The Role of Pelvic Exenteration in the Management of Locally Advanced Prostate Cancer

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Abstract

Locally advanced prostate cancer poses a clinical challenge for physicians. Despite the established role of radiotherapy and androgen-deprivation therapy in these cases, some patients with locally advanced disease experience recurrent disease or persistent disease with debilitating local symptoms, such as intractable pain and urinary symptoms. In this narrative review, we sought to evaluate the role of exenterative surgery in the management of locally advanced prostate cancer. From our search, we found that total pelvic exenteration or cystoprostatectomy represents a viable therapeutic modality to manage prostate cancer directly invading the bladder, lower urinary tract symptoms, debilitating pain caused by locally advanced disease, and as salvage treatment after failure of primary treatment among other applications. Reports on minimally invasive pelvic exenteration for prostate cancer were also retrieved, as this represents a feasible and effective treatment option for experienced clinicians. Pelvic exenteration may be an effective tool for the treatment of locally advanced prostate cancer in the surgeon's armamentarium; however, further studies are needed to establish its role in improving survival and overall patient outcomes.

Introduction

While there is no single definition of locally advanced prostate cancer (LAPca), it is generally understood to be disease extending beyond the prostatic capsule (T3 and T4 disease)[1–3]. The European Association of Urology (EAU) defines locally advanced prostate cancer as clinical cT3–cT4 or disease with positive lymph nodes (cN1)[1]. This issue has become particularly pertinent in recent years as a shift towards LAPca has been observed following the United States Preventative Task Force recommendation against routine prostate cancer screening in 2012[4].

Although there is no consensus among urologists, oncologists, and radiation oncologists on the management of LAPca, the survival benefit of radiotherapy (RT) combined with androgen-deprivation therapy (ADT) has been well established, and it has been consistently used for the treatment of LAPca[5,6]. The role of surgery in the treatment of this condition is more controversial but has been an area of intense investigation in recent years.

A meta-analysis demonstrated significant survival improvement with radical prostatectomy (RP) in LAPca, and when RP was combined with adjuvant radiotherapy, survival rates were comparable to those seen with RT and ADT[7]. The survival benefit of surgery for T4 disease in men aged < 50 years was described by Hsiao et al., who suggested that RP should be offered to men in that age group as part of a multimodal treatment approach[8].

Competing Interests

None declared.

Abbreviations

ADT androgen-deprivation therapy
CRPC castrate-resistant prostate cancer
LAPca locally advanced prostate cancer
LUTS lower urinary tract symptoms
QoL quality of life
RP radical prostatectomy
RT radiotherapy

Kim et al. stressed the importance of local treatment of the primary tumor in T4 prostate cancer with surgery, RT, or a combination of both compared to systematic therapy with ADT or chemotherapy, and reported 5-year survival rates of 57.8% for local therapy versus 33.2% for systematic therapy[9]. Given the high rates of positive surgical margins, recurrence, and occult systemic metastasis in LAPca, a combination of surgery with either adjuvant or neoadjuvant RT has been described in the literature as having improved outcomes[10].

Bothersome pelvic symptoms are frequently encountered in the management of patients LAPca. For instance, up to two-thirds of men diagnosed with castrate-sensitive prostate cancer (CSPC) experience pelvic symptoms, including perineal pain, lower urinary tract symptoms (LUTS), and urinary tract obstruction[11]. Men dying of prostate cancer experience a high incidence of urological complications[12]. Fifty percent of men dying of metastatic prostate cancer suffer from LUTS, 21% undergo lower urinary tract procedures, and 8% undergo upper urinary tract interventions[13]. In another report, 25% of prostate cancer patients who underwent palliative transurethral resection of the prostate required repeat TURP after a mean duration of 11 months[14]. LAPca can lead to chronic pelvic pain requiring opioid medications, as well as bladder outlet obstruction requiring catheterization or renal failure requiring urinary diversion or ureteral stenting. While these sequelae might not lead to increased cancer-specific mortality, they decrease the quality of life (QoL) of affected patients[15].

Pelvic exenteration is an extensive surgery that involves the removal of pelvic organs to treat pelvic malignancies[16]. It was first described by Brunschwig in 1948 for the management of gynecological cancers[17]. Currently, pelvic exenteration is most commonly performed for gynecological and locally advanced rectal tumors[18]. Total pelvic exenteration involves removal of the bladder, reproductive organs, sigmoid colon, and rectum, and creation of diversions for urine and stool. Variations include anterior pelvic exenteration, which spares the rectosigmoid, and posterior pelvic exen-teration, which spares the bladder[19]. Pelvic exenteration has also been described in the management of other pelvic tumors such as bladder cancer and pelvic sarcomas[20,21].

In this review, we aim to evaluate the role of cystoprostatectomy and pelvic exenteration in patients with LAPca by highlighting the various indications, complications, and outcomes reported in published studies, and to identify gaps in the literature that may be a focus for future studies.

Methods

This review is structured as a narrative review in accordance with the scale for the assessment of narrative review (SANRA) criteria[22].

A comprehensive literature search was performed by 2 authors using PubMed from 1980 to 2021. The search string used was ([prostate cancer] AND [pelvic exenteration] OR [cystoprostatectomy] OR [cysto-prostatectomy]). Filters included only English language papers, human subjects, and the following types of articles: case reports, classical articles, clinical studies, clinical trials, clinical trial protocols, clinical trials, comparative studies, controlled clinical trials, guidelines, journal articles, meta-analyses, multicenter studies, observational studies, practice guidelines, randomized controlled trials, reviews, and systematic review papers. The articles yielded from the final search were first screened by title, then abstract, and finally by full text. Articles on prostate sarcomas and non-adenocarcinoma tumors and articles on pelvic exenteration performed for non-prostate pelvic tumors were excluded. Letters to the editor, opinions, abstracts, summaries, videos, and reports in non-English languages were excluded. Finally, a manual search was conducted from the selected articles and search engines.

