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Prediction of short-term surgical complications in women undergoing pelvic exenteration for gynecological malignancies

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HIGHLIGHTS

- Women undergoing PE have an overall 30-day complication rate of 67%, including 27% with severe complication.
- Postoperative 30-day mortality is 0.7% and the 90-day mortality is 2.2%.
- Most common complications are urinary reconstruction complication, wound dehiscence, organ system failure, and infections.
- The surgical complexity, hemoglobin, and presence of 3+ comorbidities are independently associated with severe complication.

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ABSTRACT

Objective. Pelvic exenteration (PE) is an extensive surgery associated with high rates of postoperative morbidity and mortality. The absence of well-defined preoperative selection criteria to identify patients eligible for PE prompted the assessment of pre-operative predictors of 30-day major surgical complications.

Methods. Demographics and surgical characteristics of patients undergoing PE for gynecologic cancer in a single institution between 01/2004–12/2016 were reviewed. Postoperative complications within 30 days following surgery were graded using the Accordion grading system. Logistic regression was used to analyze potential risk factors for severe postoperative complications.

Results. A total of 138 patients were included in the cohort. Forty-five patients underwent total PE, 52 anterior PE, and 41 posterior PE. Among the 137 patients with follow-up, a severe postoperative complication was experienced by 37 patients (27.0%) and 3 patients (2.2%) experienced death within 90 days. The most frequent grade 3 complications were complications of urinary reconstruction (n = 15), wound dehiscence (n = 9), and abdominal abscess requiring intervention with drain or return to the operating room (n = 6). On multivariable analysis, independent predictors of severe postoperative complications were anterior or total PE (adjusted odds ratio (aOR): 11.66, 95% CI 2.56–53.18), pre-operative hemoglobin ≤10 mg/dl (aOR 2.70, 95% CI 1.02–7.14) and presence of 3+ comorbidities (aOR: 2.76, 95% CI 1.07–7.10).

Conclusions. Major complications after exenteration are common. Surgical complexity and patient selection play a considerable role in predicting complications. These data can be used to better risk stratify patients undergoing PE.

1. Introduction

Pelvic exenteration (PE) is a therapeutic option for patients with isolated pelvic central recurrence of gynecological cancers and for some primary advanced and persistent disease [1]. In patients previously treated with radiotherapy or chemoradiation, it may be the only curative option. PE is the radical en bloc removal of all pelvic organs, including bladder, rectum, and, when present, internal reproductive organs. Since 1948, when PE was described for the first time by Brunschwing, the development of surgical techniques and perioperative care contributed to the improvement of survival, morbidity, and mortality [2]. However, PE remains an aggressive procedure associated with a high rate of postoperative complications ranging from 51% to 82%, with 22–32% being major

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complications, and is associated with peri-operative mortality (ranging between 1 and 16%) [3]. This high morbidity and mortality risk is due both to the intrinsic patient factors such as smoking, obesity, and nutritional status, as well as disease-related factors such as prior radiation and the complexity of surgery. PE is still associated with an overall poor long-term oncological outcome, with the reported 5-year overall survival in literature being approximately 50% [4]. For all these reasons this surgery represents a challenge both for the surgeon and for the patient and the selection of appropriate candidates for this procedure is critical.

Prior studies have identified preoperative characteristics associated with morbidity and recurrence, however the literature remains sparse. The principal aim of this study is to identify risk factors for severe morbidity and mortality within 30 days after PE in a cohort of patients with gynecological malignancies treated consecutively in a single tertiary care institution. Given the paucity of data in the literature focused on short-term mortality and morbidity, this study would add to existing information to stratify the global perioperative risk and to support the clinician during the counseling process for PE.

