



Transverse myocutaneous gracilis flap reconstruction is feasible after pelvic exenteration: 12-year surgical and oncological results



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ABSTRACT

Introduction: Pelvic exenteration (PE) is the only curative treatment for certain locally advanced intra-pelvic malignancies. PE has high morbidity, and optimal reconstruction of the pelvic floor remains undetermined.

Materials and methods: A retrospective chart review was performed at a tertiary university center to assess the surgical and oncological outcomes of 39 PE procedures over a 12-year period. The majority of patients (n = 25) underwent transverse musculocutaneous gracilis (TMG) flap reconstruction for pelvic floor reconstruction.

Results: The 1- and 5-year overall survival (OS) was 72% (95%CI 58%–86%) and 48% (95%CI 31%–65%), respectively. In multivariate analysis, lymph node metastasis (HR 3.070, p = 0.024) and positive surgical margins (HR 3.928, p = 0.009) were risk factors for OS. In this population, 71.8% of the patients had at least one complication. The complication rate was 65.4% and 84.6% for patients with versus without flap reconstruction, respectively (p = 0.191). The length of stay was longer for patients with a major complication 16.0 ± 5.9 days vs. 29.4 ± 14.8 days, p = 0.001, but complications did not affect OS.

Conclusion: For selected patients, PE is a curative option for locally advanced, residual, or recurrent intrapelvic tumors. Pelvic floor and vulvovaginal defects can reliably be reconstructed using TMG flaps. TMG flaps are favored in our institution over abdominal-based flaps because the donor site morbidity is reasonable and TMG does not interfere with enterostomy.

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Abbreviations: APE, anterior pelvic exenteration; DFS, disease-free survival; DIEP, deep inferior epigastric artery perforator; OS, overall survival; PE, pelvic exenteration; PET-CT, positron emission tomography-computed tomography; PPE, posterior pelvic exenteration; TMG, transverse musculocutaneous gracilis; TPE, total pelvic exenteration; TRAM, transverse rectus abdominis musculocutaneous; VRAM, vertical rectus abdominis musculocutaneous.

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Introduction

Complete *en bloc* surgical resection with clear margins is paramount for patient survival in advanced and recurrent pelvic malignancies [1]. Pelvic exenteration (PE) is a complex surgical procedure involving partial or total removal of the pelvic organs. Total pelvic exenteration (TPE) includes removal of the rectum, genital organs, and bladder. Anterior pelvic exenteration (APE) includes partial or total removal of the vagina, removal of the uterus and bladder. Posterior pelvic exenteration (PPE) includes partial or total removal of the vagina, removal of the uterus and rectum. Based on the extent of surgical resection, pelvic exenterations are

classified as type I (supralevator), type II (infralevator), or type III (infralevator with vulvectomy). PE was first described by Brunschwig in 1948 as a palliative procedure, but PE is now performed mainly in selected patients with curative intent [2,3].

PE has considerable morbidity, and the patient's quality of life is negatively affected by one or two permanent ostomies. Furthermore, the pelvic visceral anatomy is profoundly altered, and the integrity of the pelvic floor is weakened, creating a risk of post-operative complications and functional problems. In contemporary publications, the postoperative complication rates after PE range from 56% to 94% [1,4–7], while 5-year overall survival (OS) ranges from 22% to 62% [8–11]. The most important predictors of survival are clear surgical margins [1,8,12] and negative lymph node status [13].

Reconstruction after PE entails securing the pelvic floor, filling in the dead space, and forming a neovagina in selected patients who undergo total PE. Studies show that the results of autologous reconstruction are superior to those of synthetic mesh- or acellular dermal matrix-based solutions [14]. Myocutaneous flap reconstruction has a reduced major pelvic floor wound complication rate compared to primary closure after extensive pelvic floor resection [15]. Flaps based on the inferior epigastric artery are most commonly used for pelvic floor and vaginal reconstruction, including the vertical rectus abdominis musculocutaneous (VRAM) flap, transverse rectus abdominis musculocutaneous (TRAM) flap, or, more recently, the deep inferior epigastric artery perforator (DIEP) flap [15–17]. Abdominally-based flaps interfere with abdominal wall integrity; this is noteworthy because many PE patients require urinary diversion and/or end colostomy [1,9]. Pelvic floor reconstruction by transverse myocutaneous gracilis (TMG) flap was first described by Kolehmainen et al. [18]. TMG flap is often the most feasible local option for pelvic floor and vaginal reconstruction, and this option does not impair abdominal wall integrity [19].