The included articles were then evaluated to extract the following data: number of patients included, type of exenteration surgery, the indication for exenteration, neoadjuvant or adjuvant treatments, operative outcomes (blood loss, blood transfusions, length of surgery, hospital stay), complications (including 30-day morbidity and mortality when reported), R0 resection, follow-up and the reported long-term survival outcomes.

Results

Following our search criteria, 529 articles were extracted and screened by title; 473 papers were excluded. A total of 56 abstracts were screened, and 23 papers were excluded. Thirty-three full-text articles were reviewed, of which 4 were excluded. Five articles were retrieved by a manual search, yielding a total of 34 articles included

in our results. The article screening process, the numbers included and excluded, and the reasons for exclusion are summarized in **Figure 1**.

In our review, pelvic exenteration for prostate cancer has been described in different settings based on different indications. The majority of retrospective studies reporting the indications, complications, and outcomes of pelvic exenteration for prostate cancer are summarized in **Table 1**[23–42]. **Table 2**[43–48] summarizes the reported cases of minimally invasive pelvic exenteration for prostate cancer, whether laparoscopic or robot-assisted.

Cystoprostatectomy for prostate cancer invading the bladder

Cystoprostatectomy can be performed to control LUTS in prostate cancer invading the bladder and has been described as a palliative treatment option for LUTS after failure of other treatments or as a primary treatment option for prostate cancer invading the bladder[49]. Leibovici et al. demonstrated that palliative cystoprostatectomy alleviated LUTS in 68% of patients with prostate cancer invading the bladder, whether primary or recurrent after radiotherapy, and reported significant relief of all local pain and LUTS, as well as the need for palliative lower urinary tract procedures

FIGURE 1.

The flowchart summarizes the screening process for article inclusion in this narrative review. Numbers of articles screened at each phase, the reasons for exclusion, and the final number of articles included are demonstrated in the flowchart.
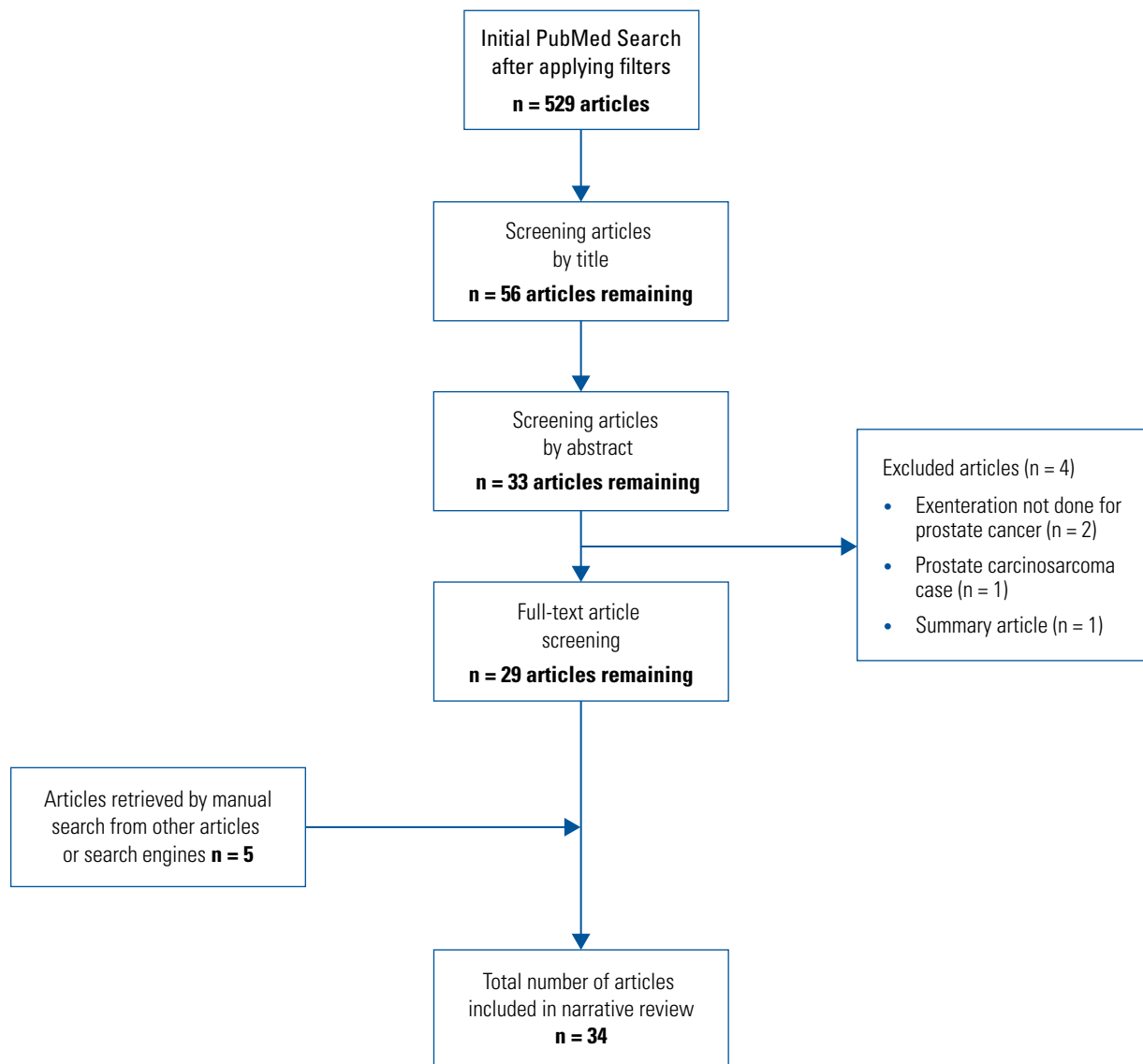
TABLE 1.