2. Materials and methods

This is a retrospective cohort study of consecutive patients who underwent pelvic exenteration at Mayo Clinic in Rochester, Minnesota, between January 2004 and December 2016. The study was approved by the Institutional Review Board, and only the medical records of patients who consented to the use of their medical record for research were reviewed. Inclusion criteria were diagnosis of primary advanced, recurrent or persistent gynecological malignancy including endometrial cancer, cervical cancer, vaginal and vulvar cancer, or complications derived from treatment of a previous gynecological cancer (i.e. fistula post radiation therapy or abscess). Patients with a diagnosis of ovarian cancer and non-gynecologic malignancy were excluded. Patient demographic, preoperative, intraoperative, and postoperative data were abstracted from the medical records including age, BMI, ASA score, smoking status, hemoglobin, creatinine and albumin levels, medical comorbidities, previous abdominal surgery, previous radiation or chemotherapy, primary oncologic diagnosis, surgical data specifying the type of pelvic exenteration and the reconstructive surgery, pathological data, and postoperative complications.

Preoperative comorbidities evaluated were history of myocardial infarction, venous thromobembolism (VTE), congestive heart failure, percutaneous coronary intervention (PCI) or prior cardiac surgery (PCS), hypertension requiring medication, diabetes mellitus, acute or chronic renal failure, chronic obstructive pulmonary disease (COPD) or recent pneumonia, peripheral vascular disease, transient ischemic attack (TIA) or cerebrovascular accident (CVA), cerebrovascular accident with neurological defect, and depression or anxiety [5].

The timing of disease indicates the moment of the natural history of the disease in which PE was performed. It was defined as primary when PE was the first therapeutic approach to the disease, persistent in case of radiological persistence or recurrence within 6 months from the end of the treatment, or recurrent in case of relapse after >6 months from the previous treatment. Previous radiation included both brachytherapy and external beam radiation. Previous chemotherapy included all patients with systemic chemotherapy but excluded those who received only radiation-sensitizing chemotherapy.

Pelvic exenteration was defined as anterior, posterior, or total according to the extent of resection and was subclassified as supralevator or infralevator according to the level of resection in agreement with the classification introduced by Magrina et al. [6]. Use of intraoperative radiation therapy (IORT) was evaluated, and in general was used in the cases where there was a positive resection margins detected with frozen section. Additional surgical procedures besides central pelvic surgery were recorded (i.e. lymphadenectomy, omentectomy, stripping peritoneum, nephrectomy, hemipelvectomy etc.). Surgical data included the type of urinary diversion when performed, intestinal and pelvic floor reconstruction, development of diverting loop ileostomy, estimated blood loss (EBL), and number of intraoperative transfusions.

We collected postoperative complications occurring during the first 30 days after surgery, and these were graded according to the Accordion classification [7]. Postoperative events requiring endoscopic or interventional radiologic procedures, re-operations, or complications resulting in organ failure were defined as Accordion grade 3. Death occurring within

Table 1
Demographic and disease characteristics of 138 patients undergoing pelvic exenteration between January 2004 and December 2016.

Patient characteristic	
Age (years)	
≥70	40 (29.0%)
<70	98 (71.0%)
BMI (kg/m^2)	
<25	53 (38.4%)
25–34.9	64 (46.4%)
35+	21 (15.2%)
ASA score	
<3	59 (42.8%)
≥3	71 (51.4%)
Unknown	8 (5.8%)
Creatinine (mg/dl)	
≤1.2	119 (86.3%)
>1.2	18 (13.0%)
Unknown	1 (0.7%)
Albumin (g/dl)	
<3.5	15 (10.9%)
≥3.5	62 (44.9%)
Unknown	61 (44.2%)
Hemoglobin (g/dl)	
≤10	28 (20.3%)
>10	110 (79.7%)
Smoking	
Never smoked	73 (52.9%)
Current/Former smoker	62 (44.9%)
Unknown	3 (2.2%)
Comorbidities at presentation	
None	35 (25.5%)
1	42 (30.4%)
2	32 (23.2%)
3+	29 (21.2%)
Hypertension requiring medication	69 (50.0%)
Depression or anxiety	30 (21.7%)
Diabetes mellitus	24 (17.4%)
History of VTE	18 (13.0%)
Renal failure (acute/chronic)	15 (10.9%)
COPD or recent pneumonia	13 (9.4%)
PCI or PCS	12 (8.7%)
Myocardial infarction	9 (6.5%)
TIA or CVA	5 (3.6%)
Congestive heart failure	3 (2.2%)
Peripheral vascular disease	3 (2.2%)
Cerebrovascular accident with neurological defect	2 (1.4%)
Prior abdominal surgery	114 (82.6%)
Disease characteristic	
Primary site	
Endometrial cancer	38 (27.5%)
Cervical cancer	51 (37.0%)
Vulvar cancer	21 (15.2%)
Vaginal cancer	18 (13.0%)
Other	10 (7.2%)
Previous EBRT +/− VBRT	112 (81.2%)
Previous systemic chemotherapy	35 (25.4%)
Timing of disease at presentation	
Primary	20 (14.5%)
Persistent	19 (13.8%)
Recurrent	88 (63.8%)
Disease-free	11 (8.0%)

