fewer superficial surgical site infections, transfusions, readmissions, and reoperations. Adjusted analysis showed a lower risk with laparoscopic surgery compared with abdominal surgery [RR: 0.75, 95% confidence interval (CI): 0.67-0.85]. Vaginal surgery showed no significant difference compared with abdominal surgery (RR: 1.09, 95% CI: 0.97-1.21). Robotic assistance increased markedly, comprising 73.5% of laparoscopic procedures in 2022.

Conclusion: Laparoscopic sacral colpopexy, particularly with robotic assistance, is associated with fewer perioperative complications compared with abdominal and vaginal approaches. These findings support minimally invasive techniques as preferred approaches for apical suspension, and further research is needed on long-term outcomes and cost-effectiveness.

Keywords: Sacral colpopexy, laparoscopic surgery, robotic surgery, apical suspension, pelvic organ prolapse, surgical outcomes

PRECIS: In an analysis of 61,524 national cases, we found that laparoscopic sacral colpopexy—especially robotic-assisted—had the lowest perioperative complication rate compared with abdominal and vaginal approaches.

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Öz

Amaç: Sakral kolpopeksi, apikal süspansiyon için iyi bilinen bir prosedürdür, ancak abdominal, laparoskopik ve vajinal yaklaşımların göreceli sonuçları hala tartışılmaktadır. Bu çalışma, ulusal bir veri tabanı kullanarak bu cerrahi yollar arasında perioperatif sonuçları karşılaştırdı ve robotik yardımdaki eğilimleri değerlendirdi.

Gereç ve Yöntemler: 2014 ve 2022 yılları arasında Amerikan Cerrahlar Koleji Ulusal Cerrahi Kalite İyileştirme Programı'ndan sakral kolpopeksi olgularını analiz ettik. Hasta demografik özellikleri, komplikasyon oranları ve cerrahi sonuçlar abdominal, laparoskopik ve vajinal prosedürler arasında karşılaştırıldı. Göreceli riskler (RR) karıştırıcı faktörlere göre ayarlandı. Laparoskopik prosedürlerde robotik sistemlerin kullanımı incelendi.

Bulgular: 61.524 olgu arasında 3.497'si (%5,7) abdominal, 22.752'si (%37,0) laparoskopik ve 35.275'i (%57,3) vajinaldi. Vajinal işlemler daha yaşlı hastalarda daha yaygınken, laparoskopik yaklaşımlar daha genç ve yüksek vücut kitle indeksli hastalarda baskınlık gösterdi. Hispanik olmayan beyaz hastalar en sık vajinal cerrahi %60,5 geçirirken, Afrika kökenli Amerikalı hastalar en sık laparoskopik işlemlere %6,4 tabi tutuldu. Laparoskopik sakral kolpopeksi en düşük komplikasyon oranına (%7,8) sahipti ve daha az yüzeysel cerrahi bölge enfeksiyonu, kan transfüzyonu, yeniden hastaneye yatış ve yeniden ameliyat gerektirdi. Ayarlanmış analiz, laparoskopik cerrahinin karın cerrahisine kıyasla daha düşük risk taşıdığını gösterdi [RR: 0,75, %95 güven aralığı (GA): 0,67-0,85]. Vajinal cerrahi, karın cerrahisine kıyasla anlamlı bir fark göstermedi (RR: 1,09, %95 GA: 0,97-1,21). Robotik destek belirgin şekilde artarak 2022 yılında laparoskopik işlemlerin %73,5'ini oluşturmuştur.

Sonuç: Laparoskopik sakral kolpopeksi, özellikle robotik destekle birlikte, abdominal ve vajinal yaklaşımlara kıyasla daha az perioperatif komplikasyonla ilişkilidir. Bu bulgular, apikal süspansiyon için tercih edilen yaklaşımlar olarak minimal invaziv teknikleri desteklemektedir ve uzun vadeli sonuçlar ve maliyet etkinliği konusunda daha fazla araştırmaya ihtiyaç vardır.

Anahtar Kelimeler: Sakral kolpopeksi, laparoskopik cerrahi, robotik cerrahi, apikal süspansiyon, pelvik organ prolapsusu, cerrahi sonuçlar

Introduction

Pelvic organ prolapse (POP) is a common condition that significantly impairs quality of life by causing pelvic pressure, urinary incontinence, bowel dysfunction, and sexual difficulties. Apical suspension surgery is central to the management of advanced POP, as restoration of the vaginal apex is critical for durable pelvic support and prevention of recurrent prolapse. Sacral colpopexy, most commonly performed using mesh, is widely considered the gold-standard procedure for apical suspension because of its robust long-term outcomes. Sacral colpopexy can be performed through abdominal, laparoscopic, or vaginal approaches. Abdominal sacrocolpopexy, historically the standard, offers durable anatomical correction, but is associated with longer recovery times and higher perioperative morbidity. Minimally invasive approaches, including laparoscopic and robotic-assisted sacral colpopexy, have been increasingly adopted given their advantages of reduced blood loss, shorter hospital stays, and faster return to normal activities. The introduction of robotic technology has further advanced minimally invasive techniques by providing enhanced visualization, improved dexterity, and ergonomic benefits. Nevertheless, concerns remain regarding costs, learning curves, and long-term outcomes, particularly in relation to mesh-related complications. Vaginal approaches, such as uterosacral ligament suspension and sacrospinous ligament fixation, remain important alternatives, especially for older patients or those unfit for abdominal surgery. While these techniques avoid abdominal entry and can be performed under regional anesthesia, they may be associated with higher recurrence rates and different complication profiles compared to abdominal and laparoscopic approaches. Despite the variety of surgical options, contemporary comparative data on demographic trends, complication risks, and outcomes by surgical route remain limited. Furthermore, the extent to which robotic assistance has transformed laparoscopic sacral colpopexy in routine clinical practice is not fully established. The objective of this study was to compare patient characteristics and perioperative outcomes among patients undergoing abdominal, laparoscopic, and vaginal sacral colpopexy using a large national surgical database and to evaluate recent trends in robotic utilization.

Materials and Methods

Study Objectives

The objective of this study was to analyze demographic trends, perioperative complications, and the impact of robotic assistance on sacral colpopexy procedures performed between 2014 and 2022. Comparisons were made among abdominal, laparoscopic, and vaginal approaches to identify the safest and most effective strategies for apical suspension in women with POP.

Data Source and Study Population

Data were obtained from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database for the years 2014-2022. Patients who underwent sacral colpopexy were identified using the following Current Procedural Terminology (CPT) codes:

- Abdominal open: 57270, 57280
- Laparoscopic: 57425
- Vaginal: 57282, 57283, 57268

Exclusion criteria included patients without colpopexy (n=4.890.409), patients with more than one route of colpopexy (n=496), patients with a cancer diagnosis (n=1.144), and patients with missing operative time (n=3). After applying exclusions, 61,524 cases were included in the final analysis. The abdominal open group was used as the reference category.

Outcomes

The primary outcome was composite perioperative morbidity, defined as the occurrence of one or more of the following complications within 30 days:

- Surgical site infection (superficial, deep, organ/space, or wound dehiscence)
- Pulmonary complications (pneumonia, unplanned intubation, prolonged ventilation)
- Cardiac complications (cardiac arrest requiring cardiopulmonary resuscitation, myocardial infarction)
- Renal complications (acute renal insufficiency, progressive renal failure)
- Sepsis (sepsis or septic shock)
- Thromboembolic events (pulmonary embolism, deep vein thrombosis, cerebrovascular accident/stroke with neurologic deficit)
- Urinary tract infection
- Postoperative blood transfusion
- Prolonged hospital stay (defined as >2 days)

Statistical Analysis

Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables were analyzed using the Student's t-test for normally distributed data and the Wilcoxon rank-sum test for skewed distributions. Categorical variables were compared using chi-square or Fisher's exact test, as appropriate. To assess the association between surgical route and composite morbidity, multivariable logistic regression was performed, adjusting for age, race, American Society of Anesthesiologists (ASA) classification, smoking status, and operative time. Results were expressed as adjusted odds ratios with 95% confidence intervals (CIs). A two-sided p-value <0.05 or a 95% CI not crossing 1.0 was considered statistically significant.

Ethics Approval

As this study used de-identified data from the NSQIP database, institutional review board approval and informed consent were not required.

Results

A total of 61,524 women who underwent sacral colpopexy between 2014 and 2022 were included. Of these, 3,497 (5.7%) underwent an abdominal approach, 22,752 (37.0%) underwent a laparoscopic approach, and 35,275 (57.3%) underwent a vaginal approach.

Patient Demographics

Patient demographics differed significantly across groups (Table 1). Women undergoing vaginal colpopexy were more likely to be aged ≥75 years (13.5%) than those undergoing laparoscopic (7.9%) and abdominal (10.0%) cases (p<0.001). Conversely, younger women (<45 years) were more frequently represented in the laparoscopic group (15.2%, p<0.001). Non-Hispanic White patients predominated across all approaches, although the proportion was lowest in the laparoscopic group (54.3%) compared with the abdominal (58.1%) and vaginal (60.5%) groups (p<0.001). Obesity (body mass index ≥30) was most common in the vaginal cohort (35.3%; p<0.001). Concomitant hysterectomy was most frequently performed laparoscopically (73.6%, p<0.001).

Operative Characteristics

Median operative time and length of hospitalization varied significantly by approach (Table 2). Prolonged operative time (>200 minutes) occurred most frequently in laparoscopic (38.1%) and abdominal (37.7%) cases, compared with vaginal cases (14.9%) (p<0.001). The abdominal approach was overwhelmingly inpatient (81.2%), whereas the laparoscopic (81.3%) and vaginal (69.2%) approaches were more commonly outpatient. Median length of stay was longest after abdominal procedures [median 2 days, interquartile range (IQR) 1-3] compared with laparoscopic and vaginal procedures (both median 1 day, IQR 0-2; p<0.001).

Trends over Time

Utilization patterns shifted markedly over the study period (Figure 1). Laparoscopic and vaginal approaches have increasingly supplanted abdominal sacrocolpopexy. Within the laparoscopic group, adoption of robotic assistance rose

Table 1. Baseline characteristics of patients undergoing sacral colpopexy, 2014-2022 (n=61,524)

Characteristic	Abdominal (n=3,497)	Laparoscopic (n=22,752)	Vaginal (n=35,275)	p-value
Age ≥75 years	10.0%	7.9%	13.5%	<0.001
Age <45 years	9.8%	15.2%	6.3%	<0.001
Race: Non-hispanic white	58.1%	54.3%	60.5%	<0.001
Race: Non-hispanic African American	5.5%	6.4%	4.1%	<0.001
Race: Hispanic	8.4%	7.9%	8.2%	0.09
BMI ≥30	33.2%	33.8%	35.3%	<0.001
BMI <30	66.8%	66.2%	64.2%	<0.001
Concomitant hysterectomy	59.2%	73.6%	64.6%	<0.001

steadily from 2014 to 2022, with nearly three-quarters of laparoscopic cases being robot-assisted by 2022 (Figure 2).

Perioperative Complications

Overall composite morbidity differed significantly across groups (Table 3). Abdominal sacrocolpopexy was associated with the highest complication rate (13.1%), followed by vaginal colpopexy (10.5%) and laparoscopic colpopexy (7.8%) (p<0.001). Abdominal procedures carried the greatest risks of superficial surgical site infection (2.6%), transfusion (4.7%), and readmission (4.7%). Laparoscopic colpopexy consistently demonstrated the lowest incidence of these events. In multivariable analysis, adjusting for age, race, ASA class, smoking, and operative time, laparoscopic colpopexy was associated with a significantly lower risk of composite morbidity compared with abdominal procedures (adjusted RR: 0.75, 95% CI: 0.67-0.85, p<0.001) (Table 4). Vaginal colpopexy demonstrated a slightly higher, but not statistically significant, risk relative to abdominal surgery (adjusted RR: 1.09, 95% CI: 0.97-1.21, p=0.12).

Graphical Comparison

Bar graph analysis (Figure 3) highlights the superior safety profile of laparoscopic procedures relative to abdominal and vaginal approaches, with consistently lower complication rates across measured outcomes.

Discussion

This study provides one of the largest contemporary analyses of apical suspension procedures in the United States, utilizing the NSQIP database from 2014-2022. By examining 61,524 patients, we identified notable demographic and outcome trends among patients undergoing abdominal, laparoscopic, and vaginal sacral colpopexy. Our results demonstrate a progressive decline in the use of open abdominal sacral colpopexy, a steady rise in minimally invasive approaches—particularly with robotic assistance—and a stable, though less frequent, role for vaginal suspension. Furthermore, we observed significantly lower composite perioperative morbidity with laparoscopic colpopexy with abdominal colpopexy; vaginal procedures demonstrated an intermediate risk profile. Although NSQIP categorizes vaginal apical suspension procedures under colpopexy-related CPT codes, true sacral colpopexy is traditionally defined as an abdominal or laparoscopic procedure involving mesh fixation to the sacral promontory. The vaginal procedures included in this study were native-tissue ligamentous suspensions, such as

Table 2. Operative and perioperative characteristics by surgical approach

Variable	Abdominal	Laparoscopic	Vaginal	p-value
Operative time >200 min	37.7%	38.1%	14.9%	<0.001
Inpatient procedure	81.2%	18.7%	30.8%	<0.001
Median hospital stay (days, IQR)	2 (1-3)	1 (0-2)	1 (0-2)	<0.001

IQR: Interquartile range

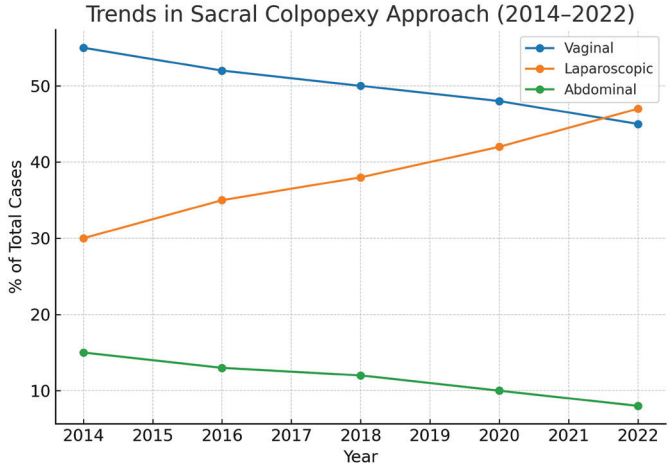

Figure 1. Trends in utilization of surgical approaches for sacral colpopexy from 2014-2022

Line graph showing relative proportions of abdominal, laparoscopic, and vaginal approaches over time

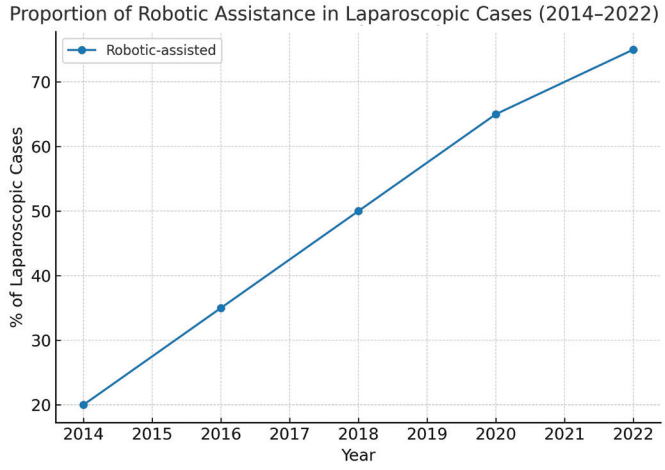

Figure 2. Trends in robotic assistance among laparoscopic sacral colpopexy cases, 2014-2022

Stacked area or line chart showing increase in robotic utilization from 39.2% (2020-2022) to 73.5% in 2022

Table 3. Perioperative complications following sacral colpopexy

Complication	Abdominal	Laparoscopic	Vaginal	p-value
Composite complication rate	13.1%	7.8%	10.5%	<0.001
Superficial SSI	2.6%	1.2%	1.0%	<0.001
Blood transfusion	4.7%	2.3%	2.4%	<0.001
Readmission	4.7%	2.3%	2.4%	<0.001
Return to OR	2.0%	1.2%	1.4%	<0.001

OR: Odds ratio, SSI: Surgical site infection

Table 4. Adjusted relative risk of composite morbidity by surgical approach

Approach	Adjusted RR	95% CI	p-value
Abdominal (reference)	1.00	–	–
Laparoscopic	0.75	0.67-0.85	<0.001
Vaginal	1.09	0.97-1.21	0.12

RR: Relative risk, CI: Confidence interval

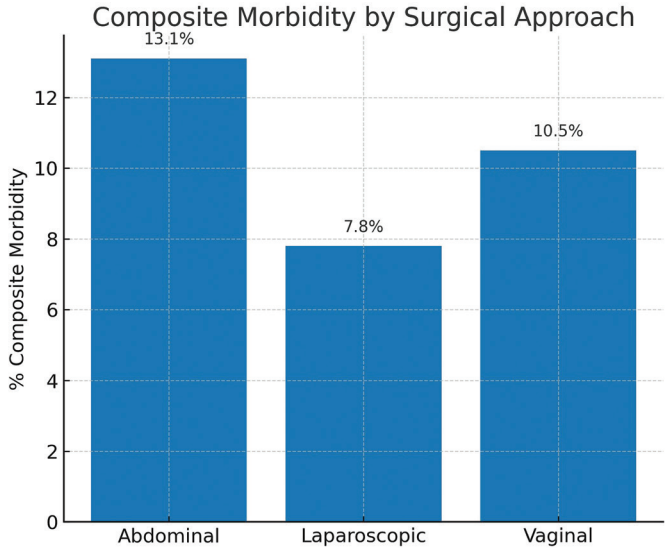

Figure 3. Composite complication rates by surgical approach

Bar graph comparing abdominal, laparoscopic, and vaginal routes with percentage complications

uterosacral ligament suspension and sacrospinous ligament fixation. This distinction should be considered when interpreting comparative outcomes across surgical routes.

Comparison with Existing Literature

Historically, abdominal sacrocolpopexy has been regarded as the gold standard for apical prolapse repair, with superior long-term anatomic durability compared with vaginal procedures[1]. Landmark studies, including randomized controlled trials, established its effectiveness in reducing recurrent prolapse and improving functional outcomes[2]. However, open abdominal surgery is associated with higher perioperative morbidity, longer hospitalization, and slower recovery[3]. Our findings are consistent with the the literature, confirming higher complication rates in the open group than in minimally invasive approaches. The adoption of laparoscopic and robotic-assisted techniques has transformed apical prolapse surgery over the past two decades. Meta-analyses demonstrate that laparoscopic sacral colpopexy achieves equivalent anatomic success compared with the open approach, but with reduced blood loss, shorter hospital stay, and faster return to activities[4,5]. Our data corroborate these advantages, showing the lowest adjusted morbidity in the laparoscopic group. Importantly, robotic assistance within the laparoscopic cohort has expanded substantially in recent years. This trend parallels national utilization studies, which show exponential increases in robotic gynecologic surgery driven by improved surgeon ergonomics, enhanced dexterity, and improved visualization[6]. While our results confirm the safety and feasibility, concerns remain regarding the high costs associated with robotic platforms, without clear evidence of superior outcomes compared to conventional laparoscopy[7]. Vaginal approaches, such as sacrospinous ligament fixation and uterosacral ligament suspension, remain widely used alternatives, particularly in older patients or those with comorbidities, in whom minimally invasive abdominal entry carries higher risks[8]. Several studies suggest that vaginal suspensions offer shorter operative times and the avoidance of general anesthesia, but may be associated with higher recurrence rates and different complication patterns, including buttock pain and ureteric injury[9]. Our findings of intermediate morbidity associated with vaginal colpopexy reflect these trade-offs. These procedures retain an important role in individualized surgical planning, particularly where durability of repair may be balanced against anesthetic and perioperative risks.

Strengths of This Study

A major strength of this study lies in the use of the ACS-NSQIP, a rigorously validated national surgical registry capturing diverse patient populations and outcomes. The large sample size across nearly a decade allowed us to observe temporal trends, evaluate demographic shifts, and assess complication profiles with adequate statistical power. Additionally, adjustment for confounders, such as age, comorbidity burden, and operative time, improves the reliability of comparisons between surgical approaches. The demonstration of increasing robotic adoption in sacral colpopexy adds further relevance, as this reflects current real-world practice and informs future policy regarding surgical innovation.

Study Limitations

Despite these strengths, several limitations must be acknowledged. First, NSQIP captures only 30-day outcomes, preventing assessment of long-term recurrence, mesh-related complications, or functional outcomes such as continence, sexual function, and quality of life. While laparoscopic sacral colpopexy demonstrated a superior perioperative safety profile in this study, its designation as the long-term gold standard rests primarily on durable anatomic outcomes. These long-term measures cannot be assessed within the 30-day follow-up framework of the NSQIP database. These outcomes are central to the ultimate success of prolapse surgery, and their absence limits the comprehensiveness of our conclusions. Second, NSQIP relies on administrative coding, which may misclassify surgical approaches or underreport complications. In particular, robotic procedures are coded within the laparoscopic umbrella, precluding granular analysis of outcomes stratified by robotic versus conventional laparoscopic approaches. Third, we cannot account for surgeon experience, hospital volume, or patient preferences, all of which likely influence surgical approach and outcomes. Finally, selection bias is inherent, as healthier patients may preferentially undergo minimally invasive surgery, while frailer patients may be directed toward vaginal routes.

Clinical Implications

The findings of this study have direct clinical relevance. The superior perioperative safety profile of laparoscopic sacral colpopexy supports its continued adoption as the preferred approach when feasible. The rapid expansion of robotic assistance reflects surgeon and institutional preferences, but the absence of demonstrable outcome superiority underscores the need for cost-effectiveness analyses to guide resource allocation. Vaginal suspension procedures continue to play a vital role, particularly for patients with significant comorbidities or for those in whom minimally invasive abdominal access is contraindicated. These results highlight the importance of individualized patient counseling. Shared decision-making should incorporate patient priorities—durability of repair, recovery time, avoidance of mesh, or anesthetic risk—alongside evidence-based data on morbidity. For example, a younger, healthier patient seeking long-term anatomic durability may benefit most from laparoscopic sacral colpopexy, whereas an older, medically frail patient may be more appropriately managed with a vaginal approach. The clinical implications of these findings should also be interpreted within the context of healthcare system variability. In regions where access to robotic platforms may be limited compared to the U.S.-based NSQIP population, such as in certain middle-income healthcare systems, conventional laparoscopy or vaginal approaches may remain predominant. Accordingly, surgical decision-making should integrate local resource availability, surgeon expertise, and institutional infrastructure when applying these findings to routine practice.

Future Directions

Future research must address several critical gaps. Long-term comparative studies are needed to evaluate durability, recurrence rates, and functional outcomes across approaches. Particularly, registry data incorporating patient-reported outcomes would provide invaluable insights into quality of life, sexual health, and continence. In parallel, ongoing surveillance of mesh safety remains imperative, given heightened regulatory scrutiny and patient concerns[10]. As the utilization of robotics continues to rise, cost-effectiveness analyses must weigh its ergonomic and technical advantages against economic sustainability considerations. Finally, training and dissemination of minimally invasive techniques should be prioritized to ensure equitable access for patients across healthcare systems.

Conclusion

In conclusion, our study demonstrates a clear shift in apical suspension surgery from open abdominal sacral colpopexy to minimally invasive sacral colpopexy, with laparoscopic and robotic-assisted approaches increasingly favored due to their lower perioperative morbidity. Vaginal approaches continue to play an important role in selected patient populations. These findings reinforce the movement toward minimally invasive surgery as the standard of care, while highlighting the need for continued evaluation of long-term outcomes, cost-effectiveness, and patient-centered metrics. Ultimately, optimizing the surgical management of POP requires a balanced, evidence-based approach that integrates evolving technology, clinical outcomes, and patient values.

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Ethics

Ethics Committee Approval: As this study used de-identified data from the NSQIP database, institutional review board approval and informed consent were not required.
Informed Consent: Not necessary.

Footnotes

Authorship Contributions

Concept: A.B.P., V.P., Design: S.B.S., Data Collection or Processing: A.B.P., V.P., Analysis or Interpretation: S.B.S., Literature Search: S.B.S., Writing: S.B.S.
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Thiol-disulfide homeostasis in ovarian cancer: comparative analysis with benign neoplasia and healthy women

Over kanserinde tiyol-disülfit homeostazı: benign neoplaziler ve sağlıklı kadınlarla karşılaştırmalı analiz

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Abstract

Objective: To evaluate thiol-disulfide (DS) homeostasis in women with ovarian cancer and to assess its ability to distinguish malignant ovarian tumors from benign ovarian neoplasia and healthy women.

Materials and Methods: This prospective comparative study included 39 women with histopathologically confirmed ovarian cancer, 30 with benign ovarian neoplasia, and 46 age- and body mass index-matched healthy women. Serum native thiol (NT), total thiol (TT), DS, and ischemia-modified albumin (IMA) levels were measured. Thiol-DS indices were calculated as DS/NT (DNT), DS/TT (DTT), and NT/TT (NTT). Data were analyzed statistically. The study was registered at ClinicalTrials.gov (NCT05011539).

Results: Compared with healthy women, the ovarian cancer group exhibited lower NT, TT, and NTT values, along with higher DS, DNT, and DTT values. When malignant and benign ovarian neoplasms were compared, NT and NTT values were lower, whereas DNT and DTT ratios were higher. IMA levels did not differ between groups. Serum CA-125 levels were positively correlated with DNT and DTT, and negatively correlated with NT, TT, and NTT.

Conclusion: Thiol-DS imbalance is more pronounced in ovarian cancer than in benign ovarian neoplasia and in healthy women, suggesting that these markers may be useful adjuncts in the preoperative evaluation of adnexal masses.

Keywords: Ovarian cancer, thiol, disulfide, oxidative stress, biomarker

Öz

Amaç: Over kanseri olan kadınlarda tiyol-disülfit (DS) homeostazını değerlendirmek ve bu dengenin malign over tümörlerini benign over neoplazileri ve sağlıklı kadınlardan ayırt etme potansiyelini araştırmaktır.

Gereç ve Yöntemler: Bu prospektif karşılaştırmalı çalışmaya histopatolojik olarak doğrulanmış over kanseri tanısı olan 39 kadın, benign over neoplazisi olan 30 kadın, yaş ve vücut kitle indeksi açısından eşleştirilmiş 46 sağlıklı kadın dahil edildi. Serum native tiyol (NT), total tiyol (TT), DS ve iskemi

PRECIS: In this prospective comparative study, women with ovarian cancer showed reduced thiol levels and increased disulfide indices compared with women with benign ovarian neoplasia and healthy women, reflecting a pronounced oxidative imbalance.

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modifiye albümin (IMA) düzeyleri ölçüldü. Tiyol-DS indeksleri; DS/NT (DNT), DS/TT (DTT) ve NT/TT (NTT) oranları olarak hesaplandı. Veriler istatistiksel olarak analiz edildi. Çalışma ClinicalTrials.gov'a kaydedilmiştir (NCT05011539).

Bulgular: Sağlıklı kadınlarla karşılaştırıldığında over kanseri grubunda NT, TT ve NTT değerleri daha düşük, DS, DNT ve DTT düzeyleri ise daha yüksek bulundu. Malign ve benign over neoplazilerinin karşılaştırılmasında NT ve NTT değerleri malign grupta daha düşükken, DNT ve DTT oranları daha yüksekti. Gruplar arasında IMA düzeyleri açısından anlamlı fark saptanmadı. Serum CA-125 düzeyleri DNT ve DTT ile pozitif, NT, TT ve NTT ile negatif korelasyon gösterdi.

Sonuç: Tiyol-DS dengesindeki bozulma, benign over neoplazileri ve sağlıklı kadınlara kıyasla over kanserinde daha belirgindir. Bu bulgular, tiyol-DS homeostazı belirteçlerinin adneksiyal kitlelerin preoperatif değerlendirilmesinde tamamlayıcı araçlar olarak kullanılabileceğini düşündürmektedir.

Anahtar Kelimeler: Over kanseri, tiyol, disülfit, oksidatif stres, biyobelirteç

Introduction

Ovarian cancer is the most lethal gynecologic malignancy, and survival outcomes have shown only limited improvement despite advances in treatment[1,2]. The absence of an effective population-based screening strategy contributes substantially to late-stage detection. Although transvaginal ultrasonography and serum CA-125 measurement are frequently used in clinical practice, CA-125 alone has restricted diagnostic accuracy due to its low specificity and variable sensitivity, particularly when distinguishing malignant from benign adnexal masses[3-5]. This limitation highlights the need for additional biochemical markers that may aid in evaluating ovarian tumors.

Oxidative stress plays an important role in carcinogenesis by promoting DNA damage, altering cell survival pathways, enhancing chemoresistance, and increasing metastatic potential[6]. These biological effects emerge from an imbalance between reactive oxygen species (ROS) and endogenous antioxidant defenses, suggesting that redox alterations may reflect underlying tumor behavior.

Thiol-disulfide homeostasis (TDH) constitutes a key component of the antioxidant system. Native thiols (NTs) can reversibly oxidize to form disulfide (DS) bonds, and the dynamic equilibrium between these two forms provides a quantitative indicator of oxidative status[7,8]. Disruption of this balance has been reported in several malignant conditions. Ischemia-modified albumin (IMA), generated through oxidative modification of serum albumin, has likewise been studied as a marker of oxidative stress in ischemic and neoplastic disorders[9,10].

The present study aimed to evaluate TDH and IMA levels in women with ovarian cancer and to compare these findings with those in benign ovarian neoplasia and healthy women. Our objective was to determine whether these oxidative markers may assist in differentiating malignant ovarian tumors from benign adnexal masses.

Materials and Methods

This prospective comparative study was conducted at a tertiary obstetrics and gynecology department between April 2021 and January 2022. Ethical approval was obtained from the University of Health Sciences Türkiye, Tepecik Training and Research Hospital Clinical Research Ethics Committee (approval number: 2021/04-10, date: 15.04.2021). All participants provided written and verbal informed consent prior to enrollment. The study was registered at ClinicalTrials.gov (NCT05011539) and conducted in accordance with the Declaration of Helsinki. All participants were evaluated and managed according to the same institutional protocols for adnexal masses.

Women presenting with a pelvic mass and scheduled for surgery were invited to participate. Only patients whose final histopathological diagnosis confirmed benign or malignant ovarian neoplasia were included. Patients with borderline ovarian tumors were excluded from the analysis. All malignant cases underwent primary surgery at our center. Patients referred after receiving neoadjuvant chemotherapy or who were previously treated elsewhere were excluded.

Similarly, women with extra-ovarian malignancies, acute inflammatory conditions, or chronic systemic diseases known to influence oxidative stress—such as diabetes mellitus, autoimmune disorders, thyroid dysfunction, or chronic inflammatory diseases—were not eligible.

Participants were also excluded if they smoked, consumed alcohol regularly, used antioxidant vitamin supplements (A, C, or E), or had cognitive limitations that could interfere with informed consent. Cognitive limitation refers to any documented neurological, psychiatric, or developmental condition impairing comprehension or decision-making.

The control group consisted of healthy women presenting for routine gynecologic check-ups during the study period. These women had no adnexal pathology, chronic systemic disease, or conditions affecting oxidative stress. They were prospectively matched to the patient groups based on two criteria: age within ±3 years and body mass index within ±2 kg/m².

Matching was performed sequentially during recruitment to ensure that participants in the ovarian neoplasia groups were comparable to those in the healthy control group.

Age, height, weight, gravida, parity, and medical history were recorded for all participants. Preoperative serum CA-125 levels for the patient groups were retrieved from the hospital information system.

For biochemical assays, 5 mL of pre-prandial venous blood was collected from surgical patients during hospitalization and from controls during outpatient visits. Samples were centrifuged, aliquoted, stored at -80 °C, and transported under appropriate conditions to an accredited, university-affiliated central laboratory.

Serum NT and total thiol (TT) levels were quantified using the automated spectrophotometric method developed by Erel and Neselioglu[8]. DS concentrations were calculated using the formula DS = (TT-NT)/2. Based on these measurements, thiol-DS indices were calculated as follows: the DS/NT ratio (DNT) was calculated as (DS/NT) x 100, the DS/TT ratio (DTT) was calculated as (DS/TT) x 100, and the native thiol/total thiol ratio (NTT) was calculated as (NT/TT) x 100.

IMA levels were measured using the albumin cobalt binding technique and expressed in absorbance units.

All women in the malignant neoplasia group underwent primary cytoreductive surgery. Staging was performed according to the International Federation of Gynaecology and Obstetrics (FIGO) ovarian cancer classification system. Benign lesions were managed surgically according to standard gynecologic practice. All pathological assessments were based on the final histopathological examination rather than on frozen-section results.

Statistical Analysis

Statistical analyses were conducted using SPSS version 22.0 (IBM, Armonk, NY, USA). The distribution of continuous variables was assessed using the Kolmogorov-Smirnov test together with Q-Q plots, while homogeneity of variances was examined using Levene's test. Comparisons between two groups were performed using the independent samples t-test when variables were normally distributed and the Mann-Whitney U test when they were not. Comparisons among three groups were analyzed using one-way ANOVA, with post-hoc testing by Tukey HSD or Tamhane, as appropriate, when the data were normally distributed, or with the Kruskal-Wallis test for non-normally distributed variables. Results were presented as mean ± standard deviation for normally distributed data and as median with interquartile range for non-normally distributed variables. A p-value below 0.05 was considered statistically significant.

Results

A total of 115 women were included in the study: 39 with malignant ovarian neoplasia, 30 with benign ovarian neoplasia, and 46 healthy controls. Among the benign lesions, the most frequent diagnoses were fibroma (23%), mature cystic teratoma (23%), endometrioma (20%), serous cystadenoma (17%), and mucinous cystadenoma (17%). In the malignant group, high-grade serous carcinoma was the predominant subtype (59%), followed by endometrioid carcinoma (13%), mucinous carcinoma (8%), granulosa cell carcinoma (8%), low-grade serous carcinoma (5%), clear cell carcinoma (5%), and dysgerminoma (2%). FIGO staging for malignant ovarian neoplasms was as follows: 14 patients were classified as stage I, 3 as stage II, 18 as stage III, and 4 as stage IV.

When demographic characteristics were compared across the three groups (malignant, benign, and control), no statistically significant differences were observed in age, body mass index, gravidity, or parity (all p>0.05) (Table 1).

Compared with healthy controls, women with malignant ovarian neoplasia had significantly higher serum DS levels and DNT and DTT ratios (p=0.009, p<0.001, and p<0.001, respectively). Conversely, NT, TT, and NTT values were significantly lower in the malignant group (all p<0.001). IMA levels did not differ significantly between the two groups (p=0.672) (Table 2).

When compared with all participants without malignancy (benign + control), the malignant group again showed significantly increased DS, DNT, and DTT values (all p<0.001) and significantly reduced NT, TT, and NTT levels (all p<0.001). IMA levels remained similar between groups (p=0.768) (Table 3).

A direct comparison of malignant and benign ovarian neoplasia revealed no significant differences in DS, TT, or IMA levels (p=0.081, p=0.057, and p=0.235, respectively). However, NT levels and NTT values were significantly lower in the malignant group (p=0.046 and p=0.012, respectively), while DNT and DTT ratios were significantly higher (both p=0.012). As expected, CA-125 levels were markedly elevated in the malignant group compared with the benign group (p<0.001) (Table 4).

Table 1. Comparison of three groups (malignant, benign, and control) according to demographic and clinical characteristics

Variables	Malignant ovarian neoplasia (n=39)	Benign ovarian neoplasia (n=30)	Control group (n=46)	p-value[a]
Age (years; mean ± SD)	53.41±7.57	49.60±7.10	52.13±5.51	0.065[b]
BMI (kg/m^2; mean ± SD)	29.46±6.12	27.29±3.15	29.27±4.94	0.155[b]
Gravidity (median, 25-75%)	2 (1-3)	3 (1-3)	2 (1-4)	0.988[c]
Parity (median, 25-75%)	2 (1-3)	2 (1-3)	2 (1-3)	0.872[c]

[a]: Significant at 0.05 level, [b]: One-way analysis of variance (ANOVA), [c]: Kruskal-Wallis test, BMI: Body mass index, SD: Standard deviation

Correlation analysis performed in women with ovarian neoplasia (benign and malignant) demonstrated a positive correlation of CA-125 with both DNT and DTT (r=0.38, p=0.001 for each). Significant negative correlations were observed between CA-125 and NT, TT, and NTT (r=-0.36, p=0.002; r=-0.34, p=0.004; and r=-0.38, p=0.001, respectively). When the analyses were repeated including only epithelial ovarian cancers from the malignant group, the results were consistent with those obtained in the overall malignant cohort.

Table 2. Comparison of malignant disease group and control group in terms of biochemical parameters

Variables	Malignant ovarian neoplasia (n=39)	Control group (n=46)	p-value[a]
Disulfide (µmol/L; median, 25-75%)	14.55 (11.25-18.95)	13.05 (11.26-14.18)	0.009[a,c]
NT (µmol/L; mean ± SD)	200.03±49.79	287.58±45.37	<0.001[a,b]
TT (µmol/L; median, 25-75%)	232.60 (204.30-260.20)	320.50 (281.20-342.70)	<0.001[a,c]
DNTx100 (median, 25-75%)	6.76 (5.37-12.75)	4.95 (3.63-5.24)	<0.001[a,c]
DTTx100 (median, 25-75%)	5.95 (4.85-10.16)	4.50 (3.39-4.74)	<0.001[a,c]
NTTx100 (median, 25-75%)	88.08 (79.68-90.28)	90.98 (90.51-93.21)	<0.001[a,c]
IMA (ABSU; median, 25-75%)	0.81 (0.73-0.94)	0.83 (0.65-0.99)	0.672[c]

[a]: Significant at 0.05 level, [b]: Independent samples t-test; [c]: Mann-Whitney U test, SD: Standard deviation, NT: Native thiol, TT: Total thiol, DNT: Disulfide/native thiol, DTT: Disulfide/total thiol, NTT: Native thiol/total thiol, IMA: Ischemia modified albumin, ABSU: Absorbance units

Table 3. Comparison of malignant disease group and others (benign + control) in terms of biochemical parameters

Variables	Malignant ovarian neoplasia (n=39)	Others (benign + control) (n=76)	p-value[a]
Disulfide (µmol/L; median, 25-75%)	14.55 (11.25-18.95)	12.60 (11.31-14.51)	0.010[a,c]
NT (µmol/L; mean ± SD)	200.03±49.79	264.29±61.78	<0.001[a,b]
TT (µmol/L; median, 25-75%)	232.60 (204.30-260.20)	304.40 (262.30-338.30)	<0.001[a,c]
DNTx100 (median, 25-75%)	6.76 (5.37-12.75)	5.19 (4.58-5.78)	<0.001[a,c]
DTTx100 (median, 25-75%)	5.95 (4.85-10.16)	4.70 (4.20-5.18)	<0.001[a,c]
NTTx100 (median, 25-75%)	88.08 (79.68-90.28)	90.58 (89.63-91.59)	<0.001[a,c]
IMA (ABSU; median, 25-75%)	0.81 (0.73-0.94)	0.82 (0.69-0.91)	0.768[c]

[a]: Significant at 0.05 level; [b]: Independent samples t-test; [c]: Mann-Whitney U test, SD: Standard deviation, NT: Native thiol, TT: Total thiol, DNT: Disulfide/native thiol, DTT: Disulfide/total thiol, NTT: Native thiol/total thiol, IMA: Ischemia modified albumin, ABSU: Absorbance units

Table 4. Comparison of malignant disease group and benign disease group in terms of biochemical parameters

Variables	Malignant ovarian neoplasia (n=39)	Benign ovarian neoplasia (n=30)	p-value[a]
Disulfide (µmol/L; median, 25-75%)	14.55 (11.25-18.95)	12.45 (11.25-15.40)	0.081[c]
NT (µmol/L; mean ± SD)	200.03±49.79	228.57±67.05	0.046[a,b]
TT (µmol/L; median, 25-75%)	232.60 (204.30-260.20)	263.10 (208.40-312.70)	0.057[c]
DNTx100 (median, 25-75%)	6.76 (5.37-12.75)	5.55 (5.22-6.69)	0.012[a,c]
DTTx100 (median, 25-75%)	5.95 (4.85-10.16)	5.00 (4.72-5.90)	0.012[a,c]
NTTx100 (median, 25-75%)	88.08 (79.68-90.28)	90.00 (88.18-90.54)	0.012[a,c]
IMA (ABSU; median, 25-75%)	0.81 (0.73-0.94)	0.77 (0.69-0.90)	0.235[c]
CA-125 (U/mL; median, 25-75%)	263.00 (57-535)	18.00 (14-42)	<0.001[a,c]

[a]: Significant at 0.05 level, [b]: Independent samples t-test, [c]: Mann-Whitney U test, SD: Standard deviation, NT: Native thiol, TT: Total thiol, DNT: Disulfide/native thiol, DTT: Disulfide/total thiol, NTT: Native thiol/total thiol, IMA: Ischemia modified albumin, ABSU: Absorbance units

Discussion

The present study demonstrates that TDH, characterized by depleted NTs and increased disulfide-derived indices, is significantly impaired in women with ovarian cancer compared with both benign ovarian neoplasia and healthy women. The inclusion of a benign neoplasia group is clinically relevant because these lesions commonly mimic malignancy radiologically or by elevation of CA-125; however, our findings indicate that the oxidative shift in thiol-DS balance is more pronounced in malignant disease. These results suggest that TDH indices reflect biological processes that are more specific to malignant transformation than to non-specific inflammatory or cystic pathology, supporting their potential role as adjunctive biomarkers in the preoperative evaluation of adnexal masses.

A possible explanation for the more pronounced thiol-DS imbalance in ovarian cancer is the persistently increased oxidative stress associated with malignant transformation. ROS are known to promote tumor progression through effects on cell survival, proliferation, and invasion, while thiols represent a major component of antioxidant defense[6,7]. In this context, lower thiol levels and higher oxidation-related ratios in the malignant group may reflect increased thiol consumption in response to tumor-related oxidative burden. A more marked alteration observed in ovarian cancer compared with benign ovarian neoplasia may therefore indicate that thiol-DS homeostasis is influenced not only by the presence of an adnexal mass but also by its malignant biological behavior.

Oxidative stress is a fundamental driver of malignant transformation. ROS facilitate DNA mutations, epigenetic instability, angiogenesis, and remodeling of the tumor microenvironment, effectively promoting multiple hallmarks of cancer[6]. ROS also influence cell survival pathways such as MAPK, PI3K/Akt, and Nuclear factor kappa B signaling, promoting proliferation while inhibiting apoptosis[11]. Ovarian cancer has been shown to exhibit distinct oxidative signatures, including increased ROS generation and metabolic reprogramming that enhances oxidative phosphorylation activity[4]. Against this biological landscape, thiols—primarily cysteine residues on proteins and glutathione—function as key antioxidants buffering oxidative stress. As thiols neutralize ROS, they undergo reversible oxidation to generate DS bonds, which can subsequently be reduced back to thiols, making TDH an indicator of dynamic redox balance[7,8].

In the present study, decreased NT, TT, and NTT levels in ovarian cancer patients reflect diminished antioxidant capacity, while elevated DS, DNT, and DTT levels represent a compensatory increase in oxidized products. These findings align with the biochemical model proposed by Erel and Erdoğan[7], who emphasized that elevated DS formation signals consumption of NTs under oxidative challenge. Mechanistically, lower thiol levels may reflect increased cellular turnover, heightened mitochondrial ROS production, and metabolic stress associated with proliferating tumor tissue. Similar thiol-DS disturbances have been described in other malignancies, including breast, lung, endometrial, cervical, and prostate cancers, in which thiol-DS balance partially normalized following tumor resection, suggesting that TDH alterations may reflect tumor presence rather than patient predisposition. The consistency of TDH derangements across distinct tumor types supports the concept that redox disruption is a shared metabolic phenotype of malignancy[12-16].

When malignant ovarian tumors were compared with benign ovarian neoplasia, our findings demonstrated significantly reduced NT and NTT, and increased DNT and DTT in malignant disease. This observation is clinically relevant because benign lesions—including endometriomas, fibromas, and mature cystic teratomas—may mimic malignant disease radiologically or through elevation of CA-125. Earlier research in benign gynecologic conditions suggests that oxidative stress is present but quantitatively less pronounced than in malignancy. For example, Karatas et al.[17] reported altered TDH in uterine fibroids but with a magnitude lower than that observed in gynecologic cancers. This distinction may explain why thiol depletion and DS elevation are more pronounced in ovarian cancer than in benign tumors.

The significant correlations observed between CA-125 and thiol-DS indices further strengthen the argument that TDH reflects tumor activity. The positive association between CA-125 and DNT/DTT and the negative association with NT/NTT suggest that as tumor burden increases, the oxidative conversion of thiols to disulfides intensifies. These relationships persisted when analyses were restricted to epithelial ovarian cancers, supporting applicability across the most clinically relevant subtypes. Similar correlations between tumor markers and oxidative parameters were observed in endometrial, cervical, and prostate cancer, suggesting potential prognostic or monitoring value[14-16]. While no conclusions about causality can be inferred due to the cross-sectional nature of our study, these findings highlight the potential of TDH parameters as dynamic biomarkers warranting longitudinal evaluation.

Unlike TDH parameters, IMA levels did not differ significantly between malignant and non-malignant groups in our cohort. This outcome is consistent with the biochemical nature of IMA formation, which is primarily driven by abrupt ischemia-reperfusion injury causing structural modification of the amino-terminal region of albumin[9]. Huang et al.[10] reported inconsistent performance of IMA in chronic gastric malignancy and suggested that IMA is more reflective of acute hypoxia than sustained oxidative stress. The chronic non-ischemic oxidative environment in ovarian cancer likely does not produce the rapid albumin modifications required to increase IMA which explains its limited diagnostic value in this context.

Beyond diagnosis, several studies have proposed prognostic implications of TDH. The partial restoration of thiol levels following radical prostatectomy and the association between TDH and disease stage in other cancers suggest that TDH may serve as a surrogate marker of tumor burden[16]. ROS-associated alterations are implicated in treatment resistance; redox-sensitive signaling influences chemotherapy response, platinum sensitivity, and ferroptosis susceptibility—critical pathways in ovarian cancer management. Therefore, future studies measuring TDH before and after cytoreduction, chemotherapy, or maintenance therapy could clarify its potential role in monitoring treatment response or predicting recurrence.

The heterogeneity of ovarian cancer presents a challenge in interpreting serum biomarkers. Distinct histopathologic subtypes exhibit characteristic metabolic and oxidative profiles: clear-cell carcinoma is characterized by glutathione-driven chemoresistance, whereas high-grade serous carcinoma displays significant genomic instability and mitochondrial dysfunction. In our study, epithelial tumors accounted for the majority of cases, and subgroup analysis yielded results consistent with those of the overall cohort. However, subtype-specific TDH signatures cannot be excluded. Future work incorporating genomic data—such as BRCA mutation status, homologous recombination deficiency, or metabolic phenotype—could identify redox-based biomarker clusters for precision stratification.

The strengths of our study include a prospective design, the inclusion of both benign and healthy control groups, and the measurement of an integrated panel of redox markers. By demonstrating TDH alterations in ovarian cancer relative to both comparison groups and identifying associations with CA-125, our findings contribute to the growing evidence that TDH may serve as an accessible adjunctive biomarker in the evaluation of adnexal masses. As healthcare systems seek cost-effective biomarkers, the simplicity, reproducibility, and low cost of thiol-DS measurement enhance its translational appeal.

Study Limitations

This study has limitations. The sample size was modest and derived from a single center. The absence of serial postoperative or treatment-associated measurements restricts insight into the temporal behavior of TDH. Furthermore, the focus on serum concentrations does not address local oxidative changes within tumor tissue. Tissue-level analysis, including markers of oxidative DNA damage and enzymatic antioxidant activity, could clarify mechanistic pathways.

Conclusion

This study demonstrated that women with ovarian cancer exhibit a distinct thiol-DS profile characterized by reduced thiol levels and increased oxidation-derived indices compared with both healthy women and those with benign ovarian neoplasia. These findings suggest that TDH reflects the heightened oxidative environment associated with malignant disease and may serve as an adjunctive biomarker in the preoperative evaluation of adnexal masses. While these results are promising, larger homogeneous cohorts and longitudinal assessments are required to establish their diagnostic, prognostic, and monitoring utility.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the University of Health Sciences Türkiye, Tepecik Training and Research Hospital Clinical Research Ethics Committee (approval number: 2021/04-10, date: 15.04.2021).
Informed Consent: All participants provided written and verbal informed consent prior to enrollment.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.K., M.S., V.K., S.K., Concept: A.K., M.S., V.K., Design: A.K., M.S., V.K., Ö.E., Data Collection or Processing: A.K., A.A.U., Ö.E., S.N., Analysis or Interpretation: A.K., S.K., A.A.U., Ö.E., S.N., A.İ., Literature Search: A.K., S.K., A.A.U., A.İ., Writing: A.K., Ö.E., S.N., A.İ.
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Effect of the new FIGO 2023 staging system on stage distribution and adjuvant therapies in endometrial cancer: A retrospective cohort study

Endometriyum kanserinde yeni FIGO 2023 evreleme sisteminin evre dağılımı ve adjuvan tedavilere etkisi: Retrospektif kohort çalışması

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Abstract

Objective: The 2023 update of the International Federation of Gynecology and Obstetrics (FIGO) staging system introduced significant changes in the classification of endometrial cancer by incorporating key pathological and molecular features. This study aimed to evaluate the impact of the revised FIGO 2023 staging system on stage distribution and adjuvant treatment decisions in patients undergoing surgical management of this malignancy.

Materials and Methods: This retrospective study included 220 patients who underwent surgical staging for endometrial cancer between January 2018 and December 2025. All patients were initially staged using the FIGO 2009 classification. Cases were subsequently reclassified according to the FIGO 2023 staging criteria, using the algorithm proposed for settings in which routine molecular classification is unavailable. The McNemar test was used to compare stage categories between the two staging systems, and the Wilcoxon signed-rank test was applied to evaluate the impact of stage migration on adjuvant treatment recommendations.

Results: Stage migration occurred in 12.7% of patients (28/220) following the application of the FIGO 2023 criteria, predominantly due to upstaging. The most common factor associated with stage reclassification was substantial lymphovascular space invasion (LVSI). The proportion of patients managed with observation alone significantly decreased from 44.5% to 32.7% ($p<0.001$), while the use of pelvic radiotherapy increased from 19.1% to 28.2% ($p=0.004$). Similarly, the proportion of patients receiving combined chemoradiotherapy significantly increased from 11.8% to 17.3% ($p=0.012$).

Conclusion: The implementation of the FIGO 2023 staging system has resulted in clinically meaningful stage migration and significantly impacted adjuvant treatment strategies. In particular, the recognition of substantial LVSI as a defining feature of stage IIC disease has led to more intensive adjuvant therapy in a subset of patients previously categorized as low risk.

Keywords: Endometrial cancer, FIGO 2023, staging system, lymphovascular space invasion, adjuvant therapy, stage migration

Öz

Amaç: Uluslararası Jinekoloji ve Obstetrik Federasyonu (FIGO) evreleme sisteminin 2023 güncellemesi, endometriyum kanserinin sınıflandırılmasında temel patolojik ve moleküler özellikleri içerecek şekilde önemli değişiklikler getirmiştir. Bu çalışmanın amacı, revize edilen FIGO 2023 evreleme sisteminin cerrahi tedavi uygulanan endometriyum kanseri hastalarında evre dağılımı ve adjuvan tedavi kararları üzerindeki etkisini değerlendirmektir.

Gereç ve Yöntemler: Bu retrospektif çalışmaya Ocak 2018 ile Aralık 2025 tarihleri arasında endometriyum kanseri nedeniyle cerrahi evreleme uygulanan hastalar dahil edilmiştir (n=220). Tüm hastalar başlangıçta FIGO 2009 sınıflamasına göre evrelendirilmiştir. Bu çalışmanın amacı doğrultusunda

PRECIS: Application of the International Federation of Gynecology and Obstetrics 2023 criteria causes significant stage migration, primarily driven by substantial lymphovascular space invasion, which leads to more intensive adjuvant radiotherapy and chemoradiotherapy recommendations.

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olgular daha sonra, rutin moleküler sınıflandırmanın yapılamadığı durumlar için önerilen algoritma kullanılarak FIGO 2023 evreleme kriterlerine göre yeniden sınıflandırılmıştır. İki evreleme sistemi arasındaki evre kategorilerini karşılaştırmak için McNemar testi, evre değişiminin adjuvan tedavi önerileri üzerindeki etkisini değerlendirmek için ise Wilcoxon işaretli sıralar testi kullanılmıştır.

Bulgular: FIGO 2023 kriterlerinin uygulanması sonrasında hastaların %12,7'sinde (28/220) evre değişimi saptanmış olup bu değişim çoğunlukla evre yükselmesi şeklinde gerçekleşmiştir. Evre yeniden sınıflandırmasına yol açan en sık faktör substantif lenfovasküler alan invazyonu (LVSI) olmuştur. Yalnızca gözlem ile takip edilen hasta oranı %44,5'ten %32,7'ye düşerken (p<0.001), pelvik radyoterapi uygulanan hasta oranı %19,1'den %28,2'ye yükselmiştir (p=0.004). Benzer şekilde kombine kemoradyoterapi uygulanan hasta oranı da %11,8'den %17,3'e artmıştır (p=0.012).

Sonuç: FIGO 2023 evreleme sisteminin uygulanması klinik olarak anlamlı evre değişimine yol açmış ve adjuvan tedavi stratejileri üzerinde önemli bir etki oluşturmuştur. Özellikle substantif LVSI evre IIC hastalığın tanımlayıcı bir özelliği olarak kabul edilmesi, daha önce düşük riskli olarak değerlendirilen bazı hastalarda daha yoğun adjuvan tedavi uygulanmasına neden olmuştur.

Anahtar Kelimeler: Endometriyum kanseri, FIGO 2023, evreleme sistemi, lenfovasküler alan invazyonu, adjuvan tedavi, evre değişimi

Introduction

Uterine body cancer, the most common gynecologic malignancy in developed countries, is rising in incidence worldwide, primarily as a consequence of prolonged life expectancy and escalating rates of obesity[1,2]. Accurate staging is essential for predicting prognosis and guiding postoperative treatment strategies[3].

The International Federation of Gynecology and Obstetrics (FIGO) staging system has historically been the primary classification method for endometrial cancer. The 2009 FIGO revision introduced important changes, including the simplification of stage I disease and an increased emphasis on surgical-pathological findings[4]. However, over time, molecular characterization and a deeper understanding of prognostic pathological factors have revealed the limitations of staging systems based solely on the anatomical extent of disease[5,6].

Based on recently published studies, further assessment of factors such as molecular classification, lymphovascular space invasion, and histological subtype has shown significant prognostic value in patients with endometrial cancer[7,8]. Molecular classification based on The Cancer Genome Atlas has further refined these risk stratification models by identifying specific subgroups associated with distinct prognoses[9]. These advances have greatly influenced modern clinical practice and risk assessment strategies.

The latest update of the FIGO staging system, published in 2023, emphasizes this comprehensive understanding of tumor biology. The new system incorporates molecular classification and refines pathological criteria, acknowledging substantial lymphovascular space invasion and aggressive histologic features as crucial prognostic factors[10]. Significantly, FIGO also provided an alternative staging algorithm for settings where routine molecular testing is unavailable, allowing the revised classification system with its updated criteria for assigning nodal status to be applied more widely across the globe[11].

Stage migration of patients previously staged according to the FIGO 2009 criteria may be observed following the introduction of the FIGO 2023 staging system. Such reclassification directly affects postoperative treatment decisions and changes the indications for both radiotherapy and chemotherapy[12-14]. Although these significant changes have occurred, there is still limited real-world evidence assessing the clinical utility of the FIGO 2023 staging system. It is critical for clinicians managing endometrial cancer to understand how this revised classification influences stage distribution and treatment planning. The objective of the current study was to investigate stage migration after the implementation of the FIGO 2023 criteria and to evaluate its consequences on postoperative therapy decisions in a surgically staged cohort diagnosed with endometrial cancer.

Materials and Methods

Study Design and Patient Population

This study was conducted at the University of Health Sciences Türkiye, Diyarbakır Gazi Yaşargil Training and Research Hospital, which is a tertiary referral center for gynecologic oncology. The Clinical Research Ethics Committee of University of Health Sciences Türkiye, Diyarbakır Gazi Yaşargil Training and Research Hospital approved the study protocol (approval number: 63, date: 12.02.2026). The study was performed in accordance with the principles of the Declaration of Helsinki.

We performed a retrospective analysis of the medical records of patients who underwent surgical staging for endometrial cancer between January 2018 and December 2025. A total of 220 patients with histologically confirmed endometrial carcinoma met the inclusion criteria and were evaluated in the final analysis. Patients with incomplete pathological data or insufficient information for precise staging were excluded from the study. The overall study population along with the process of stage reclassification is detailed in Figure 1.

