European Journal of Surgical Oncology 52 (2026) 111468

Contents lists available at ScienceDirect

European Journal of Surgical Oncology

journal homepage: www.ejso.com

Pelvic exenteration for vulvar cancer: contemporary outcomes from a multinational cohort study

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ARTICLE INFO

Keywords:
Vulvar neoplasms
Pelvic exenteration
Gynecologic oncology
Multicentre cohort study
Postoperative morbidity
Survival analysis

ABSTRACT

Introduction: Women with vulvar cancer are considerably older than those with other gynaecological malignancies, raising concerns about the tolerability of radical surgery. Yet, for locally advanced or recurrent disease, pelvic exenteration may be the only curative option. Robust evidence to guide decision-making in this population is lacking.

Material and methods: This multicentre observational cohort study used data from the COREPEX registry including women who underwent anterior or total pelvic exenteration between 2005 and 2023 across 20 European tertiary referral centres. The primary outcome was overall survival (OS); secondary outcomes were

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https://doi.org/10.1016/j.ejso.2026.111468
Received 3 January 2026; Received in revised form 30 January 2026; Accepted 15 February 2026
Available online 19 February 2026

progression-free survival (PFS) and major postoperative complications. Associations were assessed using multivariable Cox and binomial regression models adjusted for relevant covariates.
Results: Among 861 women, 79 (9.2%) had vulvar cancer. Median follow-up was 49 months for OS and 40 months for PFS. Women with vulvar cancer were older and more often overweight. Five-year OS was 32% (95% CI, 19–46) in vulvar cancer versus 29% (95% CI, 25–34) in other cancers, adjusted HR 1.05 (95% CI, 0.75–1.46). Five-year PFS was 34% versus 29%, adjusted HR 0.96 (95% CI, 0.69–1.34). Major complications occurred in 33% vs 29%, adjusted RR 1.12 (95% CI, 0.77–1.58). Lymph node metastases, positive margins, and recurrent or persistent disease independently predicted poorer survival.
Conclusion: Despite their older age, women with vulvar cancer had survival and morbidity comparable to those with other gynaecological malignancies. These findings support pelvic exenteration as a curative option for selected women with vulvar cancer when complete resection is feasible.

1. Introduction

Vulvar cancer, arising from the female external genitalia, is a rare gynaecologic malignancy with an estimated annual global incidence of ~45,000 cases [1]. Most tumours are squamous cell carcinomas (VSCC), whereas malignant melanomas and adenocarcinomas are uncommon [2]. VSCC develops through two distinct pathways: a human papillomavirus (HPV)–associated form, typically affecting younger women (median age 62 years), and an HPV-independent form, which arises in the context of chronic inflammatory disorders such as lichen sclerosus and is usually diagnosed in elderly women (median age 74 years) [3–5].

Surgery remains the cornerstone of treatment and involves local excision of the tumour with assessment of the inguinal lymph nodes by either inguinofemoral lymphadenectomy or sentinel lymph node biopsy [6,7]. Complete excision with clear margins is essential to minimise risk of recurrence and improve survival [8]. However, owing to the proximity of vital functional anatomical structures—the urethra, vagina and anus—achieving clear margins can be challenging. In locally advanced or anatomically complex disease, pelvic exenteration may therefore be required to achieve complete resection.

Similar to anal and cervical cancers, HPV-associated VSCC may be treated with primary (chemo) radiation therapy as an alternative to radical surgery. By contrast, HPV-independent VSCC, which predominantly affects elderly women, is mainly treated with surgery as these tumours seem to be less sensitive to radiation therapy [9,10].

Despite major advances in perioperative care and surgical technique since its original description by Brunschwig in 1948, pelvic exenteration remains associated with considerable morbidity and non-negligible mortality [11,12]. Consequently, patient selection remains cautious.

Because of the rarity of vulvar cancer, evidence on outcomes following pelvic exenteration is confined to small, single-centre series [13–16]. Robust data from large multicentre cohorts are needed to inform patient counselling and surgical decision-making. No previous multicentre study has compared oncologic and early postoperative outcomes of pelvic exenteration for vulvar cancer. Unlike previous single-centre series or registry-based reports that lack internal comparison groups or multivariable risk adjustment, the present multicentre study uniquely compares outcomes of pelvic exenteration for vulvar cancer against other gynaecological malignancies within the same contemporary collaborative dataset, allowing adjustment for relevant clinical, pathological, and treatment-related confounders. The objective of this study was to investigate these outcomes within the largest collaborative European dataset to date.

2. Methods

This was an observational multicentre cohort study investigating the association between vulvar cancer and oncologic as well as postoperative outcomes after pelvic exenteration.

Data were extracted from the *COmplications and REcurrence after PElvic eXenteration for Gynaecologic Malignancies* (COREPEX) database, an international registry with retrospectively collected data from 20 European tertiary referral centres specialising in surgical gynaecologic oncology.

The COREPEX database includes detailed clinical, treatment, histopathological variables, as well as oncological outcomes in patients undergoing anterior or total pelvic exenteration. A comprehensive description of recorded variables has been published previously [17].

The database is administered and led by Fondazione Policlinico Agostino Gemelli IRCCS, Rome, Italy.

Ethics approval

The study protocol was approved by the Institutional Review Board of the lead institution (No. 0011322/21) and the corresponding local ethics committees of all participating centres. This study followed the *Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE) reporting guidelines [18].