This retrospective chart review was performed to evaluate oncological outcomes and complications related to PE and TMG flap reconstruction in a tertiary university center over a 12-year period.

Materials and Methods

Selection criteria

This was a retrospective cohort study of all patients who underwent PE surgery between January 1, 2005 and December 31, 2016 for an oncological indication at Tampere University Hospital. The study was approved by our institutional review board (ETL code R16582). Patients were identified from our electronic medical records and surgical database. Preoperative evaluation included a laboratory work-up, clinical examination of the patient, and magnetic resonance imaging to evaluate the size of the tumor and its relationship with the nearby organs. Whole body positron emission tomography-computed tomography (PET-CT) was used to exclude distant metastasis. All patients underwent curative intent surgery.

Variables and measurements

The following data were obtained: patient demographics, comorbidities, operative details, histopathological results, pre- and postoperative radiotherapy, chemotherapy, and complications. Complications were classified according to Clavien-Dindo classification [20]. Complications classified as 3b or higher were categorized as severe. All complications were collected from the date of exenteration to the date of last contact. Disease relapse (local relapse or metastasis) information was determined from medical records, and deaths were identified from the national population

database. Disease-free survival (DFS) was measured from the date of exenteration to the date of recurrence, date of death or date of last contact. OS was measured from the date of exenteration to the date of death or date of last contact.

Surgical technique

All patients are evaluated with gynecologic oncologist and plastic surgeon prior the operation. Patients undergoing TPE receive sexual counselling from specialized nurse and are offered vaginal reconstruction.

The patient is placed in the dorsal lithotomy position. Colostomy and possible uretero-ileo-cutaneostomy locations, as well as TMG flap landmarks, are marked preoperatively. The pelvis is approached by a midline laparotomy incision. At laparotomy, the entire abdomen and pelvis are carefully examined for any evidence of metastatic or intraperitoneal cancer, and the lower para-aortic lymph nodes are sampled for frozen section analyses. If these are negative, a bilateral pelvic lymphadenectomy is performed, and an immediate frozen section analysis is performed to determine whether the operation should continue. The size and location of the tumor dictates the type (type I, II, or III) of exenteration that is required to obtain clear surgical margins.

Once the tumor has been resected, the reconstructive team starts the flap harvest while the oncology team performs urinary diversion. Our TMG flap harvest technique for pelvic floor and vagina reconstruction has been described in detail previously [19]. For unilateral reconstruction, a skin paddle that is approximately 8–10 cm by 20 cm is harvested with the gracilis muscle divided at the distal part near the knee joint. A bilateral TMG flap is used for vaginal reconstruction as well as in cases with extended perineal skin resection. In these cases, the skin island is approximately 6–7 cm by 20 cm. Reconstruction starts with distal skin incision and continued until muscular fascia. Fascia is opened over gracilis muscle and muscle is dissected all the way near knee joint. Anterior part of the proximal skin incision is carried out to muscle fascia. Vascular pedicle is identified under adductor muscle in it is dissected free from surrounding tissues and motor nerve is divided. Rest of the skin paddle and distal muscle insertion are incised to finalize the flap harvest. After flap harvest, a tunnel is created under the labia, and flaps are pulled through. The posterior and anterior parts of the skin island are de-epithelialized, and a neovagina is formed by suturing the skin paddles together, starting from the ventral portion of the neovagina. The posterior part of the de-epithelialized skin is sutured to Cooper's ligaments, and the distal portion of the muscles are sutured posteriorly to the pelvic floor through the laparotomy wound to fill the dead space and the pelvic floor defect and to prevent bowel herniation (Fig. 1a–h). Donor sites are closed directly with a suction drain. Key points of the reconstructive procedure are shown surgical video (Supplement 1).

