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Guideline

Minimum standards of pelvic exenterative practice: PelvEx Collaborative guideline

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Introduction

Pelvic exenteration refers to radical surgery to remove advanced or recurrent pelvic malignancies by partial or total resection of contiguously affected organs[1]. An *en bloc* resection with negative margins (R0) is the goal for an ideal prognosis[2,3]. Therefore, the extent is determined by the infiltration pattern of the tumour[1]. The human pelvis can be divided into several compartments in order to better define the topography of the tumour, to predict which structures could be invaded and to plan the extent of curative surgery. Seven compartments have been identified (*Table 1* and *Fig. 1*)[4]. Surgical procedures vary according to their involvement.

An exenteration is associated with morbidity in as many as 80 per cent of patients[2,5]. Although extensive resections result in improved radical resection rates, they come at the cost of increased morbidity and greater functional compromise, necessitating specialist perioperative care and multidisciplinary involvement[6]. Centralization of care to high-volume surgical units has facilitated this, challenging the traditional boundaries of resectability. The purpose of this document is to characterize a set of minimum standards that can be applied to the care of patients with advanced pelvic malignancy. It is not intended to be prescriptive; rather, the aim is to provide guidance for clinicians and centres alike who are developing a service, and to outline the essential components of care to which they can aspire.

Definitions

Anterior pelvic exenteration includes resection of the structures of the anterior pelvis, namely the bladder, urethra and inner reproductive organs, whereas posterior pelvic exenteration comprises resection of the structures of the posterior pelvic cavity with reproductive organs and rectum, with or without the anal canal[1]. Lateral compartment excision describes the resection of pelvic sidewall structures, such as the iliac vessels, piriformis and obturator internus muscles, and ischium, along with sacrotuberous and sacrospinous ligaments[7]. Total pelvic exenteration entails removal of the bladder, urethra, inner reproductive organs, rectum, and anus with their muscles and ligaments[1].

Multidisciplinary team guidance

The implementation of a multidisciplinary team (MDT) approach to colorectal cancer has been widely accepted and improvements in cancer-specific outcomes have been demonstrated[8,9]. This holds true nowhere more so than in the treatment of locally advanced and recurrent rectal and non-rectal cancers, especially when considering the complexity of, and great disparity in, the care of such patients[10]. This requires an ever-increasing understanding of the myriad of advances, modalities, and treatment algorithms available. It is, therefore, important to harness, involve, and coordinate the expertise of various specialists and subspecialists in order to optimize selection for surgery, minimize morbidity, improve survival, and maximize quality of life (QoL) for patients with these complex pathologies.

Several studies have reported an association between improved survival and discussion at MDT meetings, and this is more evident in complex rectal cancers, where accurate preoperative staging, mapping, and planning play a major role[11,12]. MDT meetings may confer other benefits, such as better communication among clinicians, provision of most up-to-date treatments, education, and training, and improved coordination of care. They are an important part of care for patients with complex cancer, although the resources required to run them are significant and need to be factored into service planning[13].

Ideal make-up of advanced pelvic cancer multidisciplinary team

All relevant specialties/disciplines should be represented[14]. The members should have the level of expertise and specialization relevant to advanced rectal/pelvic cancer. A clinician and specialist nurse who have met the patient who is being discussed must be present at the meeting. The make-up of the advanced pelvic cancer MDT largely depends on local institutional circumstances and availability as well as the pattern of tumour involvement. An ideal composition would be as follows. Core team members comprise: MDT lead/chair (such as colorectal, gynaeoncology or urology consultant); MDT coordinator/secretary; (at least 2) colorectal surgeons; gynaeoncology surgeon; urology surgeon; medical oncologist;

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radiation oncologist; histopathologist; radiologist; and clinical nurse specialists in colorectal/gynaeoncology/urology, as well as for sexual/pelvic floor rehabilitation support. Extended team members, joining by invitation as required according to cancer site and planned extent of procedure, include: oncoplastic surgeon; hepatopancreatobiliary surgeon; thoracic surgeon; vascular surgeon; orthopaedic surgeon/neurosurgeon; perioperative physician; physiotherapist for anticipated morbid procedure such as sacrectomy or major nerve division; palliative care team, for patients whose treatment intent is palliative; enterostomal therapists; clinical psychologist; dietician; and anaesthetist/intensivist for perioperative and postoperative care planning.

Functioning of an advanced pelvic cancer multidisciplinary team

Discussion at a dedicated advanced pelvic cancer MDT meeting is mandatory for high-risk and complex cases, such as patients with locally advanced rectal and non-rectal cancers, metastatic disease or recurrent disease[8,12,15,16]. Referral is made at the time of first diagnosis. Ideally, designated advanced pelvic cancer MDTs should be assigned, based on institutional, local, and regional referral patterns, and expertise. Referral guidelines that would trigger a referral to the designated regional or national advanced pelvic cancer MDT should be in place. Referrals should be made after completion of a standardized advanced pelvic cancer referral pro forma, to be filled by the consultant in charge, registrar or specialist nurse. This should include a predetermined minimum amount of information that would aid the MDT in its discussion and decision-making, which includes: patient demographics; diagnostic information, including a physical examination and digital rectal examination (DRE); patient fitness (performance status) and co-morbidities; history of previous malignancies, including histopathology; previous surgery and any chemo/radiotherapy; recommendations from previous and local MDTs; the patient's preferences (if known); the rationale for requiring MDT discussion; and whether the patient is suitable for any current clinical trials.

Table 1 Description of intrapelvic compartments

	Boundaries and organs
Anterior	
Anterior, above peritoneal reflection	Ureters and iliac vessels, sigmoid colon, small bowel and lateral sidewall fascia
Anterior, below peritoneal reflection	Genitourinary system and pubic symphysis
Anterior urogenital triangle	Anterior perineum, urethra, bulbospongiosus and ischiocavernosus muscles; external genitalia
Central	Rectum or neorectum, intraluminal, extraluminal and/or perirectal fat or mesorectal recurrence
Posterior	Coccyx, presacral fascia, retrosacral space and sacrum up to upper level of S1
Lateral	Ureters, external and internal iliac vessels, lateral pelvic lymph nodes, sciatic nerve, sciatic notch, S1 and S2 nerve roots, and piriformis and obturator internus muscles
Infralevator	Levator ani muscles, external sphincter complex, perineal scar (if previous abdominoperineal excision), and ischioanal fossa

Adapted from Rokan *et al.*[4]. Peritoneal reflection: level of rectovesical or rectouterine pouch.