2.1. Inclusion and exclusion criteria

Eligible patients met the following criteria: 1) Histologically verified primary diagnosis of cervical, vaginal, vulvar, or endometrial carcinoma, or recurrent/persistent disease, 2) Underwent anterior or total pelvic exenteration (PE) between January 2005 and March 2023, 3) Procedure performed with curative or palliative intent. In this cohort, 'palliative' intent did not indicate terminal or disseminated disease. Instead, the term referred to pelvic exenteration performed for severe, tumour-related or treatment-related complications, or for advanced local disease causing substantial symptom burden in situations where the prospect of complete cure was limited. These cases were therefore fundamentally different from palliative surgery for metastatic disease and were retained because they represent clinically relevant real-world indications for pelvic exenteration.

Exclusion criteria were the absence of adequate preoperative imaging (MRI or expert ultrasonography and CT or PET–CT) and posterior exenterations. The latter were excluded to ensure a homogeneous cohort, as they differ substantially from anterior and total exenterations in anatomical extent, operative field, and typical indication. Including these procedures would have introduced marked heterogeneity and compromised the validity of comparisons across diagnostic groups.

Total pelvic exenteration was defined as resection of the uterus (if present), vagina, urethra, bladder and rectum, whereas anterior pelvic exenteration referred to the same procedure excluding rectal removal. The extent of pelvic exenteration was classified according to Magrina (Supralevator, infralevator (i.e. translevator), infralevator with vulvectomy) [19].

2.2. Outcome

Primary outcome: Overall survival (OS), defined as the time from pelvic exenteration to death from any cause or last follow-up for survivors.

Secondary outcomes: Progression-free survival (PFS), defined as the time from pelvic exenteration to recurrence/progression, death, or last follow-up (if alive and recurrence-free).

Major postoperative complications, defined as Clavien–Dindo grade ≥ III within 30 days postoperatively, including all reoperations [20].

2.3. Exposure

Vulvar cancer diagnosis.

2.4. Control

Other gynaecologic malignancy (cervical, endometrial or vaginal cancer diagnosis)

2.5. Covariates

Predefined covariates and confounders included:

OS and PFS; Age, type of pelvic exenteration, American Society of Anaesthesiologist (ASA) physical status, timing of PE, extent of PE, microscopic surgical margins, lymph node metastases (pathologically confirmed after resection), year of treatment.

Postoperative major complications; Age, treatment previous to PE, body mass index (BMI), ASA physical status, type of PE, extent of PE, preoperative serum albumin, year of treatment.

2.6. Statistical analysis

Continuous variables were described using medians with interquartile ranges (IQR), whereas categorical variables were summarised as frequencies and percentages. Group differences between patients with vulvar cancer and other gynaecological malignancies were tested using Fisher's exact test or Pearson's χ^2 test, as appropriate.

Missing data were handled using multivariate imputation by chained equations (MICE), carried out with the *mice* package in R [21]. Predictive mean matching method was used for continuous variables to ensure realistic imputed values, while categorical variables were imputed using logistic or polytomous regression models, depending on the number of categories.

Associations between vulvar cancer and survival outcomes (OS and PFS) were analysed using Cox proportional hazards regression models, adjusted for: Age (<60 vs. 60–75 vs. >75 years). Age was categorised into clinically meaningful groups to allow for non-linear risk assessment and improve interpretability; modelling age as a continuous variable yielded comparable results. Models were further adjusted for type of pelvic exenteration (anterior vs. total), ASA class (I–II vs. III–IV), timing of PE (treatment-naïve vs. persistent vs. recurrent disease), extent of PE (supralevator vs. infralevator vs. infralevator with vulvectomy), microscopic surgical margins (negative vs. positive), lymph node metastases (yes vs. no vs. unknown/not assessed) and year of treatment (2005–2011 vs. 2012–2017 vs. 2018–2023).

To assess the robustness of our findings, we performed subgroup analyses stratified by lymph node metastases status. Separate Cox proportional hazards models for overall survival (OS) were fitted for patients with lymph node metastases and for those with no or unknown lymph node metastases. This approach allowed evaluation of whether the associations observed in the overall cohort were consistent across these clinically relevant subgroups.

Both univariable and multivariable models were fitted. The proportional hazards assumption was tested for all covariates, and variables violating this assumption were included as strata in the final model. Estimates are presented as hazard ratios (HR) with 95% confidence intervals (CI) and Wald *p*-values.

The association between vulvar cancer and major postoperative complications was evaluated using a log-binomial regression model fitted with the *logbin* package in R [22]. Covariates included age (<60 vs. 60–75 vs. >75 years), treatment previous to PE (none vs. surgery only vs. surgery + radiation therapy/chemoradiation [RT/CRT] vs. RT/CRT only vs. chemotherapy only), BMI (underweight vs. normal vs. overweight), ASA physical status (I–II vs. III–IV), type of PE (anterior vs. total), extent of PE (supralevator vs. infralevator vs. infralevator with vulvectomy), preoperative serum albumin (>37 vs. ≤37 g/L), and year of treatment (2005–2011 vs. 2012–2017 vs. 2018–2023). Results are presented as relative risks (RR) with 95% CI and Wald *p*-values.

Median follow-up time was estimated using the reversed Kaplan-Meier method. All statistical tests were two-sided, and a *p*-value <0.05 was considered statistically significant. Statistical analyses were performed using R version 4.4.2 [23].

3. Results

Between 2005 and 2023, 861 patients undergoing anterior or total pelvic exenteration in 20 European tertiary referral centres with expertise in surgical gynaecologic oncology were included in the analyses. Of the 861 analysed patients, 88.0% (n = 758) procedures were performed with curative intent and in 12.0% (n = 103) with palliative intent. Of the 103 procedures performed with palliative intent, 12 involved women with vulvar cancer and 91 involved women with other gynaecological malignancies. This corresponded to palliative intent in 15.6% of vulvar cancer cases and 11.6% of other gynaecological malignancies. The distribution of treatment intent did not differ significantly between diagnostic groups (p = 0.456), Table 1.

