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Palliative pelvic exenteration: A systematic review of patient-centered outcomes

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ABSTRACT

Objective: Palliative pelvic exenteration (PPE) is a technically complex operation with high morbidity and mortality rates, considered in patients with limited life expectancy. There is little evidence to guide practice. We performed a systematic review to evaluate the impact of PPE on symptom relief and quality of life (QoL).

Methods: A systematic review was conducted according to the PRISMA guidelines using Ovid MEDLINE, EMBASe, and PubMed databases for studies reporting on outcomes of PPE for symptom relief or QoL. Descriptive statistics were used on pooled patient cohorts.

Results: Twenty-three historical cohorts and case series were included, comprising 509 patients. No comparative studies were found. Most malignancies were of colorectal, gynaecological and urological origin. Common indications for PPE were pain, symptomatic fistula, bleeding, malodour, obstruction and pelvic sepsis. The pooled median postoperative morbidity rate was 53.6% (13–100%), the median in-hospital mortality was 6.3% (0–66.7%), and median OS was 14 months (4–40 months). Some symptom relief was reported in a median of 79% (50–100%) of the patients, although the magnitude of effect was poorly measured. Data for QoL measures were inconclusive. Five studies discouraged performing PPE in any patient, while 18 studies concluded that the procedure can be considered in highly selected patients.

Conclusion: Available evidence on PPE is of low-quality. Morbidity and mortality rates are high with a short median OS interval. While some symptom relief may be afforded by this procedure, evidence for improvement in QoL is limited. A highly selective individualised approach is required to optimise the risk:benefit equation.

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Introduction

Locally advanced or recurrent pelvic malignancies are notorious causes of disabling symptoms for affected patients, with significant quality of life (QoL) implications [1–3]. Symptoms often include intractable pain, bleeding, urinary and pelvic sepsis, obstruction, and fistula formation. Pelvic exenteration (PE), defined as radical en bloc resection of two or more contiguous pelvic organs, followed by reconstruction or diversion of visceral functions, and can potentially relieve symptoms, improve QoL, and increase overall survival (OS) in patients treated with curative intent [3]. PE is also associated with lengthy operating times (5–14 h), substantial blood loss, and high

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perioperative morbidity (40–90%) and mortality rates (0–24%) [4]. Therefore, indications for curative PE are carefully assessed and the procedure is typically reserved for selected patients without extra-pelvic disease who are of good general health [5].

Patients in whom an R0 resection is unlikely to be achieved, or those with un-resectable distant metastatic disease, are usually not considered for PE. These patients may, however, benefit from palliative adjuncts such as hormone and chemotherapy, radiotherapy, or palliative procedures such as a defunctioning stoma or urinary diversion. In some centers, palliative pelvic exenteration (PPE) is considered, although this practice remains controversial because of the high associated morbidity in patients with limited overall survival (OS) capacity. Furthermore, evidence for symptom control and/or QoL improvements are limited [3,6–9].

While there is little information to guide practice, interest in this topic has increased in the past few years as surgical techniques and indications have expanded. Our goal was to conduct a systematic review to identify and summarize clinical efficacy of PPE, focusing on the impact of the procedure on symptom control and patient QoL.

Methods

Data sources and eligibility

A systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [10]. The review methods were established prior to the conduct of the review. The searches were performed in duplicate (HK and ND) using the Ovid MEDLINE, EMBASe, and PubMed databases spanning a 70-year timeframe between 1948 (when Brunschwig first reported on PE) and 1st October 2018, when the last search was conducted [11].

Search terms

The following Medical Subject Headings (MeSH) terms and keywords were used: *pelvic exenteration* AND ((*palliative care* OR *palliative surgery)* AND (*pelvic neoplasms* OR *colorectal neoplasms* OR *urogenital neoplasms* OR *neoplasm metastasis)* AND (*symptom relief* OR *treatment outcome* or *survival))*. Boolean AND/OR operators were used to combine MeSH terms and keywords. The related-articles function was used to broaden the search. After the searches, titles and abstracts were screened, followed by full-text analysis of potentially eligible articles. Reference lists of full-text studies were checked for additional relevant articles.

