Management of Locally Advanced and Recurrent Rectal Cancer

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52.1 Introduction

The key principle underpinning the management of locally advanced rectal cancer (LARC) or locally recurrent rectal cancer (LRRC) is that of complete en bloc radical excision with a clear resection margin (R0) [1]. This procedure, also known as pelvic exenteration, is a complex and technically challenging procedure that can be associated with considerable post-operative morbidity. Although pelvic exenteration was first described in 1948, it was not widely accepted until two decades ago because of the high surgical mortality and morbidity [2]. With improved imaging technology, better understanding of pelvic anatomy as well as improved surgical techniques, operative mortality has declined such that most units with the expertise in pelvic exenteration report mortality rates of under 1–2 % [3–5]. Although surgical morbidity remains moderately high, most large contemporary series report an acceptable major complication rate of 24–27 % [3, 4, 6]. Coupled with the numerous case series that have reported good quality of life outcomes in recent years, [7, 8] pelvic exenteration is now accepted as established treatment of LARC or LRRC.

52.2 Magnitude of the Problem

Local recurrence following treatment of primary rectal cancer has declined dramatically since the widespread adoption of total mesorectal excision (TME) and use of neoadjuvant radiotherapy based on pre-operative magnetic resonance (MRI) staging [9–11]. Notwithstanding this, local recurrence can still occur in 5–10 % of patients [12, 13]. Of patients with LRRC, an estimated 50 % will have isolated pelvic recurrence that could be amendable to curative resection [14, 15]. Without treatment, prognosis of LRRC is invariably grim, with a median survival of 6–9 months and patients are typically highly symptomatic particularly with pain [4, 16, 17]. With chemoradiation, median survival can be prolonged to 15 months but patients can remain highly symptomatic [16, 18]. As most patients with LRRC would have previously had radiotherapy, this limits treatment options available at the time of recurrence. Even if re-irradiation is considered, prior radiotherapy limits the amount of additional radiation that can be administered

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[19, 20]. Importantly, chemoradiation alone is not curative even if it does prolong survival [21]. Thus, pelvic exenteration with a clear resection margin (R0) is the only curative option available for these patients [1].

52.3 Presentation

Most patients with LARC or LRRC are symptomatic although a small proportion of patients with LRRC may present with an asymptomatic anastomotic recurrence detectable on routine follow-up. In symptomatic patients, symptoms typically reflect the location of the disease. Common symptoms include pain, rectal bleeding, rectal discharge, tenesmus or altered bowel habits [17, 22]. Of these, pain is the most common symptom and may be the result direct nerve, muscle or bony infiltration, or the result of referred pain. Less commonly, patients may also experience lymphoedema from venous compression, malignant recto-vesical or recto-vaginal fistula or a tumor fungating through the perineum.

52.4 Pre-operative Assessment

The purposes of investigations are to confirm diagnosis and to establish the extent of local disease so as to determine resectability. Although criteria for resectability vary between institutions, several authors have published what they consider resectable (see later). It needs to be emphasized that these constitute recommendations from specialized institutions with an interest in exenterations and as such, the same guidelines are unlikely to apply to all institutions. It is also noteworthy that the goalposts for resectability are constantly changing. With improved surgical technique and experience, what used to constitute absolute contraindication such as pelvic sidewall or proximal sacral involvement have now evolved to become standard surgical practice in selected centers [2, 7, 16].

Clinical Assessment

The utility of clinical assessment depends on the location of the cancer. Cancers involving the anal canal, perineum, low rectum or anastomosis may be readily visible or palpable. However, pain, which frequently accompanies local recurrence may limit the yield of clinical assessment without anesthesia. In patients who have previously undergone an abdomino-perineal excision, clinical assessment is often limited.

Imaging

All patients should be assessed with CT, MRI and positron-emission tomography (PET). PET complement CT in the detection of metastatic disease and have been shown to alter the management in 20–40 % of patients with LARC or LRRC by detecting occult metastasis otherwise undetected on other imaging modalities [23, 24]. As PET detects metabolically active tissue, it is very useful for distinguishing between post-treatment fibrosis and recurrence although false positives can occur with benign post-treatment inflammation. Pitfalls with PET are mucinous tumors and occult peritoneal deposits where PET scans are less accurate. The development of PET-CT by fusion of PET and CT images has partly overcome the problem with small occult metastases [25].

MRI is currently the gold standard for local staging of all rectal cancers whether an early rectal cancer, LARC or LRRC. MRI has revolutionized the assessment of LRRC in that it is most accurate in determining the local extent of the disease and therefore the resectability of LRRC. In doing so, it helps guide patient selection, enables the surgeon to counsel patients appropriately about the magnitude of the anticipated surgery, likely morbidity and facilitates surgical workforce planning on the day of surgery [26]. The accuracy of MRI depends both on the compartment involved as well as the experience of the radiologist interpreting the MR [27, 28]. The major limitation with MRI resides in its inability to accurately diagnose pelvic sidewall involvement [27, 28].

