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Pelvic Exenteration as Potential Cure and Symptom Relief in Advanced and Recurrent Gynaecological Cancer

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Abstract. *Background/Aim: Pelvic exenteration is a radical procedure for certain advanced or recurrent gynaecological cancers, performed with curative or palliative intent. Its validity has evolved as operative mortality and morbidity have improved. This surgery was evaluated to determine the validity of these claims. Patients and Methods: The details of surgery and outcomes of 13 patients who underwent pelvic exenteration (6 curative intent, 7 palliative intent) for advanced or recurrent gynaecological cancers in our Department were retrospectively evaluated. Results: There were no significant differences in blood loss, surgical time, hospital stay, and complications between curative pelvic exenteration and palliative pelvic exenteration. The curative intent group had a good prognosis; the palliative-intent group showed a trend to a worse prognosis. All patients' symptoms were relieved, but in patients with short survival, symptom relief lasted for up to 3 months. Conclusion: Pelvic exenteration is an acceptable and valuable procedure for gynaecological cancers.*

Pelvic exenteration (PE) is an important and sole curative option for certain advanced primary or recurrent gynaecological cancers (1- 6). Brunschwig has reported this procedure first and noted that mortality was 23%, with significant morbidity associated with a long and difficult postoperative recovery (7). The main indication was to treat patients with advanced pelvic cancer with varying degrees of pain and other discomforts attributable to large masses of malignant tissue that had become infected, given rise to fistulas, and had previously received various forms of radiation therapy that had failed to control their growth (7). So, PE began with palliative intent, but improved perioperative mortality and morbidity, and markedly improved survival has been reported (1-6). Thus, the intention has switched from palliation to potential cure, and patients have been selected accordingly (1). However, the use of this procedure with palliative intent has been argued for a long time and remains controversial (8-15). Therefore, in this study, the records of patients who underwent PE for the treatment of primary advanced or recurrent gynaecological cancer at the Fukushima Medical University were retrospectively reviewed, and these patients were classified postoperatively into two groups based on the aim of the surgery (curative and palliative groups). The details of the surgery and survival time were evaluated in each group.

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Key Words: Pelvic exenteration, curative, palliative, complication, survival time.

Patients and Methods

After obtaining Ethics Committee approval, a retrospective review of the records of patients who underwent PE for the treatment of advanced or recurrent gynaecological cancer between December 2005 and January 2019 at the Fukushima Medical University Hospital was conducted. The collected data included age at the time of exenteration, cancer type, stage, histological results of the primary cancer, prior treatments, extent of disease, details of the operation including duration of surgery, blood loss, and complications, symptom, symptom relief, length of symptom relief, overall survival (OS) time, and present disease status. Survival times of patients alive or lost to follow-up were censored in June 2019.

PE was classified as anterior (APE), posterior (PPE), and total (TPE). APE refers to the removal of the reproductive tract, urethra, bladder, and ureter with or without the perineum; PPE refers to the removal of the reproductive tract, rectum with or without the anal canal, and perineum; and TPE refers to the removal of the

reproductive tract, urethra, bladder, ureter, rectum with or without the anal canal, and perineum (Figure 1). The preoperative selection criteria for curative intent PE were central recurrence, no gross pelvic side wall involvement, no para-aortic lymph node metastasis, no distant metastasis, and performance status (PS) 0 or 1. The operation was defined as palliative for at least one of the following reasons: distant metastasis, para-aortic lymph node metastasis, and peritoneal implants evaluated preoperatively, and unresectable pelvic tumour and peritoneal implants seen during operation. All surgical complications were assessed according to the Clavien-Dindo classification (16).

All statistical analyses were performed with SPSS ver. 21.0 (IBM, New York, NY, USA). Survival analysis was performed using Kaplan–Meier curves, and significance was determined by the log-rank test. To evaluate the data for length of hospital stay and postoperative complications, the t-test and chi-squared test were performed. Statistical analyses of duration of surgery and blood loss were performed using one-way analysis of variance with Tukey's multiple comparison test. The significance level was set at $p<0.05$.

