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Adjuvant human papillomavirus vaccination after excisional treatment for cervical precancer

Servikal prekanser için eksizyonel tedavi sonrası adjuvan insan papillomavirüsü aşılaması

Süleyman Özen[1], Eda Güner Özen[2], Gülin Özuyar Şimşek[1], İnci Başkır İşlek[1], Muzaffer Sancı[1]

[1]*İzmir City Hospital, Department of Gynecologic Oncology Surgery, İzmir, Türkiye*
[2]*İzmir City Hospital, Department of Obstetrics and Gynecology, İzmir, Türkiye*

Abstract

Objective: To evaluate whether adjuvant 9-valent human papillomavirus vaccination improves viral clearance and reduces recurrence after excisional treatment for high-grade cervical intraepithelial neoplasia (CIN2+).

Materials and Methods: This retrospective cohort study included women aged 18 years and older who underwent loop electrosurgical excision procedure for histologically confirmed CIN2+ between December 2023 and January 2026. Women with pre-treatment human papillomavirus positivity, negative surgical margins, and available post-treatment follow-up data were included. Patients were stratified according to post-treatment vaccination status. The primary outcome was human papillomavirus clearance at 24 months. Secondary outcomes included clearance at 6 and 12 months, persistent infection, time to viral clearance, and CIN2+ recurrence. Multivariable logistic and Cox regression analyses were performed.

Results: A total of 666 women were included, of whom 212 (31.8%) received adjuvant vaccination and 454 (68.2%) did not. Clearance of human papillomavirus was higher in vaccinated than in unvaccinated women at 6 months (60.8% vs. 46.3%), 12 months (78.3% vs. 58.8%), and 24 months (87.7% vs. 77.8%). Persistent infection at 24 months was lower in the vaccinated group (12.3% vs. 22.2%). CIN2+ recurrence occurred in 3.8% of vaccinated women and 11.9% of unvaccinated women. Adjuvant vaccination was independently associated with faster viral clearance (adjusted hazard ratio: 2.0, 95% confidence interval: 1.5-2.7, p<0.001).

Conclusion: Adjuvant 9-valent human papillomavirus vaccination after excisional treatment was associated with higher viral clearance and lower CIN2+ recurrence.

Keywords: Human papillomavirus vaccines, cervical intraepithelial neoplasia, uterine cervical dysplasia, recurrence, excision

Öz

Amaç: Yüksek dereceli servikal intraepitelyal neoplazi (CIN2+) nedeniyle eksizyonel tedavi uygulanan kadınlarda adjuvan 9-valan insan papillomavirüs aşısının viral klirens ve nüks üzerine etkisini değerlendirmek.

Gereç ve Yöntemler: Bu retrospektif kohort çalışmasına Aralık 2023-Ocak 2026 tarihleri arasında histolojik olarak doğrulanmış CIN2+ nedeniyle loop elektrokoter eksizyon prosedürü uygulanan 18 yaş ve üzeri kadınlar dahil edildi. Tedavi öncesi insan papillomavirüs pozitifliği, negatif cerrahi sınır ve tedavi sonrası takip verisi bulunan hastalar çalışmaya alındı. Hastalar tedavi sonrası aşılama durumuna göre gruplandırıldı. Birincil sonlanım ölçütü 24. ayda insan papillomavirüs klirensiydi. İkincil sonlanım ölçütleri 6. ve 12. ay klirensi, persistan enfeksiyon, viral klirense kadar geçen süre ve CIN2+ nüksü idi. Çok değişkenli lojistik regresyon ve Cox regresyon analizleri yapıldı.

PRECIS: Adjuvant 9-valent human papillomavirus vaccination after excisional treatment for cervical precancer was associated with higher viral clearance and lower recurrence during 24 months of follow-up.