All patients were staged according to the FIGO 2009 staging system at the time of initial treatment, which served as the baseline clinical classification throughout the study period.

Reclassification per the 2023 FIGO Staging System

All cases were reviewed according to the FIGO 2023 staging system this study. Due to the lack of routine molecular testing at our institution during the study period, staging reassessment was performed using the alternative algorithm proposed by FIGO for settings where molecular classification cannot be routinely conducted[6]. During this reassessment,

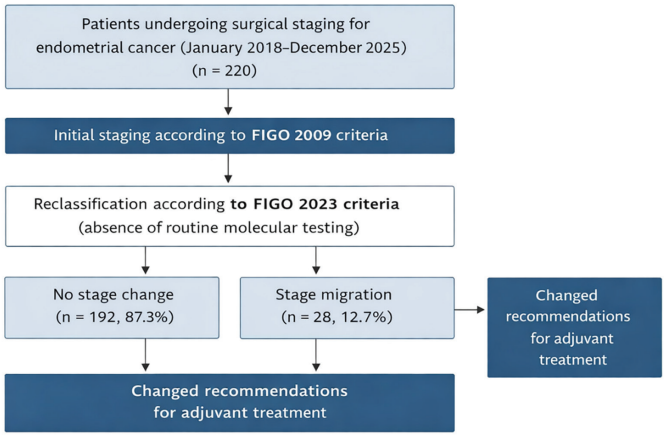

Figure 1. Flow diagram of patient selection and stage reclassification according to the FIGO 2023 staging system. Flow diagram illustrating the study population and stage reclassification process. A total of 220 patients who underwent surgical staging for endometrial cancer between January 2018 and December 2025 were initially staged according to the FIGO 2009 criteria. All cases were subsequently reclassified using the FIGO 2023 staging system in the absence of routine molecular classification. Stage migration occurred in 28 patients (12.7%), while 192 patients (87.3%) showed no change in stage. Reclassification influenced recommendations for adjuvant treatment in a subset of patients

FIGO: International Federation of Gynecology and Obstetrics

critical pathological parameters were evaluated according to the updated staging guidelines. These parameters included histological subtype, tumor grade, depth of myometrial invasion, cervical stromal involvement, lymphovascular space invasion, lymph node involvement, and distant metastases. Notably, substantial lymphovascular space invasion is a key feature that delineates stage IIC disease in the updated FIGO 2023 classification. Stage reassignment adhered strictly to the FIGO 2023 staging guidelines, and all pathology reports were evaluated according to predefined criteria.

Demographic and clinicopathological data were extracted from the institutional electronic medical records. Variables examined included age, body mass index (BMI), histological subtype, tumor grade, depth of myometrial invasion, lymphovascular space invasion, and lymph node involvement. Adjuvant management strategies were classified into four categories: observation alone, vaginal brachytherapy, pelvic external beam radiotherapy (with or without vaginal brachytherapy), and combined chemoradiotherapy. Treatment decisions were obtained from the documented postoperative management plans in the patients' medical records.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. Cross-tabulation analysis was used to evaluate the stage distribution according to the FIGO 2009 and FIGO 2023 systems. To evaluate the effect of stage reclassification on management decisions, paired comparisons of treatment approaches based on the FIGO 2009 and FIGO 2023 staging systems were conducted using the McNemar test or the Wilcoxon signed-rank test, as appropriate. Statistical significance was defined as a two-sided p-value of less than 0.05. SPSS software version 25.0 was used to conduct all statistical analyses.

Table 1. Baseline clinicopathological characteristics of patients (n=220)

Parameter	n (%)	Mean ± SD
Age (years)		62.4±9.1
Body mass index (kg/m²)		32.8±6.4
Histological type		
Endometrioid	182 (82.7%)	
Non-endometrioid (serous, clear cell, carcinosarcoma)	38 (17.3%)	
Tumor grade (endometrioid tumors, n=182)		
Grade 1	96 (52.7%)	
Grade 2	58 (31.9%)	
Grade 3	28 (15.4%)	
Myometrial invasion		
<50%	142 (64.5%)	
≥50%	78 (35.5%)	
Lymphovascular space invasion (LVSI)		
Negative	165 (75.0%)	
Focal	20 (9.1%)	
Substantial	35 (15.9%)	

Values are presented as mean ± SD or n (%), unless otherwise specified
SD: Standard deviation

Results

A cohort of 220 patients was evaluated in this study. The mean age of the study population was 62.4±9.1 years, and the mean BMI was 32.8±6.4 kilograms per square meter. In total, 182 patients, representing 82.7% of the cohort, had confirmed endometrioid histology, whereas 38 patients, representing 17.3%, exhibited non-endometrioid histological subtypes, including serous carcinoma, clear cell carcinoma, and carcinosarcoma. Among the 182 patients with endometrioid tumors, 154 (84.6%) had grade 1 or grade 2 disease and 28 (15.4%) had grade 3 disease. Myometrial invasion of 50 percent or greater was identified in 78 patients (35.5%), and substantial lymphovascular space invasion was detected in 35 patients (15.9%).

Stage Migration for FIGO 2009 and FIGO 2023

The distribution of the disease stages, adjusted to the FIGO 2009 and FIGO 2023 criteria, is summarized in Table 2. Application of the FIGO 2023 staging criteria revealed that stage migration occurred in 28 patients representing 12.7% of the cohort; all were upstaged. The overall pattern of stage reclassification, including the proportions of upstaged and unchanged cases, is detailed in Table 4. Stage changes were most frequent among patients initially classified as stage I under the FIGO 2009 system. Of 154 patients initially staged as FIGO 2009 stage I, application of the FIGO 2023 criteria resulted in stage migration in 22 patients (14.3%). The primary driver for this shift was the presence of substantial lymphovascular space invasion, which reclassified these individuals into stage IIC under the updated staging system.

Impact on Adjuvant Treatment Decisions

The consequences of stage reclassification on adjuvant treatment strategies are summarized in Table 3. Following the implementation of the FIGO 2023 staging system, the percentage of patients managed with observation alone declined significantly compared with the FIGO 2009 staging-based treatment strategy, dropping from 44.5% to 32.7% with a p-value less than 0.001. Conversely, the use of vaginal brachytherapy alone remained statistically unchanged under the new staging method. The proportion of patients treated with pelvic external-beam radiotherapy, with or without vaginal brachytherapy, rose significantly from 19.1% to 28.2%, with a p-value equal to 0.004. Likewise, the percentage of patients receiving combined chemoradiotherapy significantly increased from 11.8% to 17.3%, with a p-value of 0.012.

Discussion

Given the clinical relevance of accurate staging in oncology, this study evaluated the impact of the recently introduced FIGO 2023 staging system by exploring stage distribution and postoperative treatment strategies in patients with endometrial carcinoma. Our findings demonstrate that the implementation of the updated staging criteria produces clinically significant stage migration and alters adjuvant therapy recommendations for a select group of patients. Stage migration following the 2023 diagnostic criteria was observed in 12.7% of our cohort, which is highly consistent with rates reported in early studies assessing the adoption of the FIGO 2023 framework[15,16]. Crucially, all migration events corresponded to upstaging, indicating that the revised system may have greater sensitivity for identifying patients with high-risk disease features.

A key finding from our investigation was the prominent influence of the FIGO 2023 revision on patients who were initially diagnosed with stage I disease according to the FIGO 2009 criteria, among whom the bulk of stage migrations occurred. This shift was primarily driven by the reclassification of stage I disease as stage IIC due to substantial lymphovascular space invasion, a histological

Table 2. Comparison of stage distribution according to the FIGO 2009 and FIGO 2023 staging systems in patients with endometrial cancer (n=220)

FIGO 2009 stage	FIGO 2023 Stage I	FIGO 2023 Stage II	FIGO 2023 Stage III	FIGO 2023 Stage IV	Total
Stage I	132	14[a]	8[b]	0	154
Stage II	0	18	4[c]	0	22
Stage III	0	0	36	2[d]	38
Stage IV	0	0	0	6	6
Total	132	32	48	8	220

[a] Patients with stage IA-IB disease according to FIGO 2009 who were reclassified as stage IIC due to substantial lymphovascular space invasion (LVSI) according to the FIGO 2023 criteria
[b] Patients with aggressive histologic features or high-grade tumors reclassified into a higher stage according to FIGO 2023
[c] Patients initially classified as FIGO 2009 stage II who were reassigned to stage III due to updated lymph node involvement criteria
[d] Patients reclassified as stage IV according to revised definitions of distant metastatic disease in FIGO 2023
FIGO: International Federation of Gynecology and Obstetrics

Table 3. Impact of FIGO 2023 reclassification on adjuvant treatment strategies in patients with endometrial cancer (n=220)

Adjuvant treatment strategy	FIGO 2009 based n (%)	FIGO 2023 based n (%)	p-value
Observation only	98 (44.5%)	72 (32.7%)	<0.001
Vaginal brachytherapy (VBT)	54 (24.5%)	48 (21.8%)	0.312
Pelvic external beam radiotherapy (EBRT ± VBT)	42 (19.1%)	62 (28.2%)	0.004
Combined chemoradiotherapy	26 (11.8%)	38 (17.3%)	0.012

Changes in treatment strategy after reclassification were analyzed using the McNemar test. A p value <0.05 was considered statistically significant
EBRT: External beam radiation therapy, FIGO: International Federation of Gynecology and Obstetrics

Table 4. Stage migration after application of the FIGO 2023 staging system

Migration pattern	n (%)
No stage change	192 (87.3%)
Upstaging	28 (12.7%)
Downstaging	0

FIGO: International Federation of Gynecology and Obstetrics

feature that confers stage IIC status under the new guidelines. Many of these patients would have been categorized as low or intermediate risk under the older 2009 system. By accurately identifying this subgroup at elevated risk of recurrence, the updated classification enables patients likely to benefit from more aggressive adjuvant regimens to receive appropriate therapy.

One of the most consequential modifications implemented by the FIGO 2023 staging system is the formal inclusion of substantial lymphovascular space invasion as a defining criterion for stage IIC disease[10]. Lymphovascular space invasion has long been recognized as a potent prognostic factor in endometrial cancer, correlating strongly with lymph node metastasis, disease recurrence, and compromised survival outcomes[17,18]. Previous literature has demonstrated that patients with extensive lymphovascular space invasion experience clinical outcomes comparable to those with nodal involvement[19]. The high rate of stage migration in our cohort was primarily attributable to the presence of substantial lymphovascular space invasion, corroborating established observations. Consequently, the reclassification of these individuals from stage I under the FIGO 2009 criteria to stage IIC under the revised system had statistically and clinically meaningful effects on postoperative management.

Because treatment strategies in endometrial cancer are strictly dictated by stage and risk grouping, shifts in staging automatically reshape therapeutic recommendations[20,21]. Our data demonstrated a notable decline in observation protocols, with a concurrent increase in the use of pelvic radiotherapy and combined chemoradiotherapy after implementation of the FIGO 2023 staging system. These findings suggest that the updated staging framework provides more granular data regarding which patients stand to benefit from adjuvant management.

A major hallmark of the FIGO 2023 revision is the integration of newly characterized molecular classifications within the context of staging. These molecular subgroups, specifically POLE mutated and p53 abnormal tumors, carry profound prognostic value and have heavily advanced our understanding of endometrial cancer biology[9,22]. Nevertheless, routine molecular testing remains unavailable in many clinical settings globally. The current study utilized the alternative non-molecular staging algorithm, which accurately mirrored the clinical reality of numerous institutions worldwide. Ultimately, our findings suggest that the updated FIGO 2023 staging system refines risk stratification, even in the absence of molecular testing, by optimizing the utility of conventional pathological parameters such as lymphovascular space invasion and tumor histology. This approach ensures the early recognition of high-risk patients who would otherwise be misclassified as low-risk by purely anatomical staging systems.

In the broader clinical context, our results align well with established guidelines and historical landmark trials. The optimization of adjuvant therapy based on risk factors such as tumor grade and extension has been a cornerstone of gynecological oncology, as emphasized by classic consensus statements and clinical guidelines[3,23]. Historically, international multicenter trials like ASTEC and early PORTEC studies successfully defined the boundaries of observation versus localized interventions like vaginal brachytherapy or external beam radiotherapy in early stage diseases[24-26]. Furthermore, contemporary evidence suggests that while clinical staging guides current treatments, the transition toward personalized oncology through comprehensive molecular testing and advanced genomic profiling will ultimately dictate future selection strategies for both chemotherapy and radiation[27,28]. The integration of such risk stratification models into daily practice remains essential to prevent both overtreatment and recurrence[29].

Study Limitations

Several limitations of this study must be acknowledged. First, the retrospective design of the study carries an inherent risk of selection bias. Second, the data were gathered from a single tertiary referral center, which may limit the generalizability of our findings to other clinical settings. Third, routine molecular classification was unavailable during the study period, so staging relied on the alternative FIGO 2023 algorithm designed for non-molecular contexts. The integration of comprehensive molecular data could offer more refined risk stratification. Finally, long-term survival data were not evaluated in the current analysis. Prospective multicenter studies integrating both molecular staging and long-term survival analyses are warranted to fully validate the clinical utility of the updated FIGO staging system.

Conclusion

This study provides clinical validation of the FIGO 2023 staging system for patients with endometrial cancer, demonstrating clinically meaningful stage migration that directly impacts postoperative treatment strategies in a subset of this population. The integration of critical pathological parameters, particularly substantial lymphovascular space invasion, refines risk stratification and facilitates tailored patient management.

Ethics

Ethics Committee Approval: The Clinical Research Ethics Committee of University of Health Sciences Türkiye, Diyarbakır Gazi Yaşargil Training and Research Hospital approved the study protocol (approval number: 63, date: 12.02.2026).
Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.D.E., Concept: K.A., Design: A.D.E., Data Collection or Processing: K.A., Analysis or Interpretation: K.A., Literature Search: A.D.E., Writing: K.A.
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Review / Derleme

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Retroperitoneal anatomy and avascular spaces for pelvic surgery: Cadaveric dissection atlas

Pelvik cerrahi için retroperitoneal anatomi ve avasküler alanlar: Kadavra diseksiyon atlası

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Abstract

This paper presents a comprehensive cadaveric dissection atlas detailing the retroperitoneal anatomy essential to advanced pelvic surgery. Developed by a multidisciplinary team of anatomists, gynecologists, and gynecologic oncologists, the study provides a systematic, layer-by-layer guide for navigating the pelvic avascular spaces. It details five critical surgical corridors: the presacral (retrorectal) space, the pararectal space (divided into the Latzko and Okabayashi compartments), the paravesical space (medial and lateral compartments), the prevesical (retropubic/Retzius) space, and the medial psoas space (laterovascular plane). This atlas emphasizes the use of reliable landmarks, such as the sacral promontory, the obliterated umbilical artery, and the ureter, to define anatomical boundaries and ensure safe surgical practice. The primary objective is to maintain adequate exposure after retroperitoneal entry and to perform layer-by-layer surgical dissection to identify critical anatomical structures. The superior hypogastric plexus; hypogastric nerve; pelvic splanchnic nerves; inferior hypogastric plexus with its vesical and rectal branches; the internal iliac artery with its posterior and anterior trunk branches (including the superior gluteal, iliolumbar, lateral sacral, uterine, inferior gluteal, pudendal, obturator, middle rectal, and inferior and superior vesical arteries, and the obliterated umbilical artery); the external iliac artery; and the corresponding internal and external iliac veins were discussed. Additionally, the somatic nerves, obturator nerve, lumbosacral trunk, sacral nerves, sciatic nerve, genitofemoral nerve, and femoral nerve were reviewed. The parietal fascial planes, pubocervical fascial structure, and visceral compartments were evaluated as part of the whole. Respecting fascial planes—particularly the presacral fascia—is mandatory to avoid catastrophic hemorrhage and autonomic nerve injury. These spaces serve as the "neurovascular roadmap" for complex procedures, including radical hysterectomy, nerve-sparing pelvic surgery, pelvic lymphadenectomy, and hemorrhage control. Mastery of these interconnected retroperitoneal compartments facilitates a transition from organ-based to space-oriented surgery, significantly reducing morbidity while maintaining oncologic radicality.

Keywords: Retroperitoneum, pelvic avascular spaces, ureter, internal iliac artery, nerve-sparing surgery

Öz

Bu makale, ileri düzey pelvik cerrahi için gerekli olan retroperitoneal anatomiye dair ayrıntılı bir kadavra diseksiyon atlası sunmaktadır. Anatomistler, jinekologlar ve jinekolojik onkologlardan oluşan multidisipliner bir ekip tarafından geliştirilen çalışma, pelvik avasküler boşlukların cerrahide kullanılmasına yönelik sistematik, katman katman bir kılavuz sağlamaktadır. Beş kritik pelvik cerrahi alanı ayrıntılı olarak ele almaktadır: presakral (retrorektal) boşluk, pararektal boşluk (Latzko ve Okabayashi bölmelerine ayrılmıştır), paravezikal boşluk (medial ve lateral olarak değerlendirilir), prevezikal (retropubik/Retzius) boşluk ve medial psoas boşluğu (laterovasküler düzlem). Bu atlas, anatomik sınırları tanımlamak ve güvenli cerrahi uygulamaları sağlamak için sakral promontorium, oblitere umbilikal arter ve ureter gibi sabit referans noktalarının kullanımını vurgulamaktadır. Asıl önemli nokta, retroperitoneal girişten sonra yeterli cerrahi görünümün sağlanması ve kritik anatomik yapıları belirlemek için katman katman cerrahi diseksiyon yapılmasıdır. Superior hipogastrik pleksus, hipogastrik sinir, pelvik splanknik sinirler, enferior hipogastrik pleksus, mesane ve rektal dalları, ayrıca superior gluteal arter, iliolumbar arter ve lateral sakral arter, uterin arter, inferior gluteal arter, pudendal arter, obturator arter, middle rektal arter, enferior ve superior vesical arter ve oblitere umbilikal arter gibi posterior ve anterior kök dalları olan internal iliak arter ile external iliak arter ve bunlara karşılık gelen internal iliak ve eksternal iliak ven ele alındı. Ayrıca, somatik sinirler, obturator sinir, lumbosakral trunk, sakral sinirler, siyatik sinir, genitofemoral ve femoral sinir incelendi. Parietal fasya düzlemleri, puboservikal fasyayı oluşturan kompartmanlar ve visseral bölmeler,

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bir bütünün parçası olarak değerlendirildi. Cerrahi kanama ve otonom sinir hasarını önlemek için fasyal düzlemlere, özellikle de presakral fasyaya ve devamına özen göstermek gerekir. Bu alanlar, radikal histerektomi, sinir koruyucu pelvik cerrahi, pelvik lenfadenektomi ve kanama kontrolü de dahil olmak üzere kompleks cerrahi prosedürler için "nörovasküler yol haritası" görevi görür. Bu birbirine bağlı retroperitoneal alanların uygun kullanımı, organ odaklı cerrahiden alan odaklı cerrahiye geçişi sağlayarak, onkolojik radikalliği korurken morbiditeyi önemli ölçüde azaltır.

Anahtar Kelimeler: Retroperiton, pelvik avasküler alanlar, ureter, internal iliac arter, sinir koruyucu cerrahi

Introduction

The pelvic bones (sacrum posteriorly, pubic bone anteriorly, ilium posterolaterally on the superior side, ischium anterolaterally on the inferior side) encircle the pelvic structures. The inner layer of the pelvic bones is formed by the muscles (obturator internus laterally and levator ani at the base) and ligaments, all of which are covered by the parietal fascia. The loose, connective, and supportive fatty tissue surrounds the midline pelvic organs (the rectum posteriorly, the bladder anteriorly, and the uterus between them), and this compartment is covered by the parietal peritoneum[1]. This review focuses on the detailed surgical anatomy of the pelvic retroperitoneum as encountered during incision of the pelvic parietal peritoneum and layer-by-layer dissection from superficial to deep structures. The pelvic avascular spaces—presacral, pararectal, paravesical, and prevesical—and the laterovascular plane (medial psoas space) are well described in the literature.

Methods

This educational cadaveric dissection was performed at the Anatomy Department Laboratory of the University of Health Sciences Türkiye, Gülhane Faculty of Medicine, Ankara, Türkiye. The multidisciplinary team, consisting of anatomists, gynecologists, and gynecologic oncologists, worked collaboratively. An educational video lecture of this video can be found on the YouTube platform (https://www.youtube.com/watch?v=x_VmYaQxclM&t=1402s).

Presacral Space (Retrorectal Space) Definition and Surgical Concept

The presacral space is a midline, retroperitoneal, avascular pelvic space located anterior to the sacrum and posterior to the rectum, extending from the pelvic brim (sacral promontory) to the pelvic floor. It represents the central posterior pelvic dissection plane and serves as a critical corridor for posterior pelvic surgery, nerve identification, and en bloc resections in gynecologic oncology. The presacral space is particularly important for the orientation of the superior hypogastric plexus, hypogastric nerves, and major pelvic vessels, and it acts as the anatomical bridge between the paraaortic region and the posterior pelvic compartments.

Anatomical Boundaries (Figures 1 and 2)

The presacral space is defined by constant and easily identifiable landmarks:

• Anterior boundary:
Rectum,
Mesorectal fascia (mesorectum).
• Posterior boundary:
Sacrum,
Presacral fascia (Waldeyer's fascia).
• Lateral boundaries:
Ureters,
Common iliac artery, internal iliac artery (proximal portions).
• Superior boundary:
Pelvic brim (sacral promontory),
Inferior border of the sigmoid mesocolon.
• Inferior boundary:
Levator ani muscle,
Anococcygeal ligament.

These boundaries position the presacral space as the deepest posterior pelvic avascular plane, in close proximity to major vascular and autonomic neural structures.

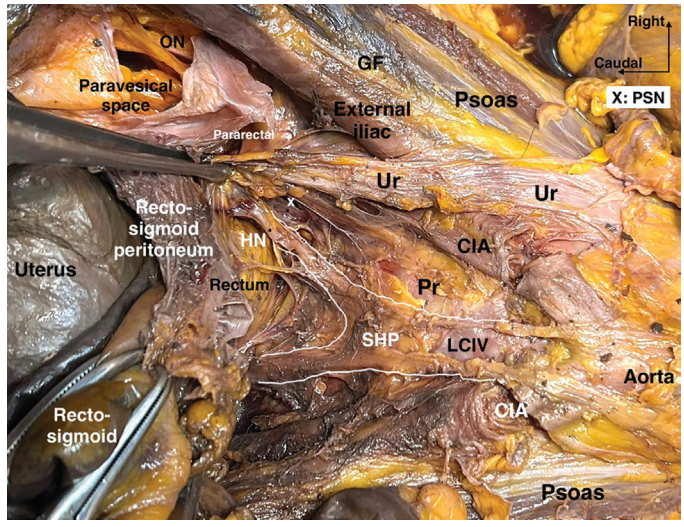


Figure 1. The presacral space, anterior to the sacrum and posterior to the rectum. Laterally, the common iliac artery and the ureter are visible. The left common iliac vein and the superior hypogastric plexus are important anatomical landmarks for the presacral space (All cadaveric dissections were performed by the author, MD-PhD İlker Selçuk, and his team)

CIA: Common iliac artery, Ur: Ureter, LCIV: Left common iliac vein, Pr: Promontorium, SHP: Superior hypogastric plexus, HN: Hypogastric nerve, ON: Obturator nerve, PSN: Pelvic splanchnic nerves, GF: Genitofemoral nerve

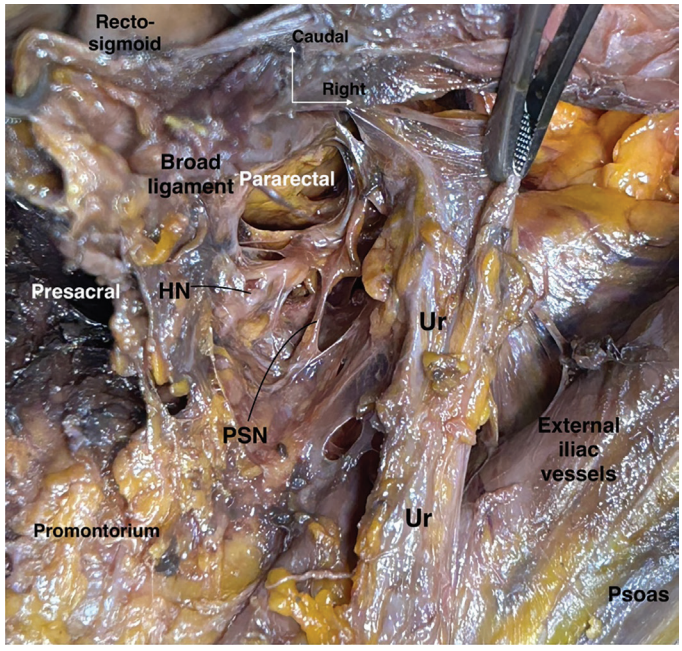


Figure 2. The anterolateral part of the presacral space with the hypogastric nerve and the pelvic splanchnic nerves. The presacral space is continuous with the pararectal space

Ur: Ureter, HN: Hypogastric nerve, PSN: Pelvic splanchnic nerves

Surgical Development (Step-by-Step)

1. Identification of the Sacral Promontory (Promontorium)

The sacral promontory is the key landmark for safe entry.
It marks the transition between the paraaortic and pelvic retroperitoneum.

2. Peritoneal Incision

The parietal peritoneum is incised:
• On the right, inferior to the radix mesenterii of the small bowel,
• On the left, along the Toldt's line after mobilization of the sigmoid colon.

3. Recognition of Critical Structures

Ureters are identified laterally.
The left common iliac vein is visualized anterior to the lumbar 5th vertebra, superior to the sacral promontory.
Superior hypogastric plexus is identified anterior to the left common iliac vein or lumbar 5th vertebra, attached to the retrorectal adipose tissue (posterior mesorectal plane).

4. Blunt Dissection

Dissection proceeds anterior to the presacral fascia.
Sharp dissection posterior to the presacral fascia must be avoided to prevent massive venous bleeding.

5. Caudal Extension

The space is deepened toward the pelvic floor.
The superior hypogastric plexus is divided into right and left hypogastric nerves.
Hypogastric nerves are followed caudally and caudolaterally at the anterior (anterolateral) part of the sacrum towards the pararectal spaces.
Proper development results in a bloodless midline surgical corridor that allows safe posterior pelvic mobilization.

Contents and Key Structures

Although the presacral space is considered avascular, its walls are closely associated with critical elements:
• Neural
Superior hypogastric plexus at the superior part, mixed nerve with dominantly sympathetic and also partially parasympathetic activity.
Bilateral hypogastric nerve lies caudolaterally at the anterolateral part of the sacrum and the posterolateral part of the rectum.
• Vascular
Median sacral artery and vein, posterior to presacral fascia.
Left common iliac vein, superiorly.
Common iliac artery, laterally.
• Fascial
Presacral (Waldeyer's) fascia, the posterior boundary, covering the sacrum.
• Lymphatic
Presacral lymphatic tissue (limited but clinically relevant).
Understanding these contents is essential to avoid catastrophic hemorrhage and autonomic nerve injury.

Surgical Applications

The presacral space has multiple critical applications in pelvic surgery:
• Radical hysterectomy
Provides a posterior access and dissection plane.
Enables safe identification and preservation of the superior hypogastric plexus and hypogastric nerve.
• Nerve-sparing surgery
Serves as the primary orientation plane for autonomic nerve preservation, the superior hypogastric plexus.
• Posterior pelvic resections
Essential for rectosigmoid mobilization.
Facilitates posterior or total pelvic exenteration.
• Ovarian cancer cytoreduction
Enables en bloc resection of the uterus, rectum, and sigmoid colon in cases of obliterated Douglas pouch.
• Hemorrhage control
Provides access to proximal vascular control when pelvic bleeding is encountered.
These applications emphasize the presacral space as a strategic posterior pelvic corridor rather than a simple anatomical cavity.

Key Surgical Insight

The presacral space is the anatomical gateway to the pelvic autonomic nervous system and to the identification of the ureter at the pelvic brim level. Respecting the presacral fascia is the single most important rule to prevent uncontrollable bleeding and nerve injury.

Pararectal Space

Definition and Surgical Concept

The pararectal space is a paired, retroperitoneal, avascular pelvic space located lateral to the rectum and medial to the internal iliac vascular system. It represents a critical surgical corridor within the posterior pelvic compartment, providing access to the uterosacral ligament, pelvic autonomic nerves, internal iliac vessels, and posterior (dorsal) parametrium. In gynecologic oncology, the pararectal space is essential for radical hysterectomy, nerve-sparing procedures, and posterior pelvic resections, serving as a key orientation space for differentiating vascular from neural planes.

Anatomical Boundaries (Figures 3 and 4)

The pararectal space is anatomically defined by the relationship between the rectum, ureter, and internal iliac system:

• Medial boundary:
Rectum,
Uterosacral ligament (posterior parametrium, rectouterine ligament/ligamentum rectouterinum),
Ureter, which divides the pararectal space into medial and lateral compartments.

• Lateral boundary:
Internal iliac artery and its branches (internal iliac vein is noticed inferior to the internal iliac artery).

• Anterior boundary:
Cardinal ligament (lateral parametrium, parauterine and paracervix tissue),
Uterine artery-vein complex with the pelvic autonomic nerves.

• Posterior boundary:
Sacrum,
Presacral fascia.

• Superior boundary:
Pelvic parietal peritoneum.

• Inferior boundary:
Levator ani muscle (iliococcygeus component).

These boundaries position the pararectal space at the crossroads of the vascular, neural, and visceral components of pelvic anatomy, making it one of the most critical pelvic spaces when approaching the frozen pelvis.

Subdivision of the Pararectal Space (Figure 5)

If the ureter is dissected and lateralized from the posterior leaf of the broad ligament, it is the key landmark dividing the pararectal space into two surgically distinct compartments:

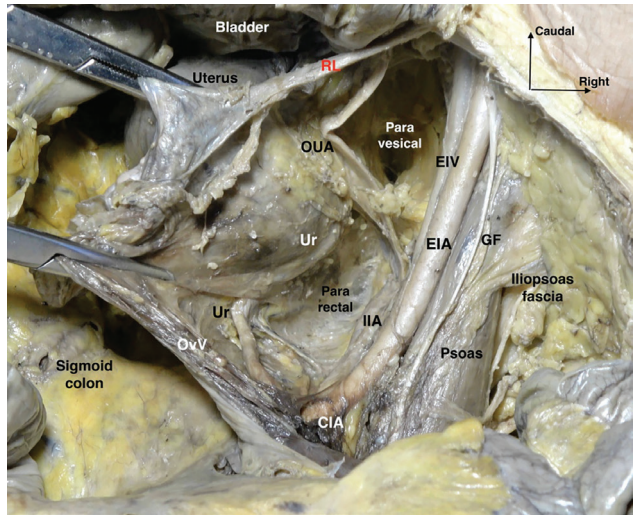


Figure 3. The anatomical boundaries of the pararectal and paravesical spaces after cutting the pelvic lateral parietal peritoneum and broad ligament

CIA: Common iliac artery, EIA: External iliac artery, EIV: External iliac vein, IIA: Internal iliac artery, GF: Genitofemoral nerve, RL: Round ligament, OvV: Ovarian vessels, OUA: Obliterated umbilical artery, Ur: Ureter

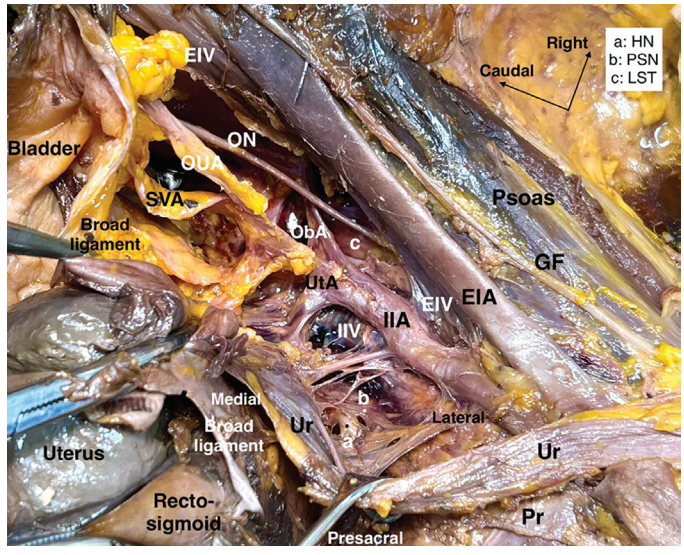


Figure 4. The pararectal and paravesical space with the obturator fossa and main anatomical components

EIA: External iliac artery, EIV: External iliac vein, IIA: Internal iliac artery, IIV: Internal iliac vein, GF: Genitofemoral nerve, HN: Hypogastric nerve, LST: Lumbosacral trunk, ObA: Obturator artery, ON: Obturator nerve, OUA: Obliterated umbilical artery, Pr: Promontory, PSN: Pelvic splanchnic nerves, SVA: Superior vesical artery, Ur: Ureter, UtA: Uterine artery

1. Lateral pararectal space (Latzko space)

Located between the ureter (medially) and the internal iliac artery (laterally),

Primarily vascular in orientation, following the internal iliac artery will lead to the uterine artery, which is the first

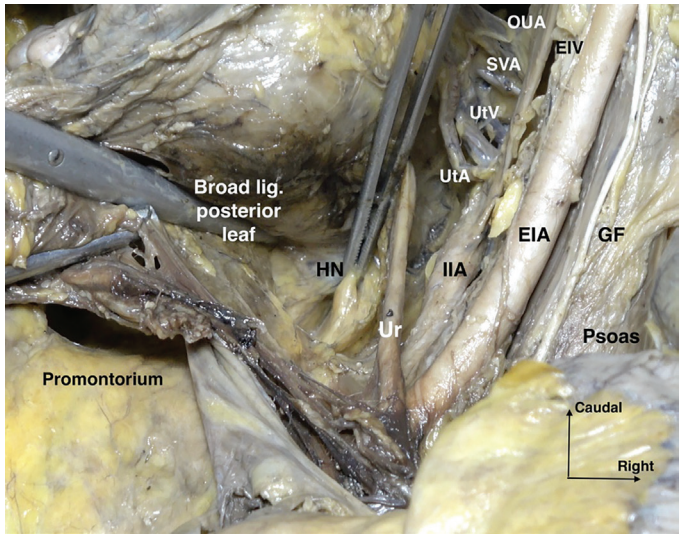


Figure 5. The medial pararectal space and the hypogastric nerve after dissection and lateralization of the ureter from the broad ligament posterior leaf

GF: Genitofemoral nerve, EIA: External iliac artery, EIV: External iliac vein, IIA: Internal iliac artery, Ur: Ureter, HN: Hypogastric nerve, UtA: Uterine artery, UtV: Uterine vein, SVA: Superior vesical artery, OUA: Obliterated umbilical artery, lig: Ligament

anteromedial branch arising from the internal iliac artery,
Contains the origin and proximal parts of the pelvic splanchnic nerves.

2. Medial pararectal space (Okabayashi space)

Located between the ureter (laterally) and the rectum/uterosacral ligament (medially),
Contains critical pelvic autonomic nerve structures, the hypogastric nerve, caudal (medial distal) parts of the pelvic splanchnic nerves, and the inferior hypogastric plexus,
This subdivision is fundamental to nerve-sparing surgical procedures (radical hysterectomy, endometriosis surgery, mesorectal resection) because neural elements are concentrated in the medial compartment.

Surgical Development (Step-by-Step)

1. Retroperitoneal entry

Achieved by incising the lateral parietal peritoneum:
• Cut the pelvic lateral parietal peritoneum, along and lateral to the infundibulopelvic ligament (ovarian vessels),
• Or medial approach, medial to the infundibulopelvic ligament, cut the posterior leaf of the broad ligament, and notice that the ureter is attached to the posterior leaf of the broad ligament inferior to the ovarian vessels.

2. Identification of the ureter

The ureter is identified at the pelvic brim, crossing over the common iliac vessels,
It is followed caudally along the posterior leaf of the broad ligament, inferior to the ovarian vessels.

3. Creation of the lateral pararectal space (Latzko)

Blunt dissection between the ureter and the internal iliac artery,
Develops a relatively avascular plane anterior to the sacrum.

4. Development of the medial pararectal space (Okabayashi)

After mobilization or lateralization of the ureter from the broad ligament posterior leaf,
Dissection proceeds between the ureter and rectum/uterosacral ligament.

5. Caudal maturation

The space deepens toward the pelvic floor and the levator ani.
Notice the internal iliac vein inferior (inferior in surgical supine position, posterior in anatomical position) to the internal iliac artery.
The hypogastric nerve, at the medial pararectal space, inferior to the ureter and attached to the perirectal visceral fascia, becomes identifiable (sympathetic activity). The ureter and the hypogastric nerve lie within the same fascial sheet, the ureterohypogastric fascia.
The pelvic splanchnic nerves, located in the lateral pararectal space at the inferomedial aspect of the internal iliac vein, arise from the sacral 2-4 foramina (parasympathetic activity). They lie obliquely medial to the paracervix and are attached to the paracervix inferior to the deep uterine or vaginal vein.
The hypogastric nerve and the pelvic splanchnic nerves merge to form the inferior hypogastric plexus at the medial part of the paracervix, inferior to the level of the (deep) uterine vein, which is a mixed ganglion with parasympathetic and sympathetic innervation.
Correct development creates a bloodless, anatomically stratified space, permitting precise oncologic and nerve-preserving dissection.

Contents and Key Structures

Although avascular, the pararectal space is closely related to critical structures:
• Neural
Hypogastric nerve, medially,
Pelvic splanchnic nerves, laterally,
Inferior hypogastric plexus, at the medial caudal compartment, closely related to the medial paracervix, lateral to the rectum and posterolateral to the upper vagina.
• Vascular
Internal iliac artery branches, in the lateral compartment,
Uterine artery, at the anterior part, superior to the ureter,
Deep uterine vein, at the anterior part, inferior to the ureter.
• Fascial
Uterosacral ligament, medially,
Presacral fascia, posteriorly.

• Visceral
Rectum, medially,
Ureter, central landmark.
• Beyond the pelvic brim, the ureter lies caudomedially within the medial aspect of the pararectal space, is situated inferior to the ovarian vessels, and is attached to the posterior leaf of the broad ligament. Between the pararectal and paravesical spaces, the ureter lies medially, interposed between the parauterine tissue—comprising the uterine artery and associated lymphatic structures (parauterine lymphatic tissue, PULT) located superior to the ureter—and the paracervix, which contains the (deep) uterine vein and related lymphatic tissue, along with the distal segments of the pelvic splanchnic nerves. Following this junction, the ureter traverses the ureteric tunnel in the lateral aspect of the upper vagina, lying between the vesicouterine ligament superiorly and the vesicovaginal ligament inferiorly. Subsequently, the ureter enters the bladder at the trigone. The vesicouterine ligament contains cervicovesical vessels, whereas the vesicovaginal ligament lies adjacent to the vesicovaginal venous plexus and bladder nerve branches. Moreover, the vesicovaginal ligament is continuous with the lateral paracervix.
Recognition of these structures is mandatory to avoid injury to the autonomic nerves and to prevent pelvic organ dysfunction.

Surgical Applications

The pararectal space is indispensable in advanced pelvic surgery.
• Radical hysterectomy
Enables posterior and lateral parametrial resection,
Essential for Querleu-Morrow type B and C procedures.
• Nerve-sparing surgery and ureteric dissection
Allows identification and preservation of the hypogastric nerve and inferior hypogastric plexus with the ureteric dissection and mobilization,
The pelvic splanchnic nerves can be identified and dissected from the paracervix.
• Pelvic lymphadenectomy
Provides orientation for obturator and internal iliac nodal dissection.
• Posterior pelvic resections
Facilitates rectosigmoid mobilization,
Essential in posterior or total pelvic exenteration.
• Complex pelvic and oncologic surgery
Crucial when the rectouterine (Douglas) pouch is obliterated by tumor or fibrosis.
• Hemorrhage control
Provides access to proximal vascular control (internal iliac and uterine arterty) when pelvic bleeding is encountered,
These applications underline the role of the pararectal space as a surgical neurovascular roadmap.

Paravesical Space

Definition and Surgical Concept

The paravesical spaces are bilateral, avascular, retroperitoneal spaces situated lateral to the urinary bladder within the pelvis. It constitutes an essential surgical corridor in the anterior pelvic compartment, facilitating secure access to the lateral pelvic wall, bladder, and parametrial structures. In gynecologic oncology surgery, the paravesical space serves as a key landmark for pelvic lymphadenectomy, radical hysterectomy, nerve-sparing procedures, and hemorrhage management.

Anatomical Boundaries (Figures 3 and 4)

The paravesical space is best understood in relation to the bladder medially and the pelvic sidewall laterally.
• Medial boundary:
Urinary bladder,
Pubocervical ligament,
Obliterated umbilical artery (OUA), which divides the paravesical space into medial and lateral compartments.
• Lateral boundary:
The external iliac vessels are observed along the medial aspect of the psoas major muscle. The external iliac artery lies medial to the psoas major muscle, and the external iliac vein lies inferomedial to the artery. The caudal (distal) ends of these vessels constitute the lateral boundary of the paravesical space.
Obturator internus muscle and fascia.
• Anterior boundary:
Superior pubic ramus, pubic bone,
Retropubic (prevesical) space lateral continuity.
• Posterior boundary:
Cardinal ligament [lateral parametrium, parauterine tissue (uterine artery) and paracervix tissue (uterine vein and pelvic autonomic nerves)],
Proximal internal iliac artery branches.
• Inferior boundary:
Pelvic floor (levator ani muscle, pubococcygeus and iliococcygeus).
• Superior boundary:
Pelvic parietal peritoneum, broad ligament anterior leaf,
These boundaries place the paravesical space at the intersection of vascular, neural, and lymphatic surgical planes, emphasizing its importance in oncologic dissection.

Subdivision of the Paravesical Space (Figure 6)

If the OUA is dissected and lateralized from the perivesical visceral fascia and fatty tissue (the umbilicovesical fascia), it is the key landmark dividing the paravesical space into two distinct compartments:

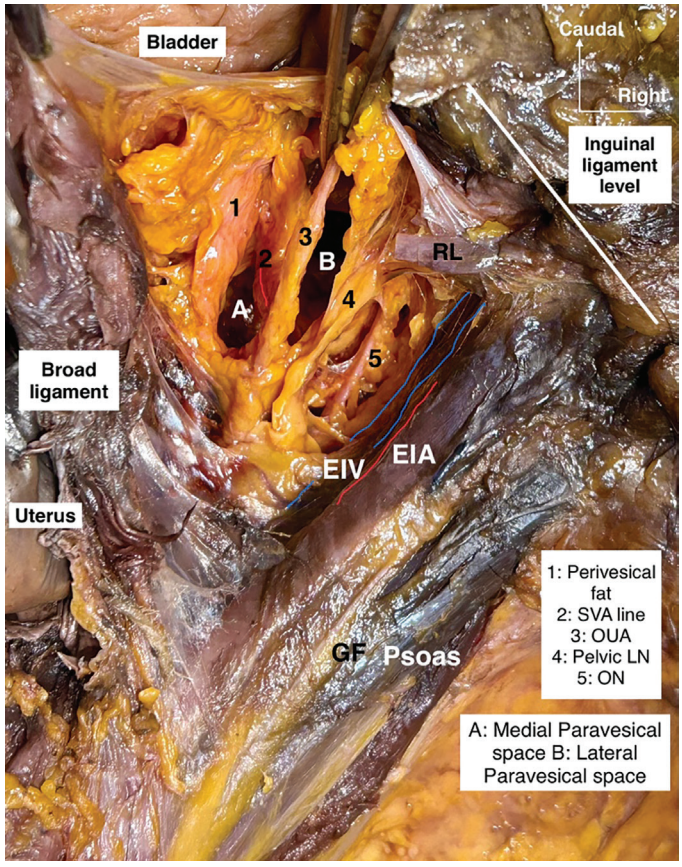


Figure 6. The medial and lateral paravesical space after dissection and lateralization of the OUA from the perivesical fatty tissue

GF: Genitofemoral nerve, EIA: External iliac artery, EIV: External iliac vein, RL: Round ligament, ON: Obturator nerve, LN: Lymph node, OUA: Obliterated umbilical artery, SVA: Superior vesical artery

1. Medial paravesical space

Located between the bladder and the OUA,
Closely related to the anterior (ventral) parametrium and bladder vascular supply.

2. Lateral paravesical space

Located between the OUA and the external iliac vessels,

Continuous laterally with the obturator fossa,
This subdivision is surgically critical because pelvic lymph node dissection is performed through the lateral paravesical compartment, whereas nerve-sparing parametrial dissection of the anterior parametrium is performed through the medial paravesical compartment.

Obturator Fossa

The obturator fossa represents the lateral extension, at the inferior aspect of the external iliac vein, of the lateral paravesical space. Its lateral boundary is delineated by the obturator internus muscle, with the obturator nerve positioned medially relative to the obturator lymph nodes. The obturator nerve exits the pelvis via the obturator canal, located at the superolateral portion of the obturator foramen. The superior margin of the obturator foramen corresponds to the superior pubic ramus. The pelvic anastomotic branches between the obturator vessels and either the inferior epigastric or external iliac vessels are called Corona Mortis vessels (pubic vessels) and are situated over the lateral aspect of the superior pubic ramus. These vessels are predominantly venous anastomoses, with their branches extending from the medial side of the obturator nerve towards the obturator canal. The obturator vessels are generally located inferior to the obturator nerve. In the cranial part of the obturator fossa, the internal iliac vein is located medial to the obturator nerve.

Surgical Development (Step-by-Step)

1. Retroperitoneal entry

Achieved by incising the pelvic lateral parietal peritoneum:
• Either by transecting the round ligament, or,
• Between the round ligament and the infundibulopelvic ligament,
• Or directly anterior to the round ligament (broad ligament anterior leaf).

2. Identification of landmarks

External iliac artery and vein laterally,
OUA medially,
Pubic bone anteriorly.

3. Blunt dissection

Gentle blunt dissection between the bladder medially and the pelvic sidewall laterally opens the paravesical space,
The loose areolar tissue allows atraumatic development.

4. Space maturation

The space is deepened caudally toward the pelvic floor (levator ani, pubococcygeus, iliococcygeus),
Posteriorly, it connects with the pararectal space at the level of the cardinal ligament (lateral parametrium),
Proper development creates a bloodless, anatomically oriented working field, essential for safe pelvic surgery.

Contents and Key Structures

The paravesical space itself is avascular, but its walls are closely related to critical structures:
• Vascular
Superior vesical artery at the posteromedial part,
Proximal branches of the internal iliac artery at the posterior part.
• Neural
Obturator nerve, laterally, in continuity with the obturator fossa.
• Lymphatic
External iliac lymph nodes,
Obturator lymph nodes, accessed via lateral paravesical extension,

PULT along the uterine artery at the posterior part, the supraureteric lymphatic pathway crossing over the OUA.

• Fascial

Pelvic parietal fascia, levator fascia inferiorly and obturator fascia laterally,

Tendinous arch of levator ani between the levator ani and obturator internus muscle fascia,

Paracervical connective tissue,

Understanding these relationships permits safe dissection and helps avoid vascular or nerve injury.

Surgical Applications

The paravesical space is indispensable in modern gynecologic oncology surgery:

• Pelvic lymphadenectomy

Provides direct access to the external iliac and obturator nodes.

• Radical hysterectomy

Facilitates identification and dissection of the paracervix and anterior parametrium,

Enables separation of the bladder from the cervix and upper vagina.

• Nerve-sparing surgery

Serves as an orientation space for preserving bladder branches of the inferior hypogastric plexus

After the vesicouterine ligament has been dissected from the superior portion of the distal ureter, the paravaginal space (Yabuki's space) can be developed between the vagina and the ureter. Inferiorly, the vesicovaginal ligament can be identified, and the bladder nerve branches of the inferior hypogastric plexus (vesical branches, parasympathetic activity) can be dissected between the ligament and the lateral paracervical tissue. At this location, the vesicovaginal venous plexus lies close to the bladder nerve branches.

• Hemorrhage control

Allows safe exposure of the internal iliac artery branches, the uterine artery,

Essential for stepwise internal iliac artery ligation.

• Pelvic exenteration and complex resections

Acts as an anterior access corridor when posterior planes are distorted, important for bladder resections,

These applications highlight the paravesical space as a foundational anatomic unit rather than a dissection cavity.

Key Surgical Insights for the Pararectal and Paravesical Spaces (Figures 7-12)

The pararectal space serves as the gateway to preservation of pelvic autonomic nerves; correct development of this space distinguishes modern nerve-sparing oncologic surgery from purely radical resection. Mastery of the paravesical space transforms pelvic surgery from an organ-based dissection to a space-oriented surgery, reducing morbidity while maintaining radicality.

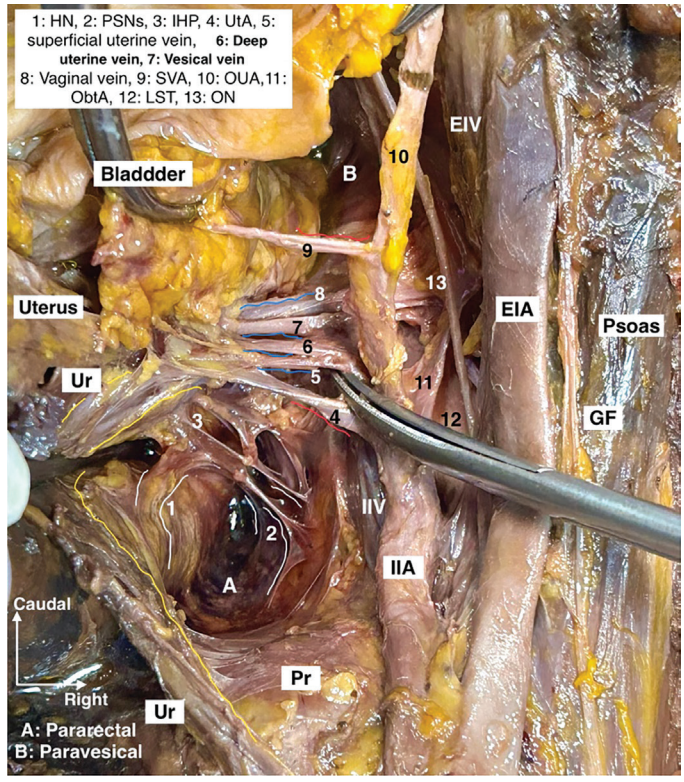


Figure 7. The lateral parametrium situated between the pararectal and paravesical spaces, along with the corresponding anatomical components. The lateral parametrium, which has historically been referred to as the cardinal ligament, is not a suspensory ligament; rather, it predominantly consists of cellulolymphatic tissue that contains the uterine artery, the uterine vein, the vesical veins, and the distal portions of the pelvic splanchnic nerves, arranged from superior to inferior. The ureter lies between the uterine artery (superior) and the uterine vein (inferior). "4-5" constitutes the parauterine tissue, and "6-8" constitutes the paracervix tissue

EIA: External iliac artery, EIV: External iliac vein, IIA: Internal iliac artery, IIV: Internal iliac vein, GF: Genitofemoral nerve, HN: Hypogastric nerve, IHP: Inferior hypogastric plexus, LST: Lumbosacral trunk, ObtA: Obturator artery, ON: Obturator nerve, OUA: Obliterated umbilical artery, Pr: Promontory, PSNs: Pelvic splanchnic nerves, SVA: Superior vesical artery, Ur: Ureter, UtA: Uterine artery

Prevesical Space (Retropubic Space of Retzius) Definition and Surgical Concept

The prevesical space, also known as the retropubic space of Retzius, is a midline, anterior, extraperitoneal, avascular compartment located between the posterior surface of the pubic bone and the anterior wall of the urinary bladder. It represents the most anterior avascular space of the pelvis and constitutes the primary surgical corridor of the anterior pelvic compartment. In pelvic surgery, the prevesical space is essential for anterior pelvic orientation, bladder mobilization, and access to the paravesical spaces.

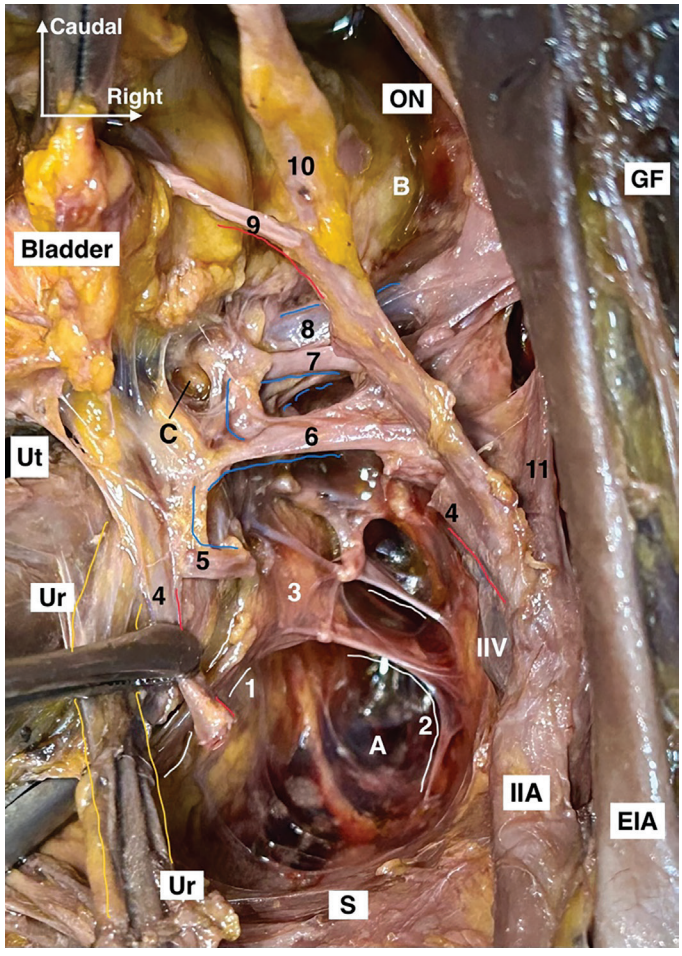


Figure 8. The lateral parametrium and pelvic autonomic nerves within the pararectal and paravesical spaces. The parauterine tissue, uterine artery, and accompanying superficial uterine vein are dissected from the superior part of the ureter. "4-5" constitutes the parauterine tissue and "6-8" constitutes the paracervix tissue

A: Pararectal space, B: Paravesical space, C: Paravaginal space, EIA: External iliac artery, IIA: Internal iliac artery, IIV: Internal iliac vein, GF: Genitofemoral nerve, ON: Obturator nerve, S: Sacrum, Ur: Ureter, Ut: Uterus, 1: Hypogastric nerve, 2: Pelvic splanchnic nerves, 3: Inferior hypogastric plexus, 4: Uterine artery, 5: Superficial uterine vein, 6: Deep uterine vein, 7: Vesical vein, 8: Vaginal vein, 9: Superior vesical artery, 10: Obliterated umbilical artery, 11: Obturator artery

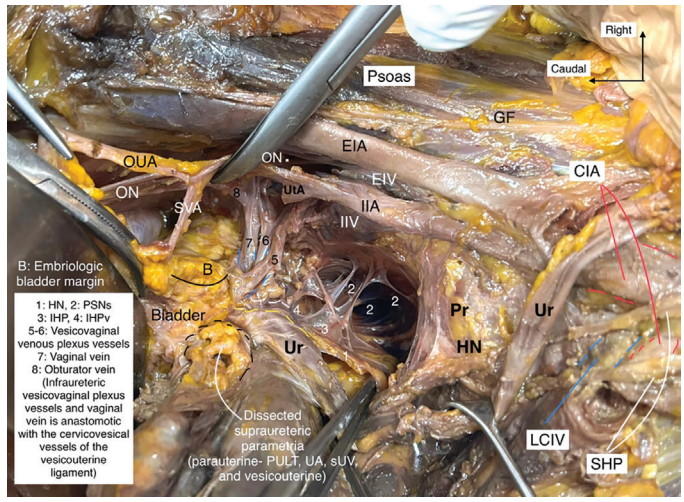


Figure 9. Deep caudal dissection of the pararectal and paravesical spaces, exposing the paracervix, vesicovaginal venous plexus, and pelvic autonomic nerves. All the supraureteric parametria are dissected and mobilized craniomedially. The "5-7" region, defined as the lateral continuity of vesicovaginal venous plexus vessels and the vaginal vein, constitutes the lateral paracervix

CIA: Common iliac artery, EIA: External iliac artery, EIV: External iliac vein, IIA: Internal iliac artery, IIV: Internal iliac vein, GF: Genitofemoral nerve, HN: Hypogastric nerve, LCIV: Left common iliac vein, ON: Obturator nerve, OUA: Obliterated umbilical artery, Pr: Promontory, PULT: Parauterine lymphatic tissue, SHP: Superior hypogastric plexus, sUV: Superficial uterine vein, SVA: Superior vesical artery, UA: Uterine artery, UtA: Uterine artery, Ur: Ureter, 1-HN: Hypogastric nerve, 2-PSNs: Pelvic splanchnic nerves, 3-IHP: Inferior hypogastric plexus, 4-IHP-v: Inferior hypogastric plexus vesical branches (bladder branches)

Anatomical Boundaries (Figure 13)

• Anterior boundary:
Posterior surface of the pubic symphysis and pubic bone.
• Posterior boundary:
Anterior wall of the urinary bladder.
• Lateral boundaries:
Pubocervical ligaments,
OUA,
Transition to the bilateral paravesical spaces.
• Superior boundary:
Anterior parietal peritoneum, reflection over the bladder dome.
• Inferior boundary:
Pelvic floor,
Endopelvic fascia(corresponds to the en bloc structure of the visceral fascia of the bladder and pelvic parietal fascia over the levator ani, pubocervical fascia),
The inferolateral border is the tendinous arch of pelvic fascia,
These boundaries position the prevesical space as a central, anterior, avascular plane that is continuous laterally with the paravesical spaces.

