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Research Article

Pelvic Exenterations for Persistent or Recurrent Cervical Cancer following Chemoradiation: Analysis of 51 cases

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Abstract

Objective: To evaluate the outcome for 51 cases of persistent or recurrent cervical cancer (PRCC) treated by pelvic exenteration (PE) following chemo radiation and based on an 11-year institutional experience. **Material and Methods:** Clinical records were analyzed for patients with cervical cancer (CC) treated with concomitant chemo radiation therapy (CCRT) in the Oncology Unit (OU) of the General Hospital of Mexico (GHM) from January 1, 2008 to December 31, 2018 and operated for PE due to tumor persistence or recurrence. **Results:** Anterior pelvic exenterations (APE) were performed on 22 cases (43.1%), total pelvic exenterations (TPE) on 26 cases (51.0%), and posterior pelvic exenterations (PPE) on 3 cases (5.9%). Postoperative major complication (MC) occurred in 12 patients (23.5%), but with no postoperative mortality. Kaplan Meier curves showed a 5-year overall survival (OS) of 5.9 % and an OS of 39.2% for 25 months Univariate analysis showed statistically significant correlations between disease-free survival (DFS) and rectal invasion ($p < 0.0001$), parametrial invasion ($p = 0.031$), presence of distant metastases ($p < 0.0001$), and surgery performed 12 months after the completion of CCRT ($p = 0.031$). Multivariate analysis showed significant association between DFS and the development of distant metastases ($p = 0.04$), and between OS and

rectal invasion ($p < 0.0001$). Twelve of the 51 patients (23.5%) developed tumor recurrences, with 9 of these (75%) occurring at distant sites. **Conclusions:** In this series of PRCC patients, DFS was significantly associated with parametrial and rectal invasion and with surgery performed 12 months after the diagnosis of recurrence. In multivariate analysis, OS was significantly associated with rectal invasion only. Since 75% of recurrences occurred at distant sites, patients at risk should be considered for adjuvant chemotherapy (CT).

Keywords: Pelvic exenteration; Cervical cancer; Chemoradiation

Abbreviations: PE: Pelvic Exenteration; PRCC: Persistent or Recurrent Cervical Cancer; CC: Cervical Cancer; OU: Oncology Unit; GHM: General Hospital of Mexico; CCRT: Concomitant Chemoradiation; APE: Anterior Pelvic Exenterations; TPE: Total Pelvic Exenterations; PPE: Posterior Pelvic Exenterations; MC: Mayor Complications; OS: Overall Survival; DFS: Disease-Free Survival; CT: Chemotherapy; RT: Radiotherapy; GY: Treatment unit of radiotherapy; IMRT: Intensity-modulated radiation therapy; VMAT: Volumetric arc therapy; FIGO: International Federation of Gynecology and Obstetrics; PW: Pelvic Wall; SCC: Squamous cell carcinoma; EBRT: External Beam Radiotherapy; GC: Gynecological Cancer; RO: Absence of residual tumor; ADC: Adenocarcinoma; CS: Clinical Stages; BT: Brachytherapy

Introduction

Cervical cancer (CC) represents a major public health problem in Mexico, with more than 4,000 deaths recorded each year [1]. CC represents 60% of hospital admissions and is usually diagnosed at an advanced stage that requires radiotherapy (RT) as the primary treatment. This disease has a high mortality rate and occurs in a population that often lacks social security [2,3]. PE offers the last chance for cure in a select group of patients with persistent or recurrent cervical cancer (PRCC) localized to the pelvis [4-6]. These patients have a morbidity of between 30% and 80% [4,7- 11], a mortality of less than 5% [9-11] and a 5-year disease-free survival (DFS) rate less than 45% [8,9,11-13]. The use of platinum concomitant with RT increases the response rate in locally advanced CC [5,6,14]. Moreover, at the authors' institution it reduces the number of laparotomies, complementary hysterectomies ± lymphadenectomies or pelvic exenterations (PE) compared to earlier experience with RT alone [15-17]. Here, we evaluated the outcome of patients with invasive PRCC who underwent PE as salvage surgery following chemoradiation. This study was based on 11 years of experience at our institution.