Study selection

Inclusion criteria were all English language publications reporting on outcomes following PPE. PPE was defined as PE performed with the aim of symptom relief in patients with known distant metastases, peritoneal disease, retroperitoneal or para-aortic lymph node metastases, and/or pelvic disease where an R0 resection with curative intent is not possible. Exclusion criteria were studies that did not mention that the procedure was done with palliative intent, studies that used the term palliative, but actually performed a PE with curative intent (i.e. complete local resection in patients without extra-pelvic disease), PE studies not analysing PPE as a separate group, review articles, single case reports, editorials and commentaries.

Data collection

The following data were extracted: first author, country, publication year, study design, number of patients, primary tumor origin, disease beyond pelvis, pelvic symptoms, hospital stay (days), 30-day morbidity and mortality rate, postoperative QoL, symptom relief, symptom-free survival, median OS and the author's conclusion on PPE.

Risk of bias assessment

Risk of bias was assessed using the Newcastle Ottawa quality assessment scale (NOS) since all included studies were cohort series [61]. The scale comprises three separate parts, using counts of * as the assessment score. The maximal NOS score is 9*: 4* for selection part, 2* for comparability part, and 3* for exposure/outcome part. A study was considered of high quality in case of a score of *>7.

Statistical analysis

Descriptive statistics were used on pooled patient cohorts and within subset analyses for cancer type. Values are provided as means and range. A meta-analysis was not appropriate because there were no comparative studies.

Results

The literature search yielded 237 articles, 232 from the primary searches and 5 additional articles were included after checking the references lists. Fifty-six duplicates were removed. After screening titles and abstracts, 68 articles remained for full-text analysis, of which 23 studies met the inclusion criteria (Fig. 1; Table 1). There were 12 studies that reported outcomes on “palliative exenteration” but were excluded as they did not fit the definition of PPE in this systematic review (Supplementary Table 1) [30,31,32,33,34,36,37,40].

The NOS risk of bias assessment of the eligible studies is shown in Supplementary Table 2. None of the identified studies qualified as a high quality study (*>7). Numerous sources of bias were identified within and across included studies: most studies were retrospective series, all studies were observational reports without comparative or randomised controlled data, patient selection and follow-up in most studies.

Study characteristics

The total number of patients from the 23 studies was 509. The median number of patients per study was 13 (4–149), and most were single-center publications from countries spanning five continents. Only one study analysed prospective data, and one reported on pooled prospective and retrospective data [3,6]. All other studies were retrospective. There were 18 cohort studies and five case series. Twelve studies reported outcomes after PPE for a single primary tumor type and eleven studies reported on the combined outcomes after PPE for different primary tumors, mostly from colorectal and gynaecological origin. Three studies also included PPE performed for sarcoma and melanoma [3,9,27]. Seventeen studies involving 395 patients specified if PPE was performed for a primary or recurrent malignancy: 82 patients underwent a PPE for a primary malignancy (20.8%) and 313 patients for tumor recurrence (79.2%) [3,6,9,13,14,16–21,23–25,27–29]. All but three studies documented extent of tumor beyond the pelvis, most combining various anatomical metastatic sites. Patients with distant metastases were included in 12 studies, locally unresectable disease in 12 studies, extra-pelvic nodal metastases in eight studies, and peritoneal metastases in seven studies [16,20,21]. Twenty studies reported results for a combined analysis of multiple symptoms. Pain was an indication for PPE in 18 studies. Other indications included symptomatic fistulas in 16 studies, bleeding in

