

Gynecologic Oncology: Pelvic Exenteration for Advanced or Recurring Cervical Cancer – A Single Center Analysis

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Abstract. *Background/Aim:* Cervical cancer is the most common gynecological indication for pelvic exenteration (PE). It is an ultima ratio approach to cure advanced or recurring tumors. This study aimed to evaluate data from a Single Center Institution in order to assess morbidity, mortality and survival data. *Patients and Methods:* Data of 24 patients, who underwent anterior (APE) or total PE (TPE) for cervical cancer at the University Hospital Marburg between 2011 and 2016, were extracted and retrospectively evaluated. Survival analysis was conducted using the Kaplan-Meier method. *Results:* Lymph node status was pN0, pN1 and pNX in 33.3%, 20.8% and 45.8% respectively. Negative margins could be achieved in 70.8%. A total of 16.7% of patients presented with metastatic disease, while 20.8%, 37.5% and 20.8% received 1, 2 or 3 modalities of treatment respectively; 20.8% underwent up-front PE. Predominant urinary diversion was an ileum conduit (66.7%). No complications were noted for 16.7%, major complications (\geq Clavien Dindo 3) in 41.7%. Overall

survival was 29.2% with a median overall survival (mOS) of 19.1 months. Curative PE was undertaken in 20 cases, with 2- and 3-year survival rates of 52.6% and 29.4% respectively, and a mOS of 24 months. Positive margins, metastatic disease, positive lymph nodes, TPE and a surgical time >6 h had a significant impact on OS. *Conclusion:* PE for cervical cancer remains a feasible option in cases of advanced or recurring tumors when alternative treatment options would fail. For selected patients it may represent a chance of cure with acceptable complication and satisfactory survival rates.

Pelvic exenteration (PE) is an ultra-radical procedure that is only performed in cases of advanced primary or recurrent carcinoma. It involves the removal of the female reproductive system, either with or without parts of the vulva and vagina, and – depending on the patient's symptoms or tumor invasion – the removal of the bladder (anterior PE; APE) and/or rectum (total or posterior PE; TPE or PPE). It is an interdisciplinary intervention that entails extensive reconstructive measures in the field of urinary and colonic diversion.

The most common gynecological indication for PE, when it was first described by Dr. A. Brunschwig, was cervical carcinoma (1) – a fact that has not changed in the last 70 years. Global Cancer Statistics 2018 showed that cervical cancer is the 4th most common cancer diagnosed and the 4th leading cause of cancer death among women worldwide with an estimated 570,000 cases and 311,000 deaths in 2018 (2). Initial treatment is conducted according to FIGO stage. Concomitant radiochemotherapy is recommended from stage IIB at the latest – often earlier – with stage IVA occupying a special position (3). Approximately 18-24 months after primary treatment an estimate of 20-30% of patients develop local recurrent disease (4, 5). However, a curative re-irradiation of the same anatomic site is mostly contraindicated and chemotherapy is ineffective due to irradiated tissue being

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Key Words: Cervical cancer, pelvic exenteration, urologic surgery, advanced gynecologic malignancy, surgical oncology.

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less vascularized (4, 6, 7). For those patients surgical treatment offers the only chance of local control and thus survival (7). This explains the significance of PE for patients with cervical cancer representing a therapeutical challenge.

Nonetheless, most studies on PE publish data obtained from all gynecological malignancies, with at least 50% of PE cases treated for cervical cancer (8-16) – only a few studies focus exclusively on cervical cancer (17-19).

Patients and Methods

Patients undergoing PE for a gynecological malignancy at the University Hospital Marburg between April 2011 and June 2016 were identified using the procedure code for PE. Those, who were operated because of cervical cancer, were specifically included in this study. Data were retrospectively analyzed.

Sociodemographic parameters such as age, BMI and ASA score (American Society of Anesthesiologists) were taken into consideration as well as histopathological parameters such as TNM classification and grading. In addition, previous therapies were evaluated. They were performed either with neoadjuvant intent or as initial treatment in case of recurrent disease. Also, type of PE (APE vs. TPE), kind of urinary diversion, operation time and blood products given were assessed. Early complications were evaluated using Clavien Dindo classification. A follow-up was conducted in January 2018 with data of comprehensive cancer center Marburg (CCC) to calculate overall survival (OS). Time of survival was either determined by death or in case of survival, last patient contact with either general practitioner or the patient's gynecologist.

Data were collected using Microsoft Excel for Mac (Version 16.39) followed by statistical analysis using IBM SPSS Statistics for Mac OS (Version 27.0.0). Continuous variables were analyzed in terms of median, mean and range whereas ordinal and nominal variables were evaluated in regard to frequencies. Correlation analysis was undertaken using Spearman Rho coefficient in case of ordinal and Pearson-Chi²-test as well as Phi test in case of nominal variables. Overall Survival was estimated applying Kaplan Meier survival analysis, finding differences or correlation using the Log-Rank (Mantel Cox) test. Statistical significance was acknowledged when *p*-value was equal or below 0.05.

