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Ovarian preservation and transposition in cervical cancer: A Retrospective Cohort Study with Long-term Oncological Follow-up

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Abstract

Background: Ovarian transposition preserves endocrine function in premenopausal women with cervical cancer undergoing pelvic radiotherapy, but its effect on long-term oncological outcomes compared with salpingo-oophorectomy remains uncertain.

Methods: We performed a retrospective cohort study of patients with histologically confirmed cervical adenocarcinoma or squamous cell carcinoma who underwent ovarian transposition (OT, n = 44) or salpingo-oophorectomy (SO, n = 52) during radical surgery, with follow-up extending to approximately 10 years. Recurrence-free survival (RFS) and overall survival (OS) were compared by Kaplan-Meier analysis with log-rank, Breslow, and Tarone-Ware tests. Cox regression assessed the association between surgical approach and recurrence, adjusted for clinicopathological covariates.

Results: The final cohort comprised 96 patients. Patients undergoing SO had significantly longer RFS than those undergoing OT (log-rank P = 0.046; Breslow P = 0.003; Tarone-Ware P = 0.009). On multivariable Cox regression, SO remained independently associated with a 59% lower hazard of recurrence than OT (adjusted HR, 0.414; 95% CI, 0.197–0.872; P = 0.020). Among 39 patients with recurrence (22 OT, 17 SO), non-pelvic recurrence was more frequent after OT (81.8% vs. 52.9%), though not statistically significant (P = 0.053). In the FIGO stage III subgroup, median RFS was 35 months after OT versus 120 months after SO (P = 0.059).

Conclusions: Ovarian transposition was associated with shorter recurrence-free survival than salpingo-oophorectomy, independent of measured clinicopathological factors. Given the retrospective, single-center design, these findings require confirmation in larger prospective studies before informing counseling on fertility- and endocrine-preserving surgery.

Keywords: Cervical cancer; Ovarian transposition; Salpingo-oophorectomy; Recurrence-free survival; Fertility preservation

1. Introduction

Cervical cancer is one of the major causes of cancer-related morbidity and mortality among women worldwide. Improvements in screening, diagnostic imaging, surgical treatment, radiotherapy, and systemic therapy have significantly improved outcomes; however, treatment-related morbidity are still a significant concern, particularly among younger women [1]. Almost 50% of cervical cancers are diagnosed in women younger than 45 years [2]. In premenopausal patients, loss of ovarian function following pelvic radiotherapy or surgical removal of the ovaries may result in premature menopause, with subsequent consequences for quality of life, sexual health, bone health, cardiovascular health, and long-term endocrine well-being. Therefore, preservation of ovarian function has become a key component of survivorship care in selected young patients with cervical cancer [3,4]. Consequently, in young patients diagnosed with cervical cancer, the eligibility for and implications of ovarian preservation should be discussed, balancing oncological safety against long-term reproductive and endocrine outcomes. Moreover, considering radiotherapy, it is well established that half of the total number of ovarian follicles are lost at doses of 2Gy (lethal dose 50%), a dose much lower than that delivered in a curative setting [5]. In this context, Ovarian transposition (OT), also known as oophoropexy, emerged. It is a surgical technique in which the ovaries are mobilized and positioned outside the anticipated pelvic radiation field with the aim of reducing radiation-induced ovarian damage. Current international cervical cancer guidelines recognize ovarian transposition as one of the options for ovarian preservation[6]. However, ovarian preservation strategies must not compromise oncological safety. The effectiveness of ovarian transposition in preserving ovarian endocrine function has been demonstrated in several studies. An updated meta-analysis reported ovarian function preservation in approximately 91–93% of women in surgical cohorts, although substantial heterogeneity existed between studies [3]. Moreover, authors stated that the efficacy of ovarian transposition may be influenced by the type and extent of subsequent radiotherapy. Another systematic review similarly concluded: ovarian transposition can reduce ovarian exposure to pelvic irradiation, but ovarian function is not guaranteed; additionally, ovarian cyst formation, remigration, and radiation scatter remain relevant limitations [4]. Although preservation of ovarian function is the principal objective of ovarian