Corresponding Author/Sorumlu Yazar: Süleyman Özen MD,
University of Health Sciences Türkiye, İzmir City Hospital, Department of Gynecologic Oncology Surgery, İzmir, Türkiye
E-mail: drsuleymanozen@gmail.com **ORCID ID:** orcid.org/0000-0002-4870-2840

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Bulgular: Toplam 666 kadın değerlendirildi; bunların 212'si (%31,8) adjuvan aşı aldı, 454'ü (%68,2) almadı. İnsan papillomavirüs klirensi aşılanan grupta 6. ayda %60,8'e karşı %46,3, 12. ayda %78,3'e karşı %58,8 ve 24. ayda %87,7'ye karşı %77,8 olarak daha yüksekti. Yirmi dördüncü ayda persistan enfeksiyon aşılanan grupta daha düşüktü (%12,3'e karşı %22,2).CIN2+ nüksü aşılanan kadınların %3,8'inde, aşılanmayanların ise %11,9'unda görüldü. Adjuvan aşılama daha hızlı viral klirens ile bağımsız olarak ilişkiliydi (düzeltilmiş tehlike oranı: 2,0; %95 güven aralığı: 1,5-2,7; p<0,001).

Sonuç: Eksizyonel tedavi sonrası uygulanan adjuvan 9-valan insan papillomavirüs aşısı, daha yüksek viral klirens ve daha düşük CIN2+ nüksü ile ilişkili bulundu.

Anahtar Kelimeler: İnsan papillomavirüs aşıları, servikal intraepitelyal neoplazi, servikal displazi, nüks, eksizyon

Introduction

Cervical cancer remains a significant global health burden, with persistent infection by high-risk human papillomavirus (HPV) recognized as the central etiological factor in its development[1,2]. While most HPV infections are transient, persistent infection—particularly with oncogenic genotypes such as HPV16—can lead to the development of high-grade cervical intraepithelial neoplasia (CIN2/3) and subsequent malignant transformation[3].

Excisional treatment, most commonly performed using loop electrosurgical excision procedure (LEEP), is the standard management for high-grade lesions. Although treatment is highly effective, a considerable proportion of women continue to exhibit persistent HPV infection or develop recurrent disease after treatment. Reported recurrence rates of CIN2+ range from approximately 5% to 15%, even among patients with negative surgical margins[4-6].

Persistent HPV infection has been consistently identified as the strongest predictor of recurrence. Women with ongoing HPV positivity after treatment are at significantly increased risk of developing recurrent high-grade lesions, highlighting the importance of post-treatment viral dynamics in clinical outcomes[5,7].

In Türkiye, HPV vaccination has not yet been incorporated into the national immunization program. Therefore, HPV vaccination is frequently recommended to women presenting in clinical practice, including those undergoing excisional treatment, such as LEEP, and those referred after such treatment. Although prophylactic HPV vaccines are primarily designed to prevent new infections rather than treat existing ones, accumulating evidence suggests that vaccination administered around the time of treatment may reduce the risk of recurrent CIN2+[8,9].However, data regarding its effect on virological outcomes, particularly HPV clearance and persistence, remain limited and inconsistent[9,10].

Given these uncertainties, further real-world data are needed to clarify the impact of adjuvant HPV vaccination on both viral and clinical outcomes following excisional treatment.

In this context, this study aimed to evaluate the effect of post-excisional administration of the 9-valent HPV vaccine on high-risk HPV clearance and on CIN2+ recurrence in women undergoing LEEP for high-grade CIN.

Materials and Methods

Study Design and Setting

This retrospective cohort study was conducted at the Gynecologic Oncology Surgery Clinic at University of Health Sciences Türkiye, İzmir City Hospital between December 2023 and January 2026. The study protocol was approved by the University of Health Sciences Türkiye, İzmir City Hospital Non-Interventional Clinical Research Ethics Committee (approval number: 2025/235, date: 21.05.2025). The study was conducted in accordance with the principles of the Declaration of Helsinki. Due to the retrospective design and the use of anonymized clinical data, the requirement for informed consent was waived.

Study Population

Eligible participants were women aged ≥18 years who underwent LEEP for histologically confirmed CIN2 or CIN3 and had documented HPV positivity prior to treatment.

To minimize the potential influence of residual disease, only patients with negative surgical margins in the excisional specimen were included. Margin negativity was defined as the absence of dysplastic epithelium at both the ectocervical and endocervical resection margins.

Inclusion also required availability of at least one post-treatment HPV test and follow-up data extending to 24 months after excisional treatment.

Patients were excluded if they had invasive cervical carcinoma at baseline, a prior history of cervical excisional treatment, known immunosuppression (including human immunodeficiency virus infection, organ transplantation, or chronic systemic immunosuppressive therapy), pregnancy at the time of treatment, incomplete clinical or virological records, or a history of prophylactic HPV vaccination prior to the index excisional procedure.