Summary of studies on pelvic exenteration (anterior or total) for locally advanced prostate cancer

Author (Year)	Total number of patients	Exenteration type (number)	Indication (number)	Neoadjuvant treatment	Blood loss	PRBC transfusion	
Mador et al. (1985)	7	Radical prostatectomy (4) Cystoprostatectomy (3)	Salvage surgery after local recurrence of prostate cancer after failure of radiotherapy with no metastasis (7)	–	NR	Mean 5.3 units	
Moul et al. (1991)	22	Radical perineal prostatectomy (4) Cystoprostatectomy with urinary diversion: ileal conduit (5), Koch pouch (3)	Salvage surgery for recurrent prostate cancer after radiotherapy (12)	–	RPP: Mean 800 ml CP: Mean 3190 ml (CP)	RPP: NR CP: Mean 6 units	
		Cystoprostatectomy with urinary diversion: ileal conduit (8), Koch pouch (1) Pelvic exenteration with colostomy and ileal conduit (1)	Locally advanced prostate cancer not amenable to standard radical prostatectomy (10)	5 of 10 patients received neoadjuvant treatment	Mean 2890 ml	Mean 7.3 units	
Zincke et al. (1992)	62	Radical prostatectomy (32) Cystoprostatectomy with ileal conduit (23) Total pelvic exenteration (7)	Salvage surgery after radiation failure, no distant metastasis in all patients at time of surgery (62)	22 patients (35%) received hormonal treatment before surgery	NR	RP: median 1.5 units, range 0–20 CP: median 1 unit, range 0–12 TPE: median 4 units, range 3–6	

[a] Data reported on a total of 18 patients: 6 prostate and 12 bladder cancer [b] Neoadjuvant and adjuvant treatments different between different institutions

PRBC: packed red blood cells; NR: not reported; postop: postoperative; CP: cystoprostatectomy; RPP: radical perineal prostatectomy; PSA: prostate specific antigen; SBO: small bowel obstruction; MI: myocardial infarction; ADT: androgen deprivation therapy; RP: radical prostatectomy;

Surgery time	Hospital stay	Reported complications	R0 resection	Follow-up	Secondary treatment	Reported outcomes
Mean 4.9h	Mean 10 days	30-day mortality 1/7 30-day morbidity 5/7 Late post-op complications 2/7	NR	–	–	6/7 patients alive at 3–22 months post-op 1/7 developed metastasis 1 year after CP
RPP: Mean 4h20min CP: Mean 8h20min	RPP: average 23 days CP: average 21.7 days	RPP: 4/4 reported post-op complications, including wound infection, urosepsis, urine leak CP and Koch pouch: 3/3 reported post-op complications, including urinoma requiring urinary diversion, urosepsis, SBO, pneumonia CP and ileal conduit: no reported complications	5/12 (41.7%)	Mean 49 months	–	4/12 no evidence of disease recurrence at follow-up 5/12 only elevated PSA at follow-up **Failure rate of salvage surgery after radiotherapy is higher than standard radical prostatectomy for localized prostate cancer (control) but not statistically significant**
Mean 8h	NR	6/10 reported post-op complications including haemorrhage requiring re-exploration, SBO, presacral abscess, Ileus, MI, rectal laceration	3/10 (30%)	Mean 59 months	–	6/10 developed metastasis and required ADT 1/10 no evidence of disease recurrence at follow-up 1/10 only elevated PSA at follow-up **CP had a significantly higher failure rate than standard radical prostatectomy controls**
RP: median 3.1h, range 1.5–5 CP: median 4.7h, range3-7.5 TPE: median 5.5h, range 3.9–8	RP: median 11.5 days, range 5–23 CP: median 12 days, range6–34 TPE median 20 days, range 12–45	RP: 30-day morbidity 10/32, 18/32 developed late complications CP: 30-day morbidity 10/23, 8/23 developed late complications TPE: 6/7 developed complications with a total of 16 reported complications and some patients experiencing several complications	RP: 24/32 (75%) CP: 15/23 (65%) TPE: 4/7 (53%)	–	17 patients (27%) received hormonal treatment after surgery	Overall 5-year survival rate: 68% **RP group had survival advantage and less recurrence compared to exenteration groups (higher residual cancer rates)** **Among the RP group, those who received adjuvant hormonal therapy had significantly less progression than those who did not**

TPE: total pelvic exenteration; LAR: low anterior resection; intra-op: intra-operative; PE: pulmonary embolus; PLND: pelvic lymph node dissection; TCC: transitional cell carcinoma; UTI: urinary tract infection; DVT: deep vein thrombosis.

TABLE 1.

Summary of studies on pelvic exenteration (anterior or total) for locally advanced prostate cancer, *Cont'd*

Author (Year)	Total number of patients	Exenteration type (number)	Indication (number)	Neoadjuvant treatment	Blood loss	PRBC transfusion	
Ahlering et al. (1992)	34	Prostatectomy (10) Cystoprostatectomy with urinary diversion (22): ileal conduit (8), continent cutaneous diversions (14) Cystoprostatectomy and LAR (1) Total pelvic exenteration (1)	Salvage surgery after failure of radiotherapy and no distant metastasis (34)	–	NR	NR	
Pontes et al. (1993)	43	Prostatectomy (35) Cystoprostatectomy (8)	Salvage surgery after failure of radiotherapy (43)	26 received hormonal surgery before or after surgery	CP: NR	CP: NR	
Lerner et al. (1995)	132	Radical prostatectomy (79–90%) Cystoprostatectomy (38–29%) Total pelvic exenteration (5–4%) PLND alone (10–7%)	Salvage surgery after failure of local radiotherapy and no distant metastasis, low co-morbidity and 10-year life expectancy (132)	–	NR	RP: median 1 unit, range 0–22 CP: median 2 units, range 0–22 TPE: median 9.5 units, range 7–97 PLND: median 1 unit, range 0–2	

a Data reported on a total of 18 patients: 6 prostate and 12 bladder cancer *b* Neoadjuvant and adjuvant treatments different between different institutions