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; COPD, chronic obstructive pulmonary disease; EBRT, external beam radiotherapy; CVA, cerebrovascular accident; PCI, percutaneous coronary intervention; PCS, prior cardiac surgery; TIA, transient ischemic attack; VBRT, vaginal brachy radiotherapy; VTE, venous thromboembolism.

30 days from surgery was defined as Accordion grade 4. A patient was classified as having a severe postoperative complication if their highest graded postoperative complication was an Accordion grade 3 or 4.

2.1. Statistical analysis

Continuous variables were descriptively summarized using mean and standard deviation (SD) or median and interquartile range (IQR), and categorical variables were described using frequencies and percentages. Univariate logistic regression analysis was performed to identify risk factors of severe postoperative complication Variable selection was performed using a least absolute shrinkage and selection operator (LASSO)-penalized logistic regression model. Determination of the optimal model was based on cross-validation using the minimal lambda minus 1 standard error rule to reduce the potential for overfitting. The reported multivariable model is based on fitting a final model including the subset of variables identified using LASSO. All statistical tests were two-sided and $p < 0.05$ was statistically significant. The analysis was performed using SAS version 9.4 (SAS Institute Inc., Cary NC) and R version 3.2.1 (R Core Team, R Foundation for Statistical Computing, Vienna, Austria).

3. Results

Between January 2004 and December 2016, 138 patients met inclusion criteria and were included in the cohort. Demographic characteristics are listed in Table 1. The mean age at surgery was 61.9 (SD: 13.1) years and mean BMI was 27.6 (SD: 6.5) kg/m^2. Over half (n = 71, 51.4%) of patients had an ASA score ≥ 3 and 74.6% (n = 103) had at least one of the identified comorbidities. Surgical indication was recurrent or persistent disease in the majority of patients (n = 107, 77.5%). Most patients (n = 112, 81.2%) had prior treatment with external beam radiation therapy +/− brachytherapy. The majority of the patients (89.9%, n = 124) were treated with curative intent, 1.5% (n = 2) were treated with palliative intent, and 8.7% (N = 12) were treated for a complication of primary treatment (such as a fistula or stenosis). Total PE was performed in 45 patients (32.6%), anterior PE in 52 (37.7%), and posterior PE in 41 patients (29.7%). There was only one case with a robotic-assisted laparoscopic approach, while all the others were performed with a midline longitudinal incision. In 35.5% of cases, pelvic surgery was perfomed concurrently with other surgical procedures such as omentectomy, appendectomy, nephrectomy, bone resection, hemipelvectomy, resection of pelvic sidewall/nerve resection, hernia repair, and stripping peritoneum (Table 2). Blood loss during surgery ranged from 100 ml to 7900 ml (median: 1100, IQR: 700–1600) and 107 patients (77.5%) received intraoperative blood transfusions (mean number of RBC units: 3.6, SD: 2.6).