Supplementary video related to this article can be found at <https://doi.org/10.1016/j.ejso.2019.04.021>.

Statistical analysis

Categorical variables were compared using a chi-square test. Continuous variables were compared using an independent sample *t*-test. DFS and OS were assessed with the Kaplan-Meier method, and statistical significance was determined using a log-rank test. Cox regression analysis was used to identify independent factors affecting survival. All statistical analyses were performed using SPSS Statistics 24.0 (IBM Armonk, NY, USA), and a *p*-value less than 0.05 was considered significant.

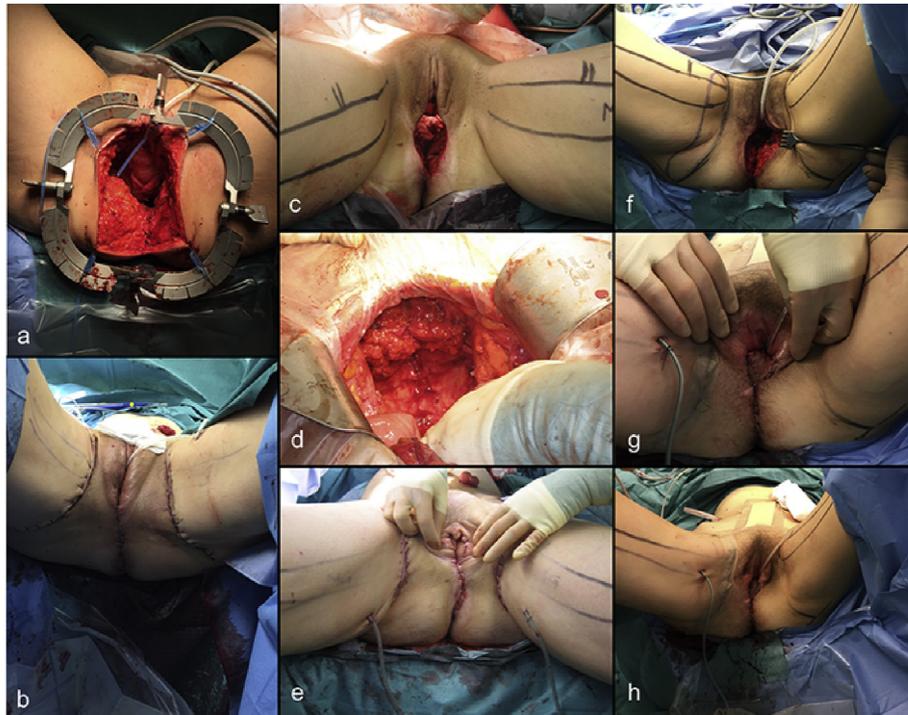


Fig. 1. PPE with most of the posterior and lateral walls resected (a) and after bilateral TMG flap reconstruction (b). Infralevator TPE (c), pelvic floor filling with de-epithelialized skin and muscle flap viewed from abdominal cavity (d) and vaginal reconstruction (e). PPE with posterior vaginal wall resection (f) with unilateral TMG flap reconstruction (g and h). PPE = posterior pelvic exenteration, TMG = transverse myocutaneous gracilis, TPE = total pelvic exenteration.

Results

During the 12-year study period, 38 women underwent a total of 39 exenteration operations. One patient underwent a first APE and then, two years later, underwent PPE after local recurrence. The mean patient age was 59.3 ± 12.2 years, and the mean follow-up was 35.1 (range 2.5–123) months. Table 1 shows the patients' demographic characteristics, comorbidities, and body mass index (BMI) values.

