Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

What Happens After Cervical Cancer Recurrence? Clinical Outcomes and Prognostic Factors in a 10-Year Retrospective Cohort Study

Morva Tahmasbi Rad

morva.t.rad@gmail.com

Johann Wolfgang Goethe University

Dario Colacurci

Johann Wolfgang Goethe University

Pouya Zahedi

Johann Wolfgang Goethe University

Giuseppe Bifulco

University Federico II

Lisa Wilhelm

Johann Wolfgang Goethe University

Ina Shehaj

Johann Wolfgang Goethe University

Khayal Gasimli

Johann Wolfgang Goethe University

Thomas Karn

Johann Wolfgang Goethe University

Sven Becker

Johann Wolfgang Goethe University

Research Article

Keywords: Cervical cancer, Recurrence, Recurrence-free survival, Post-recurrence survival, FIGO stage, Recurrence pattern

Posted Date: October 4th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10932202/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Cervical cancer remains a major global health burden despite high cure rates in early-stage disease. A substantial proportion of patients still develop recurrence within the first years after primary treatment. Recurrence patterns and their impact on survival remain incompletely characterized across FIGO stages.

Objective

To characterize recurrence patterns and treatment strategies in patients with recurrent cervical cancer, and to evaluate their impact on recurrence-free survival and overall survival after recurrence across FIGO stages.

Methods

This retrospective cohort study was conducted at a multidisciplinary gynecologic tumor center in Frankfurt, Germany. Patients discussed at the tumor board between January 2016 and December 2023 were screened, and patients with recurrent cervical cancer were followed through December 2025. Time from primary treatment to recurrence and post-recurrence overall survival were analyzed using Kaplan–Meier methods and log-rank tests. Univariable and multivariable Cox proportional hazards regression analyses were performed to identify factors associated with post-recurrence survival.

Results

Fifty-nine patients with recurrent cervical cancer were included. The median time to recurrence was 23 months (IQR, 12.5–45). Post-recurrence survival differed significantly by FIGO stage (log-rank p = 0.02), with 2-year survival of 57.4% in stage I and 0% in stage IV disease. In univariable Cox regression, higher FIGO stage was associated with increased mortality after recurrence (HR 1.373, 95% CI 1.022–1.844; p = 0.035), remaining significant after adjustment for tumor grade (HR 1.414, 95% CI 1.065–1.877; p = 0.016). Tumor grade was not independently associated with survival. Recurrence site showed a trend toward association with FIGO stage (p = 0.07), with more extrapelvic recurrences in advanced-stage disease. Adnexal management was associated with recurrence site (p = 0.03); extrapelvic recurrence occurred in 76.5% of patients undergoing ovariopexy. Neither ovariopexy nor salpingo-oophorectomy was associated with post-recurrence survival

Conclusions

Initial FIGO stage was independently associated with survival after cervical cancer recurrence, with advanced-stage disease associated with poorer post-recurrence outcomes. Adnexal management was associated with recurrence pattern but not with survival after recurrence. These findings highlight the prognostic importance of initial disease extent and support individualized surveillance and counseling in patients at risk of recurrence. Larger multicenter studies are warranted to clarify the prognostic role of recurrence timing, recurrence site, and adnexal management.

1. Introduction

Cervical cancer (CC) is one of the most common causes of cancer-related death among women worldwide [1,2]. Nevertheless, despite advances in screening, detection, and treatment of cervical lesions, CC is still a growing global burden and a major public health problem [3–5]. Indeed, primary treatment achieves high cure rates in early-stage disease [6,7]. Specifically, cure rates reach approximately 95% in early-stage CC and 40–60% in locally advanced disease [8]. However, despite these results, patients remain at high risk of pelvic recurrence or distant metastasis within the first few years after primary treatment [9]. Recurrent CC is defined as local tumor regrowth or, alternatively, as the development of nodal or distant metastases. In particular, recurrence must occur at least six months after complete regression of the primary lesion [9–12]. In this context, treatment decisions should always be discussed within a multidisciplinary team. Recurrence rates, indeed, could vary depending on primary treatment modality. After primary surgery, recurrence occurs in less than 30% of cases [13]. Conversely, fertility-sparing radical trachelectomy is associated with a considerably lower rate, of only 4% [13]. Similarly, patients previously treated with concomitant chemoradiotherapy show a recurrence rate of 32% [14,15]. Moreover, adjuvant therapy after radical hysterectomy also shapes recurrence patterns. Accordingly, a recent meta-analysis compared adjuvant chemotherapy with adjuvant radiotherapy or concurrent chemoradiotherapy, in 5,052 patients treated across 16 studies [16]. Notably, adjuvant chemotherapy was associated with lower distant recurrence and, additionally, with better overall and disease-free survival. Generally, these findings suggest that adjuvant treatment choice may influence both recurrence risk and recurrence pattern. Furthermore, an Italian multicenter retrospective study, of 327 women with recurrent CC, found that the most frequent recurrence sites are local, on the vaginal vault, and regional [17]. Likewise, the most frequent recurrence site after radical surgery was central-pelvic [18]. Indeed, central-pelvic recurrences account for approximately 30–45% of all CC relapses. Given, therefore, the substantial impact of recurrence on prognosis, on treatment-related morbidity, and on long-term quality of life, a thorough understanding of recurrence patterns and risk factors remains essential to guide clinical decision-making. In this context, we conducted a retrospective cohort study, over a 10-year period, at a multidisciplinary gynecologic tumor center in Germany. Specifically, this study aimed to characterize recurrence patterns and post-recurrence outcomes in patients with recurrent cervical cancer and to evaluate factors associated with recurrence-free survival and overall survival after recurrence across FIGO stages.