Preparation and patient selection for discussion: multidisciplinary team lead and coordinator

Owing to the potential for receiving many referrals, and for the sake of allocating adequate time to discuss each patient in sufficient detail, the MDT lead along with the MDT coordinator should vet the referrals received and ensure their suitability for discussion. They set the meeting agenda and anticipate any additional specialist presence that would be required for each individual patient (such as a urologist), and arrange it accordingly. They must also ensure that all essential staging information and reports are available, such as pathology and slides, radiology, and tumour markers. The flow of the discussion should follow an agreed sequence according to the pro forma, going through demographic details, baseline functional status and co-morbidities, route of referral, diagnostic information, histopathology, radiology, etc. to be presented by the respective specialists.

A standardized system and template for reporting of advanced pelvic cancer MDT outcomes should be adopted. This enhances communication between care providers and avoids inconsistencies in the data recorded, thereby ensuring a greater

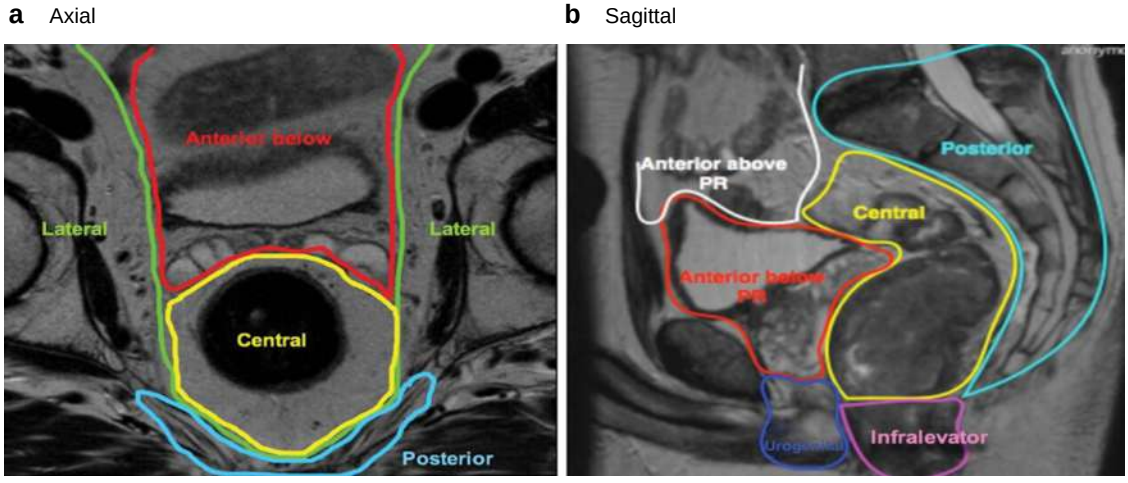

Fig. 1 MRI axial and sagittal views of defined Royal Marsden group intrapelvic compartments

a axial and **b** sagittal. PR, peritoneal reflection.

likelihood of treatment receipt or referral, guideline-adherent care, improved documentation of disease stage and performance status, and improved patient outcomes and practice patterns[17,18]. The template also supports collection of data for reporting against key performance indicators to government cancer control agencies. The MDT template should enable capture of data in discrete fields using international terminology systems, such as Systematized Nomenclature of Medicine, and would ideally be integrated into institutional electronic health records.

Staging guidelines for patients considered for pelvic exenteration

Preoperative local staging

All imaging relevant to cancer staging and preoperative planning, including time of first diagnosis, should be reviewed by an experienced gastrointestinal radiologist with a special interest in complex pelvic cancer. Radiologists require specialist experience in pelvic anatomy, types of cancer, and patterns of disease extension. Cancer type, stage, extent, response to treatment, and speed of progression vary over time. The maximum extent of cancer is frequently used to plan resection. Relevant histopathology and endoscopy findings should be made available at the time of reporting.

All patients considered for pelvic exenteration require pelvic MRI. Protocols should include multiplanar T2-weighted imaging, with a maximum slice thickness in the axial and coronal plane of no more than 3 mm. Acquisition should be perpendicular and parallel to the tumour axis in the axial and coronal planes respectively. Volumetric (Sampling Perfection with Application optimized Contrasts using different flip angle Evolution/CUBE/Volume ISotropic Turbo spin echo Acquisition) T2-weighted imaging enables multiplanar three-dimensional (3D) reconstruction, which can help assess tumour boundaries. There should be sufficient imaging to allow thorough evaluation of the inguinal, internal iliac, obturator, and external iliac lymph nodes (*Fig. 2*)[19]. Unless contraindicated, administration of buscopan as a spasmolytic can help reduce motion artefact. Diffusion-weighted sequences may be of benefit but are not mandatory. Fat-suppressed, precontrast and dynamic contrast-enhanced T1-weighted imaging is not recommended routinely[20].

Preoperative staging of distant disease

CT examination of the chest, abdomen, and pelvis is recommended routinely for staging of primary and recurrent rectal or anal cancer[21]. Whole-body MRI is not more accurate than CT for detection of metastatic disease[22], and there is no evidence to support its use for patients with recurrent colorectal cancer.

Peritoneal disease can be challenging to detect and assess accurately by CT, particularly in small-volume disease or if there is a paucity of intraperitoneal fat. Consequently, diagnostic laparoscopy is recommended when imaging is equivocal. The Peritoneal Cancer Index is used to help assess the likelihood of successful cytoreductive surgery, and is generally calculated by CT with or without laparoscopy. Diffusion-weighted MRI is a promising non-invasive tool to improve the sensitivity and specificity of radiological detection of peritoneal disease[23].

Liver MRI with hepatobiliary contrast agents and diffusion-weighted sequences should be performed in all patients with equivocal or metastatic liver lesions on CT (unless contraindicated). The authors also recommend liver MRI if there is recurrent cancer, fatty liver on CT, or adverse radiological features such as extramural vascular invasion. Use of liver MRI should be considered for detection of colorectal liver metastases (CRLMs) in patients with negative CT results as this technique has superior sensitivity to CT (91.4 *versus* 80.9 per cent)[24]. Liver MRI can more accurately inform decisions on treatment of CRLMs. However, liver MRI is not a recommended first-line modality for exclusion of CRLMs in current European Society of Medical Oncology (ESMO), Association of Coloproctology of Great Britain and Ireland (ACPGBI) or American College of Radiology (ACR) guidelines[25].