Results

Patient characteristics. Within a 5-year period, a total of 47 patients underwent PE for gynecologic malignancy. Of those, 24 patients were treated for cervical cancer. The mean age was 52.2 years (range=29.7-72.6 years). A mean body mass index (BMI) of 23.4 kg/m² was noted (range=15.1-33.1 kg/m²) across the cohort. Four patients had a BMI over 30 kg/m², whereas 2 patients had a BMI below 17.5 kg/m². Comorbidities were assessed using the ASA Score. Half of the cohort (n=12) was classified as ASA score 2, another 41.7% (n=10) as ASA score 3. For one patient each (4.2%), ASA Score 1 and 4 was noted. Although smoking status was also evaluated, it could not be obtained for 8 patients (33.3%). Of the remaining 16, 9 were smokers or past smokers (37.5%), while 7 patients did not smoke (29.2%).

Histopathological features. The majority of the cohort (87.5%, n=21) was operated based on the diagnosis of squamous cell carcinoma, 3 patients underwent PE because of adenocarcinoma (12.5%, n=3). Grading could be assessed for 20 patients with grade distribution being 50% and 33.3% for G2 and G3 respectively. Most of the tumors were a pT4 stage (62.5%, n=15), whereas pT3 and pT2 was noted in 12.5% (n=3) each. Small tumor masses in terms of pT0 and pT1 were diagnosed in one case each (4.2%). Both patients had received neoadjuvant treatment beforehand.

Positive lymph nodes were found in 5 cases (20.8%), negative lymph nodes in 8 (33.3%). In a majority of cases, lymph nodes could not be assessed with 45.8% (n=11) having a NX stage noted. Of those 11 patients 6 had undergone LNE at our institution in the past.

Negative margins (R0) could be achieved in 17 patients (70.8%) while positive margins (R1) had to be noted in 6 patients (25%). Lymphovascular and perineural space invasion was found in 29.2% (n=7) and 33.3% (n=8) of the cohort respectively. Four patients (16.7%) had metastatic disease present by the time of PE: Distant metastatic disease was present in terms of positive inguinal lymph nodes in 2 cases – one other patient had peritoneal carcinomatosis and another one hepatic lesions. Half of the cohort had primary or persistent disease (50%, n=12), the remainder (45.8%, n=11) was treated because of a recurrence. Patient data are summarized in Table I.

Adjacent therapies. Of the entire cohort, 5 patients underwent up-front PE (20.8%), having had no treatment beforehand. Another 5 (20.8%) received one treatment modality prior (3 had radiotherapy, 2 surgical treatment). Approximately a third of the cohort (37.5%, n=9) had two previous treatment modalities, 7 patients received chemo- and radiotherapy before, another 2 had radio- and surgical therapy. Five patients were treated with all three treatment modalities prior (20.8%).

In 45.8% (n=11) previous therapy was administered with neoadjuvant intent. A significant correlation between neoadjuvant treatment and the achievement of negative margins (n=11, R0) could be shown (*p*=0.006). After PE, adjuvant therapy was recommended by an interdisciplinary tumor board in 50% of the cases (n=12). Data are summarized in Table II.

Surgical management. PE was performed in 37.5% of cases as TPE (n=9), while 15 patients underwent APE (62.5%). The most common choice for urinary diversion was an ileum conduit (66.7%, n=16). In 7 cases ureterocutaneostomies (UCN) with simultaneous nephrectomy of the opposite site were performed (29.2%). In one case a continent urinary diversion (Indiana Pouch) was performed (4.2%). Median operation time was 324 minutes (range=197-540 min). In 7 cases (29.2%) surgical time was longer than 6 hours. Perioperative blood transfusion was required in 75% of cases (n=18), with a median of 2 erythrocyte concentrates (range

Table I. Summarized patient data of patients undergoing pelvic exenteration.

	Variable
Age (years)	
Median (mean)	55.7 (52.2)
Range	29.7-72.6
BMI (kg/m ²)	
Median (mean)	23 (23.4)
Range	15.1-33.1
Histological grade	
G2	12 (50%)
G3	8 (33.3%)
Tumor stage	
T0	1 (4.2%)
T1	1 (4.2%)
T2	3 (12.5%)
T3	3 (12.5%)
T4	15 (62.5%)
Positive lymph nodes	
N0	8 (33.3%)
N1 and higher	5 (20.8%)
NX	11 (45.8%)
Positive margins	
R0	17 (70.8%)
R1	6 (25%)
Vascular space invasion	
V0	15 (75%)
V1	5 (25%)
Lymphovascular space invasion	
L0	17 (70.8%)
L1	7 (29.2%)
Distant metastasis	
M0	14 (58.3%)
MX	4 (16.7%)
M1	4 (16.7%)
Recurring disease	
Yes	12 (50%)
No	11 (45.8%)
Relapse time	
≤12 months	5 (20.8%)
13 to 24 months	2 (8.3%)
≥ 25 months	4 (16.7%)

Histopathological features according to TNM-classification.

from 0 to 9). Fresh-frozen plasma concentrate was perioperatively administered in 54.2% of cases (n=13). Patient hospital stay was between 10 and 65 days with a median of 25 days. Five patients were in need of ICU treatment postoperatively, with 2 patients staying there only one day while others were admitted for 2, 3 and 10 days (n=1) each. Data are summarized in Table III.