Seventy-nine patients (9.2%) had a diagnosis of vulvar cancer, and 782 patients (90.8%) had other gynaecologic malignancies (cervical cancer (n = 573, 66.6%), endometrial cancer (n = 140, 16.2%), vaginal cancer (n = 69, 8.0%)). Centre case volume varied across institutions (median 35 cases per centre over the study period), the number of patients included by each participating European institution is provided in Supplementary Table S1. The median follow-up time for OS was 49 months (IQR: 22 to 89) and for PFS 40 months (IQR: 14 to 73).

There were distributional differences in the baseline patient and treatment characteristics by vulvar cancer and other gynaecologic malignancies, outlined in Table 1. Notably, patients with vulvar cancer had a higher mean age (66 *vs.* 55 years $p < 0.001$), were more often overweight (65 *vs.* 48%, $p = 0.009$) and were more treatment naïve before PE (18 *vs.* 11%, $p = 0.014$), see Table 1.

3.1. Overall survival

At the end of follow-up, overall, 39% (n = 333) patients were alive, 43% (n = 372) were dead due to disease. Among those who died, 11% (n = 99) died due to non-cancer causes and 6.6% (n = 57) died for unknown reasons, see Supplementary Table S2. The median time from pelvic exenteration to death was 437 days (IQR: 182 to 982), see Supplementary Table S2.

The adjusted 5-year OS in vulvar cancer patients was 32% (95% CI, 19-46) as compared to 29 % (95% CI 25-34) in other gynaecologic malignancies, HR 1.10, (95% CI 0.73 to 1.65; $p = 0.662$), see Fig. 1A. Similarly, there was no difference in OS in the crude estimate provided in Supplementary Fig. S1A.

In contrast to age and a vulvar cancer diagnosis, in the adjusted cox-regression, there was an increased hazard of death in the presence of lymph node metastases (HR 1.47, 95% CI, 1.14 to 1.88: $p = 0.002$), positive surgical margins (HR 1.72, 95% CI, 1.39 to 2.13: $p < 0.001$), total PE (HR 1.57, 95% CI, 1.29 to 1.92; $p < 0.001$), and PE at time of recurrence (HR 1.58, 95% CI, 1.12 to 2.21; $p = 0.009$) or persistent disease (HR 2.10, 95% CI, 1.43 to 3.07: $p < 0.001$), see Fig. 2A. There was no difference in OS by vulvar cancer and other gynaecological malignancies in the subgroup analysis excluding patients with lymph node metastasis, shown in Supplementary Fig. S2.

3.2. Progression-free survival

The adjusted 5-year PFS in vulvar cancer was 34% (95% CI, 21-48) as compared to 29% (95% CI, 25-33) for other gynaecologic malignancies,

Table 1
Patient and treatment characteristics of 861 women who underwent anterior or total pelvic exenteration between 2005 and 2023, stratified by vulvar cancer versus other gynaecological malignancies.

Characteristic	Vulvar cancer $n = 79$	Other[a] gynecologic cancer $n = 782$	p-value[b]
Age (Years)			
Mean (SD)	66 (10)	55 (12)	<0.001
Grouped, no (%)			
<60	16 (21)	487 (63)	
60-75	49 (63)	252 (33)	
>75	13 (17)	36 (4.6)	
Missing	1 (1)	7 (1)	
ASA physical status, no. (%)			
I	14 (22)	62 (9)	0.037
II	34 (52)	373 (57)	
III	16 (25)	196 (30)	
IV	1 (2)	26 (4)	
Missing	14	125	
BMI[c] (kg/m^2), no. (%)			
Normal weight	24 (34)	320 (44)	0.009
Overweight	46 (65)	347 (48)	
Underweight	1 (1.4)	61 (8.4)	
Missing	8	54	
Preoperative S/P-Albumin (g/L), no. (%)			
>37	22 (28)	283 (36)	0.005
≤37	22 (28)	289 (37)	
Missing	35 (44)	210 (27)	
Timing[d] of PE, no. (%)			
Naïve	14 (18)	85 (11)	0.014
Persistent disease	5 (6.3)	137 (18)	
Recurrent disease	60 (76)	560 (72)	
Treatment previous to PE, no. (%)			
Surgery only	23 (29)	94 (12)	<0.001
Surgery + RT/CRT	35 (44)	211 (27)	
RT/CRT only	6 (7.6)	358 (46)	
Chemotherapy only	1 (1.3)	29 (3.7)	
Missing	0 (0)	5 (1)	
Intent of treatment, no. (%)			
Curative	67 (84)	691 (88)	0.456
Palliative	12 (16)	91 (12)	
Type of PE, no. (%)			
Anterior PE	30 (38)	321 (41)	0.596
Total PE	49 (62)	461 (59)	
Extent[e] of PE, no. (%)			
Supralevator	5 (6.3)	337 (44)	<0.001
Infralevator	5 (6.3)	338 (44)	
Infralevator with vulvectomy	69 (87)	88 (12)	
Missing	0	19	
Microscopic surgical margins, no. (%)			
Negative margins	66 (84)	609 (79)	0.321
Positive margins	13 (16)	164 (21)	
Missing	0	9	
Lymph node metastases, no. (%)			
No	43 (54)	428 (55)	0.943
Yes	16 (20)	147 (19)	
Unknown/not assessed	20 (25)	207 (26)	
Year of treatment with PE, no. (%)			
2018–23	40 (51)	377 (48)	0.303
2012–17	34 (43)	310 (40)	
2005–11	5 (6.3)	95 (12)	

Abbreviations: SD, Standard Deviation; PE, Pelvic Exenteration; ASA, American Society of Anaesthesiologists; BMI, Body Mass Index.