transposition, its oncological safety remains an important consideration. Available retrospective studies have generally not demonstrated a clear negative effect of ovarian transposition on oncological outcomes. Moreover, the available evidence is still limited and is characterized by relatively small cohorts, heterogeneous treatment strategies, and potential selection bias. For example, a previous retrospective study of women with stage IB squamous cell cervical cancer found no significant difference in recurrence or survival between patients undergoing ovarian transposition and those undergoing oophorectomy [7]; although differences were observed in selected treatment subgroups. Most previous studies and meta-analyses have reported a insignificant risk of metastasis to the transposed ovaries, despite a relatively common incidence of ovarian cyst formation [8]. An additional systematic review and meta-analysis studied patients with rectal cancer, Ewing sarcoma, Hodgkin and non-Hodgkin lymphoma, cervical cancer, vaginal cancer, and pelvic soft-tissue sarcoma: the review reported an overall low rate of ovarian metastasis [9]. Nowadays, there is an increasing emphasis on survivorship and preservation of ovarian endocrine function. Nevertheless, long-term comparative data evaluating recurrence-free and overall survival after ovarian transposition versus salpingo-oophorectomy in cervical cancer remain limited. In particular, data with extended follow-up and adjustment for relevant clinicopathological factors are scarce. Therefore, the aim of the present retrospective cohort study was to evaluate the long-term oncological outcomes of ovarian transposition compared with salpingo-oophorectomy in patients with cervical cancer, with particular emphasis on recurrence-free survival (RFS) and overall survival (OS).

2. Materials and Methods

2.1 Study Design and Population

This retrospective cohort study was conducted at a university gynecologic oncology center in Germany, with a follow-up period extending to 10 years. A total of 243 patients discussed at the Multidisciplinary Gynecologic Tumor Board for cervical cancer between January 2016 and December 2023 were screened for eligibility. Of these, 28 patients were excluded because of metastasis from another primary tumor, histopathological subtypes other than adenocarcinoma and/or squamous cell carcinoma, or cancer of unknown primary (CUP) syndrome, leaving 215 patients with histologically confirmed adenocarcinoma and/or squamous cell carcinoma. A further 46 patients were excluded because of loss to follow-up, leaving 169 patients with adequate follow-up data. Among these, 20 patients who had disease progression or were not disease-free at the first radiologic assessment after completion of primary therapy were excluded, and an additional 53 patients were excluded because of FIGO stage IV disease or salpingectomy alone. The final analytic cohort comprised 96 patients; the entire cohort, including patients who subsequently developed recurrent disease, was followed until December 2025 (Figure 1). FIGO staging was performed according to the 2023 FIGO classification for all patients.

2.2 Treatment Strategy

All patients were discussed at a multidisciplinary gynecologic oncology tumor board, and treatment was planned according to the applicable German guidelines for the management of cervical cancer during the study period (2016–2023). Initial staging included computed tomography (CT) of the thorax and abdomen and magnetic resonance imaging (MRI) of the pelvis in all patients. Patients without evidence of distant metastases underwent surgical staging with pelvic lymph-node assessment, predominantly by laparoscopic pelvic lymphadenectomy. Sentinel lymph-node biopsy was performed in selected patients with early-stage, low-risk disease. In patients with histologically confirmed pelvic lymph-node metastases, para-aortic lymph-node assessment/lymphadenectomy was performed when clinically indicated. Definitive treatment was determined according to tumor stage and pathological findings. Patients with tumors >4 cm, parametrial involvement, or lymph-node

metastases were generally treated with definitive concurrent chemoradiotherapy. In patients with negative pelvic lymph nodes on intraoperative frozen-section examination, radical hysterectomy was performed either laparoscopically or via laparotomy, according to tumor characteristics and surgical considerations. In patients with microscopically positive surgical margins (R1), postoperative adjuvant brachytherapy was administered when indicated. In premenopausal patients with squamous cell carcinoma who wished to preserve ovarian endocrine function, ovarian preservation with ovarian transposition (oophoropexy) was considered and performed when oncologically appropriate. The decision to preserve the ovaries was individualized according to patient preference, age, menopausal status, tumor characteristics, and the anticipated need for adjuvant radiotherapy. Ovarian transposition was performed with the aim of minimizing radiation exposure to the ovaries and preserving ovarian function. Patients with recurrent disease were managed according to the site and extent of recurrence, previous treatment, and individual clinical circumstances. Pelvic recurrences were treated with concurrent chemoradiotherapy when appropriate. For isolated or resectable distant metastases, surgical resection was considered. Systemic treatment included platinum-based chemotherapy (carboplatin or cisplatin combined with paclitaxel), with the addition of bevacizumab when clinically appropriate and in the absence of contraindications. Pembrolizumab was added in selected patients according to the clinical indication and treatment availability during the study period. Depending on the location, extent, and progression of recurrent disease, additional local treatment modalities, including surgery, stereotactic body radiotherapy (SBRT), thermal ablation, or pelvic exenteration, were considered. Immunotherapy with pembrolizumab or cemiplimab was also used in selected patients according to clinical circumstances and treatment eligibility.