2. Materials and Methods

2.1. Study Design and Population

This retrospective cohort study was conducted at the Department of Gynecology and Obstetrics of Johann Wolfgang Goethe University of Frankfurt, Germany, with a follow-up period of 10 years. All patients discussed at the multidisciplinary gynecologic tumor board between January 2016 and December 2023 were screened. Patients with a diagnosis of cervical cancer were identified, and their medical records were reviewed. Among these, patients presenting with disease recurrence during the study period were selected and followed up until December 2025. Patients with persistent disease or without a disease-free interval after primary treatment were excluded. Additional exclusion criteria were: age younger than 18 years; loss to follow-up; concurrent malignancy; metastasis to the cervix originating from another primary tumor; cancer of unknown primary (CUP) syndrome; and histology other than adenocarcinoma and/or squamous cell carcinoma (Fig. 1).

2.2. Treatment Protocol

All patients were discussed at the multidisciplinary tumor board, and treatment was administered according to the German guidelines for the management of cervical cancer [19]. Treatment strategies applied between 2016 and 2023 are summarized as follows. All patients underwent radiological staging with computed tomography (CT) of the thorax and abdomen and magnetic resonance imaging (MRI) of the pelvis. Patients without evidence of distant metastasis underwent laparoscopic pelvic lymphadenectomy for surgical staging; in selected low-risk cases, sentinel lymph node biopsy was performed instead. In cases of positive pelvic lymph nodes, para-aortic lymphadenectomy was additionally performed. Patients with tumors larger than 4 cm, parametrial infiltration, or positive lymph nodes received concurrent chemoradiotherapy. When intraoperative frozen-section analysis showed negative pelvic lymph nodes, radical hysterectomy was performed, either laparoscopically or via open laparotomy. Patients with R1 resection received postoperative brachytherapy. In premenopausal patients with squamous cell carcinoma, ovarian preservation was attempted; ovarian transposition (ovariopexy) was performed when adjuvant radiotherapy was anticipated. In cases of pelvic recurrence, concurrent chemoradiotherapy was administered. For extrapelvic recurrence, treatment consisted of surgical resection of oligometastatic disease and/or systemic therapy with carboplatin or cisplatin plus paclitaxel and bevacizumab (in the absence of contraindications); pembrolizumab was added in selected cases. Local radiotherapy was additionally administered when clinically indicated. Further treatment options, selected according to imaging findings, clinical presentation, and disease course, included surgery, stereotactic body radiotherapy (SBRT) or ablative procedures, pelvic exenteration, and immunotherapy with pembrolizumab or cemiplimab.

2.3. Outcome Measures

The primary outcomes were recurrence-free survival and post- recurrence, both assessed according to FIGO stage (version 2018) at diagnosis [20]. Secondary outcomes included the anatomical site of

recurrence (pelvic versus extrapelvic) and its association with survival, and the influence of surgical approach, extent of adnexal surgery and radicality of hysterectomy, on recurrence pattern.

2.4. Statistical Analysis

Statistical analyses were performed using SPSS software (version 28.0; IBM Corp., Armonk, NY, USA). The normality of continuous variables, including age, was assessed using the Shapiro–Wilk test, skewness, and kurtosis. Normally distributed continuous variables were compared using Student's *t*-test and are presented as mean ± standard deviation (SD), whereas non-normally distributed variables were compared using the Mann–Whitney *U* test and are presented as median with interquartile range (IQR). Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate.

Time from primary treatment to recurrence was assessed using Kaplan–Meier methods. Post-recurrence overall survival was calculated from the date of recurrence to death or the last available follow-up and estimated using the Kaplan–Meier method. Survival distributions according to FIGO stage and other relevant clinical characteristics were compared using the log-rank test.

Univariable Cox proportional hazards regression analyses were performed to evaluate the association of clinical, pathological, and treatment-related variables with post-recurrence overall survival. Variables considered included FIGO stage, tumor grade, lymphatic and vascular invasion, lymph-node status, salpingo-oophorectomy, and ovariopexy. Variables with clinical relevance and/or evidence of association in univariable analysis were considered for multivariable Cox regression. The final multivariable model included FIGO stage and tumor grade. Hazard ratios (HRs) with corresponding 95% confidence intervals (CIs) were reported.

Associations between FIGO stage, recurrence site, and adnexal management were assessed using appropriate categorical-data tests. All statistical tests were two-sided, and a p-value < 0.05 was considered statistically significant.

2.5. Ethical Considerations

The study was approved by the Ethics Committee of Frankfurt am Main University Hospital (approval no. 2023 – 1151) and 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. Patient and Tumor Characteristics

Of 243 patients discussed at the multidisciplinary tumor board for cervical cancer, 215 had adenocarcinoma or squamous cell carcinoma and met the histological inclusion criteria; 169 of these had complete long-term follow-up data available. After excluding patients with disease progression without a disease-free interval (n = 20) and patients without recurrence (n = 90), 59 patients with

recurrent cervical cancer were included in the analysis (Fig. 1). The median age at diagnosis was 47 years (mean 48.1 ± 13.5 years, 95% CI 44.6–51.6), and the mean body mass index was 24.7 ± 5.5 kg/m². FIGO stage at diagnosis was distributed as follows: stage I, n = 19 (32.2%); stage II, n = 10 (16.9%); stage III, n = 23 (39.0%); and stage IV, n = 7 (11.9%). Squamous cell carcinoma was the predominant histology (n = 51, 86.4%), followed by adenocarcinoma (n = 5, 8.5%) and adenosquamous carcinoma (n = 3, 5.1%). As first-line treatment, 34 patients (57.6%) underwent radical hysterectomy and 25 patients (42.4%) received primary chemoradiotherapy. The proportion of patients treated with radical hysterectomy decreased with increasing FIGO stage (stage I, 94.7%; stage II, 60.0%; stage III, 43.5%; stage IV, 0%), while primary chemoradiotherapy use increased accordingly (stage I, 5.3%; stage II, 40.0%; stage III, 56.5%; stage IV, 100%). Patients required a mean of 3.8 ± 2.5 tumor board discussions regarding treatment decisions over the course of their disease, with no substantial difference across FIGO stages (stage I, 3.8 ± 2.3; stage II, 4.9 ± 3.5; stage III, 3.7 ± 2.5; stage IV, 3.1 ± 1.7). Patient and tumor characteristics are summarized in Table 1.