Materials and Methods

This was a retrospective study conducted at the General Hospital of Mexico (GHM) Oncology unit on 51 patients who underwent PE for PRCC following complete or incomplete concomitant chemoradiation (CCRT) between January 1, 2008 and December 31, 2018. The CCRT consisted of External Beam Radiation Therapy (50-54 Gy) with a linear accelerator, intensity-modulated radiation therapy (IMRT) or volumetric arc therapy (VMAT) + chemotherapy (CT) with Cisplatin or carboplatin weekly at conventional doses, intracavitary radiotherapy (brachytherapy 30 Gy) high 3D rate with Iridium 192 or low dose rate with Cesium 137, or Tele therapy (50-54 Gy) plus chemotherapy with Cisplatin or Carboplatin. Anterior pelvic exenteration (APE) involved resection of the uterus, adnexa, parametria, ureters, urinary bladder and pelvic lymph nodes. Total pelvic exenteration (TPE) also included the rectum, while posterior pelvic exenteration (PPE) included the rectum but preserved the urinary tract. Most surgical procedures were superior to the elevator muscle of the anus [4,18]. Following bowel preparation, a supra and infra-umbilical median laparotomy was performed and the abdominal and pelvic cavity reviewed. When there was a suspicion of abdominal activity outside the pelvis or of a tumor fixed to the pelvic wall, an intraoperative biopsy was taken of the lesion and pelvic lymph node dissection was started on the side most affected by the tumor. When there was a positive report for metastasis of the biopsied tissue, the surgical intervention was terminated and lymph node dissection was completed in the rest of the patient. The specimen was extracted in a block, with sufficient margin to the vagina and removal of the bladder and/or rectum. In patients with a trans-operative report of tumor at the margins of the vagina, these were enlarged, requiring in some patients an enlargement through the perineum. Reconstruction of the urinary tract was performed using a de-functionalized segment of the terminal ileum, Bricker's ileal conduit, [18] or with a difunctional segment of the sigmoid rectum (sigmoid conduit). A colostomy terminal was performed for TPE and PPE cases. The 2018 version of the Federation International of Gynecology and Obstetrics (FIGO) clinical classification was used [19]. This includes stage I, IB2 and IB3 lesions, as well as stage III, IIIA and IIIB neoplasms. For the evaluation of surgical procedures, the morbidity and mortality by intervention performed and by the type of previous treatment received was recorded. Surgical mortality was considered to represent death with 30 days of intervention. Morbidity events included major complications (MC) that put the patients' life at risk, such as dehiscence of the anastomotic sutures. Events that did not meet this requirement were considered to be minor complications and included infection of the surgical wound, pelvic or wall abscesses, etc. The clinic pathological variables analyzed for association with DFS and overall survival (OS) included: patient age, disease evolution

according to clinical stage, history of CCRT with or without brachytherapy, time elapsed between the completion of treatment and surgery, type of exenteration performed, presence or absence of local or regional residual disease in the surgical specimen (cervix, vagina, uterine body, parametrial invasion with or without infiltration to the pelvic wall (PW), lymphovacular infiltration, presence of tumor in section margins, metastases to the adnexa, and lymph node metastases. Also considered in the survival analyses were histologic evidence of invasion of the bladder or rectum, and the presence of hydronephrosis previously reported in preoperative imaging studies. Descriptive statistics were used to analyze the above variables, with the calculation of means and proportions for numerical and categorical variables as appropriate. Survival analysis was performed using the Kaplan-Meier method and differences between groups assessed using the log-rank test. Univariate and multivariate Cox proportional hazards models were used to identify variables that were significantly correlated with DFS and OS. Ninety five percent confidence intervals were calculated for the odds ratio (OR). P values of less than 0.05 were considered statistically significant. All statistical analyses were performed with the SPSS 22.0 statistical program.

Results

Clinicopathological characteristics

The clinical and pathological details of 51 PRCC patients in which PE was performed during the study period are shown in Table 1. The youngest patient was aged 24 years and the oldest was 75, with a mean age of 46.3 years. Squamous cell carcinoma (SCC) was diagnosed in 76.5% of patients, and 94.1% had locally advanced CC at the time of diagnosis. All patients received RT + CT as the primary treatment. APE was performed in 22 cases (43.1%), TPE in 26 (51.0%) and PPE in 3 (5.9%). Bricker's ileal conduit was the most common urinary diversion (70.5% of cases). The surgical time ranged from 3.5 hours to 6.5 hours, with a mean of 4.45. Average blood loss was 1200 cc with a range of 400 cc to 4,500 cc. The hospitalization period ranged from 7 to 42 days, with a mean of 14. The type of PE performed and the pathology details are shown in Table 2.