2.3 Statistical Approach

Statistical analysis was performed using IBM SPSS Statistics version 28.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Shapiro–Wilk test, together with evaluation of skewness and kurtosis. Normally distributed continuous variables were compared using the independent-samples Student's t-test and are presented as mean ± standard deviation (SD). Non-normally distributed continuous variables were compared using the Mann–Whitney U test and are

presented as median and interquartile range (IQR). Categorical variables were compared using the Pearson chi-square test or Fisher's exact test, as appropriate. The primary oncological endpoint was recurrence-free survival (RFS), defined as the time from initial diagnosis to the first documented disease recurrence. Recurrence was identified radiologically by computed tomography of the thorax and abdomen and magnetic resonance imaging of the pelvis, consistent with the imaging protocol used for initial staging and post-treatment assessment, with histological or cytological confirmation obtained when clinically feasible. Patients without recurrence were censored at the date of their last available follow-up. Overall survival (OS) was defined as the time from initial diagnosis to death from any cause, with patients alive at the last follow-up censored at that date. Kaplan–Meier methods were used to estimate RFS and OS distributions. Survival curves were compared between patients undergoing ovarian transposition and those undergoing salpingo-oophorectomy using the log-rank (Mantel–Cox) test. Breslow (generalized Wilcoxon) and Tarone–Ware tests were additionally used as sensitivity analyses, particularly to assess differences occurring earlier during follow-up. RFS was also analyzed separately according to FIGO stage (FIGO I, II, and III), with survival distributions compared between the ovarian management groups within each FIGO stage. Univariable Cox proportional hazards regression analyses were performed to evaluate the association between individual clinicopathological factors and RFS. Variables considered included ovarian management strategy, FIGO stage, tumor grade, lymphatic invasion, vascular invasion, perineural invasion, nodal status, tumor-related TNM characteristics, postoperative radiochemotherapy, and other clinically relevant pathological or treatment characteristics. Variables associated with RFS in univariable analysis at $P < 0.10$, together with variables considered clinically relevant a priori regardless of univariable significance, were subsequently evaluated in multivariable Cox proportional hazards regression models. Hazard ratios (HRs) with corresponding 95% confidence intervals (CIs) were reported. An HR <1 indicated a lower hazard of recurrence, whereas an HR >1 indicated a higher hazard of recurrence. All statistical tests were two-sided, and a P value <0.05 was considered statistically significant.

2.4 Ethical Approval

The study was approved by the Ethics Committee of Frankfurt am Main University Hospital (approval no. 2023-1151). The study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all patients prior to inclusion in the study.

3. Results

3.1. Cohort Characteristics

A total of 96 patients with cervical cancer were included in the analysis, comprising 44 patients who underwent ovarian transposition and 52 patients who underwent salpingo-oophorectomy. Patients either received treatment at the University Hospital Frankfurt or were referred from other centers between January 2016 and December 2023. This cohort was followed until December 2025. All patients were free of disease at the first radiologic assessment (CT of the thorax and abdomen and MRI of the pelvis) performed 3 months after completion of primary therapy. As expected, patients undergoing ovarian transposition were significantly younger than those undergoing salpingo-oophorectomy (37.7 ± 6.4 vs. 54.6 ± 12.2 years, respectively; $P < 0.001$), reflecting the clinical selection of younger, premenopausal patients for ovarian preservation. BMI was comparable between the groups (24.5 ± 6.1 vs. 26.1 ± 5.3 kg/m², respectively; $P = 0.405$). There were no statistically significant differences between the groups with regard to FIGO stage ($P = 0.605$) or tumor grade ($P = 0.486$). Similarly, the distribution of lymph-node status did not differ significantly between the ovarian-management groups ($P = 0.961$). The surgical approach also showed no significant difference between groups ($P = 0.353$). Pathological variables (resection status, lymphatic, vascular, and perineural invasion) and surgical technique were assessable only in patients who underwent primary surgical treatment, accounting for the denominators smaller than the overall group size in Table 1. Among these patients, no significant differences were observed in resection status (R0/R1; $P = 0.490$), postoperative radiochemotherapy ($P = 0.395$), lymphatic invasion ($P = 0.633$), vascular invasion ($P = 0.282$), or perineural invasion ($P = 0.560$). At the end of follow-up, 25 patients (56.8%) in the ovarian-transposition group and 38 patients (73.1%) in the salpingo-oophorectomy group were alive, although this difference did not reach statistical

significance (P = 0.095). Overall, the two groups were broadly comparable with respect to tumor-related and treatment-related characteristics, with age being the major baseline difference between the groups.