PRBC: packed red blood cells; NR: not reported; postop: postoperative; CP: cystoprostatectomy; RPP: radical perineal prostatectomy; PSA: prostate specific antigen; SBO: small bowel obstruction; MI: myocardial infarction; ADT: androgen deprivation therapy; RP: radical prostatectomy;

after surgery[42]. Similarly, Sato et al. reported effective control of LUTS in all patients who underwent cystoprostatectomy as a primary treatment for LAPca and found no significant difference in QoL or overall survival compared with RP in those without bladder neck involvement; in fact, for patients who underwent cystoprostatectomy, the 10-year disease-free survival rate was 82%[39]. A recent report by Yuan et al. described cystoprostatectomy as a therapeutic option that provides symptom control and has favorable outcomes in terms of survival and patient QoL[33]. They included 27 patients with prostate cancer invading the bladder who had not received neoadjuvant treatment and had no distant metastases. All the patients underwent open or laparoscopic cystoprostatectomy with urinary diversion (ileal conduit or cutaneous ureterostomy) and extended pelvic lymph node dissection. All patients had LUTS before surgery, and all reported relief of urinary symptoms after the procedure. QoL was also assessed using the Functional Assessment of Cancer Therapy-

Surgery time	Hospital stay	Reported complications	R0 resection	Follow-up	Secondary treatment	Reported outcomes
NR	RP: mean 7.6 days, range 6–12 Exenteration: mean 11 days, range 7–16	2 patients of the cystoprostatectomy group developed complications (ileus and SBO, requiring exploration and adhesolysis)	NR	Mean 109 months post radiotherapy	27/34 (79%) received perioperative adjuvant hormonal therapy	24/34 alive without disease 2 have elevated PSA 10/34 developed recurrence 7 of whom died from disease
CP: NR	CP: NR	CP: 2 rectal perforations intra-op repaired primarily and 1 death from PE No significant late morbidity reported for those who underwent CP	13/43 (30.2%)	Range 1–10 years	26 received hormonal surgery before or after surgery	6/9 died from metastasis 34 were alive: • 10/34 no evidence of disease • 15/34 elevated PSA • 4/34 too early to evaluate • 5/34 has metastasis **No influence of hormonal therapy on survival was seen**
NR	RP: median 8 days, range 2–44 CP: median 12 days, range 8–34 TPE: median 20 days, range 12–45 PLND: median 8 days, range 5–15	RP: 35 (44%) complications reported CP: 12 (31.6%) complications reported TPE: 6 complications reported (some patients experienced more than one) PLND: 4 (40%) complications reported	NR	–	80 (61%) received adjuvant perioperative hormonal therapy	Generally, overall survival and cause-specific survival was significantly higher for the RP group compared to the exenteration groups (due to a higher proportion of patients with organ-confined disease as well as a higher proportion of non-aneuploid cancer in the RP group) **Adjuvant hormonal therapy was associated with higher progression-free survival in patients with non-aneuploid tumors**

TPE: total pelvic exenteration; LAR: low anterior resection; intra-op: intra-operative; PE: pulmonary embolus; PLND: pelvic lymph node dissection; TCC: transitional cell carcinoma; UTI: urinary tract infection; DVT: deep vein thrombosis.

Prostate (FACT-P) questionnaire, with the total score improving significantly at 6 months and one year after surgery compared with the preoperative score. Survival outcomes were also reported with a 3-year prostate cancer-free survival of 77.8%, as all patients received adjuvant ADT, with 9 patients also receiving RT and 3 receiving chemotherapy. These survival outcomes are comparable to those reported by Kumazawa et al., who described a similar population of patients, among whom 11 (64.7%) received neoadjuvant ADT and all received adjuvant ADT and were found to have a 5-year cancer-specific survival of 87.1%[41].

Cystoprostatectomy as a salvage option after failure of other therapies

Several authors have published the outcomes of salvage surgery after failure of RT for LAPca with no distant metastasis[23,26–28,32,34]. Cystoprostatectomy rather than prostatectomy was performed to alleviate LUTS, severe local symptoms, and complications after RT

TABLE 1.

Summary of studies on pelvic exenteration (anterior or total) for locally advanced prostate cancer, *Cont'd*

Author (Year)	Total number of patients	Exenteration type (number)	Indication (number)	Neoadjuvant treatment	Blood loss	PRBC transfusion	
Gheiler et al. (1997)	8	Cystoprostatectomy with urinary diversion: ileal conduit (5), orthotopic neobladder (3)	Radio-recurrent prostate cancer with: severe fibrosis of bladder neck (2) small fibrotic bladder with severe incontinence (1) synchronous bladder TCC (2) severe incontinence due to injury of external urinary sphincter suspected invasion of prostate cancer into bladder neck	-	Ileal conduit: mean 1030 ml Neobladder: mean 800 ml	Ileal conduit: mean 1.2 units Neobladder: mean 1 unit	
Bochner et al. (1998)[a]	6	Cystoprostatectomy and orthotopic neobladder (3) Total pelvic exenteration with orthotopic neobladder (3)	Recurrent prostate cancer after radiotherapy (4) Rectoprostatic fistula after radiotherapy (2)	–	Mean 840 mL[a]	NR	
Izawa et al. (2000)	6	Cystoprostatectomy with en bloc pubic symphysectomy (3) Cystoprostatectomy (1) Prostatectomy with bladder neck closure and continent catheterizable stoma (2)	Severe complications from salvage cryotherapy after failure of primary therapy for prostate cancer (6); including: Gross hematuria, urinary incontinence, prostatopubic fistula, bladder outlet obstruction and osteitis pubis	–	NR	NR	
Sato et al. (2003)	15	Cystoprostatectomy with urinary diversion: ileal conduit (5), rectal bladder (8), Koch pouch (1), ureterocutaneostomy (1)	Prostate cancer invading the urinary bladder (15)	Surgical patients received neoadjuvant and/or adjuvant hormonal therapy	NR	NR	