Results

Thirteen patients underwent PE during this study period (Table I). The mean age of the patients was 53 years (range=23-79 years). The mean follow-up time after exenteration was 27.5 months (median, 12 months). The procedures were performed for relapsed cervical cancer (n=7), primary advanced cervical cancer with lung metastasis and a recto-vaginal fistula (n=1), recurrent endometrial cancer (n=3), primary advanced vaginal cancer with para-aortic lymph node metastasis and lung metastasis (n=1), and recurrent vulvar cancer (n=1). Six of the relapsed cervical cancer patients and two of the endometrial cancer patients had undergone both radiotherapy and chemotherapy before PE. All other patients underwent multiple courses of chemotherapy. Preoperatively, curative exenteration was planned for nine patients, but three were found to have peritoneal metastasis intraoperatively; thus, six patients underwent curative PE and seven patients underwent palliative PE. Three of the curative patients and five of the palliative patients had some clinical symptoms such as pain, urinary incontinence, abdominal pain due to ileus, and an unpleasant discharge caused by a recto-vaginal fistula. In this study, there were four APE, two PPE, and seven TPE cases. Photographs taken during curative TPE of a representative case of recurrent stage 2B cervical cancer with pelvic pain are shown in Figure 1. The surgical time and blood loss in each type of surgery classified by the aim of surgery defined postoperatively are shown in Table II. Though duration of surgery and blood loss were not significantly different between palliative PE and curative PE, there was a trend for less blood loss in palliative PE. The complications during the postoperative course evaluated by the Clavien-Dindo classification (16) are shown in Table III. The distribution of complications in each group classified by the intent of surgery was almost the same. No surgical mortality occurred. The mean length of hospital stay was 52±45 days with curative intent and 53±26 days with palliative intent. In the curative intent PE group (n=6), one patient died with disease progression and two patient had recurrent disease, but three patients achieved no evidence of disease (NED) for 17 to 162 months. In the palliative group (n=7), three patients died with disease within 12 months after PE (range=4-10 months), and two patients survived for over 12 months (range=12-41 months). With respect to relief of symptoms, all patients were relieved of their preoperative symptoms, but in patients with short, 4 to 10 months, survival (one patient in the curative intent group and two patients in the palliative intent group), symptoms were relieved for only 2 to 3 months. As shown in Figure 2, the 5-year OS rate for the patients with curative PE was 83.3% and the 3-year OS rate for the patients with palliative PE was 45.7%.

Discussion

PE is one of the most extensive procedures performed in gynaecologic oncology with the greatest morbidity (1- 6). This surgery was initially reported for palliation (7), but with improved surgical technique (1) including reconstructive techniques of urinary, digestive, and pelvic floor defects (17, 18) and perioperative management, including antibiotic therapy, intensive care monitoring, thromboembolic prophylaxis, and safer blood transfusion (1, 19, 20), curative PE has been performed. However, curative PE is not supported by level I evidence for its use (1, 2), though many reports of the utility of this surgery have been published (1-6). PE has been established as a treatment of last choice in selected patients. Now, 5-year survival after curative PE for gynaecological tumours has been reported to range from 20% to 70%, and the morbidity rate after PE is 26% to 50% (1-6). The mortality has fallen to <5% following exenteration, but severe morbidity remains >50% (1-6, 20). In the present study, the survival rate of PE with curative intent was consistent with reported rates, with postoperative grade 3 Clavien-Dindo adverse events occurring in 50% of cases. Thus, though our experience with curative PE is not extensive, this result supports its continued use in our department. Once the decision has been made to proceed with PE with curative intent, R0 resection should be attempted (1-6). Therefore, careful preoperative evaluation of resectability and distant metastasis by not only conventional CT and MRI, but also with ^{18}F-fluorodeoxyglucose positron emission tomography is needed (21).

On the other hand, palliative PE remains controversial (8-15). Palliative PE has two meanings: first, PE is performed when cure is unlikely, for example, PE continued despite pelvic side wall invasion, lymphatic involvement or peritoneal tumor observed intraoperatively, with residual