Variable	Number of patients	Percent
Age in years		
21–30	3	5.8
31–40	12	23.5
41–50	23	45
51–60	6	11.7
61–70	7	13.7
< 24, >75, mean: 46.3 years		
Pathology		
Squamous cell carcinoma	39	76.5
Adenocarcinoma	12	23.5
Clinical Stage		
I	3	5.9
II	28	54.9
III	20	39.2
Schedule of Radiotherapy		
Chemoradiation*	39	76.4
External beam radiation + Chemotherapy	12	23.5
*External beam radiation plus chemotherapy + brachytherapy		

Table 1: Clinicopathological characteristics of the 51 patients.

Variable	Number	Percent
Type of pelvic exenteration		
Anterior	22	43.1
Total	26	51
Posterior	3	5.9
Central infiltration		
Yes	34	66.7
No	17	33.3
Parametrial Invasion		
Yes	23	45.1
No	28	54.9
Pelvic Side Wall Disease		
Yes	4	7.8
No	47	92.2
Bladder Invasion		
Yes	5	9.8
No	46	90.2
Rectal Invasion		
Yes	5	9.8
No	46	90.2
Uterine Corpus Invasion		
Yes	2	3.9
No	49	96.1
Lymph Node Metastasis		
Yes	14	27.5
No	37	72.5

Table 2: Type of exenteration and pathology report information.

Morbidity and Mortality

Postoperative complications occurred in 19 patients (37.2%), of which 7 (13.7%) were considered minor and 12 (23.5%) as MC. The MC recorded for each type of PE are shown in Table 3. Only 6 of 22 (27.2%) APE patients and 6 of 26 (23.0%) TPE patients suffered MC (p = 0.740). Eleven of the 12 MC occurred in patients who received complete CCRT, (11/39, 28.2%) and the remaining 1/12, (8.3%) occurring in a patient who received external beam radiotherapy (EBRT) plus CT (p = 0.302). Nine of the 12 MC (75%) were due to dehiscence of the anastomotic sutures (Table 4), with 4 of these cases resolved by additional surgical procedures. No postoperative mortality was recorded in this series.

Previous Treatment	(a) Anterior*		(b) Total*		Posterior		Total	
	No.	%	No.	%	No.	%	No	%
(I) Complete Pelvic Cycle + Chemotherapy (39 cases)								
Persistent Cervical Cancer	3/8	37.5	4/12	33.3	0/2	-	7/22	31.8
Recurrent Cervical Cancer	2/7	28.5	2/9	22.2	-	-	4/17	23.5
(I) Total:**							11/39	28.2
(II) External beam radiation + Chemotherapy (12 cases)								
Persistent Cervical Cancer	1/5	20	0/5	-	-	-	1/10	10.0
Recurrent Cervical Cancer	0/1	-	-	-	0/1	-	0/2	-
(II) Total:**							1/12	8.3
Total global	6/22	27.2	6/51	23	0/3	-	12/51	23.5

*(a) vs (b), p = 0.740. ** (I) vs (II), p = 0.302

Table 3: Pelvic Exenteration: frequency of postoperative complications.

Complication	No.	Percent
Urinary fistula	6	11.7
Intestinal fistula	3	5.8
Pneumonia	2	3.9
Rectum vaginal fistula	1	1.9
Total	12/51	23.5

Table 4: Major postoperative complications.