Adjuvant HPV Vaccination

Participants were stratified according to HPV vaccination status following excisional treatment.

The vaccinated cohort consisted of women who initiated the 9-valent HPV vaccine (Gardasil 9®) within 90 days of the LEEP procedure and completed the standard three-dose schedule (0, 2, and 6 months). Vaccination status and timing were verified through institutional electronic medical records

and pharmacy administration records to minimize exposure misclassification.

The unvaccinated cohort included women who did not receive HPV vaccination before or after the excisional procedure.

Surgical Procedure and Histopathological Evaluation

All patients underwent LEEP. Surgical specimens were evaluated by experienced gynecologic pathologists. Histopathological examination confirmed the presence of CIN2 or CIN3 and assessed the surgical margin status according to World Health Organization classification criteria.

Follow-up Protocol

Post-treatment surveillance followed the institutional cervical dysplasia follow-up protocol. Follow-up intervals were calculated from the date of the LEEP procedure.

High-risk HPV testing and liquid-based cytology were routinely performed at 6 months and 12 months after treatment, followed by a final HPV test at 24 months.

Patients with abnormal cytology findings and/or persistent HPV positivity during follow-up underwent colposcopic evaluation. Directed cervical biopsies and endocervical curettage were performed when clinically indicated.

Follow-up completeness was assessed for all eligible participants. Patients without available follow-up data for at least one post-treatment HPV test were excluded from the analysis. For patients with partial follow-up, available data were included in time-to-event analyses until the last documented visit.

HPV Testing

High-risk HPV testing was performed using the Cobas 4800 HPV Test (Roche Diagnostics), a clinically validated real-time polymerase chain reaction-based assay that detects oncogenic HPV genotypes, including HPV16 and HPV18, and a pooled group of other high-risk HPV types. Although the assay reports HPV18 separately, no isolated HPV18-positive case was identified in the baseline dataset. Accordingly, HPV18 could not be evaluated as a separate genotype category; cases in which HPV18 was detected together with other high-risk types were included in the multiple high-risk HPV category.

When genotype-specific data were available, type-specific persistence and new genotype acquisition were distinguished. Viral clearance was defined as a negative HPV test following a previously documented positive result without subsequent detection of the same genotype during follow-up.

Persistent infection was defined as the detection of HPV at two or more consecutive follow-up visits.

Baseline demographic and clinical variables included age at treatment, histological grade (CIN2 vs CIN3), and HPV genotype category when available.

These variables were selected based on their potential association with HPV persistence and risk of recurrence, and were included as potential confounders in multivariable analyses.

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics for Windows, version 28.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro-Wilk test and are presented as mean ± standard deviation or median with interquartile range, as appropriate. Categorical variables are presented as frequencies and percentages.

Between-group comparisons were conducted using Student's t-test or the Mann-Whitney U test for continuous variables and the chi-square test or Fisher's exact test for categorical variables.

The association between HPV vaccination and HPV clearance at 24 months was evaluated using logistic regression analysis. Crude and adjusted odds ratios with 95% confidence intervals (CIs) were calculated.

Time to viral clearance and time to CIN2+ recurrence were analyzed using Kaplan-Meier survival curves, and differences between groups were assessed using the log-rank test. Cox proportional hazards regression models were used to estimate adjusted hazard ratios (aHR) while controlling for potential confounders.

The proportional hazards assumption for Cox regression models was assessed using Schoenfeld residuals. No significant violations of the proportional hazards assumption were detected.

Because the study was retrospective, a formal, a priori sample size calculation was not performed. However, a post hoc power assessment was conducted to determine whether the available sample size provided adequate statistical power to detect clinically meaningful differences between groups.

All statistical tests were two-sided, and a p-value <0.05 was considered statistically significant.

Results

Figure 1 shows the flow chart of the study population. A total of 666 women who underwent LEEP for histologically confirmed CIN2 or CIN3 and met the predefined inclusion criteria were included in the final analysis. Among these patients, 212 women(31.8%)received adjuvant 9-valent HPV vaccination following excisional treatment, whereas 454 women (68.2%) did not receive HPV vaccination and served as the comparison group.