[a] *Data reported on a total of 18 patients: 6 prostate and 12 bladder cancer* [b] *Neoadjuvant and adjuvant treatments different between different institutions*

PRBC: packed red blood cells; NR: not reported; postop: postoperative; CP: cystoprostatectomy; RPP: radical perineal prostatectomy; PSA: prostate specific antigen; SBO: small bowel obstruction; MI: myocardial infarction; ADT: androgen deprivation therapy; RP: radical prostatectomy;

Surgery time	Hospital stay	Reported complications	R0 resection	Follow-up	Secondary treatment	Reported outcomes
NR	Ileal conduit: mean 10.6 days Neobladder: mean 12.7 days	Ileal conduit: 1/5 complications (incisional hernia, required operative repair) Neobladder: 30-day morbidity 2/3 (ileus, pyelonephritis), no late complications reported	Ileal conduit: 3/5 (60%) Neobladder: 1/3 (33.3%)	–	–	Ileal conduit: 1/5 developed metastasis and died 1/5 developed PSA rise after 12 months 2/5 had no detectable PSA rise 1/5 received orchiectomy as he had PSA rise before surgery Neobladder: 3/3 patients developed PSA increase at an average 22 months after surgery
NR	Mean 9.9 days, range 8-13)[a]	30-day morbidity 3/18 (1 ileus and 2 pouch-related complications)[a] 3/18 pouch-related late complications reported, with 2 requiring repeat interventions[a]	NR	Median 28 months[a]	–	67% reported good daytime continence and 57% reported good night time continence[a]
Mean 547 minutes, range 288–748	NR	2/6 reported complications (incisional hernia, wound infection)	NR	Mean 59 months, range 54-67	–	5/6 were alive at last follow-up (death was not related to prostate cancer) At last follow-up 3/6 remained disease-free with no detectable PSA levels
NR	NR	NR	NR	–	Surgical patients received neoadjuvant and/or adjuvant hormonal therapy	Disease specific survival: 82% at 10 years (vs. 100% for prostatectomy vs. 74% for hormonal therapy) PSA relapse-free survival: 51% at 5 years (vs. 65% for prostatectomy vs. 38% for hormonal therapy)

TPE: total pelvic exenteration; LAR: low anterior resection; intra-op: intra-operative; PE: pulmonary embolus; PLND: pelvic lymph node dissection; TCC: transitional cell carcinoma; UTI: urinary tract infection; DVT: deep vein thrombosis.

TABLE 1.

Summary of studies on pelvic exenteration (anterior or total) for locally advanced prostate cancer, *Cont'd*

Author (Year)	Total number of patients	Exenteration type (number)	Indication (number)	Neoadjuvant treatment	Blood loss	PRBC transfusion	
Kumazawa et al. (2009)	17	Cystoprostatectomy with urinary diversion: ileal conduit (7), rectal neobladder (9), Koch pouch (1)	Prostate cancer invading the urinary bladder without distant metastasis (17)	11 received neoadjuvant hormonal therapy	NR	NR	
Guo et al. (2009)	18	Total pelvic exenteration	Recurrent prostate cancer invading the rectum causing intractable perineal pain after failure of initial therapy (18)	–	NR	NR	
Spahn et al. (2017)[b]	62	Cystoprostatectomy	cT4 prostate cancer with bladder invasion as part of multimodal treatment (62)	–[b]	NR	NR	
Yuan et al. (2019)	27	Cystoprostatectomy with urinary diversion (ileal conduit or cutaneous ureterostomy)	Upfront surgery for prostate cancer invading the urinary bladder (27)	None	NR	NR	

[a] *Data reported on a total of 18 patients: 6 prostate and 12 bladder cancer* [b] *Neoadjuvant and adjuvant treatments different between different institutions*

PRBC: packed red blood cells; NR: not reported; postop: postoperative; CP: cystoprostatectomy; RPP: radical perineal prostatectomy; PSA: prostate specific antigen; SBO: small bowel obstruction; MI: myocardial infarction; ADT: androgen deprivation therapy; RP: radical prostatectomy;

Surgery time	Hospital stay	Reported complications	R0 resection	Follow-up	Secondary treatment	Reported outcomes
NR	NR	11/17 (64.7%) reported perioperative complications as follows: Wound infection: 3 (17.6%) Prolonged ileus: 6 (35.3%) Pelvic abscess: 1 (5.9%) Acute pyelonephritis: 1 (5.9%)	NR	-	All received adjuvant hormonal therapy	Projected 5-year PSA recurrence-free survival rate: 62.2% 5-year cause-specific survival: 87.1% (no significant difference between pN0 and pN1)
NR	NR	NR	8/18 (44.4%)	–	All received adjuvant hormonal therapy and 17/18 received adjuvant chemotherapy	9/18 (50%) died at a mean 18 months after surgery (range 2–69 months) 9/18 (50%) alive at a mean 15 months after surgery (range 3–34 months), but 4 developed metastasis
NR	NR	NR	29 (46.8%)	Mean 2.9 years	–[b]	Clinical recurrence in 69.4% of patients at a median of 35 months Estimated prostate cancer-specific survival: 44.5% at 5 years and 39.7% at 7 years Estimated overall survival: 39.8% at 5 years and 32.4% at 7 years **Seminal vesicle invasion was found to be a strong predictor of cancer-specific survival**
Mean 258.8 mins	NR	9/27 (33.3%) patients developed complications, including hydronephrosis, wound infection, DVT, uremia, ileus, arteriouretal fistula, classified as follows: Clavien-Dindo grade 1: 5 (18.5%) patients Clavien-Dindo grade 2: 2 (7.4%) patients Clavien-Dindo grade 3: 2 (7.4%) patients	25/27 (92.6%)	Mean 46.1 months, range 20–80	All received adjuvant hormonal therapy, some also received adjuvant radiation or chemotherapy	Overall survival: 100% at 1 year, 88.9% at 3 years Clinical progression-free survival: 100% at 1 year, 77.8% at 3 years Biochemical progression-free survival: 92.6% at 1 year, 62.9% at 3 years

TPE: total pelvic exenteration; LAR: low anterior resection; intra-op: intra-operative; PE: pulmonary embolus; PLND: pelvic lymph node dissection; TCC: transitional cell carcinoma; UTI: urinary tract infection; DVT: deep vein thrombosis.