Table 1

Baseline Demographic, Histopathologic, and Treatment Characteristics of the Study Population, Stratified by FIGO Stage *Data are presented as n (%) or mean ± standard deviation (95% confidence interval), as appropriate. Percentages in the surgical approach subgroup are calculated relative to the number of patients who underwent radical hysterectomy within each FIGO stage. CI, confidence interval; FIGO, International Federation of Gynecology and Obstetrics; SD, standard deviation.*

Characteristic	FIGO I (n = 19)	FIGO II (n = 10)	FIGO III (n = 23)	FIGO IV (n = 7)	Total (N = 59)
Histopathology, n (%)					
Squamous cell carcinoma	15 (78.9)	10 (100.0)	20 (87.0)	6 (85.7)	51 (86.4)
Adenocarcinoma	3 (15.8)	0 (0.0)	2 (8.7)	0 (0.0)	5 (8.5)
Adenosquamous carcinoma	1 (5.3)	0 (0.0)	1 (4.3)	1 (14.3)	3 (5.1)
First-line treatment, n (%)					
Radical hysterectomy	18 (94.7)	6 (60.0)	10 (43.5)	0 (0.0)	34 (57.6)
Primary chemoradiotherapy	1 (5.3)	4 (40.0)	13 (56.5)	7 (100.0)	25 (42.4)
Surgical approach among patients undergoing radical hysterectomy, n (%)					
Minimally invasive	7 (38.9)	1 (16.7)	1 (10.0)	—	9 (26.5)
Open (laparotomy)	11 (61.1)	5 (83.3)	9 (90.0)	—	25 (73.5)
Patient characteristics, mean ± SD					
Age at diagnosis, years (95% CI)	47.16 ± 16.56 (39.18–55.14)	49.30 ± 8.95 (42.90–55.70)	47.87 ± 14.27 (41.70–54.04)	49.71 ± 8.20 (42.13–57.30)	48.10 ± 13.51 (44.58–51.62)
Body mass index, kg/m²	26.51 ± 5.00	24.27 ± 7.49	23.68 ± 3.94	24.20 ± 7.33	24.71 ± 5.50
Tumor board discussions, n	3.8 ± 2.3	4.9 ± 3.5	3.7 ± 2.5	3.1 ± 1.7	3.8 ± 2.5

3.2. Survival Outcomes After Recurrence

The interval from primary treatment to recurrence ranged from 4 to 458 months, with a median of 23 months (IQR, 12.5–45). Median time to recurrence varied across FIGO stages: 35 months (IQR, 2.5–61.5) for stage I, 16 months (IQR, 12.25–23.75) for stage II, 17 months (IQR, 10.5–28) for stage III, and 36 months (IQR, 17–81) for stage IV (Fig. 2; Table 2).

Table 2

Recurrence-Free Survival and Overall Survival After Recurrence, Stratified by FIGO Stage *Data are presented as median (interquartile range, IQR) [minimum–maximum], % (standard error, SE), or mean ± standard deviation (SD), as appropriate. Range was not reported for the overall cohort. FIGO, International Federation of Gynecology and Obstetrics.*

Characteristic	FIGO I (n = 19)	FIGO II (n = 10)	FIGO III (n = 23)	FIGO IV (n = 7)	Total (N = 59)
Time-to-event outcomes, months, median (IQR) [range]					
Recurrence-free survival	35 (20.50–61.50) [4–157]	16 (12.25–23.75) [8–458]	17 (10.50–28.00) [4–113]	36 (17.00–81.00) [12–300]	23 (12.50–45.00)
Survival after recurrence	28 (12.50–52.50) [1–114]	17.50 (12.25–21.25) [2–42]	14 (5.00–25.00) [1–54]	8 (4.00–19.00) [2–21]	17 (5.50–28.50)
Overall survival rate following recurrence, % (SE)					
2-year	57.4 (11.5)	23.3 (14.3)	30.4 (9.6)	0.0 (—)	35.4 (6.4)
3-year	51.0 (11.8)	11.7 (10.9)	20.3 (8.7)	—	26.7 (6.2)

Post-recurrence survival differed significantly according to FIGO stage (log-rank p = 0.02; Fig. 3). Median survival after recurrence was 28 months (IQR, 12.5–52.5) for stage I, 17.5 months (IQR, 12.25–21.25) for stage II, 14 months (IQR, 5–25) for stage III, and 8 months (IQR, 4–19) for stage IV, with a median of 17 months (IQR, 5.5–28.5) for the overall cohort. The estimated 2-year post-recurrence survival was 57.4% for stage I, while no patient with stage IV disease remained alive at 2 years.

In univariable Cox regression, increasing FIGO stage was associated with a higher hazard of death after recurrence (HR 1.373, 95% CI 1.022–1.844; p = 0.035). This association remained significant after adjustment for tumor grade (HR 1.414, 95% CI 1.065–1.877; p = 0.016), corresponding to an approximately 41% increase in the hazard of death for each one-stage increase in FIGO stage.

3.3 Factors Associated with Post-Recurrence Survival

Cox proportional hazards regression was performed to identify factors associated with overall survival after cervical cancer recurrence. In univariable analyses, FIGO stage was significantly associated with post-recurrence survival. No significant associations with post-recurrence survival were observed for lymph-node status (N(0,1,2): HR 0.804, 95% CI 0.557–1.163; p = 0.247), lymphatic invasion (LVSI: HR

0.632, 95% CI 0.310–1.286; p = 0.205), vascular invasion (HR 0.918, 95% CI 0.406–2.074; p = 0.836), salpingo-oophorectomy (HR 1.094, 95% CI 0.719–1.664; p = 0.674), or ovariopexy (HR 0.777, 95% CI 0.413–1.462; p = 0.435).

Based on the univariable analyses and clinical relevance, FIGO stage and tumor grade were entered into a multivariable Cox regression model. The overall model was statistically significant (likelihood-ratio χ^2 = 7.645, df = 2; p = 0.022). After adjustment for tumor grade, FIGO stage remained significantly associated with post-recurrence survival (HR 1.414, 95% CI 1.065–1.877; p = 0.016).