PET–CT is an option for all patients in whom pelvic exenteration is being considered, and is recommended routinely for all patients with primary anal carcinoma, often avoiding the need for sampling of enlarged inguinal or pelvic nodes[26,27]. In other pathologies, its use is reserved for characterizing possible metastases identified by standard imaging. PET–CT offers little advantage for staging of patients with primary colorectal cancer without metastases on standard CT imaging[28]. PET–CT is indicated for further evaluation of potentially metastatic lymph nodes or pulmonary nodules (8 mm or larger), or where recurrent pelvic cancer is suspected on CT or MRI. Low fluorodeoxyglucose (FDG) PET avidity is a well recognized phenomenon with mucinous adenocarcinoma and should be interpreted with caution.

Image-guided biopsy

It is common practice to obtain tissue for pretreatment histopathological assessment where feasible. Percutaneous image-guided biopsy is the most common method. The needle track should be included in the subsequent preoperative radiological roadmap for surgery. Mismatch repair status and presence of *KRAS*/*BRAF* mutations should be sought explicitly. Transrectal or transvaginal biopsy increases accessibility to biopsy.

Where biopsy is not safe or feasible, diagnosis of cancer (particularly in the setting of recurrent disease) is made through MDT consensus using a combination of clinical and imaging evidence. Imaging evidence includes that not limited to CT, MRI, and PET–CT. Interval imaging showing growth and/or response to preoperative treatment can also help in the diagnosis of cancer.

Predicting resectability

Precise, detailed communication and feedback between radiologists and surgeons is essential for assessment of patient operability. Experienced radiologists and the surgical team agree a radiological roadmap for surgery, providing a ‘dotted line’ along which surgeons can resect a specimen, surrounded by a rim of healthy tissue. The radiological roadmap considers surgical planes to create a bespoke surgical plan based on technical feasibility. The acronym BONVUE (Bones, Organs, Nerves, Vessels, Ureters, Extra-pelvic disease) is offered as a radiological aide-mémoire to help ensure a comprehensive radiological report before MDT discussion.

Neoadjuvant treatment: rectal cancer

Local control improved significantly with the introduction of total mesorectal excision (TME) surgery. The TME trial[29] subsequently demonstrated that neoadjuvant short course radiotherapy and TME combined resulted in recurrence rates of only 5.6 per cent. In locally advanced rectal cancer (LARC) and locally recurrent

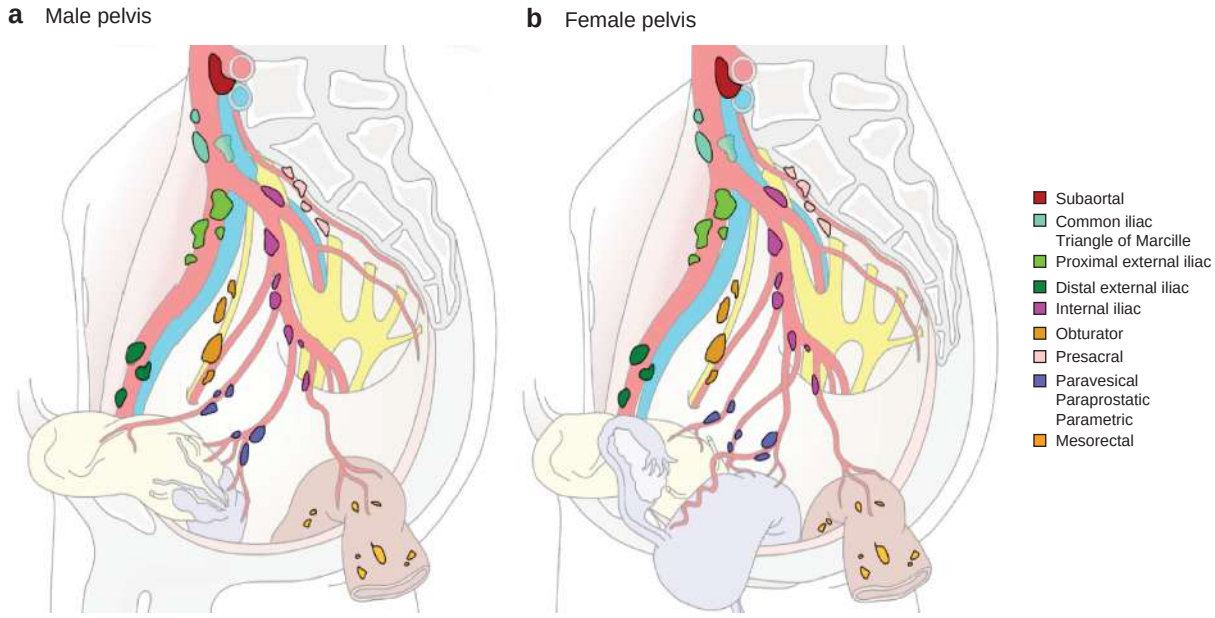

Fig. 2 Schematic diagram of pelvic lymph node compartments
Mediolateral view of right-sided **a** male pelvis and **b** female pelvis.

rectal cancer (LRRC) in particular, the risk of local recurrence is higher, which is most likely the result of incomplete resections owing to involvement of the mesorectal fascia and/or surrounding organs and structures. Preoperative downstaging may reduce the risk of incomplete resection and local recurrence. As radical resection (R0) is the main prognostic factor for survival in patients undergoing surgery for non-metastatic LARC and LRRC, preoperative downstaging may also improve survival, although this has not been demonstrated in RCTs. To achieve maximal downstaging, neoadjuvant chemoradiotherapy has been shown to be superior to short-course radiotherapy[30–32].

Neoadjuvant chemoradiotherapy for locally advanced rectal cancer

Neoadjuvant chemoradiotherapy is administered for downstaging LARC. Recommended treatment strategies include long-course chemoradiotherapy (45–50 Gy administered in 1.8–2-Gy fractions over 5–6 weeks) or short-course radiotherapy (5 Gy administered in 5 daily fractions). Chemotherapy with capecitabine in combination with radiotherapy appears to present the best possible balance between efficacy and toxicity. To optimize treatment, systemic chemotherapy can be administered before or after long-course chemoradiotherapy or short-course radiotherapy, referred to as total neoadjuvant therapy (TNT). TNT is promising in the setting of locally advanced disease; more recently, evidence from the RAPIDO and PRODIGE-23 trials of reduced disease-related treatment failures has provided further support for this approach[33–36].

Adjuvant therapy is controversial. Patients benefit in terms of locoregional control from both neoadjuvant and adjuvant radiotherapy, but neoadjuvant therapy induces downstaging of the tumour and therefore increases radical (R0) resection rates, which is the main predictor of survival. Patient compliance is generally better in the neoadjuvant setting[30,37].