3.2. Outcome

During follow-up, recurrence occurred in 22 of 44 patients (50.0%) in the ovarian transposition group and in 17 of 52 patients (32.7%) in the salpingo-oophorectomy group. Accordingly, 22 patients (50.0%) in the ovarian transposition group and 35 patients (67.3%) in the salpingo-oophorectomy group were censored. Kaplan–Meier analysis demonstrated longer recurrence-free survival (RFS) among patients who underwent salpingo-oophorectomy. The estimated mean RFS was 69.4 ± 7.7 months (95% CI, 54.4–84.4) in the ovarian transposition group and 88.4 ± 6.0 months (95% CI, 76.6–100.2) in the salpingo-oophorectomy group. The median RFS was 69 months (95% CI, 53.9–84.1) in the ovarian transposition group, whereas the median RFS in the salpingo-oophorectomy group was 113 months (95% CI, 81.2–144.8). The difference between the RFS distributions was statistically significant according to the log-rank test ($\chi^2 = 3.998$, P = 0.046). The Breslow test ($\chi^2 = 8.991$, P = 0.003) and Tarone–Ware test ($\chi^2 = 6.921$, P = 0.009) also demonstrated significant differences, consistent with a more pronounced separation of the survival curves during the earlier follow-up period. The OS curves showed a numerical separation between patients who underwent ovarian transposition and those who underwent salpingo-oophorectomy, with a trend toward lower estimated OS in the ovarian transposition group during much of the follow-up period. However, the difference in OS between the two groups did not reach statistical significance according to the log-rank test (P = 0.185) (Figure 2). To explore whether the association between ovarian management and RFS differed according to disease stage, Kaplan–Meier analyses were additionally stratified by FIGO stage (I–III). Among patients with FIGO stage I disease, no significant difference in RFS was observed between the ovarian transposition and salpingo-oophorectomy groups (log-rank $\chi^2 = 0.882$, P = 0.348). Similarly, no significant difference was observed among patients with FIGO stage II disease ($\chi^2 = 0.593$, P = 0.441), with median RFS of 65 months and 54 months in the ovarian transposition and salpingo-oophorectomy groups, respectively. In FIGO stage III disease, the Kaplan–Meier curves demonstrated greater separation, with median RFS of 35 months in the ovarian transposition group compared with 120 months in the salpingo-

oophorectomy group; however, the difference did not reach conventional statistical significance (log-rank $\chi^2 = 3.556$, P = 0.059) (Figure 3). The association between ovarian transposition and salpingo-oophorectomy was further supported by Cox proportional hazards analysis. In univariable Cox regression analysis, ovarian management was associated with RFS: patients undergoing salpingo-oophorectomy showed a lower hazard of recurrence compared with those undergoing ovarian transposition (HR, 0.530; 95% CI, 0.281–1.000; P = 0.050), an association that became stronger after multivariable adjustment, with salpingo-oophorectomy associated with a 59% lower hazard of recurrence (adjusted HR, 0.414; 95% CI, 0.197–0.872; P = 0.020). The other evaluated clinicopathological and treatment-related variables did not demonstrate statistically significant associations with RFS. The multivariable Cox model was statistically significant (likelihood-ratio $\chi^2 = 16.604$, df = 6, P = 0.011). Among the 39 patients with recurrence and documented recurrence site, pelvic recurrence occurred in 4 of 22 patients (18.2%) in the ovarian transposition group and 8 of 17 patients (47.1%) in the salpingo-oophorectomy group. In contrast, non-pelvic recurrence was observed in 18 patients (81.8%) following ovarian transposition compared with 9 patients (52.9%) following salpingo-oophorectomy. The difference in recurrence pattern showed a trend toward a higher proportion of non-pelvic recurrence among patients undergoing ovarian transposition, although this did not reach statistical significance (Pearson $\chi^2 = 3.754$, P = 0.053; Fisher's exact test, P = 0.082).

4. Discussion

Ovarian transposition is primarily performed to preserve ovarian endocrine function in young, premenopausal women who are expected to receive pelvic radiotherapy. Its rationale is to move the ovaries outside the anticipated radiation field and thereby reduce radiation-induced ovarian failure. The 2023 ESGO/ESTRO/ESP guidelines recognize ovarian transposition as an option for selected premenopausal patients [6]. The present retrospective cohort study evaluated the long-term oncological outcomes of ovarian transposition compared with salpingo-oophorectomy in patients with cervical cancer, with a follow-up period extending to approximately 10 years. The principal finding was that patients who underwent salpingo-oophorectomy demonstrated longer RFS than those who underwent ovarian transposition. The log-rank test showed a significant difference in the overall survival