Tissue Diagnosis

Tissue diagnosis is conventionally regarded as gold standard in confirming diagnosis of cancer. While this is true for LARC, tissue diagnosis is not always possible in patients with LRRC. In patients where the tumor is inaccessible via a natural orifice (such as extra-luminal nodal recurrence or previous abdominoperineal excision), one will have to question the utility of a percutaneous biopsy which would violate virginal planes that are unlikely to be included as part of the radical excision thereby posing a small but theoretical risk of tract seeding [29, 30]. Although contentious, in our exenteration practice, a hot PET scan in the presence of a corroborative history, MRI findings and CEA will be accepted as being diagnostic of local recurrence without a biopsy.

Other Investigations

A variety of other investigations are often necessary to confirm diagnosis or assist with surgical planning. They include:

- Colonoscopy
- CEA
- Cystoscopy (with or without ureteric stenting)
- CT angiography
- MR angiography

Colonoscopy and CEA are usually part of routine pre-operative assessment but the need for cystoscopy, CT or MR angiography is selective based on individual circumstances.

52.5 Resectability

The indications and contra-indications for pelvic exenteration vary widely between institutions and continue to evolve with experience. With improved surgical techniques and experience, what used to constitute absolute contraindications such as high sacral or pelvic sidewall involvement are no longer contraindications provided an R0 margin can be achieved safely [2, 5, 31]. There is little doubt that some patients are currently not offered exenteration for what would be considered routine resection in specialized centers [2]. Table **52.1** summarizes published resectability criteria.

Due to the associated surgical morbidity and mortality, pelvic exenteration is generally only offered with a curative intent. Patients with unresectable metastases are therefore not usually considered for pelvic exenteration. However, the presence of synchronous resectable visceral metastases or a history of previously treated metachronous metastases should not preclude consideration for pelvic exenteration provided the patient is medically fit for the procedure [32, 33]. Whether metasectomy and pelvic exenteration should be performed as staged or synchronous procedures and whether a metasectomy first approach is more appropriate is debatable, although synchronous procedures are likely to prolong surgical time and increase surgical morbidity considerably if a major resection is necessary.

Traditionally, pelvic sidewall recurrence was considered a formidable surgical challenge that is incurable [22, 34]. The potential involvement of major neurovascular structures essential for lower limb function coupled with the difficulties in achieving R0 resection margin have contributed to pelvic sidewall recurrence being considered a contraindication for surgical exploration [22, 35–37]. In fact, prior to the advent of MRI, referred pain in the distribution of the sciatic nerve alone was enough to preclude consideration for surgery [38, 39]. However, with improved understanding of pelvic anatomy and surgical technique, pelvic sidewall dissection has become standard practice in many centers [31]. A systematic approach to the pelvic sidewall as described by Austin and Solomon has been shown to achieve R0 resection margins in 53 % of patients with pelvic sidewall involvement, which is comparable to R0 resection rates at other sites of recurrence [6, 31]. Major iliac vessel excision and reconstruction, adopted from allied surgical specialties in the treatment of retroperitoneal soft tissue sarcomas has demonstrated that en bloc iliac vessel excision and reconstruction can improve R0 rates with acceptable morbidity and

Table 52.1 Resectability of locally recurrent rectal cancer

Institution/country	Authors year	Relative contraindication	Absolute contraindication
Leeds United Kingdom	Mirnezami et al. 2010 [26]	Distant metastasis	Encasement of external iliac vessels
		Primary stage IV disease	Extension of tumor through sciatic notch
		Extensive pelvic sidewall involvement	Presence of lower limb oedema from venous or lymphatic obstruction
		Predicted R1 or R2 resection	Poor performance status
		Sacral invasion above S2-S3 junction	
	Boyle et al. 2005[a] [5]		Presence of extensive abdominal or thoracic metastases
			Encasement of external iliac vessels
			Extension of tumor through sciatic notch
			Sacral invasion above the level of S2–3 junction
Lund Sweden	Zoucas et al. 2010[a] [35]		Adherence or invasion of sacrum at or above S2 level
			Extensive lateral or circumferential pelvic wall involvement
			Encasement of sciatic notch or external iliac vessels
			Presence of unresectable distant metastasis
Texas United States	Gannon et al. 2007 [37] and Pawlik et al. 2006[a] [36]	Ureteral obstruction	Distant metastases
		Poor candidate for surgery because of medical comorbidities	Involvement of common or external iliac vessels
		Poor candidate for surgery because of inability to care for stomas or senility	Metastasis to para-aortic nodes
			Involvement of the sacrum proximal to S1 (note: some consider S2 involvement to an absolute contraindication)
			Tumor extension through sciatic foramen
			Pelvic sidewall involvement
Washington United States	Ogunbiyi et al. 1997 [22][a]	*The authors defined resectable disease as*	Midline posterior tumors adherent or invading the distal sacrum below S2
		Isolated perianastomotic or perineal recurrence	
		Tumors invading adjacent pelvic structures such as bladder, prostate or vagina	
		Absence of invasion of lateral pelvic sidewalls, upper sacrum and pelvic nerves (ad indicated by neurologic signs and symptoms)	
		No involvement of ureters as indicated by absence of hydronephrosis on imaging	