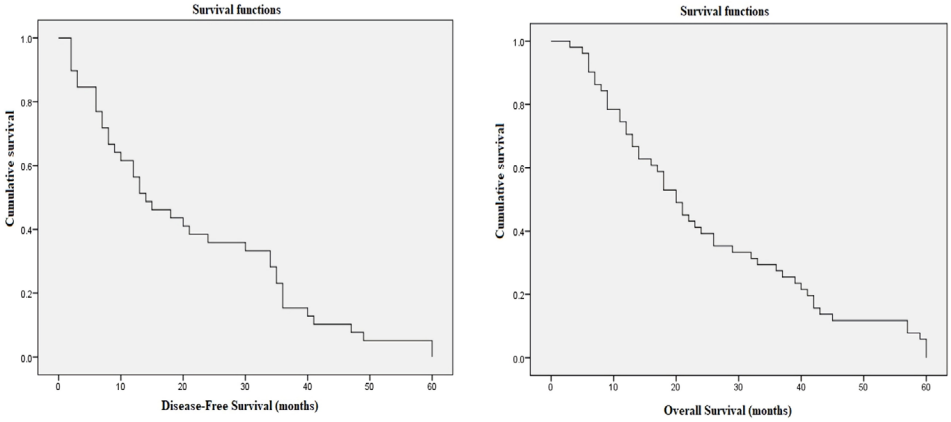

Figure 1.DFS at 24 and 60 months: 38.5% and 5.1% OS at 24 and 60 months: 39.2% and 5.9%

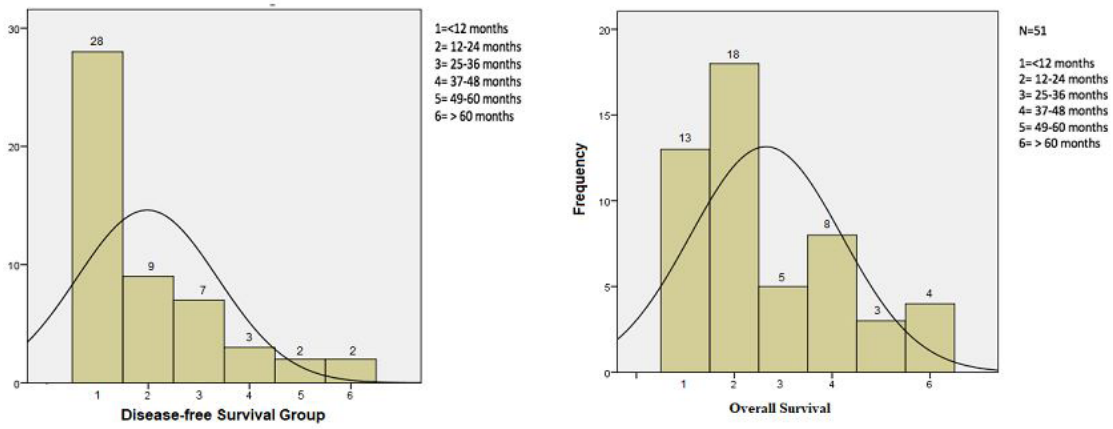

Figure 2. Disease-Free Survival, (DFS) and Overall Survival, (OS) in 51 patients. (25 months: 27.4% and 39.2% respectively)

Treatment results

Thirty-seven patients (72.0%) were lost to follow up during the first 24 months after surgery and hence the tumor status of these patients was unknown. Kaplan Meier curves showed a 5-year OS of 5.9% and OS of 39.2% for 25 and more months. Figures 1 and 2.

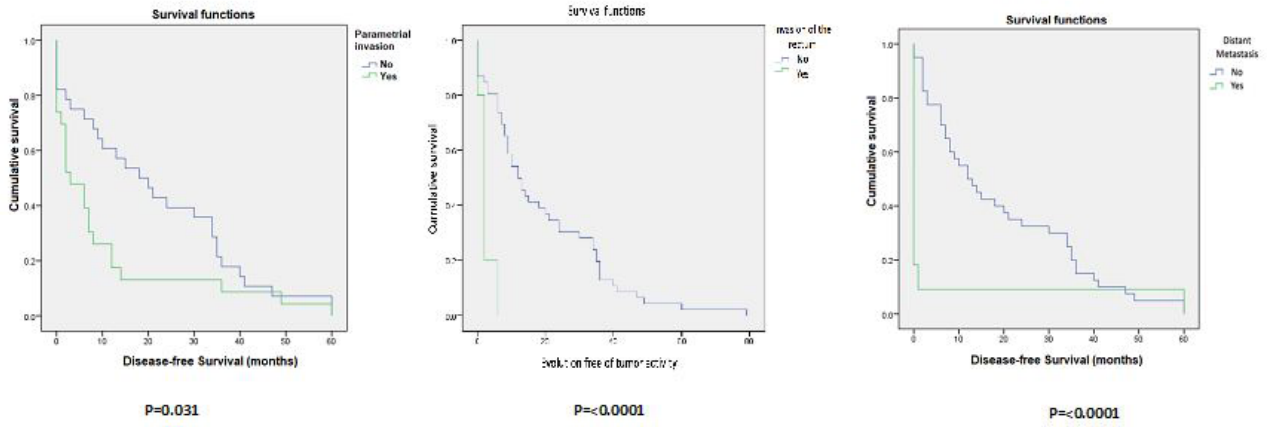

Figure 3. Curves of disease free-survival, (DFS) with significance, based on the log-rank test.