Baseline demographic and clinicopathological characteristics of the study population are summarized in Table 1. The mean age of patients in the vaccinated group was 42.9±11.1 years, compared with 43.8±11.7 years in the unvaccinated group, with no statistically significant difference between groups. Similarly, the distribution of final histological diagnoses was comparable. In the vaccinated cohort, 168 patients (79.2%) had CIN2 and 44 patients (20.8%) had CIN3, whereas 352 patients (77.5%) had CIN2 and 102 patients (22.5%) had CIN3 in the unvaccinated group.

Baseline HPV genotype distribution was also comparable between the groups. Among vaccinated women, 17.0% had HPV16 infection, 15.6% had other high-risk HPV types, and 67.5% had multiple HPV infections, whereas the corresponding proportions in the unvaccinated cohort were 38.8%, 28.9%, and 32.4%, respectively. No patient had isolated HPV18 positivity at baseline; therefore, HPV18 was not classified as a separate group. HPV18 co-infections, when present, were included in the multiple high-risk HPV category.

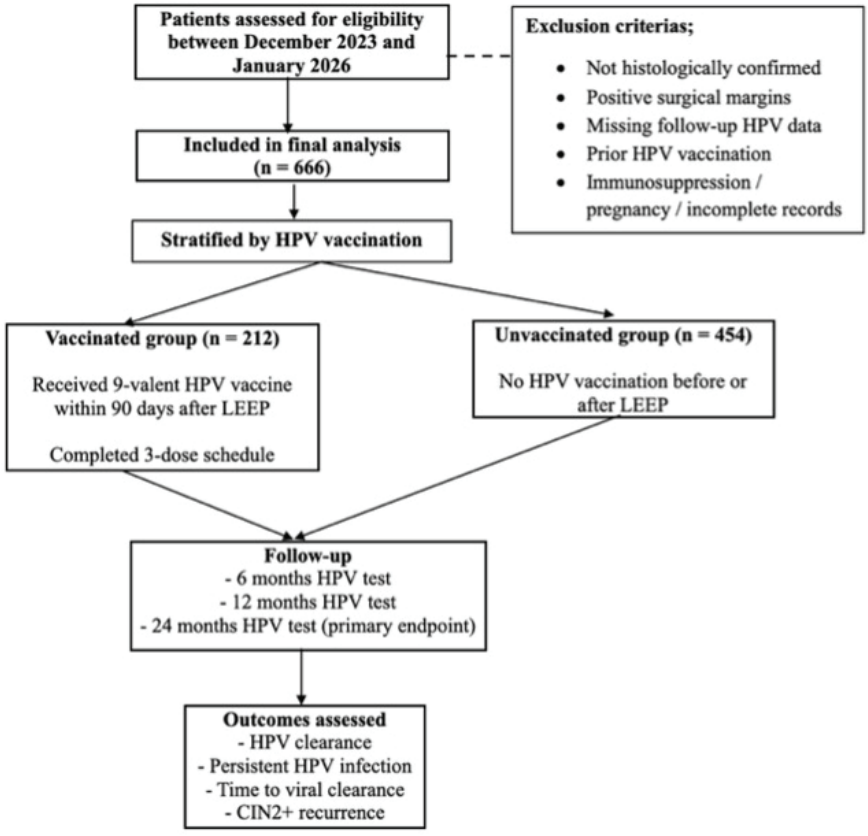

Figure 1. Flow chart of the study population

HPV: Human papillomavirus, LEEP: Loop electrosurgical excision procedure, CIN2+: High-grade cervical intraepithelial neoplasia

Table 1. Baseline demographic and clinical characteristics of women undergoing excisional treatment for high-grade cervical intraepithelial neoplasia according to HPV vaccination status

Characteristic	Vaccinated (n=212)	Unvaccinated (n=454)	p-value
Age (years)			
Mean ± SD	42.9±11.1	43.8±11.7	0.41
Final histology			
CIN2	168 (79.2%)	352 (77.5%)	0.78
CIN3	44 (20.8%)	102 (22.5%)	
Baseline HPV genotype			
HPV16	36 (17.0%)	176 (38.8%)	**0.62**
Other high-risk HPV	33 (15.6%)	131 (28.9%)	
Multiple high-risk HPV	143 (67.5%)	147 (32.4%)	

No isolated HPV18-positive case was identified at baseline. HPV18 co-infections, when present, were included in the multiple high-risk HPV category
HPV: Human papillomavirus, CIN: Cervical intraepithelial neoplasia

Overall, no statistically significant differences were observed between the two groups with respect to baseline demographic or clinicopathological characteristics.