TABLE 1.

Summary of studies on pelvic exenteration (anterior or total) for locally advanced prostate cancer, *Cont'd*

Author (Year)	Total number of patients	Exenteration type (number)	Indication (number)	Neoadjuvant treatment	Blood loss	PRBC transfusion	
Heidenreich et al. (2020)	103	Radical prostatectomy (9, 8.7%) Cystoprostatectomy (71, 68.8%) Total (23, 22.4%)	Locally advanced CRPC (84) or CSPC (19) with symptomatic infiltration into bladder, rectum or pelvic floor despite previous therapy	-	NR	14.6% required transfusions from date of admission till 90 days after surgery	
Surcel et al. (2020)	25	Cystoprostatectomy (23) Total pelvic exenteration (2) Urinary diversion: ileal conduit (18), ureterocutaneostomy (6), Mainz Pouch (1)	Palliation of cT4 prostate cancer with local invasion and local symptoms in a majority of patients, regardless of distant metastasis (25)	13 (52%) upfront surgery and 12 (48%) after ADT	NR	NR	

a Data reported on a total of 18 patients: 6 prostate and 12 bladder cancer b Neoadjuvant and adjuvant treatments different between different institutions

PRBC: packed red blood cells; NR: not reported; postop: postoperative; CP: cystoprostatectomy; RPP: radical perineal prostatectomy; PSA: prostate specific antigen; SBO: small bowel obstruction; MI: myocardial infarction; ADT: androgen deprivation therapy; RP: radical prostatectomy;

or if RP was not surgically feasible. Data on primary therapy, adjuvant therapy, and survival outcomes have not been consistently reported among studies with vast heterogeneity. The studies are presented in **Table 1**.

Exenteration surgery to control local symptoms

Direct invasion of prostate cancer into the surrounding tissues in locally advanced disease may result in symptoms such as significant perineal pain, LUTS, and urinary tract obstruction[50]. Pelvic exenteration has been described for prostate cancer with rectal and perineal invasion, causing severe symptoms that are unresponsive to RT[51]. Kamat et al. described the efficacy of total pelvic exenteration in the complete relief of perineal pain not responding to narcotics in 14 men

with prostate cancer invading the rectum and having failed ADT and RT with an average symptom-free interval of 14 months in 11 men[40]. Pelvic exenteration can alleviate symptomatic local recurrence of prostate cancer after RP, which is not possible with ADT and RT. In a small series, Leibovici et al. reported that 4 patients underwent total pelvic exenteration and 1 patient underwent wide tumor resection after RP, concluding that salvage pelvic exenteration is feasible in well-selected patients[25]. Guo et al. reported the outcomes of total pelvic exenteration after recurrent prostate cancer invading the rectum causing severe intractable perineal pain[36]. On the other hand, Surcel et al. performed cystoprostatectomy or pelvic exenteration for cT4 prostate cancer with severe local symptoms, regardless of previous treatment or distant metastasis[30].

Surgery time	Hospital stay	Reported complications	R0 resection	Follow-up	Secondary treatment	Reported outcomes
Mean 271 minutes, range 210–292	Mean 18.3 days, range 10–34	Reported complications classified as follows: Clavien-Dindo grade 2: 30.6% of patients Clavien-Dindo grade 3: 11.3% of patients Clavien-Dindo grade 4: 8.1% of patients	71/103 (68.9%)	Mean 3.04 years	–	Symptom-free survival: 89.2% at 1 year, 64.1% at 3 years Overall survival: 92.2% at 1 year, 43.7% at 3 years
NR	NR	11/25 (44%) patients developed perioperative complications, classified as follows: • Clavien-Dindo grades 1-3a: 7 (28%) patients • Clavien-Dindo grades 3b-4: 4 (16%) patients (required surgical revision: 1 colostomy, 1 complicated lymphocele, 2 ileus due to adhesions)	12/25 (48%)	Median follow-up 15 months, range 3–41	–	11/25 (44%) were alive at follow-up 8/25 died of prostate cancer 6/25 died of other causes Median overall survival: 15 months **No significant difference in survival between the group who received preoperative ADT and the group that did not**

TPE: total pelvic exenteration; LAR: low anterior resection; intra-op: intra-operative; PE: pulmonary embolus; PLND: pelvic lymph node dissection; TCC: transitional cell carcinoma; UTI: urinary tract infection; DVT: deep vein thrombosis.

Role of exenteration in castrate-resistant prostate cancer

Many patients with castrate-resistant prostate cancer (CRPC) experience local symptoms, such as hematuria, upper tract obstruction, or rectal invasion. Although the changes in the landscape of CRPC treatment have led to improvements in the overall survival of these patients from multimodal treatment and advancements in systemic therapeutics, local symptoms still pose a burden to affected patients and are projected to increase in incidence given the improved life expectancy of patients with CRPC[52,53]. In fact, approximately half of CRPC patients experience cancer-related local symptoms in their final year of life, with up to 25% requiring upper or lower urinary tract surgical interventions

for palliation[52,53]. As described earlier, invasion of the bladder or rectum may necessitate anterior or total pelvic exenteration even in patients with CRPC; however, patients should be good surgical candidates with an expected survival of over 1 year[52,53]. Recently, Heidenreich et al. reviewed 103 patients with LAPca, of whom 84 had castrate-resistant prostate cancer and underwent pelvic exenteration for symptom relief[37]. Overall, 78.6% of patients were able to obtain complete relief of symptoms in their remaining lifetime. A total of 41.7% of men reported gross hematuria before surgery, whereas none reported hematuria after pelvic exenteration. A total of 55.3% of patients had upper urinary tract obstruction before surgery managed by endoluminal stenting or percutaneous nephrostomy, all of which were removed postoperatively, with only

TABLE 2.