Surgical Development (Step-by-Step)

1. Anterior peritoneal mobilization

The bladder peritoneum is gently mobilized caudally from the anterior abdominal wall at the posterior aspect of the rectus abdominis muscle. The urachus is visible, extending from the bladder apex to the umbilicus.
This exposes the extraperitoneal plane above the bladder dome.

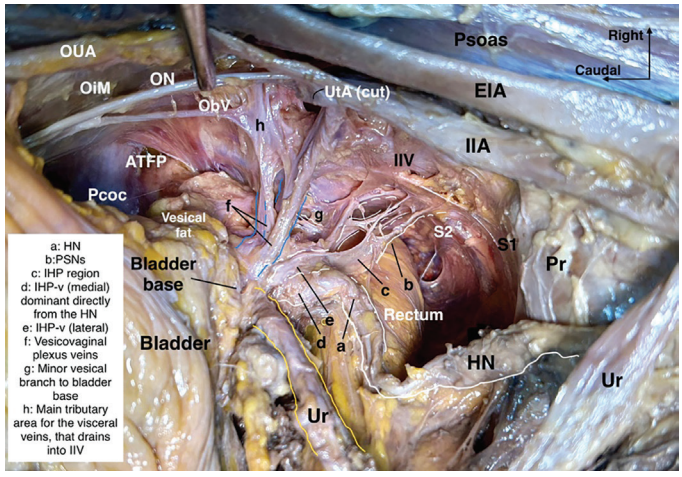


Figure 10. After total dissection of the supraureteric parametria with the medial paracervix, the anatomic exposure reveals the lateral paracervix with the vesicovaginal venous plexus and vaginal vein/deep uterine vein. The hypogastric nerve is exposed medially, inferior to the ureter, and the pelvic splanchnic nerves are dissected from the medial part of the internal iliac vein and selectively separated from the paracervix. The inferior hypogastric plexus is identified in the paracervical area; its vesical branches lie paravaginally between the vesicovaginal ligament and the lateral paracervix. "f" region, the lateral continuity of vesicovaginal plexus veins, constitutes the lateral paracervix

ATFP: Arcus tendineus fascia pelvis, EIA: External iliac artery, IIA: Internal iliac artery, IIV: Internal iliac vein, ObV: Obturator vein, OiM: Obturator internus muscle, ON: Obturator nerve, OUA: Obliterated umbilical artery, Pcoc: Pubococcygeus, Pr: Promontory, S: Sacrum, Ur: Ureter, UtA: Uterine artery, HN: Hypogastric nerve, a-HN: Hypogastric nerve, b-PSNs: Pelvic splanchnic nerves, c-IHP: Inferior hypogastric plexus, d-IHP-v: Inferior hypogastric plexus vesical branches (bladder branches)

2. Midline entry

Blunt dissection is initiated in the midline between the bladder and pubic symphysis,

Loose areolar tissue allows atraumatic entry, slightly lateral to the bladder neck, bilaterally.

3. Space expansion

Dissection proceeds caudally, along the lateral aspect of the urethra,

The bladder is gently displaced posteriorly.

4. Lateral extension

The space is widened bilaterally,

Continuity with the paravesical spaces is established,

Correct development creates a bloodless retropubic working space, enabling safe anterior pelvic surgery.

Contents and Key Structures

The prevesical space itself is avascular but contains and is closely related to critical structures:

• Vascular

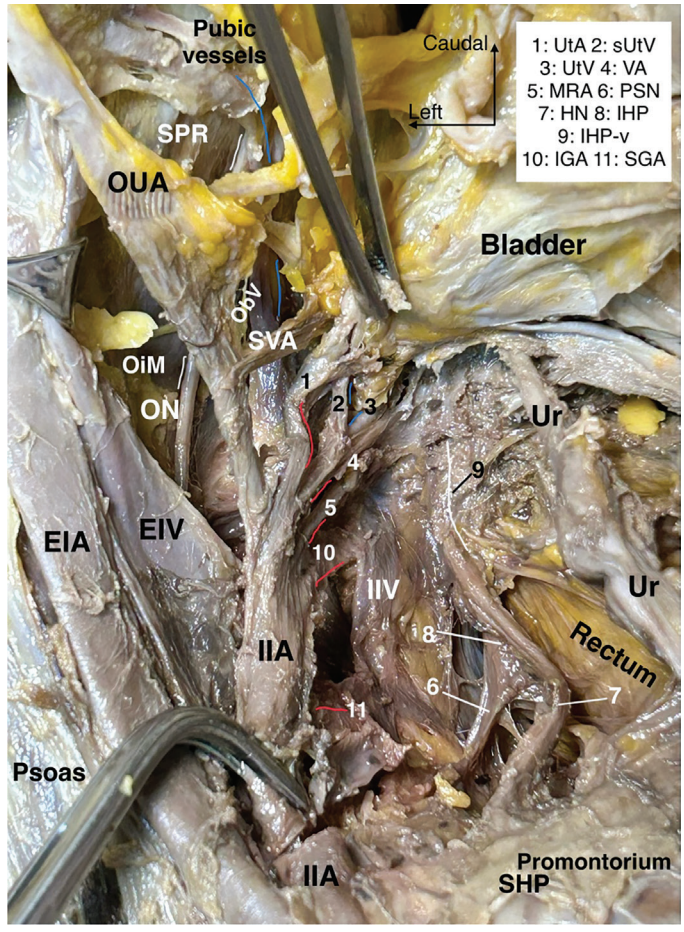


Figure 11. The pararectal and paravesical spaces, along with their anatomical components, as well as the branches of the internal iliac artery situated along the lateral parametrium ("1-4" in the figure)

EIA: External iliac artery, EIV: External iliac vein, IIA: Internal iliac artery, IIV: Internal iliac vein, ON: Obturator nerve, OiM: Obturator internus muscle, ObV: Obturator vein, SPR: Superior pubic ramus, OUA: Obliterated umbilical artery, SVA: Superior vesical artery, SHP: Superior hypogastric plexus, Ur: Ureter, 1/UtA: Uterine artery, 2/sUtV: Superficial uterine vein, 3/UtV: Uterine vein, 4/VA: Vaginal artery, 5/MRA: Middle rectal artery, 6/PSN: Pelvic splanchnic nerves, 7/HN: Hypogastric nerve, 8/IHP: Inferior hypogastric plexus, v: Vesical branches, 10/IGA: Inferior gluteal artery, 11/SGA: Superior gluteal artery

Retropubic venous plexus (Santorini plexus), lateral to the urethra at the deep paravaginal compartment,

Small pubic veins.

• Fascial

Endopelvic fascia, pubocervical fascia,

Pubovesical ligaments.

• Visceral

Urinary bladder, posteriorly,

Because of the proximity of the retropubic venous plexus, meticulous blunt dissection is essential to avoid significant bleeding.

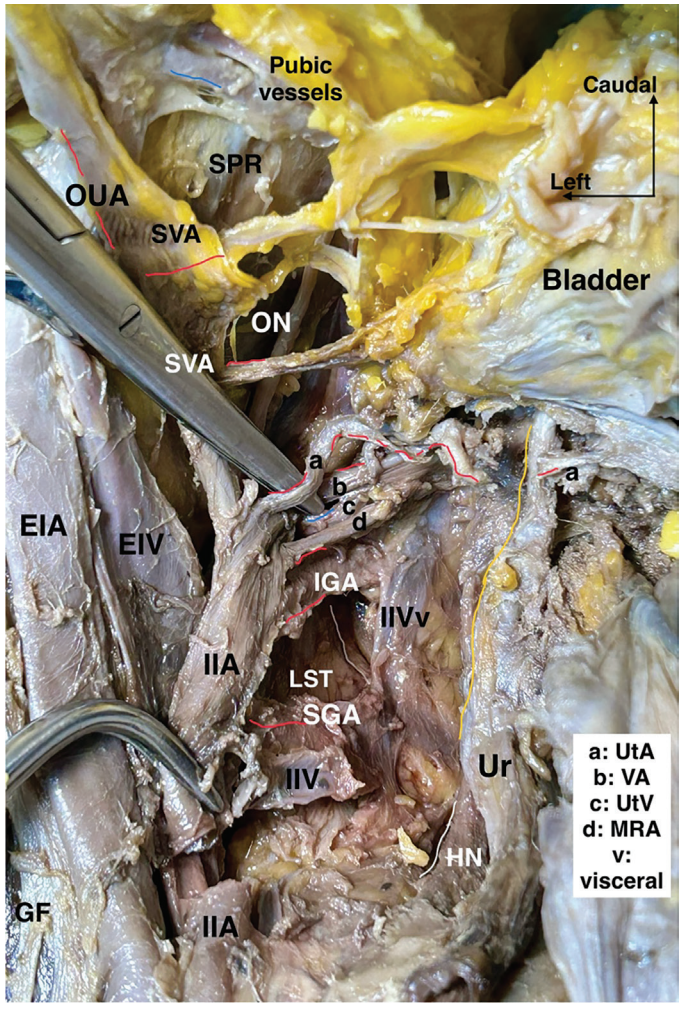


Figure 12. The pararectal and paravesical spaces, emphasizing the neurovascular anatomy associated with the lateral parametrium ("a-c" in the figure)

GF: Genitofemoral nerve, EIA: External iliac artery, EIV: External iliac vein, IIA: Internal iliac artery, IIV: Internal iliac vein, ON: Obturator nerve, SPR: Superior pubic ramus, OUA: Obliterated umbilical artery, SVA: Superior vesical artery, a/UtA: Uterine artery, b/VA: Vaginal artery, c/UtV: Uterine vein, d/MRA: Middle rectal artery, IGA: Inferior gluteal artery, SGA: Superior gluteal artery, LST: Lumbosacral trunk, HN: Hypogastric nerve, Ur: Ureter

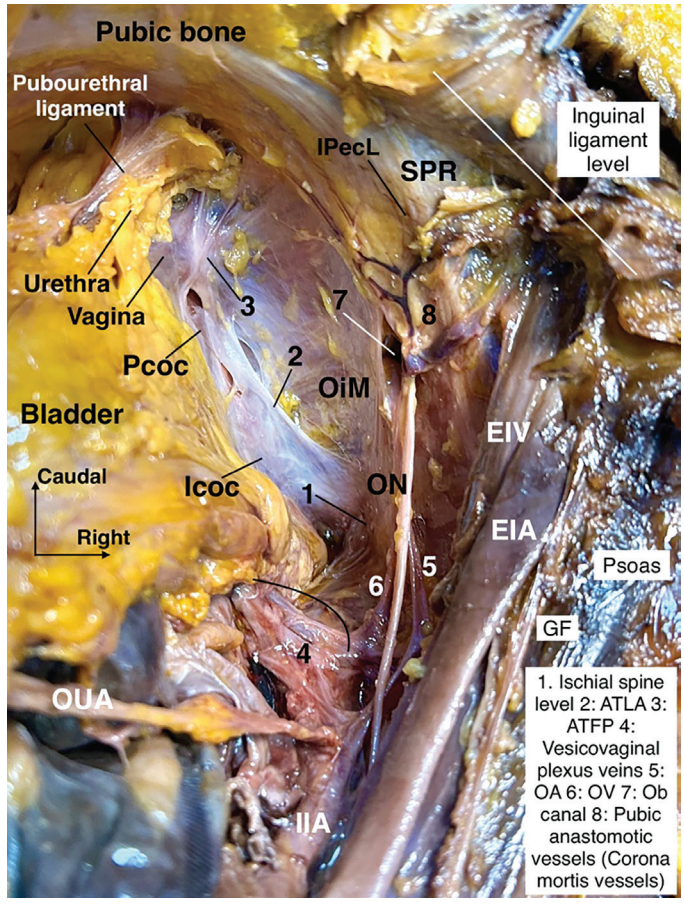


Figure 13. The prevesical space in continuation with the paravesical space. The pelvic support fascia, tendinous arch of pelvic fascia, as a condense parietal fascia between the lavator ani and obturator internus muscle. Corona Mortis, anastomotic pubic vessels, lying over the superior pubic ramus

EIA: External iliac artery, EIV: External iliac vein, Icoc: Iliococcygeus, IIA: Internal iliac artery, IPecL: Pectineal ligament, GF: Genitofemoral nerve, OiM: Obturator internus muscle, ON: Obturator nerve, OUA: Obliterated umbilical artery, Pcoc: Pubococcygeus, SPR: Superior pubic ramus, ATLA: Arcus tendineus levator ani, ATFP: Arcus tendineus fascia pelvis, OA: Obturator artery, OV: Obturator vein, Ob: Obturator

Surgical Applications (Figure 14)

The prevesical space has multiple important surgical applications:

• Radical hysterectomy

Enables anterior bladder mobilization,

Facilitates the separation of the bladder from the cervix and upper vagina in complex cases.

• Pelvic lymphadenectomy

Provides orientation for anterior pelvic anatomy before entering paravesical spaces in frozen pelvis cases.

• Hemorrhage control

Allows exposure and compression of the retropubic venous structures.

• Pelvic exenteration

Serves as the anterior dissection plane in anterior or total pelvic exenteration.

• Reconstructive and urogynecologic procedures

Provides access for retropubic sling placement (conceptually relevant for anatomical orientation), transvaginal tape procedure,

Pectineal ligament suspension (Cooper's ligament, Burch procedure),

These applications highlight the prevesical space as a foundational anterior pelvic corridor rather than a simple anatomical cavity.

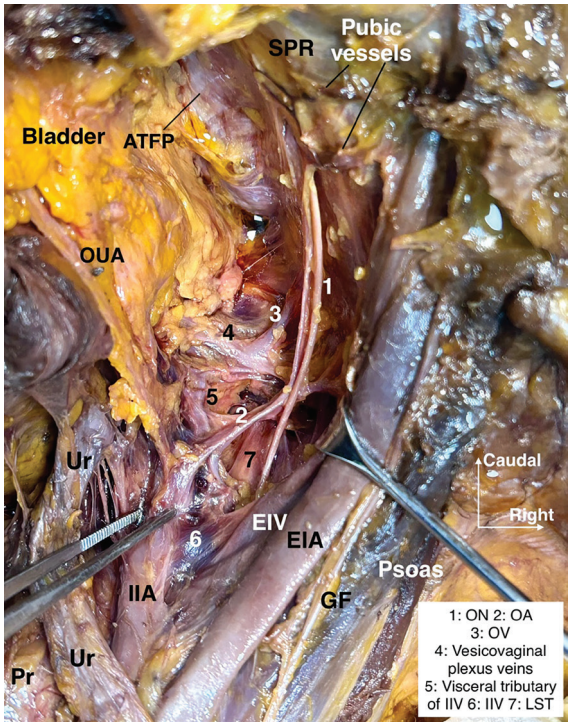


Figure 14. Lateral pelvic wall, the corridor along the prevesical and paravesical spaces, the interiliac region, and the medial psoas space

GF: Genitofemoral nerve, EIA: External iliac artery, EIV: External iliac vein, IIA: Internal iliac artery, IIV: Internal iliac vein, Ur: Ureter, Pr: Promontorium, OUA: Obliterated umbilical artery, ATFP: Arcus tendineus fascia pelvis, SPR: Superior pubic ramus, ON: Obturator nerve, OA: Obturator artery, OV: Obturator vein, LST: Lumbosacral trunk

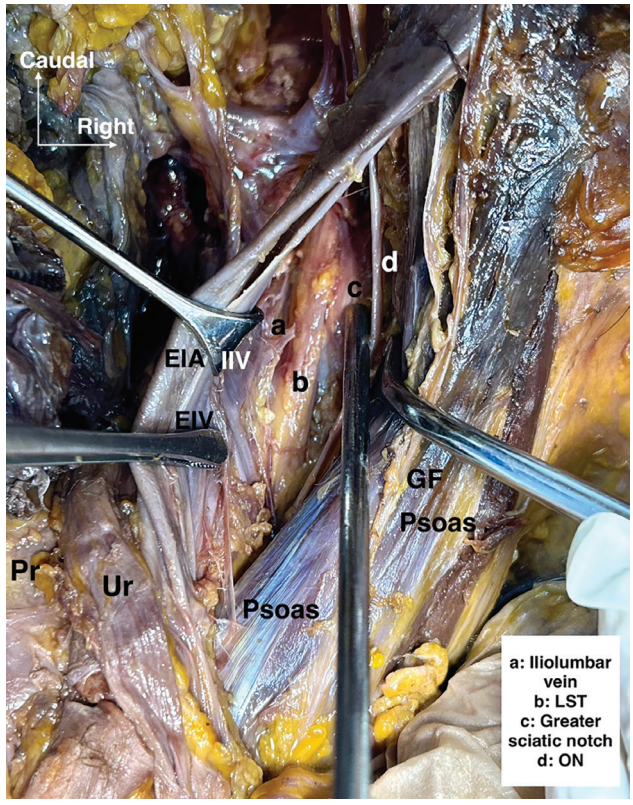


Figure 15. The laterovascular plane, medial psoas space, revealing the obturator nerve and lumboscaral trunk with the obturator and paracervical lymph nodes

EIA: External iliac artery, EIV: External iliac vein, IIV: Internal iliac vein, GF: Genitofemoral nerve, Pr: Promontory, Ur: Ureter, LST: Lumbosacral trunk, ON: Obturator nerve

Key Surgical Insight

The prevesical space is the anatomical starting point of anterior pelvic surgery; gentle midline blunt dissection and respect for the retropubic venous plexus are essential to maintain a bloodless field.

Medial Psoas Space (Laterovascular Plane) Definition and Surgical Concept

The medial psoas space, also referred to as the laterovascular plane, is a retroperitoneal anatomical plane located medial to the psoas major muscle and lateral to the iliac vessels. It is not a classical "avascular space," such as the paravesical or pararectal spaces, but rather a longitudinal dissection plane that serves as the lateral boundary for pelvic vascular and lymphatic dissection. This plane is fundamental for pelvic and paracervical lymphadenectomy, for safe exposure of the iliac vessels, the obturator region (including the obturator nerve) and the lumbosacral trunk, and for providing a stable anatomical reference along the pelvic sidewall.

Anatomical Boundaries (Figure 15)

The medial psoas space is defined by consistent muscular, vascular, and fascial landmarks:

• Lateral boundary:
Psoas major muscle,
Psoas fascia.
• Medial boundary:
External iliac artery and vein,
Internal iliac vein,
Common iliac vessels (cranially).
• Anterior boundary:
Retroperitoneal fatty-lymphatic tissue.
• Posterior boundary:
Psoas major muscle body.
• Superior boundary:
Pelvic brim, linea terminalis,
Overlying parietal peritoneum.
• Inferior boundary:
Obturator fossa region,

These boundaries position the medial psoas space as the lateral limit of pelvic oncologic dissection and the entry plane into the obturator and sacral compartments.

Surgical Development (Step-by-Step)

1. Retroperitoneal entry

Achieved by incising the pelvic lateral parietal peritoneum:
• After transection of the round ligament, or,
• Between the round ligament and the infundibulopelvic ligament.

2. Identification of the psoas major

The psoas major muscle is visualized as the first constant structure,
Its medial border defines the lateral limit of safe pelvic dissection.

3. Exposure of the vascular structures

The external iliac artery and vein are identified medial to the psoas major muscle,
Retroperitoneal lymphatic tissue and external iliac vessels are gently mobilized medially (during this step, a psoas vessel branch can be noticed).

4. Development of the laterovascular plane

Blunt dissection proceeds along the medial surface of the psoas major muscle,
This creates a longitudinal plane separating the iliac vessels from the muscle.

5. Caudal extension

The plane is followed inferiorly toward the obturator fossa,
The obturator nerve becomes visible at the superficial caudal extent, where it emerges from the posteromedial part of the psoas muscle,
Medially, the internal iliac vein can be noticed,
Inferior to the obturator nerve, the lumboscaral trunk can be dissected, at the inferomedial part cranially, and at the inferolateral part caudally,
Between the obturator nerve and the lumbosacral trunk, the iliolumbar vessels may lie. they drain into the internal iliac vein, Correct development produces a clean, tension-free lateral boundary, enabling safe nodal dissection without vascular or neural injury. Furthermore, the laterovascular plane and the caudal region of the lumbosacral trunk are accessible through the medial approach (Figure 14). During the surgical procedure, the internal iliac artery and vein, along with their associated vessels, may be sacrificed entirely or partially. Additionally, the inter-iliac region, situated between the external and internal iliac vessels, may be utilized.

Contents and Related Key Structures (Figure 16)

The medial psoas space contains or exposes several critical structures:
• Neural
Genitofemoral nerve, running on the anterior surface of the psoas muscle, lateral to the external iliac artery,
Obturator nerve, caudally, at the obturator fossa,

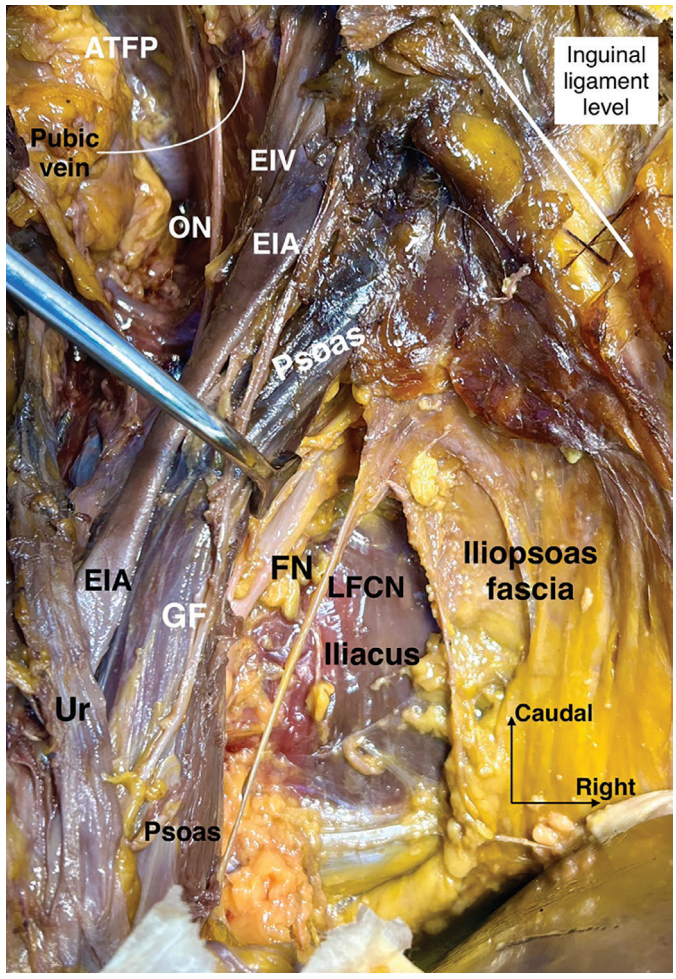


Figure 16. The iliopsoas plane revealing the femoral nerve between the psoas major and iliacus muscles

ATFP: Arcus tendineus fascia pelvis, EIA: External iliac artery, EIV: External iliac vein, FN: Femoral nerve, GF: Genitofemoral nerve, LFCN: Lateral femoral cutaneous nerve, ON: Obturator nerve, Ur: Ureter

Lumbosacral trunk, caudally, inferior to the obturator nerve, merges with the sacral 1-3 nerves to form the sciatic nerve at the infrapiriform part of the greater sciatic foramen.
• Vascular
External iliac artery and vein, medially,
Internal iliac vein, medially, inferior to the external iliac vein,
Femoral nerve is a relevant anatomical structure noticed after dissection of the iliopsoas fascia, between the psoas and iliacus muscles, located at the posterolateral aspect of the psoas major muscle.
• Urologic
Ureter, medial to the iliac vessels, crossing the pelvic brim, is a related adjacent visceral tissue.
• Lymphatic
External iliac lymph nodes,
Obturator lymphatic tissue, distally and caudally,

Paracervical lymph nodes between the obturator nerve and the lumbosacral trunk,
Deep common iliac lymph nodes,
Recognition of these structures is essential to maintain oncologic radicality while preserving nerve integrity.

Surgical Applications

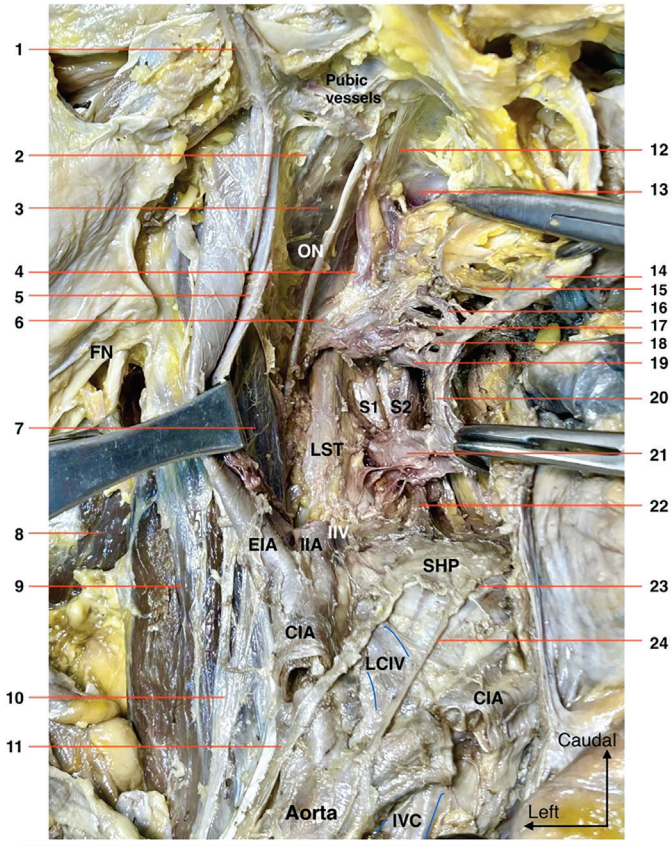
The medial psoas space (laterovascular plane) has multiple key surgical roles:
• Pelvic lymphadenectomy
Defines the lateral limit of the external iliac and cranial obturator nodal dissection,
Guides entry into the obturator fossa, from the lateral perspective.
• Radical hysterectomy
Provides orientation for safe parametrial dissection,
Protects the genitofemoral and obturator nerves,
Provides paracervical lymphadenectomy,
Provides type D resection, laterally extended parametrectomy, and endopelvic resection.
• Ureteral identification
Facilitates a reliable localization of the ureter at the pelvic brim in complex cases.
• Hemorrhage control
Maintains a clear boundary between the lymphatic tissue and major vessels.
• Advanced pelvic surgery
Serves as the lateral reference plane when extending the dissection cranially.
• Neuropelviology
Important for sciatica-related nodules and masses.

Key Surgical Insight (Figures 17-20)

The medial psoas space is the lateral guide for pelvic oncologic surgery; respecting this plane ensures vascular safety, nerve preservation, and oncologic precision.

What does This Study Add to the Literature, and Limitations

The pelvic anatomy is a complex, three-dimensional structure, which complicates its understanding. This complexity may lead to complications during pelvic surgeries. Although numerous anatomical reports have been published, this study aims to enhance understanding of surgical anatomy through a systematic, layer-by-layer dissection progressing from superficial to deep structures. It includes a comprehensive evaluation of pelvic avascular spaces, namely the presacral, pararectal, paravesical, and prevesical. In reviewing surgical anatomy, this study emphasizes the critical anatomical structures and associated surgical maneuvers, employing cadaveric dissection to detail anatomical landmarks. The primary limitation of this study is that it assesses surgical practice solely through photographs of cadaveric dissection. Nevertheless, this represents the primary strength of the study, which was originally designed to delineate the anatomical points using to observe details not identifiable during live surgery.



1: Inferior epigastric vessels, 2: Superior pubic ramus, 3: Obturator internus muscle, 4: Obturator vessels, 5: External iliac vein, 6: Obturator fascia (ischial spine level), 7: Psoas major muscle, 8: Iliacus muscle, 9: Psoas major muscle, 10: Genitofemoral nerve, 11: Thoracolumbar splanchnics, 12: Arcus tendineus fascia pelvis, 13: Pubococcygeus, 14: Obliterated umbilical artery, 15: Superior vesical artery, 16: Uterine artery, 17: Vaginal artery, 18: Middle rectal artery, 19: Inferior gluteal artery, 20: Internal iliac artery, 21: Superior gluteal artery, 22: Hypogastric nerve, 23: Promontorium, 24: Thoracolumbar splanchnics **IIV: Internal iliac vein**

Figure 17. The left pelvic sidewall anatomy. Dissection and mobilization of the internal iliac vessel system with the obturator parietal fascia

IVC: Inferior vena cava, CIA: Common iliac artery, LCIV: Left common iliac vein, SHP: Superior hypogastric plexus, EIA: External iliac artery, IIA: Internal iliac artery, IIV: Internal iliac vein, LST: Lumbosacral trunk, S: Sacral, ON: Obturator nerve, FN: Femoral nerve

Conclusion

The pelvic anatomy exhibits consistency. All the retroperitoneal compartments—including the presacral, pararectal, paravesical, and prevesical spaces—are interconnected. The laterovascular plane, also known as the medial psoas space, is part of the lateral pelvic spaces (pararectal and paravesical). Key anatomical landmarks for identifying retroperitoneal structures are the sacral promontory posteriorly (representing the anterior edge of the first sacral vertebra at the level of the pelvic brim), the pubic symphysis or the posterior surface of the body of the pubis anteriorly (serving as the superior midline component of the pubic bone), and the psoas major

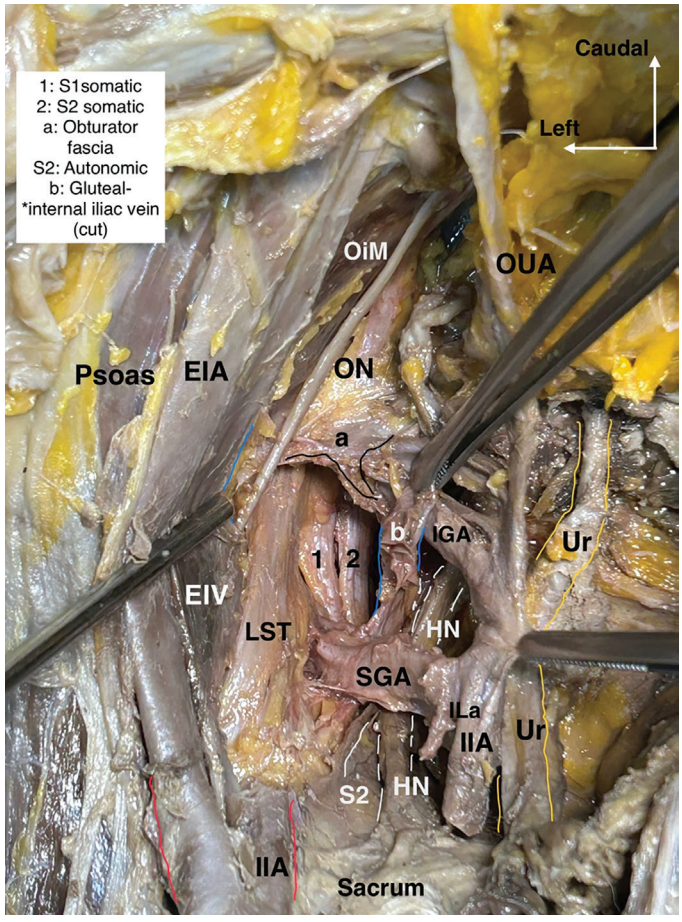


Figure 18. Lumbar and sacral plexus nerves at the left pelvic sidewall. Resection of the internal iliac vessel system will reveal the components of the sciatic nerve

EIA: External iliac artery, EIV: External iliac vein, IIA: Internal iliac artery, OiM: Obturator internus muscle, ON: Obturator nerve, OUA: Obliterated umbilical artery, Ur: Ureter, S: Sacral, HN: Hypogastric nerve, ILa: Iliolumbar artery, SGA: Superior gluteal artery, IGA: Inferior gluteal artery, LST: Lumbosacral trunk

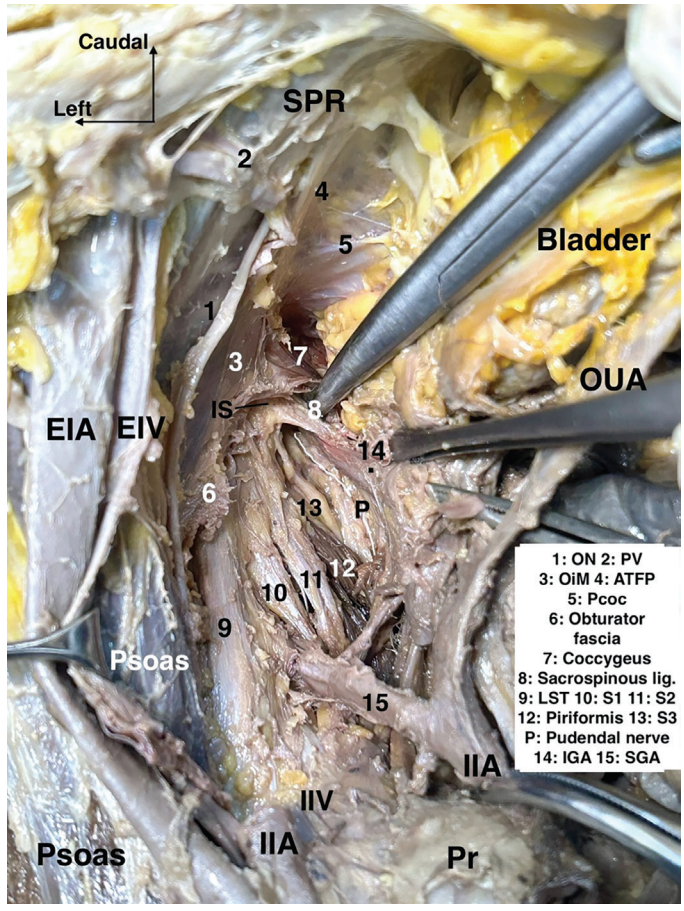


Figure 19. Somatic nerves of the left pelvic sidewall, emphasis on the sciatic and pudendal nerve with the corresponding anatomy

EIA: External iliac artery, EIV: External iliac vein, IIA: Internal iliac artery, IIV: Internal iliac vein, IS: Ischial spine, OUA: Obliterated umbilical artery, P: Pudendal, Pr: Promontory, SPR: Superior pubic ramus, 1-ON: Obturator nerve, 2-PV: Pubic vessels, 3-OiM: Obturator internus muscle, 4-ATFP: Arcus tendineus fascia pelvis, 5-Pcoc: Pubococcygeus, 6: Obturator fascia, 7: Coccygeus, 8: Sacrospinous ligament, 9-LST: Lumbosacral trunk, 10-S1: Sacral 1, 11-S2: Sacral 2, 12: Piriformis, 13-S3: Sacral 3, 14-IGA: Inferior gluteal artery, 15-SGA: Superior gluteal artery, lig: Ligament

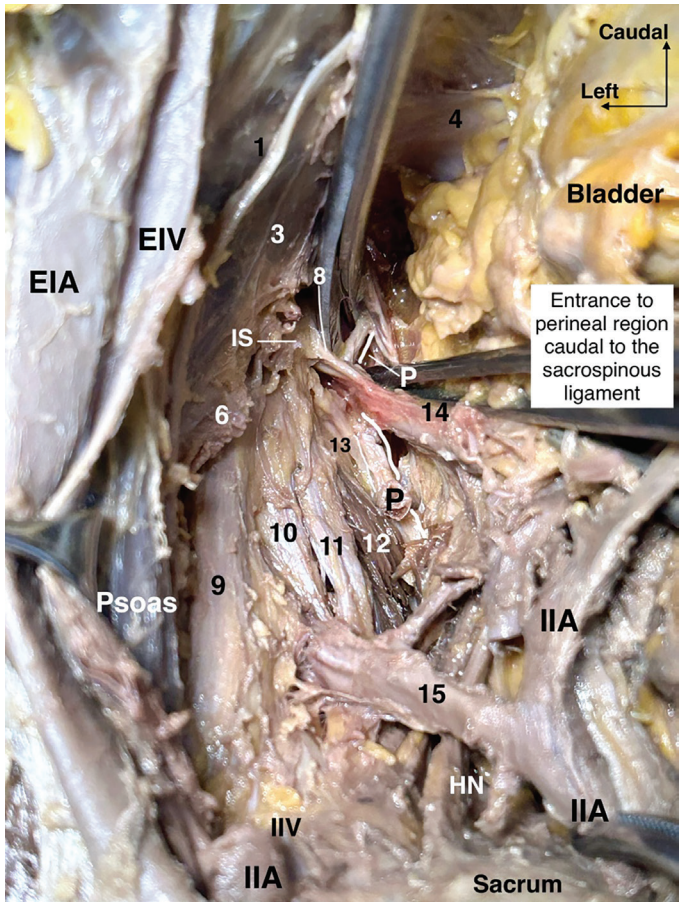


Figure 20. Entrance to the perineal region from the pelvic cavity, caudal to the sacrospinous ligament. The sciatic nerve and pudendal nerve

EIA: External iliac artery, EIV: External iliac vein, IIA: Internal iliac artery, IIV: Internal iliac vein, HN: Hypogastric nerve, IS: Ischial spine, P: Pudendal, 1-ON: Obturator nerve, 3-OiM: Obturator internus muscle, 4-ATFP: Arcus tendineus fascia pelvis, 6: Obturator fascia, 8: Sacrospinous ligament, 9-LST: Lumbosacral trunk, 10: Sacral 1, 11: Sacral 2, 12: Piriformis, 13: Sacral 3, 14-IGA: Inferior gluteal artery, 15-SGA: Superior gluteal artery

muscle laterally. Improved knowledge of retroperitoneal surgical anatomy plays a crucial role in safe pelvic surgery.

Footnotes

Authorship Contributions

Surgical and Medical Practices: İ.S., Ö.Ö., N.K., M.A.G., M.D., Concept: İ.S., Ö.Ö., N.K., M.A.G., M.D., Design: İ.S., Ö.Ö., N.K., M.A.G., M.D., Data Collection or Processing: İ.S., Ö.Ö., N.K., M.A.G., M.D., Analysis or Interpretation: İ.S., Ö.Ö., N.K., M.A.G., M.D., Literature Search: İ.S., Ö.Ö., N.K., Writing: İ.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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Review / Derleme

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Intrauterine infusion and sub-endometrial injection of autologous platelet-rich plasma for thin endometrium: A systematic review and single-arm meta-analysis

İnce endometriumda otolog trombositten zengin plazmanın rahim içi infüzyonu ve subendometrial enjeksiyonu: Sistematik bir derleme ve tek kollu meta-analiz

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Abstract

To evaluate the efficacy and safety of autologous platelet-rich plasma (PRP), administered via intrauterine infusion or subendometrial injection, for improving endometrial thickness (EMT) and pregnancy outcomes in women with thin endometrium undergoing frozen-thawed embryo transfer (FET) cycles. A comprehensive literature search was conducted across PubMed, Embase, Web of Science, and the Cochrane Library in accordance with preferred reporting items for systematic reviews and meta-analyses recommendations. Eligible studies investigating PRP treatment for thin endometrium in FET cycles were included. Methodological quality was assessed using the Methodological Index for Non-Randomized Studies. Pooled mean differences (MD) for EMT and aggregated proportions for pregnancy outcomes were calculated using R software. Fourteen studies involving a total of 523 patients were analyzed. PRP administration was associated with a significant increase in EMT [MD=1.61 mm, 95% confidence interval (CI): 1.21-2.01, p<0.05]. The pooled clinical pregnancy rate following PRP treatment was 41.5% (95% CI: 29.6-53.9%). Corresponding rates for ongoing pregnancy, implantation, and miscarriage were 27.3% (95% CI: 19.7-35.0%), 22.9% (95% CI: 8.5-37.2%), and 5.3% (95% CI: 2.3-8.2%), respectively. Subgroup analyses suggested that heterogeneity was partly attributable to differences in study design and PRP administration route. Autologous PRP may be a safe and potentially effective adjunct to enhance endometrial receptivity and reproductive outcomes in women with thin endometrium. Although current evidence from single-arm studies provides a useful clinical reference, well-designed, large-scale randomized controlled trials are still needed to validate these findings.

Keywords: Platelet-rich plasma, thin endometrium, frozen-thawed embryo transfer, intrauterine infusion, meta-analysis

Öz

Dondurulmuş-çözülmüş embriyo transferi (FET) sikluslarına giren ince endometriumlu kadınlarda otolog trombositten zengin plazmanın (PRP) rahim içi infüzyonunun veya subendometrial enjeksiyonunun endometrium kalınlığı (EMT) ve gebelik sonuçları üzerindeki etkinliğini ve güvenliğini değerlendirmek. PubMed, Embase, Web of Science ve Cochrane Kütüphanesi'nde kapsamlı bir arama yapıldı. FET sikluslarında ince endometrium için PRP kullanan çalışmalar, sistematik derleme ve meta-analizler için tercih edilen raporlama öğeleri kılavuzlarına göre seçildi. Metodolojik kalite, Rastgele Olmayan Çalışmalar için Metodolojik İndeks aracı kullanılarak değerlendirildi. EMT için birleştirilmiş ortalama farkları (MD) ve gebelik sonuçları için birleştirilmiş oranları hesaplamak üzere R yazılımı kullanılarak tek kollu bir meta-analiz gerçekleştirildi. Beş yüz yirmi üç hastayı içeren on dört çalışma dahil edildi. Meta-analiz, PRP tedavisinin EMT'yi anlamlı derecede artırdığını göstermiştir [MD=1,61 mm, %95 güven arayığı (GA): 1,21-2,01, p<0,05]. PRP müdahalesinden sonra, birleştirilmiş klinik gebelik oranı %41,5 (%95 GA: %29,6-53,9) olmuştur. Devam eden gebelik oranı %27,3 (%95 GA: %19,7-35,0), implantasyon oranı %22,9 (%95 GA: %8,5-37,2) ve düşük oranı %5,3 (%95 CI: %2,3-8,2) olmuştur. Alt grup analizleri, çalışma tasarımının ve uygulama yolunun heterojenliğe katkıda bulunduğunu göstermiştir. Otolog PRP tedavisi, ince endometriyumlu hastalarda endometriyum reseptivitesini ve üreme sonuçlarını iyileştirmek için güvenli ve etkili bir strateji gibi görünmektedir. Mevcut tek kollu

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veriler umut vadeden bir klinik ölçüt öngörse de, bu bulguları doğrulamak için standartlaştırılmış büyük ölçekli randomize kontrollü çalışmalara ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Trombositten zengin plazma, ince endometriyum, dondurulmuş-çözülmüş embriyo transferi, intrauterin infüzyon, meta-analiz

Introduction

Endometrial thickness (EMT) is a key determinant of embryo implantation and overall pregnancy outcome. Evidence indicates that insufficient EMT reduces implantation and pregnancy rates while simultaneously elevating the likelihood of early miscarriage, especially during frozen-thawed embryo transfer (FET) cycles[1,2]. Thin endometrium (TE) is characterized by inadequate endometrial thickness, often accompanied by reduced menstrual flow despite regular menstrual cycles, and is closely associated with a compromised reproductive prognosis[3]. In clinical practice, a cut-off value of 7 mm is generally accepted for the diagnosis of TE. This measurement is taken either on the day of oocyte retrieval [or human chorionic gonadotropin (hCG) trigger] during fresh in vitro fertilization (IVF) or upon commencement of progesterone in FET cycles[4]. Reports indicate that patients with an EMT ≤6 mm have pregnancy rates as low as 29.43%[5], suggesting a detrimental impact of TE on reproductive prognosis.

The treatment of TE remains a challenge in assisted reproduction. Although there is no universally accepted optimal treatment protocol, various strategies aim to promote endometrial proliferation[6,7]. Traditional treatment methods include the use of estrogen in artificial cycles, often in combination with low-dose aspirin, vitamin E, and vasodilators to improve blood flow and receptivity. However, these treatments often yield limited efficacy, and the endometrial recovery process in refractory patients is prolonged[8]. Consequently, there is an urgent need to develop safer and more efficient therapeutic strategies.

In recent years, autologous platelet-rich plasma (PRP), a bioactive preparation rich in growth factors, has demonstrated promising applications in the field of regenerative medicine. PRP is derived from peripheral blood and contains a high concentration of platelets[9,10]. Upon activation, these platelets secrete a vast array of bioactive molecules, including more than 800 proteins, cytokines, and hormones. These components are essential for driving angiogenesis, cell proliferation, and tissue repair[11,12]. Current clinical evidence indicates that administering autologous PRP, either through intrauterine infusion or sub-endometrial injection, can notably boost EMT and endometrial receptivity; this improvement, in turn, facilitates better outcomes regarding embryo implantation and pregnancy success[13,14]. For example, a study involving a cohort of 85 women with endometrial hypoplasia reported that intrauterine PRP infusion expanded the EMT by an average of 1.2 mm. Moreover, this intervention yielded a clinical pregnancy rate of 37%, which markedly surpassed the 20.2% rate observed in historical controls[15].

Although current research findings are encouraging, most existing studies have small sample sizes and heterogeneous study designs and PRP preparation protocols, leading to inconsistent conclusions. At present, key aspects of PRP application-such as preparation procedures (e.g., centrifugation parameters), routes of administration (intrauterine vs. sub-endometrial), and timing of intervention (e.g., days 10 to 13 of the hormone replacement cycle) have not been standardized. Furthermore, the safety profile of PRP therapy (e.g., risk of infection) and its long-term efficacy remain insufficiently explored. Moreover, the lack of consistent control groups across studies makes direct comparative analysis difficult. Therefore, performing a systematic review to derive a pooled efficacy estimate is essential for clarifying the actual therapeutic value of PRP.

To address this, we performed a comprehensive systematic review and a single-arm meta-analysis to assess the therapeutic efficacy of autologous PRP (administered via intrauterine infusion or sub-endometrial injection) for FET outcomes in patients with TE. By synthesizing data from existing single-arm and controlled trials, this study aims to establish clinical benchmarks for pregnancy rates and EMT improvement, providing evidence-based guidance for future research and clinical management.

Methods

Protocol and Guidance

This systematic review and meta-analysis was conducted according to the preferred reporting items for systematic reviews and meta-analyses guidelines and registered on PROSPERO (CRD420251043407) (Supplementary Table 1) [16].

Literature Search

A systematic search was performed across four electronic databases: PubMed, Embase, Web of Science, and the Cochrane Library. The literature search covered the period from database inception to April 2025. To ensure comprehensiveness, the reference lists of all included studies were also manually screened for additional relevant citations. The search terms included, but were not limited to, "PRP," "endometrial thickness," "embryo transfer," and "catheter". Detailed search strategies are provided in (Supplementary Table 2).

Eligibility Criteria

Inclusion and exclusion criteria were established based on the Participants, Intervention, Comparison, Outcome, and Study design framework.

Studies were included if they met the following criteria: (1): Participants (P): women diagnosed with a TE (<7 mm) undergoing FET cycles, irrespective of previous embryo transfer history, (2): Intervention (I): Intrauterine infusion or sub-endometrial injection of autologous PRP, with no restrictions on the mode or frequency of administration, (3): Comparison (C): Analysis of outcomes before and after intervention (self-controlled) or comparison with standard care or placebo (only PRP-arm data were extracted for this single-arm analysis), (4): Outcomes (O): The primary outcomes included changes in endometrial thickness, clinical pregnancy rate, chemical pregnancy rate, and ongoing pregnancy rate. Secondary outcomes included live birth rate, embryo implantation rate, miscarriage rate, and incidence of adverse events, (5): Study design (S): Randomized controlled trials (RCTs), non-RCTs, and observational studies (prospective or retrospective cohort studies).

Studies were excluded if they met the any of following criteria: (1): Conference abstracts, reviews, commentaries, case reports, or letters, (2): Animal studies, *in vitro* experiments, or other basic research, (3): Studies that did not involve the use of PRP, (4): Studies from which relevant data could not be extracted, (5): Studies for which the full text was unavailable.

Literature Management

Two researchers independently completed literature screening and data extraction. Any disagreements were resolved through discussion, and when consensus could not be reached, a third investigator was consulted. After removing duplicate entries using EndNote 21, we evaluated study eligibility by screening their titles and abstracts, which preceded detailed examination of the full texts.

Data Extraction and Quality Assessment

Relevant data were collected using a predefined Excel spreadsheet, covering study characteristics (including author, year, country, design, sample size, age, body mass index, infertility duration) and PRP-related details (including administration method and dosage). The methodological quality of the included studies was assessed using the Methodological Index for Non-Randomized Studies (MINORS) tool[17]. Quality assessment was conducted independently by two reviewers, with discrepancies resolved by discussion or adjudication by a third reviewer when necessary.

Definition of Outcome Measures

(1) Clinical pregnancy: The presence of a gestational sac with a fetal heartbeat identified by ultrasound 5 weeks after embryo transfer.

(2) Chemical pregnancy: Serum β-hCG ≥50 IU/L measured 14 days after embryo transfer.

(3) Ongoing pregnancy: Sustained intrauterine pregnancy beyond 12 gestational weeks.

(4) Miscarriage: Spontaneous pregnancy loss before 20 gestational weeks.

(5) Implantation rate: The ratio of gestational sacs to the number of embryos transferred.

(6) Live birth: Delivery of a viable neonate beyond 24 gestational weeks.

(7) hCG positivity: Early biochemical evidence of pregnancy (overlapping with chemical pregnancy in some reports).

Statistical Analysis

Statistical analyses were conducted in R (version 4.4.3) using the meta package. For binary outcomes (e.g., pregnancy rates), pooled proportions with 95% confidence intervals (CIs) were calculated. To stabilize the variance of proportions, the Freeman-Tukey double arcsine transformation was applied. For continuous variables (e.g., endometrial thickness), the mean difference (MD) representing the change from baseline (post-treatment minus pre-treatment) was calculated. Heterogeneity was assessed using I^2 and Cochran's Q test. I^2 >50% or $p<0.1$ indicated significant heterogeneity; in that case, a random-effects model was used; otherwise, a fixed-effects model was used. Subgroup analyses (by administration route, region, and study type) and sensitivity analyses (leave-one-out method) were conducted. For outcomes reported in ≥5 studies, publication bias was evaluated using funnel plots and Egger's test, with the trim-and-fill method applied if bias was present.

Results

Study Selection

A total of 95 records were identified through the systematic search (Figure 1). After the removal of 36 duplicate entries, 59 unique records remained for screening. Upon screening titles and abstracts, 36 studies were excluded for the following reasons: reviews or meta-analyses (n=2), conference abstracts

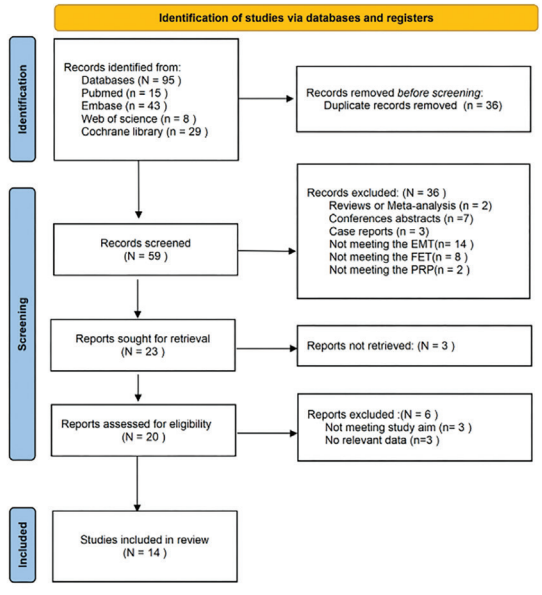

Figure 1. Flow chart of literature screening

(n=7), case reports (n=3), studies involving patients without a TE (n=14), studies not focusing on FET outcomes (n=8), and studies not involving PRP treatment (n=2). A further 23 studies were re-screened by full-text review; of these, 3 could not be accessed, 3 had research objectives unrelated to the topic, and 3 lacked relevant outcome data. Ultimately, 14 studies were included for analysis[4,14,18-29].

Study Characteristics and Quality Assessment

Fourteen studies that met the eligibility criteria were ultimately included in the analysis, encompassing 523 patients with TE whose mean age was 35.52±4.79 years. The study designs comprised 3 RCTs[19,25,26], 2 single-arm trials[18,24], 4 retrospective cohort studies[20,21,23,27], and 5 prospective cohort studies[4,14,22,28,29]. Regarding the method of PRP administration, 2 studies utilized subendometrial injection, 11 utilized intrauterine infusion, and 1 utilized both methods. The PRP injection doses ranged from 0.5 to 6 mL. The MINORS quality assessment revealed that, of the 14 studies, 12 were classified as high quality and 2 were of moderate quality. The fundamental characteristics and literature quality assessment results of the included studies are shown in Table 1.

Meta-analysis Results

Endometrial Thickness

Thirteen studies reported changes in EMT following PRP application during FET cycles in TE. The heterogeneity test indicated a high level of variability among studies (I^2=98.6%, p<0.0001); thus, a random-effects model was employed for analysis. The meta-analysis demonstrated that PRP significantly increases EMT (MD=1.61 mm, 95% CI: 1.21-2.01, p<0.05) (Figure 2A).

Because of substantial heterogeneity among the included studies, subgroup analyses were conducted to explore potential sources of heterogeneity based on study design, geographic region, and PRP administration methods (Supplementary Table 3). However, substantial heterogeneity persisted within these subgroups, suggesting that these factors may not fully explain the observed heterogeneity. Subgroup comparisons revealed that in RCTs, the increase in EMT following PRP treatment was significantly greater than in other study designs (MD=2.44 mm, 95% CI: 2.16-2.72). In Asian populations, the increase in EMT was 1.61 mm (95% CI, 1.21-2.07). Additionally, sub-endometrial injection resulted in a more pronounced increase in EMT compared to intrauterine infusion (MD=1.93 mm, 95% CI: 1.30-2.57).

Clinical Pregnancy Rate

Thirteen studies reported the clinical pregnancy rate following PRP treatment. Significant heterogeneity was observed (I^2=77.7%, p<0.0001), prompting the use of a random-effects model. The pooled clinical pregnancy rate after PRP treatment was 41.5% (95% CI: 29.6-53.9%) (Figure 2B).

Subgroup analyses were conducted to explore potential sources of heterogeneity (Supplementary Table 3). Despite stratification, high heterogeneity persisted. Subgroup analyses indicated that, in prospective cohort studies, the clinical pregnancy rate was 46.9% (95% CI: 6.7-89.4%). Furthermore, the clinical pregnancy rate following subendometrial injection was 47.2% (95% CI, 4.2-93.0%).

Chemical Pregnancy Rate

Five studies reported chemical pregnancy rates following PRP treatment. Due to high heterogeneity (I^2=90.3%, p<0.0001), a random-effects model was applied. The pooled chemical pregnancy rate was 23.5% (95% CI: 4.1-42.9%) (Figure 2C). Subgroup analyses (Supplementary Table 3) failed to fully account for the heterogeneity. However, comparisons revealed that in RCTs the chemical pregnancy rate was 40.0% (95% CI: 22.7-59.4%), whereas when PRP was administered via intrauterine infusion it was 29.8% (95% CI: 9.5-50.1%).

Ongoing Pregnancy Rate

Four studies reported the ongoing pregnancy rate following PRP treatment. No significant heterogeneity was observed among the studies (I^2=0.0%, p=0.40); thus, a fixed-effects model was employed. The pooled ongoing pregnancy rate was 27.3% (95% CI: 19.7-35.0%) (Figure 2D).

Miscarriage Rate

Six studies reported miscarriage rates following PRP treatment. No substantial heterogeneity was detected (I^2=10.3%, p=0.35); thus, a fixed-effects model was chosen to synthesize the data. The pooled miscarriage rate was 5.3% (95% CI: 2.3-8.2%) (Figure 2E).

Implantation Rate

Six studies reported the implantation rate following PRP treatment. High heterogeneity was observed (I^2=90.3%, p<0.0001), necessitating a random-effects model. The pooled implantation rate was 22.9% (95% CI: 8.5-37.2%) (Figure 2F).

Subgroup analyses (Supplementary Table 3) indicated that in RCTs, the implantation rate was 29.7% (95% CI: 10.1-49.3%). When PRP was administered via subendometrial injection, the implantation rate was notably higher, at 55.0% (95% CI: 31.5-76.9%).