distributions (P = 0.046), while the stronger significance observed with the Breslow (P = 0.003) and Tarone–Ware (P = 0.009) tests suggests that the difference between the groups was more pronounced during the earlier period of follow-up. The curves showed a more pronounced separation during earlier and intermediate follow-up, whereas they gradually converged at approximately 90–100 months and crossed toward the end of the observation period. This pattern suggests that the difference between the groups was not constant over time. The apparent late convergence or crossing should be interpreted cautiously because relatively few patients are likely to remain at risk at these later time points, making the estimates less precise. The association was further supported by Cox proportional hazards analysis. Although the univariable analysis showed a borderline association (HR, 0.53; P = 0.050), the association became stronger after multivariable adjustment, with salpingo-oophorectomy associated with a 59% lower hazard of recurrence compared with ovarian transposition (adjusted HR, 0.414; 95% CI, 0.197–0.872; P = 0.020). The consistency between the Kaplan–Meier analysis and the adjusted Cox model suggests that the observed difference in RFS was not fully explained by the clinicopathological variables included in the multivariable model. An exploratory analysis of recurrence patterns revealed a higher proportion of non-pelvic recurrence among patients undergoing ovarian transposition compared with those undergoing salpingo-oophorectomy (81.8% vs. 52.9% among patients with available recurrence-site data). Conversely, pelvic recurrence was more frequent in the salpingo-oophorectomy group. Although this difference did not reach statistical significance, the finding may warrant further investigation. The FIGO-stratified analysis provides additional context. No statistically significant difference in RFS was identified between ovarian transposition and salpingo-oophorectomy among patients with FIGO stage I or II disease. In FIGO stage III disease, however, a more pronounced separation of the curves was observed, with a median RFS of 35 months in the ovarian-transposition group compared with 120 months in the salpingo-oophorectomy group, although the difference did not reach conventional statistical significance (P = 0.059). This finding should be interpreted cautiously because of the relatively small number of patients in each subgroup. Nevertheless, it suggests that the observed overall association may be influenced by disease stage and deserves evaluation in larger cohorts. Systematic reviews and meta-analyses have demonstrated that ovarian transposition can preserve ovarian function in a substantial proportion of patients, although the reported efficacy varies

considerably according to radiation exposure, technique, age, and other treatment-related factors. Thus, the primary objective of ovarian transposition is preservation of ovarian function and prevention of premature menopause rather than improvement of oncological outcomes [10-21]. In most of these studies, a short term follow-up and the investigating the hormonal situation after ovarian transposition were the goal of study. The finding of longer RFS in the salpingo-oophorectomy group in the present study differs from several previous reports that have generally suggested that ovarian preservation does not adversely affect oncological outcomes. In a retrospective study of 92 women with stage IB squamous cell cervical cancer [8], ovarian transposition was not associated with a significant increase in recurrence compared with oophorectomy; recurrence rates were 31.6% and 26.4%, respectively, and no significant differences in 5-year disease-free or overall survival were observed. In this study, only FIGO stage IB was evaluated. A systematic review from Touhami et al. showed ovarian metastasis in 2% of women with cervical adenocarcinoma [24]. In different systematic reviews, the risk of ovarian metastasis after transposition has been discussed [3,4,23]. A potential biological explanation for the observed association between ovarian transposition and recurrence-free survival may relate to the exposure of the transposed ovaries to HPV DNA or the peritoneal environment. The PIONEER study by Bizzarri et al[22] demonstrated that human papillomavirus (HPV) DNA can be detected in the peritoneal cavity of patients with cervical cancer, with peritoneal HPV positivity observed in 28.7% of patients overall and more frequently in those with advanced, recurrent, or persistent disease. Importantly, peritoneal HPV positivity was associated with larger tumor size, high-risk HPV 16/18 infection, and peritoneal carcinomatosis, suggesting that HPV may be detectable beyond the primary cervical tumor and may reflect a broader pattern of disease dissemination or viral persistence. In the present study, patients undergoing ovarian transposition demonstrated significantly shorter RFS than those undergoing salpingo-oophorectomy, and this association remained significant after adjustment for selected clinicopathological factors (adjusted HR 0.414 for salpingo-oophorectomy, $P = 0.020$). Furthermore, among patients who developed recurrence, non-pelvic recurrence was more frequent in the ovarian-transposition group than in the salpingo-oophorectomy group (81.8% vs. 52.9%), although this difference did not reach statistical significance ($P = 0.053$). A speculative mechanism is that HPV-containing peritoneal material or tumor-associated cells could reach the transposed ovaries, potentially

creating a local environment in which occult tumor cells could implant or persist. Nevertheless, this proposed mechanism remains speculative. The PIONEER study assessed HPV DNA in peritoneal samples and did not demonstrate HPV infection or contamination of transposed ovarian tissue. Similarly, our retrospective study did not include HPV testing of the ovaries, peritoneal fluid, or recurrent lesions. Therefore, our findings cannot establish a causal relationship between ovarian transposition, peritoneal HPV positivity, and subsequent abdominal recurrence. Future prospective studies incorporating HPV genotyping of cervical tumors, peritoneal fluid, transposed ovarian tissue, and recurrent lesions could help determine whether peritoneal / ovarian HPV positivity is associated with extra-pelvic recurrence after ovarian transposition.