The log-rank test was used to analyze the effect of different variables on DFS (Table 5). Statistically significant associations were found between DFS and rectal invasion ($p < 0.0001$), parametrial invasion ($p = 0.031$), and the presence of distant metastases ($p < 0.0001$) Figure 3.

Variable	Disease-free survival (months)		Odds ratio (IC 95%)	Log Rank Test
Age group			1.247 (.708 – 2.197)	0.427
< 45 years	16.23 (15.4)	9.0 (30 -3)		
> 45 years	18.84 (20.1)	10.0 (35 – 6)		
Clinical Stage				0.334
I	24.6 (21.7)	18 (49 – 7)	.800 (.233 – 2.743)	0.723
II	14.4 (14.8)	9 (24 – 2)	1.458 (.798 – 2.665)	0.221
III	20.7 (20.9)	13 (30 – 6)	Reference	
Histological Type			1.356 (.691 – 2.660)	0.358
Squamous cell carcinoma	15.8 (16.1)	10 (24 – 2)		
Adenocarcinoma	22.9 (22.4)	10 (35 – 6)		
Type of pelvic exenteration				0.167
Anterior	18.9 (15.3)	14 (34 – 6	.347 (.100 – 1.209)	0.097
Total	17.3 (20.3)	9 (35 – 2)	.339 (.097 – 1.180)	0.089
Posterior	5.0 (4.5)	6 (9 - 0)	Reference	
Bladder Invasion			.519 (.202 – 1.331)	0.15
Yes	9.8 (14.3)	6 (6 – 2)		
No	18.3 (18.0)	12 (34 – 6)		
Rectal Invasion			.171 (.058 – 504)	P < 0.0001

Yes	2.4 (2.1)	2 (2 – 2)		
No	19.1 (17.9)	12 (34 – 6)		
Lymph Node Metastasis			.594 (.080 – 4.406)	0.593
Yes	9.0 (-)	9 (9 – 9)		
No	17.6 (17.9)	10 (34 – 3)		
			.178 (.080 - .397)	P < 0.0001
Distant metastasis				
Yes	3.0 (4.3)	0 (9 – 0)		
No	(18.0)	14 (35 – 7)		
Parametrial Invasion			1.81 (1.02 – 3.22)	0.031
Yes	9.9 (16.2)	3 (12 – 0)		
No	22.2 (20.4)	18 (35 –3)		
* SD: Standard deviation ** Q1 25th percentile, Q2 75th percentile				

Table 5: Univariate analysis of disease-free survival in relation to clinicopathologicaariables.

In univariate analysis, DFS was significantly associated with the use of CCRT (p = 0.001) and with surgery performed 12 months after the diagnosis of tumor recurrences (p = 0.031). No significant association with DFS was observed for the clinicopathological factors of stage (p = 0.334), histopathological type (p = 0.358), exenteration type (p = 0.167), and lymph node metastasis (p = 0.593) Table 5.

Similarly, no significant association with DFS was found for the presence of tumor in the surgical specimens (P = 0.190), tumor in the surgical margins (P = 0.170), or lymphovascular invasion with tumor (P = 0.235). The multivariate analysis (Cox regression) showed that distant metastases were a significant predictor of DFS (p = 0.04) Table 6.

Variable	B	Stratum effect	Odds ratio	P value
Age group	0.543	0.371	1.72	0.143
Clinical Stage	-0.155	0.273	0.856	0.57
Histological type	0.088	0.431	1.09	0.838
Type of exenteration	-0.242	0.367	0.785	0.511
Central infiltration	-0.359	0.56	0.699	0.522
Parametrial Invasion	0.379	0.482	1.46	0.432
Bladder Invasion	0.523	0.588	1.68	0.374
Rectal Invasion	0.89	0.598	2.43	0.136
Uterine Corpus Invasion	0.497	1.225	1.64	0.685
Lymph Node Metastasis	0.689	1.188	1.99	0.562
Distant Metastasis	1.442	0.502	4.22	0.004

Table 6: Multivariate Analysis for Disease-Free Survival (Cox Regression).