3.4 Recurrence Site and Associated Outcomes

Survival after recurrence also varied by anatomical site of relapse. Pelvic recurrence was associated with the longest median survival (33.5 months, SE 10.9), whereas simultaneous hepatic and pulmonary metastases were associated with the shortest (15 months, SE 6.3). Median survival for other recurrence sites was as follows: lung, 18 months; thoracic and cervical lymph nodes, 25 months; brain, 28 months; peritoneal carcinomatosis, 28.8 months; and bone, 32 months. When recurrence sites were grouped as pelvic (local/regional) versus extrapelvic (distant), pelvic recurrence was associated with a longer median survival than extrapelvic recurrence; this difference was not statistically significant (log-rank p = 0.7). Pelvic recurrences also tended to occur later than extrapelvic recurrences. The 5-year survival after recurrence was 26.7% (SE 11.4%) for pelvic recurrence versus 17.2% (SE 1.2%) for extrapelvic recurrence, a difference that did not reach statistical significance (p = 0.7). The distribution of recurrence site also varied by FIGO stage. In FIGO stage I, pelvic and extrapelvic recurrences occurred with equal frequency (50% each); the proportion of extrapelvic recurrence was higher in FIGO stage II (62.5%) and FIGO stage III (92.9%), although this trend did not reach statistical significance (p = 0.07). Patients who underwent bilateral salpingo-oophorectomy had a higher rate of pelvic than extrapelvic recurrence (56.3% vs. 43.8%). Among patients who underwent salpingectomy (with or without ovariopexy), extrapelvic recurrence predominated (15% pelvic vs. 85% extrapelvic). Among patients who underwent neither procedure, the distribution was 37.5% pelvic versus 62.5% extrapelvic. This difference between groups was statistically significant (p = 0.03). Among patients who underwent ovariopexy specifically, the rate of extrapelvic recurrence increased further, to 76.5%.

3.4. Surgical Approach and Radicality

Among the 34 patients who underwent radical hysterectomy as primary treatment, a minimally invasive approach was used in 9 patients (26.5%) and open surgery in 25 patients (73.5%) (Table 1). The proportion of minimally invasive surgery decreased with increasing FIGO stage: 38.9% (7/18) in stage I, 16.7% (1/6) in stage II, and 10.0% (1/10) in stage III; no patients with stage IV disease underwent radical hysterectomy.

4. Discussion

This study examined recurrence patterns and survival outcomes in patients with recurrent cervical cancer treated and followed over a ten-year period. In our cohort, patients who developed recurrence

required a median of three tumor board discussions before a change in treatment was made (range, 2–10). This may reflect the relatively limited number of systemic and local treatment options available for recurrent cervical cancer compared with other gynecologic malignancies, such as ovarian cancer, where treatment frequently involves multiple lines and increasingly targeted therapies [21–24].

Most recurrences in our cohort occurred in patients initially diagnosed with FIGO IB1 disease. This finding is clinically relevant in the context of the SHAPE trial [25], which demonstrated that simple hysterectomy can be safely considered in carefully selected patients with low-risk, early-stage cervical cancer. However, the occurrence of recurrence even after radical surgery in early-stage disease emphasizes that the extent of surgical resection alone does not determine recurrence risk. Tumor biology and individual patient characteristics may play an important role in determining recurrence [26–28]. These findings support careful patient selection and individualized treatment rather than relying on FIGO stage alone.

FIGO stage emerged as the most consistent prognostic factor for post-recurrence survival. Increasing FIGO stage was associated with poorer survival in both Kaplan–Meier analysis (log-rank $p = 0.02$) and Cox regression. In the multivariable model, each one-stage increase in FIGO stage was associated with a 41% higher hazard of death after recurrence (HR 1.414, 95% CI 1.065–1.877; $p = 0.016$). These findings suggest that the extent of disease at initial diagnosis may retain prognostic relevance even after recurrence has occurred. This is consistent with a previous study of 151 patients with recurrent cervical cancer, in which FIGO stage was identified as an independent prognostic factor for survival after recurrence [29].

Nevertheless, the prognostic role of initial FIGO stage after recurrence has not been consistently demonstrated. Other large studies have identified recurrence-specific characteristics, particularly disease-free interval, recurrence pattern, and treatment received at recurrence, as important determinants of post-recurrence survival [30,31]. Differences between studies may reflect variations in patient populations, initial treatment, recurrence characteristics, and access to salvage therapy. These findings emphasize that prognosis after recurrence is likely determined by a combination of the initial disease burden and the biological and anatomical characteristics of the recurrent disease.

Tumor grade showed a borderline association with post-recurrence survival in univariable analysis (HR 1.688, 95% CI 0.984–2.893; $p = 0.057$), but this association was not maintained after adjustment for FIGO stage (HR 1.372, 95% CI 0.839–2.243; $p = 0.207$). Lymphatic and vascular invasion, lymph-node status, salpingo-oophorectomy, and ovariopexy were likewise not significantly associated with post-recurrence survival. These negative findings should be interpreted cautiously given the limited sample size and statistical power of the cohort. In particular, the absence of an association with post-recurrence survival does not exclude a potential relationship between adnexal management and the anatomical pattern of recurrence.

In our cohort, adnexal management was significantly associated with recurrence site, with extrapelvic recurrence observed in 76.5% of patients who underwent ovariopexy ($p = 0.03$). However, this finding

should not be interpreted as evidence that ovariopexy causes extrapelvic recurrence. The retrospective design, small subgroup size, and potential confounding by age, FIGO stage, tumor characteristics, and treatment limit causal interpretation. Furthermore, recurrence pattern and survival after recurrence represent distinct clinical outcomes; an association with recurrence location does not necessarily translate into poorer post-recurrence survival.