A major strength of the present study is the long follow-up period, allowing evaluation of both early and late oncological events. In addition, the study used complementary survival methods, including Kaplan–Meier analysis, log-rank testing, and multivariable Cox regression, and explored outcomes according to FIGO stage. The recurrence pattern analysis provides an additional perspective beyond overall RFS and OS. Several limitations must nevertheless be acknowledged. First, the retrospective single-center design is subject to selection and information bias. Second, the relatively small sample size limits statistical power, particularly for the FIGO-stratified analyses and recurrence-site analysis. Finally, despite multivariable adjustment, residual confounding by unmeasured factors cannot be excluded. These limitations are particularly relevant when interpreting the apparently favorable RFS associated with salpingo-oophorectomy. Future studies should prospectively investigate the potential biological relationship between ovarian transposition, peritoneal HPV persistence, and extra-pelvic recurrence in cervical cancer. In particular, multicenter prospective studies should incorporate standardized HPV genotyping and longitudinal assessment of HPV DNA in the primary cervical tumor, peritoneal fluid, and, where clinically feasible, transposed ovarian tissue. In patients who subsequently develop recurrence, molecular comparison of the primary tumor, transposed ovary, peritoneal samples, and recurrent lesions could determine whether recurrent disease represents direct metastatic dissemination and whether HPV positivity is maintained across these sites. In addition, detailed documentation of the anatomical location of the transposed ovaries, distance from the pelvic

radiation field, radiation dose received by the ovaries, tumor stage, histology, HPV genotype, and adjuvant treatment would allow identification of patients at potentially higher risk of extra-pelvic recurrence. Such studies could clarify whether the observed association between ovarian transposition and shorter RFS reflects treatment-selection bias, differences in tumor biology, radiation-related factors, or a previously unrecognized interaction between peritoneal/ovarian HPV persistence and the altered anatomical position of the transposed ovaries. Ultimately, these data could help refine patient selection for ovarian transposition and establish whether specific oncological or molecular characteristics should be considered before ovarian preservation is offered.

5. Conclusions

In this retrospective cohort study, salpingo-oophorectomy was associated with longer recurrence-free survival compared with ovarian transposition, while no significant difference in overall survival was observed. The higher proportion of non-pelvic recurrences following ovarian transposition raises a hypothesis regarding the potential role of the peritoneal microenvironment and HPV persistence; however, this mechanism remains unproven. Larger prospective studies incorporating HPV and molecular analyses are warranted to clarify the oncological safety of ovarian transposition and optimize patient selection for ovarian preservation.

Author contributions:

Morva Tahmasbi Rad: Supervision; Visualization; Conceptualization; Data Collection; Methodology; Formal analysis; Writing-original draft. **Dario Colacurci:** Investigation; Formal analysis; Writing-original draft. **Pouya Zahedi:** Investigation; Data collection; Formal analysis; **Lisa Wilhelm:** Formal analysis; Writing-original draft; **Giuseppe Bifulco:** Investigation; Data collection; Formal analysis; **Khayal Gasimli:** Investigation; Data collection; Formal analysis. **Thomas Karn:** Investigation; Data collection; Formal analysis. **Sven Becker:** Supervision; Conceptualization; Methodology; Writing-review & editing.

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Ethical Approval: The study was approved by the Ethics Committee of Frankfurt am Main University Hospital (approval no. 2023–1151). The study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all patients prior to inclusion in the study.

Consent to Participate: Informed consent was obtained from all individual participants included in the study.

Data availability statement: The datasets generated and/or analysed during the current study are not publicly available due to privacy and confidentiality restrictions concerning patient-level clinical data but are available from the corresponding author on reasonable request.