Neoadjuvant chemoradiotherapy for locally recurrent rectal cancer

Neoadjuvant chemoradiotherapy is administered for downstaging of LRRC in patients who are radiotherapy-naive. Neoadjuvant chemoradiotherapy is indicated because of frequent involvement of surgical resection margins, the exceptionally high rate of local re-recurrence, and the proven efficacy of neoadjuvant chemoradiotherapy in LARC.

Neoadjuvant chemoreirradiation should be considered in patients with LRRC who received radiotherapy previously. Evidence to support the efficacy of routine reirradiation is lacking; it is offered on an individual basis. Preoperative tumour volume reduction by reirradiation appears to be safe and seems to be of additional value in obtaining R0 resection[32,38]. Further research to establish the value of reirradiation and the role of concurrent chemotherapy is needed. There is currently no evidence to suggest a benefit of adding induction chemotherapy[39]. The GRECCAR15 and PelvEx II trials will provide more evidence on the role of neoadjuvant reirradiation and induction chemotherapy in LRRC[40,41].

Radiotherapy techniques

In radiotherapy-naive patients, a treatment regimen of 45–50 Gy is administered in 25–28 fractions. For patients who have had radiotherapy previously, reirradiation with up to 30 Gy in 15 fractions appears to be safe and effective, although clinical relevance has not been demonstrated definitively[33]. However, reirradiation is not standardized and, where performed, dosing schedules vary significantly between centres and regions.

Three-dimensional conformal radiation therapy (3D-CRT) is considered acceptable but delivers high doses to critical local structures. Intensity-modulated radiotherapy is an advanced form of 3D-CRT, in which the radiation beam intensity can be changed or modulated during treatment, thus achieving maximal delivery of radiotherapy while avoiding increased toxicity[42]. Newer techniques, such as volumetric modulated arc therapy, have been shown to deliver highly conformal doses

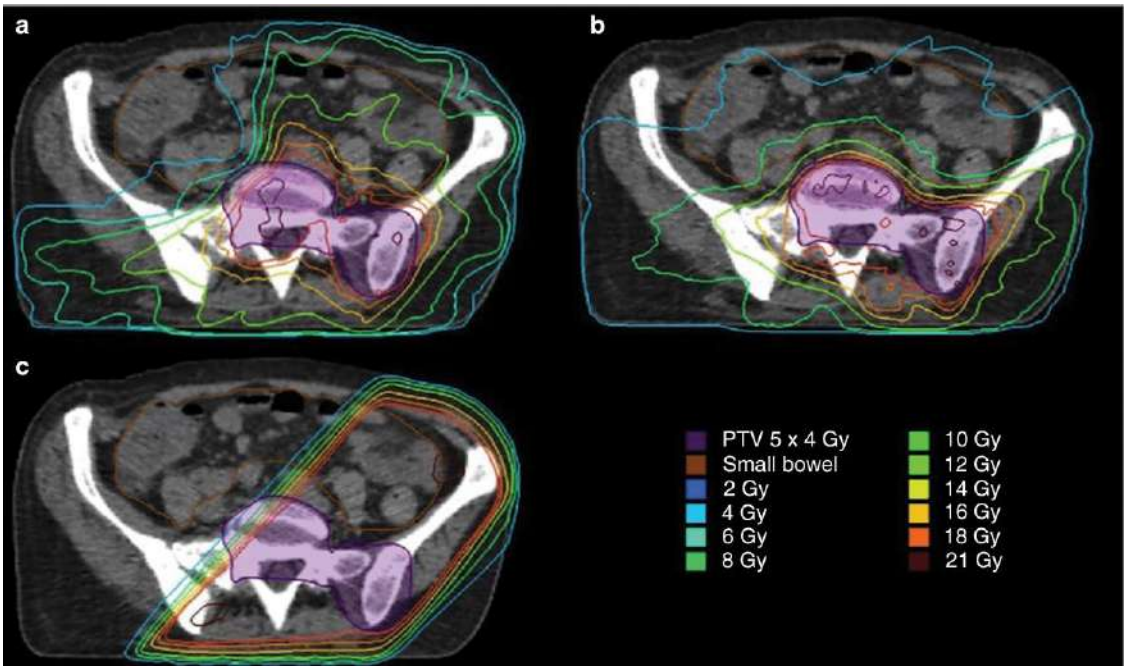

Fig. 3 Comparison of radiotherapy plan for each technique in a 68-year-old woman who presented with recurrent rectal cancer, with previous radiotherapy for metastasis to the right iliac bone, now with metastasis to L5 and left sacroiliac joint

a Modified volumetric modulated arc therapy, **b** volumetric modulated arc therapy, and **c** three-dimensional conformal radiotherapy. PTV, planning treatment volume.

leading to reduced toxicity without compromising oncological outcomes in LARC[43] (*Fig. 3*)[44].

Following neoadjuvant treatment, surgery should take place after an interval of at least 8 weeks. This facilitates further downstaging, increases the pCR rate, and improves recurrence-free survival without compromising surgical morbidity[45]. Several studies[45–47] have shown that longer intervals do not lead to worse oncological outcomes. To obviate unnecessary delay to surgery in poor responders, repeat is advised MRI 6–8 weeks after the end of the chemoradiotherapy.

Where intraoperative radiotherapy (IORT) is available in an institution, its use should be considered where margins are suspected or proven to be threatened during surgery. IORT offers the possibility of delivering a high boost of radiotherapy to areas with microscopic residual disease, while dose-limiting structures such as ureter and small bowel can be excluded from the radiation field. The role of IORT in patients with macroscopic residual (R2) disease is poorly understood. A recent study[48] demonstrated significant differences in recurrence rates in 215 patients who received different doses of IORT, suggesting a dose-dependent effect favouring high superficial doses.

Brachytherapy should be consider for palliative treatment or patients with inoperable disease. Even in LARC, a clinical complete response may be achieved after external beam radiotherapy. Major surgery may be avoided, although there are limited data available on the success rate of organ-preservation strategies in LARC. A brachytherapy boost with contact X-ray brachytherapy (Papillon) or High Dose Rate rectal endoluminal brachytherapy on small residues may further increase the chance of inducing a cCR. A minimum radiation dose of 72 Gy is necessary. The OPERA trial[49] may provide more clinical evidence for the role of brachytherapy, although patients with LARC and LRRC are not included in this trial. Proton beam therapy is a promising option for tumours that are inaccessible to brachytherapy[50].