[a] Cervical cancer (n = 573), Endometrial cancer (n = 140), Vaginal cancer (n = 69).

[b] Fisher's exact test or Pearson's Chi-squared test.

[c] Underweight: <18,5. Normal weight: 18,5 – 24,9. Overweight >24.9.

[d] Naïve: no prior treatment. Persistent: Residual tumour after treatment. Recurrent: recurrence after time of remission or progression.

[e] Defined according to the Magrina classification (infralevator equivalent to translevator) [19].

HR 1.16 (95% CI, 0.77 to 1.73; $p = 0.480$), see Fig. 1B. Similarly, there was no difference in PFS in the crude estimate provided in Supplementary Fig. S1B.

In contrast to age and a vulvar cancer diagnosis, in the adjusted cox-regression, there was an increased hazard of progression in the presence of lymph node metastases (HR 1.59, 95% CI 1.24 to 2.06; $p < 0.001$), positive surgical margin (HR 1.90, 95% CI, 1.53 to 2.37: $p < 0.001$), and PE at time of recurrence (HR 1.72, 95% CI, 1.20 to 2.45; $p = 0.003$) or persistent disease (HR 2.02, 95% CI, 1.35 to 3.01; $p < 0.001$), see Fig. 2B.

There was no absolute difference in adjusted overall or progression-free survival after pelvic exenteration by vulvar cancer or other gynaecologic malignancy year one through five after pelvic exenteration, see Fig. 3A and B.

3.3. Postoperative complications

A major postoperative complication occurred in 33% (n = 26) of patients with vulvar cancer and in 29% (n = 228) of patients with other gynaecologic malignancy, see Supplementary Table S3. In the adjusted binomial regression model, an increased risk of major postoperative complications was observed in overweight (Relative Risk (RR) 1.35, 95% CI, 1.07 to 1.70; $p = 0.011$) and underweight (RR 1.47, 95% CI 1.02 to 2.14; $p = 0.041$) patients, as well as if a total PE was performed (RR 1.25, 95% CI, 1.00 to 1.56; $p = 0.048$), see Table 2. By contrast, a decreased risk was observed if treatment with surgery and radiation therapy/chemoradiation or radiation therapy/chemoradiation alone was given prior to the pelvic exenteration, RR 0.64 (95% CI, 0.46 to 0.87; $p = 0.005$) and RR 0.75 (95% CI, 0.56 to 1.00; $p = 0.049$), respectively. Moreover, pelvic exenteration performed during the earliest time period from 2005 to 2011, decreased the risk of major postoperative complications, RR 0.55 (95% CI, 0.33 to 0.90; $p = 0.0181$), see Table 2.

The adjusted predicted probability of a major postoperative complication after pelvic exenteration with a vulvar cancer diagnosis was 33% (95% CI, 20-46) and 29% (95% CI, 26-32) for other gynaecologic malignancies, with an absolute risk difference of 4% (95% CI, −10 to 18; $p = 0.541$), see Supplementary Fig. S3. Detailed analyses of postoperative complication types and patterns in the COREPEX cohort have been reported previously [24].

4. Discussion

4.1. Main findings

In this large multinational cohort of women undergoing anterior or total pelvic exenteration, outcomes in vulvar cancer were similar to those observed in other gynaecological malignancies. Five-year overall survival and progression-free survival estimates were comparable between groups, and major postoperative complication rates did not differ materially after adjustment for relevant clinical and treatment factors. These findings provide contemporary evidence to support patient selection and counselling for pelvic exenteration in vulvar cancer, particularly in older patients in whom the procedure is often considered high risk.

Vulvar cancer demonstrates a high rate of local recurrence but a low incidence of distant metastasis [25]. In the absence of nodal or systemic dissemination, prognosis is favourable, with reported 5-year overall survival rates of 80–90% [26,27]. Accordingly, in selected patients with locally advanced or recurrent disease confined to the pelvis, pelvic exenteration may achieve durable locoregional control and long-term survival [28]. The relatively infrequent use of pelvic exenteration in vulvar cancer may be explained by the advanced age and comorbidity burden typical of this patient group, the technical demands of infralevator resections and complex reconstructions including the rarity of the disease, which limits surgical experience.