Reported cases of minimally invasive pelvic exenteration for prostate cancer,

Author (Year)	Number of patients	Exenteration surgery	Indication	Blood loss	PRBC transfusion	
Yang et al. (2015)	1	Laparoscopic total pelvic exenteration with cutaneous ureterostomy and sigmoidostomy	Recurrent prostate sarcoma causing difficult defecation	600 mL	NR	
Castillo et al. (2015)[a]	1	Robotic pelvic exenteration, bilateral EPLND, en-bloc excision of bladder and rectum, urinary and fecal diversion using double-barrel wet colostomy	CRPC after radical prostatectomy + salvage radiation followed by ADT, presenting with rectal recurrence.	600 mL	NR	
Winters et al. (2015)	3	Robotic total pelvic exenteration with laparoscopic rectus flap	Local recurrence of high-risk prostate cancer with a large malignant rectourethral fistula - biopsy revealed recurrent prostate cancer extending to the rectal side of this fistula.	800 mL	2 units	
			Prostate cancer treated with brachytherapy presented 6 years later with cT4 high-grade, squamous differentiated urothelial carcinoma involving the bladder neck, prostate, and perirectal tissues	500 mL	1 unit	
			T4N2M0 rectal adenocarcinoma treated with chemotherapy, followed by EBRT with persistent mass involving the prostate, seminal vesicles, and bladder	350 mL	NR	
Maurice et al. (2017)	1	Robotic total pelvic exenteration with intracorporeal sigmoid conduit and colostomy	Metastatic CRPC with failed primary brachytherapy but good systemic response to chemotherapy and ADT. PSA continued to rise with an enlarging prostatic pelvic mass causing progressive local symptoms	NR	NR	

[a] First reported case of robotic pelvic exenteration

UTI: urinary tract infection; EPLND: extended pelvic lymph node dissection; CRPR: castrate-resistant prostate cancer; ADT: androgen deprivation therapy; PSA: prostate-specific antigen; NR: not reported; PRBC: packed red blood cells; ICU: intensive care unit; EBRT: external beam radiotherapy;

Surgery time	Hospital stay	Reported complications	R0 resection	Follow-up	Reported outcomes
415 min	10 days	No early complications UTI after 6 months	R0 achieved	12 months	Died of recurrence
249 min	7 days	NR	NR	24 months	6 weeks later: decreased PSA = 1.39 Then treated with ADT and chemotherapy 2 years later: good quality of life, PSA = 2.37
660 min	7 days, 1 day in ICU	30-day morbidity: 1/3 (33.3%) – patient developed pelvic abscess and pyelonephritis	2/3 (66.6%)	–	All back to daily activities within 4–6 weeks
600 min	8 days, 1 day in ICU				
570 min	7 days, 1 day in ICU				
324 min (total robotic time)	8 days	DIC (resolved by blood products), TIA (no permanent disability)	NR	–	Died after 5 months due to metastatic disease but complete palliation of symptoms was achieved

DIC: disseminated intravascular coagulation; TIA: transient ischemic attack; LAR: low anterior resection; TPN: total parenteral nutrition; APR: abdomino-perineal resection.

TABLE 2.

Reported cases of minimally invasive pelvic exenteration for prostate cancer, *Cont'd*

Author (Year)	Number of patients	Exenteration surgery	Indication	Blood loss	PRBC transfusion	
Smith et al. (2020)	2	Robotic LAR + en-bloc prostatectomy	Locally advanced extracapsular prostate cancer after brachytherapy	NR	2 units	
		Robotic APR + en-bloc cystoprostatectomy + ileal conduit	Locally advanced extracapsular prostate cancer after EBRT with synchronous T1 rectal cancer	NR	2 units	
Peng et al. (2020)	1	Robotic pelvic exenteration	Prostate cancer with extracapsular extension that had persistent abutment of rectal wall and pelvic floor involvement after chemoradiation	NR	NR	

[a] First reported case of robotic pelvic exenteration

UTI: urinary tract infection; EPLND: extended pelvic lymph node dissection; CRPR: castrate-resistant prostate cancer; ADT: androgen deprivation therapy; PSA: prostate-specific antigen; NR: not reported; PRBC: packed red blood cells; ICU: intensive care unit; EBRT: external beam radiotherapy;

5.8% of patients requiring stenting later. The surgical procedures and patient outcomes are summarized in **Table 1**.

Other reported indications for pelvic exenteration in prostate cancer

Cystoprostatectomy has been described in the management of synchronous prostate and rectal cancer[54,55] and synchronous prostate and bladder cancer[56], as well as in the management of severe complications of salvage cryotherapy for prostate cancer[38].

Discussion

Pelvic exenteration, whether total or anterior, has been performed for LAPca, including CRPC, and has been described for the following indications: prostate cancer invading the bladder; salvage surgery after failure of other treatments; control of local symptoms; and synchronous prostate, bladder, or rectal tumors. In addition to the potential survival benefits associated with surgical treatment, pelvic exenteration may provide additional symptomatic benefits that investigators have evaluated in several studies.