Preoperative assessment

All patients are reviewed by an anaesthetist before surgery. The goals of preoperative assessment are the same as those for any other patient undergoing oncological resection: to determine the level of fitness and functional reserve of the patient, and to identify any features that may lead to higher perioperative risk. This assessment is best carried out by, or at least in consultation with, the anaesthetist who will oversee the procedure. It should take place within a sufficient time frame to allow any modifiable risk factors to be addressed. Patients should have a full blood count, renal function test, and blood sample for group and cross-match taken at this assessment if no recent samples are available. Other blood tests, such as haemoglobin A1c and liver function tests, can be done as indicated from the initial screening assessment. Chest X-ray is indicated only in the presence of active respiratory disease or examination findings suggestive of such disease. ECG is undertaken in all patients aged over 50 years, and younger patients with risk factors present, such as hypertension. The Revised Goldman Cardiac Index is perhaps the best tool for screening for risk of perioperative cardiac complications. Cardiopulmonary exercise testing (CPET) is an option, where available, to formally assess functional capacity. In the absence of CPET, metabolic equivalent of task (MET) assessment is a minimum requirement. Where a patient is incapable of four or fewer METs and has two or more cardiac risk factors, stress imaging, such as dobutamine stress echocardiography, is indicated[51].

Patient optimization

Prehabilitation is defined as the process of mitigating modifiable risk factors and enhancing overall health and well-being before surgery. It has been reported as an effective method of

optimizing patients and improving outcomes for major abdominal and oncological operations[52]. These same prehabilitation methods may be applied to patients undergoing pelvic exenteration to help improve outcomes.

Nutrition

Nutritional status has long been a point of interest for patient optimization. Hypoalbuminaemia, in particular, is associated with more complications and poorer overall survival[53]. Scores such as the PreOperative Nutrition Score (PONS) account for multiple measures to generate a broad picture of preoperative nutritional status. The PONS includes serum albumin, BMI, weight loss, and intake modification. Nutritional risk is defined by a BMI of less than 18.5 kg/m^2, or below 20 kg/m^2 in patients aged over 65 years, unplanned weight loss exceeding10 per cent in the past 6 months, decreased dietary intake of more than 50 per cent from normal in the past week, or serum albumin level below 3.0 g/dL[54].

Patients who are deemed to be at nutritional risk should be encouraged to increase their protein intake before surgery, as well as adding in nutritional supplements. Patients who are severely malnourished or unable to achieve sufficient oral intake should be considered for enteral tube feeding, if appropriate, or possible parenteral nutrition. At the other end of the spectrum, morbid obesity remains a significant challenge to many aspects of surgery, including technical facets, intraoperative complications, and overall recovery including proper wound healing[55]. Although reported methods for safe weight loss before surgery (including operative management) have been described, malignancy typically precludes major intervention in this aspect.

Fitness

Improving preoperative fitness may enhance perioperative physical function in major abdominal surgery[52]. A common method for determining preoperative fitness is the 6-min walk test, often in conjunction with the modified Borg scale to measure rating of perceived exertion[56]. Walk tests have been shown to reliably measure exercise capacity and ability. All patients should be provided with an incentive spirometer and exercise instructions. Although there are no concrete guidelines for preoperative exercise programmes, the American Cancer Society[57] recommends 150–300 min of moderate exercise per week or 75–150 min of vigorous exercise, as well as two or three sessions of resistance training. Patients who are deemed to have poor preoperative performance (less than 400 m in 6-min walk test) can and should be considered for referral to an exercise specialist, such as a physiotherapist or kinesiologist, for supervised prehabilitation.

Anaesthetic considerations

Combined epidural and general anaesthesia, with or without concomitant neuraxial blockade, may help attenuate the stress response associated with major surgery, as well as contributing to postoperative pain control[58–62]. Arterial line placement and insertion of large-bore vascular catheter(s) are recommended. Pre-emptive peripherally inserted central catheter placement is an option, as many patients require postoperative total parenteral nutrition and vascular access frequently becomes challenging. Arterial blood gas and haemoglobin measurements should be performed at regular intervals throughout the operation. The plasma lactate level should be kept as low as possible throughout the procedure to ensure optimal tissue perfusion and aerobic metabolism[51].

Mechanical calf compression and thromboembolus deterrent stockings are of utmost importance in pelvic exenteration, owing to the relatively higher risk of thromboembolic events in major abdominopelvic oncological surgery[63]. Furthermore, thromboprophylaxis with low molecular weight heparin is imperative and commenced at the discretion of the surgeon. The legs should be positioned carefully with pressure point protection and lowered at regular 2–4-h intervals. Anaesthetic and theatre support staff should be informed in advance if there will be a need for prone positioning to facilitate myocutaneous flap reconstruction or sacrectomy.

A minimum of 2 units of cross-matched blood should be available; more may be required in the context of major vascular resection/reconstruction. Tranexamic acid is administered in the case of massive haemorrhage[51]. Thromboelastography monitoring is an option to help provide more targeted replacement therapy and reduce inappropriate blood product administration.

If the anticipated duration of surgery is greater than 12 h, a second anaesthetic consultant should be available to assist with the procedure. Postoperative transfer to critical care facilities for invasive monitoring and/or organ support is routine but not mandatory. Should inotropy be required, noradrenaline (norepinephrine) is the drug of first choice. Fluid management is an essential component of care, with a goal-directed fluid therapy strategy generally considered more appropriate[51].

Operative approaches to pelvic exenteration: technical considerations

Open or minimally invasive surgery

In most institutions, exenteration is regarded as an open operation. Nevertheless, minimally invasive approaches using laparoscopic or robotic methods are being reported increasingly[64–66]. Although there is mostly low-level evidence from small series, minimally invasive surgery (MIS) appears feasible and safe in selected situations, particularly for locally advanced tumours; fewer reports consider recurrent tumours. Patient factors (obesity, sex, co-morbidities, extent of adhesions), tumour factors (compartments involved, degree of tumour extension into each compartment, vascular control, bony resection), surgeon factors (experience with MIS approaches), and institutional factors (access to sufficient robotic time for emergence of a MIS exenterative programme) all influence MIS utility[66,67].

Surgical approach

Whether open surgery or MIS is planned, detailed knowledge of the pelvic anatomy and the tumour's anatomical relationships is mandatory. Tumour locations are diverse and so a bespoke approach is required. Consequently, thorough preoperative radiological assessment of tumour anatomy in reference to fixed anatomical points is necessary to ensure that R0 resection is achieved; this includes planning for urological organ resection, perineal excision, resection of expendable or non-expendable pelvic vasculature, and bony excisions.

