Locally Advanced Disease and Pelvic Exenterations

Christos Kontovounisios, PhD, FRCS^{1,2} Paris Tekkis, MD, FRCS^{1,2}

¹Department of Colorectal Surgery, The Royal Marsden Hospital, Chelsea, London, United Kingdom

²Department of Surgery and Cancer, Imperial College, London, United Kingdom

Address for correspondence Paris Tekkis, MD, FRCS, Department of Colorectal Surgery, The Royal Marsden Hospital, Fulham Road, London SW3 6JJ, United Kingdom (e-mail: p.tekkis@imperial.ac.uk).

Clin Colon Rectal Surg 2017;30:404–414.

Abstract

Keywords

- ▶ primary advanced rectal cancer
- ▶ recurrent rectal cancer
- ▶ beyond total mesorectal excision
- ▶ multidisciplinary management

Advanced primary and recurrent colorectal cancer can be successfully treated by experienced, dedicated centers delivering good outcomes with low mortality and morbidity. Development and implementation of a comprehensive referral pathway is to be encouraged. Multidisciplinary team management is essential in the management of this complex group of patients and is associated with significantly more complete preoperative evaluation and more accurate provision of patient information, as well as improved access to the most appropriate individualized management plan. A structured selection process can improve outcomes through standardized approaches to service delivery to provide the highest quality of care.

Colorectal cancer (CRC) accounts for 13% of all cancers, is the third most frequent cancer after breast and prostate in the 27 countries of the European Union, and is the second most frequent cause of death after lung cancer.¹ Surveillance and prevention have led CRC incidence to decline; however, the incidence of rectal cancer in younger patients is increasing by 2.6% a year in the United States.² In the United Kingdom, 33% of the 14,000 newly diagnosed rectal cancers per year will be locally advanced on presentation.³ If left untreated, the prognosis is poor, with the median survival of rectal cancer less than 1 year and the 5-year survival less than 5%.^{4–6}

Total mesorectal excision (TME) with the addition of neoadjuvant radiotherapy has led to margin negative rates approaching 90% and local recurrence rates of 4 to 10%. Even if chemoradiotherapy (CRT) can downstage cancers so conventional TME can achieve complete surgical resection, approximately 6% of rectal cancers will still invade adjacent structures.^{7,8} Little is known about the natural history of locally advanced primary (LAP) or recurrent CRC, and there is no established protocol for these patients in terms of timing of surgery. Although CRT plays an important role in palliation and symptom control, surgical resection involving a multivisceral or exenterative approach is the only potentially curative option.^{9,10} However, prior irradiation, distorted

mesorectal planes, and aggressive tumor biology can lead to higher risks of positive resections, high rate of morbidity and decreased survival rates, and increase the difficulty of future salvage surgery.^{11–13}

Currently, there is a wide range of disparity in care for patients with multivisceral involvement from primary, locally advanced, and recurrent rectal cancer (RRC) within the United Kingdom and globally. The referral process and accessibility to high-quality care have been inconsistent, and patients may be denied potentially curative surgical treatment or delayed in being considered for surgery. There has also been only moderate data capture of activities as these patients are not generally included in standard national databases, and outcome reporting is dependent on individual center audits and publications. This article provides a general overview of the role of multivisceral, pelvic exenterations during treatment, as well as strategies and guidelines to be used when approaching locally advanced rectal cancer.

The Beyond TME Collaborative

In 2012, the Beyond TME Collaborative¹⁴ achieved consensus through Delphi methodology on the definitions and principles of management of primary advanced rectal cancer beyond

TME planes (PRC-bTME) and RRC. Prior to that effort, there was global variation in standards and no guidelines existed. The group consisted of invited experts from surgery, radiology, oncology, and pathology. The process included two international dedicated discussion conferences, formal feedback, three rounds of editing, and two rounds of anonymized web-based voting. The final consensus document included 51 voted statements, making recommendations on 10 key areas of PRC-bTME and RRC. Consensus agreement was achieved on the recommendations of 49 statements, with 34 achieving consensus in more than 95%. There was clear identification of the need for referral to a specialist multidisciplinary team (MDT) for diagnosis, assessment, and further management.