Ogunbiyi et al. defined resectability more by what was resectable rather than what was non-resectable
[a]Authors do not distinguish between relative versus absolute contraindication

graft patency rates [40, 41]. En bloc excision of sciatic nerve, where necessary to achieve R0 resection margins is a well established practice in the sarcoma literature with better than anticipated functional outcomes [42–44]. Patients typically require a foot brace to prevent foot drop but mobility is acceptable. Although patients report mild to moderate physical impairment, most prefer some degree of disability over amputation [42].

To enable even more radical resections of the pelvic sidewall for tumors extending through the sciatic notch, Nielsen et al. recently reported on their initial experience with external hemipelvectomy (hind quarter amputation) on eight highly selected patients with a variety of locally advanced or recurrent pelvic malignancies [45]. External hemi-pelvectomy is highly morbid procedure that is generally reserved for malignant sarcomas of the pelvis but where possible, a limb preserving form of hemi-pelvectomy (internal hemipelvectomy) with bony reconstruction is favored [46]. Although hemi-pelvectomy has been reported sporadically for carcinomas of the pelvis, unlike sarcomas, its role in carcinomas remains unclear [45, 47–50]. Oncological outcomes following hemi-pelvectomy in general are poor and longer term follow up data is scant [45, 47]. In the absence of long term oncological and quality of life data, these procedures should only be offered in expert centers on an individual basis where lesser surgical interventions are not possible. Patients need to be counseled appropriately and ideally, surgical, oncological and longitudinal quality of life outcomes in these patients should be assessed to further define the role of hemi-pelvectomy in LARC or LRRC.

En bloc sacrectomy may be required in 9–24 % of all pelvic exenterations in order to achieve R0 resection margins [3–6]. Sacrectomies at or below S3 are generally classed as low sacrectomies whereas high sacrectomies involves sacral transection at the level of S1 or 2. High sacrectomies are associated with increased intra-operative blood loss, surgical morbidity and post-surgical neurological deficit [4, 51–53]. Although oncological and functional outcomes following sacrectomies for a range of skeletal and soft tissue tumors are well described, literature on sacrectomy for LARC or LRRC is much more limited [51]. While low sacrectomies are widely accepted because of comparable R0, survival and morbidity rates as those who do not require en bloc sacrectomy, [54–57] high sacrectomies were traditionally considered a contraindication for surgery [5, 22]. However, as with the paradigm shift with pelvic sidewall involvement, high sacrectomies are no longer a contraindication for surgery [53, 58, 59]. In a recent study by Milne et al. which included 21 patients who underwent en bloc S1/S2 sacrectomy for LRRC, R0, median and 5 year survivals of 74 %, 59 months and 38 % were reported respectively [53]. In another study by Dozois et al. on high sacrectomy for LRRC, an R0 rate of 100 % and a 5 year survival of 30 % were reported [58]. Importantly, post-operative function seemed good with the former study reporting no difference in neurological deficits between low and high sacrectomy patients and the latter reporting acceptable post-operative ambulation, function and improved pain control [53, 58]. Although more studies are needed, favorable oncologic outcomes coupled with an acceptable morbidity profile and functional outcome necessarily means that high sacrectomy should no longer constitute a contraindication for surgery.

Rarely, pelvic exenteration may be considered for palliative purposes. These are typically patients with symptoms that cannot be adequately palliated using alternative treatment options such as uncontrolled enterovaginal or vesical fistulae, offensive fungating tumors or patients with intractable pain [22, 60]. Several small and highly selected case series have reported dramatically improved symptom control [17, 60, 61]. Naturally, such radical approach to palliation carries the risk of bringing forth the patient's demise but this also highlights the importance of quality of life and patient choice in decision making.

52.6 Treatment

Multi-disciplinary Team Approach

Treatment decision for LARC or LRRC patients should be made in a multi-disciplinary setting. These meetings should include all relevant surgical and medical specialties as well as allied health

specialists such as cancer coordinator, stomal therapists and psych-oncologists. These meetings are also useful for work force planning to ensure the necessary specialties are available on the designated operation day.