One patient without any known postoperative complications during her initial hospital stay was lost to follow-up after discharge, and was thus excluded from the remaining analyses. Among 137 patients, 92 (67.2%) had a postoperative complication within 30 days from surgery that was an Accordion grade 2 or higher. The highest experienced complication was an Accordion grade 2 for 55 (40.1%), grade 3 for 36 (26.3%), and grade 4 for one (0.7%). The most frequent Accordion grade 3 complications are listed in Table 3. One patient died within 30 days from surgery due to sepsis. This was a 73-year old woman with obesity, diabetes mellitus, and hepatic cirrhosis. She underwent posterior exenteration and experienced intraoperative hemorrhage. In the early post-operative period she developed acute renal failure, fever, and sepsis that caused death 15 days after surgery. An additional 2 patients died within 90 days for a total of 3 deaths (2.2%) within 90 days.

Table 2
Surgical characteristics of 138 patients undergoing pelvic exenteration between January 2004 and December 2016.

Surgical characteristic	
Type of exenteration	
Total	45 (32.6%)
Anterior	52 (37.7%)
Posterior	41 (29.7%)
Level of exenteration	
Infralevator	76 (55.1%)
Supralevator	62 (44.9%)
Other associated procedures performed	49 (35.5%)
Omentectomy	13 (9.4%)
Appendectomy	13 (9.4%)
Bowel resection	7 (5.1%)
Stripping peritoneum/biopsies	7 (5.1%)
Resection of pelvic sidewall/nerve	5 (3.6%)
Hernia repair	5 (3.6%)
Nephrectomy	4 (2.9%)
Bone resection (pubic symphisis)	4 (2.9%)
Inguinal lymph node dissection	2 (1.4%)
Hemipelvectomy	2 (1.4%)
Estimated blood loss (ml), Median (IQR)	1100 (700, 1600)
Intraoperative blood transfusion	107 (77.5%)
IORT	36 (26.1%)
Margin status	
Negative	96 (69.6%)
Microscopic	12 (8.7%)
Macroscopic	3 (2.2%)
Not documented	27 (19.6%)
Urinary diversion	97 (70.3%)
Type of urinary diversion (% of 97)	
Ileal conduit	69 (71.1%)
Sigmoid conduit	11 (11.3%)
Transverse conduit	15 (15.5%)
Other	2 (2.1%)
Pelvic floor reconstruction	97 (70.3%)
Type of pelvic floor reconstruction (% of 97)	
Omental flap only	57 (58.8%)
Muscular flap only	18 (18.6%)
Combination	15 (15.5%)
Other	7 (7.2%)

Abbreviations: IORT, Intraoperative radiotherapy; IQR, interquartile range.

Table 3
Descriptive analysis of reported post-operative complications among 137 of the 138 patients undergoing pelvic exenteration with postoperative follow-up.

Highest Accordion complication grade	Total N = 137
0 or 1	45 (32.8%)
2	55 (40.1%)
3	36 (26.3%)
4	1 (0.7%)
Type of Accordion grade 3 complication	**Total N = 36 (% with grade 3 complication)**
Complication of urinary reconstruction	15 (41.7%)
Ureteral anastomosis leak (N = 8)	
Conduit leak (N = 4)	
Ureteral stricture (N = 1)	
Conduit ischemia (N = 1)	
Stent obstruction (N = 1)	
Wound dehiscence requiring VAC/reoperation	9 (25.0%)
Systemic complications - organ system failure	9 (25.0%)
Respiratory failure (N = 5)	
Heart failure (N = 3)	
Renal failure (N = 1)	
Abdominal abscess requiring reoperation/drainage	6 (16.7%)
Acute ischemia of lower extremity	3 (8.3%)
Complication of intestinal reconstruction – leakage	2 (5.6%)
Bowel perforation	2 (5.6%)
Endoscopic or interventional radiology procedure	17/137 (12.4%)
Reoperation	17/137 (12.4%)
Readmission within 30 days	25/137 (18.2%)
Death within 90 days	3/137 (2.2%)

Abbreviations: VAC, vacuum assisted closure.