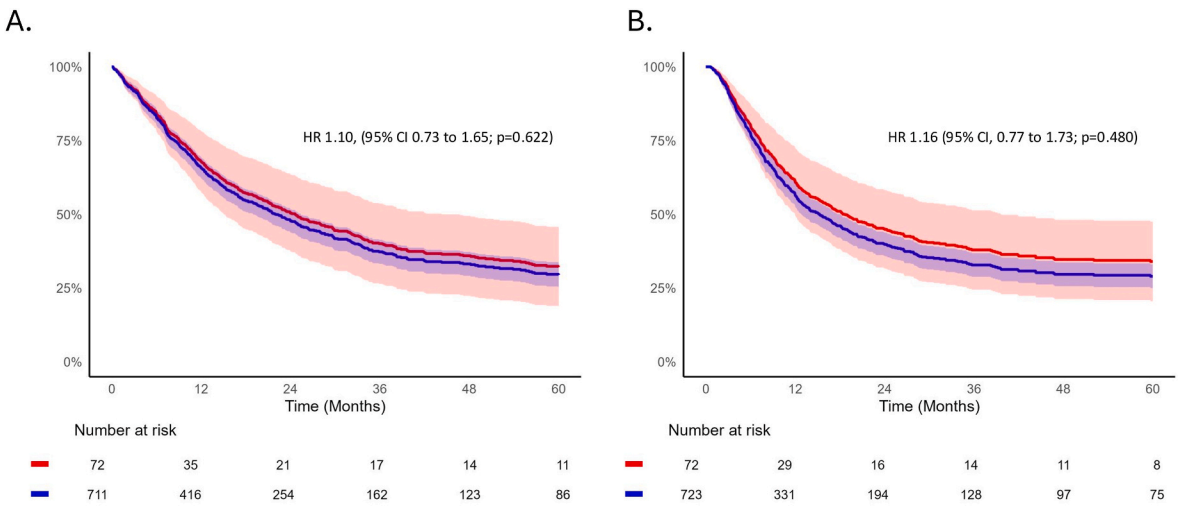


Fig. 1. Overall and progression-free survival after anterior or total pelvic exenteration in women with vulvar cancer versus other gynaecological malignancies. Red line vulvar cancer. Blue line other gynaecologic malignancies. The shadows indicate the confidence intervals.
A. Overall Survival. Adjusted for: Age (<60 vs. 60-75 vs. >75), Type of pelvic exenteration (Anterior vs. Total), ASA score (I-II vs. III/IV), Timing of PE (Naïve vs. Persistent vs. Recurrent), Extent of PE (Supralevator vs. Infralevator vs. Infralevator with vulvectomy), Microscopic surgical margins (Negative vs. Positive), Lymph node metastases (Yes vs. No vs. Unknown/Not assessed), Year of treatment (2005-11 vs. 2012-2017 vs. 2018-2023).
B. Recurrence Free Survival. Adjusted for: Age (<60 vs. 60-75 vs. >75), ASA score (I-II vs. III/IV), Timing of PE (Naïve vs. Persistent vs. Recurrent), Extent of PE (Supralevator vs. Infralevator vs. Infralevator with vulvectomy), Microscopic surgical margins (Negative vs. Positive), Lymph node metastases (Yes vs. No vs. Unknown/Not assessed), Year of treatment (2005-11 vs. 2012-2017 vs. 2018-2023). The variables Extent of PE (Supralevator vs. Infralevator vs. Infralevator with vulvectomy), Type of pelvic exenteration (Anterior vs. Total), and ASA score (I-II vs. III/IV) did not meet the proportional hazards assumption and were therefore included as strata.

4.2. Results of the study in the context of previous findings

Previous studies examining outcomes after pelvic exenteration for vulvar cancer have reported 5-year overall survival rates ranging from 39% to 70%, which is higher than the 32% observed in the present cohort [13–16]. However, these investigations were limited by small sample sizes, absence of comparison groups or adjustment for relevant covariates, fewer patients with adverse prognostic factors such as non-radical resections or recurrent disease and single-institution designs conducted over extended time periods, thereby restricting generalisability. Conversely, the present study incorporates a large, contemporary, multicentre cohort with an internal comparison group, providing robust and generalisable estimates. Importantly, survival outcomes were consistent with those reported for other gynaecological malignancies undergoing pelvic exenteration, corroborating previous evidence [29–34].

As in previous reports, lymph node metastases, non-radical excision, and recurrent or persistent disease were associated with poorer survival in our study [30,34–41]. Given the established prognostic impact of nodal disease, extra regional lymph node metastases have traditionally been regarded as a contraindication to pelvic exenteration with curative intent, however opinions on regional/pelvic lymph node metastases differ [42]. In the present cohort, 20% of women had nodal involvement. The COREPEX dataset did not capture details on lymphadenectomy procedures or institutional criteria for case selection, which may account for variability across centres. Nevertheless, after excluding women with lymph node metastases, survival remained similar between vulvar cancer and other gynaecologic malignancies.

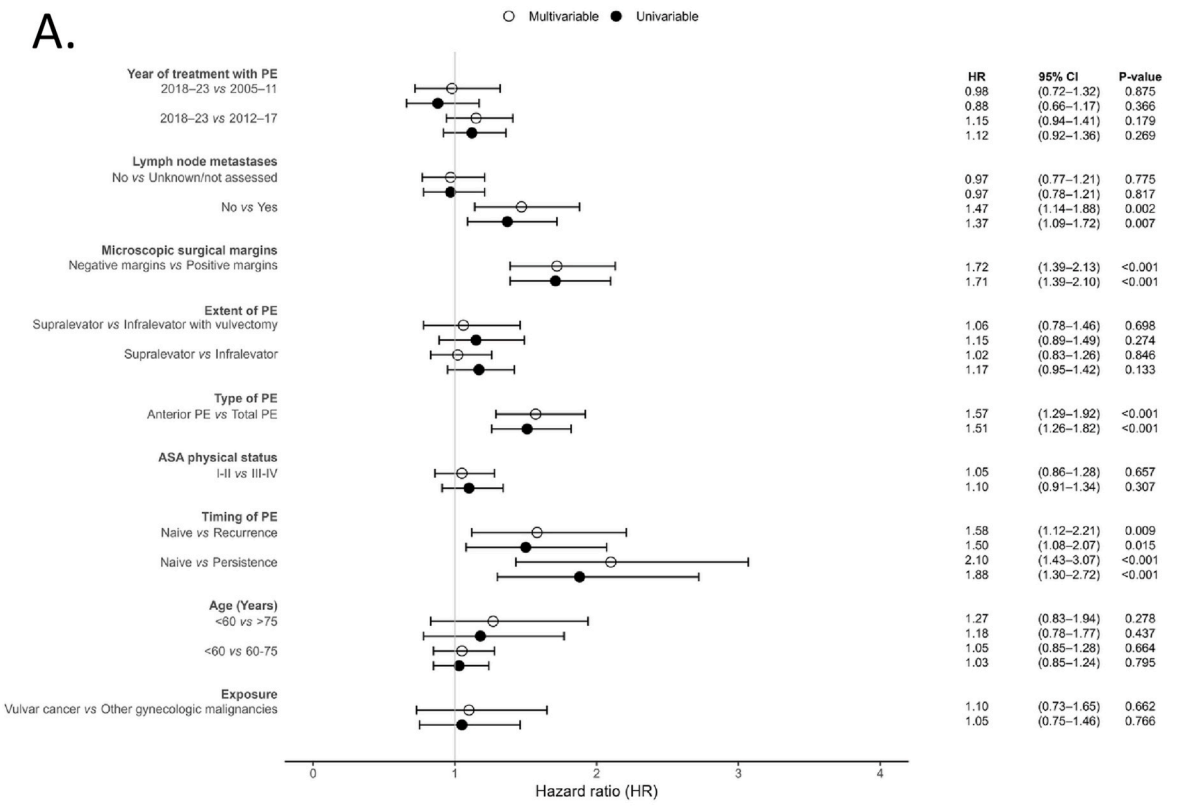
Population-based data has suggested that undertreatment—rather than age itself—may contribute to poorer outcomes [43,44]. In the present cohort, age had no significant impact on PFS or OS. Notably, age ≥75 years was not associated with poorer oncological outcomes or increased postoperative morbidity.