Pre-operative Chemoradiation

Patients who are radiotherapy naïve should undergo pre-operative long course chemoradiation [62]. The role of re-irradiation in patients previously irradiated patients is currently unclear [19]. Re-irradiation options include external beam radiotherapy, intensity modulated radiotherapy (IMRT) or intra-operative radiotherapy (IORT). IMRT is a relatively new radiotherapy technique that delivers differential radiation doses precisely to better conform to the three-dimensional shape of the tumor. In doing so, parts of the tumor can receive higher doses while protecting surrounding critical structures [63]. IORT can deliver a much higher biological dose directly to the tumor bed without increasing tissue toxicity but requires purpose built operating theaters to do so [19]. This seems useful where resection margins may have been compromised but this simply underscores the importance of an R0 resection margin [19, 64, 65].

The role of re-staging after chemoradiation is currently unclear although the consensus from an international collaboration, the Beyond TME collaboration, recommends restaging with MRI and PET to assess treatment response prior to exenteration (manuscript in preparation).

Compartments of the Pelvis and Dissection Planes

Conceptually, the pelvis can be divided into five compartments (Fig. 52.1). They are the central, anterior, posterior and the two lateral compartments. Each compartment overlaps at their periphery and are each centered on a different structure. The central compartment is centered on the tip of the coccyx, while the anterior, posterior and lateral compartments are centered on the urethra, the third sacral vertebra and the ischial spines respectively. The contents of each compartment are listed in Table 52.2. Within each compartment are different extra-TME dissection planes and this is illustrated in Fig. 52.2. With these in mind, the surgeon can then conceptualize the three-dimensional anatomy of the cancer so as to formulate a surgical plan when the pelvic MRI is reviewed with an experienced MR radiologist.

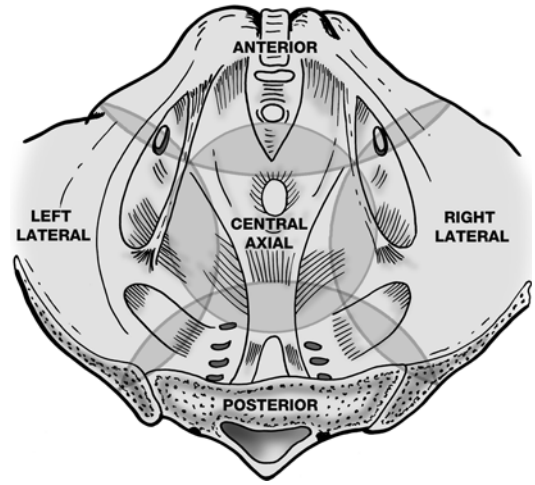

Fig. 52.1 Diagram of the pelvis illustrating the five pelvic compartments, each overlapping at their periphery. Each compartment is centered on a different structure with the anterior, central, posterior and lateral compartments centered on the urethra, the tip of the coccyx, the third sacral vertebra and the ischial spines respectively

Surgical Technique

Pelvic exenteration is a heterogeneous group of operations where the specific procedure will vary depending on the location and the extent of the tumor. Because of this, there is no standardized surgical approach although broad principles can be applied. Of note, there is no universally accepted terminology for types of exenteration. Terms such as central, visceral, complete and total exenteration are often used interchangeably while others would use composite resection or abdominosacral resection to imply en bloc sacral resection. For clarity, exenteration is best defined

Table 52.2 Contents within the compartments

Compartment	Viscera	Muscle	Bone	Others
Anterior	Bladder	Obturator internus	Pubic symphysis	Dorsal venous complex
	Urethra	Obturator externus	Superior pubic ramus	
	Males: prostate, seminal vesicles, vas deferens	Anterior pelvic floor (pubococcygeus, puborectalis part of levator)	Inferior pubic ramus	
	Females: anterior vagina			
Central	Females: posterior half of vagina, uterus, cervix, ovaries, fallopian tubes, broad ligament, round ligament	Pelvic floor muscles (iliococcygeus part o levator ani)	S4 and 5 sacral vertebra	
	Rectum		Coccyx	
Posterior	Rectum	Pelvic floor muscles (coccygeus)	Sacrum (S1-S5)	Branches and tributaries of the internal iliac vessels
		Piriformis	Coccyx	Sacral nerve roots (S1–S4)
				Anterior sacroccocygeal ligament
				Medial sacrotuberous ligament
				Sacrospinous ligament
Lateral	Ureter	Piriformis	Ischial spine	Internal iliac artery and vein
		Obturator internus	Ischial tuberosity	External iliac artery and vein
		Coccygeus		Obturator artery and vein
				Lateral sacrotuberous ligament
				Sacrospinous ligament
				Lumbosacral trunk
				Sciatic nerve distal to ischial spine
				Obturator nerve

Because the compartments overlap at their periphery, some structures appear more than once within the table

as complete or partial based on the number of compartments excised.