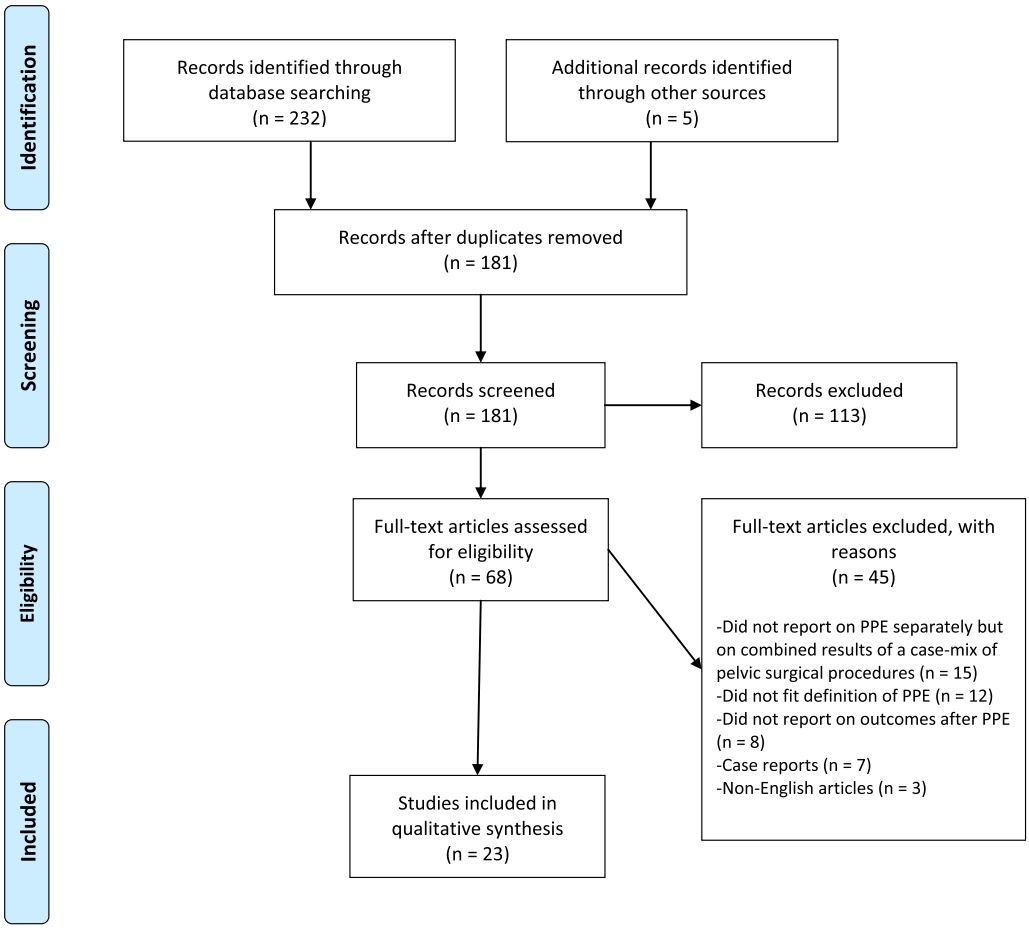

Fig. 1. PRISMA flowchart for the selection of studies according to the inclusion criteria. (PPE: palliative pelvic exenteration).

11 studies, malodourous discharge in six, urinary or bowel obstruction in five, pelvic sepsis in five, haematuria in four, and urinary or faecal incontinence in two studies. The majority of the studies included multiple types of exenterations: total exenterations were performed in 21 studies, anterior exenterations in 11 studies and posterior exenterations in 13 studies [3,18].

Table 2 provides an overview of reported indications for PPE as reported in the 23 studies that were included in this systematic review.

Short-term post-operative outcomes and survival

Hospital stay was reported in 13 studies (247 patients) with a median stay of 22 days (8–51 days). Pooled postoperative in-hospital morbidity was 53.6% (13–100%), reported in 22 studies (450 patients); 12 of these studies (172 patients) reported a pooled in-hospital morbidity of 40.1% (0–79.5%) for severe complications (e.g. reoperation, abdominal sepsis, pulmonary embolism, myocardial infarction and cerebral ischemic accident) specifically(Table 1). In-hospital mortality was reported in all 23 studies, with a pooled percentage of 6.3% (0–66.7%). OS interval was reported in all 23 studies with a median of 14 months (4–40 months).

Quality of life

Seven studies (n = 135 patients) reported on QoL after PPE. The best quality study was performed by Quyn et al. who had prospective validated follow-up QoL questionnaires completed by 39 consecutive patients (SF-36v2 was used, with no disease-specific QoL instrument reported). These data showed that PPE patients experienced a sustained decline in QoL after surgery until death [3]. There was only one other prospective study reporting on QoL after PPE describing an 88% improvement in 35 patients. However, this study used a non-validated ad-hoc questionnaire designed specifically for their study [6]. The remaining five studies stated improved QoL after PPE but did not mention how QoL was assessed making interpretation difficult [8,9,24,26,29].