Complication rate. Complications were graded using the Clavien Dindo Classification. Overall, 16.7% had no complications at all (n=4). Minor complications were observed in 41.7% (n=10) as 5 patients each (20.8%) experienced complications according to

Table II. Summary of adjacent therapies (neoadjuvant, prior and adjuvant) received by patients undergoing pelvic exenteration.

	Variable
No. of previous therapy modalities	
None	5 (20.8%)
One	5 (20.8%)
Surgery	2 (8.3%)
Radiotherapy	3 (12.5%)
Two	9 (37.5%)
Chemo- and radiotherapy	7 (29.2%)
Surgical- and radiotherapy	2 (8.3%)
Three	5 (20.8%)
With neoadjuvant intent	11 (45.8%)
Adjuvant therapy	
None	11 (45.8%)
Yes	12 (50%)
Chemotherapy	3 (12.5%)
Radiotherapy	4 (16.7%)
Chemo- and radiotherapy	5 (20.8%)

Table III. Perioperative data including complications after pelvic exenteration and urinary diversion.

	Variable
Type of PE	
Anterior PE	15 (62.5%)
Total PE	9 (37.5%)
Operation time (minutes)	
Median	324 min
Range	197-540 min
Blood products given	
No	6 (25%)
Yes	18 (75%)
≤2	9 (37.5%)
>2	9 (37.5%)
Urinary diversion	
Ileum Conduit	16 (66.7%)
Uretero-cutaneostomy	7 (29.2%)
Pouch	1 (4.2%)
Total hospital stay (days)	
Median (mean)	25 (28.5)
Range	10-65
ICU admissions	5 (20.8%)

PE: Pelvic exenteration.

Clavien Dindo I and II. Major complications were noted in 41.7% (n=10) and distributed as follows: 8.3% (n=2) experienced complications in need of radiological, endoscopic or surgical treatment under local anesthesia (Clavien Dindo IIIa), 25% (n=6) needed intervention under general anesthesia (Clavien Dindo IIIb). One patient experienced a complication that called for ICU treatment (Clavien Dindo IVa) and one

Table IV. Postoperative complication rate stratified by Clavien Dindo Classification.

	Variable
Postoperative complications	
None	4 (16.7%)
Yes	20 (83.4%)
Minor (Clavien Dindo <III)	10 (41.7%)
Major (Clavien Dindo ≥III)	10 (41.7%)
Clavien Dindo I	5 (20.8%)
Clavien Dindo II	5 (20.8%)
Clavien Dindo IIIa	2 (8.3%)
Clavien Dindo IIIb	6 (25%)
Clavien Dindo Iva	1 (4.2%)
Early mortality (Clavien Dindo V)	1 (4.2%)

patient died within the early postoperative phase (Clavien Dindo V), representing early mortality (4.2%). Complication rates are summarized in Table IV.

Survival. Median follow-up for the entire cohort was 46 months (range 19 to 82 months). Median OS (mOS) was 19.1 months (range=0.4-35.6 months) with 1-, 2- and 3-year survival rate of 58.3%, 43.5% and 23.8% respectively. By the time of follow-up, 7 of 24 patients were still alive representing an OS-rate of 29.2% (Figure 1).

Patients who underwent curative PE (n=20) showed an OS-rate of 35% with a median OS of 24 months and 2- and 3-year survival rates of 52.6% and 29.4% respectively (Figure 2). For those with oligo distant metastatic disease (n=4) a median overall survival of 8.3 months was evaluated, which was significantly worse ($p<0.001$) than OS compared to patients without metastases.

Also, resection status showed a significant impact on survival. R1-status correlated with significantly worse mOS compared to R0-status (5 months vs. 24 months, $p<0.05$, Figure 3). Furthermore, a significant difference was found regarding lymph node status ($p=0.047$). For patients with pN0, mOS was not reached as 5 out of 8 patients were still alive. In comparison, mOS for those with pNX and pN1 or higher was 7.5 months and 8.9 months respectively (Figure 4).

Regarding surgical management, a significant benefit in mOS for those with APE vs. TPE (28 months vs. 5.8 months, $p<0.05$) was found as well as for those with an operation time under 6 hours (28 months vs. 7.5 months, $p<0.005$; see Figure 5 and Figure 6). Further analysis of survival data is summarized in Table V and Table VI.

No differences regarding mOS were found concerning complication rates (none vs. minor vs. major, $p=0.3$), primary or persistent disease vs. recurring disease ($p=0.23$), time to recurrence (within 12 months vs. 12 to 24 months vs. over 24 months, $p=0.78$), number of previous therapies

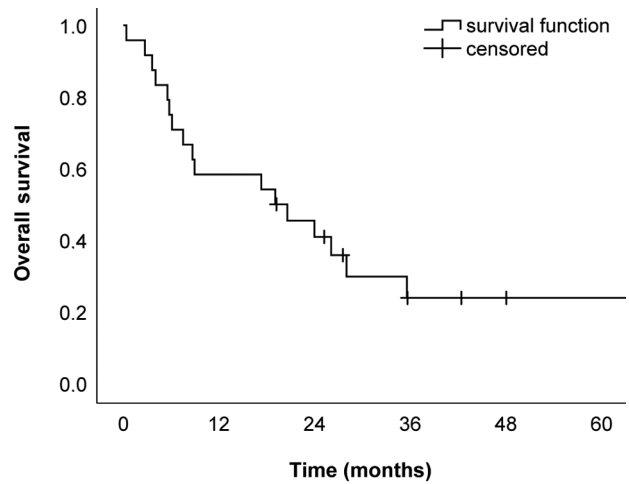


Figure 1. Overall survival for the entire cohort.