Of the 39 patients, 26 (66.7%) underwent TPE, 11 (28.2%) underwent PPE, and 2 (5.1%) underwent APE. The mean surgical time was 428 ± 56 min for TPE and 374 ± 49 min for combined APE and PPE ($p = 0.032$). The mean length of stay was 22.5 days for the TPE group and 15.5 days for the combined PPE and APE groups ($p = 0.024$). The length of stay was 16.0 ± 5.9 days for patients without severe complications and 29.4 ± 14.8 days for patients with severe complications ($p = 0.001$). While 15 (38.5%) patients had a

Table 1

The demographic characteristics, comorbidities, body mass index values, tumor types, and radiotherapy status of 39 patients who underwent pelvic exenteration.

	Mean	Range
Age	59,3	30–78
Body mass index	26,2	16,0–38,0
	N	%
Diabetes	4	10,3
Chronic heart disease	2	5,1
Chronic pulmonary disease	1	2,6
Primary tumor	15	38,5
Tumor recurrence	24	61,5
Radiotherapy		
Pre-operative	29	74,4
Post-operative	1	2,6
None	9	23,0

primary surgical procedure, 24 (61.5%) had a secondary salvage procedure after previously failed primary therapy. A total of 29 (74.4%) patients had pre-operative radiotherapy, and 1 (2.6%) patient had post-operative radiotherapy. Table 2 lists the primary locations and histology of the tumors. Nine (23.1%) patients had local lymph node metastasis.

We found that 27 (69.2%) patients underwent flap reconstruction for pelvic floor and/or vaginal reconstruction. Of these, 17 (43.6%) had bilateral TMG flap reconstruction, 9 (23.1%) had unilateral TMG flap reconstruction, and 1 (2.6%) had TRAM flap reconstruction; 12 (30.8%) patients had no flap reconstruction for the pelvic floor defect (Fig. 2). Out of 26 patients who underwent TPE, 12 (46.2%) had vaginal reconstruction. Bilateral TMG flap was used for all vaginal reconstructions in the TPE group.

The 1- and 5-year DFS of all patients was 58% (95%CI 43%–74%) and 45% (95%CI 28%–68%), respectively, and the 1- and 5-year OS of all patients was 72% (95%CI 58%–86%) and 48% (95%CI 31%–65%), respectively. Factors affecting OS in univariate analysis were BMI over 30 ($p = 0.028$), lymph node metastasis ($p = 0.048$), and positive surgical margins ($p = 0.001$) (Table 4). When these were applied to multivariate analysis, only positive surgical margins ($p = 0.009$) and lymph node metastasis ($p = 0.027$) were significant factors that contributed to OS (Table 4). The mean OS for patients with negative surgical margins was 84 months (95%CI 64–105 months) versus 17 months (95%CI 7.8–27 months) for patients with positive surgical margins ($p < 0.001$) (Fig. 3a). The 1-year OS of patients with intralesional surgical (R2) resection ($n = 3$) was 33% (OS range, 10–15 months). The mean OS was 20 months (95%CI 12–29 months) for patients with lymph node metastasis and 77 months (95%CI 58–97 months) for patients without lymph node metastasis ($p = 0.039$) (Fig. 3b).

There was a total of 49 complications in 28 (71.8%) patients. The complication rate was 65.4% and 84.6% for patients with versus without flap reconstruction, respectively ($p = 0.191$). Prior

Table 2

Tumor histology and primary location of the tumor in 39 patients who underwent pelvic exenteration.

Histology	N	%
Adenocarcinoma	20	51,3
Spino-cellular ca	12	30,8
Melanoma	5	12,8
Cystadenocarcinoma	2	5,1
Primary location		
Cervix	12	30,8
Vagina	7	17,9
Vulva	6	15,4
Uterus	5	12,8
Rectum	5	12,8
Ovary	3	7,7
Urethra	1	2,6

radiotherapy, BMI, diabetes, and age did not affect the complication rate. A total of 12 patients (30.8%) had at least one severe complication, and the most common complications were infection (43,6%) and local wound dehiscence (33,3%) (Table 3). There was one complication that was directly flap-related, a minor edge necrosis of a TMG flap that was treated with excision and direct closure. The most severe complication of each patient according to Clavien-Dindo classification is shown in Table 3.