A previous large registry-based analysis identified vulvar cancer as an independent risk factor for postoperative morbidity [45]. However, this dataset lacked key surgical and oncological variables, limiting the reliability of this conclusion. Consistent with previous results, postoperative morbidity was comparable to that of other gynaecologic malignancy in our study [29,31,33,40,46–48]. Several factors may explain why morbidity was not higher in vulvar cancer despite the older age and higher prevalence of obesity in this group. Pelvic exenteration for vulvar cancer is less often preceded by pelvic radiotherapy or extensive prior surgery, both of which increase operative complexity. Together, these factors likely mitigated the higher baseline surgical risk expected in this older, comorbid group.

Consistent with broader surgical literature, both overweight and underweight patients demonstrated increased postoperative morbidity in our cohort, underscoring the relevance of nutritional and metabolic status in preoperative risk stratification 49–52.

Treatment received prior to pelvic exenteration, including surgery, radiotherapy and chemoradiation, is detailed in Table 1 and was included as an adjustment variable in the multivariable complication model. The lower morbidity observed among previously irradiated patients should be interpreted cautiously. This association most likely reflects confounding by indication: radiotherapy was predominantly administered to younger, fitter women with cervical cancer, rather than having any protective effect itself. Given that radiotherapy is uncommon in vulvar cancer, this finding should not be extrapolated to that population.

Apparent temporal differences in postoperative morbidity also warrant cautious interpretation. To mitigate potential temporal confounding arising from evolving surgical techniques, perioperative care, and referral patterns over the study period, year of treatment was included as a predefined adjustment variable in all multivariable models. Lower complication rates in the earliest study period (2005–2011) likely reflect differences in case selection, with earlier years including a higher proportion of anatomically favourable, less complex procedures. As surgical experience increased and referral pathways evolved, more challenging cases were undertaken in later years. These trends suggest that the temporal variation observed is largely attributable to evolving case mix rather than changes in surgical quality or perioperative care.