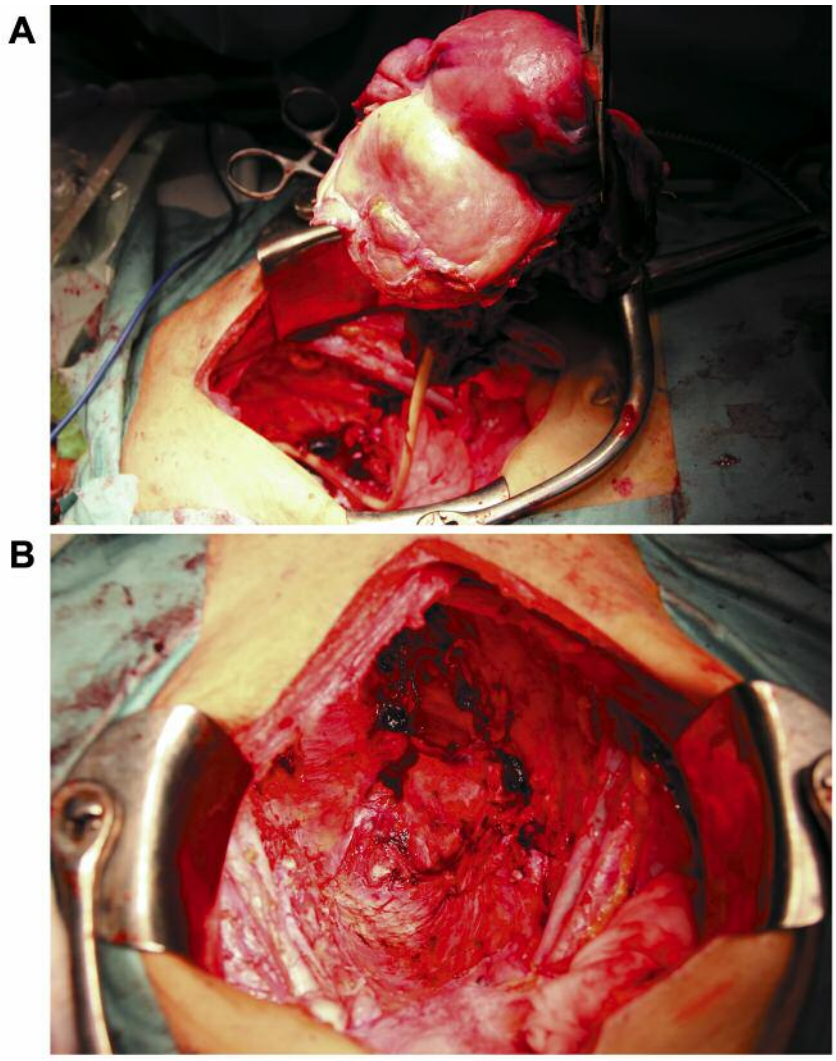

Figure 1. *Total pelvic exenteration for recurrent cervical cancer, after concurrent radiotherapy, that invaded the bladder and rectum causing severe pelvic pain. A. Specimen has just been removed from the pelvis. B. Pelvis after total pelvic exenteration.*

disease remaining postoperatively and second, palliative PE is performed to alleviate or prevent pain or suffering in patients (1, 9-11, 13, 15). In the past, from the 1970s to 1990s, some reports claimed that PE could not provide any improvement of quality of life (QOL) and should not be considered palliative, given that recovery can take several months, and patients may not live long enough to benefit (8, 12, 13). However, in some recent reports, the authors recognized that palliative PE is a procedure with high morbidity and mortality rates that should only be offered to highly selected patients, and, although controversial, palliative PE might be the only method that can offer long-term survival in highly selected patients (10). Moreover, David *et al*. have recently reported that half of gynaecologic oncologists seem to be willing to offer palliative PE (14). In addition, Matsuo has reported that, as chemotherapy options to control of non-symptomatic distant metastases have improved, PE as a treatment option has expanded to include PE for palliative use (22). The survival rate of palliative PE has been reported to be less than that of curative surgery. Two-year survival rates range from 10% to 47% for palliative PE compared to 5-year survivals of 20%-60% for PE in general (9-11, 13, 15). Pathiraja has reported good symptom control with a mean overall survival of 11 months and a postoperative complication rate of about 50% after palliative PE (9). Guimarães has reported that actuarial 2-year overall survival after palliative PE was 15.4%, and the overall complication rate was 38.4% (10). These reports described

Table I. *Patient characteristics*.