Live Birth Rate

Seven studies reported live-birth rates following PRP treatment. Due to high heterogeneity (I^2=91.5%, p<0.0001), a random-effects model was employed. The pooled live birth rate was 23.6% (95% CI: 12.5-44.4%) (Figure 2G).

Subgroup analyses (Supplementary Table 3) showed that in retrospective cohort studies, the live birth rate was 42.4% (95% CI: 1.3-83.5%). Following subendometrial injection, the live birth rate was 37.9% (95% CI, 8.6-100.0%).

HCG Positivity Rate

Four studies reported hCG positivity rates following PRP treatment. Heterogeneity was significant (I^2=65.9%, p=0.032);

Table 1. Specific information about the included studies

Author	Year	Country	Study design	n	Age	BMI (kg/m2)	Duration of infertility (years)	PRP administration methods	PRP dosage	Outcome indicators	Minors
Cakiroglu et al.[7]	2025	Türkiye	NRCT	100	36.90±5.70	26.70±5.80	-	Injection	4-6 mL	①②⑦⑧	High
Eftekhar et al.[19]	2018	Iran	RCT	40	31.98±2.26	-	-	Infusion	0.5-1 mL	①②④⑤⑥	High
Coksuer et al.[20]	2019	Türkiye	Retrospective	34	29.41±4.54	26.35±4.41	7.66±2.87	Infusion	1 mL	②③⑤⑦	High
Dogra et al.[4]	2022	India	Prospective	20	32.35±3.89	25.60±4.14	7.85±4.61	Infusion	0.5-1 mL	①②⑥⑦	High
Fujii and Oguchi[21]	2024	Japan	Retrospective	70	38.30±0.50	22.50±0.40	3.10±0.20	Infusion	1 mL	①②③⑤⑦⑧	High
Gangaraju et al.[22]	2023	India	Prospective	9	33.67±6.46	-	-	Infusion	0.8 mL	①②	High
Shrivastava et al.[23]	2024	India	Retrospective	20	35.75±6.88	27.15±6.43	10.37±6.03	Injection	1 mL	①②③⑤⑥⑦	High
Kim et al.[14]	2019	Korea	Prospective	20	38.40±4.30	23.30±3.10	5.70±2.60	Infusion	0.7-1.0 mL	①②④⑥⑦⑧	High
Nagireddy et al.[24]	2019	India	NRCT	28	32.00±3.79	-	-	Infusion	-	①②④⑤⑥⑦	Moderate
Nazari et al.[25]	2019	Iran	RCT	30	33.93±2.76	24.30±2.24	-	Infusion	0.5 mL	①②③	High
Obidniak et al.[26]	2017	Russian	RCT	45	28-39	-	-	Infusion	2 mL	②⑥	Moderate
Wang et al.[27]	2024	China	Retrospective	47	36.90±1.13	21.61±0.61	2.09±0.68	Infusion	1 mL	①②④⑤⑧	High
Zadehmodarres et al.[28]	2017	Iran	Prospective	10	34.00±3.23	-	-	Infusion	0.5 mL	①③	High
Zaha et al.[29]	2023	Romania	Prospective	23	39.16±3.12	26.20±3.60	5.20±1.80	Infusion	2 mL	①	High
				27	37.26±2.32	24.50±5.80	3.40±1.40	Injection			

PRP: Platelet-rich plasma, BMI: Body mass index, RCT: Randomized controlled trial, NRCT: Non-randomized controlled trial, ①: Endometrial thickness, ②: Clinical pregnancy rate, ③: Chemical pregnancy rate, ④: Ongoing pregnancy rate, ⑤: Miscarriage rate, ⑥: Implantation rate, ⑦: Live birth rate, ⑧: hCG positivity rate:

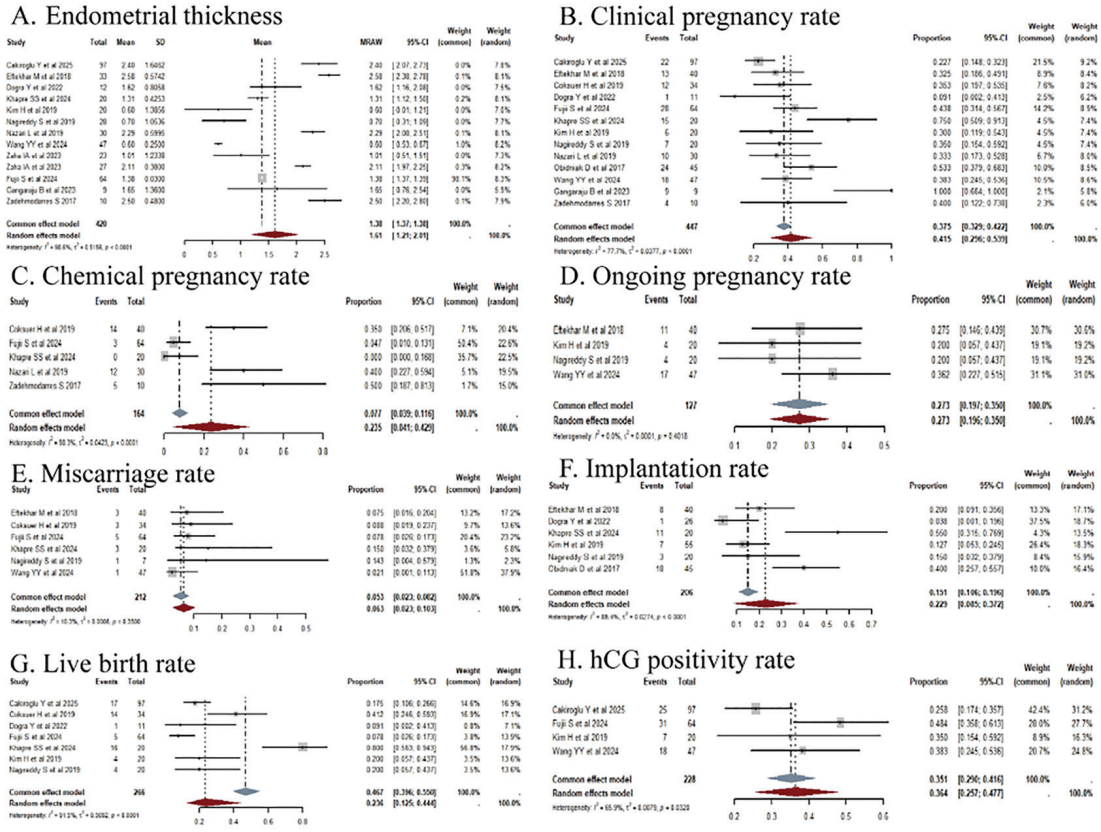

Figure 2. Forest plot of the effect of PRP on endometrial thickness and pregnancy outcomes

PRP: Platelet-rich plasma, hCG: Human chorionic gonadotropin

thus, a random-effects model was used. The pooled hCG positivity rate was 36.4% (95% CI: 25.7-47.7%) (Figure 2H). Subgroup analyses (Supplementary Table 3) indicated that both study design and PRP administration method contributed to heterogeneity. In retrospective cohort studies, the hCG positivity rate was 44.0% (95% CI: 34.4-53.9%). When PRP was administered via intrauterine infusion, the rate was 42.7% (95% CI: 34.2-51.4%).

Sensitivity Analysis and Publication Bias

A sensitivity analysis was performed using a leave-one-out approach for outcome measures that included more than five studies. Sensitivity analyses revealed that removal of any single study did not materially alter the pooled estimates for endometrial thickness, clinical pregnancy rate, chemical pregnancy rate, or miscarriage rate. These findings indicate a high degree of robustness and stability in the synthesized outcomes. As shown in Supplementary Figure 1.

For outcome measures with more than five included studies, publication bias was assessed using funnel plots and Egger's test. The results indicated no significant publication bias for EMT (p=0.58) and clinical pregnancy rate (p=0.16); both P-values exceeded 0.05. However, significant publication bias was detected for chemical pregnancy rate (p=0.02), miscarriage rate (p=0.02), implantation rate (p=0.02), and live birth rate (p=0.03); all p-values were <0.05. To further evaluate potential publication bias, we applied the trim-and-fill approach. After adjustment, the results suggested that the degree of publication bias was small and did not materially influence the reliability of the pooled outcomes. As shown in (Supplementary Figures 2-4).

Discussion

In this systematic review and single-arm meta-analysis, data from 14 relevant studies were pooled to assess the efficacy and safety of autologous PRP administered by intrauterine or subendometrial injection in women with TE. Overall, PRP administration was associated with significant gains in EMT and improvements across multiple reproductive endpoints, including pregnancy and implantation outcomes. These findings support the potential role of PRP in optimizing the endometrial environment and promoting receptivity.

This meta-analysis demonstrated that PRP treatment was associated with a meaningful increase in EMT, consistent with earlier reports. In a representative study by Kim et al.[14], 24 women with TE (EMT <7 mm) and a history of ≥2 failed IVF cycles were treated with two to three intrauterine PRP infusions, resulting in an average EMT gain of 0.6 mm

relative to the preceding cycle. Our subgroup analyses further suggested that the magnitude of benefit was greater in RCTs and that direct intra-endometrial administration produced more favorable outcomes than intrauterine infusion alone. Together, these observations imply that both the route and technique of PRP delivery may modulate treatment efficacy. From a biological perspective, PRP is enriched with multiple growth factors—including vascular endothelial growth factor, platelet-derived growth factor, transforming growth factor beta, and epidermal growth factor —which may collectively promote endometrial repair and receptivity in patients with TE[30]. These growth factors may enhance endometrial structure and function by promoting angiogenesis, epithelial cell proliferation, and stromal remodeling. Moreover, PRP may improve endometrial receptivity by modulating the local cytokine milieu and immunological microenvironment, thereby facilitating embryo implantation[31].

Regarding clinical pregnancy outcomes, the pooled clinical pregnancy rate following PRP intervention was 41.5%, which was comparable to or even exceeded that of conventional treatment strategies[19], and reached as high as 46.9% in some prospective studies. Furthermore, the ongoing pregnancy rate after PRP treatment was 27.3%, with a relatively low miscarriage rate of 5.3%, suggesting that PRP may not only enhance initial implantation but also contribute to pregnancy maintenance. This trend may be associated with PRP's ability to promote endometrial vascularization and stabilize the maternal-embryo interface. A notable improvement in implantation rate was also observed (22.9%), with even more pronounced effects reported in RCTs (exceeding 35%), supporting the viability of PRP as an adjunctive intervention. However, substantial variability was noted in chemical pregnancy rates, ranging from 4.1% to 42.9%, indicating high inter-study heterogeneity. Additionally, wide CIs were observed in certain subgroup analyses, likely due to the limited sample size of available studies. The observed heterogeneity may be attributable to differences in PRP dosage, timing of administration, and baseline endometrial conditions, thereby underscoring the need for standardized research designs and intervention protocols in future studies[32].

Study Limitations

Although the major outcomes demonstrated overall positive effects of PRP, several limitations remain: (1): The single-arm experimental design lacks a control group, which limits the ability to draw comparative inferences. However, subgroup data from RCTs consistently show that improvements with PRP are superior to those achieved with the standard hormone treatment regimen. (2): High heterogeneity was observed across key outcome variables. Even after performing subgroup analyses by study design, geographic region, and intervention mode, the sources of heterogeneity could not be fully accounted for. (3): The lack of standardization in PRP preparation and administration represents one of the most critical confounding factors affecting treatment efficacy. Considerable variability exists across studies regarding the source of PRP, centrifugation protocols, activation status, dosage, injection site, and frequency, all of which may directly influence the concentration of growth factors and subsequent biological effects[33]. (4): Beyond the PRP protocol itself, additional potential confounders include differences in the methods of EMT measurement, cycle regulation strategies (natural versus artificial cycles), and concomitant therapies such as estrogen supplementation or granulocyte colony-stimulating factor, which may further bias the meta-analytic results. (5): With regard to safety, no serious adverse events directly attributable to PRP have been reported to date, which is likely due to its autologous origin and low immunogenicity. However, invasive procedures, particularly subendometrial injection, may carry risks, including uterine perforation or infection, especially in the absence of standardized operating procedures; thus, they should be approached with caution. Moreover, incomplete reporting of adverse events in some studies limits the ability to perform a comprehensive assessment of long-term safety. (6): Currently, systematic research evaluating the long-term maternal and neonatal outcomes associated with PRP treatment, including potential birth defects and placental complications, is lacking. Accordingly, future research should focus on extended follow-up and the establishment of national or international prospective registries to systematically collect safety and outcome data. (7): Although correlations have been observed, causal mechanisms linking EMT to pregnancy success remain poorly defined, necessitating focused cellular, molecular, and translational studies.

Despite the aforementioned limitations, this study represents one of the few existing systematic reviews evaluating PRP treatment for TE, filling a critical gap in the current body of literature. As a low-cost, minimally invasive, and patient-friendly intervention, PRP has shown promise, particularly in TE patients who respond poorly to conventional therapies. Based on the findings of this analysis, future clinical applications may benefit from several strategic optimizations, including: (1): Optimizing the timing of intervention (e.g., intrauterine PRP infusion on days 10-12 of a hormone replacement cycle); (2): Developing standardized protocols for PRP preparation, including concentration grading, activation methods, and injection techniques; (3): Promoting multicenter, prospective RCTs with appropriately designed control groups (e.g., placebo or conventional treatment) to more accurately assess clinical efficacy; (4): Strengthening mechanistic studies to explore the roles of PRP in modulating endometrial immunity, activating stem cells, and enhancing the local microenvironment; (5): Establishing maternal-neonatal health outcome databases to systematically evaluate the potential impact of PRP on birth and long-term developmental outcomes.

Conclusion

Overall, autologous PRP administered via intrauterine infusion or sub-endometrial injection is associated with a significant increase in EMT in women with TE undergoing FET cycles. Available evidence also suggests potential benefits for pregnancy and implantation outcomes, with a possible reduction in miscarriage risk, supporting its role as a useful adjunct in clinical practice. Although heterogeneity and methodological differences remain across existing studies, PRP continues to show promise in assisted reproductive technology. Future research should prioritize well-designed, multicenter RCTs that integrate mechanistic insights with clinical outcomes and establish consensus protocols for treatment and safety evaluation to support evidence-based application in reproductive medicine.

Footnotes

Authorship Contributions

Concept: Z.T., Design: M.L., X.W., Data Collection or Processing: Z.T., X.W., Analysis or Interpretation: Ş.H., M.L., Z.T., X.W., Literature Search: M.L., Z.T., X.W., Writing: M.L., Z.T., X.W.

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Letter to the Editor / Editöre Mektup

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Sphingosine-1-phosphate in ovarian hyperstimulation syndrome: Biomarker promise and therapeutic peril

Yumurtalık hiperstimülasyon sendromunda sfingozin-1-fosfat: Biyobelirteç vaadi ve tedavi riski

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Keywords: Ovarian hyperstimulation syndrome, sphingosine-1-phosphate, reproductive medicine, vascular permeability, assisted reproductive technology

Anahtar Kelimeler: Yumurtalık hiperstimülasyon sendromu, sfingozin-1-fosfat, üreme tıbbı, vasküler geçirgenlik, yardımcı üreme teknolojisi

To the Editor,

Ovarian hyperstimulation syndrome (OHSS) is a serious, potentially life-threatening iatrogenic complication of excessive ovarian response to stimulation during fertility treatments, such as in vitro fertilization, which is part of assisted reproductive technology. It is often triggered by human chorionic gonadotropin (hCG), when used to induce oocyte maturation. Compared with LH, hCG's prolonged luteotropic effect induces vasodilation, increases vascular permeability, and shifts fluid into the third space, leading to ascites, pericardial and pleural effusions, and generalized edema. Severe cases may result in complications such as adult respiratory distress syndrome, thromboembolism, and acute renal failure. Clinically, OHSS presents with enlarged cystic ovaries, abdominal distention, and pain[(1)].

OHSS is a serious complication with unclear pathophysiology. Lipids play important roles in cellular function and various diseases; hence, lipid alterations were investigated by lipidomic analysis of follicular fluid samples obtained from OHSS patients, revealing a significant reduction in some lipid classes, including LPC, dMePE, LdMePE, PI, PE, PC, TG, and sphingomyelin (SM), and an elevation of ChE in the OHSS group. These differential lipids might serve as biomarkers. Notably, sphingosine 1-phosphate (S1P) is a bioactive lipid mediator produced from SM. S1P is found abundantly in blood and regulates vascular permeability, cell recruitment, and clotting during inflammatory processes. This role of S1P is mediated by S1PR1, a member of the family of G protein-coupled receptors, through a signaling pathway. Hence, S1P emerges as a promising biomarker and therapeutic target[(2)]. Future randomized controlled studies should focus on refining the role of S1P as a predictive marker for OHSS.

Studies suggest that women with OHSS have lower S1P levels in their follicular fluid than women without OHSS. This drop in S1P could act as an early warning sign, allowing timely intervention. Identifying such changes may help improve patient safety during fertility treatments[(3)]. In an OHSS rat model, S1P treatment reduced ovarian weight and serum progesterone levels, increased the number of healthy antral follicles, decreased the number of corpora lutea and cystic structures, lowered steroidogenic acute regulatory protein levels, and reduced endothelial swelling. It also restored N-cadherin and VE-cadherin levels while enhancing the expression of claudin-5, occludin, and S1P receptor 1,

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indicating that S1P holds potential as both a diagnostic marker and a therapeutic option for OHSS[4].

S1P shows promise as an early marker for ovarian hyperstimulation syndrome, but its current evidence is derived mainly from *in vitro* cell studies rather than from studies using human ovarian tissue. While these models offer useful insights, they cannot fully capture the complexity of real patients, making direct clinical application uncertain. To move forward, well-designed human research is essential to confirm its accuracy and usefulness in early detection[5]. The use of S1P to treat OHSS could inadvertently exacerbate or trigger conditions such as endometriosis, adenomyosis, and fibroids. That's because S1P encourages cell growth, angiogenesis, and inflammation, the same processes that promote these disorders. While it may help with OHSS, it carries the risk of exacerbating other hormone-related diseases, thereby limiting its therapeutic potential[6].

The new findings identify S1P as a putative biomarker and therapeutic candidate in OHSS, based on lipidomic data from follicular fluid and animal models in which it inhibits vascular permeability and reduces ovarian size. However, the data presented are limited to *in vitro* and animal studies because S1P has been reported to worsen disorders such as endometriosis. To translate these findings into clinical practice, most S1P human observational studies must be conducted to validate predictive accuracy; small clinical trials must be performed to ensure localized delivery and reduce systemic risk; and studies of selected modulators of the S1P receptor must be undertaken to develop safer interventions. The endpoint of these activities is to improve risk stratification and therapeutic approaches, thereby improving patient safety in assisted reproductive technologies[1,2,4].

Future research on S1P in OHSS should start with human observational studies to confirm its predictive value and determine safe ranges. Because current evidence derives from animal and lab models, initial human trials should be small and closely monitored, and should preferably use local or targeted delivery to reduce side effects. Safer alternatives may include selective S1P receptor modulators or neutralizing agents, particularly in women with conditions such as endometriosis. Careful patient selection and monitoring will be vital before wider clinical use.

Footnotes

Authorship Contributions

Concept: S.M.H., M.U., Literature Search: F.K.K., Writing: M.T.

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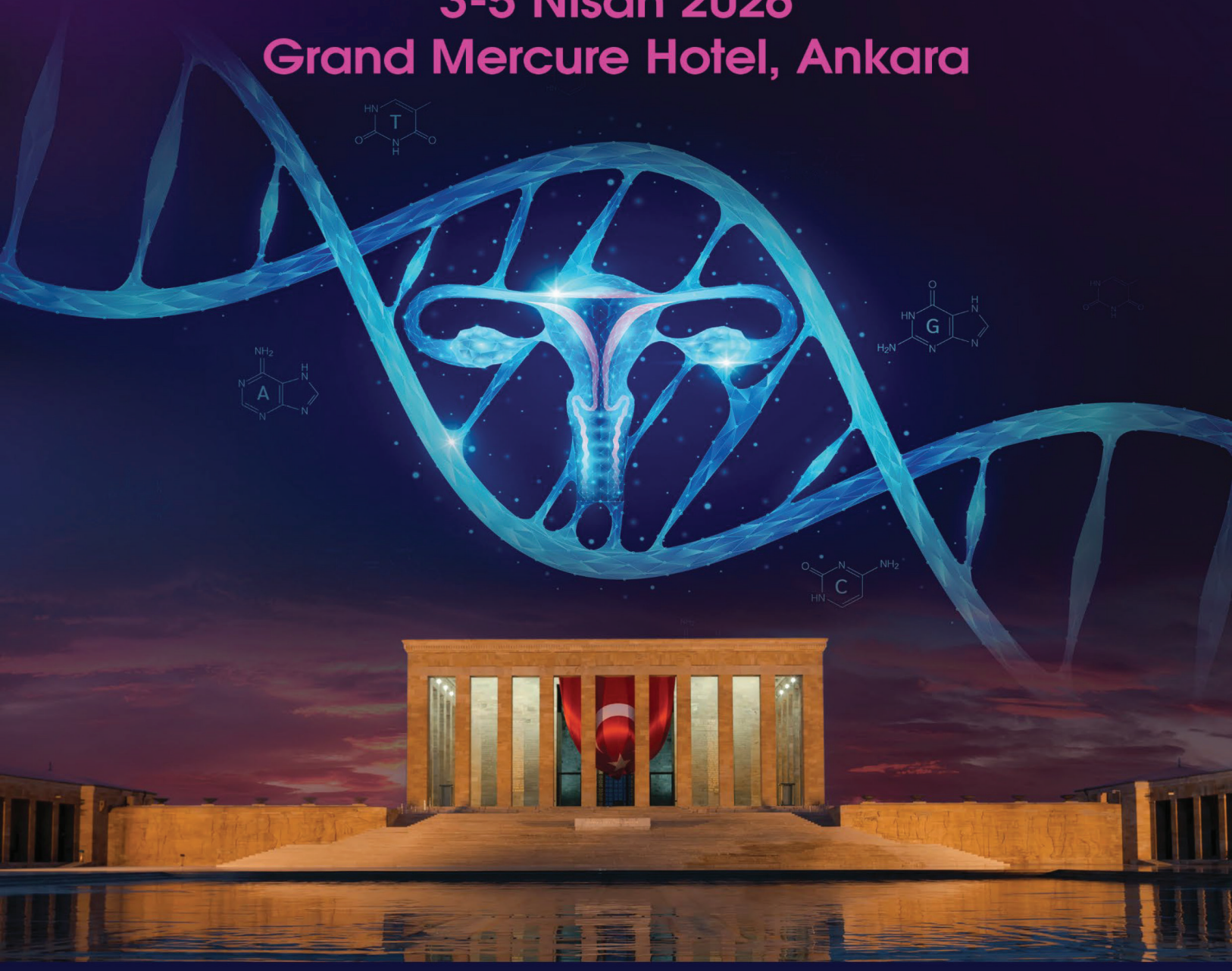

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POSTER BİLDİRİLER

[PS-001]

Jinekolojik malignitelere bağlı vajinal kanamada uterin arter embolizasyonu: Dört olguluk olgu serisi

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Amaç: Jinekolojik malignitelere bağlı vajinal kanamalar masif olduğunda hayatı tehdit eden bir komplikasyon olup hızlı ve etkili hemostaz gerektirir. Bu çalışmada vajinal kanama nedeniyle uterin arter embolizasyonu uygulanan jinekolojik maligniteli hastaların klinik sonuçlarının değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: Ocak 2020-Şubat 2026 tarihleri arasında jinekolojik malignitelere bağlı kontrolsüz vajinal kanama nedeniyle uterin arter embolizasyonu uygulanan dört hasta retrospektif olarak değerlendirildi. Hastaların klinik özellikleri, tanıları, işlem öncesi ve sonrası hemoglobin düzeyleri, transfüzyon ihtiyaçları ve işlem sonuçları incelendi.

Bulgular: Çalışmaya bir endometriyum kanseri ve üç serviks kanseri olgusu dahil edildi. Serviks kanseri olgularından biri yeni tanı inoperable hastalık, ikisi rekürren hastalık olarak değerlendirildi. Endometriyum kanseri olgusunda vajinal nüks saptandı. Embolizasyon öncesinde üç hastada ortalama hemoglobin düzeyi 7,07 g/dL idi ve bu hastalara 2 ünite eritrosit süspansiyonu ile 2 ünite taze donmuş plazma transfüzyonu uygulandı. Bir hastada hemoglobin düzeyi 11,1 g/dL olup transfüzyon ihtiyacı olmadı. Vajinal tampon ile kanaması kontrol altına alınamayan ve radyoterapiye uygun olmayan hastalara girişimsel radyoloji tarafından uterin arter embolizasyonu uygulandı. Embolizasyon sonrası ortalama hemoglobin düzeyi 9,16 g/dL olarak ölçüldü. Tüm hastalarda işlem sonrası erken dönemde kanama kontrolü başarıyla sağlandı ve majör komplikasyon gözlenmedi.

Sonuç: Uterin arter embolizasyonu jinekolojik malignitelere bağlı hayatı tehdit eden vajinal kanamalarda hızlı ve etkili hemostaz sağlayan güvenli bir minimal invazif tedavi seçeneğidir. Özellikle ileri evre veya rekürren hastalarda cerrahiye alternatif bir yaklaşım olarak değerlendirilebilir ve hastaların stabilizasyonuna katkı sağlayarak ileri onkolojik tedavilerin planlanmasına olanak tanıyabilir.

Anahtar Kelimeler: Serviks kanseri, vajinal kanama, embolizasyon

[PS-002]

Successful surgical management of a mesenteric spindle cell tumor mimicking an adnexal cyst: A case report

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Objective: Large pelvic masses in reproductive-age women often pose diagnostic challenges, with adnexal origins presumed based on imaging, yet mesenteric tumors can mimic these presentations, necessitating multidisciplinary approaches for optimal resection and fertility preservation.

Case: A 25-year-old nulliparous woman presented with a pelvic mass suspected to be adnexal. The laboratory examinations were within normal ranges, including tumor markers α-fetoprotein (AFP), carcinoembryonic antigen (CEA), and cancer antigen (CA 19-9), CA125, CA 15-3. Preoperative imaging included pelvic magnetic resonance imaging demonstrating an 165x110 mm solid-cystic lesion filling the pelvis with suprapubic extension, unrelated to uterine or adnexal structures; pelvic computed tomography revealing a 185x115 mm lobulated, multiseptated cystic mass originating from the left adnexal region, extending superiorly to the liver and displacing adjacent tissues; and colonoscopy showing sigmoid colon narrowing with mucosal edema suggestive of extrinsic compression. Exploratory laparotomy via midline incision was performed by gynecologic oncology and general surgery teams. Intraoperative findings revealed a 20 cm mass originating from the colonic mesentery, encasing the sigmoid colon and extending to the rectum, with bilateral grade 1 hydronephrosis due to ureteral compression. No ascites was present, and peritoneal washings were obtained. The uterus, bilateral ovaries, and tubes appeared normal. The inferior mesenteric artery was sacrificed for en bloc resection. The patient underwent low anterior resection with complete excision of the mass and primary anastomosis. Frozen pathology indicated a spindle cell tumor of unclear primary origin, pending final histopathology. Postoperative recovery was uneventful with no early complications.

Discussion: Mesenteric spindle cell tumors are rare neoplasms that include a heterogeneous group such as gastrointestinal stromal tumors (GIST), desmoid-type fibromatosis, and other mesenchymal sarcomas. Because of their deep intra-abdominal location and potential to grow to large sizes, they may mimic adnexal masses on preoperative imaging, particularly in young women presenting with pelvic symptoms. Several reports have highlighted that even advanced imaging modalities may fail to accurately determine the tumor origin when lesions displace adjacent pelvic organs. In such cases, intraoperative assessment and frozen section analysis become essential to guide the surgical strategy. Complete surgical excision with negative margins remains the cornerstone of treatment for most mesenteric spindle cell tumors. Our case further emphasizes the importance of multidisciplinary collaboration to achieve optimal oncologic resection while preserving reproductive organs in young patients.

Conclusion: Mesenteric spindle cell tumors may masquerade as adnexal masses, underscoring the need for vigilant preoperative imaging interpretation and intraoperative frozen section to guide extent of resection. Multidisciplinary cytoreductive surgery facilitates complete excision without fertility compromise in young patients, optimizing oncologic outcomes and highlighting the value of collaborative expertise in ambiguous pelvic neoplasms.

Keywords: Adnexal disease, cytoreduction surgical procedure, mesenteric neoplasm

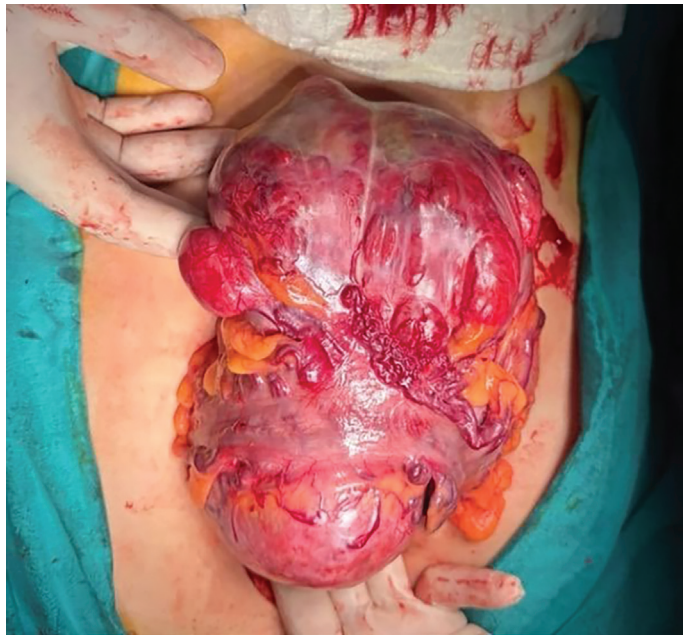

Figure 1. Intraoperative view of the pelvic mass

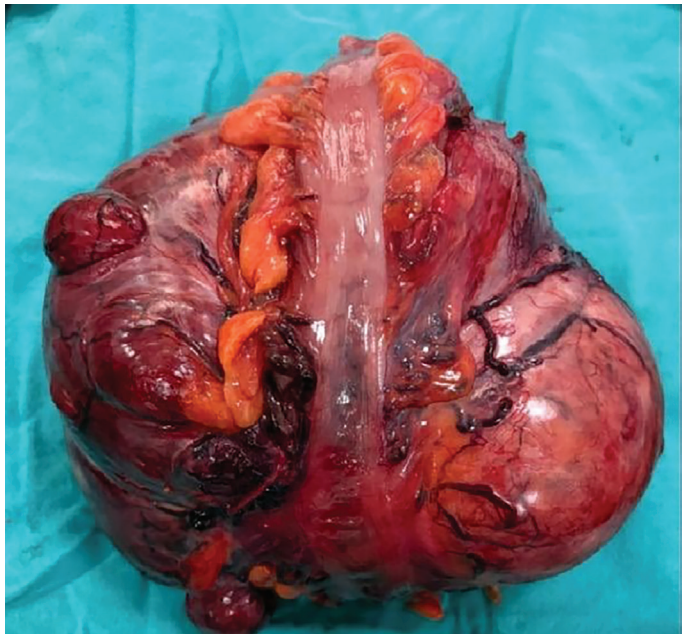

Figure 2. Total excision of the mass with low anterior resection

[PS-003]

Isolated pulmonary recurrence of pelvic synovial sarcoma after two successful pregnancies without adjuvant therapy: A rare case report

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Objective: Synovial sarcoma (SS) is a rare, high-grade soft tissue sarcoma with a marked tendency for local recurrence and pulmonary metastasis. The influence of pregnancy-related hormonal changes on SS behavior is not well established. We report an unusual clinical course of a young woman with pelvic SS who remained free of local recurrence following complete surgical resection and experienced isolated pulmonary metastasis only after two consecutive pregnancies.

Case: A 28-year-old woman presented with a large pelvic mass in May 2023. Magnetic resonance imaging demonstrated a pelvic mass independent of the uterus. At surgery, the uterus and bilateral ovaries appeared normal. Wide excision of the pelvic mass was performed with negative margins (R0 resection). Histopathology confirmed synovial sarcoma. The patient declined adjuvant chemotherapy or radiotherapy to preserve fertility. Subsequently, she completed two full-term pregnancies, during which routine surveillance showed no evidence of local recurrence. During follow-up in December 2025, imaging revealed a solitary pulmonary nodule consistent with metastatic SS, while evaluation of the primary pelvic site demonstrated no recurrence. The patient remained asymptomatic and clinically stable.

Discussion: Pelvic SS is an uncommon malignancy in which complete surgical resection is the primary determinant of local disease control. In this patient, R0 resection allowed prolonged local disease-free survival despite the absence of adjuvant therapy and exposure to pregnancy-related hormonal changes. The subsequent development of a solitary pulmonary metastasis underscores the ongoing risk of distant recurrence, even when local control is achieved. This case aligns with literature emphasizing the importance of complete surgical excision and supports the notion that, in selected young patients, fertility-sparing approaches can be considered without necessarily compromising local disease control. While hormonal influences during pregnancy did not appear to accelerate local recurrence in this instance, clinicians should remain vigilant for distant metastases and continue long-term surveillance. These observations may inform counseling and management strategies for reproductive-aged women diagnosed with SS.

Conclusion: This report illustrates that complete surgical resection in pelvic SS can provide durable local control, even in the absence of adjuvant therapy and following pregnancy. Nonetheless, the potential for delayed distant metastasis persists, reinforcing the need for long-term follow-up. Fertility preservation may be feasible in carefully selected patients without adversely affecting local oncologic outcomes.

Keywords: Pelvic synovial sarcoma, pregnancy, pulmonary metastasis

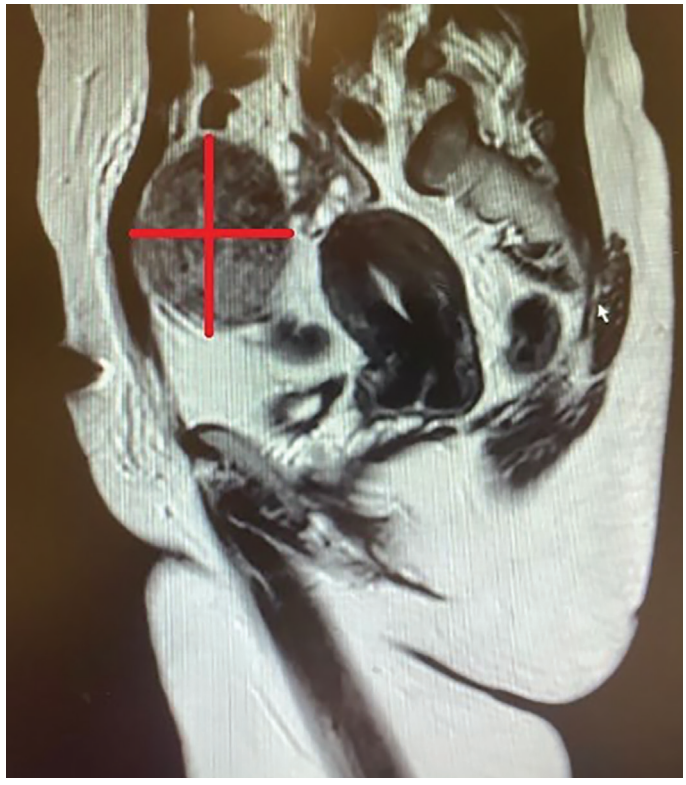

Figure 1. Magnetic resonance imaging of a 15x10 cm pelvic mass

[PS-004]

Disseminated gastrointestinal signet-ring cell adenocarcinoma mimicking ruptured ectopic pregnancy with DIC and elevated β-hCG: A rare case of tubal metastasis

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Objective: Acute abdominal pain with positive β-human chorionic gonadotropin (β-hCG) in reproductive-age women is most commonly suggestive of ectopic pregnancy and often necessitates urgent surgical evaluation. However, rare non-gestational malignancies may present with low-level β-hCG positivity and mimic gynecologic emergencies. Advanced gastrointestinal adenocarcinomas may also present with disseminated intravascular coagulation (DIC), a life-threatening coagulopathy associated with high mortality. Tubal metastasis from gastrointestinal malignancies is extremely rare.

Case: A reproductive-age woman presented with acute abdominal pain. Laboratory evaluation showed hemoglobin 7.2 g/dL, β- hCG 57 IU/L (confirmed on repeated measurements), and severe thrombocytopenia (22,000/μL). Follow-up tests demonstrated progressive hemoglobin decline to 5.1 g/dL, platelets 13,000/μL, diffuse intra-abdominal fluid, and a DIC score of 7. Due to hemodynamic deterioration and suspected ruptured ectopic pregnancy, diagnostic laparoscopy was performed six hours after admission following platelet transfusion. Intraoperatively, diffuse serohemorrhagic fluid and a hydropic right fallopian tube were observed, while both ovaries appeared normal. Right salpingectomy and endometrial curettage were performed. No gestational tissue was identified in curettage specimens. The patient was discharged on postoperative day three but was readmitted two days later with recurrent ascites. During further evaluation, she developed intracranial hemorrhage secondary to DIC and died on hospital day five. Histopathology of the fallopian tube revealed metastatic signet-ring cell adenocarcinoma. Immunohistochemistry demonstrated CK7 negativity with CK20 and *CDX2* positivity, while β-hCG and PAX8 were negative, supporting a gastrointestinal—most likely colorectal—origin. Tumor markers were markedly elevated (CA19-9: 10,567 U/mL; CEA: 310 ng/mL). Magnetic resonance imaging also demonstrated bone infiltration, suggesting disseminated disease.

Discussion: This case illustrates several important diagnostic challenges. First, although β-hCG positivity typically indicates pregnancy, non-gestational malignancies may rarely cause low-level β-hCG elevation and lead to diagnostic confusion. In such cases, reliance solely on β-hCG may result in misinterpretation of the clinical picture. Second, malignancy-associated DIC is a well-recognized but often under-recognized complication of advanced gastrointestinal cancers. Tumor-related activation of the coagulation cascade can result in severe thrombocytopenia, consumption coagulopathy, and life-threatening bleeding complications such as intracranial hemorrhage. In contrast, primary coagulopathy is uncommon in ectopic pregnancy; therefore, the presence of profound thrombocytopenia or DIC should raise suspicion for alternative systemic causes. Finally, metastasis of gastrointestinal adenocarcinoma to the fallopian tube is extremely rare. While ovarian metastases from gastrointestinal tumors are relatively well described, isolated tubal involvement is seldom reported and may present with symptoms mimicking gynecologic emergencies.

Conclusion: β-hCG positivity does not always indicate pregnancy. In patients presenting with suspected ectopic pregnancy accompanied by severe thrombocytopenia or DIC, underlying systemic malignancy should be considered. Gastrointestinal cancers may rarely present with tubal metastasis and mimic acute gynecologic conditions. Malignancy-associated DIC may progress rapidly and lead to fatal complications.

Keywords: Ectopic pregnancy mimic, signet-ring cell adenocarcinoma, tubal metastasis

[PS-005]

Şilöz asit ile prezente olan Meigs sendromu: Nadir bir olgu sunumu

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Amaç: Meigs sendromu; plevral efüzyon, asit ve benign over tümörü ile karakterize nadir görülen klinik bir tablodur. Genellikle over fibromu ile ilişkili olup ovaryan tümörün cerrahi olarak eksize edilmesi sonrasında plevral efüzyonun ve asitin gerilemesi Meigs sendromunda tipiktir. Asit sıklıkla seröz vasıfta olmakla birlikte, şilöz asit varlığı oldukça nadir olarak görülmektedir. Şilöz asit, lenfatik sistemden kaynaklanan ve triliserid miktarı açısından zengin sıvı ile karakterizedir. Bu olgu sunumunda, şilöz asit ile prezente olan ve yapılan cerrahi sonrası gerileyen nadir bir Meigs sendromu olgusunun sunulması amaçlanmıştır.

Gereç ve Yöntemler: Elli iki yaşında, nullipar, ek hastalığı olmayan kadın hasta, nefes darlığı ve progresif karın şişliği şikayetleri ile merkezimize başvurdu. Yapılan fizik muaynede sol hemitoraksta solunum seslerinde azalma ve yaygın abdominal distansiyon saptandı. Yapılan görüntülemelerde (toraks BT ve tüm batın MR), sağ over kaynaklı yaklaşık 17 cm solid kitle, yaygın asit ve sol plevral efüzyon izlendi. Hastaya uygulanan torasentez ve parasentez sonucu elde edilen sıvının süt beyazı görünümde olduğu ve trigliserid düzeyinin yüksek olduğu belirlenerek şilöz asit tanısı konuldu. Tümör belirteçlerinden CA125: 2005 U/mL olarak bulundu. Hastaya operasyon planlandı; total abdominal histerektomi, frozen uygulandı. Frozen patoloji fibrom olarak bildirildi.

Bulgular: Yapılan postoperatif histopatolojik değerlendirme sonucunda lezyonun benign over fibromu ile uyumlu olduğu saptandı. Postoperatif dönemde hastanın plevral efüzyonunun ve asitinin belirgin şekilde gerilediği ve takiplerde tamamen kaybolduğu izlendi. Buna paralel olarak hastanın şikayetleri de tamamen geriledi.

Sonuç: Meigs sendormu nadir görülen klinik bir durum olmakla birlikte, özellikle over kaynaklı benign kitleler ile birlikte plevral efüzyon ve asit varlığında ayırıcı tanıda akılda tutulmalıdır. Şilöz asit ile birlikteliği oldukça nadir olup, maligniteyi taklit edebilen klinik bir tabloya neden olabilir. Bu nedenle dikkatli bir değerlendirme yapılması önem arz etmektedir. Cerrahi olarak tümörün eksize edilmesi çoğunlukla hem tanısal hem de tedavi edici olup, asit ve plevral efüzyonun gerilemesi ile sonuçlanır. Sunulan bu olgu, Meigs sendromunun atipik bir prezentasyonu olan şilöz asit ile birlikteliğini göstermesi açısından literatüre katkı sağlamaktadır.

Anahtar Kelimeler: Meigs, fibrom, asit

[PS-006]

Cerrahi evrelenmiş evre 1 endometrioid endometriyum kanserinde hastalıksız sağkalımı belirleyen faktörler

Arife Ebru Taşcı

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Amaç: Erken evre endometriyum kanserinde evre, grade, myometriyal invazyon derinliği ve lenfovasküler alan invazyonu (LVSI) onkolojik sonuçları belirlemektedir. Çalışmamızda, evre I endometrioid endometriyum kanserinde klinikopatolojik özelliklerin ve hastalıksız sağkalımı (HS) etkileyen prognostik faktörlerin tanımlanması amaçlandı.

Gereç ve Yöntemler: Lenfadenektomi yapılmış evre I endometrioid endometriyum kanserli 149 hasta retrospektif olarak değerlendirildi. Non-endometrioid tümör tipi olanlar ve senkronize malignitesi olanlar çalışmaya dahil edilmedi. HS cerrahiden rekürrense veya son takip edilen zamana kadar olan süre olarak tanımlandı. Yaşam analizi Kaplan-Meier yöntemiyle değerlendirildi ve sonuç log-rank testiyle karşılaştırıldı. Evrelemede FIGO 2009 kriterleri kullanıldı.

Bulgular: Çalışma grubunun ortalama yaşı 61,9±9,9 yıldı. Ortanca tümör boyutu 40 mm (aralık; 2-120) ve ortanca çıkarılan lenf nodu sayısı 35'ti (aralık; 2-105). Evre hastaların %59,7'sinde IA'ydı. Grade düzeyi hastaların %54,4'ünde 1, %36,2'sinde 2 ve %9,4'ünde 3'tü. Myometriyal invazyon hastaların %6'sında yokken %40,3'ünde ≥%50'ydi. Çalışma grubunun %14,8'inde LVSI mevcuttu. Peritoneal sitoloji tüm olgularda negatifti. Hastaların %44,3'ünün adjuvan radyoterapi aldığı ve evre IB'de adjuvan radyoterapinin belirgin şekilde daha fazla verildiği (%90 vs. %13,5; p<0,0001) belirlendi. Ortanca takip süresi 25 aydı (aralık; 1-50). Bu süre içinde 7 hastada (%4,7) rekürrens geliştiği ve bunlardan 1'inin (%0,7) hastalıktan dolayı kaybedildiği saptandı. Rekürrenslerin 4'ü sistemik rekürrens şeklindeydi. Çalışma grubunda 5 yıllık HS %93 ve genel sağkalım %99'du. Yaş, evre, grade düzeyi, myometrial invazyon varlığı ve derinliği, tümör boyutu, servikal glandüler yayılım, LVSI, çıkarılan lenf nodu sayısı, adjuvan tedavi alıp almadığı HS ile ilişkili değildi. Ancak, evre (IA vs. IB) ve grade düzeyi (1-2 vs. 3) anlamlı olma eğilimindeydi. 5 yıllık HS ileri evrede (%96 vs. %87; p=0,071) ve grade 3'te (%95 vs. %75; p=0,054) daha kötüydü. Bu iki parametreyi bir arada değerlendirdiğimizde (evre IB ve grade 3 vs. diğerleri) HS belirgin olarak yüksek riskli hasta grubunda (evre IB ve grade 3) daha düşüktü. 5 yıllık HS bu hasta grubunda %33 iken çalışma grubunun geri kalanında %95'ti (p<0,001).

Sonuç: Cerrahi evrelenmiş evre I endometrioid endometriyum kanserinde onkolojik sonuçlar iyi olmakla birlikte özellikle evre IB grade 3'te belirgin biçimde kötüleşmekteydi. Bulgularımız, bu hasta grubunda mutlaka adjuvan tedavi verilmesi gerektiğini göstermektedir.

Anahtar Kelimeler: Endometrioid endometriyum kanseri, hastalıksız sağkalım, rekürrens

Tablo 1. Genel özellikler (n=146)

Faktör		Ortalama±SD	Ortanca (Aralık)
Yaş (yıl)		61.9±9.9	62 (27-81)
Tümör boyutu (mm)		44.4±24.2	40 (2-120)
Çıkarılan lenf nodu sayısı		36.3±19.6	35 (2-105)
		n	%
2009 FIGO evre	IA	89	59.7
	IB	60	40.3
FIGO grade	1	81	54.4
	2	54	36.2
	3	14	9.4
Myometrial invazyon	Yok	9	6
	<1/2	80	53.7
	≥1/2 [1]	60	40.3
Servikal yayılım	Yok	144	96.6
	Glandüler	5	3.4
Lenfovasküler alan invazyonu	Negatif	127	85.2
	Pozitif	22	14.8
Peritoneal sitoloji	Negatif	149	100
	Pozitif	-	-

[1]: Seromal yayılımı olan hastalar dahil değil

Tablo 2. Hastalıksız yaşam oranını belirleyen faktörler

Faktör		5-yıl Hastalıksız Yaşam (%)	*p* Değeri
Yaş [1]	<62	94	*0.698*
	≥62	93	
Yaş [2]	<65	95	*0.295*
	≥65	91	
FIGO 2009 evre	IA	96	*0.071*
	IB	87	
FIGO grade	1	95	*0.155*
	2	96	
	3	75	
FIGO grade	1 ve 2	95	*0.054*
	3	75	
FIGO 2009 evre ve FIGO grade	Diğerleri	95	***<0.001***
	IB ve grade 3	33	
Myometrial invazyon	Yok	100	*0.187*
	<1/2	96	
	≥1/2 [3]	87	
Tümör boyutu (mm) [1]	≤40	96	*0.155*
	>40	90	
Servikal yayılım	Negatif	94	*0.088*
	Glandüler	80	
Lenfovasküler alan invazyonu	Negatif	94	*0.939*
	Pozitif	91	
Çıkarılan lenf nodu sayısı [1]	≤35	94	*0.626*
	>35	93	
Adjuvan tedavi	Almadı	93	*0.956*
	Aldı	94	

[1]: Ortanca değerler;
[2]: Geriatrik yaş
[3]: Seromal yayılımı olan hastalar dahil değil;

[PS-007]

Radikal histerektomi planlanan serviks kanseri hastasında insidental pelvik ektopik böbrek; olgu sunumu

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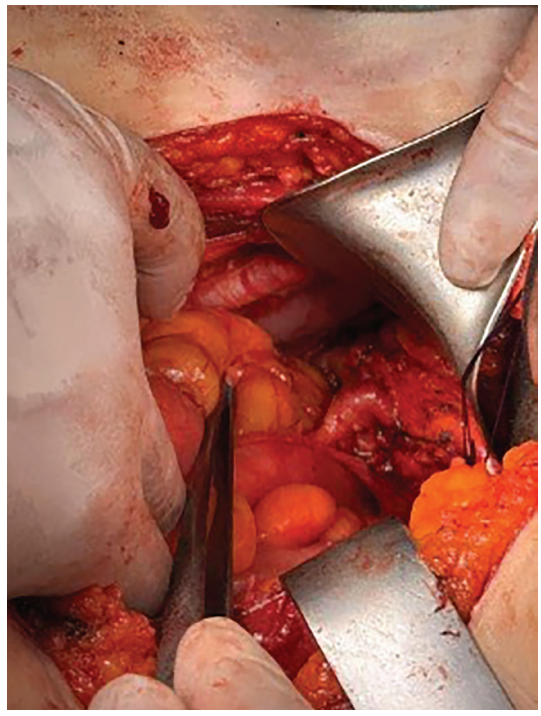
Amaç: Ektopik pelvik böbrek, embriyolojik gelişim sürecinde böbreğin normal retroperitoneal lojuna çıkamaması sonucu ortaya çıkan anatomik bir farklılıktır. Üreterlerin ve iliak damarların diseksiyonunun yapıldığı olgularda pelvis yerleşimli bir böbreğin bulunması cerrahiyi zorlaştırabilmekte ve komplikasyon riskini arttırmaktadır. Bu olgu sunumunda serviks kanseri (skuamöz hücreli karsinom) tanısı almış ve preoperatif değerlendirmede sol böbreğin pelvik yerleşimli olduğu tespit edilen bir hastaya başarıyla uygulanan tip 2 radikal histerektomi (Wertheim operasyonu) ve lenf nodu diseksiyonu anlatılmaktadır.

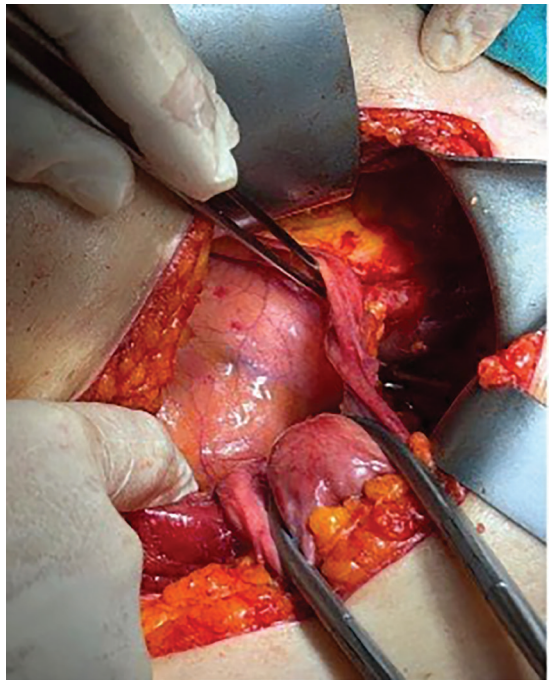
Olgu: Altmış yaşında gravida 3, parite 2 kadın hasta yapılan rutin smear taramasında HPV tip 16 pozitifliği ve ASCUS raporlanması üzerine kolposkopik değerlendirmeye alınmış; yapılan kolposkopik biyopsi sonucunda skuamöz hücreli karsinom tanısı alması sonucunda tarafımıza başvurmuştur. Hastaya preoperatif olarak cerrahi evreleme ve anatomi değerlendirilmesi amacıyla yapılan pelvik ve üst batın MR görüntülemesinde serviks seviyesinde 4 mm'lik tümöral oluşum saptanmasına ek olarak sol böbreğin normal şartlar altında olması gereken yer olan retroperitoneal lojda izlenmediği ve pelvise lokalize olduğu raporlanmıştır. Preoperatif anestezi konsültasyonundan ASA-3 risk skoru alan, apendektomi ve hipotiroidi haricinde geçirilmiş cerrahisi ve komorbiditesi olmayan hastaya SCC ön tanısı ile genel anestezi altında Wertheim ameliyatı ve bilateral pelvik lenf nodu diseksiyonu yapılması planlandı. Bu çerçevede batına pfannelstiel insizyon ile girilmesiyle uterus ve adneksler atrofik yapıda olduğu; sol böbreğin ise pelvis yerleşimli olduğu gözlemlendi. Bilateral pararektal ve paravezikal alanlar genişletilerek eksternal iliak ve obturator lenf nodları diseke edildi. Ektopik böbrek komşuluğunda retroperitoneal diseksiyona özen gösterilerek bilateral üreter ve uterin arterlerin hipogastrik arter seviyesine kadar desketelizasyonu tamamlandı ve bu seviyeden bağlandı. İntraoperatif komplikasyon gelişmeksizin operasyon 90 dakikada tamamlandı. Postoperatif değerlendirilmeler sonrasında takipleri sorunsuz seyreden hasta 3. gününde şifa ile taburcu edildi.

Sonuç: Sunumu yapılmış bu olguda serviks kanseri (SCC) tanısı ve nadir bir anatomik varyasyon olan ektopik böbrek birlikteliği olan hastaya cerrahi tedavi uygulanan tip 2 radikal histerektomi ve lenf nodu diseksiyonu başarı ile tamamlanmıştır. İntraoperatif dönemde majör vasküler ya da ürolojik komplikasyon yaşanmaması cerrahi anlamda olumlu bir sonuç olması ile birlikte böbreğin pelvik lokalizasyonu bu işlemin zorluğunu belirgin şekilde artırmaktadır. Bu noktada preoperatif radyolojik görüntülemeler ile anatomik haritalandırma yapılması ve intraoperatif süreçte dikkatli şekilde retroperitoneal diseksiyon tekniklerinin kullanılması değişkenlik gösteren anatomik referans noktalarının güvenle değerlendirilmesi, iyatrojenik yaralanma risklerinin en aza indirilmesi ve anatomik varyasyon halinde cerrahi stratejinin buna uyumlu şekilde yönetilmesi bu olgu sunumunun kilit noktasını oluşturmaktadır.

Anahtar Kelimeler: Serviks kanseri, radikal histerektomi, insidental pelvik ektopik böbrek



Şekil 1. Pelvik ektopik böbrek 1



Şekil 2. Pelvik ektopik böbrek 2

[PS-008]

Nadir görülen bir jinekolojik patoloji: Miyomektomi zemininde saptanan STUMP olgusu

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Amaç: Uterin STUMP (smooth muscle tumors of uncertain malignant potential) histolojik olarak benign karakterli leiomyom ile malign karakterli leomyosarkom spektrumu arasında yer alan, oldukça nadir görülen ve malignite potansiyeli net bir şekilde öngörülemeyen düz kas tümörlerindendir. Genel olarak preoperatif dönemde miyom tanısı alır ve kesin tanı ancak miyomektomi yada histerektomi operasyonu sonrasında çıkartılan materyalin histopatolojik olarak incelenmesiyle konulabilmektedir. Biyolojik seyrindeki malignite konusundaki belirsizlikler ve maligniteye dönüşebilme riski bu tümörlerin cerrahi yönetimi ve postoperatif takip açısından zorlu bir süreç oluşturmaktadır. Bu posterde miyomektomi sonrası patolojisi STUMP olarak raporlanmış ve kliniğimizde evreleme/debulking cerrahisi uygulanmış bir hastanın sunumu yapılmıştır.

Olgu: Kırk iki yaşında; gravida 4, parite 4 olan kadın hasta yaklaşık 3 ay önce dış merkezde miyom ön tanısıyla miyomektomi geçirmiş olup çıkartılan 8x6 cm boyutlarındaki materyalin patoloji sonucunun "sitolojik atipi ve sellülarite artışı içeren, ancak nekroz izlenmeyen STUMP" olarak raporlanması üzerine, onkolojik açıdan inceleme yapılması ve ileri cerrahi planlanması için tarafımıza refere edilmiştir. Preoperatif olarak anesteziden cerrahi için onay alınarak hastaya jinekolojik onkoloji prensiplerine uygun şekilde operasyon planlanmıştır. Batına pfannenstiel insizyon ile girilmiş, uterusun, tubaların ve overlerin atrofik olarak görülmesi üzerine hastaya total abdominal histerektomi, bilateral salpingo-ooferektomi (TAH + BSO), bilateral pelvik (eksternal iliak ve obturator) lenf nodu diseksiyonu ve omentum biyopsisi uygulanması sonrasında batın içi yıkama sıvısından sitoloji örneği alınmıştır. İntraoperatif komplikasyon gelişmeyen ve sonrasında postoperatif dönemi stabil seyreden, vital bulguları normal olan, spontan diürezi ve gaz çıkışı olan hasta postoperatif 3.gününde şifa ile taburcu edilmiştir.