The main strengths of this study include the relatively long follow-up through December 2025, allowing assessment of mature survival outcomes, and the consistent multidisciplinary tumor board setting. However, several limitations should be acknowledged. The retrospective, single-center design limits generalizability and introduces the possibility of selection and treatment-related biases. The relatively small cohort restricted the power of subgroup and multivariable analyses, particularly for advanced FIGO stages and less frequent adnexal procedures. Treatment after recurrence was heterogeneous and may have influenced both recurrence patterns and subsequent survival. In addition, recurrence-specific factors such as disease-free interval, recurrence site, and treatment response require further investigation in larger cohorts.

Overall, our findings indicate that initial FIGO stage remains an important prognostic factor after cervical cancer recurrence, while adnexal management appears to be more closely related to recurrence pattern than to survival after recurrence. Future multicenter studies should integrate initial tumor characteristics with recurrence-specific and molecular factors to improve individualized risk stratification and guide surveillance and treatment strategies after cervical cancer recurrence.

5. Conclusions

In this cohort of patients with recurrent cervical cancer, initial FIGO stage was significantly associated with post-recurrence survival and remained an independent prognostic factor in multivariable analysis. Adnexal management was associated with recurrence site, with a higher proportion of extrapelvic recurrence observed after ovariopexy; however, neither ovariopexy nor salpingo-oophorectomy was associated with survival after recurrence. These findings highlight the prognostic importance of initial disease extent while emphasizing the potential relevance of recurrence-specific characteristics. Larger multicenter studies incorporating stage, recurrence timing, recurrence site, treatment at recurrence, and molecular or biological markers are needed to improve individualized risk stratification and guide surveillance and treatment strategies after cervical cancer recurrence.

Abbreviations

BMI: Body mass index

CC: Cervical cancer

CI: Confidence interval

CT: Computed tomography

CUP: Cancer of unknown primary

FIGO: International Federation of Gynecology and Obstetrics

HPV: Human papillomavirus

IQR: Interquartile range

MRI: Magnetic resonance imaging

SBRT: Stereotactic body radiotherapy

SD: Standard deviation

SE: Standard error

Declarations

Funding: None.

Conflict of interest: The authors have no conflicts of interest.

Ethical Approval: Ethical approval was granted by the Ethics Committee Goethe University Frankfurt (Reference number approval no. 2023–1151).

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

Data availability statement: In accordance with the journal's guidelines, we will provide our data for the reproducibility of this study if our institution approves the request.

Author contribution: 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; **Giuseppe Bifulco:** Investigation; Data collection; Formal analysis; **Lisa Wilhelm:** Investigation; Data collection; Formal analysis. **Ina Shehaj:** Investigation; Data collection **Khayal Gasimli:** Formal analysis, review & editing, **Thomas Karn** Data analysis and methogology **Sven Becker:** Supervision; Conceptualization; Methodology; Writing—review & editing.

References

1. Mangold BR. Self-Collected Samples in Cervical Cancer Screening: Results of HPV and Pap Self-Collected Samples Compared to Physician-Obtained Specimens. Acta Cytol 2019;63:379–84.

https://doi.org/10.1159/000499373.

2. Miccò M, Lupinelli M, Mangialardi M, Gui B, Manfredi R. Patterns of Recurrent Disease in Cervical Cancer. J Pers Med 2022;12:755. https://doi.org/10.3390/JPM12050755.
3. Mangold BR. Self-Collected Samples in Cervical Cancer Screening: Results of HPV and Pap Self-Collected Samples Compared to Physician-Obtained Specimens. Acta Cytol 2019;63:379–84. https://doi.org/10.1159/000499373.
4. O'Hara CA, Khoo ZKH, Dimech C, Chong NZY, Sim GHZ, Ismail-Pratt I, et al. Screening of human papilloma virus-related anogenital cancers in immunocompromised women: a systematic review of clinical practice guidelines. Int J Gynecol Cancer 2025;35. https://doi.org/10.1016/J.IJGC.2025.102131.
5. Carlea A, Colacurci D, D'Apice G, Mazzarelli LL, Pellicano M, Falco L, et al. Human papillomavirus persistence and clearance in women living with HIV: A five-year retrospective analysis from an Italian university center. Acta Obstet Gynecol Scand 2026. https://doi.org/10.1111/AOGS.70299.
6. Lin H, Wu CH, Fu HC, Ou YC. Recent advances in cervical cancer treatment: Innovations from early-stage to advanced disease. Taiwan J Obstet Gynecol 2025;64:608–15. https://doi.org/10.1016/j.tjog.2025.04.006.
7. Schaafsma M, Plante M, Mom CH, Van Trommel NE. Is less more in the surgical treatment of early-stage cervical cancer? Curr Opin Oncol 2022;34:473–89. https://doi.org/10.1097/CCO.0000000000000863.
8. Bendifallah S, de Foucher T, Bricou A, Ouldamer L, Lavoue V, Varinot J, et al. Cervical cancer recurrence: Proposal for a classification based on anatomical dissemination pathways and prognosis. Surg Oncol 2019;30:40–6. https://doi.org/10.1016/j.suronc.2019.05.004.
9. Peiretti M, Zapardiel I, Zanagnolo V, Landoni F, Morrow CP, Maggioni A. Management of recurrent cervical cancer: A review of the literature. Surg Oncol 2012;21:e59–66. https://doi.org/10.1016/j.suronc.2011.12.008.
10. Marshall C, Rajdev MA, Somarouthu B, Ramaiya NH, Alessandrino F. Overview of systemic treatment in recurrent and advanced cervical cancer: a primer for radiologists. Abdom Radiol (NY) 2019;44:1506–19. https://doi.org/10.1007/S00261-018-1797-4.
11. Geeitha S, Prabha KPR, Cho J, Easwaramoorthy SV. Bidirectional recurrent neural network approach for predicting cervical cancer recurrence and survival. Sci Rep 2024;14. https://doi.org/10.1038/S41598-024-80472-5.
12. Fontenot VE, Francoeur A, Tewari KS. Review of emerging biological therapies for recurrent and advanced metastatic cervical cancer. Expert Opin Biol Ther 2024;24:709–13. https://doi.org/10.1080/14712598.2024.2373320.
13. Manning-Geist B, Grace MA, Sonoda Y. Trachelectomy and fertility-sparing procedures for early-stage cervical cancer: A state of the science review. Gynecol Oncol 2024;181:179–82. https://doi.org/10.1016/j.ygyno.2024.01.014.