Aim of PE	Age (y)	Cancer type	Stage	Histology	Status	Prior treatment	Site of disease (preo-perative)	Identified disease as palliative (intra-operative)	Type of PE	Symptom	Symptom relief	Length of symptom relief (months)	Survival time after PE (months)	Disease status
Curative	41	Cervical	IIB	SCC	Recurrence	Surgery, CCRT, chemo	Vaginal stump, vaginal wall		Total	None			162	NED
	33	Cervical	IIB	SCC	Recurrence	Chemo, CCRT	Uterus, bladder		Total	Pain	Improved	48	48	NED
	21	Cervical	IIB	SCC	Recurrence	Surgery, CCRT, chemo	Vaginal stump, pelvic lymph node		Total	Pain	Improved	3	5	DOD
	67	Cervical	IIB	SCC	Recurrence	CCRT, surgery, chemo	Vaginal stump		Posterior	None			17	NED
	65	Endo-metrial	IIIC	Endo-metrioid G1	Recurrence	Surgery, chemo, RT, chemo	Vaginal stump		Anterior	None			24	AWD
	67	Vulva	IB	GIST	Recurrence	Surgery, chemo	Vaginal stump, vaginal wall		Posterior	Pain	Improved	7	17	AWD
Palliative	54	Cervical	IIA	SCC	Recurrence	Surgery, CCRT, chemo	Vaginal stump	Peritoneum, cecum	Total	Pain, ileus	Improved	41	41	NED
	63	Cervical	IVB	SCC	Primary	Chemo	Uterus, bladder, rectum, lung, para-aortic lymph node		Total	Pain, fistula discharge	Improved	12	12	AWD
	44	Cervical	IB1	LCNEC	Recurrence	Surgery, chemo	Vaginal stump, liver		Anterior	Pain	Improved	5	6	AWD
	52	Cervical	IIB	SCC	Recurrence	CCRT, chemo	Cervix, paramatrium pelvic lymph node	Peritoneum	Anterior	Pain	Improved	2	4	DOD
	51	Endo-metrial	IA	Clear	Recurrence	Surgery, chemo, surgery, RT	Vaginal stump, pelvic side wall	Peritoneum	Total	None			5	AWD
	65	Endo-metrial	IVB	Carcino-sarcoma	Recurrence	Surgery, chemo	Bladder, lung		Total	None			6	DOD
	67	Vaginal	IVB	Clear	Primary	Chemo	Vaginal wall, urethra, lung para-aortic lymph node		Anterior	Pain	Improved	3	10	DOD

SCC: Squamous cell carcinoma; G1: Grade 1; GIST: gastrointestinal stromal tumor; CCRR: concurrent chemo-radiotherapy; RT: radiotherapy; PE: pelvic exenteration; NED: no evidence of disease; DOD: dead of disease; AWD: alive with disease.

the surgical time or postoperative morbidity, but they did not compare them with the results of curative PE. In the present study, mean survival time was 12 months, and 71% (5/7) of patients who underwent palliative PE had some kind of postoperative complications. Moreover, duration of surgery, blood loss, and hospital stay were no different between palliative and curative PE. These results suggest that palliative PE could be performed safely, but the feasibility and acceptability of this procedure could not be determined based on these results, because this was a very small

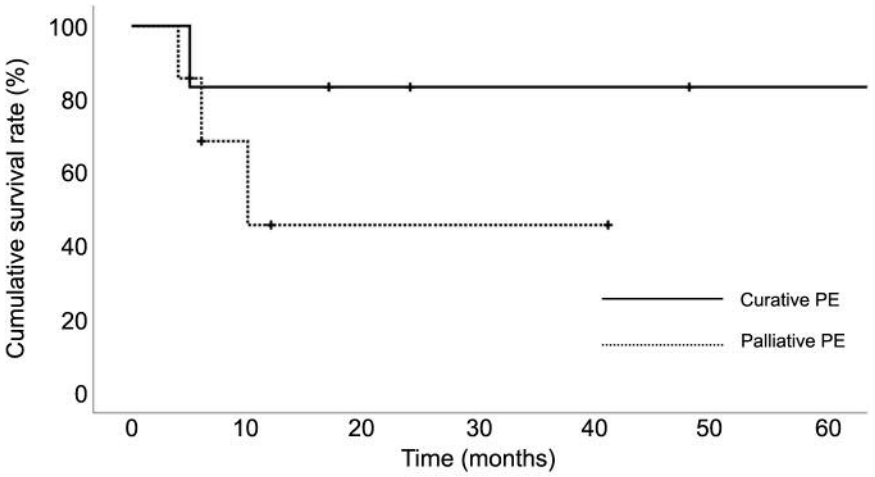

Figure 2. *Overall survival of 13 patients who underwent pelvic exenteration (PE) by intent (curative or palliative).*

Table II. *Surgical time and blood loss by intent of surgery.*

Intent of surgery defined postoperatively	Type of surgery	Duration of surgery (min)	Blood loss (ml)	Hospital stay (days)
Curative (n=6)	Total exenteration (n=3)	673 (483-844)	2216 (1,110-4,160)	52.3 (24-122)
	Anterior or Posterior exenteration (n=3)	579 (533-590)	1941 (930-2,895)	
Palliative (n=7)	Total exenteration (n=4)	782 (615-958)	1503 (1,000-2,000)	52.7 (27-102)
	Anterior or Posterior exenteration (n=3)	469 (411-563)	1075 (580-1,420)	

Table III. *Postoperative complications according to the Clavien-Dindo classification.*