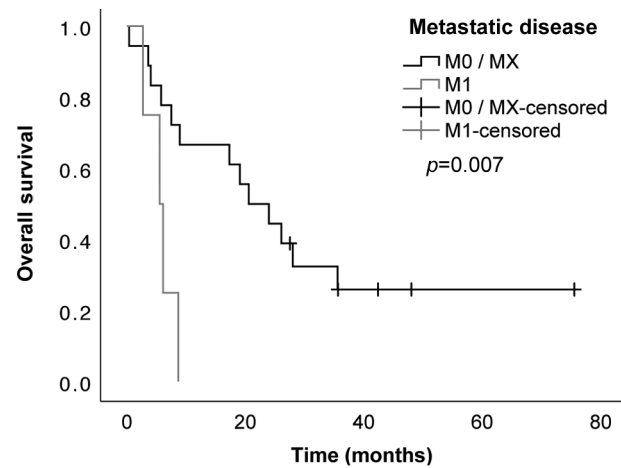


Figure 2. Overall survival in regard to metastatic disease present by the time of pelvic exenteration (PE). M0: No metastatic disease; M1: metastatic disease; MX: metastasis cannot be assessed.

(none vs. one vs. two vs. three, $p=0.33$) or neoadjuvant treatment ($p=0.79$). A tendency towards worse mOS in patients receiving adjuvant treatment was displayed (17.3 vs. 35.6 months, $p=0.065$). Analysis of further factors such as sociodemographic or histopathologic ones impacting mOS is summarized in Table V and Table VI.

Discussion

Nowadays, approximately 70% of women with cervical carcinoma are treated with concomitant chemoradiotherapy (4). However, about 20% to 30% develop recurrent disease within the radiation field with risk of recurrence increasing according to the initial FIGO stage (4). In case of local recurrence,

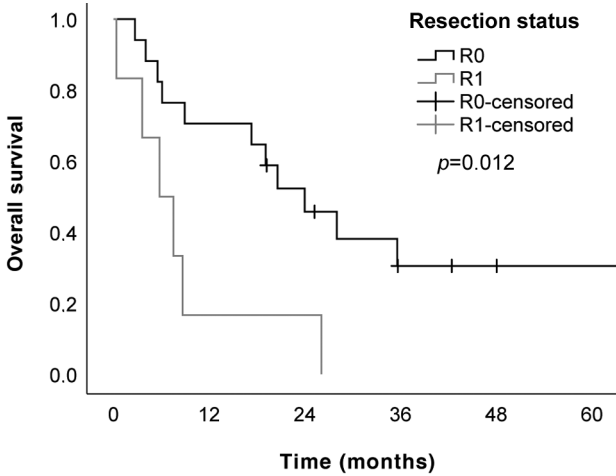


Figure 3. Overall survival in regard to resection status. R0: No microscopic residual tumor; R1: microscopic residual tumor.

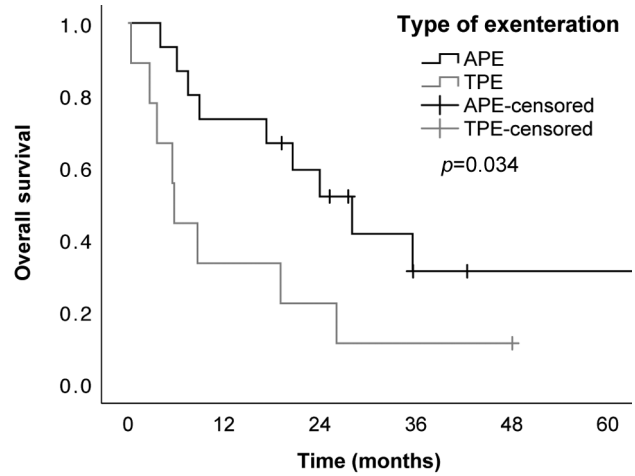


Figure 5. Overall survival in regard to anterior pelvic exenteration (APE) vs. total pelvic exenteration (TPE).

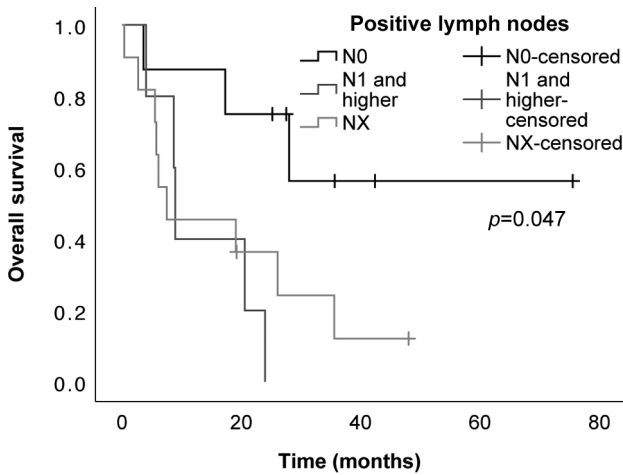


Figure 4. Overall survival in regard to lymph node status. N0: No regional lymph node metastasis; N1: regional lymph node metastasis; NX: lymph nodes cannot be assessed.