14. Kushwah AS, Gupta MK, Singh R, Banerjee M. Cytokine gene variants and treatment outcome of cisplatin-based concomitant chemoradiotherapy in cervical cancer. Br J Biomed Sci 2020;77:81–6. https://doi.org/10.1080/09674845.2020.1714164.
15. Li K, Chen J, Hu Y, Wang YZ, Shen Y, Chen G, et al. Neoadjuvant chemotherapy plus camrelizumab for locally advanced cervical cancer (NACI study): a multicentre, single-arm, phase 2 trial. Lancet Oncol 2024;25:76–85. https://doi.org/10.1016/S1470-2045(23)00531-4.
16. Lee KB, Shim SH, Lee JM. Comparison between adjuvant chemotherapy and adjuvant radiotherapy/chemoradiotherapy after radical surgery in patients with cervical cancer: a meta-analysis. J Gynecol Oncol 2018;29:e62. https://doi.org/10.3802/JGO.2018.29.E62.
17. Zola P, Fuso L, Mazzola S, Piovano E, Perotto S, Gadducci A, et al. Could follow-up different modalities play a role in asymptomatic cervical cancer relapses diagnosis? Gynecol Oncol 2007;107:S150–4. https://doi.org/10.1016/j.ygyno.2007.07.028.
18. Kobayashi R, Yamashita H, Okuma K, Ohtomo K, Nakagawa K. Details of recurrence sites after definitive radiation therapy for cervical cancer. J Gynecol Oncol 2016;27. https://doi.org/10.3802/jgo.2016.27.e16.
19. German Cancer Society GCAA. German Guideline Program in Oncology: Diagnosis, Treatment, and Follow-Up in Patients with Cervical Carcinoma Long version 2.2, AWMF Registration Number: 032/033OL. 2022.
20. Bhatla N, Berek JS, Cuello Fredes M, Denny LA, Grenman S, Karunaratne K, et al. Revised FIGO staging for carcinoma of the cervix uteri. International Journal of Gynecology & Obstetrics 2019;145:129–35. https://doi.org/10.1002/ijgo.12749.
21. Ozga M, Aghajanian C, Myers-Virtue S, McDonnell G, Jhanwar S, Hichenberg S, et al. A systematic review of ovarian cancer and fear of recurrence. Palliat Support Care 2015;13:1771–80. https://doi.org/10.1017/S1478951515000127.
22. Webb MJ, Symmonds RE. Site of recurrence of cervical cancer after radical hysterectomy. Am J Obstet Gynecol 1980;138:813–7. https://doi.org/10.1016/S0002-9378(16)32742-9.
23. Kang O, Koh J, Lee S, Park J, Lee M, Chung JH, et al. Neoadjuvant Paclitaxel-Carboplatin Chemotherapy Followed by Cesarean Radical Hysterectomy in Pregnant Patients With Cervical Cancer: Obstetric, Neonatal, and Surgical Outcomes. J Obstet Gynaecol Res 2026;52. https://doi.org/10.1111/JOG.70403.
24. Shinghal A, Chakravarty A, Singla T, Kapoor A, Datta A, Giridhar P, et al. Outcomes of cervical carcinoma patients treated with chemoradiation and single-application two-fractions schedule of high-dose-rate brachytherapy: A retrospective review (SATF study). J Contemp Brachytherapy 2026;18:154–62. https://doi.org/10.5114/JCB.2026.163310.
25. Plante M, Kwon JS, Ferguson S, Samouëlian V, Ferron G, Maulard A, et al. Simple versus Radical Hysterectomy in Women with Low-Risk Cervical Cancer. New England Journal of Medicine 2024;390:819–29. https://doi.org/10.1056/NEJMOA2308900;PAGEGROUP:STRING:PUBLICATION.

26. Colacurci D, Bifulco G, Ascione M, Shehaj I, Tahmasbi Rad M, Gasimli K, et al. Robotic Surgery in Gynecology: Balancing Clinical Benefit, Cost-Effectiveness, and Accessibility. Journal of Clinical Medicine 2026, Vol 15, Page 3628 2026;15:3628. https://doi.org/10.3390/JCM15103628.
27. Fan Y, Wang W, Sun Y, Guo S, He Y. The Expression and Clinical Value of miR-483-5p in Cervical Cancer and Its Regulation of Cervical Cancer via TIMP2. J Obstet Gynaecol Res 2026;52. https://doi.org/10.1111/JOG.70396.
28. Sun X, Qian S, Ye G, Wang Q, Yue EC, Zhang J. The ubiquitination of CD274 at MERCs enhances the anti-tumor immunity of cervical cancer. Autophagy 2026. https://doi.org/10.1080/15548627.2026.2708579.
29. Cibula D, Dostálek L, Jarkovsky J, Mom CH, Lopez A, Falconer H, Scambia G, Ayhan A, Kim SH, Isla Ortiz D, Klat J, Obermair A, Di Martino G, Pareja R, Manchanda R, Kosťun J, Dos Reis R, Meydanli MM, Odetto D, Laky R, Zapardiel I, Weinberger V, Benešová K, Borčinová M, Cardenas F, Wallin E, Pedone Anchora L, Akilli H, Abu-Rustum NR, Barquet-Muñoz SA, Javůrková V, Fischerová D, van Lonkhuijzen LRCW. Post-recurrence survival in patients with cervical cancer. Gynecol Oncol. 2022 Feb;164(2):362-369. doi: 10.1016/j.ygyno.2021.12.018. Epub 2021 Dec 23. PMID: 34955236; PMCID: PMC9406127.
30. Thongkhao P, Janmunee N, Tangkananan A. Prognostic factors for post-recurrence survival among patients with locally advanced cervical cancer who underwent definitive concurrent chemoradiation. Rep Pract Oncol Radiother. 2022 Sep 19;27(4):615-623. doi: 10.5603/RPOR.a2022.0078. PMID: 36196420; PMCID: PMC9521700.
31. Yoshida K, Kajiyama H, Utsumi F, Niimi K, Sakata J, Suzuki S, Shibata K, Kikkawa F. A post-recurrence survival-predicting indicator for cervical cancer from the analysis of 165 patients who developed recurrence. Mol Clin Oncol. 2018 Feb;8(2):281-285. doi: 10.3892/mco.2017.1530. Epub 2017 Dec 8. PMID: 29435288; PMCID: PMC5776414.