List of abbreviations

BMI - Body mass index

CI - Confidence interval

CUP - Cancer of unknown primary

ESGO - European Society of Gynaecological Oncology

ESP - European Society of Pathology

ESTRO - European Society for Radiotherapy and Oncology

FIGO - International Federation of Gynecology and Obstetrics

HPV - Human papillomavirus

HR - Hazard ratio

OS - Overall survival

OT - Ovarian transposition

RFS - Recurrence-free survival

SCC - Squamous cell carcinoma

SO - Salpingo-oophorectomy

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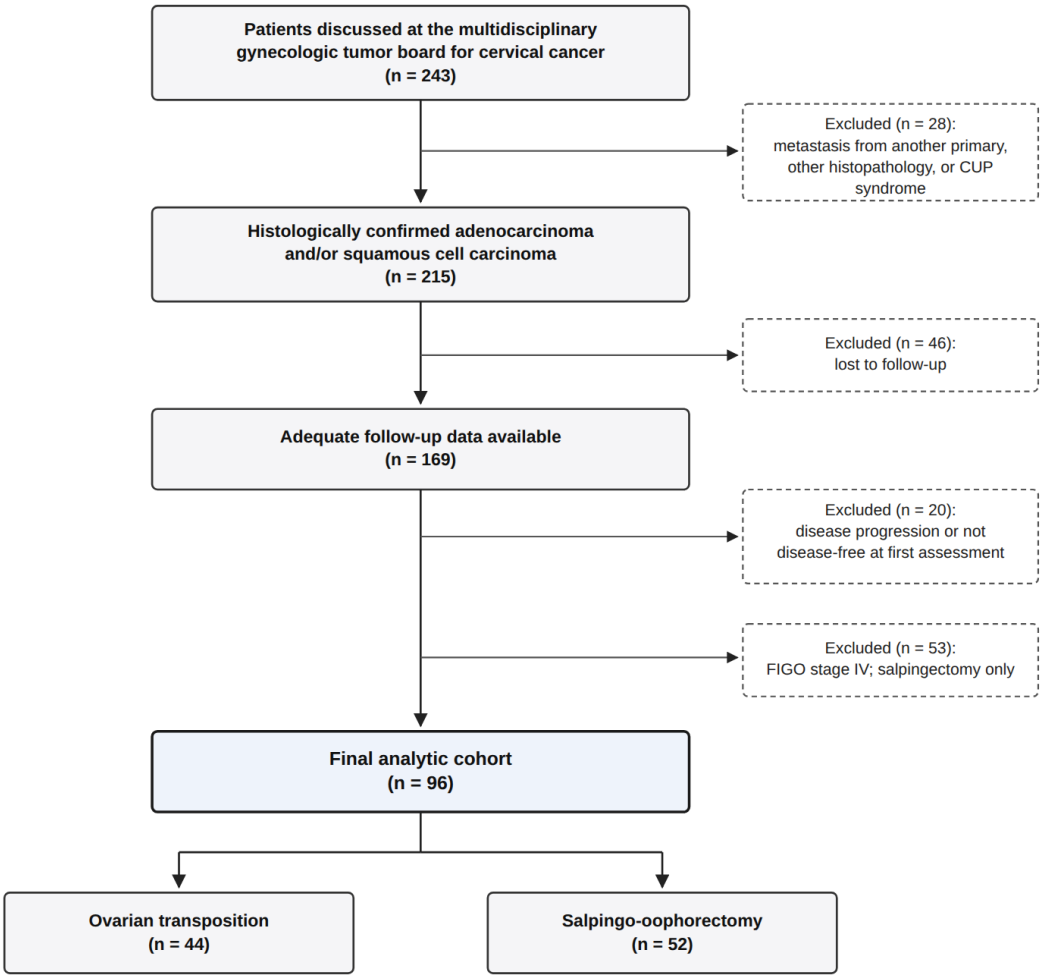
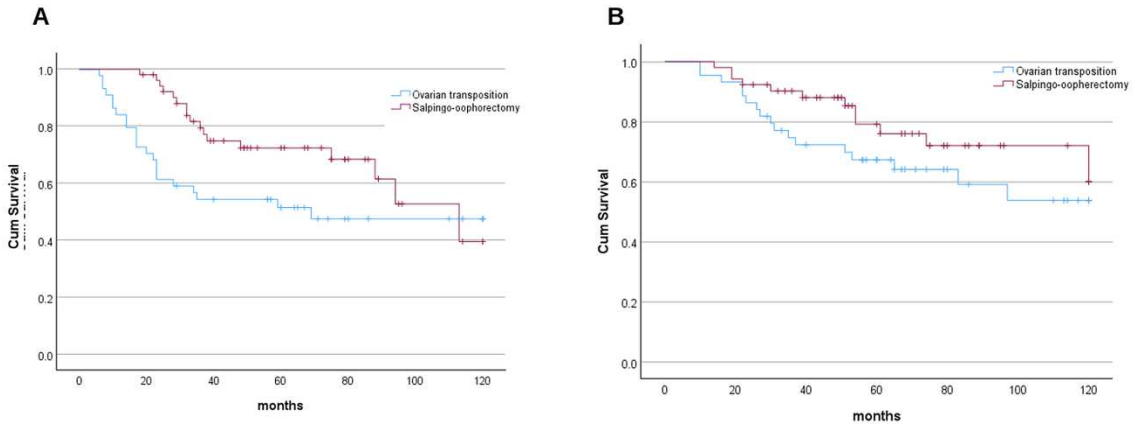


Figure 1. Flowchart of study population.