All procedures can be subdivided into an exploratory phase, a dissection phase and a reconstructive phase. All procedures begin with an exploratory phase where the aim is to rule out occult metastatic disease that may preclude curative resection and to isolate the pelvic cancer from all small bowel loops by meticulous adhesiolysis, en bloc excision of contiguously involved small bowel loops and dividing the colon along its anatomical planes.

The aim of the dissection is to achieve a clear microscopic margin (R0). As a general principle, a compartmental approach is adopted whereby involvement of a compartment would necessitate

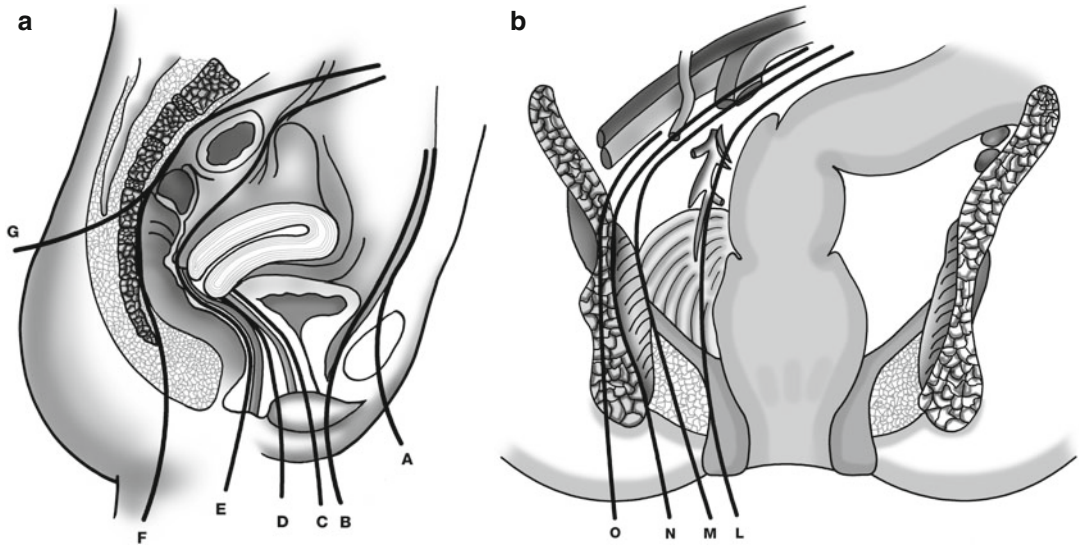

Fig. 52.2 (**a**) Sagittal section of a female pelvis demonstrating possible dissection planes. *Plane A–G* are the surgical dissection planes available. (**b**) Coronal section of a pelvis demonstrating possible dissection planes. *Plane L* is the TME plane; *plane M* is the extra-vascular plane which would involve excision of iliac vasculature; *plane N* is the plane that involves en bloc excision of obturator internus; *plane O* involves en bloc excision of ischial spine or ischial tuberosity

complete excision of the compartment at its soft tissue bony junction or if the tumor extends very close to this margin, en bloc excision of the adjacent bone. Attempting to obtain a soft tissue margin in the former is likely to result in an unacceptably high rate of involved margins. In LRRC, the dissection planes are often poorly defined due to fibrosis from previous radiotherapy and total mesorectal excision. While detailed technical description of each exenteration procedure is beyond the scope of this chapter, it is important to highlight the modern breakthroughs in exenteration techniques.

Lateral Neurovascular Approach

Central to pelvic sidewall dissection is the appreciation that key neurovascular structures are organized in a "layered" manner where the ureter lies superficial to iliac arteries, iliac veins, lumbosacral trunk and obturator internus (Fig. 52.3). To gain access to a deeper structure, the superficial lying structure is dissected out so as to "float" it off the pelvic sidewall (Fig. 52.3). Lateral compartment dissection begins with ureterolysis and pelvic lymphadenectomy which facilitates vascular dissection and exposes the sacral plexus. The appropriate dissection plane is usually predetermined by the staging MRI (Fig. 52.2). Where possible, the internal iliac artery should be ligated distal to the gluteal branches so as to