Symptom relief

Eleven studies (n = 110 patients) reported on symptom relief [7–9,13,16,17,20,24,25,28,29]. Pooled data showed 79% of patients experienced some reduction in reported symptoms (50–100%). While most studies reported on the nature of the symptoms that were palliated, there were few data in any of the studies about the magnitude of the effect. Five studies (n = 53 patients) reported on pain relief specifically with a reduction in 50–100% of the patients [7,16,17,20,24]. The duration of symptom relief was reported in 6 studies (n = 47 patients), with a median of 14 months (8–18 months) [8,16,20,25,28,29]. Of note, Quyn et al., reported prospectively mainly on QoL, but did also report that there was no durable palliation of symptoms in their patients [3].

Specific tumor types

Eight studies (n = 65 patients) reported on PPE for colorectal

Table 1
Series in English literature reporting on outcomes of palliative pelvic exenteration surgery for symptomatic patients.

Author, country, year	Study design	Number of patients	Age (range)	Primary tumor origin (%)	Surgery for primary or recurrence (%)	Disease beyond pelvis (%)	Pelvic Symptoms	Type of exenteration performed (%)
Quyn, Australia, 2016 [3]	Pooled retrospective and prospective cohort	39	63 (40–75)	Colorectal (79) Gynaecological (8) Bladder (5) Sarcoma (5) Melanoma (3)	Primary (23) Recurrence (77)	Distant (liver) metastases (12) Nodal metetastases (21) Peritoneal metetastases (21) Irradical pelvic resection (48)	Pain Bleeding Fistula Prognosis	Resection of tumor and 2 + adjacent neurovascular structures, involving 3/5 or more of pelvic compartments
Schmidt, Switzerland, 2016 [12]	Retrospective cohort	9	63.5 (43–78)	Endometrial	–	Distant metastases Peritoneal metastases Irradical pelvic resection (R1)	Fistula Pain Bowel obstruction	Total Anterior Posterior
Pathiraja, United Kingdom, 2014 [13]	Retrospective cohort	18	54 (26–79)	Cervical (67) Vulva (27) Endometrial (6)	Recurrence	Irradical pelvic resection	Pain Malodourous Bleeding Fistula	Total (50) Anterior (27) Posterior (22)
Schmidt, Switzerland, 2012 [14]	Retrospective cohort	149	50 (23–79)	Cervical	Primary (29) Recurrence (71)	Distant metastases Peritoneal metastases Irradical pelvic resection (R1)	>5 cm tumor Fistula Recurrences meeting the criteria for primary exenteration	Total (96) Anterior (2) Posterior (2)
Guimaraes, Brazil, 2011 [9]	Retrospective cohort	13	58 (29–93)	Cervical (69) Endometrial (15) Leiomyosarcoma (15)	Recurrence	Distant metastases Retroperitoneal nodal metastases Peritoneal metastases Irradical pelvic resection	Fistula Pain Malodourous Bleeding	Total
Fotopoulou, Germany, 2010 [15]	Retrospective cohort	22	52.5 (37–78)	Cervical Vaginal Ovarian[5]	–	Distant metastases/ para-aortic lymph nodes Peritoneal metastases	Bleeding Bowel obstruction Fistula	Total Anterior Posterior[5]
Puntambekar, India, 2009 [16]	Retrospective cohort	7	41 (28–52)	Cervical	Recurrence	–	Malodorous Bleeding Pain Fistula Constipation Haematuria	Total
Leibovici, USA, 2005 [17]	Retrospective case series	5	66 (53–71)	prostate	Recurrence	Pre-operative irradical pelvic resection expected	Haemoturia Obstructive uropathy Pain Fistula	Total (80) 'wide tumor resection' (20)
Vieira, Brazil, 2004 [18]	Retrospective cohort	9	56 (15–84)	Colorectal	Primary	R1 and R2 resections Abdominal or systemic metastases	Pain Weight loss Bleeding Change in bowel habits, mucorhea Fistula Fever Pneumaturia[5]	Colectomy and en bloc 1 or more organs/structures
Kakuda, USA, 2003 [19]	Retrospective cohort	5	64 (50–78)	Colorectal	Recurrence	Distant metastases (40) Irradical pelvic resection (100)	Pain Fistula Infected tumor	Total
Kamat, USA 2003 [20]	Retrospective cohort	14	67.2 (54–75)	Prostate	Recurrence	None	Pain Dysuria haematuria faecal and urinary incontinence	Total
Yamada, Japan, 2002 [21]	Retrospective cohort	13	63	Colorectal	Primary (8) Recurrence (92)	–	Pain	Total±sacrum Posterior±sacrum Anterior
Magrina, USA, 1997 [22]	Retrospective cohort	30	59 (16–85)	Cervical cancer Endometrial Vaginal Colorectal Vulva	–	Nodal metastases pelvic, aorta, side wall	Bleeding Malodorous Pain Irresectable nodal metastases	Total Anterior Posterior 'Extended'
Woodhouse, UK, 1995 [8]	Retrospective case series	10	59	Colorectal Bladder Vulva/vaginal Cervical Anal	–	Local Nodal metastases Pelvic side wall involvement Bone involvement Irradical pelvic	Pain Discharge Haematuria/ dysuria	Total (60) Anterior (40)