Intraoperative ureteric stenting may facilitate both identification and protection of the ureters. After this, the operation usually commences with an abdominal phase, although an initial pelvic or prone approach is appropriate in certain patients. The abdominal phase commences with a

thorough exploration for metastatic disease and division of adhesions. Subsequent surgical steps depend on the compartment(s) and organs involved, and the nature of any previous surgery. Typically, dissection begins with the identification of ureters and major pelvic vasculature, with the placement of slings around the key anatomical structures. Purely for descriptive ease, the types of dissection are described in order below. Anteriorly, dissection may incorporate the bladder, prostate, and dorsal venous complex in men, or, more anteriorly, the pubic bones and/or symphysis pubis. Laterally, dissection may extend to include ureters, iliac vessels, obturator internus muscle and fascia, sciatic nerve, and ischial spine[67]. Posteriorly, the plane of dissection may include piriformis, sciatic nerve roots, sacral ligaments, periosteum, and sacral bone.

Pelvic sidewall

Dissection in the pelvic sidewall may be required in the following circumstances: most commonly, to achieve R0 resection with *en bloc* excision of a tumour mass[68]; to clear potentially involved lymph nodes; to gain and control iliac vessels bilaterally before *en bloc* sacrectomy; and, if there is posterolateral tumour extension, to allow resection of sacral nerve roots, piriformis and internal obturator muscles, and sciatic nerve where involved. Potentially involved lymph nodes are cleared either by means of a vessel-preserving lymphadenectomy or *en bloc* excision of the sidewall with associated vasculature. If there are nodes containing extracapsular tumour spread, R0 excision may require extended resection of the tissue around the node, typically with *en bloc* vessel resection. Furthermore, after neoadjuvant chemoradiotherapy, many patients develop significant pelvic sidewall fibrosis, rendering vessel-preserving lymphadenectomy impossible and risking significant haemorrhage from thin-walled large-calibre veins surrounded by dense fibrosis. In this situation, *en bloc* excision of the sidewall may be safer[69,70].

Distant disease and palliative resections

Although resectable metastases are not an absolute contraindication, they signify poorer prognosis, and the precise sequencing of surgery in the presence of distant resectable disease remains unclear[71]. A metastasis-first approach is often advocated based on the observation that many such patients will ultimately manifest with further disease in time owing to occult micrometastatic disease becoming apparent. In this situation, conducting lower-risk lung or liver metastatectomy that has less impact on QoL, with restaging at each time point, may be more sensible to allow the disease trajectory to be declared. These approaches may be reversed when the extent of metastatic resection would compromise future exenteration (such as resection of excessive lung or liver parenchyma). In selected circumstances, synchronous resections of liver or peritoneal metastases may be combined with the exenterative procedure[71,72]. The presence of synchronous distant disease (or the likely failure to achieve R0 resection) indicate a palliative approach[73]. Data in this setting are sparse but, in general, some symptom relief is achievable, although with little improvement in QoL and a short survival time[74].

Reconstructive options

Bladder

Partial cystectomy with or without ureteric reimplantation can be considered if the remnant cystic volume is adequate for good function. As partial cystectomy often results in small bladder capacity and nerve dysfunction, patients should be aware of the risk of postoperative urinary retention and a long-term need for self-intermittent catheterization.

In the event of radical cystectomy, different methods of urinary diversion are available, and restoration or reconstruction is rarely offered[75]. The ileal conduit is considered the standard. Although other bowel segments, such as sigmoid or transverse colon, may be used, they are often avoided owing to the perceived higher rate of malignancy. Comparative studies on urinary diversion are scarce and the data are inconsistent. Morbidities, such as reintervention for ureteral stenosis, treatment for recurrent pyelonephritis, metabolic acidosis and parastomal hernia, are frequent. Continent urinary diversions and orthotopic neobladders are infrequently used in exenterations for colorectal malignancy, possibly because of the complex nature of exenterative procedures, and their association with higher morbidity and risk of recurrence[76]. However, there is some support for these types of reconstruction in anterior exenteration as alternatives to incontinent ileal conduits. Recently, there has been an increase in the reported use of double-barrelled wet colostomies, an option in patients with short ureters or inability to exteriorize the ileal conduit (for example, in obesity, short mesentery)[77]. Cutaneous ureterostomy or conjunction of the ureters with nephrostomy should be regarded as a last-resort option or temporary solution because of the appreciable long-term morbidity. The need for percutaneous drainage and frequent changing of nephrostomy catheters should be taken in consideration.

Pelvic/perineal flaps

When performing pelvic exenteration, many patients require flap reconstruction owing to tissue loss. Perineal flap reconstruction is further complicated by neoadjuvant (chemo)radiotherapy, increased pelvic dead space, poor tissue vascularity, fluid accumulation, and bacterial contamination. Flap complication rates have been reported in 16–68 per cent[78,79]. Based on region, the following types can be discerned: abdominal— vertical or oblique rectus abdominis myocutaneous/muscle flap, deep inferior epigastric perforator (DIEP) flap; gluteal region—myocutaneous or fasciocutaneous VY-plasty, inferior gluteal artery perforator flap; upper thigh—anterolateral thigh with or without vastus lateralis flap, gracilis flap; gluteal fold/perineal—internal pudendal artery perforator or perineal turnover perforator flap; and omental.

Women can be considered for vaginal reconstruction after posterior vaginal wall resection. This can be achieved using a rectus abdominis myofascial flap, DIEP flap, bilateral gracilis flaps, or gluteus maximus special flap. Female sexual function and body image after flap reconstructions have been sparsely studied and attention in future investigations is paramount.

Bone stabilization

Functional benefits of reconstruction must be weighed against the risks of longer operating time, wound and prosthetic/allograft infection, and pseudoarthrosis or non-union. A history of radiotherapy limits prosthetic incorporation. Adequate soft tissue coverage is imperative for all types of prostheses. Biological reconstruction is preferred over prosthetic reconstruction in patients with high functional demand, as well as in those who are not able to engage in frequent radiological and/or clinical follow-up. Examples of biological reconstructions include arthrodesis, allograft or fibular autograft, using struts with or without vascularity, or allograft-prosthetic composites.

A classification system for bony pelvis resection has been proposed by Enneking and Dunham[80].

Ilium (type I)

Reconstruction is generally not warranted when resection includes the iliac wing only. Where resections include the sciatic buttress, the continuity of the pelvic ring is compromised and iliosacral reconstruction with an allograft, autograft, and/or metallic prosthesis is necessary to preserve limb length.

Periacetabular (type II)

Resections involving the periacetabular region are generally considered the most challenging in terms of both resection and reconstruction. Recovery times are longer and the associated morbidity is substantial. Options include resection arthroplasty, saddle prosthesis, allograft/prosthetic composites or custom-made implant devices.