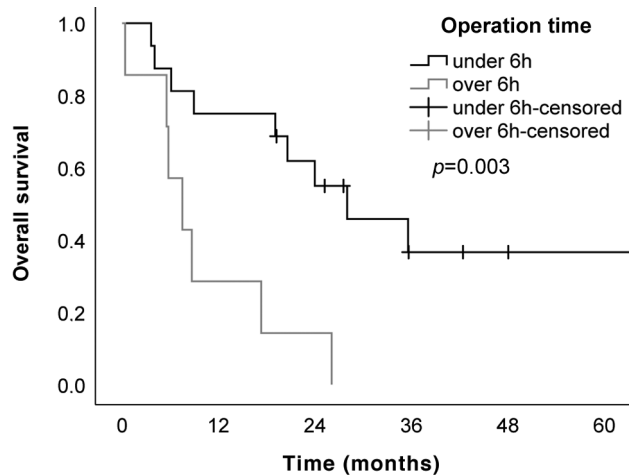


Figure 6. Overall survival in terms of operation time under vs. over 6 hours.

treatment options are limited – another radiotherapy of the same anatomic site is seen as contraindicated and chemotherapy is perceived to be ineffective due to the tumor being less vascularized when recurring in previously irradiated tissue (4). This gives meaning to the word “ultima ratio” treatment and explains why PE – in carefully selected patients – is the treatment of choice in case of recurrent or persistent disease. In case of tumor invasion into adjacent organs (FIGO IVA) and fistula formation, upfront PE, which was performed in 20.8% patients in this cohort, is justifiable (3).

In such complex cases, where patients have received one or more previous therapies, high morbidity rates after such

extensive interventions need to be expected. However, in our extensively pretreated cohort (79.2%), 16.8% of patients did not experience any complications with another 41.7% only suffering minor complications with need of conservative treatment. We report a major complication rate of 41.7%. This rate is in accordance with other reported morbidity rates such as Schmidt *et al.*'s 51% (17). Previous pelvic irradiation and operative time are known factors to influence morbidity (4). However, in our cohort complication rate was not influenced by either one of these.

Also, no differences in complication rates were found in regard to urinary diversion. In this cohort, 7 patients (29.9%)

Table V. Analysis of factors impacting overall survival.

Variable (n)		p-Value
BMI	<25 kg/m ² (17)	0.89
	>25 kg/m ² (7)	
Age	<65 years (21)	0.71
	>65 years (3)	
ASA-Score	1 (1)	0.36
	2 (12)	
	3 (10)	
	4 (1)	
Recurrence	No (12)	0.23
	Yes (n=11)	
Time to recurrence (n=11)	<12 months (5)	0.78
	12-24 months (2)	
	>24 months (4)	
Number of previous therapies	None (5)	0.33
	1 (5)	
	2 (9)	
	3 (5)	
Neoadjuvant treatment	Yes (11)	0.78
	No (13)	
Adjuvant treatment	Yes (12)	0.07
	No (12)	
Complication rate	None (4)	0.3
	Minor (10)	
	Major (10)	
Type of urinary diversion	Ileum conduit (16)	0.96
	UCN (7)	
	Pouch (1)	
Type of PE	APE (15)	0.034
	TPE (9)	
Operation time	<6 h (16)	0.003
	>6 h (7)	

APE: Anterior pelvic exenteration; TPE: total pelvic exenteration. Significant p-Values are shown in bold.

received an UCN with simultaneous nephrectomy whereas 66.7% were treated with an ileum conduit. This differs from recently published studies in which UCN was rarely performed. In patients with cervical carcinoma hydronephrosis is common due to tumor invasion often resulting in loss of kidney function. If indicated, a preoperative MAG-III scan can be helpful to determine split renal function. In case of lost renal function, UCN with simultaneous nephrectomy may be a wise choice of urinary diversion as it does not require complicated reconstruction techniques, keeping operation time as short as possible. Especially patients undergoing PE would benefit most, as they are known to have concomitant comorbidities and are more prone to extensive complications. Furthermore, UCN is a valid choice for previously irradiated patients for which surgeons would fear postoperative intestine anastomosis- and wound healing insufficiencies.

Almost half of the patients undergoing PE had neoadjuvant treatment prior to PE. In this cohort, all of these cases showed negative margins in surgical specimen. Our data supports the statement made by Landoni and coworkers,

Table VI. Analysis of histopathological factors impacting overall survival.