Table 1 (*continued*)

Author, country, year	Study design	Number of patients	Age (range)	Primary tumor origin (%)	Surgery for primary or recurrence (%)	Disease beyond pelvis (%)	Pelvic Symptoms	Type of exenteration performed (%)
						resection None		
Brophy, USA, 1994 [6]	Retrospective cohort of prospective collected data	35	60 (30–82)	Colorectal Bladder/renal/urethra Cervical/Ovary	Recurrence	Distant metastases Irradical pelvic resection None	Pain (34) Bleeding (31) Fistula (20) Obstruction (17)	Total (31) Anterior (37) Posterior (31) (Extended in 48%)
Yeung, Canada, 1993 [7]	Retrospective cohort	20	55.3 (31–77)	Colorectal	–	Irradical resection 'Extrapelvic disease'	Pain (100) Bleeding (15) Fistula (25) Obstruction (15) Urinary symptoms (25)	Total
Wanebo, USA, 1992 [23]	Retrospective cohort	6	47	Colorectal	Recurrence	'Extraplevic disease'	Fistula Ulcer/Infection Pain Malodorous	Total Posterior
Temple, Canada, 1990 [24]	Retrospective case series	7	61 (49–70)	Colorectal Prostate (n = 1)	Recurrence	Distant metastases Irradical pelvic resection	Pain Malodorous Pelvic sepsis	Total Posterior
Pearlman, USA, 1989 [25]	Retrospective Cohort	4	- (35–88)	Colorectal	Recurrence	Distant metastases Nodal metastases para-aortic	Pain	Total posterior
Lindsey, USA, 1985 [26]	Retrospective cohort	23	58.5 (22–92)	Colorectal Cervical Bladder Vulva	–	Extrapelvic metastases	Fistula Pelvic sepsis Bleeding Pain	Total (57) Anterior (41) Posterior (2)
Stanhope, USA, 1985 [27]	Retrospective cohort	59	51 (16–81)	Cervical Vaginal/vulva Endometrial Colorectal Bladder/urethra Melanoma	Primary (25) Recurrence (75)	Nodal metastases (pelvic or para-aortic; 66) Peritoneal metastases (15) Distant metastases (10) Irradical pelvic resection (8)	Fistula Intra-operatively due to no curative resection possible	Total (57) Anterior (41) Posterior (2)
Wanebo, USA, 1981 [28]	Retrospective case series	4	56 (39–65)	Colorectal	Recurrence	Distant metastases Nodal metastases	Pain Infected tumors	Posterior Extended
Deckers, USA, 1976 [29]	Retrospective case series	8	63	Cervical (50) Bladder (25) Colorectal (25)	Primary (63) Recurrence (37)	Distant metastases Peritoneal metastases Nodal metastases para-aortic Non-cancerous (hydronephrosis, dementia, cardiac)	Fistula Pain Bleeding Infected tumors Incontinence	Total (63) Anterior (37)