Table 7 shows the results of the log-rank test for OS. Significant correlations with OS were observed for the type of exenteration (APE and TPE vs PPE, p = 0.012) and for the presence of rectal invasion (p < 0.0001) Figure 4 & Table 7.

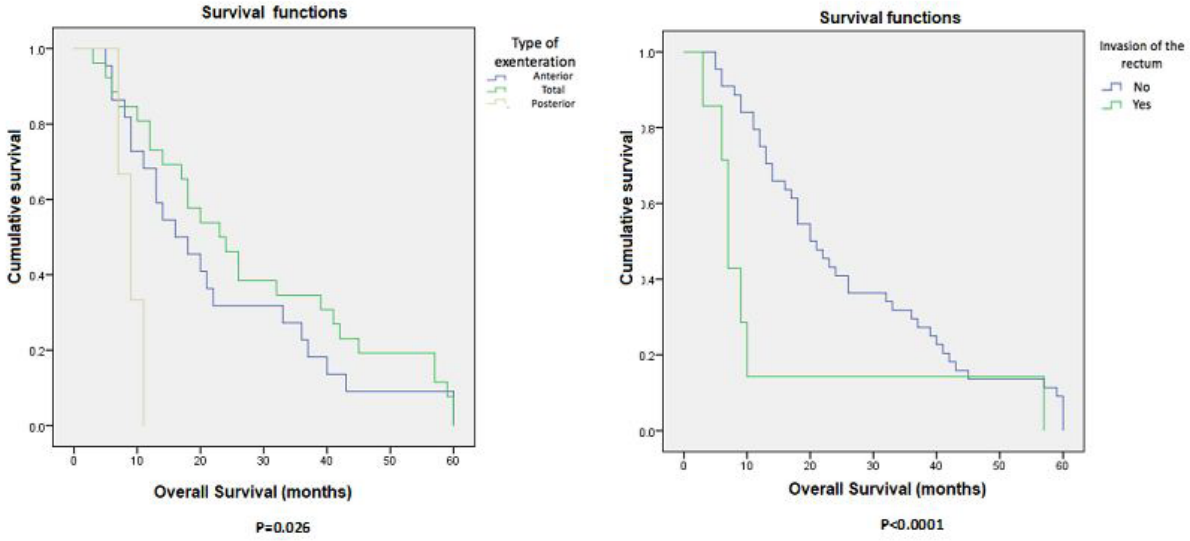

Figure 4 Curves of Overall Survival (OS) with significance, based on the log-rank test.

Variable	Overall survival (months)		Odds ratio	Log Rank Test
Age group			1.206 (.690 – 2.109)	0.504
< 45 years	25.1 (20.5)	20 (36 -11)		
> 45 years	29.2 (25.4)	20 (41 –12)		
Clinical Stage				0.472
I	30.6 (23.0)	21 (57 – 14)	.992 (.291 – 3.377	
II	23.4 (19.7)	18 (32 – 9)	1.410 (.783 – 2.539)	
III	31.8 (27.0)	21 (39 – 13)	Reference	
Histological type			1.405 (.721 – 2.739)	0.307
Squamous cell carcinoma	24.7 (20.7)	20 (39 - 11)		
Adenocarcinoma	34.5 (28.7)	22 (37 – 12)		
Type of exenteration				0.026
Anterior	26.6 (27.6)	16 (36 – 9)	.186 (.049 - .705)	
Total	29.3 (21.4	23 (42 – 12)	.171 (.045 - .649)	
Posterior	9.0 (2.0)	9 (11 – 7)	Reference	
Bladder invasion			.530 (.206 – 1.363)	0.175
Yes	17.2 (13.6))	9 (26 – 8)		
No	28.2 (23.5	20 (40 – 12)		
Rectal invasion			.066 (.019 - .228)	P < 0.0001
Yes	6.4 (2.1)	7 (7 – 6)		
No	29.4 (23.0)	21 (40 – 13)		
Parametrial Invasion			.638 (.363 – 1.122)	0.11

Yes	22.0 (24.2)	13 (26 – 8)		
No	31.3 (21.3)	23 (42 – 17)		
Lymph Node Metastasis			.271 (.035 – 2.082)	0.172
Yes	11.0 (--)	11 (11 – 11)		
No	27.4 (23.0)	20 (39 – 12)		
Distant metastasis			.648 (.322 – 1.305)	0.215
Yes	20.7 (10.6)	18 (29 – 11)		
No	28.9 (25.1)	20 (40 – 11)		

* SD: Standard deviation ** Q1 25th percentile, Q2 75th percentile

Table 7: Univariate analysis of overall survival (OS) in relation to clinicopathological variables.