Table 4
Univariate logistic regression analysis of predictors of severe postoperative complications (Accordion grade 3 or higher) within 30 days following surgery in 137 of the 138 patients undergoing pelvic exenteration with postoperative follow-up.

Characteristic	N (%) with a severe postoperative complication	Unadjusted OR (95%CI)	p-Value
Age (years)			
≥70	11 (28.2%)	1.09 (0.48, 2.49)	0.84
<70	26 (26.5%)	Referent	
BMI (kg/m^2)			
<25	16 (30.2%)	1.84 (0.78, 4.34)	0.16
25–34.9	12 (19.0%)	Referent	
35+	9 (42.9%)	3.19 (1.10, 9.28)	**0.033**
ASA			
≥3	20 (28.6%)	1.17 (0.54, 2.57)	0.69
<3	15 (25.4%)	Referent	
Comorbidities at presentation			
None	7 (20.0%)	Referent	
1	11 (26.2%)	1.42 (0.48, 4.17)	0.61
2	14 (30.4%)	0.96 (0.28, 3.24)	0.17
3+	13 (44.8%)	3.25 (1.08, 9.82)	**0.016**
Comorbidities at presentation			
Hypertension requiring medication			
Yes	22 (32.4%)	1.72 (0.80, 3.70)	0.16
No	15 (21.7%)	Referent	
Depression or anxiety			
Yes	7 (24.1%)	0.83 (0.32, 2.14)	0.70
No	30 (27.8%)	Referent	
Diabetes mellitus			
Yes	9 (37.5%)	1.82 (0.72, 4.61)	0.21
No	28 (24.8%)	Referent	
History of VTE			
Yes	4 (22.2%)	0.74 (0.23, 2.43)	0.62
No	33 (27.7%)	Referent	
Renal failure (acute/chronic)			
Yes	6 (40.0%)	1.96 (0.64, 5.94)	0.24
No	31 (25.4%)	Referent	
COPD or recent pneumonia			
Yes	2 (15.4%)	0.46 (0.10, 2.19)	0.33
No	35 (28.2%)	Referent	
PCI or PCS			
Yes	7 (58.3%)	4.43 (1.13, 15.00)	**0.017**
No	30 (24.0%)	Referent	
Myocardial infarction			
Yes	4 (44.4%)	2.30 (0.58, 9.10)	0.23
No	33 (25.8%)	Referent	
TIA or CVA			
Yes	0 (0.0%)	0.23 (0.01, 4.29)	0.37
No	37 (28.0%)	Referent	
Congestive heart failure			
Yes	2 (66.7%)	5.66 (0.50, 64.33)	0.16
No	35 (26.1%)	Referent	
Peripheral vascular disease			
Yes	2 (66.7%)	5.66 (0.50, 64.33)	0.16
No	35 (26.1%)	Referent	
Cerebrovascular accident with neurological defect			
Yes	0 (0.0%)	0.53 (0.02, 11.20)	0.74
No	37 (27.4%)	Referent	
Creatinine (mg/dl)			0.24
≤1.2	30 (25.4%)	Referent	
>1.2	7 (38.9%)	1.87 (0.66, 5.26)	
Albumin (g/dl)			0.89
<3.5	3 (20.0%)	Referent	
≥3.5	15 (24.2%)	1.28 (0.32, 5.13)	
Hemoglobin (g/dl)			
≤10	12 (42.9%)	2.52 (1.05, 6.02)	**0.038**
>10	25 (22.9%)	Referent	
Smoking			0.47
Never smoked	18 (25.0%)	Referent	
Current/former smoker	19 (30.6%)	1.33 (0.62, 2.83)	
Primary site			
Endometrial cancer	7 (18.4%)	Referent	
Cervical cancer	15 (29.4%)	1.85 (0.67, 5.11)	0.69
Vulvar cancer	6 (30.0%)	1.90 (0.54, 6.69)	0.71
Vaginal cancer	7 (38.9%)	2.82 (0.81, 9.87)	0.21
Other	2 (20.0%)	1.11 (0.19, 6.39)	0.57
Timing of disease at presentation			
Primary	4 (20.0%)	0.30 (0.06, 1.51)	0.23
Persistent/recurrent	28 (26.4%)	0.43 (0.12, 1.52)	0.61
Disease-free	5 (45.5%)	Referent	
Prior EBRT +/− VBRT			
Yes	33 (30.8%)	2.90 (0.94, 9.01)	0.065
No	4 (13.3%)	Referent	
Prior systemic chemotherapy			
Yes	10 (28.6%)	1.11 (0.47, 2.61)	0.81
No	27 (26.5%)	Referent	
Prior abdominal surgery			
Yes	33 (29.2%)	2.06 (0.66, 6.50)	0.22
No	4 (16.8%)	Referent	
Type of exenteration			
Total	19 (42.2%)	13.88 (2.98, 64.75)	**0.002**
Anterior	16 (30.8%)	8.44 (1.81, 39.34)	**0.007**
Posterior	2 (5.0%)	Referent	
Level of exenteration			
Infralevator	26 (34.7%)	2.46 (1.10, 5.52)	**0.029**
Supralevator	11 (17.7%)	Referent	
Pelvic floor reconstruction			
Yes	31 (32.3%)	2.78 (1.06, 7.31)	**0.038**
No	6 (14.6%)	Referent	
IORT			
Yes	9 (25.0%)	0.87 (0.36, 2.08)	0.75
No	28 (27.7%)	Referent	
EBL (ml)			
≥750	32 (34.4%)	8.66 (1.95, 38.40)	**0.005**
<750	2 (5.7%)	Referent	
Intraoperative blood transfusion			
Yes	31 (29.0%)	2.24 (0.71, 7.05)	0.17
No	4 (15.4%)	Referent	