Definitions

Tumors requiring extended resection include those beyond the magnetic resonance imaging (MRI) predicted circumferential resection margin (CRM), those invading the sphincter with or without involvement of the levator complex, and those with abnormal side-wall lymph nodes deemed by appropriate imaging and MDT assessment to contain cancer.

Primary Rectal Cancer beyond Total Mesorectal Excision Planes

In the literature, there are several definitions of locally advanced rectal cancer among institutions. This heterogeneity can be explained due to different editions of the tumor node metastasis (TNM) classification by different international coloproctology societies, differing methods of preoperative imaging for staging of rectal cancer (ultrasonography, computed tomography [CT], MRI), different criteria for what constitutes locally advanced disease, and varying anatomical definitions of the rectum itself.^{15–18}

Examples of different uses of the term *locally advanced disease* in recent studies include the German rectal cancer trial (any T N+, or T3/T4), the MERCURY study (T3c, T3d, or T4), the EXPERT study (T1–4 N2; low T3; T4; threatened CRM), and the Berlin rectal cancer trial (ultrasound defined [u] T2 N+; any T3, T4 excluded).¹⁹ In the Beyond TME Collaborative consensus document, PRC-bTME includes tumors that are predicted by MRI to require an extended surgical resection beyond the TME plane to achieve a pathological R0 resection. pT4a were considered tumors invading the visceral peritoneum, and pT4b were considered tumors invading the adjacent structures or organs. Tumors with abnormal side-wall lymph nodes considered by imaging and MDT assessment to contain cancer would also require extended resection. T4a upper rectal tumors can be excluded from this category as they would not necessitate an extended resection (but are at high risk of local recurrence through intracoeleomic seeding and also widespread abdominal recurrence). The term *high-risk rectal cancer* is used to define tumors generally recommended for neoadjuvant therapy to reduce the risk of recurrence, but not requiring an extended surgical resection. This subgroup would include tumors with a potentially threatened CRM such as T3c/d middle and

upper rectal tumors, and any T3 tumor in the lower third of the rectum, or any TN1 or TN2 diseases. The term *low-risk rectal cancer* is used to define earlier stages. A proposed algorithm to diagnose and assess resectability of PRC-bTME is shown in ►Fig. 1.¹⁴

Recurrent Rectal Cancer

Pelvic recurrence includes anastomotic and tumor bed recurrences, as well as recurrence within lymphatics such as residual mesorectal nodes and pelvic side wall lymph nodes.²⁰ Para-aortic disease, by definition beyond the definition of the rectum, is considered as distant disease. Also included is inguinal node recurrence and disease manifesting along drain tracts and surgical scars (abdominal or perineal). The time frame for recurrence is typically within the first 2 years after resection of the primary tumor. However, with improved CRT and adjuvant therapies, recurrence may occur as late as 10 years following primary surgery.²¹ A proposed algorithm to diagnose and assess resectability of RRC is shown in ►Fig. 2.

Neoadjuvant Treatment in Locally Advanced Disease

Preoperative CRT is now the preferred treatment when compared with postoperative CRT due to overall compliance rate, improved local control, reduced toxicity, and increased sphincter preservation rate in low-lying tumors. It is often preferred in patients with resectable rectal cancer due to a significant decrease in local failure, acute toxicity, and chronic toxicity.²² There are two different approaches to preoperative radiation therapy: (1) an intensive short-course radiotherapy with large fractions (5 × 5 Gy) for 1 week followed by surgery or (2) 5 to 6 weeks of conventional fractions (1.8–2.0 Gy), combined with concurrent chemotherapy, and surgery 4 to 6 weeks later (long-course preoperative radiotherapy). Larger tumors (cT3–4 and/or N+) in which the goal is downstaging or downsizing, full-course preoperative CRT (50.4 Gy plus concurrent chemotherapy) is recommended. Patients with a cT3N0, cT4N0, and cTxN+ should be also considered for a neoadjuvant CRT. Overtreatment may be possible especially in some cT3N0 patients, but overall benefit outweighs risks, resulting in lower regional recurrence rate compared with postoperative radiotherapy or CRT.²³