Discussion

PE remains the only curative alternative for certain locally advanced, residual, or recurrent tumors of the pelvic organs, especially those involving the female reproductive organs. Even though a majority of the patients in this series experienced surgical or medical complications, the 5-year OS rate approached 50% with no perioperative mortality.

Careful patient selection, planning, and a multidisciplinary team approach are paramount for successful PE. Patient age was not

associated with an increased risk of complications or with OS, highlighting the importance of individualized decision making for this patient group [10,21]. Patients require close follow-up in the post-operative period, as complications are common after PE. Patients also required interventions by multiple specialties during the post-operative period. The overall length of stay of 22.5 days for TPE was similar to that in other cohorts [1,13,22].

PE can be performed for curative intent in patients who present with advanced or recurrent pelvic malignancies. Our 5-year OS of 48% was comparable to that in larger patient cohorts [2,4]. BMI affected OS in univariate analysis but not in multivariate analysis. Obesity has not been shown to affect recurrence or OS in patients who undergo PE for a gynecological indication [23]. In multivariate analysis, only negative surgical resection margins (R0) and negative lymph node status had a positive effect on patient survival. Both negative surgical margins [1,9,13,24] and negative lymph node status [13,24] have been shown to be predictive for survival.

There was a tendency toward a lower complication rate in the flap reconstruction, cohort, although this did not reach statistical significance. Flap closure is superior to primary closure for pelvic floor defects following oncologic resection [15]. Reconstruction after PE has three main goals: securing the pelvic floor in order to prevent perineal herniation of the bowel; filling in the dead space; and forming a vagina, either partially or entirely. A variety of methods have been described, ranging from free skin and bowel grafts to local flaps, muscle flaps, and myocutaneous flaps [25,26]. Of these alternatives, only vascularized fasciocutaneous or myocutaneous flaps can achieve all three of these goals. Both mesh and acellular dermal matrix have been used previously to support the pelvic floor, but these are associated with increased infection rate and fistulas [14]. Furthermore, autologous reconstruction is needed for patients who want to be able to have intercourse.

The TMG flap is conveniently located in the upper thigh, providing a pliable flap with a width of 6–10 cm and a length up to 26 cm, and, together with the gracilis muscle, has enough bulk to fill in the pelvic floor. It can be raised as a unilateral or bilateral flap, depending on the reconstructive requirements and the amount of expendable tissue. We found that TMG flaps are versatile tool for pelvic floor and vaginal reconstruction after PE. Bilateral TMG reconstruction is indicated for TPE patients who wish to have vaginal reconstruction and PPE patients whose vaginal resection included, not only posterior wall of the vagina, but resection extended to the lateral wall. Bilateral TMG flaps are also required for some patients who undergo concomitant radical vulvectomy. Remaining of the defects can be reliably reconstructed with unilateral TMG flap. Horizontally oriented skin paddle in TMG flap was reliable with only one minor skin edge necrosis in this series. Reconstructing the pelvic floor and vagina with a unilateral or bilateral TMG flap has been our preferred choice since 2011 [19]. Vaginal reconstruction was offered to all patients with TPE and was performed on 12 patients.

TMG flaps have two additional advantages over abdominal-based flaps (VRAM/TRAM or DIEP flaps). First, patients undergoing TPE required urinary diversion and colostomy through the abdominal wall. Harvesting the flap from the abdomen is associated with significant donor site morbidity as it weakens the anterior abdominal wall resulting abdominal wound complication rate up to 48% [16]. Some prefer gracilis flap over abdominal flap when bilateral ostomies are needed [27]. However, there is no clear evidence that use of abdominal flap would increase abdominal herniation risk [15,28]. Second, harvesting the TMG flaps and reconstruction of the pelvic floor can be performed while the urologist performs urinary diversion. Our mean surgical time of 428 min was comparable to the 335–725 min reported for reconstructions with abdominal-based flaps in previously published