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CI, confidence interval; EBL, estimated blood loss; EBRT, external beam radiotherapy; IORT, Intraoperative radiotherapy; OR, odds ratio; VBRT, vaginal brachy radiotherapy.

In univariate analysis, BMI ≥ 35 kg/m^2 was associated with an increased risk of a severe (grade 3–4) postoperative complication compared to those with BMI 25–34.9 (odds ratio [OR]: 3.19; 95% confidence interval [CI]: 1.10–9.28). Other preoperative variables univariately associated with an increased risk of severe complications included presence of 3 or more comorbidities (versus those with 0 comorbidities, OR: 3.25, 95%CI: 1.08–9.82) and pre-operative hemoglobin ≤10 g/dl (OR: 2.52, 95%CI: 1.05–6.02). We found that older age, ASA score ≥ 3, smoking, history of prior abdominal surgery, pre-operative albumin and creatinine level were not significantly associated with a higher risk of postoperative complications (Table 4). The type of primary disease (endometrial vs. cervical vs. vaginal vs. vulvar cancer) and the timing of surgery (primary vs. recurrent/persistent) were also not associated with a higher risk of severe complications. On the other hand, we reported a trend towards a higher rate of complications among patients previously treated with external beam radiation therapy +/− brachytherapy compared with non-irradiated patients (30.8% vs. 13.3% respectively, p = 0.065).

Surgical complexity in terms of the type and level of PE was a major predictor of severe postoperative complications. Specifically, the 30-day severe complication rate increased from 5% for posterior PE, to 30.8% for anterior PE (p = 0.007) and 42.2% for total PE (p = 0.002). Patients undergoing supralevator PE experienced a severe postoperative complication less commonly (17.7%) compared to those undergoing infralevator exenteration (34.7%, p = 0.029) (Table 4). The risk of severe

Table 5
Multivariable logistic regression analysis of predictors of severe postoperative complications (Accordion grade 3 or higher) within 30 days following surgery in 137 of the 138 patients undergoing pelvic exenteration with postoperative follow-up.