Author, country, year	Hospital stay (days)	In-hospital Morbidity (%) (severe in-hospital morbidity (%))	Hospital mortality (%)	Post-operative quality of life	Symptom relief (%)	Median symptom free survival (months)	Median overall survival (months)	Conclusion on palliative exenteration
Quyn, Australia, 2016 [3]	18	79 (79)	0	Worse than preoperative	–	–	24	Controversial and questionable effect
Schmidt, Switzerland, 2016 [12]	–	30[5]	11[5]	–	–	–	40	May be considered in case of severe symptoms
Pathiraja, United Kingdom, 2014 [13]	24	78 (55.6)	0	–	78	–	11	Technically feasible in carefully selected patients
Schmidt, Switzerland, 2012 [14]	–	51[5]	5[5]	–	–	–	14	Previous contraindication should be reconsidered
Guimaraes, Brazil, 2011 [9]	15	38.4	15	Improved	100	–	5	In highly selected patients only: role yet to be established
Fotopoulou, Germany, 2010 [15]	29[5]	82	8.5[5]	–	–	–	4	Considerable in highly selected patients to improve quality of life
Puntambekar, India, 2009 [16]	8	43 (0)	0	–	100 (pain 86%; bleeding 86%; fistula 43%)	8	11	Technically feasible in carefully selected patients
Leibovici, USA, 2005 [17]	12	60 (40)	0	–	80 (haemoturia 60%; pain 40%; renal failure 40%)	–	17	Salvage surgery is feasible and safe, and

(*continued on next page*)

Table 1 (*continued*)

Author, country, year	Hospital stay (days)	In-hospital Morbidity (%) (severe in-hospital morbidity (%))	Hospital mortality (%)	Post-operative quality of life	Symptom relief (%)	Median symptom free survival (months)	Median overall survival (months)	Conclusion on palliative exenteration
								provides effective palliation
Vieira, Brazil, 2004 [18]	11[5]	77.8	66.7	–	–	–	3.1	Could benefit selected patients when cautiously indicated
Kakuda, USA, 2003 [19]	8	80 (40)	0	–	–	–	8.4	There may be a benefit in selected patients, however, operative morbidity is high
Kamat, USA 2003 [20]	–	50 (36)	0	–	79 (pain)	14.1	24	Feasible in highly selected patients
Yamada, Japan, 2002 [21]	51[5]	56[5]	1.6[5]	–	(Minority of the patients)	(Temporarily or not at all)	10	Controversial and dismal prognosis after palliative exenteration
Magrina, USA, 1997 [22]	26.6[5]	57[5]	6.7[5]	–	–	–	14	Shorter survival after palliative exenteration
Woodhouse, UK, 1995 [8]	–	20 (20)	0	Improved in 80%	80	>18	17	In highly selected patients and appropriate multi-speciality care, exenteration can be of palliative value
Brophy, USA, 1994 [6]	–	47 (17)	3	Improved in 88%	–	–	20	Aggressive treatment can be considered in selected patients after a multimodality approach
Yeung, Canada, 1993 [7]	38[5]	25[4] (45)	25	Improved	50 (pain relief)	–	10	There is a role in selected low-risk patients with intractable symptoms
Wanebo, USA, 1992 [23]	–	76[5]	8.5[5]	–	–	–	9	inappropriate to resect for palliative purposes in case you cannot expect cure (discussion by Dr. Wood)
Temple, Canada, 1990 [24]	21–28	57 (0)	0	Improved in all patients, 3 returned to work	100 (pain relief)	–	12	Safe to perform and provides superb palliation for very selected patients
Pearlman, USA, 1989 [25]	–	50 (50)	0	–	55[5]	Until death or last follow-up[5]	9	Hesitant to perform exentaration in case of extrapelvic disease because the degree of palliation is unclear
Lindsey, USA, 1985 [26]	–	44.1[5]	8.7	Improved in the majority	'in the majority of patients'	–	11	Feasible in severely symptomatic patients
Stanhope, USA, 1985 [27]	22	–	5.1	–	–	–	19	Reasonable in selected patients by experienced pelvic surgeons if good clearance of cancer can be achieved
Wanebo, USA, 1981 [28]	–	14 complications in 11 patients[5]	0	–	75	8	6	feasible and may provide good palliation in most patients
Deckers, USA, 1976 [29]	–	13 (0)	0	Improved in all patients	100	15	15	To be considered in symptomatic patients