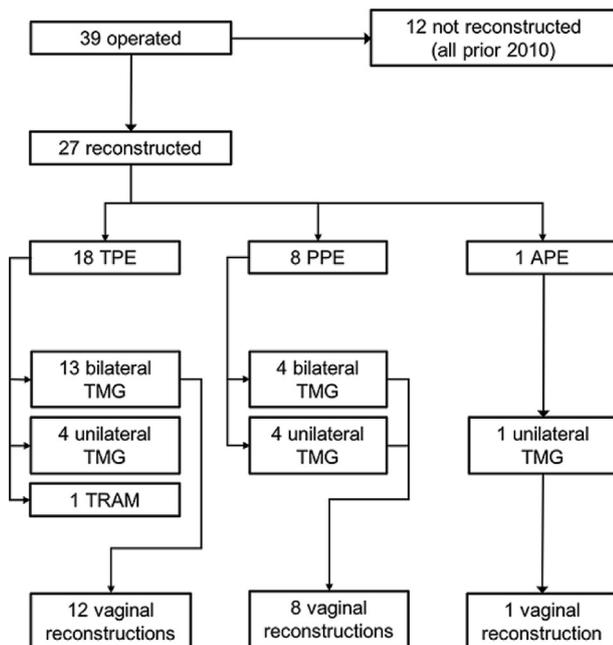


Fig. 2. Exenterations and their reconstructions. TPE = total pelvic exenteration, PPE = posterior pelvic exenteration, APE = anterior pelvic exenteration. TMG = transverse myocutaneous gracilis flap, TRAM = transverse rectus abdominis flap.