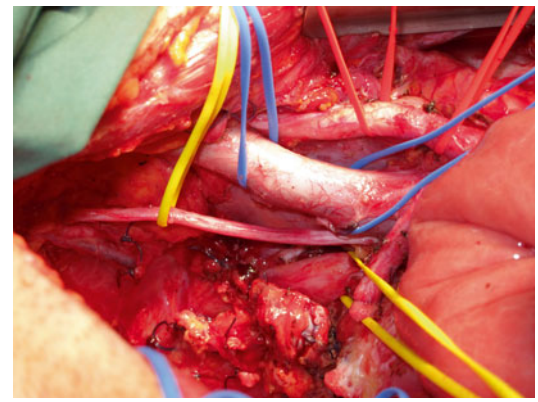

Fig. 52.3 Intra-operative photo of pelvic sidewall demonstrating the right common, external and ligated internal iliac arteries (*red* vessel loops); the right common, external and ligated internal iliac veins (*blue* vessel loops); obturator nerve and lumbosacral trunk (*yellow* vessel loops). This photo demonstrates the "layered" organization of the lateral compartment neurovascular structures. Ligation of internal iliac artery and vein allows and common and external iliac systems to be "floated" off the pelvic sidewall

reduce the likelihood of buttock claudication and to preserve the option of a gluteal artery based flap. Even where formal excision of the internal iliac vasculature is not necessary, in situ ligation of these vessels can help limit blood loss when a distal sacrectomy is planned.

Dissection of the iliac veins is much more challenging due to the variable anatomy and thin walled veins. Loss of venous control is more commonly the cause of catastrophic bleeding in exenterative surgery. The surgeon can usually expect at least a visceral, spinal (or presacral) branch and a gluteal tributary at each level. Pre-emptive suture ligation after dissection of an appropriate venous cuff will ensure vascular control and progressively devascularize the pelvis. In LRRC, the extra-vascular plane is often virginal compared to the TME plane and may be comparatively easier to dissect even if vascular excision is not required.

Identification of the lumbosacral trunk is a key step in lateral compartment dissection as it leads to obturator internus muscle and ischial spine. Preserving the lumbosacral trunk for lower limb motor function is generally possible even if a distal sacrectomy is necessary. To completely excise the lateral compartment, obturator internus can be excised at its origin with or without en bloc excision of ischial spine or ischial tuberosity.

Anterior Compartment Dissection

Conventionally, the anterior dissection plane is the retro-pubic plane at the junction between bladder and pubic bone. As with the principles of en bloc bony excision in the lateral and posterior compartments to improve R0 resection, the same can be applied to the anterior compartment. In LRRC where there is extensive prostatic involvement or involvement of the membranous urethra following previous abdomino-perineal excision in men, en bloc pubic bone excision and excision of proximal penile urethra may be required to achieve a clear resection margin. In a study by Solomon et al. patients with LRRC who underwent en bloc cystectomy had a R0 rate of 64 % but this contrasts with an R0 rate of 100 % in patients who underwent en bloc cystectomy and pubic bone excision (pubic symphysis or bilateral inferior pubic ramus excision) when the membranous urethra was involved (manuscript in preparation). Although long term oncological data from pubic bone excision is not yet available, this demonstrates technique modification can further improve R0 resection rates. Of note, even if central pubic excision is performed, internal fixation is typically not required. Mesh reconstruction to the divided ends of pubic rami with overlying flap reconstruction is generally all that is required.

Posterior Compartment Dissection

The surgical approach for high versus low sacrectomy differ in that a high (S1/S2) sacrectomy generally requires a prone approach whereas a low sacrectomy (S3 and distal) can be performed via an abdominolithotomy approach. High sacrectomies can be highly morbid because division of proximal sacral nerve roots which can cause considerable lower limb motor and sensory deficits. Division of distal sacral nerve roots can result in an atonic bladder. Therefore, patients should be counseled appropriately about en bloc cystectomy even if it is not required oncologically. In patients where there is central involvement of L5 or S1, a central anterior table excision can be performed for L5 and S1 leaving the remainder of the sacrum intact thus preserving pelvic stability and sacral nerve roots.

Sacrectomy is usually the final step after completion of both the abdominal (lateral, anterior and other posterior dissections) and perineal phases of the procedure. This includes abdominal and perineal reconstruction where a prone sacrectomy is required. Posterior dissection begins in the TME plane but stops about 2 cm above the point where tumor adheres to sacrum. For distal sacrectomy, piriformis and sacral nerve roots are divided. After completion of the remainder of perineal dissection, the perineal surgeon disconnects gluteus maximus and tunnels immediately posterior to the coccyx and sacrum to the level of intended sacral division. A malleable retractor is then inserted to protect natal cleft tissue as the abdominal surgeon performs the sacrectomy using a 20 mm osteotome and mallet (Fig. 52.4).