- Not reported; [2] 5-year survival in %; [3] 2-year survival in %; [4] total number complications; [5] reported for entire palliative and curative exenteration cohort; [6] 3-year survival in %.

cancer only [7,18,19,21,23–25,28]. In these patients, pooled median hospital stay was 38 days (8–51 days) as reported in five studies (n = 53 patients). In-hospital morbidity and mortality rates were reported in all eight studies and showed pooled percentages of 56% (5–100%) and 8.5% (0–66.7%), respectively. Symptom relief, mostly reported for pain, was achieved in 65% (50–100%) as described in three studies (n = 31 patients) [7,24,28]. Median OS was 10 months (3.1–12 months). Four studies concluded that PPE can be applied in highly selected patients with colorectal cancer, two studies were undetermined about its role, and another two discouraged its use.

Five studies reported on PPE for a mix of gynaecological cancers: endometrial, cervical, vaginal, vulva, and ovarian [12–16]. Pooled median hospital stay was 24 days (8–29 days) with a pooled postoperative morbidity of 51% (30–82%), in-hospital mortality of 5% (0–11%), and a median OS of 14 months (range 4–40 months). All gynaecological articles expressed a positive opinion in favour of

Table 2
Overview of reported indications for palliative pelvic exenteration surgery as reported in the 23 included studies in this systematic review.

Primary tumor origin	Main indication for PPE	Extent of tumor beyond the pelvis
Colorectal and anal	Pain	Locally unresectable tumor
Colon	Bleeding	Nodal metastases
Rectum	Haematuria	Pelvic/lateral
Anus	Rectal	Inguinal
Gynaecological	Vaginal	Para-aortic
Vulva	Obstruction	Peritoneal metastases
Vagina	Urine	Distant metastases
Cervix	Bowel	
Uterine/ endometrium	Incontinence	
Ovary	Urine	
Urological	Faecal	
Urethra	Fistula	
Prostate	Recto-vesical	
Bladder	Recto-prostatic	
Melanoma	Recto-vaginal	
Sarcoma	Vesico-vaginal	
	Ulcerative/fungating tumor	
	Pelvic sepsis	
	Fever	
	Malodourous	

PPE: palliative pelvic exenteration.

PPE.

Two studies reported results after PPE for patients with advanced prostate cancer, with one reporting a hospital stay of 12 days. In-hospital morbidity was 50% and 60% with no mortality reported [17,20]. Symptom relief was experienced in 80% (mostly urinary symptoms) and median survival was 17 and 24 months. Both articles concluded that PPE can provide effective palliation in selected patients with advanced prostate cancer.

Overall recommendations

Of the 23 articles included in the systematic review, five discouraged performing PPE in any patient regardless of presentation [3,21–23,25]. The other 18 studies concluded that PPE may be considered in highly selected patients.

Discussion

We conducted a systematic review of PPE and its impact of patient QoL and symptom relief. In total, 23 studies including 509 patients were identified. The results suggest that, although there may be some improvement in symptom control based on retrospective data, PPE is a highly morbid procedure with little evidence to support an improvement in QoL after surgery. Median survival interval is also short (14 months), particularly when recovery time from the procedure is taken into account. This supports the reluctance of some to perform PPE [3,8,9,21–23,25] and the approach of using less morbid palliative options where possible, such as a diverting stoma, suprapubic catheter or nephrostomy, hormone therapy, chemotherapy, radiotherapy and palliative pain management with multi-modal analgesia [3,14,41–43]. These options can be applied in isolation or in combination, and in an individualised fashion to target the specific symptoms affecting the patient at any given time. Nonetheless, there may remain a role for PPE in highly selected patients, where other palliative options have been exhausted or are not feasible [1,2,12,44].