Denost et al²⁴ has studied the impact of changing the surgical strategy according to tumor response in rectal cancer mrT4b. Patients with nonmetastatic T4b rectal cancer at two tertiary referral centers between 2008 and 2013 were grouped as “responders” ypT0–3abNx versus “nonresponders” ypT3cd-4Nx and divided into three surgical procedures: TME, extended-TME (e-TME), and beyond-TME (b-TME). Among 883 patients with rectal cancer, 101 were included. Responders had a higher rate of induction chemotherapy (59.7 vs. 38.2%; $p = 0.04$). Morbidity and definitive stoma formation were significantly higher in nonresponders. R0 was not impacted by either the tumor response or the surgical procedures. The 3-year local recurrence was lower in responders (14%) compared with nonresponders (32%) (HR: 1.6; 95% confidence interval: 1.02–2.59; $p = 0.041$) and was twofold higher in e-TME compared with b-TME in nonresponders, whereas no difference was found in responders. The 3-year disease-free

Fig. 1 Algorithm to diagnose and assess resectability of primary rectal cancer beyond total mesorectal excision planes (PRC-bTME). Boxes with shading represent areas of particular controversy. CEA, Carcinoembryonic antigen; CT, computed tomography; EUA, examination under anesthesia; FDG, fluorodeoxyglucose; MRI, magnetic resonance imaging; PET, positron emission tomography; sMDT, specialist multidisciplinary team; TAP, thorax, abdomen, and pelvis.

survival (DFS) was higher in responders irrespective to the surgery (71 vs. 47%; $p = 0.07$). Therefore, in responders, TME or e-TME is technically and oncologically feasible and should be given preference over b-TME. In nonresponders, allowing for high rates of morbidity and local recurrence in patients with e-TME, b-TME procedures should be preferred.

Intraoperative Radiotherapy for Locally Advanced Disease

Intraoperative radiotherapy (IORT) is a specialized method of delivering radiation higher doses where there is concern about tumor margins, without compromising the surrounding organs at risk. The low rate of recurrence in IORT fields, and a convergence of survival curves for R0 and R1/2 resections seen in studies with long-term data support the concept that IORT may offer an oncological advantage in selected patients. Mayo Clinic has achieved with IORT reduced incidence of local failure (40 vs. 93% at 3 years) and improved overall survival (19 vs. 7% at 5 years; $p < 0.001$). Others have found a significant survival benefit in patients who received IORT compared with patients who did not (3-year survival rate: 43 vs. 5%; $p < 0.001$).²⁵ A

recent European multinational study of 605 patients demonstrated that 55% of patients with a positive resection margin who received IORT remained free from local recurrence.²⁶ Dubois et al randomized clinical trial that included 142 patients with T3–4 primary and/or recurrent tumors; compared external beam radiotherapy (EBRT) using 40 Gy alone with the same EBRT plus an IORT boost (an additional 18 Gy) did not confirm any DFS benefits from IORT treatment ($p = 0.781$).²⁷ In this series, it is possible that the population of T3 and T4 tumors contributed to these negative results.

Adjuvant Treatment in Locally Advanced Disease

To date, adjuvant chemotherapy is recommended by most centers in Western countries for a period of 4 to 6 months following surgery. The aim is the reduction of local failures achieved through preoperative treatment, with a reduction of distant metastasis and thereby an increase in survival. A recent pooled analysis of five randomized studies demonstrating a 20% absolute survival benefit with postoperative chemotherapy, administered for 6 to 18 months +/- postoperative radiotherapy, compared with observation or postoperative

Fig. 2 Algorithm to diagnose and assess resectability of recurrent rectal cancer (RRC). Boxes with shading represent areas of particular controversy. CEA, Carcinoembryonic antigen; CT, computed tomography; EUA, examination under anesthesia; FDG, fluorodeoxyglucose; MRI, magnetic resonance imaging; PET, positron emission tomography; sMDT, specialist multidisciplinary team; TAP, thorax, abdomen, and pelvis.

radiation alone.²⁸ Adjuvant treatment including fluoropyrimidine-based chemotherapy is effective in those patients who show downstaging (pT1–pT2) after preoperative treatments (CRT or radiotherapy). Several retrospective studies have shown that patients with a pathological complete response have a better long-term prognosis even if adjuvant therapy is omitted.²⁹ Furthermore, it is not possible to determine whether this better outcome depends on inherent characteristics of these tumors, with response to preoperative CRT, or whether this prognosis is a result of tumor response to preoperative treatment. Response to preoperative CRT may also indicate chemosensitivity with intact cell death pathways and a potential positive impact on the efficacy of postoperative treatment. At present, adjuvant infusional 5-fluorouracil (5-FU)/folinic acid or capecitabine for 6 months is recommended.³⁰ Oxaliplatin-based regimens as postoperative chemotherapy are considered in some cases, in particular in patients in whom 5-FU-based CRT did not lead to a downsizing.