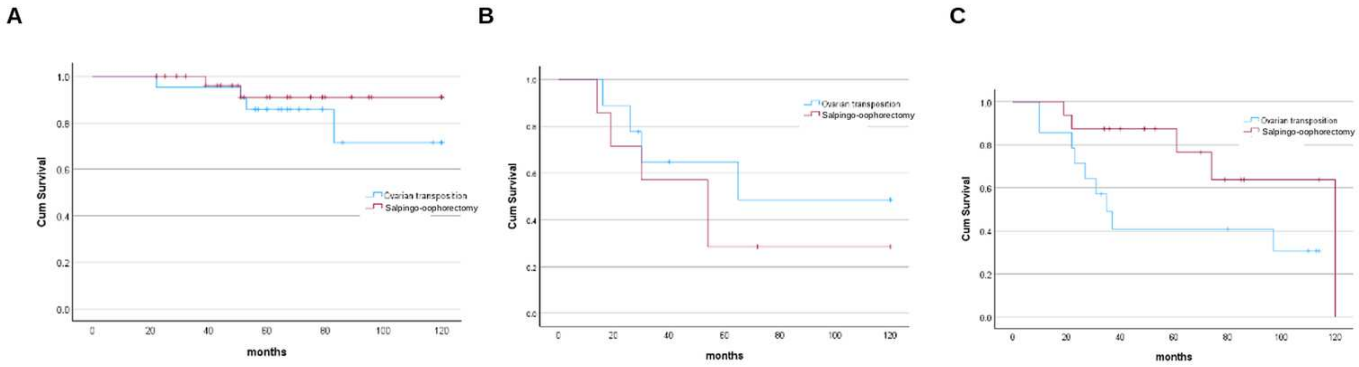
462

463 **Figure 2.** Kaplan–Meier estimates of (A) recurrence-free survival and (B) overall survival according

464 to ovarian management strategy (ovarian transposition, blue; salpingo-oophorectomy, maroon). Tick

465 marks indicate censored observations. Log-rank P = 0.046 for recurrence-free survival; P = 0.185 for

466 overall survival.



467

468 **Figure 3.** Kaplan–Meier estimates of recurrence-free survival according to ovarian management

469 strategy (ovarian transposition vs. salpingo-oophorectomy), stratified by FIGO stage: (A) FIGO I, (B)

470 FIGO II, (C) FIGO III. Tick marks indicate censored observations.

471

Characteristic	Ovarian transposition (n=44)	Salpingo-oophorectomy (n=52)	P-value
Age at first diagnosis, years	37.68 ± 6.39	54.62 ± 12.22	**<0.001**
BMI, kg/m²	24.48 ± 6.10	26.13 ± 5.28	0.405
FIGO stage			0.605
I	21 (47.7%)	29 (55.8%)	
II	9 (20.5%)	7 (13.5%)	
III	14 (31.8%)	16 (30.8%)	
Tumor grade (n=43 vs. n=50)			0.486
G1	3 (7.0%)	1 (2.0%)	
G2	26 (60.5%)	33 (66.0%)	
G3	14 (32.6%)	16 (32.0%)	
Vital status at last follow-up			0.095
Alive	25 (56.8%)	38 (73.1%)	
Deceased	19 (43.2%)	14 (26.9%)	
TNM nodal status			0.961
Nx	1 (2.3%)	2 (3.8%)	
N0	28 (63.6%)	34 (65.4%)	
N1	11 (25.0%)	12 (23.1%)	
N2	4 (9.1%)	4 (7.7%)	
Hysterectomy technique (n=30 vs. n=40)			0.353
Robotic-assisted (DaVinci)	4 (13.3%)	1 (2.5%)	
Laparotomy	15 (50.0%)	22 (55.0%)	
Laparoscopy (LSK)	9 (30.0%)	15 (37.5%)	
Transverse laparotomy	2 (6.7%)	2 (5.0%)	
Resection status (n=14 vs. n=12)			0.490
R0	12 (85.7%)	9 (75.0%)	
R1	2 (14.3%)	3 (25.0%)	

Postoperative radiochemotherapy (n=28 vs. n=39)			0.395
No	22 (78.6%)	27 (69.2%)	
Yes	6 (21.4%)	12 (30.8%)	
Lymphatic invasion (n=44 vs. n=51)			0.633
L0	22 (50.0%)	23 (45.1%)	
L1	22 (50.0%)	28 (54.9%)	
Vascular invasion (n=34 vs. n=43)			0.282
V0	27 (79.4%)	38 (88.4%)	
V1	7 (20.6%)	5 (11.6%)	
Perineural invasion (n=39 vs. n=49)			0.560
Pn0	30 (76.9%)	35 (71.4%)	
Pn1	9 (23.1%)	14 (28.6%)	

Table 1. Baseline and clinicopathological characteristics of different groups.

Notes: Bold values indicate statistically significant differences (P < 0.05).

Variable	Adjusted HR	95% CI	P-value
Salpingo-oophorectomy vs. ovarian transposition	0.414	0.197–0.872	**0.020**
Tumor grade	0.904	0.593–1.379	0.639
Lymphatic invasion	1.710	0.710–4.119	0.232
Vascular invasion	1.655	0.697–3.927	0.253
Perineural invasion	1.627	0.677–3.909	0.277
FIGO III vs. I–II	1.465	0.981–2.186	0.062

Table 2. Multivariable Cox regression analysis of recurrence free survival.

Notes: Bold values indicate statistically significant differences (P < 0.05).