Where a prone sacrectomy is to be performed, to ensure that sacral transection is performed at

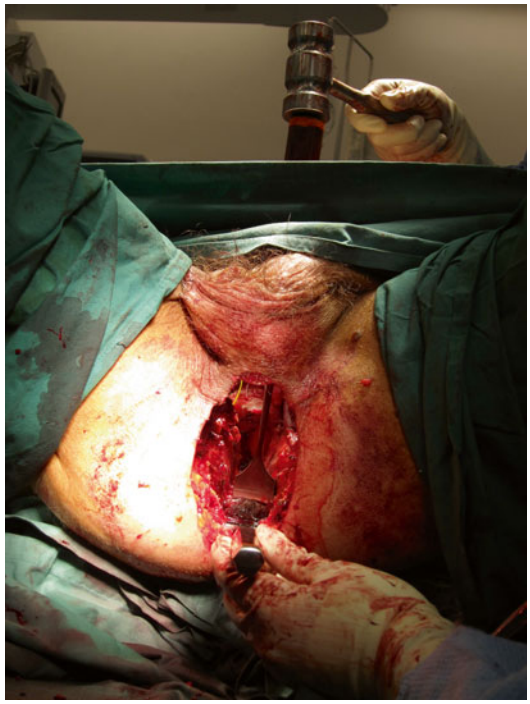

Fig. 52.4 Distal sacrectomy performed via an abdomino-lithotomy approach using a 20 mm osteotome. Natal cleft tissues are protected with a malleable retractor

the appropriate level, an orthopedic staple is secured into the sacrum 2 cm above the desired point of transection. The position of this staple is checked with intra-operative x-ray to confirm the point of sacral transection. It is also useful in these cases to have both lumbosacral trunks marked with a yellow vessel loop and a suture to orientate the rectus abdominis myocutaneous flap to avoid flap malrotation. Abdominal sponges are also left in the pelvis anterior to the sacrum to prevent small bowel from coming into contact with the anterior aspect of sacrum which may be inadvertently injured as the sacrum is being divided from the prone approach using an oscillating saw. Dural sac should be ligated in high sacrectomies to prevent ongoing cerebro-spinal fluid leakage.

Reconstruction

Consideration has to be given to visceral, abdominal and perineal reconstruction. Where cystectomy is performed, an ileal or colonic conduit will be required. Although ileal conduits are preferred, it may not be advisable in patients where small bowel loops have been heavily irradiated. A colonic conduit out of the radiation field may be associated with less complications in this setting [66]. The use of orthotopic neobladder reconstruction is popular within gynae-oncology literature [67, 68] but few are considering the technique in LARC or LRRC [69]. Where a segmental ureteric excision was performed, options include an end-to-end ureteric anastomosis, bladder re-implantation with a psoas hitch or nephrectomy. Re-implanting the ureter into the contralateral ureter or the use of a gastric or jejunal interposition graft are alternatives but the former is avoided if possible to prevent potential repercussions on both kidneys should surgical complications ensue.

In patients where a wide perineal excision or high sacrectomy has been performed, consideration needs to be given to reconstruction using a myocutaneous flap [70]. A rectus abdominis myocutaneous flap is the workhorse for this reconstruction as flap harvest can be incorporated to the laparotomy incision in addition to providing a bulky and well-vascularized tissue with a skin paddle for reconstruction. In patients with previous bilateral stomas, assessing patency of the inferior epigastric artery is recommended. Alternative tissue flaps include gluteal V-Y advancement flaps, inferior gluteal artery perforator based flaps or anterior thigh flaps [71–74]. It is important that skin paddle harvested is not excessive as this will only introduce donor site morbidity. If a rectus abdominis myocutaneous flap is harvested, mesh reconstruction of the abdominal wall will be necessary.

52.7 Outcomes and Prognosis

Reported surgical mortality rates range between 0.3 and 8 % although larger series in recent years have tended to report mortality rates of under 1 % [3, 4, 75]. Published complication rates vary even

Table 52.3 Common complications experienced in exenteration patients

Septic
Urinary tract infection
Wound infection
Pneumonia
Deep seated intra-abdominal/pelvic collections
Osteomyelitis
Gastrointestinal complications
Prolonged ileus
Small bowel obstruction
Enterocutaneous fistula
Anastomotic leak
Colo-vaginal fistula
Cardiorespiratory
Atrial fibrillation or other cardiac arrthymias
Myocardial infarction
Pulmonary embolism (deep venous thrombosis)
Wound complications
Wound dehiscence
Persistent perineal sinus
Perineal flap necrosis
Infected prosthetic mesh
Hematomas
Urological
Urinary retention
Urological leak
Colovesical fistula
Neurological
Sciatic nerve palsy
Stomal complications
Stomal dehiscence
Ischemia

more widely between 21 and over 70 % [3, 38, 76, 77]. The widely disparate complication rates reflect the lack of consistency in reporting. While some authors only report major complications, other report all documented complications. However, major complication rates of about 25 % are generally reported by the larger and more recent studies. Common complications are listed in Table 52.3.