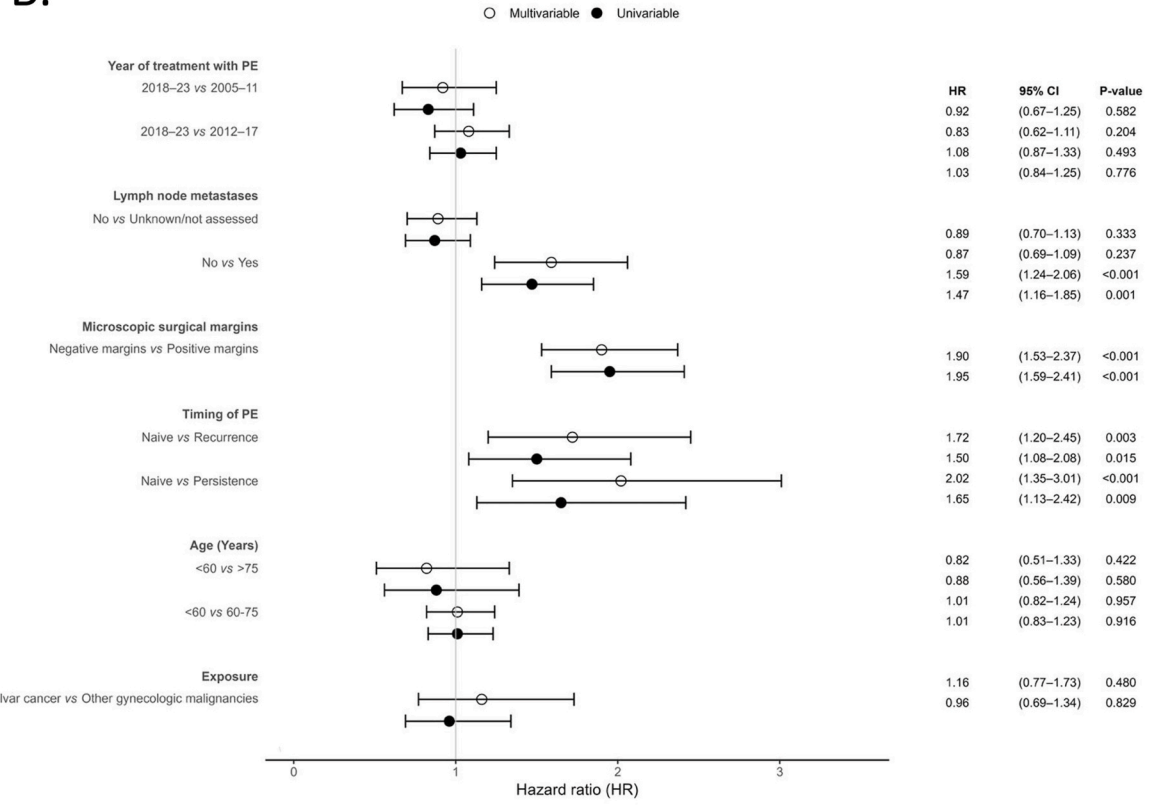


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Fig. 2. Forest plot of uni- and multivariable Cox regression for overall and progression-free survival after anterior or total pelvic exenteration, stratified by vulvar cancer versus other gynaecological malignancies.
Black circle: Unadjusted estimate. White circle: Adjusted estimate.
Abbreviations: PE, Pelvic Exenteration; HR, Hazard Ratio; CI, Confidence Interval; ASA, American Society of Anaesthesiologists.
A. Overall survival. Adjusted estimate adjusted for all included variables.
B. Progression-free survival. Adjusted for all included variables. The variables Extent of PE, ASA physical status, and Type of PE did not meet the proportional hazards regression and were therefore included as strata.

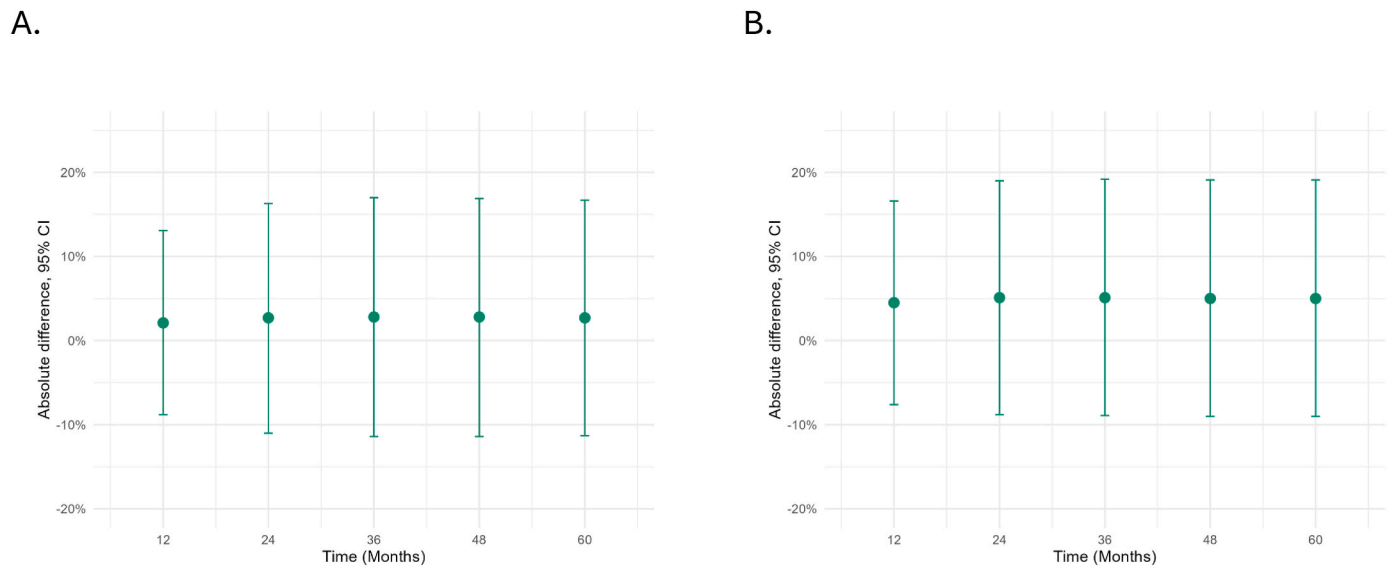

Fig. 3. Absolute difference in adjusted overall and progression-free survival between vulvar cancer and other gynaecological malignancies, from year 1 to year 5 after pelvic exenteration.
A. Overall Survival. Adjusted for: Age (<60 vs. 60-75 vs. >75), Type of pelvic exenteration (Anterior vs. Total), ASA score (I-II vs. III/IV), Timing of PE (Naïve vs. Persistent vs. Recurrent), Extent of PE (Supralevator vs. Infralevator vs. Infralevator with vulvectomy), Microscopic surgical margins (Negative vs. Positive), Lymph node metastases (Yes vs. No vs. Unknown/Not assessed), Year of treatment (2005-11 vs. 2012-2017 vs. 2018-2023).
B. Progression-Free Survival. Adjusted for: Age (<60 vs. 60-75 vs. >75), ASA score (I-II vs. III/IV), Timing of PE (Naïve vs. Persistent vs. Recurrent), Extent of PE (Supralevator vs. Infralevator vs. Infralevator with vulvectomy), Microscopic surgical margins (Negative vs. Positive), Lymph node metastases (Yes vs. No. vs., Unknown/Not assessed), Year of treatment (2005-11 vs. 2012-2017 vs. 2018-2023). The variables Extent of PE (Supralevator, vs., Infralevator vs. Infralevator with vulvectomy), Type of pelvic exenteration (Anterior vs. Total), and ASA score (I-II vs III/IV) did not meet the proportional hazards assumption and were therefore included as strata.