Figures

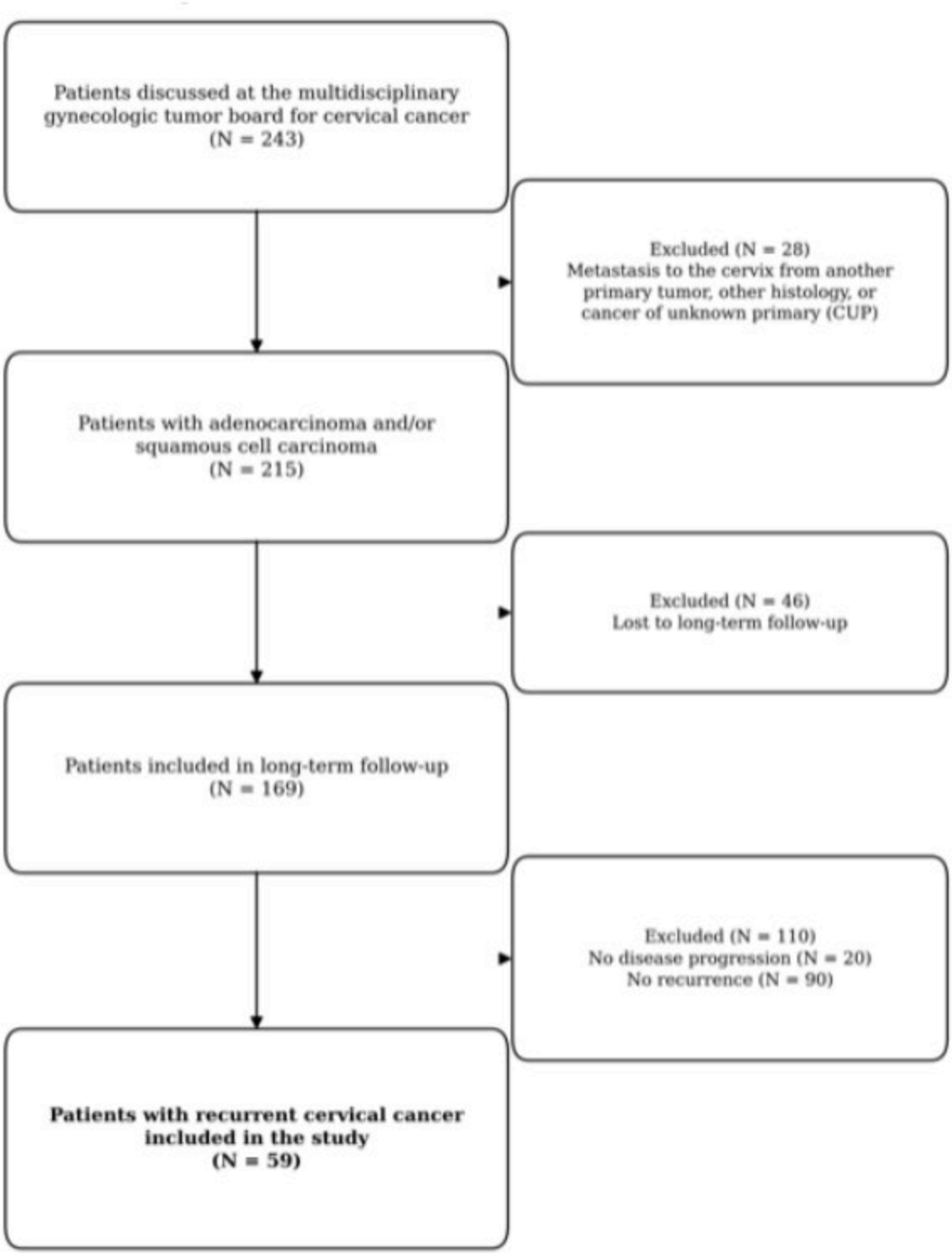

Figure 1

Study flow diagram illustrating patient selection and exclusion criteria.