Reconstruction after hemipelvectomy, type I resections (involving the ilium) and type II resections (periacetabular region) are less common.

Ischiopubic (type III)

This region, which extends from the pubic symphysis to the acetabulum, adds to the structural stability of the pelvis. Patients can experience muscular weakness after resection of the muscular attachments of the abdominal, gluteal, and leg musculature. Bony reconstruction is not required, provided that the continuity between the acetabulum and axial skeleton is intact. Tissue flaps with or without the use of mesh can prevent herniation of the internal organs through the created defect.

Sacrum (type IV)

Sacrum-stabilizing sacroiliac and lumbosacral ligaments are spared with low sacrectomy (below S3–S4), whereas they are often sacrificed along with the sacrospinous and sacrotuberous ligaments in high sacral resections (above S3–S4). Iliolumbar arthrodesis is recommended in case of complete sacrectomy, as the axial skeleton loses support and flails, only attached by remaining muscles and ligaments. However, it is strongly recommended in the event of iliolumbar ligamentous instability. The axial skeleton can be stabilized by using modern rod and screw constructions for iliolumbar fixation. This entails a combination of bone grafts, fixation bars, and spinal fixation in the distal lumbar vertebral bodies.

Histopathological guidelines for exenterative specimens in locally advanced and recurrent rectal cancer

Securing an accurate perception of the exenterative specimen for the pathologist

The surgeon request form (see example in *Appendix S1*) should describe the exenterative specimen, outlining the MRI findings, procedures performed, structures/organs resected, and the area expected to have the shortest resection margin. Structures in the lateral and posterior compartment, including ureters, pelvic sidewall and presacral fascia, iliac vessels, lateral lymph nodes, muscles, ligaments, and nerves are often difficult for the pathologist to identify. As such, the structure representing the outermost lateral and posterior margin should be marked specifically with sutures of different colours or different numbers of knots.

Margin involvement is reported according to residual tumour (R) classification as no residual tumour (R0), microscopic residual tumour (R1), or macroscopic residual tumour (R2). Microscopically, the circumferential resection margin (CRM) is considered uninvolved (R0) if the distance to the tumour is over 1 mm and involved (R1) if the distance is 1 mm or less[81]. Multiple other biomarkers with prognostic implications for rectal cancer have also been identified, and should also be reported for both locally advanced and recurrent cases as outlined below[82].

Macroscopic examination

Protocols for macroscopic examination, dissection, and tissue sampling of colorectal specimens, like those developed by the Royal College of Pathologists[83] and the College of American Pathologists[84], should be followed where applicable. Before fixation of the specimen, the proximal part of the bowel is opened anteriorly to a maximum of 1–2 cm from the tumour, and absorbent material is inserted into the remaining lumen to aid fixation. Additional hollow viscera, including urinary bladder, prostate, and uterus, are opened anteriorly. The specimen should then be fixated for a minimum of 24–48 h before further dissection.

After fixation, the resected bowel is measured, and any mesorectal defects or perforations are recorded if not done previously. The intact specimen should be photographed, preferably from the anterior, posterior, and both lateral aspects. Annotation of the images to help identify organs, structures, and suture markings is recommended. The CRM, including all non-peritonealized surfaces of adjacent organs and structures, is inked according to an agreed colour code. A suggested division of the CRM for inking is anterolateral right, anterolateral left, and posterior. Before further dissection, accessible margins, except for the CRM and distal longitudinal bowel margin, are sampled. These include the proximal longitudinal bowel margin (optional if 30 mm or more from macroscopic tumour), the superior rectal or inferior mesenteric vascular margin, and other relevant longitudinal margins (such as ureters, urethra, vas deferens, vagina, and iliac vessels).

The number of blocks needed to map tumour infiltration and the CRM will vary according to specimen and tumour size, additional resected organs and structures, and the extent to which the tumour is evident macroscopically or replaced by fibrosis after preoperative therapy. If available, the use of megablocks is recommended to facilitate measurements and radiological correlation. These may be combined with standard blocks from the same slices to demonstrate structures and margins of special interest. To minimize decalcification of viscera and soft tissues, bone tissue should generally be dissected from slices before sampling, and the resulting new surfaces inked in a specified colour. If macroscopic or microscopic findings suggest tumour near the bone, this should be decalcified for microscopic examination. In rare cases of a known or possible synchronous primary of other origin in an attached organ, dissection and sampling should be performed according to an appropriate protocol for the organ in question.

Microscopic examination

The microscopic examination should follow standard guidelines for colorectal cancer histopathology with a special focus on tumour involvement of the CRM, and of adjacent structures and organs. If no tumour is initially found in the area with the expected shortest CRM distance (as specified by the surgeon),

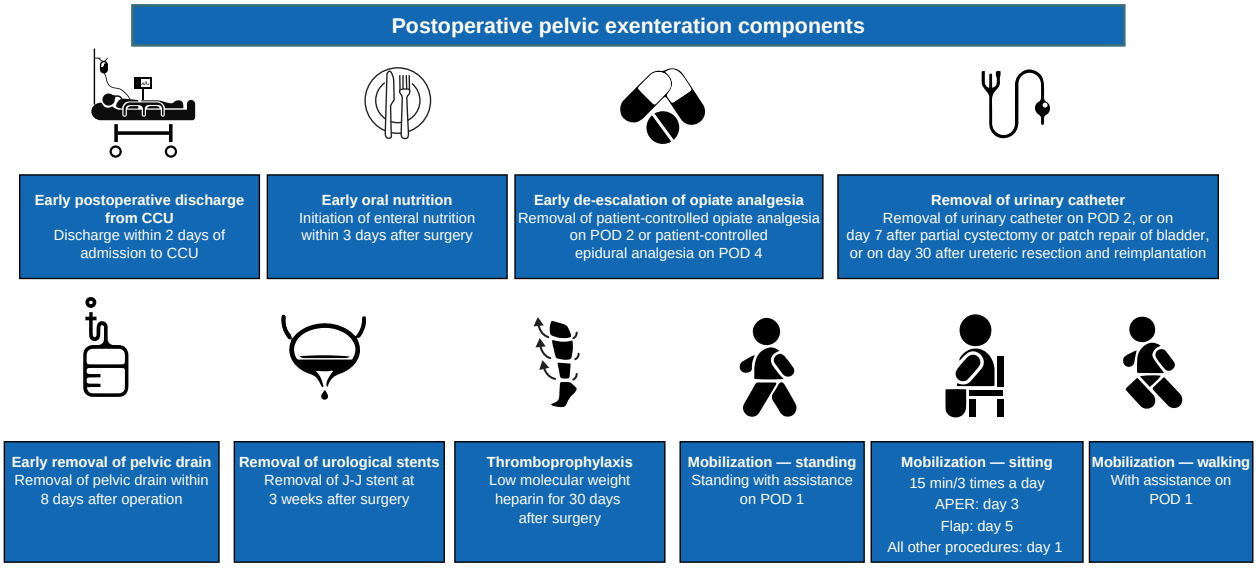

Fig. 4 Essential care after pelvic exenteration

CCU, critical care unit; POD, postoperative day; APER, abdominoperineal excision of rectum.