Rates of HPV clearance during follow-up are presented in Table 2. At 6 months after LEEP, HPV clearance was observed in 129 of 212 vaccinated patients (60.8%), compared with 210 of 454 unvaccinated patients (46.3%). Persistent HPV infection at this time point remained in 39.2% of vaccinated women and 53.7% of unvaccinated women.

At the 12 months follow-up, viral clearance increased in both groups but remained higher among vaccinated patients. Specifically, 166 vaccinated patients (78.3%) achieved HPV clearance, whereas 267 unvaccinated patients (58.8%) tested negative for HPV.

At 24 months, which represented the primary endpoint of the study, HPV clearance was documented in 186 vaccinated patients (87.7%), compared with 353 unvaccinated patients (77.8%). Persistent HPV infection at 24 months was therefore observed in 26 vaccinated patients (12.3%) and 101 unvaccinated patients (22.2%).

Persistent HPV infection during follow-up occurred less frequently in the vaccinated group. At the 24 months follow-up, 26 vaccinated patients (12.3%) remained HPV positive compared with 101 patients (22.2%) in the unvaccinated cohort.

In crude comparative analysis, adjuvant HPV vaccination was associated with an approximately 50% reduction in the odds of persistent HPV infection.

During the follow-up period, histologically confirmed CIN2+ recurrence occurred in 62 patients across the entire cohort. Recurrent disease was observed in 8 of 212 vaccinated patients (3.8%), whereas 54 of 454 unvaccinated patients (11.9%) developed CIN2+ recurrence.

Thus, the incidence of recurrent high-grade cervical disease was substantially lower among women who received adjuvant HPV vaccination compared with those who did not.

Figure 2 presents the Kaplan-Meier curves for time to HPV clearance following LEEP according to HPV vaccination status. Kaplan-Meier analysis demonstrated a higher cumulative probability of HPV clearance among vaccinated women compared with unvaccinated patients throughout the 24 months follow-up period. The difference between groups was statistically significant according to the log-rank test (p<0.001).

In multivariable Cox proportional hazards regression analysis adjusting for age, histological grade, and baseline HPV genotype, adjuvant HPV vaccination was independently associated with a significantly increased rate of viral clearance (aHR: 2.0, 95% CI: 1.5-2.7, p<0.001),indicating an approximately twofold higher rate of HPV clearance over time.

Discussion

Principal Findings

In this retrospective cohort study, adjuvant 9-valent HPV vaccination following LEEP for CIN2+ was associated with improved virological and clinical outcomes. Vaccinated women demonstrated higher HPV clearance rates at all follow-up points, reaching 60.8% at 6 months and 87.7% at 24 months, compared with 46.3% and 77.8% in unvaccinated patients, respectively. This was accompanied by a lower rate of persistent infection (12.3% vs. 22.2%) and a reduced

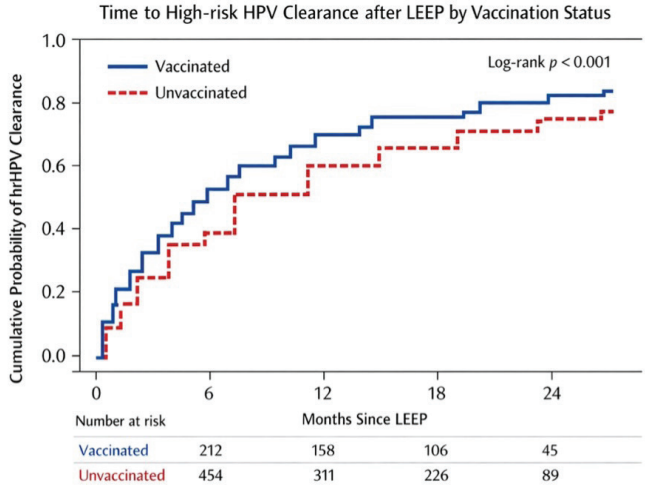

Figure 2. Kaplan-Meier curves for time to hrHPV clearance following LEEP according to HPV vaccination status

hrHPV: High-risk human papillomavirus, LEEP: Loop electrosurgical excision procedure

Table 2. Comparison of HPV clearance and clinical outcomes according to HPV vaccination status