Tartışma: STUMP olguları, net bir şekilde leiomyosarkom niteliğinde olmasa da literatüre bakıldığında %8,7 ile %11 arasında değişen oranlarda nüks etme ve metastaz riski barındırdığından dolayı dikkatle yönetilmesi önem arz etmektedir. Tedavi seçimi yapılırken hastanın yaşını ve fertilite isteğini değerlendirmek gereklidir. Fertilite isteği olmayan hastalarda standart tedavi yaklaşımı olgumuzda da olduğu gibi histerektomi ve bilateral salpingo-ooferektomidir. Ancak bizim olgumuzda da görülebileceği gibi miyomektomi sonrasında "tesadüfi" olarak yakalanmış STUMP olgularında hastalığın gerçek yayılımını belirlemek ve okült maligniteyi dışlayabilmek için pelvik lenf nodu diseksiyonu, omentektomi ve sitolojiyi içeren sekonder bir evreleme cerrahisi oldukça rasyonel ve güvenli bir yaklaşımdır. Nükslerin yıllar sonra bile ortaya çıkabileceği göz önünde bulundurulduğunda bu cerrahi yaklaşım yalnızca kesin tanıyı sağlamaz aynı zamanda hastanın uzun dönem sağ kalım oranını maksimize etmektedir.

Sonuç: Miyom ön tanısı ile opere edilen hastalarda STUMP tanısı her ne kadar nadir gözlense de atlanmaması gereken sürpriz bir tanıdır. Kesin tanı sonrasında hastanın jinekolog onkologlar tarafından değerlendirilmesi, operasyon sonrası rezidü doku bırakılmaması ve evrelemenin tamamlanması hastalığın yönetilmesi açısından anahtar rol oynamaktadır. Bu hastalarda cerrahi sonrası uzun dönem ve yakın klinik izlem hayati önem arz etmektedir.

Anahtar Kelimeler: Miyomektomi, STUMP, TAH + BSO

[PS-009]

Retroperitonun gizli tümörü: Retroperitoneal liposarkom olgu sunumu

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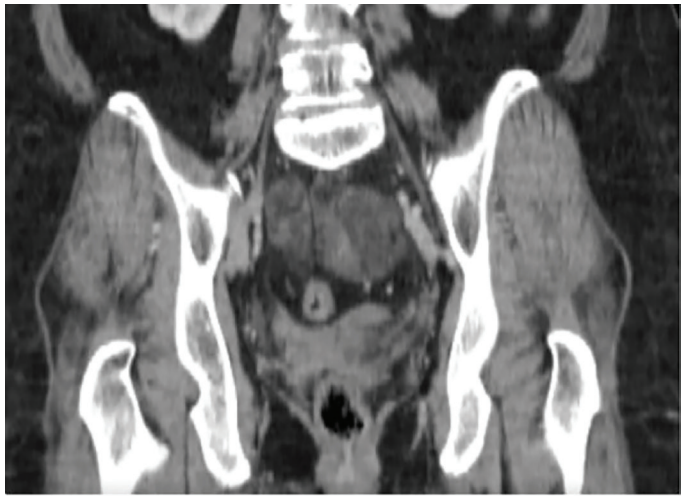
Amaç: Liposarkomlar mezenkimal kökenli malign yumuşak doku tümörleri olup en sık retroperitoneum ve ekstremitelerde görülür. Jinekolojik sistemde uterus kaynaklı liposarkomlar oldukça nadirdir. Bu tümörler klinik ve radyolojik olarak sıklıkla benign uterin kitlelerle karışabilmektedir. Tanı genellikle cerrahi sonrası yapılan histopatolojik inceleme ile konulmaktadır. Bu çalışmada uterusta liposarkom tanısı alan hastanın klinik özellikleri, cerrahi tedavisi ve takip süreci sunulmuştur.

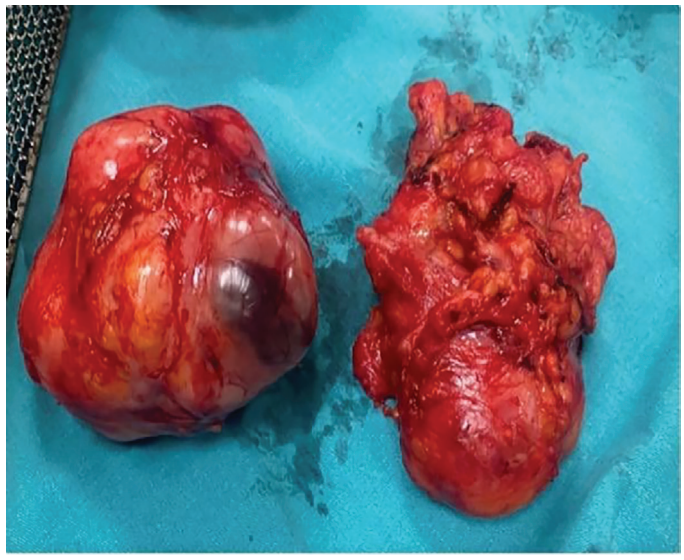
Olgu: Altmış yaşında kadın hasta kliniğimize karında sertlik şikayetiyle başvurdu. Hastanın öyküsünde Ocak 2024 tarihinde karında sertlik ve şişlik nedeniyle başka bir merkezde değerlendirilmiş olduğu ve Haziran 2024 tarihinde karın içinden yaklaşık 7 kg ağırlığında sarkom kitlesi eksize edildiği öğrenildi. Ameliyat sonrası erken dönemde gelişen hemoraji nedeniyle hasta postoperatif ilk gün tekrar opere edilmiştir. Hasta 2024 yılı içerisinde toplam 9 kür kemoterapi tedavisi almıştır. Hastanın özgeçmişinde diyabetes mellitus öyküsü bulunmakta olup düzenli ilaç kullanımı olmadığı öğrenildi. Ayrıca periferik arter hastalığı nedeniyle rivaroksaban (Xarelto 20 mg) kullanımı olduğu bildirilmiştir. Soygeçmişinde kızında meme kanseri öyküsü olduğu öğrenildi. Mevcut değerlendirme sonucunda hastaya sitoredüktif cerrahi ve insizyonel herni onarımı planlanarak cerrahi tedavi uygulandı. Genel anestezi altında göbek altı ve üstünü içeren median insizyonla batına girildi. Batın ön duvarına yapışık insizyonel herni ve yaygın intraabdominal adhezyonlar izlendi. Adhezyonlar keskin ve künt diseksiyon ile ayrılarak batın eksplorasyonu yapıldı. Barsak pasajını sağlamak ve anatomiyi restore etmek amacıyla barsaklar arasındaki adhezyonlar makas ve koter yardımıyla diseke edildi. Pelviste sağ lateral bölgede iliak damarlar, üreter ve sigmoid kolona komşu yaklaşık 7 cm boyutlarında retroperitoneal kitle saptandı. Retroperitoneal alana girilerek bilateral üreterler vizualize edilip, kitle çevre dokulardan diseksiyon ile ayrılarak eksize edildi. Ayrıca sağ iliak arter komşuluğunda ve sakrum önünde yaklaşık 4-5 cm boyutlarında bilobüle presakral kitle palpe edilerek eksize edildi. Omentektomi yapılarak çıkarılan kitleler ve omentum batın dışına alındı. Pelvise Foley dren yerleştirildi. Fasya 1/0 loop PDS ile kontinü, deri altı 2/0 Vicryl, deri 2/0 Prolen matres sütür ile kapatıldı.

Sonuç: Uterin liposarkom oldukça nadir görülen malign mezenkimal tümörlerdendir. Klinik ve radyolojik olarak benign uterin kitlelerle karışabilmesi nedeniyle kesin tanı çoğunlukla histopatolojik inceleme ile konulmaktadır. Erken tanı ve uygun cerrahi tedavi hastalık yönetiminde önemlidir. Nüks ve metastaz riski nedeniyle hastaların uzun dönem takip edilmesi önerilmektedir.

Anahtar Kelimeler: Retroperitoneal liposarkom, TAH-BSO



Şekil 1. Retroperitoneal liposarkom 1



Şekil 2. Retroperitoneal liposarkom 2

[PS-010]

Vulvar malign melanom olgusunda metakron meme kanseri

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Amaç: Vulvar malign melanom, jinekolojik maligniteler arasında nadir görülen ancak agresif seyirli bir tümördür. Prognoz başlıca tümör invazyon derinliği ve bölgesel lenf nodu tutulumu ile ilişkilidir. Vulvanın kompleks lenfatik drenajı ise metastatik yayılım paterninin öngörülmesini güçleştirebilir.

Olgu: Altmış dört yaşındaki kadın hastaya, sağ labium majusta lokalize vulvar malign melanom (Breslow 5 mm, Clark düzeyi IV) tanısıyla radikal vulvektomi ve ipsilateral inguinal lenf nodu diseksiyonu uygulandı. İlk patolojik değerlendirmede ipsilateral lenf nodu metastazı saptanmadı. İzlemin birinci yılında erken evre metakron meme kanseri tanısı alan hastada, 22. ayda izole sol inguinal lenf nodu nüksü gelişti ve yeniden opere edildi.

Tartışma: Başlangıçta ipsilateral nodların negatif olduğu lateralize bir tümörde geç dönemde kontralateral inguinal nüks gelişmesi, vulvanın bilateral ve değişken lenfatik drenajını göstermektedir. Bu olgu, vulvar malign melanomda uzun dönem yakın izlemin ve multidisipliner yaklaşımın önemini vurgulamaktadır.

Sonuç: Primer vulvar malign melanomda ipsilateral lenf nodları negatif sonuçlansa bile yüksek Breslow; invazyon derinliği (5 mm ve üzeri) bu malignitenin sistemik ya da aberran lenfatik yollarla yayılabilme potansiyeline sahip olduğunu göstermektedir. Bu hasta popülasyonunda metakron meme kanseri gibi ikinci primer maligniteleri gelişme riski yüksek olduğu için; jinekolojik muayene, PET-BT ve meme taramalarını içeren sıkı ve multidisipliner onkolojik takipler hayat kurtarıcıdır.

Anahtar Kelimeler: Meme kanseri, vulvar malign melanom

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[PS-012]

Primer endometriyal taşlı yüzük hücreli adenokarsinom: Olgu sunumu ve literatür incelemesi

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[2]*Sağlık Bilimleri Üniversitesi, İstanbul Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, İstanbul*

[3]*İstanbul Aydın Üniversitesi, VM Medical Park Florya Hastanesi, Jinekolojik Onkoloji Kliniği, İstanbul*

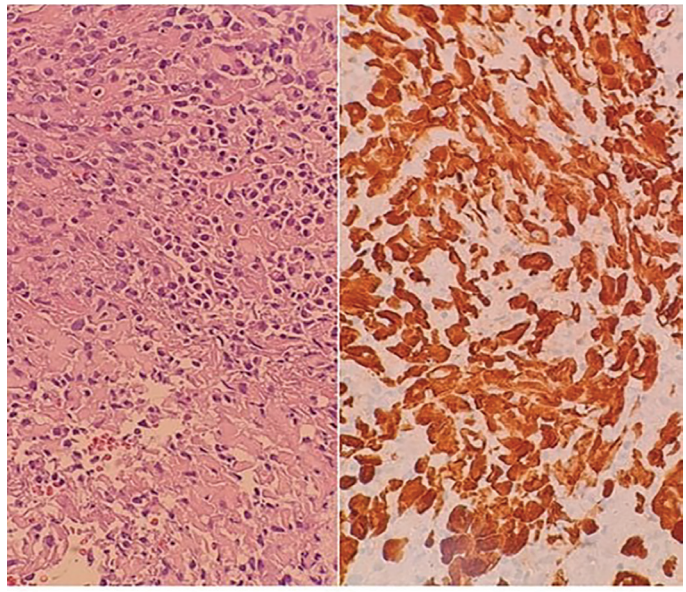
Amaç: Primer endometriyal taşlı yüzük hücreli adenokarsinom son derece nadir görülen bir histolojik alt tiptir ve çoğu olguda genital sistem dışı malignitelerin metastazı ile karışabilmektedir. Bu çalışmada nadir bir olgunun sunulması ve mevcut literatürün gözden geçirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Bu çalışma retrospektif olgu sunumu olarak planlandı. Hastadan yazılı onam alındı. Klinik veriler hasta dosyalarından elde edilerek anonim hale getirildi. Literatürde bildirilen olguları değerlendirmek amacıyla PubMed ve Google Scholar veri tabanlarında "Primary Endometrial Carcinoma with Signet Ring Cells" anahtar kelimeleri ile dil ve zaman kısıtlaması olmaksızın tarama yapıldı ve mevcut olgular incelendi. Sağlık Bilimleri Üniversitesi, İstanbul Eğitim ve Araştırma Hastanesi, Patoloji Anabilim Dalı'ndan Dr. Gonca Kavşut'a mikroskobik görüntülerin sağlanmasındaki katkıları için teşekkür ederiz.

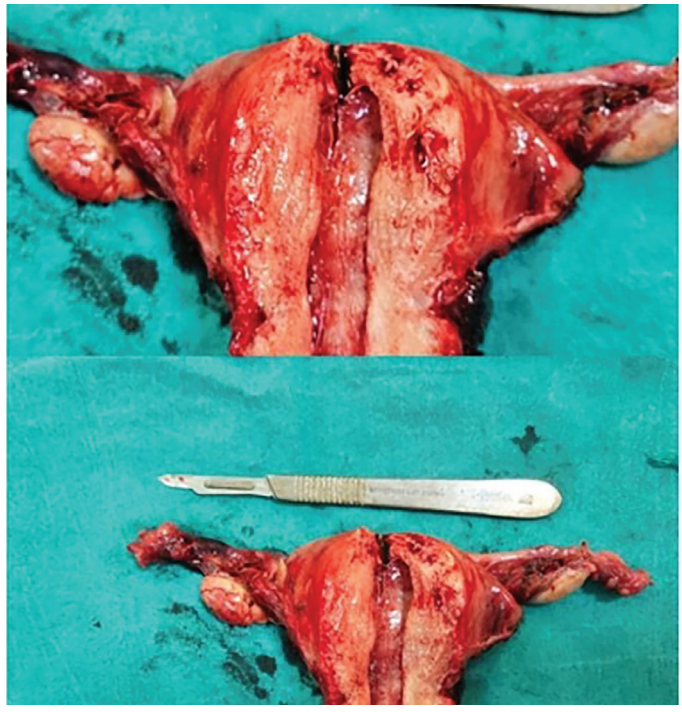
Bulgular: Altmış yedi yaşında, 11 vajinal doğum öyküsü bulunan, yedi yıldır postmenopozal olan hasta dizüri ve sık idrara çıkma şikayeti ile başvurdu. Özgeçmişinde yalnızca diabetes mellitus mevcuttu. Jinekolojik muayenede patoloji saptanmadı. Transvajinal ultrasonografide endometriyum kalınlığı 7 mm ve düzensiz olarak izlendi. Pipelle ile yapılan endometriyal örneklemede zayıf koheziv taşlı yüzük hücreli karsinom enfiltrasyonu raporlandı. Ekstragenital primer odak açısından yapılan değerlendirmede tümör belirteçleri (CEA, CA125, CA15-3, CA19-9) normal bulundu. Gastroskopi, kolonoskopi, meme değerlendirmesi, mamografi, PET-BT ve MRG incelemelerinde malignite lehine bulgu saptanmadı. Hastaya total laparoskopik histerektomi ve bilateral salpingo-ooferektomi uygulandı. Operasyon sırasında serozal yüzeylerde ve overlerde endometriotik odaklar izlendi. Nihai patolojide tümöral oluşum saptanmadı; servikal intraepitelyal neoplazi (CIN I) ve adneksiyel endometriozis raporlandı. Postoperatif 20. ayda hasta hastalıksız olarak izlenmektedir. Literatür incelemesinde olguların çoğunun postmenopozal dönemde ve anormal uterin kanama ile başvurduğu, tanı sonrası gastrointestinal ve meme kaynaklı primerlerin mutlaka dışlanması gerektiği görüldü.

Sonuç: Primer endometriyal taşlı yüzük hücreli adenokarsinom, son derece nadir görülmesi ve sıklıkla gastrointestinal sistem veya meme kaynaklı metastatik tümörlerle karışabilmesi nedeniyle tanısal açıdan önemli zorluklar barındırmaktadır. Bu nedenle, histopatolojik tanı sonrası olası ekstragenital primer odakların dışlanması amacıyla gastroskopi, kolonoskopi ve ileri görüntüleme yöntemlerini içeren kapsamlı bir değerlendirme yapılması gereklidir. İmmünohistokimyasal analizler tanı sürecinde belirleyici rol oynamaktadır. CK7 pozitifliği ve CK20 negatifliği primer endometriyal köken lehine güçlü bulgular sunarken, ters immünprofil kolorektal metastazları düşündürmektedir. Ayrıca GATA3 negatifliği meme kaynaklı tümörleri dışlamada önemli katkı sağlarken, PAX8 pozitifliği Müllerian kökeni destekleyen güvenilir bir belirteçtir. Buna karşın, CEA'nın literatürde heterojen sonuçlar göstermesi nedeniyle gastrointestinal kökenin dışlanmasında sınırlı tanısal değere sahip olduğu anlaşılmaktadır. Literatür verileri, olguların çoğunlukla postmenopozal dönemde ve anormal uterin kanama ile başvurduğunu göstermektedir; ancak asemptomatik olguların varlığı klinik şüphenin önemini ortaya koymaktadır. Histopatolojik olarak, tümörün tamamen taşlı yüzük hücrelerinden oluşup oluşmamasına göre terminolojik ayrım yapılması önerilmektedir. Bu nadir tümör alt tipinde tedavi yaklaşımları standart olmayıp cerrahi, kemoterapi ve radyoterapi uygulamaları olgular arasında değişkenlik göstermektedir. Sonuç olarak, doğru tanı için multidisipliner yaklaşım, kapsamlı immünohistokimyasal değerlendirme ve ekstragenital primerlerin titizlikle dışlanması esastır. Daha geniş olgu serilerine ihtiyaç duyulmakta olup, bu sayede hastalığın klinik seyri ve optimal tedavi stratejileri daha net ortaya konulabilecektir.

Anahtar Kelimeler: Endometriyal neoplazmlar, taşlı yüzük hücreli adenokarsinom



Şekil 1. ×40 büyütmede yan yana mikroskobik görüntüler. Sol: Hematoksilen-eozin (H&E) boyalı kesitte, fibrinöz zemin içerisinde dağınık olarak izlenen, intrasitoplazmik müsin içeren ve taşlı yüzük morfolojisi ile uyumlu atipik epiteloid hücre kümeleri. Sağ: Pansitokeratin (PCK) ile yapılan immünohistokimyasal boyamada, tümör hücrelerinde yaygın ve güçlü sitoplazmik pozitiffik izlenmekte olup epitelyal kökeni desteklemektedir



Şekil 2. Makroskopik incelemede histerektomi spesimeninde malignite lehine herhangi bir bulgu saptanmadı. Cerrahi materyal açılarak ayrıntılı şekilde değerlendirildi ve tümöral kitle ya da şüpheli lezyon izlenmedi

Tablo 1.

Olgu	Yazar	Yaş	Semptom	Cerrahi	Evre	Adjuvan tedavi	Takipte hastalıksız sağkalım
1	Mooney ve ark. 1997	65	Asemptomatik	TAH + BSO + pelvik/paraaortik LND + omentektomi + batın sitolojisi			6 ay
2	Chebib ve ark. 2010	51	Trousseau sendromu, assit ve kilo kaybı	TAH + BSO + bilateral pelvik lenfadenektomi + batın sitolojisi	IVB	6 siklus karboplatin + paklitaksel	Metastaz sonucu ölüm
3	Boyd ve ark. 2010	46	Aşırı menstrüel kanama	Subtotal histerektomi			
4	Boyd ve ark. 2010	59	Postmenopozal kanama	TAH			
5	Pusiol ve ark. 2014	53	Aşırı menstrüel kanama	TAH + BSO + pelvik/paraaortik LND	IB		22 ay
6	Akkalp ve ark. 2015	77	Postmenopozal kanama	TLH + BSO + bilateral pelvik lenfadenektomi	IA	RT	14 ay
7	Ota v ark. 2015	66	Postmenopozal kanama	Radikal histerektomi + BSO + pelvik/ paraaortik LND	IB	6 siklus karboplatin + paklitaksel	17 ay
8	Shahin ve ark. 2015	80	Postmenopozal kanama	LaVAH + BSO, omental biyopsi + batın sitolojisi	IA		48 ay
9	Marketkar ve ark. 2016	64	Postmenopozal kanama	Endometrial biyopsi		Sisplatin ve pelvik RT	7 ay
10	Sierra ve ark. 2020	73	Postmenopozal kanama	TAH + BSO + pelvik/paraaortik LND + omentektomi	IIIA	6 siklus karboplatin + paklitaksel + RT	28 ay
11	Ali ve ark. 2022	72	Postmenopozal kanama	TAH + BSO + bilateral pelvik lenfadenektomi	IIIC1	KT + RT	10 ay
12	Hoang ve ark. 2023	64	Postmenopozal kanama	TAH + BSO + bilateral pelvik lenfadenektomi	IIB	KT	Takipte
13	Sunulan olgu	67	Asemptomatik	TLH + BSO	IA		20 ay takipte

Primer endometriyal taşlı yüzük hücreli adenokarsinom: bildirilen olgular. TAH: Total abdominal histerektomi, TLH: Total laparoskopik histerektomi, LaVAH: Laparoskopi yardımlı vajinal histerektomi, BSO: Bilateral salpingo-ooferektomi, LND: Lenf nodu diseksiyonu

[PS-014]

Gebelikte dejenere myom nedeniyle myomektomi: Olgu sunumu

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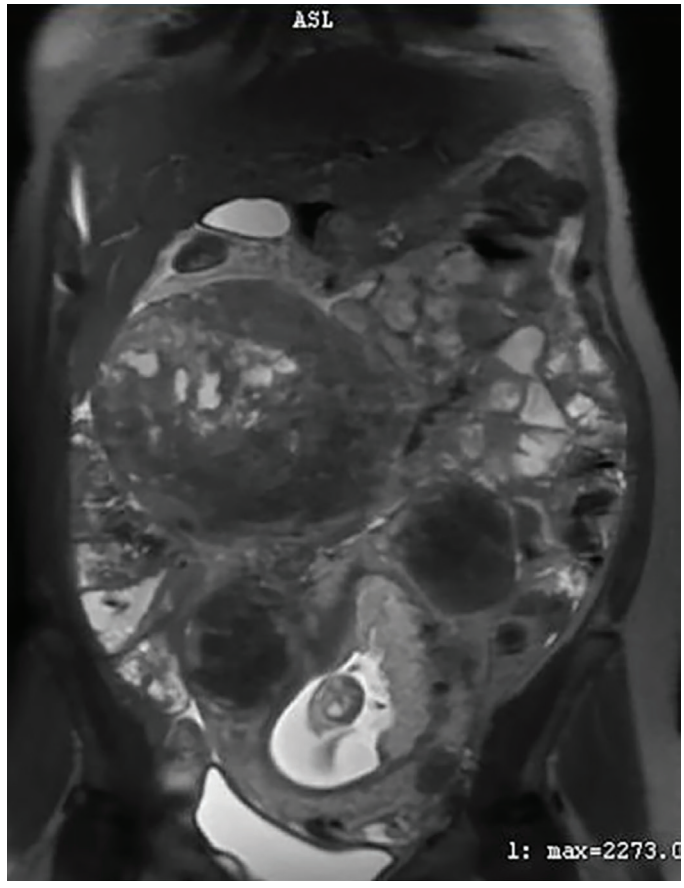
Amaç: Uterin leiomyomlar, üreme çağındaki kadınlarda en sık görülen benign jinekolojik tümörlerdir. Gebelik sırasında artan hormonal uyarı ve myom hacmindeki değişikliklere bağlı olarak dejeneratif değişiklikler gelişebilir. Dejenere myomlar, özellikle şiddetli karın ağrısı ile prezente olarak akut abdomen tablosunu taklit edebilir ve ayırıcı tanıda önem taşır. Gebelikte dejenere myomların tanınması, maternal semptomların uygun yönetimi ve gebelik sürecinin güvenli şekilde sürdürülebilmesi açısından klinik önem arz etmektedir. Bu posterde, 13 hafta 2 günlük gebeliği bulunan ve şiddetli karın ağrısı nedeniyle kliniğimize başvuran, myomektomi uygulanan bir olgu sunulmaktadır.

Olgu: Otuz üç yaşında, evli, gravida 2, parite 1 olan hasta, çok şiddetli sağ yan ağrısı şikayeti ile kliniğimize başvurdu. Yapılan obstetrik ultrasonografik değerlendirmede 13 hafta 2 günlük intrauterin gebelik saptandı; fetal kardiyak aktivitenin pozitif olduğu ve crown-rump length (CRL) ölçümünün 12 gebelik haftası ile uyumlu olduğu izlendi. Ultrasonografide sağ üst kadranda yaklaşık 16×15 cm boyutunda, dejenerasyon bulguları gösteren myom ile uyumlu kitle lezyonu saptandı. Ayrıca uterin anterior duvarda 5 cm ve 6 cm boyutlarında ek myom nodülleri izlendi. Her iki over doğal görünümde değerlendirildi. Klinik ve radyolojik bulgular eşliğinde hastanın mevcut yakınmalarının dejenere myoma bağlı olduğu düşünülerek cerrahi tedavi planlandı. İntraoperatif değerlendirmede fundustan kaynaklanan saplı, nekrotik-dejenere myom izlendi ve hastaya myomektomi uygulandı. Olgu, gebelikte dejenere myomun tanı ve yönetimindeki klinik yaklaşım açısından sunulmaya değer bulundu.

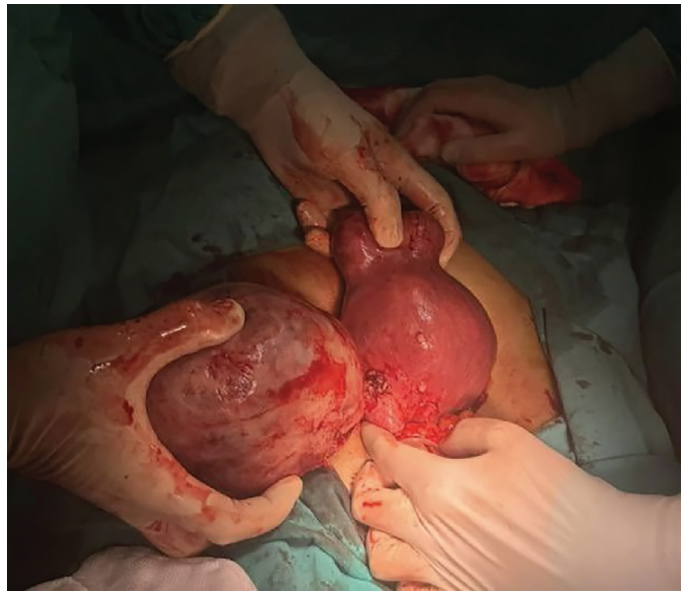
Bulgular: Gebelikte uterin leiomyomlar çoğu zaman asemptomatik seyretmekle birlikte, özellikle büyük boyutlu myomlarda gelişen dejenerasyon şiddetli karın ağrısına yol açarak akut abdomen tablosunu taklit edebilmektedir. Bu durum, gebelikte apandisit, adneksiyel torsiyon, ablatio plasenta ve diğer cerrahi aciller ile ayırıcı tanının dikkatli şekilde yapılmasını gerekli kılmaktadır. Özellikle hızlı büyüme gösteren veya kanlanması bozulan myomlarda ortaya çıkan dejeneratif değişiklikler, konservatif tedaviye dirençli ağrı ile prezente olabilir. Gebelikte dejenere myomların yönetiminde ilk yaklaşım çoğunlukla konservatif tedavi olmakla birlikte, medikal tedaviye yanıt vermeyen şiddetli ağrı, tanısal belirsizlik veya maternal durumun kötüleşmesi halinde cerrahi müdahale gündeme gelebilir. Gebelikte myomektomi, kanama ve gebelik kaybı riski nedeniyle çekinceyle yaklaşılan bir işlem olsa da, seçilmiş olgularda ve uygun cerrahi koşullarda güvenli şekilde uygulanabileceği bildirilmektedir. Özellikle semptomatik, büyük ve dejenerasyon gösteren myomlarda cerrahi tedavi maternal semptomların kontrol altına alınmasında etkili olabilir. Bizim olgumuzda da ikinci trimesterin erken döneminde şiddetli karın ağrısı ile başvuran hastada, ultrasonografik değerlendirmede büyük boyutlu dejenere myom saptanmış, intraoperatif olarak fundustan kaynaklanan saplı, nekrotik-dejenere myom izlenmiş ve klinik bulgular eşliğinde cerrahi tedavi uygulanmıştır. Bu olgu, gebelikte dejenere myomların nadiren cerrahi müdahale gerektirebileceğini ve uygun hasta seçimi ile myomektominin başarılı bir tedavi seçeneği olabileceğini göstermektedir. Sonuç olarak, gebelikte şiddetli abdominal ağrı ile başvuran hastalarda dejenere myom ayırıcı tanıda akılda tutulmalı; tedavi yaklaşımı gebelik haftası, semptomların şiddeti, myomun boyutu ve lokalizasyonu ile maternal-fetal durum göz önünde bulundurularak bireyselleştirilmelidir.

Sonuç: Gebelikte dejenere myom, akut abdomeni taklit edebilen ve tanı-yönetim açısından klinik güçlük oluşturabilen önemli bir durumdur. Her ne kadar ilk basamak yaklaşım konservatif tedavi olsa da, seçilmiş olgularda myomektomi başarılı sonuçlar sağlayabilmektedir. Olgumuz, gebelikte şiddetli karın ağrısı ile başvuran hastalarda dejenere myomun ayırıcı tanıda göz önünde bulundurulması gerektiğini ve uygun hasta seçimi ile cerrahi tedavinin etkin bir seçenek olabileceğini göstermektedir.

Anahtar Kelimeler: Dejenere myom, myomektomi, gebelik



Şekil 1. BT



Şekil 2. İntraop

[PS-015]

Plasenta akreata spektrumunda sezaryen histerektomi: Maternal ve neonatal sonuçlar

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Amaç: Plasenta akreata spektrumu (PAS), artan sıklığı ve yüksek morbidite riski nedeniyle önemli bir obstetrik sorundur. Bu çalışmada, PAS nedeniyle sezaryen histerektomi uygulanan olgularda maternal ve neonatal sonuçların değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: Sağlık Bilimleri Üniversitesi, Ankara Bilkent Şehir Hastanesi Perinatoloji Kliniği'nde 2023-2025 yılları arasında PAS şüphesiyle takip edilen 188 gebeden; sezaryende segmental rezeksiyon, balon uygulaması gibi yöntemler uygulanan veya PAS çıkmayan olgular dışında; histerektomi uygulanan 12 olgunun verileri retrospektif olarak incelendi. Maternal (kan kaybı, transfüzyon, komplikasyon, yoğun bakım) ve neonatal (doğum haftası, doğum ağırlığı, Apgar, yenidoğan yoğun bakım ünitesi ihtiyacı) sonuçlar analiz edildi. Veriler SPSS (Statistical Package for the Social Sciences) ile değerlendirilerek uygun istatistiksel yöntemlerle sunuldu.

Bulgular: Çalışmaya dahil edilen olguların ortalama yaşı 35,2±5,0 yıl olup, ileri maternal yaş dikkat çekmektedir. Median gravida sayısı 3,5 ve median parite sayısı 2 olup, median geçirilmiş sezaryen sayısı 2; eşlik eden hastalık ve ilaç kullanım oranlarının düşük olduğu görülmüştür. Median operasyon haftası 34 hafta olup; doğumların önemli bir kısmının preterm dönemde gerçekleştiği gözlenmiştir. Tüm hastalara intraoperatif transfüzyonun verilmiş olduğu görüldü. Neonatal değerlendirmede median doğum ağırlığı 2297 gr olup prematürite ile uyumludur. Apgar skorlarının 1. dakikada görece düşük (5,3±1,6), 5. dakikada artış göstermesi (7,4±1,2) ise neonatal adaptasyonun zamanla düzeldiğini düşündürmektedir. Yenidoğan yoğun bakım ünitesi (YYBÜ) ihtiyacının yüksek olduğu izlenmiştir. Maternal komplikasyon oranı düşük düzeyde olup, maternal yoğun bakım ihtiyacı sınırlı sayıda olguda gözlenmiştir. Neonatal mortalite nadir olarak saptanmıştır. Genel olarak bu bulgular, ileri maternal yaş ve geçirilmiş sezaryen öyküsüne sahip bu hasta grubunda preterm doğum, artmış transfüzyon gereksinimi ve belirgin neonatal bakım ihtiyacı ile karakterize yüksek riskli bir klinik tabloyu ortaya koymaktadır.

Sonuç: PAS nedeniyle sezaryen histerektomi uygulanan hastalar, yüksek oranda maternal morbidite ve preterm doğuma bağlı neonatal risk taşımaktadır. Özellikle kan transfüzyonu gereksinimi, preterm yoğun bakım ihtiyacı ve cerrahi komplikasyon riski bu hasta grubunda ön plandadır. Prenatal tanı ve multidisipliner yaklaşımla planlanan cerrahilerin, maternal ve neonatal sonuçları iyileştirmede önemli rol oynadığı görülmektedir. Bu nedenle PAS olgularının erken tanınması ve deneyimli merkezlerde yönetilmesi, komplikasyon riskinin azaltılması açısından kritik öneme sahiptir.

Anahtar Kelimeler: Plasenta akreata spektrumu, plasenta previa, perinatoloji

Tablo 1.

	n=12	
Yaş		35,25±5,01
Gravida		3,5 (2-5)
Parite		2 (1-3)
Yaşayan		1,92±0,51
Ek hastalık		0,42±0,51
İlaç kullanımı		0,25±0,45
Geçirilmiş sezaryen sayısı		2 (0-2)
Demografik özellikler		

Tablo 2.

	n=12	
Operasyon haftası		34 (25-37)
YYBÜ		0,83±0,39
Apgar 1.dk		5,33±1,56
Apgar 5.dk		7,42±1,24
Doğum ağırlığı (gr)		2297 (595-2700)
Komplikasyon		0,17±0,39
Neonatal ölüm		0 (0-1)
Yoğun bakım (anne)		0,33±0,49
Maternal ve neonatal sonuçlar		

[PS-016]

Gebelikte adneksiyel kitle nedeniyle takip edilen hastaların sonuçları

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Amaç: Gebelikte adneksiyel kitleler, prenatal ultrasonografinin yaygın kullanımı ile sık karşılaşılan bir durumdur. Çoğunluğu fonksiyonel kist olup ikinci trimesterde spontan gerileme gösterse de, persiste eden olgularda torsiyon, rüptür, obstetrik komplikasyonlar ve nadir malignite riski bulunmaktadır. Bu retrospektif çalışmanın amacı, gebelikte adneksiyel kitle tanısı alan hastaların demografik özelliklerini, ultrasonografik bulgularını, yönetim yaklaşımlarını (konservatif veya cerrahi) ve maternal-fetal sonuçlarını değerlendirmek ve literatür verileriyle karşılaştırmaktır.

Gereç ve Yöntemler: Çalışmamız Sağlık Bilimleri Üniversitesi, Ankara Bilkent Şehir Hastanesi'nde 2023 Ocak-2026 Aralık tarihleri arasında gebelikte adneksiyel kitle nedeniyle takip edilen 12 hasta çalışmaya dahil edildi. 6 cm'den küçük basit kistli olgular hariç tutuldu. Demografik veriler, ultrasonografik özellikler, tümör markerleri [CA125 (kanser antijeni-125), CA-15.3 (kanser antijeni-15.3), CA-19.9 (kanser antijeni-19.9), AFP (Alfa fetoprotein), CEA (karsinoembriyonik antijen)], yönetim şekli ve perinatal sonuçlar hastane kayıt sisteminden retrospektif olarak incelendi. İstatistiksel analiz SPSS 23.0 programı ile yapıldı; nicel veriler ortalama ± standart sapma olarak ifade edildi.

Bulgular: Hastaların ortalama yaşı 29,00±4,16 yıl, gebelik tanı haftası 20,27±9,18 hafta, ortalama kist boyutu 107,86×83,86 mm idi. Tanıların %33,3'ü birinci, %58,3'ü ikinci, %8,3'ü üçüncü trimesterde konuldu. Ultrasonografik olarak 5 (%41,7) basit kist, 5 (%41,7) kompleks kist, 1 endometrioma ve 1 hemorajik kist görünümündeydi. Basit kist grubunda %60 (n=3), kompleks kist grubunda %80 (n=4) cerrahi gereksinim oldu; toplam cerrahi oranı %58 idi. Spontan gerileme oranı %42 olarak bulundu. Cerrahi endikasyonları torsiyon (n=1, dermoid), rüptür (n=1, dermoid), obstetrik nedenli sezaryen eşliğinde kistektomi (n=3; 1 seröz, 2 müsinöz kistadenom) ve diğer nedenler idi. Tüm patolojiler benign olup malignite saptanmadı. Ortalama doğum haftası 35,67±4,47 idi; tümör markerleri normal sınırlarda kaldı.

Sonuç: Gebelikte adneksiyel kitlelerin büyük kısmı benign seyir gösterir ve konservatif takip ile iyi perinatal sonuçlar elde edilir. Ancak büyük boyutlu ve kompleks kistlerde komplikasyon (torsiyon, rüptür) riski artmakta, bu olgularda ikinci trimesterde veya sezaryen eşliğinde cerrahi müdahale güvenli bir seçenektir. Rutin ultrason taramaları erken tanı için kritik öneme sahiptir. Bulgularımız literatürle uyumludur; daha geniş prospektif çalışmalarla yönetim protokollerinin optimize edilmesi önerilmektedir

Anahtar Kelimeler: Gebelik, adneksiyel kitle, tümör markırları

Tablo 1. Çalışmaya dahil edilen hastalara ait değişkenler

Değişken	Ort ± SS
Yaş	29,00±4,16
Tanı haftası	20,27±9,18
Gravida	2,71±1,79
Parite	1,14±0,90
Boyut (milimetre)	107,86x83,86±(52,85x33,09)
CA125	23,82±17,38
CA-15.3	16,64±4,39
CA-19.9	12,67±7,83
AFP	87,38±80,03
CEA	0,64±0,401
Doğum haftası	35,67±4,47

Tablo 2. Hastalara ait sonuçlar

Hasta no.	Kist natürü	Tanı haftası	Sonuç	Patoloji
1	Basit	21w4d	31w2d obstetrik nedenli C/S + Kistektomi	Seröz kistadenom
2	Basit	5w3d	6. haftada spontan abortus sonrası laparatomi	Hidrosalpenks
3	Basit	23w5d	38w6d miad NSD sonrası rüptür	Corpus luteum kisti
4	Basit	7w4d	9. haftada spontan Abortus sonrası spontan gerileme	
5	Basit	9w1d	39. hafta MİAD NSD sonrası spontan gerileme	
6	Kompleks	24w1d	29w3d obstetrik nedenli C/S + Kistektomi	Müsinöz kistadenom
7	Kompleks	27w6d	39. hafta NSD sonrası spontan gerileme	
8	Kompleks	18w1d	18. haftada laparatomi/Torsiyone, 38w1d miad doğum	Dermoid kist
9	Kompleks	28w3d	29w3d obstetrik nedenli C/S + Kistektomi	Müsinöz kistadenom
10	Kompleks	24w0d	24. haftada rüptür, laparatomi, 38w5d miad doğum	Dermoid kist
11	Endometrioma	5w3d	36. hafta NSD, operasyon gereği olmadı	
12	Hemorajik	21w4d	32w3d obstetrik nedenli CS, Gebelikte spontan gerileme	

[PS-017]

Serviksin ileri evre non-Hodgkin lenfoması: Olgu sunumu

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Amaç: Non-Hodgkin lenfomalar erişkinlerde görülen lenfomaların büyük çoğunluğunu oluşturmakta olup diffüz büyük B hücreli lenfoma (DBBHL) en sık görülen histolojik tiptir. Hastalık çoğunlukla lenf nodlarında görülmekle birlikte ekstranodal yerleşimler de izlenebilir. Serviks yerleşimli lenfoma oldukça nadir olup klinik bulguları non-spesifiktir ve tanısı güç olabilir. Bu çalışmada serviks yerleşimli diffüz büyük B hücreli lenfoma tanısı alan olgunun sunulması amaçlanmıştır.

Gereç ve Yöntemler: Olgu sunumu şeklinde planlanan bu çalışmada 2025 yılında smear sonucu ASC-US saptanması üzerine jinekolojik onkoloji kliniğine yönlendirilen hastanın klinik süreci retrospektif olarak değerlendirildi. Jinekolojik muayenede servikste damarlanma artışı izlenmesi üzerine kolposkopi planlandı ve biyopsi alındı.

Bulgular: Yirmi yedi yaşındaki hastanın smear sonucu ASC-US ve HPV negatif olarak raporlandı. Muayenede servikal damarlanma artışı saptanması üzerine 30 Nisan 2025 tarihinde kolposkopi yapılarak saat 9 ve 11 hizasından biyopsi alındı ve endoservikal küretaj uygulandı. Patoloji sonucu diffüz büyük B hücreli lenfoma olarak raporlandı. İmmünohistokimyasal incelemede CD20 yaygın pozitif, BCL-1 ve MUM1 ile fokal reaktivite izlenmiş olup Ki-67 proliferasyon indeksi %75-80 olarak saptandı. CD5, CD10, CD23 ve TdT negatif bulundu. Hasta hematoloji bölümüne yönlendirildi. Kemik iliği biyopsisinde tutulum izlenmedi. 04 Haziran 2025 tarihinde yapılan PET incelemesinde servikal bölge ile birlikte mediastinal ve abdominopelvik lenf nodlarında artmış FDG tutulumu saptandı. Diyaframın üstü ve altında lenf nodu tutulumu olması nedeniyle hastaya Ann Arbor evre III diffüz büyük B hücreli lenfoma tanısı konuldu ve üç haftada bir uygulanacak şekilde altı kür R-CHOP kemoterapisi başlandı. Üçüncü kür sonunda yapılan ara değerlendirme PET incelemesinde tam metabolik yanıt saptandı. Altı kür tedavi tamamlandıktan sonra hasta tam hematolojik yanıt ile takibe alındı.

Sonuç: Serviks yerleşimli lenfoma oldukça nadir görülen bir hastalıktır ve klinik bulguları çoğu zaman non-spesifiktir. Tanı genellikle biyopsi ile konulmaktadır. Bu hastalarda cerrahinin rolü sınırlı olup temel tedavi yaklaşımını sistemik kemoterapi oluşturmaktadır. Erken tanı ve uygun kemoterapi tedavisi ile başarılı tedavi sonuçları elde edilebilmektedir.

Anahtar Kelimeler: Serviks, lenfoma, non-Hodgkin

SÖZLÜ BİLDİRİLER

[SS-001]

HPV genotip dağiliminin yüksek dereceli servikal intraepitelyal lezyonlarla (CIN2+) ilişkisi

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Amaç: Serviks kanseri, önlenebilir maligniteler arasında yer almakla birlikte dünya genelinde kadınlarda önemli morbidite ve mortalite nedenidir. Yüksek riskli insan papilloma virüsü (HR-HPV) enfeksiyonu servikal karsinogenezde temel etiyolojik faktördür. Özellikle HPV 16 ve HPV 18 genotipleri invaziv serviks kanserlerinin yaklaşık %70'inden sorumludur. Güncel olarak Amerikan Kolposkopi ve Servikal Patoloji Derneği (ASCCP) tarafından önerilen risk temelli yönetim yaklaşımı, hastaların mevcut ve geçmiş HPV genotip sonuçlarına göre CIN3+ gelişme riskini hesaplayarak klinik karar vermeyi önermektedir. Bu nedenle bölgesel HPV genotip dağılımının belirlenmesi, risk stratifikasyonu ve hasta yönetimi açısından kritik öneme sahiptir. Bu çalışmada merkezimizde saptanan HPV genotip dağılımının yüksek dereceli servikal lezyonlarla (CIN2+) ilişkisini değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Bu retrospektif kesitsel çalışmada Şubat 2025-Ocak 2026 tarihleri arasında HPV DNA testi ve eş zamanlı servikal biyopsi sonucu bulunan 312 hasta değerlendirildi. Hastalar histopatolojik sonuçlarına göre düşük dereceli lezyon (normal/CIN1) ve yüksek dereceli lezyon (CIN2, CIN3, adenokarsinoma *in situ*) olmak üzere iki gruba ayrıldı. HPV genotipleri HPV 16, HPV 18 ve diğer yüksek riskli tipler olarak sınıflandırıldı. Demografik ve klinik veriler hastane bilgi sisteminden elde edildi. Gruplar arası karşılaştırmalar ki-kare testi ile yapıldı. CIN2+ gelişimi için bağımsız risk faktörleri çok değişkenli lojistik regresyon analizi ile değerlendirildi. Modele yaş, sigara kullanımı, sitoloji sonucu (ASC-US/LSIL/HSIL), HPV 16 ve HPV 18 pozitifliği ile diğer yüksek riskli HPV genotipleri dahil edildi.

Bulgular: Çalışmaya dahil edilen 312 hastanın yaş ortalaması 38,6±9,4 yıl idi. Hastaların medyan paritesi 2 (0-4) olup ortalama vücut kitle indeksi 27,4±4,6 kg/m² olarak saptandı. Olguların %27,2'sinde (n=85) CIN2+ lezyon tespit edildi. HPV 16 pozitifliği CIN2+ grubunda düşük dereceli lezyonlara göre anlamlı olarak daha yüksek bulundu (%48,2 vs %19,5; p<0,001). HPV 18 pozitifliği özellikle glandüler lezyonlarda daha sık gözlendi (p=0,027). Çok değişkenli lojistik regresyon analizinde HPV 16 pozitifliği CIN2+ gelişimi için bağımsız ve güçlü bir risk faktörü olarak saptandı (OR: 3,84; %95 GA: 2,10-7,02; p<0,001). Diğer yüksek riskli HPV tipleri ile CIN2+ arasında daha zayıf ve sınırda anlamlı bir ilişki gözlendi (OR: 1,62; %95 GA: 0,92-2,84; p=0,080). Parite, vücut kitle indeksi ve sigara kullanımı ile CIN2+ gelişimi arasında istatistiksel olarak anlamlı bir ilişki saptanmadı (p>0,05).

Sonuç: Bu çalışmada HPV genotip dağılımı ile yüksek dereceli servikal intraepitelyal lezyonlar arasındaki ilişki değerlendirildiğinde, HPV 16 pozitifliğinin CIN2+ gelişimi ile güçlü ve bağımsız şekilde ilişkili olduğu gösterilmiştir. Diğer yüksek riskli HPV genotipleri ile CIN2+ arasında daha zayıf bir ilişki gözlenirken, parite, vücut kitle indeksi ve sigara kullanımı ile yüksek dereceli lezyon gelişimi arasında anlamlı bir ilişki saptanmamıştır. Bulgularımız, yüksek dereceli servikal lezyonların öngörülmesinde HPV genotiplemenin önemini desteklemekte ve HPV 16 varlığının risk stratifikasyonunda önemli bir belirteç olduğunu göstermektedir. Bu sonuçlar, servikal kanser tarama programlarında ve klinik yönetim algoritmalarında genotip temelli risk değerlendirmesinin önemini vurgulamaktadır.

Anahtar Kelimeler: Human papillomavirus, servikal intraepitelyal neoplazi, yüksek riskli HPV

Tablo 1. Çalışmaya dahil edilen hastaların demografik ve klinik özellikleri

Değişken	
Yaş (yıl)	38,6±9,4
Parite (n)	2 (0-4)
Vücut kitle indeksi (kg/m²)	27,4±4,6
Sigara kullanımı (n, %)	78 (%25,0)
CIN2+ lezyon varlığı (n, %)	85 (%27,2)
Düşük dereceli lezyon (normal/CIN1), (n, %)	227 (%72,8)

Tablo 2. CIN2+ gelişimi ile ilişkili faktörlerin tek değişkenli ve çok değişkenli lojistik regresyon analizi

	Tek değişkenli analiz OR (%95 GA)	p değeri	Çok değişkenli analiz OR (%95 GA)	p değeri
HPV 16 pozitifliği	4,02 (2,35-6,87)	<0,001	3,84 (2,10-7,02)	<0,001
HPV 18 pozitifliği	1,89 (1,07-3,31)	0,027	1,74 (1,06-2,86)	0,027
Diğer yüksek riskli HPV tipleri	1,71 (0,98-2,97)	0,061	1,62 (0,92-2,84)	0,080
Parite	1,11 (0,95-1,30)	0,193	1,08 (0,91-1,29)	0,365
Vücut kitle indeksi	1,03 (0,98-1,08)	0,245	1,02 (0,97-1,07)	0,416
Sigara kullanımı	1,28 (0,85-1,92)	0,239	1,21 (0,78-1,87)	0,392

[SS-002]

Endometrial intraepitelyal neoplazide eşlik eden endometriyum kanseri için klinik ve ultrasonografik prediktörler

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Endometrial intraepitelyal neoplazi (EIN), endometriyum kanseri gelişimi açısından yüksek risk taşıyan premalign bir lezyon olarak kabul edilmektedir. EIN tanısı alan hastalarda eşlik eden endometriyum kanserinin erken dönemde öngörülmesi, uygun tedavi stratejisinin belirlenmesi açısından önem taşımaktadır. Bu çalışmada, EIN tanısı alan hastalarda endometriyum kanseri varlığı ile ilişkili klinik ve ultrasonografik risk faktörlerinin değerlendirilmesi amaçlanmıştır. Çalışmamıza Ocak 2022-Aralık 2025 tarihleri arasında Sağlık Bilimleri Üniversitesi, Bursa Yüksek İhtisas Eğitim ve Araştırma Hastanesi, Kadın Hastalıkları ve Doğum Kliniği'nde EIN tanısı ile cerrahi tedavi uygulanan 56 hasta dahil edildi. Hastaların demografik özellikleri, obstetrik öyküleri, menopoz durumu, postmenopozal kanama varlığı, hipertansiyon ve diabetes mellitus gibi komorbid hastalıkları, serum CA125 düzeyleri ve transvajinal ultrasonografi ile ölçülen endometrial kalınlık değerleri incelendi. Hastalar nihai histopatolojik sonuçlara göre yalnızca EIN saptanan hastalar ve EIN ile birlikte endometriyum kanseri saptanan hastalar olmak üzere iki gruba ayrıldı. Endometriyum kanseri varlığını öngören bağımsız risk faktörlerini belirlemek amacıyla çok değişkenli lojistik regresyon analizi uygulandı. Çalışmaya dahil edilen 56 hastanın 19'unda (%33,9) nihai histopatolojik incelemede endometriyum kanseri saptandı. Kanser saptanan hastaların ortalama yaşı (p=0,021) ve vücut kitle indeksi (p=0,009) anlamlı olarak daha yüksekti. Postmenopozal durum (p=0,031) ve postmenopozal kanama varlığı (p=0,002) kanser grubunda daha sık gözlendi. Ayrıca kanser grubunda endometrial kalınlık ve CA125 düzeyleri daha yüksek bulundu. Çok değişkenli lojistik regresyon analizinde postmenopozal kanama (OR: 4,21; %95 GA: 1,48-11,92; p=0,006), obezite (OR: 2,92; %95 GA: 1,14-7,48; p=0,024), postmenopozal durum (OR: 2,98; %95 GA: 1,07-8,31; p=0,036) ve artmış endometrial kalınlık (OR: 1,17; %95 GA: 1,05-1,33; p=0,007) eşlik eden endometriyum kanseri için bağımsız risk faktörleri olarak saptandı. Endometrial kalınlık için en iyi eşik değeri 14 mm olup duyarlılık %74 ve özgüllük %73 olarak saptandı. Endometrial intraepitelyal neoplazi tanısı alan hastalarda postmenopozal kanama, obezite, postmenopozal durum ve artmış endometrial kalınlık eşlik eden endometriyum kanseri açısından önemli risk faktörleridir. Bu klinik ve ultrasonografik parametrelerin birlikte değerlendirilmesi yüksek riskli hastaların belirlenmesine katkı sağlayabilir ve cerrahi tedavi kararının verilmesinde yol gösterici olabilir. Daha geniş hasta serileri ile yapılacak prospektif çalışmalar bu bulguların doğrulanmasına yardımcı olacaktır.

Anahtar Kelimeler: Endometrial intraepitelyal neoplazi, endometrial kalınlık, endometrial kanser

Tablo 1. EIN tanısı alan hastaların nihai histopatoloji sonuçlarına göre demografik, klinik, laboratuvar ve ultrasonografik özellikleri

	EIN (n=37)	EIN + endometriyum kanseri (n=19)	p
Yaş (yıl)	51,9±7,6	57,1±8,2	0,021
Vücut kitle indeksi (kg/m^2)	29,8±4,3	33,4±4,8	0,009
Gravida (n)	3 (0-6)	3 (1-7)	0,412
Parite (n)	2 (0-5)	2 (0-6)	0,538
Postmenopozal durum (n, %)	14 (%37,8)	13 (%68,4)	0,031
Postmenopozal kanama varlığı (n, %)	6 (%16,2)	11 (%57,9)	0,002
Hipertansiyon (n, %)	10 (%27,0)	9 (%47,4)	0,132
Diabetes mellitus (n, %)	7 (%18,9)	6 (%31,6)	0,291
Jinekolojik kanser aile öyküsü (n, %)	3 (%8,1)	4 (%21,1)	0,178
CA125 (U/mL)	18 (10-32)	29 (14-58)	0,044
Endometrial kalınlık (mm)	11,8±3,9	16,2±4,6	0,001

Tablo 2. EIN tanısı alan hastalarda endometriyum kanseri varlığını öngören çok değişkenli lojistik regresyon analizi

	Odds ratio (OR)	%95 güven aralığı	p
Yaş	1,05	1.00-1.11	0,141
Obezite	2,92	1.14-7.48	0,024
Postmenopozal durum	2,98	1.07-8.31	0,036
Postmenopozal kanama	4,21	1.48-11.92	0,006
Hipertansiyon	1,72	0.59-5.01	0,309
Diabetes mellitus	1,59	0.52-4.86	0,418
Endometrial kalınlık	1,17	1.05-1.33	0,007
CA125	1,03	1.00-1.06	0,139
Jinekolojik kanser aile öyküsü	2,09	0.55-7.86	0,274

[SS-003]

Mol hidatiformda kontrolsüz uterin kanama nedeniyle acil histerektomi

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Amaç: Gestasyonel trofoblastik hastalık, benign hidatiform molden malign gestasyonel trofoblastik neoplazilere uzanan geniş bir klinik spektrumu kapsar. Günümüzde molar gebelikler çoğunlukla erken dönemde tanınmakla birlikte, bazı olgularda masif vajinal kanama gibi yaşamı tehdit eden komplikasyonlar gelişebilmektedir. Bu olguda, mol hidatiform zemininde gelişen kontrolsüz uterin kanama nedeniyle uygulanan acil histerektomi yaklaşımının klinik özelliklerinin ve yönetim sürecinin sunulması amaçlandı.

Gereç ve Yöntemler: Kırk yaşındaki, fertilite isteği olmayan kadın hasta, yaklaşık 15 gün önce molar gebelik nedeniyle dilatasyon ve küretaj uygulanması sonrası artan vajinal kanama nedeniyle değerlendirildi ve jinekolojik onkoloji kliniğine yönlendirildi. Hastanın klinik bulguları, görüntüleme yöntemleri, seri total beta-insan koryonik gonadotropin (β-hCG) düzeyleri, laboratuvar parametreleri, cerrahi bulguları, transfüzyon gereksinimi, postoperatif seyri ve histopatolojik inceleme sonuçları retrospektif olarak değerlendirildi. Kontrol altına alınamayan abondan vajinal kanama nedeniyle 10 Ocak 2026 tarihinde acil cerrahi uygulandı.

Bulgular: Başvuru sırasında total β-hCG düzeyi 144,416 IU/L idi. Dilatasyon ve küretaj sonrası takipte β-hCG düzeylerinde beklenen düşüş izlenmedi; postoperatif erken dönemde değer 51,339 mIU/mL olarak saptandı. Ameliyat günü hemoglobin değeri 9.2 g/dL, hematokrit yaklaşık %28 idi. Preoperatif koagülasyon parametreleri büyük ölçüde korunmuş olmakla birlikte, operasyon sonrası erken dönemde fibrinojen düzeyi 2.24 g/L'ye geriledi ve INR 1.2 olarak izlendi. Operasyonda uterus normalden iri ve yumuşak kıvamda izlendi, bilateral over ve tubalar doğal görünümdeydi. Hastaya pfannenstiel insizyon ile total abdominal histerektomi ve bilateral salpenjektomi uygulandı. İntraoperatif dönemde 2 ünite eritrosit süspansiyonu ve 1 ünite taze donmuş plazma transfüzyonu yapıldı. Postoperatif dönemde hasta yoğun bakım ünitesinde takip edildi, ardından servise devredildi. Histopatolojik incelemede mol hidatiform ve egzajere plasental yerleşim saptandı.