In patients who did not receive neoadjuvant radiotherapy or CRT, adjuvant treatment should be considered after radical resection rectal cancer. In the setting of postoperative CRT, a long-course radiotherapy (45–50.4 Gy in 1.8 Gy fractions) regimen in combination with chemotherapy (protracted infusion of 5-FU or capecitabine) is usually administered.²³

Surgical Approaches: Pelvic Exenterations

Pelvic exenteration is a surgical procedure that is indicated for the management of advanced primary or locally recurrent pelvic malignancies. The operation may involve removal of numerous pelvic structures, including the bladder, uterus and fallopian tubes, vagina, rectum, pelvic blood vessels and nerves, and pelvic bone. The procedure was first described in 1948 for management of advanced pelvic malignancies.³¹ Since that time, pelvic exenteration surgery has evolved to become an established procedure for the treatment of a variety of primary and recurrent pelvic malignancies.

Surgical techniques have become more complex over time, largely due to:

- Advances in the resection of tumors that involve lateral pelvic bone and/or the sacrum.
- Advances in urinary diversion surgery and plastic surgical reconstructive techniques.
- Introduction of IORT in some surgical centers.³²

Operative approaches to the pelvis can also be defined according to the four main anatomical compartments that comprise the pelvic anatomy.³³ Surgery may involve more than one pelvic compartment:

- Axial compartment: this consists of the vagina, uterus, ovaries, fallopian tubes, broad ligament, round ligament of uterus, rectum, and pelvic floor muscle (iliococcygeus part of levator ani).
- Anterior compartment: this consists of the bladder, prostate, seminal vesicles, vas deferens, urethra, urogenital diaphragm, dorsal vein complex, obturator internus and externus muscles, anterior pelvic floor muscle (pubococcygeus and puborectalis part of the levator ani), pelvic bone (pubic symphysis, superior and inferior pubic rami), and obturator nerves and vessels.
- Posterior compartment: this consists of the rectum, pelvic floor (coccygeus muscle), internal iliac vessels branches and tributaries, piriformis muscle, sacral nerves S1–S4, pelvic bone (sacrum and coccyx), anterior sacrococcygeal ligament, and medial sacrotuberous and sacrospinous ligaments.
- Lateral compartment: this consists of the pelvic side wall structures, ureter, internal iliac vessels, external iliac vessels, piriformis and obturator internus muscles around the ischial spine, coccygeus muscle, lateral sacrotuberous and sacrospinous ligaments attached to ischium, ischium including tuberosity and spine, lumbosacral trunk, and sciatic nerve distal to ischial spine.

Three types of pelvic exenteration surgery have been described in the literature: anterior, posterior, and total; however, sometimes modifications are required by the surgical team due to variations in site and size of tumors or organs involved^{32,34}:

- Anterior exenteration involves removal of pelvic structures toward the front of the pelvic cavity, including the reproductive organs, bladder, and urethra.
- Posterior exenteration removes organs at the back part of the pelvic cavity. These include the reproductive organs, plus the lower part of the bowel.
- Total exenteration removes the bladder, urethra, rectum, anus, and supporting muscles and ligaments, together with the reproductive organs.

Various pelvic classifications have been proposed to assess tumor resectability. In addition to assisting with decision-making regarding resectability, classification adds information about prognosis. Central recurrences have been shown to have improved results over posterior or lateral recurrences (–Table 1 and –Figs. 3 and 4).^{35–37}

Role of the Multidisciplinary Team

Studies have shown that MDT input in complex diseases results in greater patient satisfaction, changes in management, improved staging, increased operative experience, and enhanced survival. It is also well established that surgery by trained specialists results in improved outcomes, especially for rectal cancer. Efficient identification of patient eligibility for operative management is a key element in surgical outcomes and survival. Multivisceral resections can have a major impact on physical appearance, physical functioning (bowel, urinary, and sexual), and emotional health; therefore, management will necessitate clinical and psychosocial support in addition to the chance for cure.