Outcome	Vaccinated (n=212)	Unvaccinated (n=454)	Crude OR (95% CI)	p-value
hrHPV clearance at 6 months	129 (60.8%)	210 (46.3%)	1.81	<0.001
hrHPV clearance at 12 months	166 (78.3%)	267 (58.8%)	2.53	<0.001
hrHPV clearance at 24 months	186 (87.7%)	353 (77.8%)	2.05	0.004
Persistent hrHPV infection at 24 months	26 (12.3%)	101 (22.2%)	0.49	0.004
CIN2+ recurrence	8 (3.8%)	54 (11.9%)	0.29	<0.001

OR: Odds ratio, CI: Confidence interval, CIN2+: High-grade cervical intraepithelial neoplasia, hrHPV: High-risk human papillomavirus

incidence of CIN2+ recurrence (3.8% vs. 11.9%), indicating a clinically relevant benefit in the post-treatment setting.

Biological Plausibility and Interpretation

Persistent HPV infection is a well-established driver of recurrent cervical disease. Previous studies have shown that type-specific persistence, particularly HPV16, significantly increases the risk of CIN2+ recurrence even in margin-negative patients[3,7]. In our cohort, the approximately 10% absolute reduction in persistence among vaccinated women likely contributed to the observed reduction in recurrence. Notably, clearance rates in the unvaccinated group were consistent with expected ranges after excisional treatment (40-55% at 6 months and 65-80% at 24 months) supporting the internal validity of our findings[8,11]. Evidence from observational studies has reported improved viral clearance and reduced persistence following vaccination[12-15].

Comparison with Existing Literature

Our findings are consistent with previous studies that demonstrate a protective effect of HPV vaccination following excisional treatment. A large meta-analysis including over 21,000 women reported a 59% reduction in recurrent CIN2+ (RR 0.41) among vaccinated individuals[16]. Similarly, other meta-analyses and systematic reviews have reported risk reductions ranging between 50% and 80%[14,15]. A large prospective project demonstrated that post-treatment HPV vaccination achieved approximately 80% effectiveness in preventing disease relapse, with sustained benefits observed over long-term follow-up[17]. Similarly, systematic reviews evaluating HPV-positive adult women have reported that vaccination after conization reduces CIN2+ recurrence by up to 87% and improves viral clearance rates to approximately 72.4%, compared with 45.7% in unvaccinated controls[18]. These findings closely parallel the higher clearance rates and reduced persistence observed in our cohort.

In pooled analyses of clinical trials, prior HPV vaccination was associated with a marked reduction in subsequent HPV-related lesions, with decreases exceeding 85-95% for vaccine-type disease endpoints[19]. Likewise, post-hoc analyses of randomized controlled trials have demonstrated approximately 88% efficacy in preventing recurrent CIN2+ after surgical treatment[20].

A recent large retrospective cohort study reported that completion of the 9-valent HPV vaccination schedule was independently associated with significantly higher HPV clearance rates at 12 months, irrespective of excisional treatment status[21]. This supports our observation of consistently higher clearance rates across all follow-up time points (60.8%, 78.3%, and 87.7%), suggesting that vaccination may enhance immune-mediated viral elimination beyond that of surgical excision alone. The natural history of cervical disease after excisional treatment underscores the importance of viral persistence. Longitudinal data indicate that approximately 10-20% of infections persist after treatment, representing a key mechanism underlying recurrence[22]. The reduction in persistent infection observed in our study (12.3% vs. 22.2%) is, therefore, likely a key mechanism underlying the decreased recurrence rates.

Heterogeneity of Evidence

The interpretation of adjuvant HPV vaccination remains challenging because of substantial heterogeneity across study designs and clinical contexts. While our findings demonstrate a clinically meaningful reduction in recurrence (3.8% vs. 11.9%) and a nearly twofold increase in the rate of viral clearance over time (aHR≈2.0), randomized evidence remains limited and less consistent.

Recent evidence syntheses have emphasized this uncertainty. A 2025 Cochrane review concluded that HPV vaccination administered around conisation may reduce CIN2+ risk, but rated much of the evidence as low to very low certainty and noted that randomized evidence was limited to only two trials[23]. A subsequent 2026 systematic review and meta-analysis including 17 studies, four of which were randomized controlled trials, reported an overall reduction in CIN2+ recurrence with adjuvant vaccination, while also underlining between-study heterogeneity and the need for stronger randomized data[24].