The main limitation in assessing the impact of pelvic exenteration in LAPca is the heterogeneity and limitations of the published studies. The majority of the studies have had small sample sizes and varied patient characteristics. Data on previous therapies, neo-adjuvant treatments, and adjuvant treatments have not been consistently reported and have insufficient details. Different survival parameters and follow-up durations have been reported. Surgical procedures and techniques were different between studies; for example, different types of urinary diversion were used with all being feasible, but no data reported on the superiority of one over the other. Not all studies have reported operative outcomes, including the need for blood transfusions and length of hospitalization. Reporting of complications was not standardized among studies, with few using the Clavien-Dindo classification. Comparisons made within the studies were also heterogeneous. For example, Gheiler et al.[35] compared all outcomes after cystoprostatectomy based on the type of urinary diversion used; Zincke et al.[34] and Lerner at al.[26] compared the outcomes between different types of surgery performed as salvage treatment after radiotherapy; and Ward et al.[32] reported the difference in need for blood transfusions and early complication rates in patients undergoing cystoprostatectomy based on the year of their surgery. Finally, there are scarce reports on the outcomes of long-term follow-up, including the need for further urological interventions, number of readmissions, and objective assessment of QoL.

Surgery time	Hospital stay	Reported complications	R0 resection	Follow-up	Reported outcomes
480 min	15 days, 1 day in ICU	Ileus (required TPN), atrial fibrillation	R0 achieved	12 months	No recurrence for both at 12 months follow-up
360 min	11 days, 1 day in ICU	NR	R0 achieved		
NR	NR	NR	R0 achieved	–	–

DIC: disseminated intravascular coagulation; TIA: transient ischemic attack; LAR: low anterior resection; TPN: total parenteral nutrition; APR: abdomino-perineal resection.

Pelvic exenteration represents a major surgery that can lead to significant morbidity and that may harbor a perioperative mortality risk. The major complication rates reported in the literature range between 44% to 55%. The impact of minimally invasive surgery for pelvic exenteration in prostate cancer is still unclear, given the small number of cases reported. Although there are no clear outcomes, a minimally invasive approach is possible, with few reported complications.

Most authors concluded that exenteration may be feasible for well-selected patients despite the increased operative risk. Therefore, the decision to proceed should be tailored according to patient comorbidities, projected life expectancy, impact of symptoms on QoL, and availability of experienced surgeons to perform these complex operations.

LAPca management remains a clinical challenge despite advances in systemic therapies over the past decade[57,58]. Even though systemic agents as well as traditional ADT have been successful in decreasing the progression and improving the survival of patients with advanced prostate cancer, they may not palliate or address the symptoms associated with the direct invasion of LAPca. Pelvic exenteration, on the other hand, may not be curative in locally advanced disease but may be associated with a durable disease response, particularly in combination with systemic treatments.

The rationale for the use of cytoreductive surgery involves multiple postulations. Decreasing the bulk of the disease would render systemic therapy more effective, since the same dosage is used against a smaller number of malignant cells. Another theory is that surgical debulking decreases the number of cells that can undergo somatic mutations and become castrate-resistant in cases of prostate cancer[59,60]. Another rationale is extrapolation from the concept of index lesions in prostate cancer and clonality, which is the scientific basis of prostate focal therapy[61]. Exenteration would treat the index lesion, which would eventually lead to metastasis and castration resistance.

The evidence for cytoreductive surgery in metastatic prostate cancer is not as robust but is an area of interest for many investigators. A study using the SEER database showed that such patients who underwent local therapy had a survival benefit over those who did not receive local therapy[62]. Another national cancer database study showed that cytoreductive prostatectomy and primary radiotherapy provide an overall survival benefit in metastatic prostate cancer[63]. However, these were retrospective database studies and did not provide robust evidence to change current practice guidelines or currently available systemic treatment options. Recently, the STAMPEDE trial has shown a survival benefit of local radiation therapy in low-volume metastatic prostate cancer[64].

While pelvic exenteration may provide an oncologic benefit for locally advanced or metastatic prostate cancer, a more compelling reason for surgical intervention is the control of local symptoms. However, there is no standardized quantifiable QoL indicator because symptomatology is variable given the heterogeneous nature of this disease and its classification. Future studies using validated QoL questionnaires would help to address these questions in these patients[65].

Recently, with the introduction of theranostics and the emerging widespread adoption of functional imaging studies such as positron emission tomography using prostate-specific membrane antigen (PET-PSMA), variations in clinical management are expected[66]. These would include surgical planning in cases of advanced disease requiring exenteration.

The improvement in the perioperative and postoperative outcomes of salvage robot-assisted radical prostatectomy might open the door for better utilization of neoadjuvant RT for LAPca[67,68]. The role of neoadjuvant RT is well established for several different types of malignancies and is considered the standard of care for some patients[69,70]. The rationale for its preoperative use in cases of prostate cancer is that RT induces long-term growth arrest in prostate cancer cells rather than acute apoptosis[71]. These cells would still be positive if present at the resection margin; however, a positive margin after neoadjuvant radiation therapy might indicate the presence of sterilized cancer cells that later die due to necrosis[71].

The role of neoadjuvant RT in prostate cancer has not been well studied, and neoadjuvant RT is not part of the standard of care for the management of patients with prostate cancer. Carlson et al. reported their results on 18 patients who received neoadjuvant RT doses ranging from to 40 to 70 Gy followed by radical prostatectomy 1 to 2 months afterwards, with minimal postoperative morbidity and 67% of patients metastasis-free at 5 years[72]. Several phase I and phase II trials of neoadjuvant RT followed by radical prostatectomy have confirmed the safety of the surgery with minimal side effects and improvement in biochemical progression-free survival[73]. This approach should be investigated in patients with LAPca who might be good candidates for pelvic exenteration.

Conclusion

Pelvic exenteration can be offered to patients with LAPca, whether for cure or for palliation of local symptoms; however, it is not a widely used management option. Retrospective data indicated that pelvic exenteration may help alleviate local pain and LUTS and improve patient QoL. However, the oncological benefits of such procedures have not been well established. Furthermore, this extensive surgical treatment option is associated with high complication rates. There is an urgent need for prospective multicenter studies that use a standardized methodology to report complications, incorporate patient-reported outcomes, and examine novel endpoints such as the need for adjunct upper and lower urinary tract procedures and the need for hospitalization for complications related to the primary tumor. These studies will help define the future role of pelvic exenteration as a treatment modality for LAPca.

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