Sonuç: Mol hidatiform olgularında standart yaklaşım çoğu hastada uterin evacuasyon olmakla birlikte, kontrolsüz uterin kanama, ileri yaş ve fertilite isteğinin bulunmaması gibi seçilmiş durumlarda histerektomi yaşam kurtarıcı ve etkili bir tedavi seçeneği olabilir. Bununla birlikte histerektomi, persistan trofoblastik hastalık riskini tamamen ortadan kaldırmadığından yakın β-hCG takibi sürdürülmelidir. Bu olgu, molar gebeliğin halen akut hemorajik tablo ile prezente olabileceğini ve tedavinin hastanın hemodinamik durumu ile bireysel özellikleri birlikte değerlendirilerek planlanması gerektiğini göstermektedir.

Anahtar Kelimeler: Gestasyonel trofoblastik hastalık, acil histerektomi, kontrolsüz uterin kanama

Tablo 1. Hastanın klinik ve laboratuvar seyri

Tarih	β-hCG	Hb/Hct	INR	Fibrinojen	Klinik durum
07.01.2026	144,416 mIU/mL	7,8 g/dL/%23,8	1,0	3,60 g/L	Yatış, aktif vajinal kanama
08.01.2026	—	9,1 g/dL/%27,4*	1,1	4,31 g/L	Klinik izlem
09.01.2026	124,157 mIU/mL	8,6 g/dL/%25,4*	1,0	3,81 g/L	Persistan kanama/izlem
10.01.2026	—	9,2 g/dL/%27,6	—	—	Ameliyat günü, preop
10.01.2026	—	9,4 g/dL/%28,0	—	—	Erken postop
10.01.2026	—	8,5 g/dL/%25,5	1,2	2,24 g/L	Postop yoğun bakım izlemi
11.01.2026	51,339 mIU/mL	9,8 g/dL/%28,0*	1,0	2,35 g/L	Erken postop izlem
12.01.2026	23,463 mIU/mL	9,1 g/dL/%26,2	1,0	3,72 g/L	Servis izlemi
13.01.2026	15,575 mIU/mL	9,4 g/dL/%28,2	1,0	4,72 g/L	Klinik toparlanma
14.01.2026	10,530 mIU/mL	9,8 g/dL/%28,5	1,1	2,47 g/L	Postop izlem
15.01.2026	7,565 mIU/mL	8,7 g/dL/%26,8	1,1	4,01 g/L	Biyokimyasal gerileme sürüyor

* Kangazı total hemoglobin

Tablo 2. Cerrahi ve histopatolojik bulgular

Başlık	Bulgular
Cerrahi endikasyon	Kontrol altına alınamayan abondan vajinal kanama
Uygulanan cerrahi	Total abdominal histerektomi + bilateral salpenjektomi
İntraoperatif gözlem	Uterus iri ve yumuşak kıvamda, over ve tubalar doğal
Transfüzyon	2 ünite eritrosit süspansiyonu + 1 ünite taze donmuş plazma
Histopatoloji	Mol hidatiform, egzajere plasental yerleşim
Postop izlem	Yoğun bakım sonrası servis devri

[SS-004]

Tek over ve aplastik anemi varliğinda fertilite prezervasyonu

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Amaç: Kanser ya da kanser dışı nedenlerle gonadotoksik tedavi planlanan ve düşük yumurtalık kapasitesi ya da erken menapoz riski altında olan olgularda fertilite koruma yöntemlerinin önemini vurgulamak.

Olgu: Ocak 2026 tarihinde aplastik anemi tanısı ile gonadotoksik tedavi planlanan 36 yaşında bekar hasta hematoloji kliniği tarafından fertilite koruma amacıyla tarafımıza refere edildi. Hastanın hikayesinde, Kasım 2025 tarihinde bilateral overyan kitle (patoloji: benign seröz kistanadenom) nedeni ile sağ unilateral salpingo-ooferektomi ve sol over kistektomi operasyonu mevcut idi. Hastada over rezervi belirgin azalmış olup AMH 0,2 ng/mL saptandı. Siklusun üçüncü gününde antagonist protokol ile rekombinant FSH 300 IU ve rekombinant LH 150 IU başlandı. Altıncı gün kontrolünde sol overde ≥15 mm boyutunda üç folikül izlenmesi üzerine rekombinant hCG ile ovulasyon tetiklemesi yapıldı. Trigger günü hemoglobin 5,2 g/dL ve trombosit sayısı 16.000/mm^3 olan hastaya eritrosit ve trombosit süspansiyonu transfüzyonu uygulandı. Otuz altı saat sonra transvajinal yoldan gerçekleştirilen oosit toplama işleminde elde edilen iki adet matür (MII) oosit vitrifikasyon yöntemi ile kriyoprezerve edildi.

Sonuç: Cerrahiye bağlı azalmış over rezervi ve ağır hematolojik bozukluk varlığında dahi uygun multidisipliner yaklaşım ile fertilite prezervasyonu mümkün olabilir. Gonadotoksik tedavi öncesinde zaman kaybetmeden fertilite korumaya yöntemleri ile ilgili danışmanlık verilmelidir. Sınırlı sayıda oosit elde edilse bile, gelecekteki üreme potansiyelinin korunmasına katkı sağlanabilir.

Anahtar Kelimeler: Fertilite prezervasyonu, oosit freezing

[SS-005]

Ulusal serviks kanseri tarama programında yüksek riskli HPV prevalansı ve yaşa göre genotip dağılımı: Tek merkez sonuçları

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Amaç: HPV-DNA testi ile serviks kanseri taraması, serviks kanserine bağlı morbidite ve mortalitenin azaltılmasında temel stratejilerden biridir. Bu çalışmada, ulusal serviks kanseri tarama programı kapsamında HPV pozitif saptanan kadınlarda HPV genotip dağılımının ve klinik sonuçların yaş gruplarına göre değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Bu retrospektif çalışmada Ocak 2019-Temmuz 2025 tarihleri arasında Sağlık Bilimleri Üniversitesi, Dr. Abdurrahman Yurtaslan Ankara Onkoloji Eğitim ve Araştırma Hastanesi'nde ulusal tarama programı kapsamında HPV pozitif saptanan 30-65 yaş arası kadınlar değerlendirildi. Histerektomi öyküsü, daha önce CIN tedavisi veya radyoterapi öyküsü olan hastalar ile 30 yaş altı ve 65 yaş üzeri hastalar çalışma dışı bırakıldı. Hastaların sitolojik, kolposkopik, biyopsi ve cerrahi sonuçları (LEEP, soğuk konizasyon, histerektomi) incelendi. İstatistiksel analizde ki-kare testi kullanıldı ve $p<0,05$ değeri istatistiksel olarak anlamlı kabul edildi.

Bulgular: Ocak 2019-Temmuz 2025 tarihleri arasında HPV pozitif saptanan toplam 2.136 hasta değerlendirilmiş, dışlama kriterleri sonrası 1.888 hasta analizlere dahil edilmiştir. HPV genotip dağılımı incelendiğinde 567 (%30) hastada HPV16, 150 (%7,9) hastada HPV18, 77 (%4) hastada HPV16/18 birlikte ve 1.094 (%57,9) hastada HPV16/18 dışı tipler saptanmıştır. Kolposkopi sonuçlarına göre ≥CIN2 oranı HPV16 grubunda %30,2, HPV18 grubunda %20, HPV16/18 birlikte pozitif olanlarda %33,8 ve HPV16/18 dışı tiplerde %13,4 olarak bulunmuştur. HPV16 genç kadınlarda (30-50 yaş) anlamlı derecede daha sık görülürken, HPV18 ve non-16/18 tipler ileri yaş grubunda (51-65 yaş) daha sık saptanmıştır ($p<0,05$). Genç yaş grubunda hem LSIL hem HSIL sitolojisi daha sık görülmüş ($p<0,05$) ve CIN2+ lezyonlar anlamlı olarak daha yüksek bulunmuştur ($p<0,001$). Tedavi yöntemleri incelendiğinde genç hastalarda LEEP ve soğuk konizasyon daha sık uygulanırken, ileri yaş grubunda histerektomi oranı daha yüksek bulunmuştur ($p<0,001$). Eksizyonel işlemler sonrası CIN2+ oranları yüksek saptanmakla birlikte yaş grupları arasında final patoloji sonuçları açısından anlamlı fark izlenmemiştir ($p=0,5$).

Sonuç: Bu çalışmada ulusal serviks kanseri tarama programı kapsamında HPV pozitif kadınlarda HPV genotip dağılımı ve klinik sonuçlar yaş gruplarına göre değerlendirilmiştir. HPV16'nın özellikle genç yaş grubunda daha sık görülmesi ve bu grupta yüksek dereceli sitolojik anormallikler ile CIN2+ lezyonların daha fazla saptanması HPV16'nın yüksek onkojenik potansiyelini desteklemektedir. Buna karşılık HPV18 ve HPV16/18 dışı tiplerin ileri yaş grubunda daha sık görülmesi yaşla birlikte HPV genotip dağılımında değişiklik olabileceğini düşündürmektedir. Bu bulgular, serviks kanseri tarama ve yönetiminde HPV genotipi ve yaşın birlikte değerlendirilmesinin önemini göstermektedir.

Anahtar Kelimeler: HPV, serviks kanseri, tarama

[SS-006]

Multidisciplinary secondary cytoreduction with nephroureterectomy for recurrent high-grade serous ovarian carcinoma

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Objective: Recurrent high-grade serous ovarian carcinoma (HGSOC) with urinary tract and pelvic organ involvement represents a surgical challenge, yet multidisciplinary secondary cytoreduction can achieve R0 status in select cases, potentially improving progression-free survival.

Case: A 30-year-old woman with history of cesarean section with ovarian biopsy confirming HGSOC, neoadjuvant chemotherapy (4 cycles), and cytoreduction surgery (total abdominal hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic and para-aortic lymphadenectomy) presented with recurrence. Initial laboratory results including alpha- fetoprotein (AFP), carcinoembryonic antigen (CEA), CA125 and Ca15-3 within normal limits; whereas CA19-9 was 481 U/mL. Preoperative evaluation included pelvic examination noting an 8 cm vaginal cuff mass; positron emission tomography-computed tomography (PET-CT) identifying a 5 cm hypermetabolic mass (SUV_{max} 8.4) encasing the left ureter, bladder, bowel, peritoneal reflections, and vaginal cuff; normal colonoscopy; cystoscopy showing extrinsic bladder compression without mucosal invasion; and renal scintigraphy demonstrating 4% left kidney function. Surgery involved laparoscopic left nephrectomy, followed by midline laparotomy for partial cystectomy, and en bloc resection preserving rectal anterior wall and bladder mucosa. Exploration disclosed a 5-6 cm lobulated indurated tumor extending from the left pelvic sidewall to levator ani, involving the rectal anterior wall, bladder base, vaginal cuff, and dilated left ureter with a hydronephrotic, nonfunctional kidney (2-3 times enlarged). En bloc excision included the tumor, ureter, and kidney, achieving R0 margins without fragmentation. Bladder integrity was confirmed with leak testing and reinforcement sutures. No residual disease was evident in the vaginal cuff, bladder, or pelvic floor. Postoperative recovery was uneventful.

Discussion: Recurrent HGSOC involving the urinary tract and pelvic organs presents a significant surgical challenge due to complex anatomy and the need to balance maximal cytoreduction with organ preservation. Achieving complete (R0) resection is a well-established prognostic factor for improved progression-free and overall survival in recurrent HGSOC, yet urinary tract involvement often complicates standard cytoreductive approaches. In this case, careful preoperative evaluation—including PET-CT, renal scintigraphy, cystoscopy, and colonoscopy—enabled precise mapping of tumor extent and assessment of organ function, particularly the left kidney which was found to be nonfunctional. This guided the decision for en bloc resection with nephroureterectomy while preserving bladder mucosa and rectal integrity, demonstrating that aggressive multidisciplinary surgery can achieve R0 margins even in advanced recurrences without compromising patient safety. Our experience aligns with recent reports emphasizing the role of combined gynecologic-oncologic and urologic interventions in selected patients with pelvic recurrence. Preservation of functional tissue where feasible may reduce postoperative morbidity and maintain quality of life. However, careful patient selection is critical; not all recurrences are amenable to such an approach, and functional assessments are essential to avoid unnecessary organ sacrifice.

Conclusion: In recurrent HGSOC with urinary tract compromise, preoperative functional assessment and multidisciplinary surgery enable R0 cytoreduction, preserving adjacent organs and function despite advanced involvement. This approach highlights the value of precise dissection in reducing morbidity and supports aggressive intervention in selected patients for improved survival, advocating integrated urologic-oncologic strategies in complex pelvic recurrences.

Keywords: Cytoreduction surgical procedures, nephrectomy, ovarian epithelial carcinoma

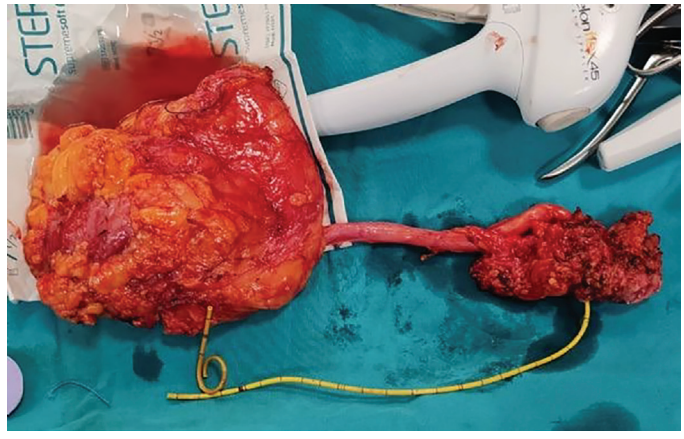

Figure 1. Excision of the tumor, ureter, and kidney as a block

[SS-007]

Orta Anadolu'da bir tersiyer merkezde kolposkopi uygulanan hastalarda HPV genotip dağılımı ve CIN2+ lezyonlar için bağımsız risk faktörleri

Mustafa Bakırcı

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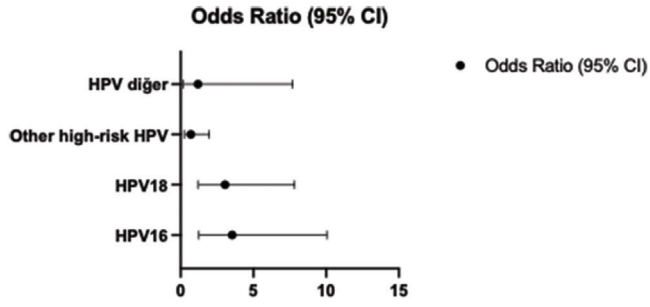
Amaç: Human papilloma virüs (HPV) enfeksiyonu servikal intraepitelyal neoplazi ve serviks kanserinin en önemli etiyolojik faktörüdür. HPV genotiplerinin servikal lezyon dereceleri ile ilişkisi klinik yönetim açısından önem taşımaktadır. Bu çalışmanın amacı kolposkopi uygulanan hastalarda HPV genotip dağılımını belirlemek ve HPV genotiplerinin yüksek dereceli servikal lezyonlar (CIN2+) ile ilişkisini değerlendirmektir.

Gereç ve Yöntemler: Bu kesitsel çalışmada kolposkopi yapılan ve HPV genotiplendirme sonucu bulunan toplam 229 hasta retrospektif olarak değerlendirildi. Hastaların demografik verileri, HPV genotip sonuçları ve kolposkopik/histopatolojik bulguları kayıt altına alındı. Servikal lezyonlar CIN2- (negatif ve LSIL/CIN1) ve CIN2+ (HSIL/CIN2, HSIL/CIN3 ve adenokarsinom) olarak iki gruba ayrıldı. HPV genotipleri ile CIN2+ lezyonlar arasındaki ilişki ki-kare testi ve odds oranları (OR) ile değerlendirildi. Bağımsız risk faktörlerini belirlemek amacıyla çok değişkenli lojistik regresyon analizi uygulandı. İstatistiksel anlamlılık düzeyi p<0,05 olarak kabul edildi.

Bulgular: Toplam 229 hastanın kolposkopi sonuçları incelendiğinde %49,8'inde negatif bulgu, %35,8'inde LSIL/CIN1, %5,2'sinde HSIL/CIN2, %8,3'ünde HSIL/CIN3 ve %0,9'unda adenokarsinom saptandı. En sık görülen HPV genotipleri HPV16 (%39,3) ve HPV18 (%16,6) idi. CIN2+ lezyon gelişimi açısından HPV genotipleri değerlendirildiğinde HPV16 pozitifliğinin CIN2+ riskini anlamlı şekilde artırdığı saptandı (OR: 2,08; %95 GA: 1,30-5,90; p=0,007). Benzer şekilde HPV18 pozitifliği de CIN2+ lezyonlarla anlamlı ilişki gösterdi (OR: 2,60; %95 GA: 1,12-6,06; p=0,022). Multiple HPV enfeksiyonu bulunan hastalarda da CIN2+ riski anlamlı olarak yüksek bulundu (OR: 2,75; %95 GA: 1,29-5,84; p=0,007). Diğer HPV tipleri ile CIN2+ lezyonlar arasında anlamlı ilişki saptanmadı (p=0,333). Hastaların yaş ortalamaları CIN2- ve CIN2+ gruplarında benzerdi (47,5±9,7 vs. 46,5±9,1 yıl; p=0,574). Çok değişkenli lojistik regresyon analizinde HPV16 (OR: 3,54; %95 GA: 1,25-10,06; p=0,018) ve HPV18 (OR: 3.06; %95 GA: 1,20-7,82; p=0,019) bağımsız olarak CIN2+ lezyonlarla ilişkili bulundu. Model istatistiksel olarak anlamlıydı (Omnibus testi p=0,013) ve iyi uyum gösterdi (Hosmer-Lemeshow p=0,779).

Sonuç: Bu çalışmada kolposkopi uygulanan hastalarda en sık saptanan HPV genotipleri HPV16 ve HPV18 olup, bu genotiplerin yüksek dereceli servikal lezyonlar ile anlamlı şekilde ilişkili olduğu gösterilmiştir. Özellikle HPV16 ve HPV18 pozitifliği CIN2+ gelişimi açısından bağımsız risk faktörleri olarak bulunmuştur. Bulgularımız, bölgemizdeki tarama programlarında HPV16 ve 18 pozitifliği saptanan hastaların, diğer yüksek riskli tiplere oranla daha agresif bir kolposkopik değerlendirme ve takip sürecine alınması gerektiğini desteklemektedir. Bu bulgular HPV genotiplendirmesinin servikal lezyonların risk sınıflandırılmasında ve hasta yönetiminde önemli bir rol oynayabileceğini göstermektedir.

Anahtar Kelimeler: HPV genotipleri, human papilloma virüs, kolposkopi



Şekil 1. Yüksek dereceli servikal lezyonlarla (CIN2+) ilişkili HPV genotiplerinin çok değişkenli lojistik regresyon analizi (Forest Plot)

Tablo 1. Kolposkopi sonuçlarına göre HPV genotip dağılımı, n (%)

	Negatif	LSIL/CIN1	HSIL/CIN2	HSIL/CIN3	Adenokarsinom	Toplam
HPV (-)	1 (0,4)	2 (0,9)	0	0	0	3 (1,3)
HPV11	1 (0,4)	1 (0,4)	1 (0,4)	0	0	3 (1,3)
HPV16	43 (18,8)	27 (11,8)	8 (3,5)	11 (4,8)	1 (0,4)	90 (39,3)
HPV18	14 (6,1)	14 (6,1)	4 (1,7)	5 (2,2)	1 (0,4)	38 (16,6)
HPV31	11 (4,8)	3 (1,3)	1 (0,4)	1 (0,4)	0	16 (7,0)
HPV33	1 (0,4)	0	0	2 (0,9)	0	3 (1,3)
HPV35	2 (0,9)	3 (1,3)	0	0	0	5 (2,2)
HPV39	11 (4,8)	9 (3,9)	2 (0,9)	1 (0,4)	0	23 (10,0)
HPV45	2 (0,9)	9 (3,9)	0	2 (0,9)	0	13 (5,7)
HPV51	10 (4,4)	4 (1,7)	1 (0,4)	4 (1,7)	0	19 (8,3)
HPV52	7 (3,1)	7 (3,1)	2 (0,9)	1 (0,4)	0	17 (7,4)
HPV56	14 (6,1)	1 (0,4)	0	0	0	15 (6,6)
HPV58	4 (1,7)	1 (0,4)	0	1 (0,4)	0	6 (2,6)
HPV59	6 (2,6)	6 (2,6)	1 (0,4)	1 (0,4)	0	14 (6,1)
HPV66	4 (1,7)	6 (2,6)	0	0	0	10 (4,4)
HPV68	15 (6,6)	3 (1,3)	1 (0,4)	1 (0,4)	0	20 (8,7)
HPV diğer	14 (6,1)	14 (6,1)	1 (0,4)	1 (0,4)	0	30 (13,1)
Toplam	114 (49,8)	82 (35,8)	12 (5,2)	19 (8,3)	2 (0,9)	229 (100)

Tablo 2. HPV tipleri ve CIN2+ lezyonlar arasındaki *çok* değişkenli lojistik regresyon analizi

	OR	95% CI	p
HPV16	3,538	1,245-10,056	0,018
HPV18	3,060	1,198-7,817	0,019
Diğer high-risk HPV	0,706	0,254-1,962	0,504
HPV diğer	1,188	0,183-7,697	0,856

OR: Odds ratio, CI: %95 güven aralığı; "Other high-risk HPV": HPV11, 31, 33, 35, 3S, 45, 51, 52, 5C, 58, 5S, CC, C8; Model, Omnibus testine göre istatistiksel olarak anlamlıdır (p<0,05) ve Hosmer-Lemeshow testi ile uygun uyum gösterir.

[SS-008]

Yolk sak tümörü öyküsü olan hastada metastazı taklit eden FDG-PET pozitif pelvik kitle: Leiomyom olgusu

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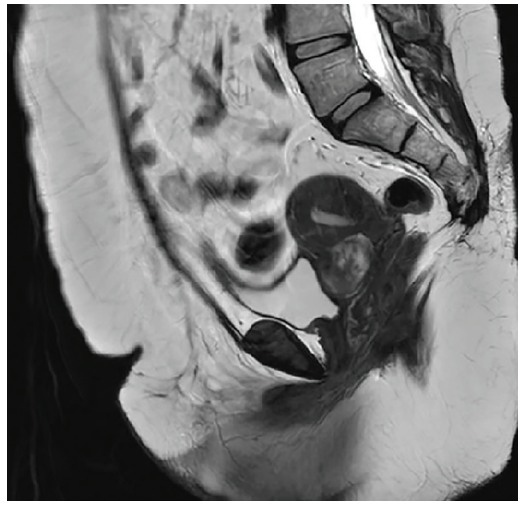
Amaç: Yolk sak tümörü overin nadir ancak agresif germ hücreli malignitelerinden biridir ve sıklıkla çocukluk veya genç yaşta görülür. Günümüzde sağkalımın artmasıyla birlikte bu hastaların uzun dönem takiplerinde saptanan pelvik kitlelerin ayırıcı tanısı klinik açıdan önem kazanmıştır. Görüntüleme yöntemlerinde saptanan metabolik aktivite çoğu zaman rekürrens veya metastaz lehine yorumlanmakla birlikte, bazı benign lezyonlar maligniteyi taklit edebilmektedir.

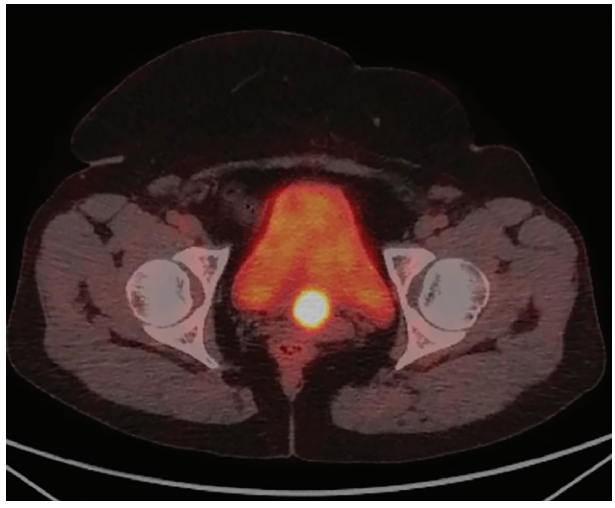
Olgu: Yirmi sekiz yaşında kadın hasta, üç yaşında tanı aldığı yolk sak tümörü nedeniyle uzun yıllardır takip edilmekte olup bu süreçte toplam 14 cerrahi operasyon geçirmiştir. Rutin kontroller sırasında yapılan Manyetik Rezonans Görüntüleme incelemesinde uterus inferior anterior komşuluğunda yaklaşık 34×24 mm boyutlarında ve interval dönemde büyüme gösteren kitle lezyonu saptandı (Şekil 1). Hastanın tümör belirteci olan Alfa-Fetoprotein düzeyi 1,54 ug/L olup normal sınırlarda idi. Buna rağmen metastaz olasılığı nedeniyle yapılan Pozitron Emisyon Tomografisi incelemesinde lezyonda belirgin FDG tutulumu izlendi ve SUVmax değeri 17.30 olarak ölçüldü (önceki incelemede 20.18) (Şekil 2). Hasta girişimsel radyolojiye yönlendirilmiş, ancak yapılan biyopsi tanısal bulunmamış ve biyopsi tekrarının önerilmesi üzerine cerrahi değerlendirme amacıyla kliniğimize yönlendirilmiştir. Laparotomi ile yapılan eksplorasyonda uterus inferior anterior komşuluğunda lokalize kitle tespit edilerek total olarak eksize edildi. Bu girişim hastanın on beşinci abdominal cerrahisi idi. Histopatolojik incelemede SMA, Desmin ve MSA pozitifliği saptanmış ve lezyon benign düz kas tümörü ile uyumlu olarak değerlendirilerek Leiomyom tanısı konulmuştur.

Sonuç: Malignite öyküsü bulunan hastalarda FDG-PET pozitif pelvik kitleler sıklıkla metastaz lehine yorumlanmaktadır. Ancak leiomyom gibi benign lezyonlar da yüksek FDG tutulumu gösterebilir ve yanlış pozitif sonuçlara yol açabilir. Bu olgu, özellikle tümör belirteçleri normal olan hastalarda görüntüleme bulgularının dikkatli değerlendirilmesi ve ayırıcı tanıda benign patolojilerin de göz önünde bulundurulması gerektiğini vurgulamaktadır.

Anahtar Kelimeler: Leiomyom, Yolk sak tümörü



Şekil 1. Pelvik kitleyi gösteren MR görüntüsü



Şekil 2. Lezyonda artmış FDG tutulumu gösteren PET görüntüsü

[SS-009]

TAH-BSO'dan 25 yıl sonra masif asit ve yüksek CA125 ile ileri evre pelvik maligniteyi taklit eden over fibroması: Atipik meigs sendromu olgu sunumu

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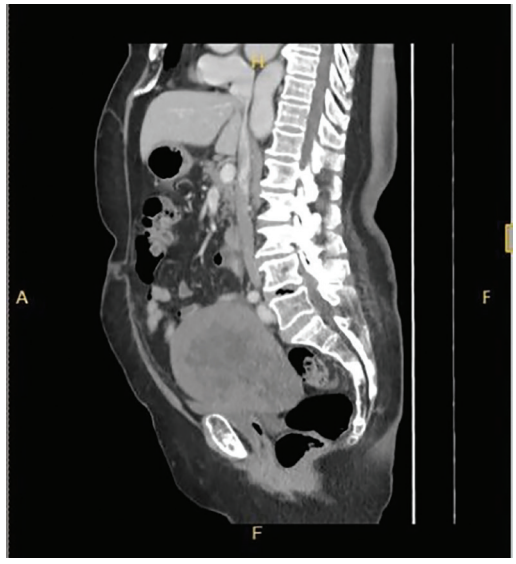
Amaç: Meigs sendromu benign over tümörü, asit ve plevral efüzyon birlikteliği ile karakterize nadir bir klinik tablodur. Tümörün eksizyonu sonrasında asit ve plevral efüzyonun spontan olarak gerilemesi sendromun ayırt edici özelliğidir. Bununla birlikte bazı olgularda klinik triadın eksik olduğu atipik formlar görülebilmektedir. Bu çalışmada masif asit, yüksek CA125 düzeyi ve pelvik kitle ile ileri evre pelvik maligniteyi taklit eden, ancak histopatolojik incelemede over fibroması olarak tanı alan nadir bir olgunun sunulması ve tanısal güçlüğün vurgulanması amaçlanmıştır.

Olgu: Altmış dokuz yaşında postmenopozal kadın hasta pelvik kitle, asit ve belirgin CA125 yüksekliği nedeniyle ileri değerlendirme amacıyla üçüncü basamak bir merkeze refere edilmiş olup hastanın özgeçmişinde 25 yıl önce yapılmış total abdominal histerektomi ve bilateral salpingo-ooferektomi öyküsü mevcuttu. Klinik değerlendirmede fizik muayene, laboratuvar incelemeleri, transvajinal ultrasonografi ve torakoabdominopelvik bilgisayarlı tomografi gerçekleştirildi. Asit etiyolojisi için tanısal abdominal parasentez uygulandı. Klinik ve radyolojik bulgular doğrultusunda pelvik malignite ön tanısı ile hasta jinekolojik onkoloji kliniğine yatırılarak eksploratif laparotomi planlandı. Operasyon sırasında pelvik kitlenin eksizyonu gerçekleştirildi ve frozen inceleme yapıldı. Nihai tanı histopatolojik ve immünohistokimyasal inceleme ile konuldu. Fizik muayenede abdominal distansiyon saptandı ve bimanuel pelvik muayenede Douglas boşluğunu dolduran fikse bir kitle palpe edildi. Laboratuvar incelemelerinde serum CA125 düzeyi 281.6 U/mL olarak yüksek bulundu. Transvajinal ultrasonografide yaklaşık 12 cm çapında pelvik kitle ve serbest sıvı izlendi. Torakoabdominopelvik bilgisayarlı tomografide Douglas boşluğundan suprapubik alana uzanan yaklaşık 121×112 mm boyutlarında, heterojen kontrast tutulumu gösteren ve merkezinde kistik dejeneratif alanlar içeren semisolid bir lezyon saptandı. Tanısal parasentezde serum-asit albumin gradyanı 0.9 g/dL olup eksüdatif asit ile uyumlu bulundu. Hastanın ileri yaşı, asit varlığı, pelvik kitle ve belirgin CA125 yüksekliği nedeniyle pelvik malignite ön tanısı ile eksploratif laparotomi gerçekleştirildi. İntraoperatif olarak kitlenin barsaklar ve anterior abdominal duvar ile adezyonlar gösterdiği izlendi. Frozen inceleme sonucu dejeneratif leiomyoma ile uyumlu mezankimal neoplazm olarak raporlandı. Postoperatif dönemde hastanın klinik durumu hızla düzeldi ve asit tamamen geriledi. Nihai histopatolojik incelemede tümör over fibroması olarak tanımlandı. İmmünohistokimyasal incelemede inhibin ve WT1 diffüz pozitif, desmin ve caldesmon negatif olarak saptandı. Olgumuzda plevral efüzyon izlenmemesi nedeniyle klinik tablo atipik Meigs sendromu ile uyumlu olarak değerlendirildi.

Sonuç: Meigs sendromu ve varyantları hastalarda asit, pelvik kitle ve CA125 yüksekliği ile ileri evre pelvik maligniteyi taklit edebilir. Bu durum klinisyenler için tanısal güçlük oluşturabilir. Bu nedenle asit ve CA125 yüksekliği ile birlikte pelvik kitle saptanan hastalarda benign over tümörleri, özellikle fibroma, ayırıcı tanıda mutlaka göz önünde bulundurulmalıdır.

Anahtar Kelimeler: CA125, Meigs sendromu, over fibroması



Şekil 1. Torakoabdominopelvik BT görüntüsü

[SS-010]

Testesteron salgılayan granüloza hücreli tümör: Olgu sunumu

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Amaç: Granüloza hücreli tümör, seks kord-stromal tümörlerin %70'ini oluşturan nadir görülen, düşük dereceli, malign karakterde bir tümördür. Bu tümör grubu tüm over tümörlerinin %5'inden daha azını oluşturur. Bu tümörlerin yaklaşık %70'i hormonal olarak aktiftir; klinik belirtileri hastanın yaşına ve adet durumuna bağlıdır. Nadir olarak androjen salgılayabilirler ve hastada virilizasyona neden olabilirler. Bu olgu sunumunda sekonder amenore, hirsutizm ve pelvik kitle bulguları ile seyreden bir testesteron salgılayan granüloza hücreli tümör olgusunun sunulması amaçlanmıştır.

Gereç ve Yöntemler: Otuz sekiz yaşında, multipar kadın hasta amenore, hirşutizm ve erkek tipi saç dökülmesi nedeniyle dış merkeze başvuran hastanın yapılan tahlillerinde pelvik kitle ve testesteron yüksekliği saptanması üzerine tarafımıza yönlendiriliyor.

Hastanın yapılan fizik muaynesinde vajinal muaynesinde klitoral hipertrofi mevcuttu, şiddetli hirşutizm belirtileri göstermekteydi. Yapılan hormon testleri total testesteron 1500, serbest testesteron >15, FSH ve LH <0,3 U/L, E2: 91.3 ng/L, DHEA-SO4 378 µg/dL olarak sonuçlandı. ACTH, tiroid fonksiyon testleri, GH ve tümör markerları normal olarak izlendi. Pelvik MR incelemesinde sağ over lojunda nodüler tarzda kontrast tutan yaklaşık 4 cm kitle izlendi. Bu kitle lezyonuna ek olarak patolojik lenf nodu veya asit mevcut değildi.

Hastaya operasyon planlandı. Hastaya sol salpingooferektomi, sağ over biyopsi, bilateral periton biyopsisi, omentum biyopsisi, eksfolyatif sitoloji ve frozen uygulandı. Frozen patoloji seks kord stromal tümör olarak bildirildi.

Bulgular: Yapılan postoperatif histopatolojik değerlendirme sonucunda sol over granüloza hücreli tümör tanısı konulmuştur. Tümör boyutu 3.5 cm olup kapsülü düzgündür. Düşük dereceli FIGO 1A olarak değerlendirilmiştir. Hastanın alınan sağ over biyopsisi, periton biyopsileri, omentum biyopsisi ve sitoloji örneklerine malign tümör hücrelerine rastlanmadı. Lokal erken evre (evre 1a) olarak kabul edilen hasta klinik olarak takibe alındı. Hastanın ilk üç aylık kontrolündeki hormon testlerinde FSH: 5,43 U/L, LH: 2,58 U/L, E2: 23,8 ng/L, total testesteron 24,71 olarak görüldü. Hastanın hirşutizm belirtilerinin büyük oranda gerilediği izlendi.

Sonuç: Granüloza hücreli tümör nadir olarak görülen endokrin bir ovaryan tümördür. Epitelyal over tümörlerinin aksine, erken teşhis edilirler. Genç hastalarda görülebilir ve tipik olarak karın şişliği, ağrı veya nadiren hiperöstrojenizm veya virilizasyon belirtileriyle kendini gösterir. Klinik olarak amenore ve hiperandojenemi görülmesi nadirdir; polikistik over sendromu ile karıştırılabilir. Bu nedenle anormal derecede testesteron seviyesi yüksek olan hastalarda bu adneksiyel kitle de bulunuyorsa ayırıcı tanıda göz önünde bulundurulmalıdır.

Anahtar Kelimeler: Amenore, testesteron, virilizasyon

[SS-011]

İleri evre over kanserinde rektosigmoid rezeksiyon uygulanan hastalarda klinikopatolojik özelliklerin değerlendirilmesi

Ayşe Buran

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Amaç: İleri evre over kanseri sıklıkla yaygın peritoneal ve pelvik tutulum ile seyretmekte olup optimal sitoredüksiyon cerrahisi hastaların prognozunu belirleyen en önemli faktörlerdendir. Bu hasta grubunda rektosigmoid kolon rezeksiyonu en sık uygulanan gastrointestinal rezeksiyonlardan biridir. Ancak bu rezeksiyon çoğu zaman tek başına yeterli olmayabilir ve rezidüel tümör bırakmamak için ek cerrahi prosedürler gerekebilir. Bu çalışmada sitoredüktif cerrahi sırasında rektosigmoid rezeksiyon uygulanan ileri evre over kanseri hastalarının klinikopatolojik özellikleri ve rektosigmoid rezeksiyon dışında uygulanan diğer cerrahi prosedürlerin tanımlanması amaçlandı.

Gereç ve Yöntemler: Bu retrospektif kohort çalışmasına, 2020-2025 yılları arasında Sağlık Bilimleri Üniversitesi, Ankara Bilkent Şehir Hastanesi Jinekolojik Onkoloji Cerrahisi Kliniği'nde ileri evre over kanseri nedeniyle sitoredüksiyon cerrahisi sırasında rektosigmoid rezeksiyon uygulanan toplam 69 hasta dahil edildi. Hastaların demografik özellikleri, uygulanan cerrahi prosedürler ve patolojik bulgular hastane kayıtları üzerinden retrospektif olarak incelendi.

Bulgular: Hastaların median yaşı 59 yıl (34-89) idi. Median CA125 düzeyi 414 U/mL (9-11149) olarak saptandı. Cerrahi sırasında çıkarılan median lenf nodu sayısı 29 (1-83) olup metastatik lenf nodu sayısı ise 4 (1-53) idi. Hastaların 25'i (%36,2) neoadjuvan kemoterapi almıştı. Altmış altı hastaya (%95,7) retroperitoneal lenfadenektomi yapıldı. Retroperitoneal lenfadenektomi uygulanan hastaların 50'sinde lenf nodu metastazı saptandı. Otuz bir hastada (%44,9) asit saptandı. Sitoloji 50 hastadan alınmış olup bunların 46'sında pozitif sitoloji saptandı. Histopatolojik incelemede tümör tipi 64 hastada seröz karsinom, 3 hastada clear cell karsinom ve 2 hastada ovaryan karsinosarkom olarak raporlandı. Hastaların %34,8'ine splenektomi, %65.2'sine diyafram periton stripping, %33.3'üne karaciğer kapsül veya parankim rezeksiyonu, %11.6'sına ince barsak rezeksiyonu, %4,3'üne distal pankreatektomi ve %24.7'sine kardiyofrenik lenf nodu eksizyonu yapıldı. Sitoredüksiyon sonucu, verisi mevcut olan 62 hastada değerlendirildi. Elli beş hastada (%88,7) maksimal, 6 hastada (%9.7) optimal ve 1 hastada (%1.6) suboptimal sitoredüksiyon sağlandı.

Sonuç: İleri evre over kanserinde rektosigmoid rezeksiyon uygulanan hastalarda sitoredüktif cerrahi sıklıkla çoklu üst abdominal ve pelvik cerrahi prosedürleri gerektirmektedir. Çalışmamızda yüksek oranda maksimal sitoredüksiyon sağlanması, uygun hasta seçimi ve deneyimli merkezlerde geniş kapsamlı cerrahi yaklaşımların etkin şekilde uygulanabildiğini göstermektedir. Bu bulgular, ileri evre over kanserinde optimal sitoredüksiyon elde etmek için agresif cerrahi stratejilerin önemini desteklemektedir.

Anahtar Kelimeler: İleri evre over kanseri, rektosigmoid rezeksiyon, sitoredüktif cerrahi

Tablo 1. Hastaların klinikopatolojik özellikleri

Yaş (yıl)	59 (34-89)	
CA125 (U/mL)	414 (9-11149)	
Çıkarılan lenf nodu sayısı	29 (1-83)	
Çıkarılan metastatik lenf nodu sayısı	4 (1-53)	
Asit varlığı	31	44,9
Omentektomi	69	100
Retroperitoneal lenfadenektomi	66	95,6
Apendektomi	34	49,3
Karaciğer kapsül veya parankim eksizyonu	23	33,3
Splenektomi	24	34,8
Diyafram periton stripping	45	65,2
Diyafram tam kat rezeksiyonu	19	27,5
İnce barsak rezeksiyonu	8	11,6
Diğer kolon segmentlerinin rezeksiyonu	14	20,3
Distal pankreatektomi	3	4,3
Kardiyofrenik lenf nodu eksizyonu	17	24,7

1. sütun: Değişken adı 2. sütun: Değer (median veya n) 3. sütun: Yüzde (%)

[SS-012]

Reprodüktif dönemde servikal konizasyonun kadın cinsel fonksiyonları üzerine etkisi

Hasan Can Toyganözü

Özel Medline Adana Hastanesi, Adana

Amaç: Bu çalışmanın amacı, servikal intraepitelyal neoplazi nedeniyle uygulanan servikal konizasyon işleminin kadın cinsel fonksiyonları üzerindeki etkisini değerlendirmektir.

Gereç ve Yöntemler: Bu prospektif çalışma, Temmuz 2024-Temmuz 2025 tarihleri arasında servikal intraepitelyal neoplazi tanısı ile konizasyon planlanan reprodüktif dönemdeki hastalar üzerinde gerçekleştirildi. Çalışmaya cinsel olarak aktif 100 hasta dahil edildi. Menopozda olanlar ve cinsel fonksiyonları etkileyebilecek psikiyatrik, nörolojik veya sistemik hastalığı bulunanlar çalışmaya dahil edilmedi. Hastaların demografik verileri, obstetrik öyküleri ve klinik özellikleri kaydedildi. Kadın cinsel fonksiyonlarının değerlendirilmesinde Kadın Cinsel Fonksiyon İndeksi (Female Sexual Function Index, FSFI) kullanıldı. FSFI ölçeği, konizasyon işlemi öncesinde ve postoperatif 3. ayda uygulandı. FSFI ölçeği; istek, uyarılma, lubrikasyon, orgazm, doyum ve ağrı olmak üzere altı alt gruptan ve toplam 19 sorudan oluşmaktadır.

Bulgular: Çalışmaya dahil edilen hastaların yaş ortalaması 36,72±6,44 yıl, vücut kitle indeksi ortalaması ise 26,45±2,53 kg/m^2 idi. Hastaların ortalama gebelik sayısı 2,21±1,29 ve doğum sayısı 1,86±1,34 olarak saptandı. Patoloji sonuçlarına göre olguların %6'sında CIN 2 ve %94'ünde CIN 3 tespit edildi. İşleme bağlı herhangi bir komplikasyon gelişmedi. Konizasyon sonrası üriner sistem yakınması %16,8 oranında, pelvik ağrı ise %44,7 oranında gözlendi. FSFI toplam skorları karşılaştırıldığında işlem öncesi ve sonrası arasında istatistiksel olarak anlamlı bir fark saptanmadı (p=0,256). Ancak FSFI alt ölçekleri değerlendirildiğinde istek (p=0,041), lubrikasyon (p=0,047) ve orgazm (p=0,021) puanlarında konizasyon sonrası anlamlı düzeyde azalma olduğu görüldü. Cinsel fonksiyonun iyi veya kötü olarak sınıflandırılması açısından konizasyon öncesi ve sonrası arasında anlamlı bir fark bulunmadı (p=0,258).

Sonuç: Servikal konizasyon işleminin kadın cinsel fonksiyonları üzerine etkisi FSFI skorlama sistemi ile değerlendirildiğinde toplam cinsel fonksiyon skorunda anlamlı bir değişiklik saptanmamıştır. Bununla birlikte bazı alt ölçeklerde görülen değişiklikler, servikal cerrahinin cinsel fonksiyonun belirli bileşenlerini etkileyebileceğini düşündürmektedir. Konizasyon öncesinde hastaların işlem ve olası sonuçları hakkında yeterli bilgilendirilmesi, oluşabilecek anksiyetenin azaltılmasına katkı sağlayabilir.

Anahtar Kelimeler: Cinsel fonksiyon, konizasyon, servikal intraepitelyal neoplazi

[SS-013]

Postmenopozal kanama ile başvuran östrojen salgılayan over tümörü: Erişkin tip granüloza hücreli tümör olgusu

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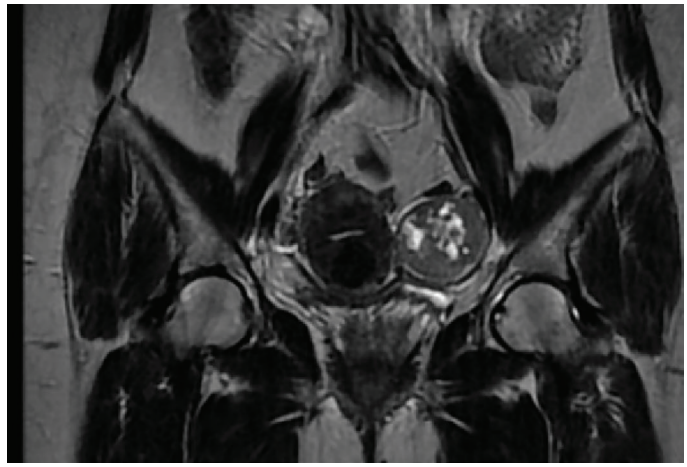
Amaç: Erişkin tip granüloza hücreli tümörler (AGCT), overin nadir görülen seks kord-stromal tümörleri olup tüm over malignitelerinin yaklaşık %2-5'ini oluşturur. Bu tümörler sıklıkla hormonal olarak aktiftir ve östrojen salgılayabilirler; bu durum endometriyal proliferasyona ve anormal uterin kanamaya yol açabilir. Görüntüleme bulguları ve tümör belirteçlerinin çoğu zaman spesifik olmaması nedeniyle preoperatif tanı güç olabilir. Bu yazıda, tümör belirteçleri normal olan ve postmenopozal kanama ile başvuran bir erişkin tip granüloza hücreli tümör olgusu sunulmuştur.

Olgu: Elli dört yaşında, postmenopozal bir kadın hasta (G4P4), 20 gündür devam eden postmenopozal kanama şikayeti ile başvurdu. Menopozunun dört yıl önce gerçekleştiği öğrenildi. Vücut kitle indeksi 32 kg/m^2 idi. Transvajinal ultrasonografide endometriyum kalınlığı 8 mm olarak ölçüldü, ayrıca posterior yerleşimli 35 mm intramural miyom ve sol overde 59×50 mm boyutlarında kompleks solid-kistik lezyon saptandı. Endometriyal biyopsi düzensiz proliferatif endometriyum ile uyumlu bulundu. Pelvik manyetik rezonans görüntülemede yaklaşık 5.2×4.3 cm boyutlarında, kontrast tutan ve T2 hiperintens komponentler içeren sol adneksiyal kitle izlenerek malignite açısından şüpheli olarak değerlendirildi. Serum tümör belirteçleri (CA125, CEA ve CA 19-9) normal sınırlarda idi. Hastaya total laparoskopik histerektomi ve bilateral salpingo-ooferektomi uygulandı. Operasyon sırasında sol adneksiyal bölgede yaklaşık 6 cm'lik kitle saptandı. İntraoperatif frozen kesit incelemesi granüloza hücreli tümör ile uyumlu bulundu. Nihai histopatolojik incelemede tümör hücrelerinin mikrofolliküler patern oluşturduğu ve karakteristik Call-Exner cisimciklerinin varlığı gösterildi. İmmünohistokimyasal incelemede inhibin pozitifliği saptanarak erişkin tip granüloza hücreli tümör tanısı doğrulandı. Tümörün over ile sınırlı olduğu, lenfovasküler ve perinöral invazyon saptanmadığı belirlendi ve hasta FIGO evre IA olarak değerlendirildi.

Tartışma: Erişkin tip granüloza hücreli tümörler en sık perimenopozal ve postmenopozal dönemde görülür ve tanı yaşı ortalaması yaklaşık 50-55 yıl olup bu durum olgumuz ile uyumludur. Bu tümörler sıklıkla östrojen salgılayarak endometriyal proliferasyon, hiperplazi ve anormal uterin kanamaya yol açabilir; bu bulgular hastaların yaklaşık %70'inde bildirilmektedir. Görüntüleme bulguları genellikle spesifik değildir ve AGCT'ler solid, kistik veya miks özellikte adneksiyal kitleler şeklinde izlenebilir. Ayrıca serum tümör belirteçleri sıklıkla normal olduğundan, preoperatif dönemde epiteliyal over malignitelerinden ayırımı zor olabilir. Bu nedenle histopatolojik inceleme tanıda altın standarttır. Mikroskopik olarak AGCT'ler mikrofolliküler yapı ve Call-Exner cisimcikleri ile karakterizedir. İmmünohistokimyasal olarak inhibin pozitifliği tanı için oldukça duyarlı ve özgüldür. Son yıllarda, AGCT'lerin büyük çoğunluğunda *FOXL2* mutasyonu tanımlanmış olup önemli bir moleküler belirteç olarak kabul edilmektedir. Cerrahi tedavi yönetimin temelini oluşturur. Postmenopozal hastalarda total histerektomi ve bilateral salpingo-ooferektomi standart tedavi yaklaşımıdır. AGCT'ler genellikle iyi prognoza sahiptir ve erken evre hastalıkta 5 yıllık sağkalım oranı %90'ın üzerindedir. Bununla birlikte, bu tümörler geç nüks potansiyeline sahiptir ve ilk tedaviden yıllar sonra bile nüks görülebilir; bu nedenle uzun dönem takip büyük önem taşır.

Sonuç: Postmenopozal kanama ile birlikte adneksiyal kitle saptanan hastalarda, tümör belirteçleri normal olsa bile granüloza hücreli tümörler ayırıcı tanıda düşünülmelidir. Erken tanı ve uygun cerrahi tedavi, optimal hasta sonuçları için kritik öneme sahiptir.

Anahtar Kelimeler: Adneksiyel kitle, granüloza hücreli tümör, over tümörü



Şekil 1. Pelvik manyetik rezonans görüntülemede sol adneksiyal bölgede yaklaşık 5.2×4.3 cm boyutlarında, kontrast tutan ve T2 hiperintens komponentler içeren kitle lezyonu izlenmektedir

[SS-014]

Vulvada nadir bir malignite: Mammariyan gland tipi adenokarsinom ile başvuran bir olgu

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Amaç: Vulva malignitelerinin büyük çoğunluğunu skuamöz hücreli karsinomlar oluştururken, primer vulvar adenokarsinomlar oldukça nadir görülmektedir. Mammariyan gland tipi adenokarsinom ise vulvada bulunan anogenital mammary-like glandlardan geliştiği düşünülen ve literatürde sınırlı sayıda bildirilen nadir bir tümördür. Klinik olarak benign vulvar kitleleri taklit edebilmesi tanıda gecikmelere yol açabilmektedir. Bu olguda, başlangıçta benign vulvar kitle ön tanısı ile eksize edilen ve histopatolojik inceleme sonrası mammariyan gland tipi adenokarsinom olarak tanı alan nadir bir vulvar malignite sunulmuştur.

Olgu: Yetmiş üç yaşında, hasta vulvada kitle şikayeti ile jinekoloji polikliniğine başvurdu. Yapılan fizik muayenesinde üretra komşuluğunda yaklaşık 3.5-4 cm boyutlarında kitle saptandı. Pelvik bilgisayarlı tomografide (BT) sol vulvada üretra komşuluğunda saat 2 yönünde yaklaşık 35 mm boyutlarında heterojen kontrastlanan nodüler lezyon izlendi. Lipom ön tanısı ile sol labiumdan yaklaşık 5 cm'lik hemorajik ve dejenere görünümlü kitle eksize edildi. Eksizyon materyalinin patolojik incelemesinde malign epitelyal tümör saptanması üzerine hasta jinekolojik onkoloji kliniğine yönlendirildi. Muayenede sol labiumda insizyon skarı izlenmekteydi, serviks doğal görünümdeydi. Tümör belirteçleri negatifti. PET-BT'de sol labium düzeyinde minimal FDG tutulumu dışında metastaz lehine bulgu izlenmedi. Mamografi benign (BIRADS-2) ile uyumluydu. Hastaya radikal vulvektomi, bilateral inguinofemoral lenf nodu diseksiyonu uygulandı. Histopatolojik incelemede fibrotik stromada kribriform, solid ve kistik yapılardan oluşan tümöral infiltrasyon izlendi. İmmünohistokimyasal incelemede ER, PR ve GATA3 pozitifliği saptandı. Nihai tanı iyi diferansiye mammariyan gland tipi adenokarsinom olarak raporlandı. Tümör boyutu 2.5 cm olup cerrahi sınırlar negatifti. Lenfovasküler ve perinöral invazyon izlenmemiştir. İnguinal lenf nodlarında metastaz saptanmamıştır. Nadir bir tümör olması nedeniyle hasta medikal ve radyasyon onkolojisi ile multidisipliner olarak değerlendirildi ve adjuvan tedavi önerilmedi. Postoperatif takiplerinde nüks veya metastaz saptanmadı.

Tartışma: Mammariyan gland tipi vulvar adenokarsinomlar genital bölgede bulunan mammary-like glandlardan köken alan nadir tümörlerdir. Tanı çoğunlukla eksizyon sonrası histopatolojik ve immünohistokimyasal inceleme ile konur. Literatürde bildirilen primer vulvar mammariyan gland tipi adenokarsinom olgularının büyük çoğunluğu postmenopozal kadınlarda görülmekte olup, bu tümörlerin immünohistokimyasal olarak sıklıkla ER, PR ve GATA3 pozitifliği göstermesi ayırıcı tanıda önemli ipuçları sağlamaktadır. Primer meme karsinom metastazının dışlanması önemlidir. Tedavide temel yaklaşım cerrahi eksizyondur ve lenf nodu değerlendirmesi önerilmektedir. Literatürde optimal adjuvan tedaviye ilişkin net bir görüş birliği bulunmamaktadır. Metastatik olgularda trastuzumab gibi medikal tedavi seçenekleri bildirilmiştir. Bu olguda adjuvan tedavi planlanmamıştır.

Sonuç: Vulvada benign görünümlü kitleler nadir de olsa malignite içerebilir. Mammariyan glandtipi adenokarsinomlar nadir görülmeleri ve tanısal güçlükleri nedeniyle klinisyenlerin ayırıcı tanıda akılda bulundurması gereken tümörlerdir. Erken tanı ve uygun cerrahi tedavi ile başarılı sonuçlar elde edilebilir.

Anahtar Kelimeler: Mammary-like gland tümör, vulvar adenokarsinom

[SS-015]

Maligniteyi taklit eden adneksiyal kitle: Sklerozan stromal tümör

Arife Ebru Taşcı

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Amaç: Sklerozan stromal tümör (SST), overin seks kord-stromal tümörleri içerisinde yer alan nadir benign neoplazmdır. Chalvardjian ve Scully tarafından 1973 yılında tanımlanmıştır. Bu tümörler klinik, histopatolojik ve immünohistokimyasal özellikleri ile diğer stromal tümörlerden ayrılmaktadır. SST çoğunlukla genç kadınlarda görülmekte olup bildirilen olguların büyük kısmı yaşamın ikinci ve üçüncü on yılında ortaya çıkmaktadır. Tümörler genellikle unilateraldir. Bununla birlikte görüntüleme yöntemlerinde solid ve kistik komponentlerin birlikte bulunması nedeniyle malign over tümörlerini taklit edebilmektedir. Bu durum özellikle genç hastalarda cerrahi plan ve fertilite korunması açısından tanısal zorluk oluşturur.

Olgu: On dokuz yaşında kadın hasta adneksiyal kitle ön tanısı ile opere edildi. Operasyon öncesinde yapılan kontrastlı bilgisayarlı tomografi incelemesinde sağ adneksiyal lojda 10 cm çapında, periferik yoğun vaskülarizasyon ve kontrastlanma gösteren, santralinde hipodens nekrotik alanlar içeren solid kitle lezyonu izlendi. Hastanın preoperatif laboratuvar değerlendirmesinde hemoglobin düzeyi 13,5 g/dL, lökosit sayısı 7300/μL, C-reaktif protein (CRP) düzeyi 19,5 mg/L, beta-human koryonik gonadotropin (β-hCG) düzeyi <2 mIU/mL, alfa-fetoprotein (AFP) düzeyi <1,3 ng/mL, karsinoembriyonik antijen (CEA) düzeyi <0,5 ng/mL, kanser antijeni 125 (CA125) düzeyi 15,3 U/mL, kanser antijeni 19-9 (CA 19-9) düzeyi 5,35 U/mL ve kanser antijeni 15-3 (CA 15-3) düzeyi 14,5 U/mL olarak saptandı. İntraoperatif değerlendirmede uterus, sol over ve tuba normal görünümdeydi. Sağ over kaynaklı yaklaşık 10 cm çapında, tubayı içine alan, solid ve kistik komponentler içeren kitle izlendi. Sağ overde normal over parankimi izlenmemesi üzerine sağ unilateral salpingo-ooferektomi uygulandı. Frozen incelemede kesin tanının parafin kesit değerlendirmesi ile konulacağı bildirildi. Kesin histopatolojik incelemede sağ overde 9×6×5 cm boyutlarında sklerozan stromal tümör saptandı. İmmünohistokimyasal incelemede tümör hücrelerinde SF-1 ve östrojen reseptörü ile diffüz boyanma, inhibin ile fokal boyanma izlendi. Ki-67 proliferasyon indeksi %8-10 olarak raporlandı.