Variable (n)		p-Value
Histology	Squamous cell (21)	0.76
	Adeno cell (3)	
Grading	G2 (12)	0.72
	G3 (8)	
	Tumor size	
Tumor size	T2 (3)	0.43
	T3 (3)	
	T4 (15)	
	Positive lymph nodes	
Positive lymph nodes	N0 (8)	0.047
	N1 (5)	
	NX (11)	
Positive margins	R0 (17)	0.012
	R1 (6)	
Lymphovascular invasion	L0 (17)	0.996
	L1 (7)	
	Vascular invasion	
Vascular invasion	V0 (15)	0.4
	V1 (5)	
	Metastatic disease	
Metastatic disease	M0 (20)	0.007
	M1 (4)	

Histopathological features according to TNM-classification. Significant p-Values are shown in bold.

who proposed that neoadjuvant chemotherapy may have a positive impact on prognosis of seemingly poorer candidates (20). They showed that negative margins could be achieved in 74% of patients receiving neoadjuvant chemotherapy opposed to 80% of those, who underwent up-front PE. Patients who received neoadjuvant treatment initially faced poorer prognostic factors due to more frequent pelvic side wall disease and larger tumor masses. However, there was no significant difference regarding OS between those two groups, which lead the authors to conclude that neoadjuvant treatment represents a feasible therapeutic option with comparable complication rates for those who are seemingly poor candidates for up-front PE (20).

While a significant influence of neoadjuvant treatment on margin status could be shown in our data, there were no significant findings in regard to OS. As described by Sardain *et al.*, tumor free resection margins are known to be “a major significant and independent prognostic factor” impacting OS (4). The impact of other histopathological factors is still debated as no consensus has yet been found. Our data show that survival correlated significantly with pelvic lymph node status ($p < 0.05$) supporting other reported data (10, 21–25). However, other groups found that survival is not negatively impacted by positive pelvic lymph nodes (11, 18). Schmidt *et al.* could not find a significant difference in OS regarding pelvic lymph node involvement, whereas the presence of para-aortic lymph nodes impacted survival significantly (17). Goldberg *et al.* reported that they would abort the procedure when positive lymph nodes were detected intraoperative (9). Ruthledge and McGuffee concluded that although patients with pelvic lymph nodes have

a poorer prognosis some long-term survivals can be achieved making PE feasible in case of pelvic lymph nodes in order to improve quality of life or to extend life (26).

In addition, a significant difference regarding OS was found with respect to type of PE ($p=0.034$), as those who received TPE seemed to have a poorer prognosis. This may go hand in hand with worse survival of those, who had an operation time over six hours – a difference that was also significant in our cohort ($p=0.003$). Five of 8 TPEs lasted longer than 6 hours, another 3 lasted just a bit shorter (340, 356 and 358 min). None were shorter than 324 min, which was the median surgical time for the entire cohort. This is most likely due to a more extensive nature of the operation as well as more complicated reconstruction techniques. Interestingly, there was no significant difference in terms of Clavien Dindo classification between those who underwent APE vs. TPE ($p=0.36$). Tumors for which TPE has to be performed are normally more advanced which may also impact survival. Also, Yoo *et al.* observed a negative impact of rectal involvement (18); a fact that has not been observed by others and may be subject of future studies.

PE remains to be an ultima-ratio procedure that may present cure for patients with far advanced or recurring carcinoma. In case of curative PE, overall survival was 35% with a mOS of 24 months. Our data are in line with findings of Graves *et al.*, who analyzed data from 313 women using the National Cancer Database and also found an mOS of 24 months (25). Overall, differing 5-year-OS rates have been reported in the past. The majority of published data cover all gynecologic malignancies and is therefore not directly comparable to our data. A meta-analysis published by Sardain *et al.* reported cervical carcinoma-specific 5-year-OS-rates between 24.4% to 64% (8, 9, 16–18, 24). Nonetheless, it should be acknowledged that these differences could occur because of cohort selection. Schmidt *et al.* for instance enrolled a total of 282 patients into their study (17). However, the published 5 year OS-rate of 64% reflects the OS of those with negative resection margins ($n=133$), since only their PE was considered curative - a fact which can only be determined postoperatively (17). The 5-year-OS-rate for the entire cohort was 41% (17). In 1948, initially reported surgical mortality was 23% (1). Surgical techniques as well as postoperative care have improved over the past decades, so that – 70 years later – perioperative mortalities between 0% and 5% can be noted (9, 17, 19). This is also reflected by our data.

Overall, PE remains to be a highly morbid procedure that requires extensive patient counselling before and careful follow-up afterwards. It represents a challenge for the entire medical staff involved. Nevertheless, for certain patients – especially in case of tumor invasion into the bladder and/or the rectum, fistula formation or recurrence after previous therapies – it represents the only treatment that can offer cure in otherwise “lost cases” with satisfactory survival rates.

Limitations and strengths. Certain limitations influence the findings of this study: Most important, its retrospective character and the rather small cohort size, which made overall statistical analysis difficult and did not allow multivariate analysis. The fact that late morbidity was not evaluated after initial discharge from University Hospital Marburg can also be seen as a further limitation of this study design. It was not possible to consider all late complications that occurred after PE, as many patients returned home far from University Hospital Marburg, which is a high-volume center. Thus, possible late complications might have been treated elsewhere. Therefore, it was decided not to collect late morbidity data as the data would have been incomplete.