4.3. Limitations

Our study has several limitations. Its observational design introduces the potential for selection bias, information bias, unmeasured confounding and loss to follow-up. The absence of a predefined sample-size calculation, together with the relatively small number of women with vulvar cancer, limits the ability to detect modest differences in outcomes between diagnostic groups and raises the possibility of type II error. Institutional heterogeneity may also have influenced results, as detailed data on operative selection criteria—including in the presence of nodal disease—were not available. Although all participating institutions were high-volume tertiary referral centres, formal multilevel modelling of centre-specific effects was not feasible due to limited per-centre event counts. Moreover, details regarding institutional criteria for nodal assessment (sentinel lymph node biopsy, PET findings, frozen section) and eligibility for exenteration in node-positive disease were not uniformly captured in COREPEX and may therefore have varied across centres. Posterior exenterations were excluded to preserve a homogeneous surgical cohort, and the findings may not be generalisable to patients undergoing posterior procedures. The inclusion of cases labelled as 'palliative' in COREPEX may introduce some variation in surgical intent; however, these procedures were performed for severe local symptoms and reflect real-world indications for exenteration. Data on comorbidities were lacking, and multiple imputation was required for several variables, which may have affected the precision of the estimates. In addition, COREPEX did not uniformly capture tumour biological variables such as HPV status, p53 expression, histological subtype, lymphovascular or perineural invasion. Their absence may further limit the precision of survival risk adjustment. Furthermore, quality-of-life and functional outcomes were not uniformly captured across centres. Future multicentre exenteration registries should systematically incorporate patient-reported outcome measures to better inform shared decision-making and patient counselling for this highly morbid procedure. Despite these limitations, this analysis represents the largest contemporary multicentre study of pelvic exenteration for vulvar cancer, providing evidence on outcomes following an uncommon procedure performed for an even rarer malignancy.

4.4. Conclusion

Women with vulvar cancer had comparable survival and major postoperative complication rates after pelvic exenteration as compared to those with other gynaecological malignancies, and advanced age did not adversely affect outcomes. These findings provide reassurance that pelvic exenteration can be considered a curative option for carefully selected women with vulvar cancer, when complete resection is technically feasible.

CRediT author contributions

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Table 2
Association between pelvic exenteration and major postoperative complications[a] including patients with vulvar cancer.

	Univariate analysis		Multivariate analysis	
Variable	RR (95% CI)	*p*-value[b]	RR (95% CI)	*p*-value[b]
Exposure				
Vulvar cancer	1		1	
Other cancer types	0.89 (0.63 -1.24)	0.476	0.87 (0.57 - 1.33)	0.522
Age (Years)				
<60	1		1	
60-75	1.08 (0.86 - 1.35)	0.504	1.03 (0.81 - 1.30)	0.805
>75	1.38 (0.95 - 2.02)	0.093	1.27 (0.87 - 1.85)	0.217
Treatment previous to PE				
None	1		1	
Surgery only	0.78 (0.54 - 1.13)	0.190	0.72 (0.50 - 1.04)	0.080
Surgery and RT/CRT	0.65 (0.46 - 0.90)	0.010	0.64 (0.46 - 0.87)	**0.005**
RT/CRT	0.77 (0.58 – 1.04)	0.088	0.75 (0.56 – 1.00)	**0.049**
Chemotherapy only	0.78 (0.43 -1.43)	0.421	0.72 (0.40 – 1.30)	0.280
BMI[c]				
Normal weight	1		1	
Overweight	1.32 (1.06 - 1.66)	0.014	1.35 (1.07 - 1.70)	**0.011**
Underweight	1.48 (1.02 - 2.15)	0.038	1.47 (1.02 – 2.14)	**0.041**
ASA physical status				
I-II	1		1	
III-IV	0.97 (0.78 - 1.21)	0.791	0.92 (0.73 - 1.15)	0.466
Type of PE				
Anterior PE			1	
Total PE	1.30 (1.04 - 1.62)	0.020	1.25 (1.00 - 1.56)	**0.048**
Extent[d] **of PE**				
Supralevator	1		1	
Infralevator	1.37 (1.08 - 1.73)	0.010	1.26 (0.99 - 1.60)	0.060
Infralevator with vulvectomy	1.30 (0.97 - 1.74)	0.084	1.05 (0.72 - 1.52)	0.794
Preoperative S/P-Albumin (g/L)				
>37	1		1	
≤37	1.18 (0.96 - 1.45)	0.124	1.09 (0.88 - 1.35)	0.421
Year of treatment with PE				
2018–23	1		1	
2012–17	0.87 (0.70 - 1.08)	0.203	0.95 (0.77 - 1.18)	0.629
2005–11	0.51 (0.33 - 0.81)	0.004	0.55 (0.33 – 0.90)	**0.018**

Abbreviations: RR, Relative Risk: CI, Confidence Interval: PE, Pelvic Exenteration; BMI, Body Mass Index; RT, Radiation Therapy; CRT, Chemoradiation; ASA, American Society of Anesthesiologists.
[1]Adjusted for all tabulated variables.
[a] Defined according to Clavien Dindo ≥ III within 30 days of PE.
[b] Walds test of significance.
[c] Underweight: <18,5. Normal weight: 18,5 – 24,9. Overweight: >24.9.
[d] Defined according to the Magrina classification (infralevator equivalent to translevator).

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Data availability statement

The data that support the findings of this study are not publicly available owing to restrictions related to patient confidentiality, data protection, and ethical approvals. De-identified, aggregated data may be made available from the corresponding author upon reasonable request, subject to review and approval by the COREPEX collaborative and in accordance with institutional and ethical requirements. The full dataset may be made available to the journal's editorial team for the purposes of peer review, where required.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest

All authors declare no conflict of interest.

Acknowledgements

The authors thank the patients whose data contributed to this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2026.111468.

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