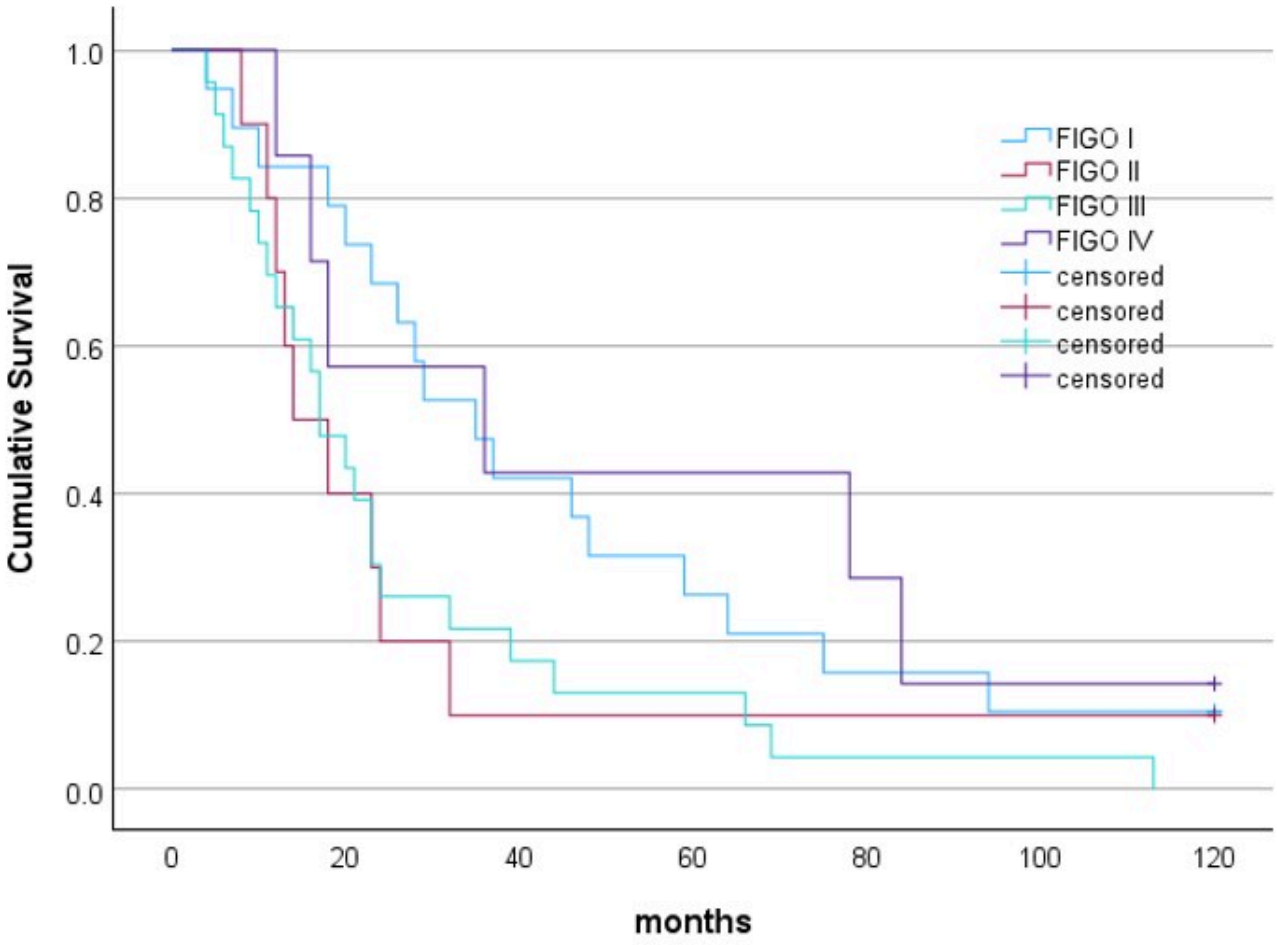

Figure 2

Kaplan-Meier Curves of recurrence free survival, Stratified by FIGO Stage

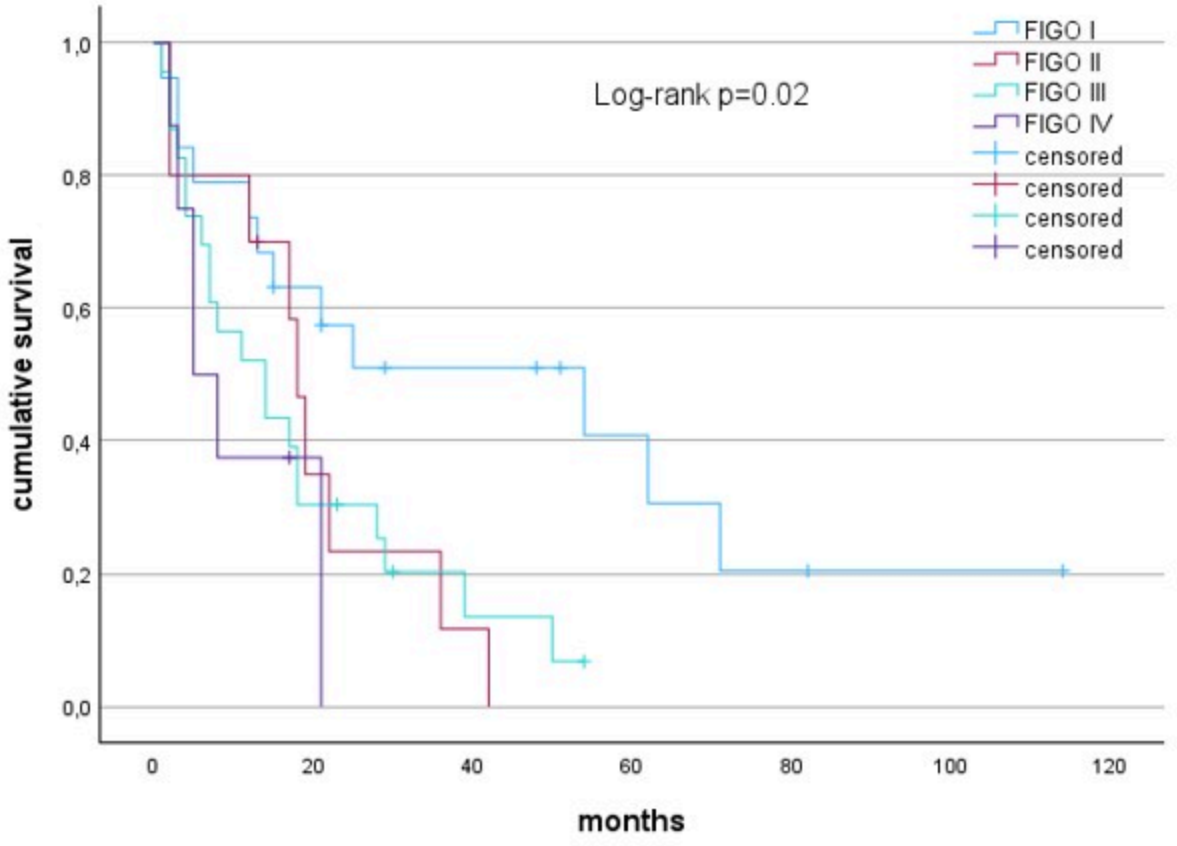

Figure 3

Kaplan-Meier Curves of Overall Survival After Recurrence, Stratified by FIGO Stage