PE is an ultra-radical procedure that requires a highly skilled medical team. Due to its extensive nature, not every patient qualifies as fit enough for PE. This both results in PE being rarely performed, thus leading to small cohort sizes. Our data were collected over a short period of five years, which stands out amongst other studies, for which data were collected over decades. Herein we see the strength of the data published as we thereby ensured a comparable setting in terms of preoperative staging, tumor board decision-making as well as intra- and postoperative management. Because data collection was more individual compared to broad statistical analysis, a more thorough assessment, particularly of complication rates, is possible when medical records are reviewed individually. Furthermore, most published studies concentrate on PE for gynecologic malignancies rather than cervical carcinoma in particular. However, as tumor biology and pathology differ from entity to entity, publishing data specifically for cervical cancer represent another strength of our study as it aims to improve future patient care and decision making for this specific gynecologic malignancy.

Conflicts of Interest

The Authors declare no conflicts of interest in relation to this study.

Authors' Contributions

A. Hegele and U. Wagner conceptualized the project. A Hegele administered and supervised, J. Boekhoff and L. ter Glane collected the data, L. ter Glane conducted statistical analysis and wrote the original draft, A. Hegele, U. Wagner and J. Boekhoff reviewed and edited the draft.

References

- 1 Brunschwig A: Complete excision of pelvic viscera for advanced carcinoma; a one-stage abdominoperineal operation with end colostomy and bilateral ureteral implantation into the colon above the colostomy. *Cancer* 1(2): 177-183, 1948. PMID: 18875031. DOI: 10.1002/1097-0142(194807)1:2<177::aid-cnrcr2820010203>3.0.co;2-a