Variable	Adjusted OR (95% CI)	p-Value
Type of exenteration		
Posterior	Referent	
Anterior or total	11.66 (2.56, 53.18)	0.002
Hemoglobin (g/dl)		
≤10	2.70 (1.02, 7.14)	0.046
>10	Referent	
Number of comorbidities at presentation		
<3	Referent	
≥3	2.76 (1.07, 7.10)	0.035

Abbreviations: CI, confidence interval; OR, odds ratio.

postoperative complications was 34.4% in cases with intraoperative EBL ≥ 750 ml, compared to 5.7% for EBL < 750 ml ($p = 0.005$).

Given that we have 37 patients with severe postoperative complications, we restricted the multivariable model to include variables accounting for no >3 degrees of freedom. We also chose to consider hemoglobin instead of estimated blood loss in order to focus on variables available for preoperative counseling. Upon considering number of comorbidities (<3 vs. 3+) instead of the individual comorbidities, independent predictors of severe postoperative complications in the final multivariable model included anterior or total PE (adjusted odds ratio 11.66 [95% CI, 2.56–53.18]), hemoglobin ≤10 g/dl (2.70 [1.02–7.16]) and presence of 3+ comorbidities (2.76 [1.07–7.10]) (Table 5). Given the far lower risk of complication in the posterior exent group compared to anterior and total exenteration, we confined anaylsis to this subgroup of patients. Similar to our other findings, multivariable analysis shows and confirms that hemoglobin, complexity of surgery, and comorbidities are the drivers of complications (Table 6).

4. Discussion

Pelvic exenteration remains a radical curative opportunity for patients with recurrent pelvic cancer when other medical and more conservative treatments fail. However, it continues to have a consistent rate of therapeutic failure and high postoperative morbidity [3]. We decided to focus specifically on early morbidity (within 30 days) to catch all complications purely related to the surgery. This study is one of the largest series reported in the literature from a single institution, with the aim to identify factors that could mainly affect early postoperative morbidity. Consistent with data reported in literature, we found that: i) the overall rate of 30-day postoperative complications is still high, affecting 67.2% of patients; ii) 26.8% of patients experienced an Accordion grade 3–4 complication; iii) patient related factors such as morbid obesity, presence of 3+ comorbidities, low preoperative hemoglobin level (≤10 mg/dl) are associated with grade 3–4 complications; iv) increased surgical complexity is associated with grade 3–4 complication including anterior and total PE, infralevator PE, pelvic floor reconstruction, and EBL >750 cc; and v) the extent of surgery, low preoperative hemoglobin and presence of 3+ comorbidities are the only factors independently affecting the complication rate.

Table 6
Multivariable logistic regression analysis of predictors of severe postoperative complications (Accordion grade 3 or higher) within 30 days following surgery in patients undergoing only anterior/total pelvic exenteration.

Variable	Adjusted OR (95% CI)	p-Value
Level of exenteration		
Infralevator	3.10 (1.06, 9.01)	0.038
Supralevator	Referent	
Hemoglobin (g/dl)		
≤10	3.90 (1.25, 12.20)	0.019
>10	Referent	
Number of comorbidities at presentation		
<3	Referent	
≥3	3.06 (1.06, 8.80)	0.038

Abbreviations: CI, confidence interval; OR, odds ratio.

Several attempts to build predictive models of postoperative complications in gynecological cancers have been made, but few data are focused exclusively on this type of surgery. These data are consistent with the data in advanced ovarian cancer where surgical complexity is a driver of surgical morbidity [8,9]. Obesity is a known risk factor for early and late postoperative complications, making the surgery more challenging and longer. This data has been verified from other authors on complex gynecologic surgery demonstrating an increased risk of complication in obese patients [8]. Here we observed an increase in the 30-day complication rate in women with morbid obesity, ranging from 19.0% for BMI 25–34.5 to 42.9% for BMI 35+ ($p = 0.033$). Iglesias et al. focused on the impact of BMI on PE, reported a prolonged hospital stay and increased risk of wound dehiscence but the overall late complication rate was not different to that of non-obese woman [10]. Consistent with data reported in literature from Huang et al. [11], advanced age, particularly those without multiple co-morbidities, is not an absolute contraindication to PE, with rates of both early and late complications being no different in young versus elderly women in our cohort.