Variable	B	Stratum effect	Odds ratio	P value
Years Group	-0.015	0.363	0.985	0.967
Clinical Stage				0.512
I	0.052	0.792	1.053	0.948
II	0.412	0.378	1.51	0.275
III	Reference	Reference	Reference	Reference
Histological type	0.154	0.437	1.166	0.724
Type of exenteration				0.422
Anterior	1.641	1.291	5.161	0.204
Total	1.355	1.21	3.877	0.263
Posterior	Reference	Reference	Reference	Reference
Central infiltration	-0.026	0.429	0.974	0.951
Parametrial Invasion	-0.425	0.393	0.654	0.279
Pelvic Side Wall Disease	-0.071	0.911	0.932	0.938
Bladder Invasion	-0.631	0.635	0.532	0.321
Rectal Invasion *	-3.396	0.906	0.034	P < 0.0001
Uterine Corpus Invasion	-0.456	1.017	0.634	0.654
Lymph Node Metastasis	-2.692	1.848	0.068	0.147
Distant Metastasis	-181	0.502	0.834	0.718

Table 8: Multivariate analysis for Overall Survival (Cox Regression).

Multivariate analysis (Cox regression) revealed that rectal invasion was the only independent predictor of OS ($p < 0.0001$) Table 8.

Tumor recurrence

Twelve of the 51 patients (23.5%) developed a tumor recurrence between 6 and 26 months after surgery (mean of 13.5 months) and were lost with tumor activity. Recurrences occurred in 8 of 26 (30.7%) TPE; 1 of 22 APE (4.5%), ($p = 0.044$), and 3 of 3 PPE (100%) patients. Recurrences also occurred in 6 of 20 (30.0%) stage IIIB and 6 of 28 (21.4%), ($p = 0.499$) stage II patients, as well as in 9 of 39 (23.7%) SCC and 3 of 12 (25%) adenocarcinoma (ADC) patients ($p = 0.999$). Recurrences at a distant site occurred in 9 of the 12 patients (75%), and exclusively at a distant site in 6 patients (50%) Table 9.

Location	Anatomical site (s)	No.	%
Local and distant	Retroperitoneal lymph nodes. *	1 of 12	8.3
Regional		1 of 12	8.3
Locoregional		2 of 12	16.6
Locoregional and distant	1.Retroperitoneal lymph nodes. *	2 of 12	16.6
	2. Inguinal lymph nodes		
Distant	1 Inguinal lymph nodes		
	2.CNS **, mediastinum, Retroperitoneal lymph nodes. *		
	3. Mediastinum CNS. ** Retroperitoneal lymph nodes. *		
	4. Lung, mediastinum, Retroperitoneal lymph nodes. *	6 of 12	50
	5. CNS. ** Bones.		
	6. Lung, mediastinum, Retroperitoneal lymph nodes. *		
Total:		12 of 51	23.5

* Retroperitoneal lymph nodes. **Central Nervous System (CNS)

Table 9: Tumor recurrences.