Brunschwig first reported on PE in 1948 and, in fact, described it as a purely palliative technique [11]. Initial results were discouraging with mortality rates of 23–33%. In the subsequent decades, PE was increasingly performed as a curative procedure and consensus was formed about its relative contraindications: distant metastases and spread of tumor into major nerves, vessels, and/or pelvic bones [38,39,41,45]. Over the past seven decades, new multimodality strategies, and improvements in technology and peri-operative care have broadened the indications of PE with curative intent. With this, the indications for palliative exenteration have become less well-defined. The World Health Organization states that palliative care neither hastens nor postpones death but provides relief from distressing symptoms [46]. In view of this, we chose to define PPE as PE performed with the aim of symptom relief in patients with known distant metastases, peritoneal disease, retroperitoneal or para-aortic lymph node metastases, and/or pelvic disease where an R0 resection with curative intent is expected not to be possible [2,3,9,41].

Outcomes of PPE are known to be worse compared with PE performed with curative intent. Our work shows that in-hospital mortality is higher (6.3%), and hospital stay is longer (22 days) when compared to PE performed with curative intent (2.2% and 15 days, respectively), while median OS after PPE is only 14 months [47–49]. While 11 included studies demonstrated relief of symptoms in 79% of patients, these results have to be interpreted with great caution as most did not report which symptoms were improved and by how much. Furthermore, in contrast to PE with curative intent where there is good evidence showing QoL improves rapidly 2–9 months after surgery [50,51], we found little evidence to support this in the palliative setting. The only prospective validated QoL analysis, showed that after PPE, QoL only reduced further, and did not recover before death [3].

These results suggest that if PPE is contemplated, meticulous patient selection should be a key factor in optimising any potential gains and avoiding harm or futile intervention [29]. In general terms, the data show that the ideal candidate for a PPE would be a medically fit patient, with limited and chemo-responsive distant disease, and pelvic symptoms that are thought treatable with exenteration, and which cannot be otherwise palliated with less invasive options. Due to the complexity in decision-making, a specialised multi-disciplinary team (MDT) setting is essential [3,35,52]. Quyn et al. reported that the introduction of a dedicated exenteration MDT meeting resulted in a reduction in the percentage of patients undergoing PPE from 11% to 8% over a 20-year period [3]. When a patient is found surgically and medically eligible for a PPE by MDT consensus, the treating clinician must inform the patient and his/her relatives thoroughly and discuss the procedure in detail, providing them with a realistic assessment regarding its efficacy in terms of palliation and potential adverse outcomes. It is also important to clearly discuss limits on subsequent care, and what other options are available. An open, frank, shared decision-making process should be actively encouraged [53,54].

Some limitations of this systematic review must be addressed. Firstly, due to the historical evolution of the definition and indications for PE, there were a significant number of studies that performed palliative procedures on patients that would now be considered candidates for curative surgery (Supplementary Table 1). The word “palliative” was also not always used as per our definition, with some authors using the term “palliative” to emphasize symptom relief for patients who all had a curative resection [55–57]. We therefore only included studies that fit our present definition, as the inclusion of curative intent patients would have biased the results. Furthermore, most of the included studies were retrospective series and no comparative data were available. Due to the scarce information on the inclusion criteria,

high heterogeneity in outcomes such as in-hospital morbidity, symptom relief and overall survival rates, and different endpoints used in the included studies, it was therefore not possible to perform a meta-analysis. None of the studies defined patient selection criteria for PPE and many did not report data on QoL or symptom relief. Finally, there was great heterogeneity of the data as most studies reported on a wide range of primary tumor types, PE techniques, and symptoms for which PPE was performed making comparisons between studies challenging.

In the future, it is likely that the definitions and indications for PPE will continue to evolve with the introduction of more effective systemic and local therapies, such as immunotherapy, precision radiotherapy, and radiological chemo-embolization. The role for minimally invasive surgery remains undefined, but there are reports of its feasibility in case series on laparoscopic and robotic PPE [13,55,58–60]. Despite this, currently there is no good evidence regarding the current role of PPE [2,3,13,41]. In order to define this further, a prospective comparative study with other established palliative treatment options, and using validated QoL instruments, is required.

Conclusion

Available evidence on PPE is of low-quality. Morbidity and mortality rates are high with a short median OS interval. While some symptom relief may be afforded by this procedure, evidence for improvement in QoL is limited. A highly selective individualised approach is required to optimise the risk:benefit equation.

Declarations of interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2019.06.011.

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