Tartışma: Sklerozan stromal tümör overin nadir görülen benign stromal tümörlerinden biridir ve over seks kord-stromal tümörlerinin yaklaşık %2-6'sını oluşturur. Klinik olarak hastalar sıklıkla pelvik ağrı şikayeti ile başvurmaktadır. Histopatolojik olarak SST'nin en karakteristik özellikleri psödolobüler mimari, stromal ödem ve belirgin vasküler ağdır. İmmünohistokimyasal incelemede inhibin, calretinin ve SF-1 pozitifliği seks kord-stromal kökeni desteklemektedir. Radyolojik olarak heterojen solid-kistik yapı göstermesi nedeniyle malign over tümörleri ile karışabilmektedir. Ancak benign klinik seyri nedeniyle doğru tanı konulduğunda fertilite koruyucu cerrahi genellikle yeterli olmaktadır ve rekürrens oldukça nadir bildirilmektedir.

Sonuç: Sklerozan stromal tümör nadir görülmesine rağmen özellikle genç hastalarda saptanan adneksiyal kitlelerin ayırıcı tanısında akılda tutulmalıdır. Bu tümörün doğru tanınması gereksiz radikal cerrahinin önlenmesine ve fertilite koruyucu cerrahi yaklaşımın uygulanmasına olanak sağlamaktadır.

Anahtar Kelimeler: Fertilite koruyucu yaklaşım, sklerozan stromal tümör

[SS-016]

Yaşlı serviks kanserli hastalarda Hb/RDW oranı prognostik mi?

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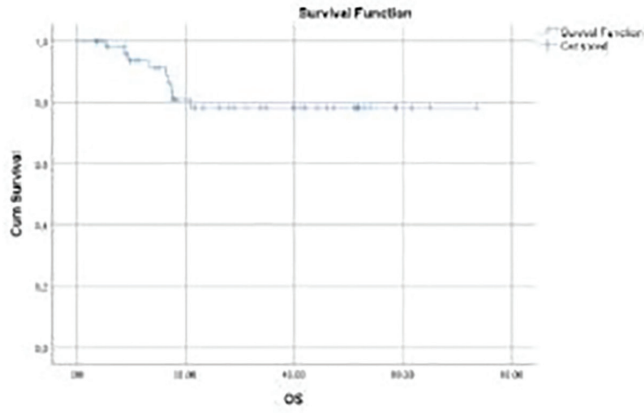
Amaç: Bu çalışmada, kemoradyoterapi (KRT) uygulanan 60 yaş ve üzeri serviks kanserli hastalarda hemoglobin/eritrosit dağılım genişliği (Hb/RDW) oranının prognoz üzerindeki etkisinin değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: Bu çalışmaya ≥60 yaş olan 54 serviks kanseri hastası dahil edildi. Hastaların demografik, klinik ve tedavi özellikleri ile tedavi öncesi Hb ve RDW değerleri retrospektif olarak kaydedildi. Hb/RDW oranının nüks ve mortaliteyi öngörmedeki performansı ROC analizi ile değerlendirildi. Sağkalım analizleri Kaplan-Meier yöntemi ile yapıldı.

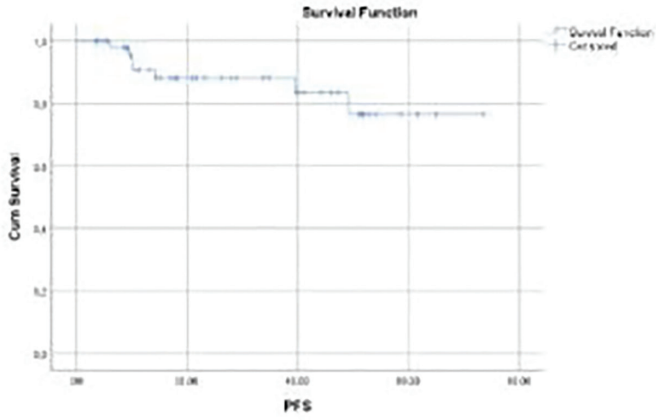
Bulgular: Medyan yaş 67 (60-83) olup hastaların büyük çoğunluğunun performans durumu iyiydi (ECOG 0-1: %88,9). En sık görülen histopatolojik tip skuamöz hücreli karsinom (%88,9) ve en sık görülen evre FIGO IIIC1 (%46,3) idi. Hastaların hepsine yoğunluk aarlı radyoterapi yöntemi (IMRT) ile görüntü kılavuzluğunda external radyoterapi (IGRT), external radyoterapi sonrası 3 boyutlu Brakiterapi uygulanmıştır. Hastaların %98,1'ine eş zamanlı kemoterapi verilmiş olup tedavi dağılımı homojen özellik göstermekteydi. Medyan 21,3 aylık takip süresinde 7 hastada (%13) nüks, 9 hastada (%16,7) ölüm gözlendi. Bir ve 2 yıllık progresyonsuz sağkalım (PFS) oranları sırasıyla %90 ve %85, genel sağkalım (OS) oranları ise %94 ve %78 olarak saptandı. Hb/RDW oranının prognostik değeri değerlendirildiğinde; nüks için AUC: 0,663 (p=0,168) ve mortalite için AUC: 0,563 (p=0,554) bulunmuş olup istatistiksel olarak anlamlı ilişki gösterilemedi.

Sonuç: Çalışmamızda Hb/RDW oranının yaşlı serviks kanserli hastalarda nüks ve mortaliteyi öngörmede anlamlı bir prognostik belirteç olmadığı sonucuna ulaşılmıştır. Bu durum; düşük olay sayısı, kısa takip süresi ve hasta grubunun homojen ve iyi prognostik özellikler göstermesi ile açıklanabilir. Ayrıca yaşlı popülasyonda Hb ve RDW düzeylerinin kanser dışı faktörlerden etkilenmesi, bu oranın prognostik değerini sınırlamış olabilir.

Anahtar Kelimeler: Serviks, kanser, hemoglobin



Şekil 1. Genel sağkalım grafiği



Şekil 2. Progresyonsuz sağkalım grafiği

[SS-017]

Endometriyum karsinosarkomu ile senkron tubal yüksek dereceli seröz karsinom birlikteliğinde rabdomyosarkom diferansiyasyonu: Olgu sunumu

Süleyman Özen[1], Eda Güner Özen[2], Muzaffer Sancı[1]

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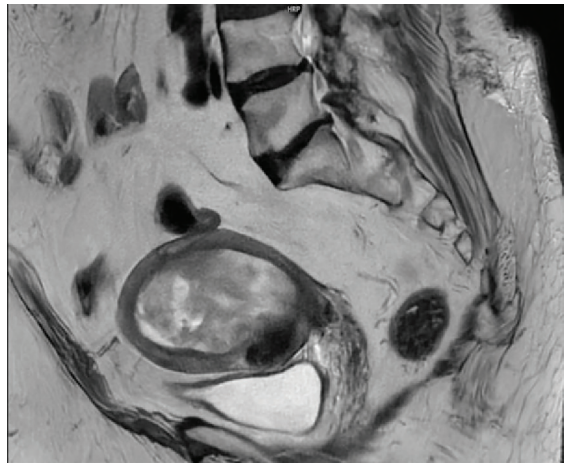
Amaç: Karsinosarkomlar, epitelyal ve mezenkimal bileşenlerin birlikte bulunduğu, nadir ancak yüksek derecede agresif seyirli malign neoplazmlardır. Bu tümörlerde heterolog diferansiyasyon alanlarının varlığı, tümörün biyolojik davranışı ve prognozu üzerinde belirleyici olabilmektedir. Bu olgu sunumunda, endometriyum kökenli karsinosarkoma eşlik eden senkron tubal yüksek dereceli seröz karsinom birlikteliği ile rabdomyosarkom komponentinin klinik ve histopatolojik öneminin ortaya konulması amaçlandı.

Gereç ve Yöntemler: Seksen bir yaşında, multipar ve eşlik eden hipertansiyon, diabetes mellitus ile koroner arter hastalığı bulunan hasta, dış merkezde endometrioid adenokarsinom ön tanısıyla opere edilmesini takiben ileri değerlendirme amacıyla kliniğimize refere edildi. Hastaya evreleme ve sitoredüksiyon amacıyla total abdominal histerektomi, bilateral salpingo-ooferektomi, omentektomi ile bilateral pelvik ve paraaortik lenfadenektomi uygulandı. İntraoperatif frozen incelemede malign miks Müllerian tümör lehine bulgular elde edildi. Preoperatif görüntüleme ve tümör belirteçlerinde ileri evre hastalığı düşündüren bulgu saptanmadı.

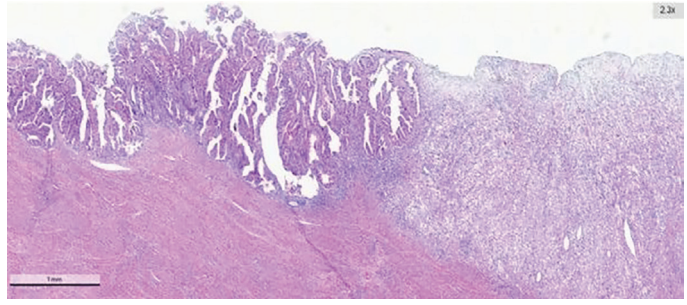
Bulgular: Makroskopik olarak 9×6×4,2 cm boyutlarında olan tümörün myometriuma yüzeyel invazyon gösterdiği belirlendi. Histopatolojik incelemede epitelyal komponentin yüksek dereceli seröz karsinom morfolojisi sergilediği, mezenkimal komponentin ise geniş alanlarda rabdomyosarkom diferansiyasyonu içerdiği izlendi. Lenfovasküler invazyon saptanmadı ve pelvik ile paraaortik lenf nodlarında metastatik tutulum izlenmedi. Sağ tuba uterinada bağımsız odak şeklinde yüksek dereceli seröz karsinom varlığı saptanarak senkron tümör lehine değerlendirildi. İmmünohistokimyasal incelemede sarkom komponentinde desmin, myogenin ve MyoD1 pozitifliği; kaldesmon negatifliği izlendi. Her iki komponentte p16 ekspresyonu mevcut olup MLH1 ekspresyonunda fokal kayıp dikkat çekti.

Sonuç: Bu olgu, endometriyum karsinosarkomu ile senkron tubal yüksek dereceli seröz karsinom birlikteliğinin nadirliğini ortaya koymaktadır. Rabdomyosarkom diferansiyasyonu, tümörün biyolojik agresifliğini yansıtan önemli bir histopatolojik özellik olarak değerlendirilebilir. Ayrıca senkron tümör varlığı, tanı ve tedavi sürecinde multidisipliner yaklaşımın gerekliliğini vurgulamaktadır. Moleküler düzeyde yapılacak ileri incelemelerin, tümörün patogenezinin aydınlatılmasına ve hedefe yönelik tedavi stratejilerinin geliştirilmesine katkı sağlayabileceği düşünülmektedir.

Anahtar Kelimeler: Endometriyum karsinosarkomu, senkron tümör, tubal seröz karsinom



Şekil 1. MRI görüntüleme



Şekil 2. Patoloji

[SS-018]

Perioperatif IVC filtresi kullanımıyla yönetilen tromboembolik riskli hastada senkron endometriyum ve over tümörü: Olgu sunumu

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Amaç: Endometriyum kanserlerinin en sık görülen histolojik alt tipi endometrioid adenokarsinom olup çoğunlukla düşük dereceli olgularda daha iyi prognoz ile ilişkilidir. Buna karşın berrak hücreli karsinom, nadir görülmesine rağmen daha agresif klinik seyir ve yüksek nüks riski ile ilişkili olabilen non-endometrioid bir alt tiptir. Endometriyum ve overde eş zamanlı (senkron) malignitelerin varlığı; cerrahi evreleme, adjuvan tedavi stratejisi ve moleküler/immünohistokimyasal değerlendirme açısından klinik önem taşır. Bu posterde, endometriyumda endometrioid adenokarsinom (G1) ile overde berrak hücreli karsinom birlikteliği saptanan ve cerrahi olarak evrelenen bir olgu, immünohistokimyasal bulgular eşliğinde sunulmaktadır.

Olgu: Kırk yedi yaşında hasta karın ağrısı ve anormal uterin kanama yakınmaları ile başvurdu. Özgeçmişinde, planlanan cerrahiden yaklaşık bir ay önce gelişen pulmoner emboli ve sol popliteal vende derin ven trombozu öyküsü mevcuttu. Perioperatif tromboembolik riskin azaltılması amacıyla kardiyovasküler cerrahi tarafından preoperatif dönemde inferior vena cava (IVC) filtresi yerleştirildi. Ardından total abdominal histerektomi ve bilateral salpingo-ooforektomi ile birlikte batından sitoloji örneklemesi, pelvik lenf nodu diseksiyonu ve omentum biyopsisi gerçekleştirildi. IVC filtresi postoperatif ikinci günde sorunsuz şekilde çıkarıldı. Makroskopik incelemede histerektomi materyali 306 g ağırlığında olup 13,5×7,5×5 cm ölçülerindeydi; serviks 4 cm çapta ve endoservikal kanal 3 cm uzunlukta izlendi. Endometrial kavitede anterior ve posterior duvarda 3×1 cm boyutlarında infiltratif nitelikte tümoral lezyon saptandı. Tümörün en derin invazyon alanında myometriyuma 3 cm derinlikte invazyon izlenirken sağlam duvar kalınlığı 0,4 cm olarak ölçüldü. Lenfovasküler invazyon saptanmadı ve olgu evre IA olarak değerlendirildi.

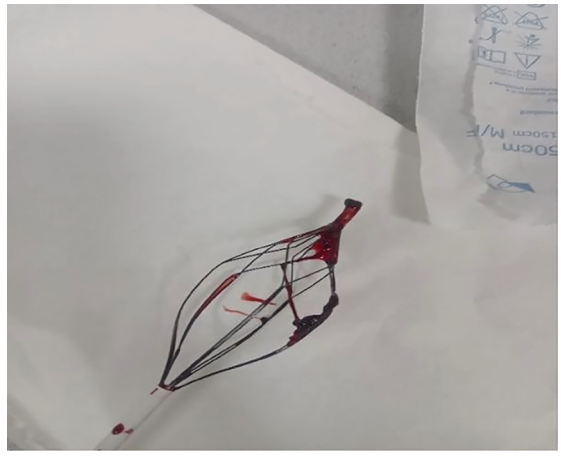
Sonuç: Sunulan olguda endometriyumda düşük dereceli endometrioid adenokarsinom ile overde berrak hücreli karsinom birlikteliği mevcuttur ve cerrahi evreleme sonrası olgu evre IA olarak sınıflandırılmıştır. Lenfovasküler invazyonun olmaması prognostik açıdan olumlu bir bulgu olmakla birlikte, iki farklı histolojinin eş zamanlı varlığı klinik yönetimde ayrıntılı patolojik ve immünohistokimyasal karakterizasyonun önemini artırmaktadır. Bu bağlamda immunohistokimyasal profil; tümör biyolojisinin daha iyi anlaşılması, olası ek değerlendirme gereksiniminin belirlenmesi ve takip stratejisinin şekillendirilmesi açısından posterin temel odak noktalarından biri olarak sunulmuştur. İmmunohistokimyasal çalışmalar: MMR protein ekspresyonu: MSH6 her iki tümörde kaybolmuş: PMS2 ise sadece endometriyum tümöründe azalmış, over tümöründe korunmuş. p53: Her iki tümörde normal boyanma paterni gözlenmiş.

ER: Endometriyum tümöründe %10 güçlü pozitif, over tümöründe negatif. Klinik not: MSH6 kaybı genetik danışmanlık ve ileri moleküler inceleme için önemli olabilir.

Anahtar Kelimeler: Endometriyum kanseri, over kanseri, vena kava filtresi

Tablo 1. Belirteçler

Marker	Endometrium tümörü	Over tümörü
ER	%10 güçlü (+)	(-)
p53	Wild-type	Wild-type
PMS2	Kayıp	Korunmuş
MSH6	Kayıp	Kayıp



Şekil 1. Filtre fotoğrafı

[SS-019]

Meigs sendromu şeklinde prezente olan erişkin tip over granüloza hücreli tümörü: Olgu sunumu

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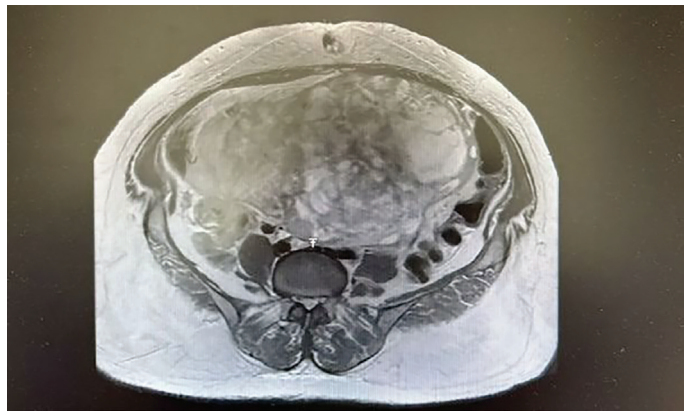
Sağlık Bilimleri Üniversitesi, İzmir Şehir Hastanesi, İzmir

Amaç: Bu olgu sunumunun amacı, postmenopozal bir kadında Meigs sendromu şeklinde ortaya çıkan nadir bir erişkin tip over granüloza hücreli tümör olgusunu sunmak ve ileri evre over malignitesine benzerliği nedeniyle oluşturduğu tanısal güçlükleri vurgulamaktır.

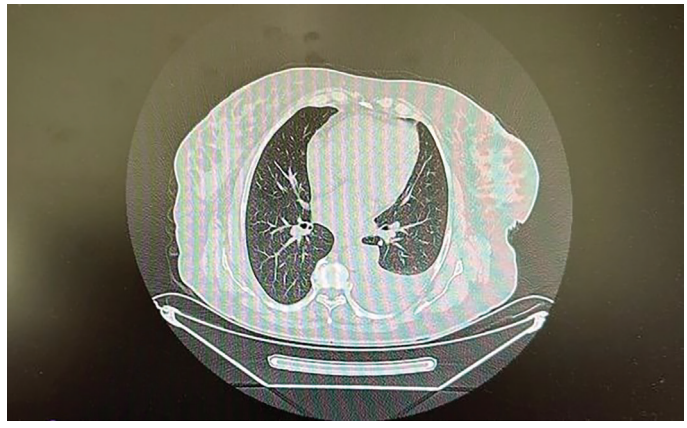
Olgu: Elli altı yaşında postmenopozal kadın hasta, vajinal kanama ve ilerleyici abdominal distansiyon yakınmaları ile başvurdu. Hastanın ayrıca plevral efüzyon nedeniyle göğüs hastalıkları kliniğinde yatırılarak izlendiği öğrenildi. Pelvik manyetik rezonans görüntülemede, 275×249×147 mm boyutlarında, septasyonlar, kontrastlanan septalar ve solid bileşenler ile solid alanlarda difüzyon kısıtlılığı içeren büyük bir sağ adneksiyal kitle ve eşlik eden pelvik serbest sıvı saptandı. Ayrıca 22 mm kalınlığında sol plevral efüzyon izlendi. Hastaya total abdominal histerektomi, bilateral salpingo-ooforektomi, omentektomi, bilateral pelvik lenf nodu örneklemesi, periton biyopsisi ve sitolojik örnekleme uygulandı. İntraoperatif frozen kesit incelemesinde, granüloza hücreli tümör lehine şüpheli non-epitelyal over tümörü düşünüldü. Nihai histopatolojik incelemede, sağ over kaynaklı 33×20×18 cm boyutlarında erişkin tip granüloza hücreli tümör tanısı doğrulandı. Tümör kapsülü intakt olup lenfovasküler invazyon izlenmedi. Omentum, pelvik lenf nodları ve periton biyopsilerinde metastatik tümör tutulumu saptanmadı. İmmünohistokimyasal incelemede inhibin ve kalretinin ile fokal pozitiflik, PR ile %40 oranında güçlü nükleer boyanma izlenirken; EMA, SALL4, ER ve p16 negatif bulundu, p53 ise wild-type patern gösterdi.

Sonuç: Bu nadir olgu, düşük dereceli bir malignite olarak tanımlanan erişkin tip over granüloza hücreli tümörünün, Meigs sendromunu tablosu ile prezente olabileceğini ve ileri evre, yüksek dereceli over malignitesini taklit edebileceğini göstermektedir. Bu birlikteliğin bilinmesi, uygun cerrahi planlamayı ve perioperatif dönemde daha doğru tanısal değerlendirmeyi kolaylaştırabilir.

Anahtar Kelimeler: Erişkin tip granüloza hücreli tümör, Meigs sendromu, overin seks kord-stromal tümörü, plevral efüzyon, asit



Şekil 1. Pelvik manyetik rezonans görüntülemede, 275×249×147 mm boyutlarında, septasyonlar, kontrastlanan septalar ve solid bileşenler ile solid alanlarda difüzyon kısıtlılığı içeren büyük bir sağ adneksiyal kitle



Şekil 2. Toraks BT'de 22 mm kalınlığında sol plevral efüzyon

[SS-020]

Yüksek proliferatif indeksli dev uterin PEComa: Fatal septik seyir ile sonlanan nadir bir olgu

Esma Doğan, Tolga Çiftpınar

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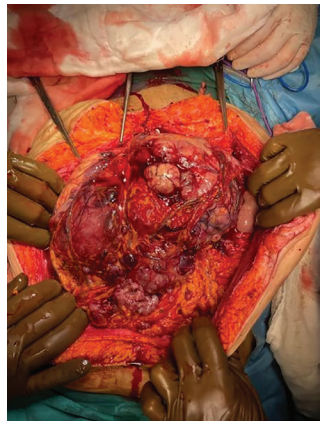
Amaç: Perivasküler epiteloid hücreli tümörler (PEComa), nadir görülen mezenkimal tümörlerdir ve uterin yerleşimleri oldukça seyrektir. Klinik davranışları benign seyirden agresif maligniteye kadar değişkenlik gösterebilir. Literatürde PEComa'larda malign potansiyeli öngörmede; tümör çapının 5 cm'den büyük olması, infiltratif büyüme paterni, nekroz, yüksek mitotik aktivite ve artmış Ki-67 proliferasyon indeksi gibi kriterler tanımlanmıştır. Bu çalışmada, yüksek proliferatif indeks ile seyreden ve postoperatif dönemde fatal septik komplikasyon gelişen dev uterin PEComa olgusunun sunulması ve klinik- patolojik özelliklerinin literatür eşliğinde değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Elli yaşındaki hasta, CA125 yüksekliği (136 U/mL) ve pelvik kitle nedeniyle değerlendirilmiştir. Preoperatif görüntüleme bulguları doğrultusunda total abdominal histerektomi, bilateral salpingo-ooferektomi, total omentektomi ve pelvik- paraaortik lenfadenektomi içeren optimal debulking cerrahisi uygulanmıştır. Postoperatif klinik seyir ile patolojik bulgular retrospektif olarak analiz edilmiştir.

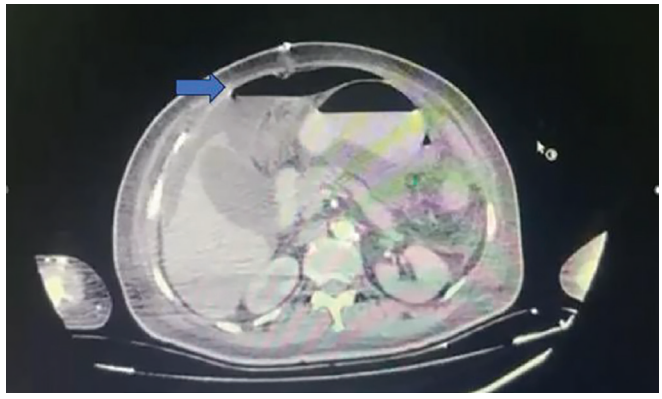
Bulgular: Preoperatif görüntülemede ve intraoperatif değerlendirmede yaklaşık 15-16 cm boyutlarında kitle izlenmiş; patolojik incelemede omentum ve peritona yayılım ile tümör yükünün daha geniş bir intraabdominal alanı kapsadığı saptanmıştır. Tümörün uterus korpusundan köken aldığı, serozayı aşıp batın içine uzandığı ve omentum ile peritonda yaygın implantlar oluşturduğu gözlenmiştir. Lenf nodu metastazı izlenmemekle birlikte, batın içi sıvı sitolojisi malign olarak değerlendirilmiştir. İmmünohistokimyasal incelemede HMB45 ve Cathepsin K pozitifliği saptanmıştır. Tümör proliferatif aktivitesini gösteren Ki-67 indeksi %50-60 olarak raporlanmıştır. Postoperatif üçüncü gün içerisinde hastada hızlı klinik kötüleşme gelişmiş; CRP ve prokalsitonin düzeylerinde belirgin artış izlenmiştir. Gelişen klinik tablo üzerine yapılan görüntülemede serbest intraperitoneal hava saptanmış ve acil relaparotomi uygulanmıştır. İntraoperatif değerlendirmede sigmoid kolonda perforasyon ve buna bağlı yaygın fekal kontaminasyon izlenmiştir. Barsak anslarının ileri derecede ödemli ve frajil olması nedeniyle primer onarım uygun görülmemiş ve Hartmann prosedürü uygulanmıştır. Ancak, postoperatif dönemde derin metabolik asidoz ve septik şok gelişmiş, yoğun bakım tedavisine rağmen hasta kaybedilmiştir.

Sonuç: Yüksek proliferatif indeksli dev uterin PEComa'ların agresif biyolojik davranış sergileyebileceği ve ciddi postoperatif septik komplikasyonlar ile mortal seyredebileceği görülmektedir. Bulgularımız, yüksek Ki-67 indeksinin kötü prognoz ile ilişkili olabileceğini desteklemektedir. Ayrıca, bu tümörlerin yalnızca tümör agresifliği açısından değil, aynı zamanda fatal sistemik inflamatuar komplikasyonlar yönünden de yüksek risk taşıyabileceği düşünülmektedir. Literatürde, uterin PEComa olgularında yüksek Ki-67 indeksi ile sistemik enflamatuvar yanıt ve septik mortalite arasındaki ilişkiyi birlikte ortaya koyan veri son derece sınırlıdır. Bu bulgular ışığında, bu hasta grubu perioperatif dönemde yüksek riskli olarak değerlendirilmeli; inflamatuar parametreler yakından izlenmeli ve olası komplikasyonlara karşı erken ve agresif yönetim stratejileri uygulanmalıdır.

Anahtar Kelimeler: Ki-67, septik şok, uterin PEComa



Şekil 1. Debulking cerrahisi sırasında kitlenin çevre dokularla ilişkisi ve adezyon bölgeleri gösterilmektedir



Şekil 2. Kontrastlı abdominal bilgisayarlı tomografi kesitinde, serbest intraperitoneal hava görünümü (ok ile işaretli) izlenmektedir. Bulgular gastrointestinal perforasyon ile uyumludur

Tablo 1. Olgunun klinik ve patolojik özellikleri

Özellik	Bulgular
Yaş	50 yıl
Başvuru	Pelvik kitle
CA125	136 U/mL
Lokalizasyon	Fundustan köken alan, yaygın intraabdominal yayılım gösteren
Tümör boyutu	~15-16 cm
Cerrahi	TAH + BSO + omentektomi + pelvik paraaortik lenfadenektomi
Histopatoloji	PEComa
İmmünohistokimya	HMB45 (+), cathepsin K (+)
Ki-67	%50-60
Yayılım	Omentum, periton
Lenf nodu	Negatif
Sitoloji	Malign

Tablo 2. Postoperatif klinik seyir ve komplikasyonlar

Parametre	Bulgular
CRP	116 → 394 mg/L
Prokalsitonin	0,62 → 36,06 ng/mL
Klinik durum	Hızlı kötüleşme
Görüntüleme	Serbest intraperitoneal hava
Girişim	Relaparotomi
İntraoperatif bulgu	Sigmoid kolon perforasyonu, fekal kontaminasyon
Ek cerrahi	Hartmann prosedürü
Kan gazı	pH: 7,22, Laktat: 12,6 mmol/L, HCO_3: 15 mmol/L
Komplikasyon	Septik şok, metabolik asidoz
Sonuç	Eksitus

[SS-021]

Predictors of lymph node metastasis endometrial cancer after systematic laparoscopic lymphadenectomy

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Objective: Lymph node metastasis is an important prognostic factor in endometrial cancer and plays a key role in guiding adjuvant treatment decisions. Identifying clinicopathological factors associated with nodal involvement may improve the accuracy of surgical staging. This study aimed to determine the predictors of lymph node metastasis and to evaluate the pattern of para- aortic involvement in patients with endometrial cancer who underwent laparoscopic pelvic and para-aortic lymphadenectomy.

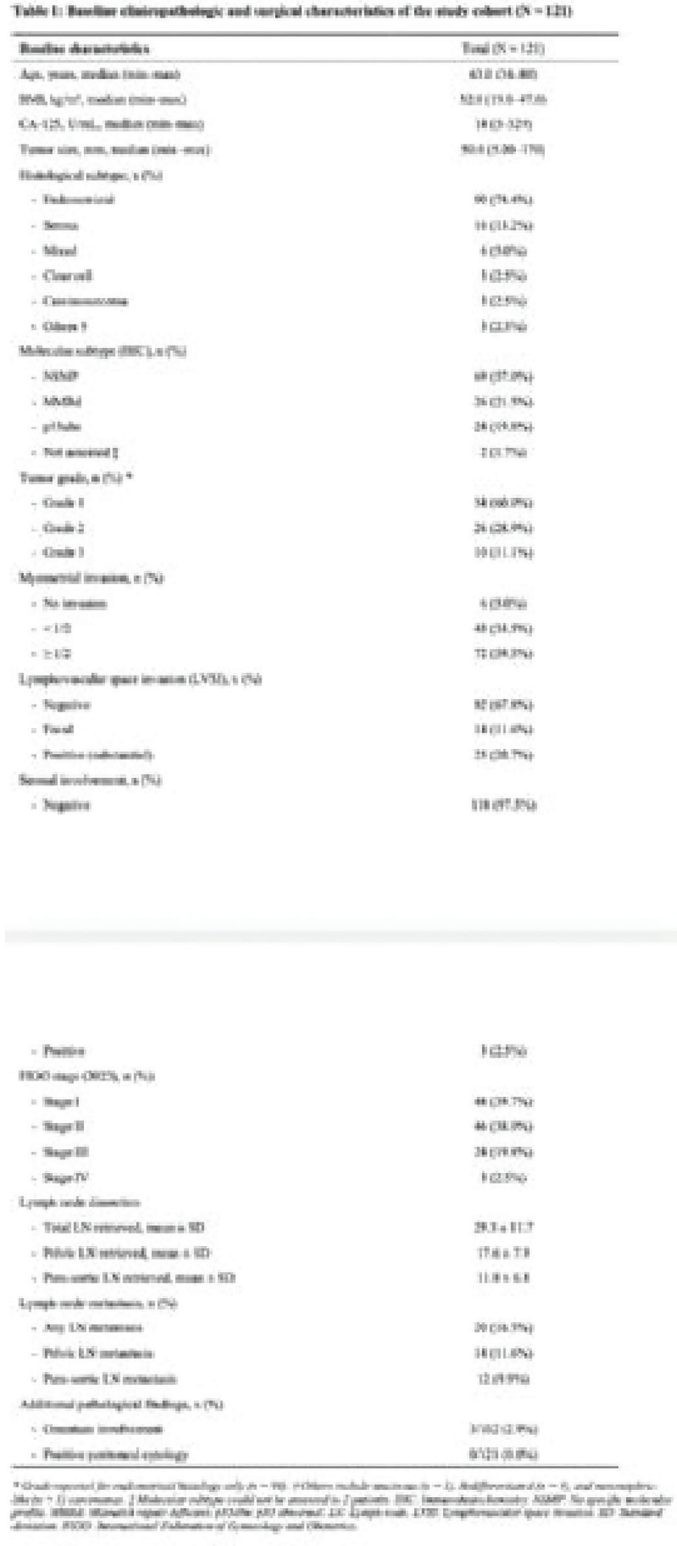
Materials and Methods: In this retrospective single-center study, 121 patients with endometrial cancer who underwent laparoscopic pelvic and para-aortic lymphadenectomy were included. The following variables were analyzed: age, body mass index (BMI), tumor size, histological type, tumor grade, depth of myometrial invasion, lymphovascular space invasion (LVSI), molecular subtype, and FIGO stage. The primary outcome was the presence of lymph node metastasis. Para-aortic metastasis patterns were also evaluated. Univariate and multivariate analyses were performed.

Results: A total of 121 patients were analyzed. The median age was 63 years and the median BMI was 32 kg/m². The most common histological type was endometrioid carcinoma (74.4%). Lymph node metastasis was detected in 20 patients (16.5%). Pelvic metastasis was observed in 11.6% (n=14), and para-aortic metastasis in 9.9% (n=12). The mean number of retrieved lymph nodes was 29.3±11.7, and the mean number of para-aortic lymph nodes was 11.8±6.8. In univariate analysis, LVSI was significantly associated with nodal metastasis (p=0.002). In multivariate analysis, prominent LVSI was identified as an independent predictor (OR: 5.44; 95% CI: 1.67-17.65; p=0.005). Additionally, LVSI was also an independent predictor of para- aortic metastasis (OR: 6.98; 95% CI: 1.81-26.78; p=0.005).

Conclusion: LVSI appears to be the strongest predictor of both pelvic and para-aortic lymph node metastasis in endometrial cancer. Assessment of LVSI may guide surgical staging and decision-making regarding the necessity of para-aortic lymphadenectomy.

Keywords: Endometrial cancer, lymph node metastasis, laparoscopy

Tablo 1.



Turk J Obstet Gynecol 2026;23(Suppl 1):S35-S45

Tablo 2.

Table 2: Univariate analysis of factors associated with lymph node metastasis

Variable	LN Negative (n = 168)	LN Positive (n = 28)	p value
Continuous variables			
Age, years, median (range)	63 (34–79)	63 (40–80)	0.899
BMI, kg/m², median (range)	32 (19–47)	30 (22–42)	0.113
CA-125, U/mL, median (range)	13 (5–329)	28 (3–203)	0.207
Tumor size, mm, median (range)	50 (5–170)	53 (10–140)	0.810
Categorical variables			
Histological type			0.556
- Endometrioid	74 (73.3%)	16 (80.0%)	
- Non-endometrioid	27 (26.7%)	4 (20.0%)	
Molecular subtype (IHC)			0.386
- NSMP	58 (57.4%)	11 (55.0%)	
- MMRd	19 (18.8%)	7 (35.0%)	
- p53abn	22 (21.8%)	2 (10.0%)	
- Not assessed	2 (2.0%)	0 (0.0%)	
Tumor grade *			0.329
- Grade 1	46 (62.2%)	8 (50.0%)	
- Grade 2	19 (25.7%)	7 (43.8%)	
- Grade 3	9 (12.2%)	1 (6.3%)	
Myometrial invasion			0.189
- No invasion	6 (5.9%)	0 (0.0%)	
- < 1/2	90 (88.6%)	4 (20.0%)	
- ≥ 1/2	56 (55.5%)	16 (80.0%)	
LVSI			**0.002**
- Negative	74 (73.3%)	8 (40.0%)	
- Focal	12 (11.9%)	2 (10.0%)	
- Positive (substantial)	15 (14.9%)	10 (50.0%)	
Serosal involvement			0.433
- Negative	98 (97.0%)	20 (100.0%)	
- Positive	3 (3.0%)	0 (0.0%)	
Cervical invasion			0.323
- Negative	85 (84.2%)	15 (75.0%)	
- Positive	16 (15.8%)	5 (25.0%)	
Ovarian involvement			0.427
- Negative	99 (98.0%)	19 (95.0%)	
- Positive	2 (2.0%)	1 (5.0%)	

*Bold p values indicate statistical significance (p < 0.05). Mann-Whitney U test used for continuous variables. Chi-square or Fisher's exact test used for categorical variables. * Grade reported for endometrioid histology only (n = 90). LN: Lymph node. LVSI: Lymphovascular space invasion. IHC: Immunohistochemistry. NSMP: No specific molecular profile. MMRd: Mismatch repair deficient. p53abn: p53 abnormal.*

[SS-022]

Evre I endometriyum kanserinde adjuvan radyoterapi öncesi hematolojik parametrelerin ve moleküler özelliklerin prognostik değeri

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Amaç: Evre I endometriyum kanserinde adjuvan radyoterapi uygulanan hastalarda prognozu belirleyen faktörlerin ortaya konulması önemlidir. Son yıllarda rutin kan parametrelerinden elde edilen enflamasyon belirteçlerinin çeşitli malignitelerde prognostik değeri olabileceği gösterilmiştir. Bu çalışmada evre I endometriyum kanseri nedeniyle adjuvan radyoterapi uygulanan hastalarda radyoterapi öncesi hematolojik parametrelerin ve tümör biyolojik özelliklerinin sağkalım sonuçları ile ilişkisinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Bu retrospektif çalışmada Eylül 2019-Ağustos 2025 tarihleri arasında evre I endometriyum kanseri tanısı ile adjuvan radyoterapi uygulanıp kemoterapi uygulanmayan toplam 210 hasta analiz edilmiştir. Hastaların klinik, patolojik ve tedavi özellikleri retrospektif olarak incelenmiştir. Radyoterapi öncesi periferik kan sayımlarından nötrofil/lenfosit oranı (NLR), trombosit/lenfosit oranı (PLR), monosit/lenfosit oranı (MLR) ve sistemik immün inflamasyon indeksi (SII) hesaplanmıştır. Sağkalım analizleri Kaplan-Meier yöntemi ile yapılmış, gruplar arasındaki fark log-rank testi ile değerlendirilmiştir. Progresyonsuz sağkalım (PFS) ve genel sağkalım (OS) ile ilişkili faktörler Cox regresyon analizi ile araştırılmıştır. İstatistiksel analizler IBM SPSS Statistics yazılımının 26.0 sürümü kullanılarak gerçekleştirilmiştir.

Bulgular: Hastaların medyan yaşı 65 yıl (45-90) olup %40,5'i evre IA, %59,5'i evre IB olarak sınıflandırılmıştır. Olguların %91,4'ü endometrioid, %8,6'sı non-endometrioid histolojiye sahipti. Tümör derecesi açısından %76,8'i grade 1-2, %23,2'si grade 3 idi. p53 mutasyonu hastaların %17,1'inde saptandı. Adjuvan tedavi olarak %79,5 hastaya brakiterapi, %18,1 hastaya eksternal pelvik radyoterapi (EBRT), %2,4 hastaya ise kombine tedavi uygulandı. Hasta, tümör ve tedavi özellikleri Tablo 1'de özetlenmiştir. Medyan takip süresi 33 ay (1-70 ay) olarak hesaplandı. Takip süresince 16 hastada (%7,6) nüks, 13 hastada (%6,2) ölüm gelişti. Medyan progresyonsuz sağkalım 65,4 ay olup medyan PFS'ye ulaşılamadı. ROC analizinde radyoterapi öncesi hematolojik parametrelerin nüks gelişimini öngörmede anlamlı bir ayırt ediciliği olmadığı görüldü. Cox regresyon analizinde NLR, PLR, MLR ve SII değerlerinin progresyonsuz sağkalım ile anlamlı ilişki göstermediği saptandı (p>0,05). Histolojik alt tip progresyonsuz sağkalım açısından anlamlı bulundu ve non-endometrioid histolojiye sahip hastalarda progresyon riskinin daha yüksek olduğu görüldü (HR: 4,18; p=0,013). Ayrıca p53 mutasyonu bulunan hastalarda progresyon riskinin anlamlı derecede arttığı saptandı (HR: 5,22; p=0,046). Evre IA ve IB hastalar arasında progresyonsuz sağkalım açısından anlamlı fark izlenmedi (p=0,714). Evre ile uygulanan radyoterapi tipi arasında da anlamlı ilişki saptanmadı (p=0,639). Genel sağkalım analizinde medyan OS 66,4 ay olarak hesaplandı ve medyan OS'ye ulaşılamadı. Genel sağkalım analizinde de p53 mutasyonu ile sağkalım arasında anlamlı ilişki saptanmış, p53 mutant hastalarda sağkalımın daha düşük olduğu izlenmiştir (p=0,009).

Sonuç: Evre I endometriyum kanserinde adjuvan radyoterapi uygulanan hastalarda radyoterapi öncesi hematolojik enflamasyon belirteçlerinin prognostik değeri gösterilememiştir. Buna karşılık non-endometrioid histoloji ve p53 mutasyonu progresyonsuz sağkalım açısından önemli prognostik faktörler olarak bulunmuştur. Bulgularımız erken evre endometriyum kanserinde tümör biyolojisinin sağkalım sonuçları üzerindeki belirleyici rolünü desteklemektedir.

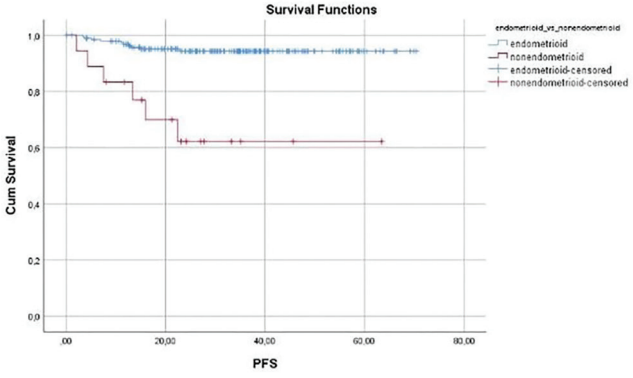
Anahtar Kelimeler: Endometriyum kanseri, radyoterapi, prognostik belirteçler

Tablo 1. Hasta, tümör ve tedavi özellikleri

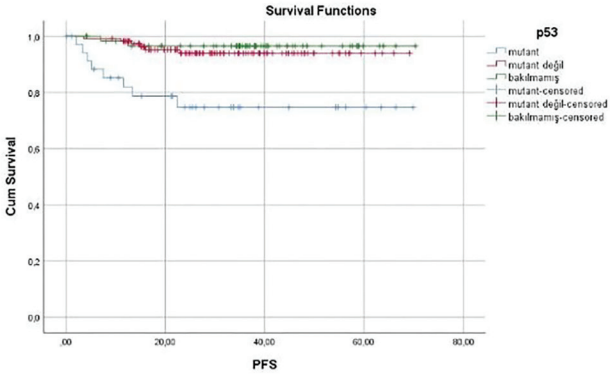
Değişken	n (%)
Yaş (medyan, aralık)	65 (45-90)
Evre IA	85 (40,5)
Evre IB	125 (59,5)
Endometrioid histoloji	192 (91,4)
Non-endometrioid histoloji	18 (8,6)
Grade 1-2	159 (76,8)
Grade 3	48 (23,2)
p53 mutant	36 (17,1)
p53 mutant değil	114 (54,3)
p53 bakılmamış	60 (28,6)
Sadece brakiterapi	167 (79,5)
Sadece eksternal radyoterapi	38 (18,1)

Tablo 2. Evreye göre radyoterapi dağılımı

Evre	Sadece EBRT	Sadece brakiterapi	EBRT + Brakiterapi
IA	16 (18,8%)	66 (77,6%)	3 (3,5%)
IB	22 (17,6%)	101 (80,8%)	2 (1,6%)
p=0,639			



Şekil 1. Histolojik alt tipe göre progresyonsuz sağkalım (PFS) için Kaplan-Meier eğrileri



Şekil 2. p53 durumuna göre progresyonsuz sağkalım (PFS) için Kaplan-Meier eğrileri

[SS-023]

Fumarat hidrataz eksikliği ile ilişkili uterin leiomyom olgusu: STUMP ayırıcı tanısı ve HLRCC açısından klinik önemi

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Amaç: Uterin düz kas tümörleri benign leiomyomlardan leiomyosarkomlara uzanan geniş bir spektrum oluşturur. Bu spektrumda yer alan ve atipik histopatolojik özellikler gösteren lezyonlar, özellikle malignite potansiyeli belirsiz düz kas tümörleri (STUMP) ile fumarat hidrataz (FH) eksikliği gösteren leiomyomlar arasında ayırıcı tanıda güçlük yaratabilmektedir. FH eksikliği gösteren leiomyomlar nadir olup (%0,4-1,6), belirgin nükleer atipi, epiteloid morfoloji ve alışılmadık vasküler yapılar nedeniyle STUMP ve leiomyosarkomu taklit edebilir. Ayrıca Herediter leiomyomatozis ve renal hücreli karsinom (HLRCC) sendromu ile ilişkili olabilmeleri nedeniyle doğru tanı klinik açıdan önem taşır. Bu çalışmada başlangıçta myoma uteri ön tanısı ile opere edilen ve postoperatif olarak FH eksikliği gösteren leiomyom tanısı alan bir olgu sunulmuştur.

Olgu: Yirmi beş yaşında, nulligravid hasta rutin kontrol amacıyla başvurdu. Özgeçmişinde hipofiz adenomu dışında özellik yoktu. Transvajinal ultrasonografide yaklaşık 10 cm çapında myom ile uyumlu kitle izlendi. Pelvik MRG'de intrauterin yerleşimli, 9×10 cm boyutlarında, internal septasyonlar içeren kistik lezyon saptandı. Tümör belirteçleri normaldi. Pfannenstiel insizyon ile yapılan myomektomide uterin kaviteyi dolduran yaklaşık 10 cm'lik intramural kitle enüklee edildi. Histomorfolojik incelemede epiteloid ve yer yer rabdoid hücreler, alveolar tip ödem, belirgin nükleollü nükleuslar, perinükleer halo ve geyik boynuzu benzeri damar yapıları izlendi. Nekroz saptanmadı, mitotik aktivite 10 büyük büyütme alanında 2-3 idi. Bu bulgular FH eksikliği lehine olmakla birlikte epiteloid STUMP ile de örtüşebilmesi nedeniyle immünohistokimyasal inceleme yapıldı. FH ekspresyon kaybı saptandı; SMA, desmin ve kaldesmon diffüz pozitif, Ki-67 düşük, p16 negatif bulundu. Olgu FH eksikliği gösteren leiomyom olarak raporlandı ve HLRCC açısından genetik danışmanlık ile ürolojik değerlendirme önerildi. İki yıllık takipte ek patoloji izlenmedi.

Tartışma: FH eksikliği gösteren leiomyomlar, belirgin sitolojik atipi ve karakteristik vasküler paternleri nedeniyle STUMP veya leiomyosarkom ile karışabilmektedir. FH gen mutasyonları HLRCC sendromu ile ilişkili olup, bu sendromda uterin ve kutanöz leiomyomlar ile agresif renal hücreli karsinom gelişebilir. Bu nedenle FH kaybının gösterilmesi yalnızca tanı açısından değil, genetik danışmanlık ve renal tümör taraması açısından da önemlidir. Literatürde FH eksik tümörlerin önemli bir kısmının STUMP olarak sınıflandırılabildiği ve bu olguların bir bölümünde germline FH mutasyonu saptandığı bildirilmiştir. Ayrıca STUMP grubunun bir kısmının gerçekte FH eksik leiomyom spektrumunda yer aldığı gösterilmiştir. FH eksik leiomyomlar genellikle benign seyirli olmakla birlikte, özellikle genç hastalarda HLRCC'nin ilk bulgusu olabilir. Bu nedenle atipik morfoloji gösteren uterin düz kas tümörlerinde Fumarat hidrataz immünohistokimyası ve gerekli durumlarda genetik inceleme önerilmektedir.

Sonuç: FH eksikliği gösteren leiomyomlar nadir ancak klinik açıdan önemli tümörlerdir. STUMP ile morfolojik örtüşme gösterebilirler ve doğru tanı için immünohistokimyasal değerlendirme gereklidir. Özellikle genç hastalarda FH ekspresyonunun değerlendirilmesi ve HLRCC açısından genetik danışmanlık verilmesi önem taşımaktadır.

Anahtar Kelimeler: Fumarat hidrataz eksikliği, HLRCC, leiomyom

[SS-024]

Şiddetli anemi ve hidronefroza neden olan prolabe pedinküle dev submüköz leiomyom: Olgu sunumu

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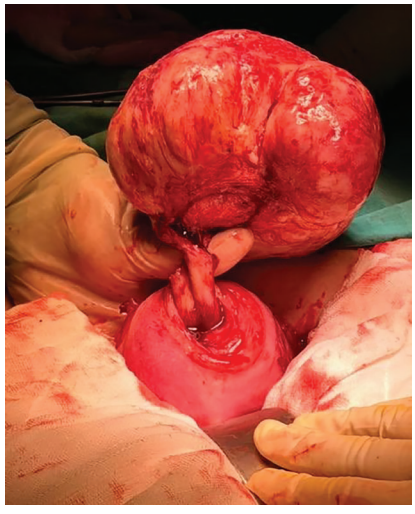
Amaç: Uterin leiomyom, üreme çağındaki kadınlarda sık görülen, yerleşim yerine göre farklı belirtiler verebilen benign tümörlerdir. Submüköz myomlar uterin kaviteye doğru büyüyüp fazla kanama ile kendini gösterdikleri için genellikle erken dönemde tanı alırlar. Vajene doğmuş pedinküllü submüköz myomlar ise nadir görülür ve genellikle yine anormal uterin kanama ile prezente olurlar. Bu olguda, ileri derecede anemi ve hidronefroza neden olan pedinküllü dev submüköz myom olgusunu sunmayı amaçladık.

Olgu: Yirmi iki yaşında, virigo hasta; yoğun vajinal kanama, sık idrara çıkma ve sağ yan ağrısı şikayetleri ile başvurdu. Hastanın anamnezinde tekrarlayan kan transfüzyonlarına rağmen hemoglobin düzeylerinde artış sağlanamadığı öğrenildi. Pelvik ultrasonda 12 cm kadar karın ön duvarını kaplayan kitle izlendi. Myom ön tanısıyla pelvik MR istendi. Başvuru anında hemoglobin değeri 5 g/dL olarak ölçüldü. Pelvik manyetik rezonans görüntüleme 'uterin fundus yerleşimli yaklaşık 12 cm çapında myom ve sağ böbrekte grade 2-3 hidronefroz saptandı' olarak raporlandı. Kan transfüzyonları sonrası operasyon kararı alındı. Açık cerrahi ile batına girildiğinde, gözlemde uterus ve ovlerlerin normal olduğu görüldü, vajen ön duvarına yapılan kesi ile myoma ulaşıldı, uterin fundustan ince bir sapla köken alarak vajene doğru ilerleyen yaklaşık 15 cm boyutunda pedinküllü myom olduğu, mesane basısı, sağ üreter basısı buna bağlı üreterde ileri derece dilatasyon olduğu görüldü. Myom pedinkülü ile birlikte eksize edildi. Bir ay sonraki kontrolünde hastanın hemoglobin değerinin 10,8 g/dL olduğu, kanamasının normale döndüğü, sık idrara çıkma şikayetinin operasyondan hemen sonra bittiği, hidronefroz bulgusunun da gerilediği görüldü.

Tartışma: Prolabe pedinküle submüköz leiomyomlar nadir görülmekle birlikte, ciddi kanama ve anemiye yol açabilir. Bu olguda hemoglobin düzeyinin 5 g/dL olması klinik tablonun ciddiyetini göstermektedir. Görüntüleme yöntemleri her zaman myomun yerleşimini doğru yansıtmayabilir. Bu olguda da preoperatif olarak fundal myom düşünülmesine rağmen intraoperatif olarak vajene prolabe submüköz myom saptanmıştır. Üriner semptomlar genellikle mesane basısına bağlıdır ancak bu olguda nadir olarak üreter basısına bağlı hidronefroz geliştiği görülmüştür.

Sonuç: Dev prolabe submüköz leiomyomlar şiddetli anemiye, sık idrara çıkma gibi üriner semptomlara ve nadiren hidronefroza neden olabilir. Tanıda özellikle virigo hastalarda görüntüleme yöntemleri yanıltıcı olabilir. Cerrahi eksizyonla klinik iyileşme oldukça hızlıdır.

Anahtar Kelimeler: Hidronefroz, anemi, prolabe pedinküle dev submüköz leiomyom



Şekil 1. Prolabe pedinküle dev submüköz leiomyom

[SS-025]

Tuba kanseri cerrahisi sırasında insidental saptanan apendiks nöroendokrin tümörü: Olgu sunumu

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Amaç: Apendiks nöroendokrin tümörleri (NET), apendiksin en sık görülen primer neoplazmları olup genellikle asemptomatik seyirli ve insidental olarak saptanan lezyonlardır. Apendektomi materyallerinde görülme sıklığı %0,3-2,3 arasında bildirilmektedir. Primer tuba uterina kanseri ise nadir görülen bir jinekolojik malignite olup klinik ve patolojik özellikleri nedeniyle tanıda güçlük yaratabilmektedir. Jinekolojik maligniteler ile eş zamanlı insidental apendiks NET saptanması oldukça nadir olup genellikle bağımsız ikinci primer tümörler olarak değerlendirilmektedir. Bu olgu sunumunda, tuba/over kaynaklı malignite nedeniyle opere edilen bir hastada insidental olarak saptanan iyi diferansiye apendiks NET olgusunun sunulması ve bu nadir birlikteliğin klinik öneminin literatür eşliğinde tartışılması amaçlanmıştır.

Gereç ve Yöntemler: Altmış üç yaşında, postmenopozal kadın hasta ishal, karın ağrısı ve abdominal şişkinlik yakınmaları ile başvurdu. Ön değerlendirmede gastrointestinal nedenler araştırıldı; endoskopi ve kolonoskopide malignite lehine bulgu saptanmadı. Tümör belirteçlerinde CA125 ve CA 72-4 yüksekliği izlenmesi üzerine ileri görüntüleme yapıldı. Manyetik rezonans görüntülemede sol overde yaklaşık 21 mm çapında, kistik ağırlıklı ve 5 mm'lik nodüler solid komponent içeren, O-RADS 3 kategorisinde değerlendirilen lezyon saptandı. Postmenopozal durum, tümör belirteç yüksekliği ve görüntüleme bulguları nedeniyle jinekolojik malignite ön tanısı ile eksploratif laparotomi planlandı. Hastaya total abdominal histerektomi, bilateral salpingo-ooforektomi, omentektomi ve pelvik-paraaortik lenf nodu diseksiyonu uygulandı. Cerrahi evreleme kapsamında profilaktik apendektomi de yapıldı.

Bulgular: Operasyon sırasında apendiks makroskopik olarak doğal görünümdeydi. Histopatolojik incelemede sol over ve sol tuba uterinada yüksek dereceli seröz karsinom saptandı; tubal fimbrialarda intraepitelyal karsinom odakları izlendi. Tümörün over kapsülünü fokal olarak invaze ettiği, ancak makroskopik ekstraovaryan yayılım göstermediği görüldü. İmmünohistokimyasal incelemede WT-1 ve p53 pozitifliği, Ki-67 proliferasyon indeksinin yaklaşık %70 olduğu raporlandı. Omentum ve 30'dan fazla pelvik-paraaortik lenf nodunda metastaz saptanmadı. Apendektomi materyalinin mikroskopik incelemesinde ise apendiks ucunda 0.8 cm çapında, submukozal yerleşimli, iyi diferansiye nöroendokrin tümör saptandı. Tümör serozaya ulaşmamış, organa sınırlı izlenmiş ve cerrahi sınırlar negatif bulunmuştur. Mitoz ve nekroz izlenmeyen lezyonda Ki-67 proliferasyon indeksi yaklaşık %1 olup Grade 1 nöroendokrin tümör ile uyumlu olarak değerlendirildi. İmmünohistokimyasal incelemede kromogranin-A, sinaptofizin ve CD56 pozitifliği izlendi. Bu bulgular insidental saptanan, düşük dereceli ve tamamen çıkarılmış apendiks nöroendokrin tümörü tanısını destekledi. Tubal yüksek dereceli seröz karsinom nedeniyle hasta adjuvan kemoterapi programına alındı; apendiksteki düşük dereceli ve küçük boyutlu nöroendokrin tümör için ek cerrahi veya medikal tedavi planlanmadı, klinik izlem önerildi.