the block(s) should be sectioned in at least two additional levels. A complete tumour regression response to neoadjuvant therapy can be reported if no residual tumour is found in the whole tumour site, preferably after examination of each block in five levels. Samples from adjacent organs should be examined for other incidental findings, and detection of a synchronous primary tumour of other origin should prompt further embedding and reporting according to relevant guidelines.

As a minimum, the final report must include all core elements provided by the International Collaboration on Cancer Reporting[85]. Additional information required for exenterative specimens is: presence of adjacent structures/organs involved by tumour and identification of the structure or organ with the shortest resection margin; presence of metastatic lateral (pelvic sidewall) lymph nodes; and, for recurrent rectal cancer, the number of tumours should be recorded. The convention y (pretreatment), p (pathological), and r (recurrent) should be used in conjunction with the TNM system.

Follow-up and surveillance

Follow-up protocol after exenterative procedures

In the immediate postoperative phase, the patient's general recovery with respect to healing and function of stomas and flaps, as well as strength and mobility, are prioritized (*Fig. 4*)[86]. Psychological support should be offered after very extensive surgery. Considering the excess burden of the exenterative procedure and the chance of late complications (such as urinary tract dilatation–renal function deterioration, small bowel adhesion, fistula, myocutaneous flap circulatory problems) long-term follow-up is recommended. In addition, planning with respect to any long-term rehabilitation needs is crucial.

Patients are usually kept under medical surveillance for a minimum 5 years. Follow-up protocols specific to pelvic exenteration have yet to be defined, but surveillance should be largely in keeping with those for primary colorectal cancer. Physical examination, informal patient satisfaction report[87], and laboratory tests are undertaken on a regular basis, at a frequency that decreases over time in line with clinical need. There is no evidence to suggest a shorter-interval follow-up schedule should be used routinely in more complex cases. Therefore, once yearly follow-up is suggested. A final check-up is undertaken at the end of the fifth year.

Appropriate surveillance consists of annual CT of the chest, abdomen, and pelvis combined with measurement of carcinoembryonic antigen (colorectal cancer) or other tumour markers. Further laboratory tests are indicated when liver and/or kidney involvement is relevant. If there is a suspicious lesion on CT, correlation with tumour markers is advised and MDT discussion is recommended. PET–CT has an important role in confirming or ruling out distant metastases, as well as differentiating between scar and tumour tissue in the pelvis. Normally occurring FDG-avid take-up sites and inflammatory foci must be taken into consideration when evaluating results. PET–CT has no role where the initial pathology was mucinous adenocarcinoma.

Colonoscopy is performed throughout the patient's life if the primary tumour was of colorectal origin. The suggested time interval is every 3 years if no new lesion is found. When any intervention has been necessary, repeat colonoscopy is at the discretion of the endoscopist. If the first endoscopy was incomplete, thorough evaluation of the colon must take place within 6 months of the index operation.

When extended procedures have been performed, such as bone resection, special care must be taken to rehabilitate the patient, noting that this process usually takes several months to a year to complete. The appropriate specialty (such as orthopaedics or rehabilitation team) should be involved during follow-up. The optimal follow-up schedule after urinary diversion has not been defined, but it is suggested that renal function should be monitored regularly in consultation with a nephrologist, and radiological surveillance of the upper urinary tract be undertaken annually for life.

Follow-up is best carried out by the surgeon who performed the operation, as he or she knows the subtleties of the situation and can take further action as needed. However, consultation with other members of the MDT is paramount and dictated by the clinical scenario.

Patient support groups may help considerably in coping mentally and physically with the recovery process and should be encouraged. Detailed, step-by-step series of advice for patients can be found under different headings at several websites, such as: American Society of Clinical Oncology (read the entire guideline endorsement); Guide to Colorectal Cancer; Colon Cancer Survivorship Care Plan; Survivorship; Up Care After Cancer Treatment; and Coping With the Fear of Recurrence.

Patient involvement

Patient (and family) involvement at each stage is vital as part of the doctor–patient shared decision-making process. Despite this, relatively little is known about the true scale of the impact of treatment for advanced pelvic cancer on patients[88]. Radical surgery impairs QoL and physical functioning may never return to previous levels[89,90]. Symptoms such as pain and fatigue may never abate[91]. However, many patients who undergo surgery can expect their QoL to return to baseline around 6 months after operation, and some exhibit better-than-normal mental health compared with the general population[2,89]. This suggests that not only is exenteration oncologically justified in appropriately selected patients, but that it may confer a psychological benefit to patients who are faced with an otherwise dismal prognosis.

Nowhere in this process is shared decision-making more relevant than in obtaining consent. Given the nature of exenterative procedures, patients may find it difficult to truly appreciate the associated morbidity, particularly for the index operation. Furthermore, they may be unwilling to fully engage with alternative, less radical options, given the poor outcome they will likely face. Therefore, it is important that consent is obtained by the consultant surgeon or senior member of the surgical team, and that other involved subspecialties contribute as needed. Clinicians must take the time to find out what is important to the patient and explain how this may be influenced by exenterative surgery or (neo)adjuvant treatments; fertility is an example. This process should begin at first diagnosis and be revisited before formally obtaining consent before operation.

There is a growing interest in patient-reported outcome measures (PROMs) as a means to evaluate the impact and outcomes of oncological surgery. Use of validated questionnaires is increasing over time, but more research with standardized formats is needed in order to better inform clinicians, allowing them to provide practical insight into what patients can expect at each step in their journey[88]. Patient decision aids (PDAs) have also been suggested as a valuable tool to help guide informed patient decision-making. However, a recent review[92] found no such examples meeting international standards in the context of complex rectal cancer. It is vital that research into PROMs and PDAs pertains to specific pathologies and treatments/operations, and that it feeds back into each of the areas outlined in this document in order to comprehensively assess and improve the experience of patients with advanced pelvic malignancy.

Collaborators

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Supplementary material

Supplementary material is available at *BJS* online.

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