The main aim of surgery is to achieve an R0 margin [1]. Many studies have now demonstrated the survival difference between patients who have R0, R1 and R2 resection margins [3–5]. R0 rates within the literature vary between 38 and 85 % depending on the type of exenteration offered and the experience of the institution [3, 5, 34, 76, 78, 79]. Table 52.4 summarizes R0 and survival data from the larger case series published in the last 5 years.

Numerous other studies have attempted to characterize prognostic indicators for LRRC. Wanebo et al. and Yamada et al. reported that an elevated CEA conferred a worse prognosis compared to patients with normal CEA [34, 59]. Hahnloser et al. and Suzuki et al. found that patients with symptomatic recurrence, particularly when the symptom was pain was associated with a worse prognosis [4, 38]. In the large study by Hahnloser et al. from the Mayo clinic, the number of points of fixation within the pelvis was also found to be predictive of survival [4].

Quality of life in patients following pelvic exenteration is an area that remains understudied [80]. A meta-analysis by Thaysen et al. reported found only seven studies that evaluated quality of life in exenteration patients [80]. Based on existing studies, what is known is that quality of life in exenteration patients can be comparable with patients after TME for primary rectal cancer and that bony resection, the need for double stomas, gender or age do not influence quality of life [7, 8]. The issue of chronic pain in this group of patients is even more under-studied. In a recent study by You et al. pain is predictive of poorer quality of life and is associated with reduced survival [81]. More prospective studies with longer follow ups are required. However, within the confines of current knowledge, it would appear that the quality of life of patients are not worse than that of patients with primary rectal cancer [7].

In the only study that evaluated the cost effectiveness of pelvic exenteration, the authors concluded that surgery is cost effective particularly when calculated using utilities derived from patient preferences [82].

Table 52.4 R0 and survival data from the larger series in the last 5 years

Authors/year	N	R0 (%)	5 year survival (%)	R1/R2 survival	Comments
Heriot et al. 2008 [3]	160	98 (61)	49	25 % for R1 9 % for R2	
Kusters et al. 2009 [83]	170	92 (54)	40		Anastomotic and presacral recurrences had the best and the worst outcomes respectively
Jiang et al. 2011 [84]	187	87 (47)	31	17.2 % for R1 0 % for R2	Patients with lymph node metastases had worse survival
Rahbari et al. 2011 [6]	92	54 (59)	47	26 % 3 year OS for R1 11 % 3 year OS for R2	Exenteration in the setting of metastatic disease can lead to good outcomes if clear margins for pelvic disease can be achieved
Neilsen et al. 2012 [85]	40	15 (38)	17		LARC had better survival than LRRC even when both had R0
Zoucas et al. 2010 [35]	33	19 (64)	Not reported		2 year survival of 75 %

LARC Locally Advanced Rectal Cancer, *LRRC* Locally Recurrent Rectal Cancer

Conclusions

Pelvic exenteration is a complex procedure that requires meticulous pre-operative planning and specialized post-operative care. The boundaries of resectability are constantly being challenged. Improved surgical technique has reduced surgical mortality and morbidity to an acceptable level. Increased surgical radicality over the years has also improved R0 rates thereby increasing the prospects of long term survival. As with oncological results with many other cancers, best results with exenteration is most likely from high volume centers. Smaller centers are therefore encouraged to consider onward referral and to collaborate with larger centers for best outcomes.

Key Points

- Locally advanced primary rectal cancer and locally recurrent rectal cancer require the same meticulous surgical planning, intra-operative surgical approach and post-operative care
- Criteria for resectability continue to evolve. Boundaries are constantly being pushed and smaller centers are encouraged to collaborate with more experienced centers and to consider onward referral if appropriate. The most important determinant for resectability is the ability to achieve a clear resection margin.
- The single most important factor predicting long term survival is a clear resection margin (R0). Others include an elevated CEA (>10), symptomatic presentation (especially pain) and number of points of fixation in the pelvis
- Patient selection for surgery is based on a high quality pelvic MRI and PET scan. MRI determines the extent of local disease so as to determine resectability and the latter rules out distant metastasis.
- All patients require input from a multidisciplinary team including allied health specialists (cancer coordinator, stomal therapy, psychologists, physiotherapists and dieticians)

- A major breakthrough in the surgical approach to locally recurrent rectal cancer is the compartmental approach adopted from sarcoma surgery
- Anatomically, the pelvis can be divided into five compartments including the anterior, central, posterior and two lateral compartments. Within each compartment are different possible dissection planes.
- With improved surgical technique and better understanding of pelvic anatomy, surgical mortality and major complications in large contemporary series are usually under 1 % and about 25 % respectively.
- Quality of life studies following pelvic exenteration are relatively scant but based on available data, global quality of life seems acceptable. The need for bony resection or double stomas does not appear to affect quality of life. The impact of pain on quality of life and survival needs further evaluation.
- Follow up after pelvic exenteration is currently not well defined.

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