Sonuç: Apendiks nöroendokrin tümörleri genellikle iyi diferansiye, düşük proliferasyon indeksine sahip ve indolent seyirli neoplazmlar olup çoğunlukla insidental olarak saptanmaktadır. Küçük (<1 cm) ve düşük dereceli lezyonlarda apendektomi yeterli ve küratif tedavi sağlamaktadır. Bu olguda da 0,8 cm çapında, grade 1 apendiks NET için ek cerrahi gereksinimi olmamış ve kılavuzlarla uyumlu bir yaklaşım benimsenmiştir. Jinekolojik maligniteler ile eş zamanlı apendiks NET birlikteliği nadir olup, genellikle bağımsız ikinci primer tümörler şeklinde karşımıza çıkmaktadır. Bu nedenle jinekolojik onkoloji cerrahisi sırasında uygulanan profilaktik apendektomi, klinik olarak sessiz seyreden ve aksi halde tanı alamayacak lezyonların erken saptanmasına olanak sağlayabilir. Bu olgu, çıkarılan apendiks materyallerinin rutin histopatolojik değerlendirilmesinin önemini vurgulamakta ve özellikle jinekolojik malignite cerrahilerinde profilaktik apendektominin tanısal katkısını desteklemektedir.

Anahtar Kelimeler: Apendiks nöroendokrin tümörü, yüksek dereceli seröz karsinom, insidental tümör

[SS-026]

Semptomatik miyomatozis nedeniyle yapılan histerektomi sonrasında saptanan insidental uterin perivasküler epiteloid hücreli tümör (PEComa): Olgu sunumu

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Amaç: Perivasküler epiteloid hücreli tümörler (PEComa), melanositik ve düz kas farklılaşmasını birlikte gösteren nadir mezenkimal neoplazmlardır. Uterus, jinekolojik PEComa'nın en sık bildirilen yerleşim yeridir; ancak preoperatif klinik ve görüntüleme bulguları leiomyomdan ayırt edilmeye olanak tanımadığından tanı sıklıkla cerrahi sonrası histopatolojik incelemeyle konulmaktadır. Bu olguda, semptomatik miyomatozis nedeniyle uygulanan histerektomi materyalinde insidental olarak saptanan düşük riskli uterin PEComa'nın klinikopatolojik özellikleri ve iki yıllık izlem sonuçları sunulmaktadır.

Gereç ve Yöntemler: Kırk dokuz yaşında premenopozal kadın hasta (gravida 3, para 3), on sekiz aydır ilerleyici menoraji, dismenore ve pelvik basınç yakınmaları ile başvurdu. Transvajinal ultrasonografide en büyüğü 6,4 cm olan çoklu intramural ve subserozal leiomyomlar saptandı; adneksiyal patoloji izlenmedi. Endometriyal biyopside proliferatif endometriyum ile uyumlu bulgular elde edildi; hiperplazi veya malignite bulgusu yoktu. Didrogesteron (2×10 mg/gün, 30 gün) ve traneksamik asit (2×500 mg/gün, 25 gün) ile yeterli kanama kontrolü sağlanamadı. Medikal tedaviye dirençli kanama ve semptomatik miyomatozis nedeniyle aydınlatılmış onam sonrası laparoskopik total histerektomi ve bilateral salpingo-ooforektomi uygulandı. Cerrahi materyal, ayrıntılı makroskopik örnekleme, mikroskopik inceleme ve kapsamlı immünohistokimyasal panel ile değerlendirildi.

Bulgular: Makroskopik incelemede intramural yerleşimli, en büyüğü 4,5 cm olan toplam sekiz adet miyom nodülü izlendi. Mikroskopik incelemede miyom nodüllerinin arka planında 1 cm çaplı, iyi sınırlı, nodüler yapıda bir tümöral odak saptandı. Tümör hücreleri berrak-granüler eozinofilik sitoplazma ve yuvarlak-oval nükleuslardan oluşmaktaydı. Elli büyük büyütme alanında mitotik figür izlenmedi; nekroz, lenfovasküler invazyon ve perinöral invazyon saptanmadı; cerrahi sınırlar negatifti. İmmünohistokimyasal incelemede vimentin ve HMB-45 diffüz pozitif, desmin pozitif, kaldesmon fokal pozitif; S-100, CD34 ve CD117 negatif; Ki-67 proliferasyon indeksi %1'in altındaydı. SMA ve Melan-A non-spesifik boyanma gösterdi. Bulgular, ICD-O kodu 8714/0 ile uyumlu "PEComa, NOS, benign" tanısını destekledi. Olgu jinekolojik onkoloji multidisipliner konseyinde değerlendirildi; düşük riskli patolojik özellikler ve komplet eksizyon göz önünde bulundurularak adjuvan tedavi önerilmedi. Postoperatif 15. gün, 3. ay, 1. yıl ve 2. Yıl kontrollerinde nüks, metastaz veya tümöre atfedilebilir bulgu saptanmadı.

Sonuç: Uterin PEComa, miyomatozis nedeniyle çıkarılan histerektomi materyallerinde beklenmedik bir tanı olarak karşımıza çıkabilir. Bu olgu, benign ön tanıyla yapılan histerektomilerde dahi sistematik makroskopik örnekleme ve immünohistokimyayı kapsayan ayrıntılı patolojik değerlendirmenin önemini vurgulamaktadır. Doğru tanı, uygun risk sınıflaması ve bireysellestirilmiş izlem planının oluşturulması multidisipliner yaklaşımı gerektirmektedir.

Anahtar Kelimeler: PEComa, histerektomi, miyomatozis

[SS-027]

Lokal ileri serviks kanserinde laparoskopik lenf nodu disseksiyonu ve over transpozisyonu

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Amaç: Serviks kanseri, Dünya Sağlık Örgütü verilerine göre dünya genelinde kadınlarda en sık görülen jinekolojik malignitedir. Lokal ileri evre hastalıkta standart tedavi eş zamanlı kemoradyoterapi olup, pelvik radyoterapi özellikle genç hastalarda over fonksiyonlarının kaybına yol açabilmektedir. Bu olgu sunumunda, genç yaştaki lokal ileri evre serviks kanseri tanılı bir hastada uygulanan laparoskopik lenf nodu diseksiyonu ve over transpozisyonu ile doğru evreleme sağlanması, postoperatif tedavi planının belirlenmesi ve morbiditenin azaltılması ile overlerin radyoterapinin olumsuz etkilerinden korunması amaçlanmıştır.

Gereç ve Yöntemler: Otuz beş yaşında kadın hasta, dış merkezde yapılan smear testinde ASC-US saptanması üzerine uygulanan kolposkopik biyopsi sonucunda skuamöz hücreli karsinom tanısı alarak merkezimize başvurdu. Pelvik manyetik rezonans görüntülemede, servikste endoservikal kanalı ekspanse eden yaklaşık 51×32 mm boyutlarında, vajen üst 1/3 posterior duvara uzanım gösteren kitle lezyonu izlendi. Parametrial yağ planlarının heterojen ve düzensiz görünümü parametrial invazyon lehine değerlendirildi. Ayrıca sol tarafta en büyüğü 10×5 mm, sağ internal iliak bölgede ise 7×5 mm boyutlarında lenf nodları saptandı. Pozitron emisyon tomografi-bilgisayarlı tomografi (PET-CT) incelemesinde, serviksten vajen proksimaline uzanan yaklaşık 4×4 cm boyutlarındaki kitlede artmış 18F-florodeoksiglukoz (FDG) tutulumu (SUV_{max}: 25,03) izlendi. Sağ internal iliak bölgede 1,5×1,3 cm (SUV_{max}: 6,99) ve sol external iliak bölgede 1,7×1,4 cm (SUV_{max}: 3,55) boyutlarında lenf nodlarında patolojik FDG tutulumu saptandı. Hastaya genel anestezi altında muayene, servikal biyopsi ve sistoskopi uygulandı. Jinekolojik muayenede serviks alt dudakta yaklaşık 3-4 cm çapında ülsere lezyon izlendi. Vajinal forniksler doğal, serviks sola deviye idi. Rektovajinal muayenede sağ parametriyum serbest, sol parametriyum kısalmış olarak değerlendirildi. Sistoskopide mesane mukozası ve bilateral üreter orifisleri doğal izlendi. Alınan biyopsi materyalinin histopatolojik incelemesi sonucunda nonkeratinize tip skuamöz hücreli karsinom tanısı doğrulandı.

Bulgular: Hastada doğru evreleme, over fonksiyonlarının korunması ve radyoterapi alanının belirlenmesi amacıyla laparoskopik retroperitoneal lenf nodu diseksiyonu, bilateral salpenjektomi, bilateral over transpozisyonu ve batın sitolojisi planlandı. Laparoskopik olarak batına girilerek öncelikle peritoneal sitoloji örneği alındı. Eksplorasyonda bilateral pelvik bölgede yaklaşık 2 cm boyutlarında bulky lenf nodları izlendi ve bilateral pelvik lenf nodu örneklemesi yapıldı. Üreterler bilateral olarak visualize edilerek doğal seyirde izlendi. İntraoperatif frozen incelemeye gönderilen lenf nodları malignite açısından negatif olarak raporlandı. Takiben bilateral salpenjektomi uygulandı. Overler ligamentum ovarii propriumdan serbestlenerek mobilize edildi. İnfundibulopelvik ligament, üreterlerle olan ilişkisi korunarak dikkatli şekilde disseke edildi. Overler, pelvik radyoterapi alanının dışında kalacak şekilde üst abdominal bölgeye doğru mobilize edilerek alt parakolik alandaki peritona transpoze edildi. Overlerin lokalizasyonunu belirlemek amacıyla periton hemoklip ile işaretlendi. Hemostaz kontrolü ve batın temizliği sonrası operasyon sonlandırıldı. Nihai patoloji sonucunda lenf nodları reaktif olarak değerlendirildi, batın sitolojisi ve tubal örneklerde malignite saptanmadı. Hasta konseyde evre IIB skuamöz hücreli serviks kanseri olarak değerlendirildi.

Sonuç: Erken evre serviks kanserinde primer tedavi seçeneği cerrahi iken, lokal ileri evre hastalıkta lenf nodu değerlendirmesi, evreleme, tedavi planlaması ve prognoz açısından kritik öneme sahiptir. Bu olguda uygulanan laparoskopik lenf nodu diseksiyonu ve over transpozisyonu ile hem doğru evreleme sağlanmış hem de overlerin radyoterapinin olumsuz etkilerinden korunması hedeflenmiştir. Bu yaklaşım, uygun hasta grubunda tedavi planlamasına katkı sağlamakta ve özellikle genç hastalarda hormonal fonksiyonların korunmasına olanak tanımaktadır.

Anahtar Kelimeler: Lenf nodu diseksiyonu, laparoskopi, serviks kanseri

[SS-028]

Preliminary değerlendirme: Türkiye'de sağlık çalışanları ve genel popülasyonda HPV farkındalığı ve aşılanma-bilgi düzeyi ve aşılanma oranlarının değerlendirilmesi

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Amaç: Bu çalışmanın amacı, Türkiye'de sağlık çalışanları, sağlık çalışanı olmayan hastane personeli ve genel popülasyonda insan papilloma virüsü (HPV) ve HPV aşısına ilişkin farkındalık ve bilgi düzeylerini değerlendirmek, gruplar arasında karşılaştırmak ve mevcut bilgi boşluklarını ortaya koymaktır. Bu özet, devam eden çalışmanın ön bulgularını sunmaktadır.

Gereç ve Yöntemler: Bu kesitsel anket çalışması üç farklı grupta yürütülmüştür: Kadın hastalıkları ve doğum kliniği dışında çalışan kadın hemşireler (n=45), sağlık çalışanı olmayan kadın hastane personeli (n=57) ve jinekoloji polikliniğine başvuran kadınlar (n=57). Veriler, Waller ve arkadaşları tarafından geliştirilen ve Türkçe geçerlik–güvenirlik çalışması Demir Bozkurt ve arkadaşları tarafından yapılan HPV Bilgi Ölçeği kullanılarak elde edilmiştir. Ölçek toplam puanı, ilgili maddelerin puanlarının toplanması ile hesaplanmış olup, daha yüksek puanlar daha yüksek bilgi düzeyini ifade etmektedir. Katılımcıların sosyodemografik özellikleri ile HPV enfeksiyonu, bulaş yolları, ilişkili hastalıklar ve korunma yöntemlerine yönelik bilgi düzeyleri gruplar arasında karşılaştırılmıştır.

Bulgular: Çalışmaya toplam 159 katılımcı dahil edilmiştir. Katılımcıların %93,7'si serviks kanserini duyduğunu, %69,8'i bu konuda bilgi sahibi olduğunu bildirmiştir. HPV'yi duyma oranları gruplar arasında benzer bulunurken (p>0,05), HPV testini duyma (p=0,007) ve HPV aşılanma oranları (p=0,003) açısından anlamlı farklılık saptanmıştır. HPV aşılanma oranı hemşirelerde %2,2, sağlık çalışanı olmayan hastane personelinde %14,0 ve genel popülasyonda aşılı birey saptanmamıştır. HPV farkındalık ölçeği toplam puanı açısından gruplar arasında anlamlı fark izlenmemiştir (p=0,184). Bununla birlikte, eğitim ve gelir düzeyi arttıkça HPV farkındalık puanlarının anlamlı şekilde arttığı gösterilmiştir (tüm p<0,001). Lojistik regresyon analizinde gelir düzeyinin HPV farkındalığı üzerinde bağımsız olarak anlamlı etkisi olduğu saptanmıştır (p=0,007).

Sonuç: Bu çalışmanın ön bulguları, HPV ve HPV aşısına ilişkin farkındalığın yalnızca genel popülasyonda değil, sağlık çalışanları ve hastane personelinde de beklenen düzeyin altında olduğunu göstermektedir. Özellikle hemşire grubunda bilgi düzeyinin sınırlı olması ve tüm gruplarda HPV aşılanma oranlarının son derece düşük kalması dikkat çekicidir. Genel popülasyonda aşılanmış birey saptanmamış olması, toplum düzeyinde HPV aşısına erişim ve kabulün yetersizliğini çarpıcı biçimde ortaya koymaktadır. Bu bulgular, HPV ile mücadelede yalnızca topluma yönelik değil, sağlık çalışanlarını ve hastane personelini de kapsayan hedefe yönelik eğitim ve müdahale stratejilerine ihtiyaç olduğunu göstermektedir. Ayrıca, bilgi düzeyindeki artışın koruyucu davranışlara yansımaması, sağlık politikalarının aşıya erişimi ve kabulünü artıracak şekilde yeniden yapılandırılması gerektiğini düşündürmektedir.

Anahtar Kelimeler: Anket çalışması, HPV aşı, HPV farkındalık

[SS-029]

Over kaynaklı mezonefrik-like adenokarsinom: Nadir görülen bir olgu sunumu

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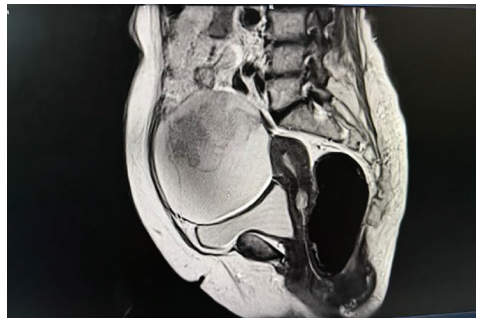
Amaç: Mezonefrik adenokarsinom (MA), kadın genital sisteminde mezonefrik (Wolff) kanal artıklarından gelişen nadir görülen malign tümörlerdir. Bu nedenle uterus, serviks, vajen, ovaryan hilus ve broad ligament gibi bölgelerden kaynaklanabilir. Mezonefrik-like adenokarsinom (MLA) ise doğrudan mezonefrik epitelden köken almamasına rağmen uterus ve adnekslerde görülebilen; histolojik, immün ve moleküler özellikleri açısından mezonefrik adenokarsinomlara benzerlik gösteren tümörlerdir.

Olgu: Seksen iki yaşında, parite 2 olan hasta batında şişlik şikâyetiyle kliniğimize başvurdu. Hastanın hipertansiyon dışında ek hastalığı ve geçirilmiş cerrahi öyküsü yoktu. Ultrasonografide sağ adneksiyel alanda 20×25 cm çapında kitle izlendi. İçerisinde 5,5×4,5 cm boyutlarında papiller yapı içeren solid alan mevcuttu. Douglas boşluğunda sıvı saptanmadı. Ayırıcı tanıda seröz kistadenom ve over karsinomu düşünüldü. CA125 (cancer antigen), CEA (carcinoembryonic antigen), CA19-9, CA15-3 ve AFP (alpha-fetoprotein) normal sınırlardaydı. Manyetik rezonans görüntülemesinde kitlenin sağ over lojundan kaynaklandığı ve ön planda seröz kistadenom ile uyumlu olabileceği değerlendirildi. Batın içinde ek patolojik lezyon veya lenfadenopati saptanmadı. Hastaya laparotomi ile cerrahi girişim planlandı. Eksplorasyonda sağ overde, yer yer solid alanlar içeren yaklaşık 25 cm çapında kitle görüldü. Sağ salpingo-ooferektomi yapılarak frozen incelemeye gönderildi. Frozen sonucunun düşük dereceli over tümörü ile uyumlu gelmesi üzerine histerektomi, sol salpingo-ooferektomi, pelvik ve paraaortik lenf nodu diseksiyonu ile total omentektomi uygulandı. Operasyon sonunda tam sitoredüksiyon sağlandı. Nihai patolojide kitlenin MLA ile uyumlu olduğu bildirildi. Tümör, sağ over kaynaklı olup içinde 6×6×3 cm mikrokistik alan içeren solid kitle görünümündeydi. İmmünohistokimyasal incelemede ER (estrogen receptor) negatif, PR (progesterone receptor) pozitif, *PAX8* (paired box gene 8) pozitif, p53 pozitif, *WT-1* (Wilms tumor gene) pozitif; CD 10 (cluster of differentiation), GATA3 (GATA binding protein 3) ve TTF-1 (tiroid transkripsiyon faktörü -1) negatif saptandı. Batın sıvısında ve çıkarılan 34 adet lenf nodunda metastaz görülmedi.

Sonuç: MA ve MLA nadir görülen jinekolojik malignitelerdir. MLA'larda en sık KRAS (Ki-ras2 Kirsten rat sarcoma viral oncogene homolog) ve PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha) mutasyonları bildirilmektedir. İmmünohistokimyasal olarak genellikle ER/PR negatifliği, GATA3, PAX8, TTF-1 ve CD10 pozitifliği, non-diffüz p16 pozitifliği ve wild-type p53 ekspresyonu görülebilir. Bizim olgumuz Evre IA olarak değerlendirilmiştir. Görüntüleme yöntemleri tanıyı kesinleştirmede yeterli olmayıp, kesin tanı patolojik ve immünohistokimyasal inceleme ile konulmuştur. Tümör tek overde sınırlı olup diğer organlarda yayılım saptanmamıştır. Bu hasta için üç aylık aralıklarla izlem kararı verildi. MLA nadir görülmesi nedeniyle tanı, tedavi ve prognostik faktörler açısından daha geniş serilere ihtiyaç duyulan bir tümör grubudur. Kesin tanı için immünohistokimyasal inceleme önem taşır. Over kitlesi ile başvuran hastalarda sık görülen tümörlerin yanı sıra MLA da ayırıcı tanıda düşünülmeli ve patolojik değerlendirmede bu olasılık göz önünde bulundurulmalıdır.

Anahtar Kelimeler: Mezonefrik-like adenokarsinom, over tümörleri



Şekil 1. Adneksiyal kitlenin manyetik rezonans görüntülemesi

[SS-030]

Uterin karsinosarkomlarda klinik ve histopatolojik özelliklerin prognostik değeri: 43 olguluk seri

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Amaç: Uterin karsinosarkom yüksek dereceli karsinomatöz ve sarkomatöz bileşenlere sahip agresif bir tümör tipidir. Hastalar genellikle anormal uterin kanama ve pelvik kitle şikayetiyle başvururlar. Hastaların %50'si tanı anında Evre 3-4'tedir. Bu çalışmada merkezimizde tanı alan 43 karsinosarkom olgusunun klinikopatolojik özelliklerinin analiz edilmesi amaçlanmıştır.

Gereç ve Yöntemler: 2012-2022 yılları arasında tanı alan toplam 43 karsinosarkom olgusu çalışmaya dahil edildi. Yaş, tümör boyutu ve yayılımı, uzak metastaz varlığı, tümör marker düzeylerini içeren klinik ve demografik veriler hastane bilgi sisteminden elde edildi. Olguların tümü histolojik bileşenler açısından tekrar gözden geçirildi. Endometrioid karsinom bileşenine sahip olguların moleküler alttipi belirlendi. Histolojik alttipler ve diğer prognostik veriler arasındaki ilişki istatistiki açıdan analiz edildi.

Bulgular: Hastaların ortalama yaşı 67,8±6,9 olarak belirlendi. Epitelyal komponent olguların %65,1'inde endometrioid karsinom, %20,9'unda seröz karsinom, %7,0'sinde şeffaf hücreli karsinom, %7,0'sinde andiferensiye karsinomdu. Sarkomatöz komponent ise 36 (%83,7) olguda homolog yani yüksek dereceli sarkom, NOS, 7 olguda heterolog [5 (%11,6) kondrosarkom/osteosarkomatöz diferensiyasyon, 2 (%4,7) olguda rhabdomyosarkomatöz diferensiyasyon] sarkomdu. Endometrioid karsinom bileşenine sahip 28 olgunun 22'si (%78,5) p53 mutant alttip, 3'ü (%10,7) MMR deficient, 3'ü (%10,7) ise NSMP alttüründeydi. Olguların %65,1'inde myometrial %50'nin üstündeyken, %46,5'inde alt uterin segment ve servikal stromal tutulum, %30,2'sinde ise uterin seroza tutulumu mevcuttu. Olguların %62,8'sinde lokal/bölgesel yayılım mevcut olup, en sık yayılım over, tuba uterina ve omentumaydı. Uzak metastaz ise %23,3 olguda izlendi ve en sık metastatik odaklar karaciğer ve akciğer olarak belirlendi. Uzak metastaz izlenen 10 olgunun 9'unda metastatik odakta sadece karsinomatöz komponent izlenirken 1 olguda hem karsinomatöz hem de sarkomatöz komponent mevcuttu. Olguların 31'inde (%72,1) lenfovasküler invazyon, 21'inde (%48,8) ise lenf nodu tutulumu mevcut olup, bu metastazların büyük çoğunluğu pelvik lenf nodlarınaydı. Asit sıvısı %74,4 olguda tümör pozitifti. Hastaların tanı anındaki tümör belirteçleri Tablo 2'de belirtilmiş olup, CA125 olgularda anlamlı yükseklik gösterdi ($p<0,05$). Olguların %34,9'u tanı anında FIGO evre II, %46,5'i evre III, %18,6'sı evre IV'te idi. Hastaların takip süresi en az 48 ay olup, 11 (%25,6) hasta yaşamakta, 32 (%74,4) hasta ölmüştü. Sağkalım süreleri çok değişken aralıkta olup ortalama sağkalım 30 ay (6-76 ay) olarak belirlendi. Epitelyal komponentin tipi ile klinikopatolojik veriler arasında anlamlı ilişki bulunmazken, mezenkimal olarak heterolog eleman içeren tümörler ile servikal stromal tutulum, lenf nodu tutulumu ve bölgesel yayılım arasında anlamlı ilişki saptandı ($p<0,05$). Epitelyal komponent olarak endometrioid karsinom içeren olgular moleküler alttip açısından değerlendirildiğinde p53 mutant alt türün diğerlerine göre kısa sağkalım ile ilişkili bulundu ($p<0,05$). Epitelyal komponent türü ile FIGO evresi ve sağkalım arasında anlamlı ilişki bulunmazken, heterolog eleman içeren mezenkimal komponente sahip olgular anlamlı şekilde ileri FIGO evresi ve kısa sağkalım ile ilişkili saptandı ($p<0,05$).

Sonuç: Uterin karsinosarkomlar nadir görülmekle birlikte agresif davranış potansiyeline ve kötü prognoza sahip tümörlerdir. Çalışmamızda olguların büyük çoğunluğunun ileri evrede tanı alması ve ortalama sağkalımın 30 ay ile sınırlı kalması literatür verileriyle uyumludur. Epitelyal komponent dağılımında endometrioid morfoloji ve p53 mutant alttipin daha kötü sağkalım ile ilişkili bulunması, moleküler sınıflamanın prognostik önemini ortaya koymaktadır. Çalışmamızın en dikkat çekici bulgularından biri, heterolog mezenkimal komponent varlığının daha ileri evre, artmış lenf nodu metastazı ve daha kötü sağkalım ile ilişkili olmasıdır. Bu sonuç, heterolog diferansiyasyonun tümör agresifliğini artıran önemli bir faktör olabileceğini desteklemektedir.

Anahtar Kelimeler: Uterin, karsinosarkom

Tablo 1. Klinikopatolojik özellikler

Parametre	n (%)
Myometrial invazyon	
<%50	15 (34,9)
>%50	28 (65,1)
Lenfovasküler invazyon (LVSI)	
Yok	12 (27,9)
Var	31 (72,1)
Servikal stromal tutulum	
Yok	23 (53,5)
Var	20 (46,5)
Alt uterin segment tutulumu	
Yok	23 (53,5)
Var	20 (46,5)
Uterin seroza tutulumu	
Yok	30 (69,8)
Var	13 (30,2)
Diğer organ/doku tutulumu	
Yok	27 (62,8)
Var	16 (37,2)
Lenf nodu metastazı	
Yok	22 (51,2)
Var	21 (48,8)
Uzak metastaz	
Yok	33 (76,7)
Var	10 (23,3)
Batın sıvısı	
Negatif	11 (25,6)
Pozitif	32 (74,4)

Tablo 2. Tanı anında tümör markerları

Marker	Ortalama ± SS	Medyan	Min-maks
CA125	363,8±387,6	214	5,5-1476
CA19-9	5,96±5,84	4,2	0,1-26
CA15.3	5,36±3,82	5,0	0,2-18,7
CEA	2,60±3,96	1,7	0,2-22

Turk J Obstet Gynecol 2026;23(Suppl 1):S41-S45

[SS-031]

Overin seks kord tümörlerine benzeyen uterin tümörler: Olgu sunumu ve tanısal zorluklar

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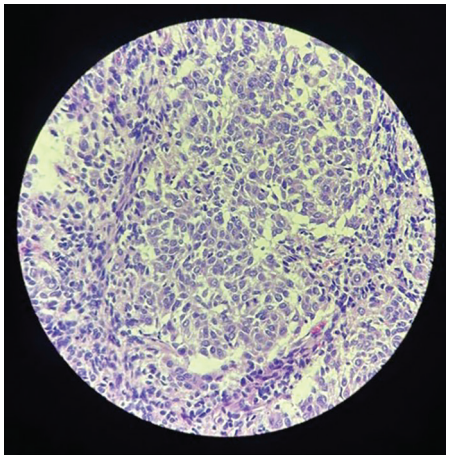
Amaç: Overin sex cord tümörlerine benzer uterin tümörler (UTROSCT), histogenezi belirsiz ve malign potansiyeli belirsiz nadir ve ayırt edici bir neoplazmdır. Bu tümörler sıklıkla yaşamın 4. ile 6. dekadı arasında izlenir. Submokozal, intramural veya polipoid kitlelerdir. Basit histerektomi genellikle tedavi edicidir.

Olgu: Altmış beş yaşında, 3 doğum yapmış (gravida 3, para 3) bir kadın hasta, anormal uterin kanama ve karın ağrısı şikayetleri ile jinekolojik onkoloji kliniğimize başvurdu. Ultrasonografi ile uterus corpus'unda 4 cm boyutunda bir lezyon tespit edildi ve endometrial kalınlık 11 mm olarak ölçüldü. Overler normal ve atrofik görünüyordu. Manyetik rezonans görüntüleme, uterin corpus ve fundus seviyesinde, kontrast tutulum gösteren ve maligniteyi dışlayamayacak şekilde en büyük boyutu 48x40 mm olan bir lezyon saptadı. Daha sonra yapılan endometrial biyopsi hiperplastik polip belirledi. Bu bulgulara dayanarak, laparoskopik histerektomi ve bilateral salpingo-ooforektomi yapılmasına karar verildi. Postoperatif olarak, patoloji raporu, myometriumda yer alan ve düşük malignite potansiyeli olan bir overin sex cord tümörüne benzeyen uterin tümör varlığını gösterdi. İmmünohistokimyasal analiz, kalretinin, CD10, vimentin, CD99 ve CD56 için pozitif, Ki-67 için <%1 ve inhibin için negatif sonuçlar verdi. Üç yıllık takip süresince, nüks belirtileri olmadı ve hasta izlenmeye devam edilmektedir.

Sonuç: Bu olgu, anormal uterin kanama ile başvuran hastalarda overin sex cord tümörlerine benzer uterin tümörlerin nadirliğini vurgulamaktadır; bu durum genellikle leiomyomlara atfedilmektedir. Malignite potansiyeli göz önünde bulundurulduğunda, kliniklerin benzer olguları yönetirken bu farklı tanıyı düşünmeleri kritik öneme sahiptir.

Anahtar Kelimeler: Over tümörleri, UTROSCT



Şekil 1. İmmünohistokimyasal boyama, tümör hücrelerinde CDGG için pozitifliği göstermektedir (HEx40)

[SS-032]

Malign perivasküler epiteloid hücreli tümörün adneksiyal kitle şeklinde prezentasyonu

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Amaç: Adneksiyal kitle olarak prezente olan nadir bir malign perivasküler epiteloid hücreli tümör (PEComa) olgusunu sunmak ve ayırıcı tanıda değerlendirilmesini sağlamak.

Gereç ve Yöntemler: Otuz bir yaşında, gravida 1 parite 1 olan hasta, yaklaşık 6 aydır devam eden karın ağrısı ve abdominal distansiyon şikâyetleri ile başvurdu. Pelvik muayenede sağ adneksiyal kitle saptandı. Transvajinal ultrasonografide 105×100 mm boyutlarında, solid mural komponent içeren ve yoğun vaskülarizasyon gösteren komplike kistik lezyon izlendi. Manyetik rezonans görüntülemede solid ve vejetan alanlar içeren kistik kitle izlenerek over malignitesi ön tanısı düşünüldü. Tümör belirteçleri genel olarak normal sınırlarda olup yalnızca CA 19-9 hafif yüksek (42 U/mL) bulundu. Bilgisayarlı tomografide uzak metastaz saptanmadı. Hasta adneksiyal malignite ön tanısı ile opere edildi.

Bulgular: İntraoperatif değerlendirmede overlerin ve tubaların doğal olduğu, sağ parametrium ve üreter komşuluğunda retroperitoneal yerleşimli kitle saptandığı görüldü ve eksize edildi. Apendikste ek bir kitle daha saptandıve appendektomi yapıldı. Retroperitoneal kitlenin histopatolojik incelemesinde nükleer atipi, nekroz, lenfovasküler invazyon ve lenf nodu metastazı varlığı ile uyumlu malign PEComa tanısı konuldu. Aynı zamanda sitolojide pecoma ile uyumlu malignidi. İmmünohistokimyasal bulgular tanıyı destekledi. Ayrıca insidental olarak düşük dereceli apendiks müsinöz neoplazisi (LAMN) saptandı. Postoperatif dönem sorunsuz seyreden hasta onkolojik değerlendirmeye yönlendirildi.

Sonuç: PEComalar nadir görülen mezenkimal tümörler olup non-spesifik klinik ve radyolojik bulgular nedeniyle preoperatif dönemde adneksiyal maligniteleri taklit edebilir. Kesin tanı histopatolojik ve immünohistokimyasal inceleme ile konulmaktadır. Malign PEComalar agresif seyir gösterebileceğinden yakın takip gerektirir. Bu olgu, atipik adneksiyal kitlelerin ayırıcı tanısında PEComa'nın akılda tutulması gerektiğini vurgulamaktadır.

Anahtar Kelimeler: Pecoma, adneksiyel kitle, LAMN

[SS-033]

Pelvik eksenterasyon sonrası 2 ve 5 yıllık sağ kalım oranları

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Amaç: Jineko-onkolojik ileri evre kanserlerde, lokal pelvik nüks durumlarında küratif amaçlı standart tedavilere yanıt vermeyen ve cerrahi negatif olma şansı olan hastalarda bazen zor bir cerrahi işlem olarak pelvik ekzenterasyon yapılabilir. Pelvik ekzenterasyon neredeyse jinekolojide yapılan en zor ve komplikasyon oranı yüksek amaliyatlardan biridir ve kanserin bulunduğu yere göre gerek duyulan işlemin içeriği açısından mesane ve üretranın korunduğu posterior yada rektumun korunduğu anterior yada hepsinin alındığı total ekzenterasyon olarak 3'e ayrılır. En sık ileri evre ve sonrasında pelvik nüks yapmış serviks kanser olgularında uygulanır. Cerrahi işlem sonrası hastaya ihtiyacına göre idrar çıkışı, gayta çıkışı veya seksüel aktivite durumu söz konusu ise vagina gibi yeniden yapılandırma işleminin de yapılması gerekmektedir. Tümör boyutu küçük, nüks çok uzun süre sonra gerçekleşmiş ve cerrahi sınırlar temiz ise hastaların sağ kalım oranları uzun olabilir. Genel kabul olarak 2 yıl ve üzerinde nüks görülmeyen olgularda sağ kalım beklentisi artmaktadır. Cerrahi sonrası ortalama yaşam süresi 58 aydır. Genel olarak 5 yıllık sağkalım oranları %30-60 arasındadır. Bizim 17 pelvik egzenterasyon olgumuzda 2 ve 5 yıllık sağ kalım oranlarını hesapladık. Bizim amacımız Süleyman Demirel Üniversitesi Jineko-Onkoloji Kliniği'nde yapılan pelvik egzenterasyon olgularındaki 2 ve 5 yıllık sağ kalım oranlarını paylaşmaktır.

Gereç ve Yöntemler: 2012-2022 yılları arasında Süleyman Demirel Üniversitesi Jineko-Onkoloji Kliniği'nde 12 serviks kanser ve 5 endometriyum kanser takipli ve lokalize pelvik nüks olgularında standart tedavilere cevap vermeyen hastalara yapılan pelvik egzenterasyon olgularına ait bilgiler hasta takip dosyalarından kaydedildi. Serviks kanser grubunda pelvik egzenterasyon yapılma ortalama yaşı 50,6 (38-65) iken endometriyum kanserinde 60 (50-80). Total grubun ortalama operasyon yaşı 53,7 idi. Serviks kanseri için 2 yıllık sağ kalım oranı %33,3 iken 5 yıllık sağ kalım oranları %16,7. Benzer oranlar endometriyum kanser olgularında sırasıyla hem 2 hem de 5 yıllık sağ kalım oranları %20 idi. Total 2 ve 5 yıllık sağ kalım oranları ise sırasıyla %29,4 ve %17,6.

Sonuç; Pelvik egzenterasyon operasyonları son derece zor, komplikasyon oranları yüksek ve riskli operasyonlardır. Operasyon sonrası hastaların fiziksel fonksiyonlarının 6-12 ayda ve duygusal/zihinsel sağlık skorlarının ise ortala 18 ayda ameliyat öncesi seviyelerine döndüğü raporlanmaktadır. Buna karşılık 2 yıllık sağ kalım oranları ortalama %30 ve 5 yıllık sağ kalım oranları 18 gibi oldukça düşük oranlardadır. Bu nedenle doğru ve kür şansı olan hastaların bu operasyon için seçilmesi çok önemlidir.

Anahtar Kelimeler: Endometriyum kanseri, pelvik ekzenterasyon, serviks kanseri

Tablo 1. Pelvik ekzenterasyonda 2 ve 5 yıllık sağ kalım oranları

Kanser türü	Ortalama yaş (Min-maks)	2 yıllık sağkalım (%)	5 yıllık sağkalım (%)
Serviks	50,6 (38-65)	%33,3	%16,7
Endometriyum	60 (50-80)	%20	%20
Total	53,7 (38-80)	%29,4	%17,6

[SS-034]

Grade 2 evre 1B endometrioid endometrial kanserde port site ve vajen cuff metastazı: Olgu sunumu

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Amaç: Port site metastazı (PSM), jinekolojik malignitelerde minimal invazif cerrahi sonrası nadir görülen bir rekürrens formudur. Endometrial kanser hastalarında özellikle düşük ve orta risk grubunda oldukça nadir bildirilmektedir. Bu çalışmada robotik cerrahi sonrası gelişen port site metastazı ve eş zamanlı vajen cuff rekürrensi olan evre 1B grade 2 endometrioid endometrial kanser olgusunun sunulması ve literatür eşliğinde değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Olgu sunumu şeklinde planlanan bu çalışmada, 2019 yılında postmenopozal kanama nedeniyle başvuran 63 yaşındaki hastanın klinik süreci retrospektif olarak değerlendirildi. Tanısal küretaj sonucunda iyi diferansiye adenokarsinom saptanan hastaya robotik cerrahi ile total histerektomi, bilateral salpingooferektomi ve bilateral sentinel lenf nodu diseksiyonu uygulandı. Cerrahi sırasında umblikal ve paraumblikal bölgelerde toplam beş trokar kullanıldı. Nihai patoloji sonucunda tümör çapı 3,5×2,5×2 cm, histolojik grade 2 ve FIGO evre 1B olarak raporlandı. Hasta adjuvan vajinal brakiterapi aldı ve rutin takip programına alındı.

Bulgular: Hasta yaklaşık 4 yıl boyunca hastalıksız takip edildi. Mayıs 2024 kontrolünde karın ön duvarında deri altında ele gelen kitle ve vajen cuff bölgesinde yaklaşık 2 cm erode lezyon saptandı. F-18 FDG PET/BT incelemesinde vajen cuff düzeyinde ve karın ön duvarında artmış metabolik aktivite gösteren lezyonlar izlendi. Umbilikus düzeyinde karın ön duvarında yaklaşık 3,8×2,8×4,5 cm boyutlu lezyon ve bunun devamında FDG tutulumu gösteren yumuşak doku alanı saptandı (SUV_{max}: 9,33). Vajen cuff bölgesinde de artmış FDG tutulumu izlendi (SUV_{max}:10,37). Karın ön duvarı ve vajen cuff bölgelerinden alınan biyopsiler adenokarsinom enfiltrasyonu ile uyumlu bulundu. Ekim 2024 tarihinde hastaya cerrahi rezeksiyon uygulandı. Sağ eksternal ve internal iliak lenf nodları eksize edildi, vajen cuff rekürrens alanı ve port site metastazı tamamen çıkarıldı. Patolojik incelemede adenokarsinom metastazı saptandı ve cerrahi sınırlar tümörsüz olarak raporlandı. Hasta sistemik tedavi planlanması amacıyla tıbbi onkolojiye yönlendirildi.

Sonuç: Port site metastazı endometrial kanserli hastalarda oldukça nadir görülmesine rağmen düşük veya orta riskli olgularda da gelişebilmektedir. İzole port site metastazı veya vajen cuff rekürrensi ile birlikte ortaya çıkabilir. Bu nedenle minimal invazif cerrahi sonrası takiplerde port giriş yerlerinin dikkatli değerlendirilmesi önemlidir. Cerrahi rezeksiyon çoğu olguda temel tedavi yaklaşımını oluşturmakta olup uygun hastalarda radyoterapi ve kemoterapi gibi ek tedaviler de uygulanabilir.

Anahtar Kelimeler: Endometriyum kanseri, port site, metastaz

[SS-035]

Histerektomi yapılmayan pas olgularında kanama öngörüsü ve şok indeksi

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Amaç: Plasenta akreta spektrumu (PAS), ciddi maternal morbidite ve mortalite ile ilişkili önemli bir obstetrik durumdur. Bu çalışmada, histerektomi uygulanmayan PAS olgularında kan replasmanı gereksinimi ile ilişkili klinik faktörlerin ve şok indeksinin değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: Bu retrospektif çalışmaya, Ocak 2025-Ocak 2026 tarihleri arasında kliniğimizde izlenen ve PAS tanısı alan, histerektomi yapılmayan 42 hasta dahil edildi. Hastalar kan replasmanı yapılan (n=13) ve yapılmayan (n=29) olarak iki gruba ayrıldı. Demografik özellikler, obstetrik öykü, laboratuvar parametreleri ve şok indeksi (kalp hızı/sistolik kan basıncı) karşılaştırıldı. İstatistiksel analizde Mann-Whitney U ve ki-kare testleri kullanıldı.

Bulgular: Toplam 42 hasta çalışmaya dahil edildi. Hastaların 13'ünde (%31) kan replasmanı uygulanırken, 29'unda (%69) uygulanmadı. Kan replasmanı yapılan hastalarda BMI, gravida, parite ve önceki sezaryen sayısı anlamlı olarak daha yüksek bulundu ($p<0,05$). Ayrıca preoperatif hemoglobin düzeyi daha düşük ve şok indeksi anlamlı olarak daha yüksek saptandı ($p=0,008$). Yaş, DCC öyküsü ve postoperatif hemoglobin düzeyi açısından gruplar arasında anlamlı fark izlenmedi ($p>0,05$).

Sonuç: Çalışmamızda, kan replasmanı yapılan grupta vücut kitle indeksi, gravida, parite ve önceki sezaryen sayısının anlamlı olarak daha yüksek olduğu saptandı. Bu durum, artmış obstetrik yük ve özellikle tekrarlayan sezaryenlerin PAS gelişimi ve şiddeti ile ilişkili olduğunu desteklemektedir. Preoperatif hemoglobin düzeyinin kan replasmanı yapılan hastalarda daha düşük bulunması, bu hastaların cerrahiye daha düşük hematolojik rezerv ile girdiğini göstermektedir. Bu durum, intraoperatif ve postoperatif dönemde kan transfüzyonu gereksinimini artırabilecek önemli bir faktördür. Şok indeksi, kalp hızı ve sistolik kan basıncının oranı olarak hesaplanan, hemodinamik durumu hızlı ve pratik şekilde yansıtan bir parametredir. Bu bulgu, PAS olgularında erken dönemde hemodinamik instabilitenin öngörülmesinde şok indeksinin klinik olarak değerli erken uyarıcı bir belirteçtir. Sonuç olarak, PAS olgularında artmış parite, sezaryen öyküsü, düşük preoperatif hemoglobin düzeyi ve yüksek şok indeksi kan replasmanı gereksinimi ile ilişkili bulunmuştur. Şok indeksinin, bu hastalarda erken risk değerlendirilmesi açısından pratik ve değerli bir parametre olarak kullanılabileceği düşünülmektedir

Anahtar Kelimeler: Şok indeksi, invazyon, plasenta akreata spektrumu

Tablo 1. Kan transfüzyonu yapılan ve yapılmayan PAS olgularının klinikodemografik verileri

Değişken	Kan transfüzyonu yapılmayan (n=29)	Kan transfüzyonu yapılan (n=13)	p-değeri
Yaş (yıl)	28 (25-35)	30 (25-34)	0,989*
VKİ (kg/m^2)	24,8 (21,9-29,1)	28,4 (25,8-35,1)	0,009*
Gravida	2 (1-3)	3 (3-5)	0,012*
Parite	1 (0,1,5)	2 (2-2)	0,002*
Önceki sezeryan ≥1 (n)	8 (%27,6)	10 (%76,9)	0,002*
DCC (n)	5 (%17,2)	2 (%15,4)	0,460
Preop Hb (g/dL)	11,9 (10,9-12,6)	10,9 (9,6-12,1)	0,043*
Postop Hb (g/dL)	10,2 (9,6-11,5)	9,5 (8,5-10,7)	0,119*
Şok indeksi ≥1	0 (%0)	13 (%100)	0,008 *

Sürekli değişkenler medyan (çeyrekler arası aralık) olarak verilmiş olup gruplar arasında karşılaştırmalar Mann-Whitney U testi ile yapılmıştır. Kategorik değişkenler sayı (yüzde) olarak sunulmuş ve karşılaştırmalarda ki-kare testi veya Fisher'ın kesin testi kullanılmıştır. $p<0,05$ değeri istatistiksel olarak anlamlı kabul edilmişti

[SS-036]

Lenf nodu tutulumu pozitif olan seröz borderline over tümörü olgu sunumu

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Amaç: Seröz borderline over tümörleri (SBOT), düşük malign potansiyelli epitelyal over tümörleri arasında yer almakta olup genellikle genç yaş grubunda görülür ve prognozu iyidir. Lenf nodu tutulumu SBOT'larda nadir olmakla birlikte görüldüğünde klinik yönetim açısından belirsizlik yaratır. Bu olguda, primer tümör borderline özellikte olmasına rağmen pelvik lenf nodlarında pozitiflik saptanan bir hastayı sunuyoruz.

Olgu: Yirmi dört yaşında, daha önce sağlıklı kadın hasta pelvik ağrı ve karında şişlik şikâyetiyle başvurdu. Ultrasonografi ve BT görüntülemede sol overde 135x88 mm multiloküler kistik kitle izlendi. CA125 hafif yüksek bulundu (37,2 U/mL). Hastaya eksploratif laparotomi yapıldı. İntraoperatif değerlendirmede sol overde papiller çıkıntılar içeren kistik kitle izlendi, karşı over ve uterus doğal görünümde idi.

Hastaya, batın yıkama sıvısı örneği alınmasını takiben, sol salpingo-ooforektomi, omentum biyopsisi, periton biyopsisi ve bilateral pelvik lenf nodu diseksiyonu işlemleri uygulandı.

Patoloji sonucunda:

• Histolojik tip: Mikroinvazyon ve mikropapiller alanlar içeren lenf nodu tutulumlu seröz borderline tümör (sol over),

• Peritoneal yüzeylerde implant izlenmedi,

• Omentum negatif,

• Ancak 1 pelvik lenf nodunda seröz borderline tutulumu saptandı.

Hastanın FIGO evresi IIIA1 olarak değerlendirildi. Multidisipliner konseyde hastaya oosit donasyonu takiben tamamlayıcı cerrahi önerilmesi, hastanın reddetmesi halinde adjuvan tedavi önerilmesi planlandı.

Bulgular: SBOT'larda cerrahi yaklaşım hastanın fertilite beklentisine göre değişmektedir. Fertilite beklentisi varsa tek taraflı kistektomi/salfingoooferektomiye ek olarak batın yıkama sıvısı örneği, omentum biyopsisi, periton biyopsisi alınması önerilir. Fakat (bulky) lenf nodu örneklemesi rutinde yoktur. Olguda görüldüğü üzere (bulky) lenf nodu örneklemesinin yapılması, seröz borderline over tümöründe (özellikle daha agresif olduğu düşünülen mikropapiller morfolojik alt tipte) evreleme ve hastanın tedavisinin devamı açısından önem teşkil etmektedir.

Sonuç: Seröz borderline over tümörlerinde lenf nodu pozitifliği nadir görülse de özellikle daha agresif seyreden mikropapiller morfolojik alt tipte hastanın operasyon sonrası takip ve yönetiminde önemli rol oynar.

Anahtar Kelimeler: Seröz borderline over tümörü, mikropapiller morfolojik alt tip, lenf nodu pozitifliği, metastaz, olgu sunumu

[SS-037]

Gastrik Krukenberg tümörlerinin vNOTES cerrahi ve PIPAC ile yönetimi olgu serisi

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Amaç: Gastrik adenokarsinomdan kaynaklanan Krukenberg tümörlerinin tedavisinde vNOTES (vajinal doğal orifis transluminal endoskopik cerrahi) ile PIPAC (basınçlı intraperitoneal aerosol kemoterapi) yöntemlerinin birleştirilmesinin uygulanabilirliğini ve klinik geçerliliğini ortaya koymak.

Gereç ve Yöntemler: Gastrik adenokarsinom ve ardından yumurtalık metastazları (Krukenberg tümörleri) öyküsü olan, vNOTES yoluyla sitoredüktif cerrahi ve PIPAC kullanılarak intraperitoneal kemoterapi uygulanan üç kadın hasta (32, 39 ve 47 yaşında). Her üç olguda da vNOTES tekniği kullanılarak histerektomi ve bilateral salpingo-ooforektomi gerçekleştirilmiştir. Sitoredüksiyonun ardından, birinci olguda mitomisin C, ikinci olguda sisplatin + doksorubisin, üçüncü olguda ise oksaloplatin ile PIPAC uygulanmıştır. Periton boşluğuna GelPOINT® cihazı ile erişilmiş ve kemoterapi 12 mmHg basınç altında aerosolize edilmiştir.

Bulgular: İntraoperatif komplikasyon görülmedi. Histopatoloji, peritoneal tutulum olmaksızın Krukenberg metastazlarını doğruladı. Üç hasta da prosedürü iyi tolere etti; hızlı iyileşme gösterdi ve postoperatif majör morbidite görülmedi. Bu, Krukenberg tümörü tedavisinde vNOTES ve PIPAC'ın eş zamanlı kullanımını gösteren ilk klinik rapordur.

Sonuç: vNOTES ve PIPAC'ın kombinasyonu, mide kaynaklı izole yumurtalık metastazı olan seçilmiş hastalar için uygulanabilir, güvenli ve minimal invazif bir yaklaşım olarak görünmektedir. Bu teknik, daha iyi lokal kontrol ve hasta konforu sağlayabilir. Uzun vadeli onkolojik sonuçlarını doğrulamak için daha fazla klinik çalışma yapılması gerekmektedir.

[SS-038]

İndosiyanin yeşili eşliğinde sentinel lenf nodu haritalaması ile görüntüleme yöntemleriyle saptanamayan nodal metastazın ortaya konduğu vulva skuamöz hücreli karsinom olgusu

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Amaç: Vulva skuamöz hücreli karsinomda lenf nodu tutulumu, prognoz ve tedavi stratejisinin belirlenmesinde temel belirleyicilerden biridir. Sentinel lenf nodu (SLN) biyopsisi, uygun hasta grubunda cerrahi morbiditeyi azaltırken yüksek tanısal doğruluk sağlamaktadır. Bununla birlikte, klinik ve radyolojik olarak nod negatif değerlendirilen olgularda mikrometastatik hastalığın saptanması halen önemli bir klinik sorun teşkil etmektedir. İndosiyanin yeşili (ICG) ile gerçekleştirilen SLN haritalaması ile okült nodal metastaz saptanan bir olgunun sunulması ve bu bulgunun evreleme ile adjuvan tedavi kararına etkisinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Altmış yaşında, gravida 4 parite 4, hipertansiyon öyküsü bulunan hasta, yaklaşık altı aydır olan vulvar lezyon nedeniyle değerlendirildi. Klinik muayenede üretra sağ lateralinde, sağ labium minus iç yüzüne uzanan yaklaşık 3,5×3 cm boyutlarında, düzensiz sınırlı ve frajil karakterde lezyon izlendi. Vulva biyopsi sonucu yüksek dereceli skuamöz hücreli karsinom olarak raporlandı. Pelvik manyetik rezonans görüntüleme ve kontrastlı torakoabdominal bilgisayarlı tomografi incelemelerinde patolojik lenf nodu ya da uzak metastaz lehine bulgu izlenmedi. Genel anestezi altında tümör çevresine dört kadrandan peritümoral ICG enjeksiyonu uygulandı. Bunu takiben floresan görüntüleme eşliğinde bilateral inguinofemoral SLN haritalaması gerçekleştirildi. Tespit edilen sentinel lenf nodları eksize edildi ve ek olarak bilateral yüzeyel ve derin inguinofemoral lenf nodu diseksiyonu uygulandı. Primer tümör için anterior modifiye radikal vulvektomi gerçekleştirildi.

Bulgular: Histopatolojik incelemede 3×2,5 cm boyutlarında, grade 3 skuamöz hücreli karsinom saptandı. Tümör invazyon derinliği 6 mm olarak ölçüldü. Lenfovasküler invazyon ve perinöral invazyon saptandı. Sağ inguinofemoral sentinel lenf nodunda metastaz saptanmazken, sol tarafta derin yerleşimli sentinel lenf nodunda 0,9 cm çapında metastatik odak ve ekstranodal yayılım mevcuttu. Sentinel dışındaki lenf nodlarının tamamı metastaz açısından negatif olarak değerlendirildi. Preoperatif görüntüleme yöntemlerinin nodal hastalık açısından negatif olmasına rağmen metastazın yalnızca sentinel lenf nodunda saptanması, SLN biyopsisinin mikrometastatik hastalığın belirlenmesindeki yüksek duyarlılığını desteklemektedir. Elde edilen bulgular doğrultusunda hasta FIGO evre IIIC olarak evrelendirildi. Postoperatif dönemde küratif radyoterapi ile eş zamanlı haftalık sisplatin tedavisi uygulandı.

Sonuç: Bu olgu, klinik ve radyolojik olarak nod negatif vulva kanseri hastalarında ICG eşliğinde gerçekleştirilen sentinel lenf nodu haritalamasının okült metastatik hastalığın saptanmasında önemli bir tanısal değer taşıdığını göstermektedir. Bu yaklaşım, yalnızca doğru evreleme sağlamakla kalmayıp, aynı zamanda adjuvan tedavi kararlarını doğrudan etkileyerek hasta yönetiminde belirleyici rol oynamaktadır. Özellikle konvansiyonel görüntüleme yöntemlerinin sınırlı kaldığı durumlarda SLN biyopsisinin uygun hastalarda rutin klinik pratiğe entegrasyonu önerilebilir.

Anahtar Kelimeler: Vulva kanseri, sentinel lenf nodu biopsisi, indosiyanin yeşili, lenf nodu metastazı, vulvektomi

[SS-039]

Acil ve planlı plasenta perkreata doğumlarında segmental uterin rezeksiyonun fetal ve maternal sonuçları

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Amaç: Bu çalışmanın amacı, segmental uterin rezeksiyon ile tedavi edilen, plasenta previa eşlik eden plasenta perkreata olgularında acil ve planlı ameliyatların maternal ve fetal sonuçlarını karşılaştırmaktır.

Gereç ve Yöntemler: Retrospektif olarak, plasenta previa ve plasenta perkreata tanısı ile segmental uterin rezeksiyon uygulanan hastalar değerlendirildi. İntraoperatif bulgulara dayanarak tanıları doğrulanan hastalar çalışmaya dahil edildi. Fetal anomali, ikiz gebelik ve 24 haftadan önce plasenta perkreata tanısı konulan (kliniğimizde yaşayabilirlik sınırı 24. gebelik haftası) ve histerektomi geçiren hastalar çalışmadan çıkarıldı. Plasenta akreta spektrumu tanısı konulmuş ancak postpartum patolojik plasenta perkreata tanısı konmamış hastalar da çalışmadan çıkarıldı. Olgular acil ve planlı cerrahi uygulananlar olarak iki gruba ayrıldı. Demografik veriler, hemorajik morbidite, intraoperatif ve postoperatif komplikasyonlar, ameliyat süresi, hastanede yatış süresi ile perinatal ve neonatal sonuçlar karşılaştırıldı.

Bulgular: Bu çalışmaya toplam 141 plasenta perkreata olgusu dahil edildi. Bunların 25'i (%17,73) acil, 116'sı (%82,27) planlı segmental uterin rezeksiyon grubundaydı. Postoperatif hemoglobin değişiklikleri, ameliyat süreleri, toplam kan transfüzyonu, mesane yaralanması ve hastanede kalış süresi gruplar arasında anlamlı farklılık göstermedi (sırasıyla p=0,7, p=0,6, p=0,9, p=0,9 ve p=0,2). Fetal ağırlıklar, 5 dakikalık Apgar skorları ve yenidoğan yoğun bakım ünitesine yatış oranları gruplar arasında anlamlı farklılık göstermedi. Kanama ile başvuran hastaların doğumdaki gebelik yaşı, aktif doğum eylemiyle başvuran ve elektif cerrahi geçiren hastalara göre daha düşüktü [32 hafta %95 güven aralığı (GA): 26-37 vs. 35 hafta %95 GA: 34-35; p=0,037].

Sonuç: Deneyimli bir multidisipliner ekip eşliğinde uygulanan segmental uterin rezeksiyon, plasenta perkraeta olgularında uterus koruyucu bir yaklaşım olarak acil ve planlı olgularda benzer maternal ve fetal sonuçlar vermektedir. Bu bulgular uygun merkezlerde ve seçilmiş hastalarda konservatif cerrahi yaklaşımın güvenli bir seçenek olabileceğini düşündürmektedir.

Anahtar Kelimeler: Plasenta akreata, plasenta perkreta, acil

[SS-040]

Gebelikte tanı alan ileri evre meme kanseri olgusunda gebelik terminasyonu kararı ve gebelikte kanser olgu sunumu ve literatür eşliğinde değerlendirme

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Gebelikle ilişkili meme kanseri (pregnancy-associated breast cancer, PABC), gebelik sırasında veya postpartum ilk yıl içerisinde tanı alan meme kanserlerini kapsamakta olup nadir görülmesine rağmen yönetimi oldukça kompleks bir klinik durumdur. Maternal prognoz ile fetal güvenlik arasındaki denge, tedavi planlamasında temel belirleyicidir. Bu olgu sunumunda, gebeliğin ikinci trimesterinde ileri evre meme kanseri tanısı alan ve multidisipliner değerlendirme sonucunda gebelik terminasyonu önerilen bir hasta sunulmaktadır. Olgu, mevcut literatür ve kılavuzlar eşliğinde tartışılmıştır.

Anahtar Kelimeler: Gebelikle ilişkili meme kanseri, ileri evre meme kanseri, multidisipliner yaklaşım, gebelik terminasyonu, maternal ve fetal güvenlik