Results from randomized or trial-derived data have not been uniformly supportive. In pooled analyses of clinical trials, prior HPV vaccination was associated with a marked reduction in subsequent HPV-related lesions, with decreases exceeding 85-95% for vaccine-type disease endpoints[19]. Likewise, post-hoc analyses of randomized controlled trials demonstrated substantial efficacy in preventing recurrent CIN2+ after surgical treatment[20]. Conversely, a post-hoc analysis of a randomized controlled trial of the HPV16/18 AS04-adjuvanted vaccine did not show a clear effect on viral persistence or lesion recurrence despite modest reductions in new HPV infections[10]. The VIVA randomized placebo-controlled trial in previously treated anal or vulvar high-grade squamous intraepithelial lesion (HSIL) also reported no significant reduction in HSIL recurrence or HPV persistence after nonavalent vaccination[25]. In a related population-based analysis of women with CIN2 managed by active surveillance, vaccination after diagnosis did not reduce progression to CIN3+[26].

In contrast, observational and real-world studies have reported more favorable outcomes, including reductions in recurrence rates approaching 50-60% in pooled analyses[27]. These discrepancies likely reflect differences in baseline risk, margin status, timing of vaccination, HPV genotype distribution, outcome definitions, and residual confounding inherent to non-randomized designs.

Importantly, HPV vaccines are prophylactic rather than therapeutic. Their mechanism is based on the induction of neutralizing antibodies that prevent viral entry[28]. Therefore,

the observed benefits are unlikely to reflect the direct clearance of established infection. Instead, vaccination may reduce reinfection risk[10,29], enhance immune-mediated viral control following excision[30], and provide cross-protection against related HPV genotypes[31].

Clinical Implications

In Türkiye, where HPV vaccination is not included in the national immunization program, the observed reductions in persistence and recurrence support a pragmatic strategy of offering vaccination following excisional treatment. This approach is consistent with European Society of Gynecological Oncology recommendations advocating individualized counseling for HPV vaccination in patients with HPV-related disease[32].

The strengths of this study include a relatively large sample size, a real-world clinical setting, and a standardized follow-up protocol with serial HPV testing at predefined intervals. Importantly, this study offers context-specific evidence from a healthcare setting where HPV vaccination is not part of the national immunization program. In such settings, our findings have direct clinical relevance and support the implementation of opportunistic vaccination strategies following treatment.

Study Limitations

This study has several limitations. Its retrospective design may have introduced selection bias and residual confounding. In addition, vaccination was not randomly assigned, and unmeasured post-LEEP behavioral factors, including smoking status, acquisition of new sexual partners, condom use, and partner HPV status, may have influenced HPV clearance and recurrence. Because these variables were not systematically available in the medical records, their potential effect could not be adjusted for in the multivariable models. The higher proportion of HPV16 infection in the unvaccinated group may also have contributed to the observed between-group differences, given the known association between HPV16 persistence and recurrence risk. Furthermore, baseline differences in HPV genotype distribution may have affected virological outcomes. Accordingly, residual confounding cannot be fully excluded despite multivariable adjustment.

Conclusion

Adjuvant 9-valent HPV vaccination following LEEP was associated with higher HPV clearance rates, reduced persistence of infection, and a significantly lower incidence of CIN2+ recurrence. These findings suggest that vaccination may enhance post-treatment viral control and contribute to a clinically meaningful reduction in recurrence risk. However, given the heterogeneity of existing evidence and the absence of a direct therapeutic effect, these results should be interpreted with caution. In settings where HPV vaccination is not routinely implemented, such as Türkiye, offering vaccination after excisional treatment may represent a pragmatic strategy to improve outcomes. Further prospective, randomized studies are needed to confirm these findings and define optimal patient selection.

Ethics

Ethics Committee Approval: The study protocol was approved by the University of Health Sciences Türkiye, İzmir City Hospital Non-Interventional Clinical Research Ethics Committee (approval number: 2025/235, date: 21.05.2025).
Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.Ö., G.Ö.Ş., İ.B.İ., M.S., Concept: S.Ö., Design: S.Ö., Data Collection or Processing: S.Ö., E.G.Ö., G.Ö.Ş., İ.B.İ., Analysis or Interpretation: S.Ö., E.G.Ö., M.S., Literature Search: S.Ö., E.G.Ö., G.Ö.Ş., İ.B.İ., Writing: S.Ö., E.G.Ö., M.S.
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