We found that surgical complexity is a main driver of complications. Extent of exenteration, including level of levator excision, and whether urinary conduit is necessary by the addition of an anterior component excision, both increase the complication rate. It is important to note the high degree of complications associated with urinary conduits, begging the question, should urinary diversions be performed by gynecologic oncologists or by urologists that are specialized in these procedures. Certainly high volume surgery makes for better outcomes and even at our high volume institution, the overall volume of urinary diversions is quite low. However, our complications rate is consistent with other studies about cystectomies for urologic pathologies reporting morbidity rates <30 days after surgery between 20 and 56% [12].

We also found a higher risk of complications in patients carrying 3 or more preoperative comorbidities, raising the importance of the overall health status of the patient which is consistent with other studies [13]. Several studies reported the need of more comprehensive evaluation taking in account multiple factors. In this context preoperative serum albumin level has been recognized as important risk factor for early and late complications in several types of surgery [8,14]. In our study the lack of albumin levels for many patients did not allow us to confirm an association, however we believe albumin and pre-operative nutritional status likely remains an important consideration for surgical risk stratification.

Most patients in this series had recurrent disease and had prior surgery, radiation, and/or chemotherapy. In a large case series focused specifically on morbidity after PE, Chiantera et al. [15] reported a higher risk of surgical complications in patients submitted to previous radiation therapy (61% versus 33.5%), although not statistically significant. These data are sustained in our results, where there is a clear trend for a higher complication rate in patients previously irradiated compared to naïve patients (respectively 30.8% vs. 13.3%, $p = 0.06$). This could be a hint to tailor surgery, especially the reconstructive procedure, in these patients. Furthermore, this data has been validated in several studies from general surgery in which previous radiation is an independent risk factor for overall anastomotic complications [16]. Preoperative anemia is another well-known adverse factor for postoperative outcome and, more specifically, Hb < 11 mg/dl increases the risk of anastomotic leak 6.5 fold [16,17]. The rational of such finding can be related to a decreased capacity of oxygen transportation that lead to a higher risk of complications or as a marker of increased frailty or increased surgical complexity.

Strengths of this study include the relatively large sample size, from a single-institution over a 13-year period, treated with a uniform approach to care. Limitations are inherent to the retrospective design of

the study and, moreover, evaluating a population treated in a tertiary care clinic could increase the risk of referral bias by including more likely patients with more severe disease. Further, we treated comorbidities equally while some are likely to confer higher surgical risk than others.

In conclusion, there are no clear exclusion criteria to discourage patients from this surgery, especially when PE represents the last curative chance. We found that posterior supra-levator PE is a different and quite safe procedure, compared to more extensive surgery. As per our results, complications are related to the high intrinsic hazard and complexity of this surgery and for this reason are poorly reducible. Therefore, these patients should be referred to high volume specialized centers, especially for more complex cases. The right balance between quality of life, risk of postoperative complications and life expectances needs to be done. In this subset of patients, where the estimated median overall survival is poor, the evaluation of long-term oncologic outcome is mandatory. However, an improved and standardized preoperative assessment, evaluating BMI, preoperative hemoglobin, comorbidities, previous treatments, and likely surgical complexity should be performed in order to help the physicians during the counseling with the patient.

Conflict of interest statement

The authors have no conflicts of interest to declare.

Author contribution

Authors participated in conception and design (TL, WAL, KA), acquisition and analysis of data (TL, MKC, WAL, KA), drafting the article or revising critically for important intellectual content (TL, CJ, MKC, WAL, MF, GGE, CWA, SG, KA), and gave final approval of the manuscript.

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