- 2 Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA and Jemal A: Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 68(6): 394-424, 2018. PMID: 30207593. DOI: 10.3322/caac.21492
- 3 Bhatla N, Aoki D, Sharma DN and Sankaranarayanan R: Cancer of the cervix uteri. *Int J Gynaecol Obstet* 143 Suppl 2: 22-36, 2018. PMID: 30306584. DOI: 10.1002/ijgo.12611
- 4 Sardain H, Lavoue V, Redpath M, Bertheuil N, Foucher F and Levêque J: Curative pelvic exenteration for recurrent cervical carcinoma in the era of concurrent chemotherapy and radiation therapy. A systematic review. *Eur J Surg Oncol* 41(8): 975-985, 2015. PMID: 25922209. DOI: 10.1016/j.ejso.2015.03.235
- 5 Peiretti M, Zapardiel I, Zanagnolo V, Landoni F, Morrow CP and Maggioni A: Management of recurrent cervical cancer: a review of the literature. *Surg Oncol* 21(2): e59-e66, 2012. PMID: 22244884. DOI: 10.1016/j.suronc.2011.12.008
- 6 Marnitz S, Köhler C, Müller M, Behrens K, Hasenbein K and Schneider A: Indications for primary and secondary exenterations in patients with cervical cancer. *Gynecol Oncol* 103(3): 1023-1030, 2006. PMID: 16890276. DOI: 10.1016/j.ygyno.2006.06.027
- 7 Höckel M and Dornhöfer N: Pelvic exenteration for gynaecological tumours: achievements and unanswered questions. *Lancet Oncol* 7(10): 837-847, 2006. PMID: 17012046. DOI: 10.1016/S1470-2045(06)70903-2
- 8 Berek JS, Howe C, Lagasse LD and Hacker NF: Pelvic exenteration for recurrent gynecologic malignancy: survival and morbidity analysis of the 45-year experience at UCLA. *Gynecol Oncol* 99(1): 153-159, 2005. PMID: 16054678. DOI: 10.1016/j.ygyno.2005.05.034
- 9 Goldberg GL, Sukumvanich P, Einstein MH, Smith HO, Anderson PS and Fields AL: Total pelvic exenteration: the Albert Einstein College of Medicine/Montefiore Medical Center Experience (1987 to 2003). *Gynecol Oncol* 101(2): 261-268, 2006. PMID: 16426668. DOI: 10.1016/j.ygyno.2005.10.011
- 10 Maggioni A, Roviglione G, Landoni F, Zanagnolo V, Peiretti M, Colombo N, Bocciolone L, Biffi R, Minig L and Morrow CP: Pelvic exenteration: ten-year experience at the European Institute of Oncology in Milan. *Gynecol Oncol* 114(1): 64-68, 2009. PMID: 19411097. DOI: 10.1016/j.ygyno.2009.03.029
- 11 Benn T, Brooks RA, Zhang Q, Powell MA, Thaker PH, Mutch DG and Zigelboim I: Pelvic exenteration in gynecologic oncology: a single institution study over 20 years. *Gynecol Oncol* 122(1): 14-18, 2011. PMID: 21444105. DOI: 10.1016/j.ygyno.2011.03.003
- 12 McLean KA, Zhang W, Dunsmoor-Su RF, Shah CA, Gray HJ, Swensen RE and Goff BA: Pelvic exenteration in the age of modern chemoradiation. *Gynecol Oncol* 121(1): 131-134, 2011. PMID: 21256580. DOI: 10.1016/j.ygyno.2010.11.044
- 13 Baiocchi G, Guimaraes GC, Rosa Oliveira RA, Kumagai LY, Faloppa CC, Aguiar S, Begnami MD, Soares FA and Lopes A: Prognostic factors in pelvic exenteration for gynecological malignancies. *Eur J Surg Oncol* 38(10): 948-954, 2012. PMID: 22818842. DOI: 10.1016/j.ejso.2012.07.002
- 14 Chiantera V, Rossi M, De Iaco P, Koehler C, Marnitz S, Fagotti A, Fanfani F, Parazzini F, Schiavina R, Scambia G, Schneider A and Vercellino GF: Morbidity after pelvic exenteration for gynecological malignancies: a retrospective multicentric study of 230 patients. *Int J Gynecol Cancer* 24(1): 156-164, 2014. PMID: 24362721. DOI: 10.1097/IGC.0000000000000011
- 15 de Gregorio N, de Gregorio A, Ebner F, Friedl TWP, Huober J, Hefty R, Wittau M, Janni W and Widschwendter P: Pelvic exenteration as ultimate ratio for gynecologic cancers: single-center analyses of 37 cases. *Arch Gynecol Obstet* 300(1): 161-168, 2019. PMID: 31011878. DOI: 10.1007/s00404-019-05154-4
- 16 Kaur M, Joniau S, D'Hoore A, Van Calster B, Van Limbergen E, Leunen K, Penninckx F, Van Poppel H, Amant F and Vergote I: Pelvic exenterations for gynecological malignancies: a study of 36 cases. *Int J Gynecol Cancer* 22(5): 889-896, 2012. PMID: 22617477. DOI: 10.1097/IGC.0b013e31824eb8cd
- 17 Schmidt AM, Imesch P, Fink D and Egger H: Indications and long-term clinical outcomes in 282 patients with pelvic exenteration for advanced or recurrent cervical cancer. *Gynecol Oncol* 125(3): 604-609, 2012. PMID: 22406639. DOI: 10.1016/j.ygyno.2012.03.001
- 18 Yoo HJ, Lim MC, Seo SS, Kang S, Yoo CW, Kim JY and Park SY: Pelvic exenteration for recurrent cervical cancer: ten-year experience at National Cancer Center in Korea. *J Gynecol Oncol* 23(4): 242-250, 2012. PMID: 23094127. DOI: 10.3802/jgo.2012.23.4.242
- 19 Tanaka S, Nagase S, Kaiho-Sakuma M, Nagai T, Kurosawa H, Toyoshima M, Tokunaga H, Otsuki T, Utsunomiya H, Takano T, Niikura H, Ito K and Yaegashi N: Clinical outcome of pelvic exenteration in patients with advanced or recurrent uterine cervical cancer. *Int J Clin Oncol* 19(1): 133-138, 2014. PMID: 23404487. DOI: 10.1007/s10147-013-0534-9
- 20 Landoni F, Zanagnolo V, Rosenberg PG, Lopes A, Radice D, Bocciolone L, Aletti G, Parma G, Colombo N and Maggioni A: Neoadjuvant chemotherapy prior to pelvic exenteration in patients with recurrent cervical cancer: single institution experience. *Gynecol Oncol* 130(1): 69-74, 2013. PMID: 23474343. DOI: 10.1016/j.ygyno.2013.02.038
- 21 Westin SN, Rallapalli V, Fellman B, Urbauer DL, Pal N, Frumovitz MM, Ramondetta LM, Bodurka DC, Ramirez PT and Soliman PT: Overall survival after pelvic exenteration for gynecologic malignancy. *Gynecol Oncol* 134(3): 546-551, 2014. PMID: 25014540. DOI: 10.1016/j.ygyno.2014.06.034
- 22 Shingleton HM, Soong SJ, Gelder MS, Hatch KD, Baker VV and Austin JM Jr: Clinical and histopathologic factors predicting recurrence and survival after pelvic exenteration for cancer of the cervix. *Obstet Gynecol* 73(6): 1027-1034, 1989. PMID: 2726106. DOI: 10.1097/00006250-198906000-00024
- 23 Symmonds RE, Pratt JH and Webb MJ: Exenterative operations: experience with 198 patients. *Am J Obstet Gynecol* 121(7): 907-918, 1975. PMID: 1115180. DOI: 10.1016/0002-9378(75)90908-4
- 24 Baiocchi G, Guimaraes GC, Faloppa CC, Kumagai LY, Oliveira RA, Begnami MD, Soares FA and Lopes A: Does histologic type correlate to outcome after pelvic exenteration for cervical and vaginal cancer? *Ann Surg Oncol* 20(5): 1694-1700, 2013. PMID: 23212765. DOI: 10.1245/s10434-012-2768-6
- 25 Graves S, Seagle BL, Strohl AE, Shahabi S and Nieves-Neira W: Survival after pelvic exenteration for cervical cancer: A National Cancer Database study. *Int J Gynecol Cancer* 27(2): 390-395, 2017. PMID: 27984375. DOI: 10.1097/IGC.0000000000000884
- 26 Rutledge FN and McGuffee VB: Pelvic exenteration: prognostic significance of regional lymph node metastasis. *Gynecol Oncol* 26(3): 374-380, 1987. PMID: 2435621. DOI: 10.1016/0090-8258(87)90029-1

Received January 3, 2022
 Revised February 28, 2022
 Accepted March 17, 2022