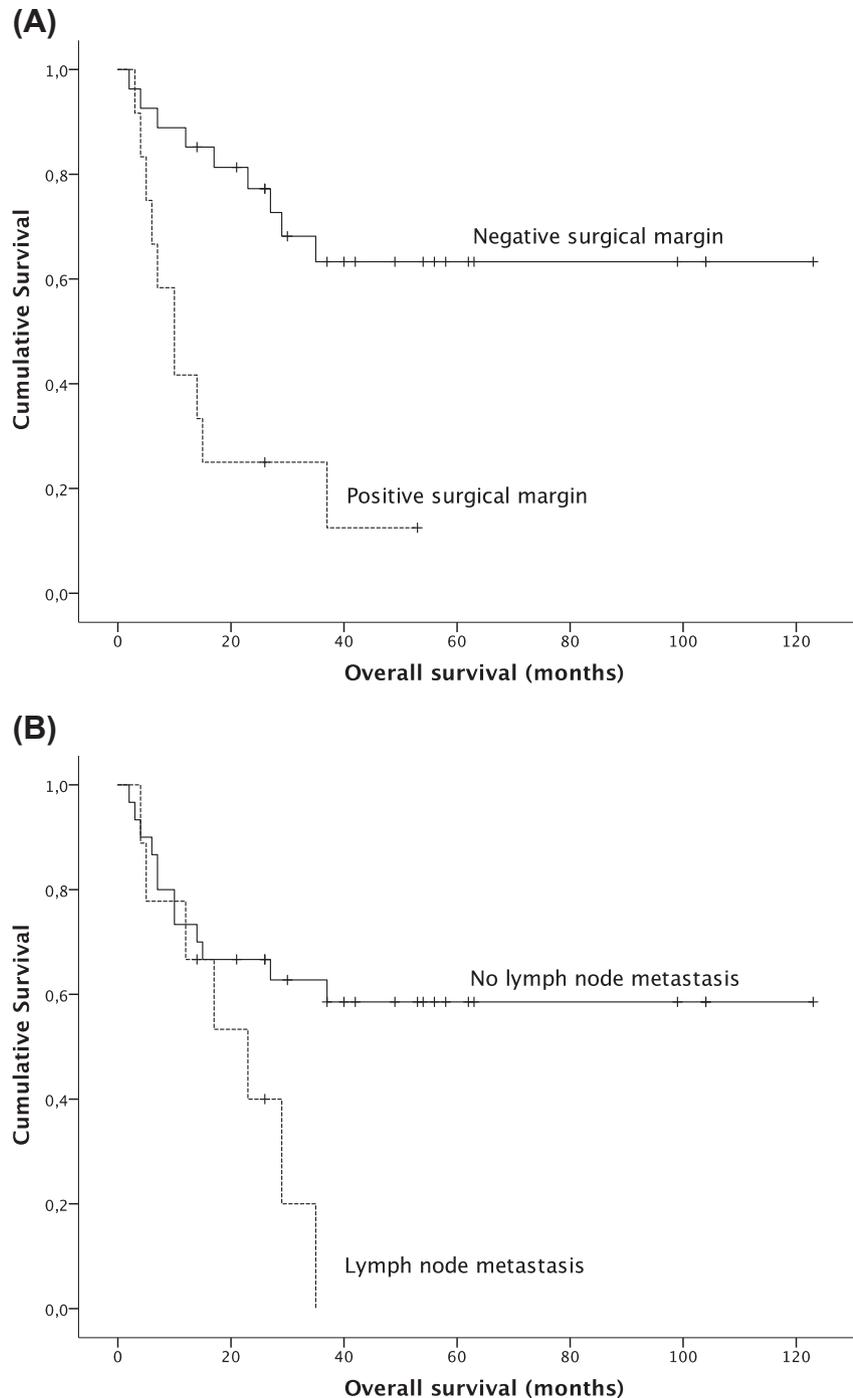


Fig. 3. Kaplan-Maier plots showing overall survival (OS) in patients with R0 or R1/2 resection margins (A) with or without lymph node metastasis (B).

series [17,29]. There are no prospective studies comparing thigh or abdominal based flaps for pelvic floor and vaginal reconstruction. No differences were detected on outcomes or complications when thigh and abdominal flaps were compared in meta-analysis or recent retrospective studies [15,27,30].

Our overall complication rate of 71.8% was similar to the rates in previous publications [1,9,13]; notably, earlier reports did not always define complication severity. Here we stratified complication severity using the Clavien-Dindo classification. In our cohort, the majority of complications were minor complications, and the severe complication rate was 30.8%. Severe complications prolonged

the length of stay but did not affect the DFS or OS. The most common complications were infectious complications, and the majority of these were managed with antimicrobial treatment. Wound dehiscence was the most common operatively-managed complication. There were three post-operative decubital ulcers. We were not able to retrace the timing of these ulcers nor could we determine whether proper preventive measures failed or whether the decubital ulcer risk was disregarded during post-operative care. There was only one direct flap-related complication with partial flap loss in this cohort. Our flap-related complication rate was lower than in series that used abdominal-based flap reconstruction

Table 3

Complications (number and percentage) and the grade of the most severe complication in 39 patients who underwent pelvic exenteration.

Complication	n	%
Infection	17	43,6%
Wound dehiscence	13	33,3%
Enteral fistula	3	7,7%
Postoperative decubital ulcer	3	7,7%
Acute kidney injury	2	5,1%
Pelvic evisceration	1	2,6%
Urinary fistula	1	2,6%
Urinary incontinence	1	2,6%
Cardiac insufficiency	1	2,6%
Hernia/bulging	1	2,6%
Thromboembolic complication	1	2,6%
Flap loss		
Partial	1	2,6%
Total	0	0%
Clavien-Dindo grade	n	%
1	4	10,3%
2	8	20,5%
3a	4	10,3%
3b	10	25,6%
4a	2	5,1%

[16,17].

One limitation of this study was its retrospective nature. Although the number of patients who underwent PE during the 12-year study period was comparable to the number in some earlier reports [5,13], the heterogeneity of the tumor location and histology limited its statistical power for detecting risk factors for complications as well as histology-specific survival. No patient-reported outcome measures were available for this patient cohort.

In conclusion, in carefully selected patients who are treated by an experienced multidisciplinary team, PE is a possible curative option for recurrent gynecological, urological, and gastrointestinal cancers. Clear surgical margins are paramount for survival and should be the goal in every case. Pelvic floor and vulvovaginal defects can be reconstructed with TMG flaps without additional morbidity.

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Conflict of interest

None of the authors have conflict of interest to declare.

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