Discussion

Surgical intervention is well established for the treatment of PRCC and provides a final opportunity to achieve disease control. Left to follow the natural course of disease, these patients will otherwise die from the effects of metastatic tumor [4, 5, 6,19-21]. In the current series, 95% of patients had advanced lesions when they received conventional treatment. This is associated with a 23%, 42% and 74% likelihood of failure for stages IIB, III, and IVA, respectively [22]. TPE was performed in 51.1% of patients and APE in 43.1%. Urinary diversions were resolved in 73.5% of patients using ileal conduits. This is the procedure of choice used by most authors for patients previously treated with RT [5,11,13,18,20]. Postoperative complications were recorded in 19 cases (37.2%) in this series, of which 12 (23.5%) were considered MC, and 9 of these (75%) were due to dehiscence of the anastomotic sutures. This type of MC is similar to that published in the literature, with up to 80% reported in some studies [8,10,21,22]. In our setting, Teran-Moncayo et al [23] from the National Cancer Institute previously reported an incidence of 65.3% complications in a series of 42 patients operated with PE for CC. The operative mortality of PE was as high as 20% in early studies [4] and has progressively decreased to less than 5% in recent years [8, 10,11,12,24,25]. Recent publications on exenterations for gynecological cancer (GC) have also reported very low rates of postoperative mortality. Bacalbasa et al [10] reported an operative mortality of 3% in 100 cases of pelvic cancer, of which 56 were caused by CC. The mortality rate was 1.7% in a series of 523 cases, of which 108 were due to CC [25]. In a review of 2647 cases due to GC, Matsuo et al [8] reported a mortality rate of 1.9%. No postoperative deaths were recorded in the present series of 51 PRCC. The mean follow-up for 25 months in this series was 39.2%. In all, 37 (72.5%) patients in this series of 51 were lost to follow-up without evidence of disease during the first two years after their surgery. The tumor status of these patients was therefore unknown. The Mexican federal government provides the resources for cancer care at the authors' institution, with the patients lacking any type of social security. Seventy percent of the patients did not reside in Mexico City and came from the interior of the country. This makes it difficult to obtain adequate follow-up once they are discharged from hospital [26].

A study of 411 cases of PE due to PRCC and collected internationally between 1995 and 2006 showed a 5-year survival rate of 42.8% [7]. Maggioni et al [24] reported a 5-year survival rate of 52% for 62 cases. Balcabasa N [10] reported a 2-year survival rate of 63% for 100 PE cases due to recurrent pelvic cancer. The 5-year survival rate without evidence of disease for PE studies published in the first decade of this century ranges from 20% to 60% [5,7,13,27]. Recent publications have highlighted the value of absence of residual tumor (R0) in the surgical specimen in determining the prognosis of PE due to malignant neoplasms of the pelvis [10,25,28]. Kelly et al [25] reported a 3-year tumor-free survival rate of 49% for patients with R0 specimens in a series of 523 PE for GC collected from 22 centers. In the present study, DFS was significantly correlated when rectal invasion ($p < 0.0001$), parametrial invasion ($p = 0.031$) and with the presence of distant metastases ($p < 0.001$). DFS was also positively associated with CCRT treatment ($p = 0.001$) and with surgery performed 12 months after the diagnosis of tumor recurrences ($p = 0.031$).

Multivariate analysis revealed that rectal invasion ($p = 0.002$) and the presence of distant metastases ($p < 0.0001$) were independently associated with DFS. OS was significantly correlated with the type of PE used (APE and TPE vs PPE) ($p = 0.012$) and with the presence of rectal invasion ($p < 0.0001$). Some of the published studies on PE due to CC report that APE is associated with better prognosis than TPE, presumably because resection of the rectum presupposes a greater tumor burden and is accompanied by greater operative morbidity and mortality [27,28]. In a study of 203 PE due to advanced pelvic cancers, 65.5% of which were CC, Fleish et al [29] found no significant differences in survival between the types of exenterations performed. However, these authors did not specify the pathological findings behind the intervention. In the present work, multivariate analysis showed significant differences in DFS and OS between APE and TPE vs PPE. The relevant prognostic factors reported by Shingleton et al [30] were: tumor volume <3 cm, parametrial invasion that does not affect the PW, and recurrence one year after the completion of RT. These patients had a 5-year DFS of 58%. Patients with large tumors, fixed PW lesions, and a short disease-free period after RT showed 5-year DFS of 42%.

Twelve of the 51 patients (23.5%) in the present study developed tumor recurrences. These occurred in 8 of 26 (30.7%) TPE, 1 of 22 APE, (4.5%, $p = 0.044$) and 3 of 3 PPE (100%) cases. The recurrences were located at distant sites in 9 of the 12 cases (75%). In 6 (50%) of these patients the recurrence occurred exclusively at a distant site, suggesting that administration of adjuvant CT to such patients should be considered.

Conclusions

In this series of PRCC, DFS was significantly correlated with parametrial invasion, rectal invasion, and with surgery performed 12 months after the diagnosis of recurrence, Multivariate analysis revealed that rectal invasion was a significant and independent predictor of DFS and OS. Twelve of the 51 patients (23.5%) developed tumor recurrences. In 9 of these cases (75%) the recurrences were distant and in 6 of these (50%) they occurred exclusively at distant sites, suggesting that administration of adjuvant CT to such patients may be warranted.

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