Clavien-Dindo grade	Aim of Surgery		Type of intervention
	Curative (n=6)	Palliative (n=7)	
I-II	3	3	Antibiotics for 6 patients
IIIa	1	2	Wound cleaning and dressing for 3 patients
IIIb	2	0	Exploratory laparotomy for ileus for 2 patients

retrospective study. However, there were unique points in the present study: in the palliative PE group, four patients had distant metastasis, and the other three patients had peritoneal tumour. Generally, peritoneal tumour and distant metastasis have been described as contraindications to PE. In the present study, three patients had lung metastasis and one patient had liver metastasis diagnosed preoperatively, and the other three patients had peritoneal disease diagnosed intraoperatively. One patient had primary stage IVB cervical cancer with local bladder and rectum invasion, pelvic and para-aortic lymph node metastases, and lung metastasis. She was initially treated by chemotherapy, but a rectovaginal fistula occurred that required colostomy. Pelvic tumour persisted and malodorous discharge continued after the colostomy, so palliative PE was performed. After PE, she continued to undergo chemotherapy because of progression of lung disease, but her QOL improved remarkably. The other patient with recurrent cervical cancer who was diagnosed as having characteristics of neuroendocrine carcinoma with liver metastasis had pelvic pain and renal dysfunction due to hydronephrosis caused by tumour invasion. She underwent PE with liver resection, and her pain improved, but multiple

lung metastases were diagnosed, so she had to continue to chemotherapy; her pain improved, and improved renal function assisted with compliance with chemotherapy. Among patients who had peritoneal tumour, one died only 5 months after PE, while one patient who had ileus due to invasion to the ileum by peritoneal tumour achieved long-term survival with no recurrence, and the other patient is now being administered an immune checkpoint inhibitor, and Complete Response was achieved on CT scan 6 months after PE. From these patients' clinical courses, it is clear that some patients who have distant metastases and peritoneal tumour could benefit from PE. By considering the characteristics of each recurrent tumour, such as histological type, growth speed, and location of tumour precisely, some patients who could benefit from palliative PE can be identified. Thus, accumulation of patients' detailed clinical data, indications for PE, and assessments of QOL after palliative PE are essential and valuable to argue the validity of palliative PE for patients with distant metastasis. To show the validity of palliative PE, a prospective comparison with other established treatment options with validated QOL instruments, which is the only way to define the role of pelvic exenteration in relieving severe symptoms from pelvic tumours in patients with incurable disease, should be conducted (1, 9-11, 13). As for symptom relief, including patients who underwent curative and palliative PE, all patients were relieved of their preoperative symptoms, but the duration of this relief depended on survival time. Thus, the three patients who had preoperative symptoms and did not achieve long-term survival (4 months, 5 months, and 10 months) had quite short relief of symptoms (2 months, 3 months, and 3 months). Since the number of patients in the present study was small, the feasibility and acceptability of PE for eliminating symptoms could not be analysed scientifically, but it seemed clear that these patients could benefit from this procedure. One patient with recurrent cervical cancer had severe pain and required non-steroidal anti-inflammatory drugs and opioids as analgesics, and she could not walk by herself and used a wheelchair all of the time; after curative PE, she could walk and enjoy a trip with her family while she was symptom-free for 3 months, though she survived for only 5 months after PE. Although she benefited for only a short time, we believe that it was valuable for her and her family. Thus, from the perspective of symptom relief, if long survival after PE cannot be achieved, the validity of this procedure is judged by the patients themselves and their families, and it is difficult to be evaluated scientifically. We know that this is a subjective view of surgeons who offer PE, so the effort to establish the evidence to support the feasibility and acceptability of palliative PE should be continued (10, 23, 24). Moreover, this issue emphasizes the need for moral education and ethical reflection by all who provide treatment, as well as sensibility to the patient's physical, emotional, and existential condition (10).

Conclusion

In the present small study, PE was found to have acceptable morbidity and mortality, and curative PE achieved acceptable survival times, whereas palliative PE had shorter survival times than curative PE, but the morbidity of PE was not different between curative and palliative PE. Moreover, some patients treated with palliative intent had a long survival. Thus, if sufficient counselling and information could be offered by a multidisciplinary team before and after PE, PE could be an acceptable therapeutic option, since it is the only method that can be performed with both curative and palliative intent and can result in long-term survival.

Conflicts of Interest

The Authors declare no conflict of interest in regard to this study.

Authors' Contributions

Conception and design: Shu Soeda, Shigenori Furukawa, Takafumi Watanabe, Toshifumi Takahashi, Keiya Fujimori; Acquisition of data: Shu Soeda, Tetsu Sato, Makiho Ueda, Norihiro Kamo, Takahiro Endo, Manabu Kojima, Shinzi Nomura, Masao Kataoka, Shotaro Fujita, Hisahito Endo; Performed the analysis: Shu Soeda, Shigenori Furukawa; Wrote the paper: Shu Soeda.

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