Preoperative Assessment

Preoperative optimization is essential to minimize perioperative morbidity and requires a multispecialist approach. That includes anesthetists, respiratory physicians, urologists, cardiologists, and stoma nurses. Formal cardiopulmonary testing is an objective test to assess fitness and diagnose cardiovascular and lung pathophysiology.³⁸ Areas for potential improvement can be identified, including ischemic heart disease.³⁹ Admission 24 hours before surgery into a critical care setting may allow maximal preoperative optimization in special cases. Intraoperative monitoring, such as esophageal Doppler, in association with other invasive monitoring provides further information on the physiological status of the patient.⁴⁰ Routine cross-matching of blood, clotting products, and platelets should be available at short notice in case of severe bleeding. Hemostatic materials can assist in sealing bleeding of surfaces. Preoperative stoma counseling/marketing should be performed. Selective ureteric stenting to clearly identify the ureteric course is also helpful.

Postoperative intensive care is necessary after any exenteration. The major postoperative inflammatory response requires close physiological monitoring to maintain organ perfusion and function. Prolonged postoperative ileus is common. Consideration should be given to early postoperative parenteral nutrition if the likelihood of prolonged ileus is likely. Some patients with end stomas undergoing certain exenterative procedures are likely to be able to feed orally at an early stage.

R0 versus R1 versus R2 Resection

The key to successful long-term survival is the ability to achieve an R0 resection. Bhangu et al⁴¹ on 100 pelvic exenterations demonstrated that resection margin status is more important than primary or recurrent cancer in predicting long-term outcome. R0, R1, and R2 resections were achieved in 78, 15, and 7 cases, respectively. R0 rates were significantly higher in LAP cancer than in RRC (91 vs. 62%, $p = 0.001$). Three-year DFS for R0, R1, and R2 resections was 67, 49, and 0%, respectively ($p < 0.001$). For R0 resections only, DFS in LAP cancer was 76 and 57% in RRC ($p = 0.212$). On multivariate analysis, a positive resection margin (hazard ratio: 4.04; $p < 0.001$) and positive lymph node staging (hazard ratio, 2.43; $p = 0.022$) were significant predictors of reduced DFS. Three-year local recurrence free survival

Table 1 Classification systems in use for locally recurrent rectal cancer

Study group	Classification	Definitions		Outcomes
Mayo Clinic	Symptoms	S0	Asymptomatic	Pain-free patients had better survival
		S1	Symptomatic without pain	
		S2	Symptomatic with pain	
	Degree and site of fixation	F0	No fixation	More points of fixation resulted in more complications and worse survival
		F1	Fixation to one point	
		F2	Fixation to two points	
		F3	Fixation to more than two points	
Yamada et al	Pattern of pelvic fixation	Localized	Invasion to the adjacent pelvic organs or tissue	5-y survival 38%
		Sacral invasive	Invasion to lower sacrum (S3, S4, S5), coccyx, perosteum	5-y survival 10%
		Lateral invasive	Invasion to sciatic nerve, greater sciatic foramen, lateral pelvic wall, upper sacrum (S1, S2)	5-y survival 0%
Wanebo et al	Five stages	TR1	Limited invasion of the muscularis	
		TR2	Full-thickness penetration of the muscularis propria	
		TR3	Anastomotic recurrences with full-thickness penetration beyond the bowel wall and into the perirectal soft tissue	
		TR4	Invasion into the adjacent organs without fixation	
		TR5	Invasion of the bony ligamentous pelvic including sacrum, pelvic/side walls, or sacrotuberous/ischial ligaments	
Memorial Sloan Kettering Cancer Center	Anatomical region involved	Axial	Anastomotic, mesorectal, perirectal soft tissue, perineum (APER)	Axial-only recurrence has 90% likelihood of R0; lateral recurrence associated with 36% likelihood of R0
		Anterior	Genitourinary tract	
		Posterior	Sacrum and presacral fascia	
		Lateral	Soft tissues of the pelvic side wall and the lateral bony pelvis	
Leeds	Anatomical region involved	Central	Tumor confined to the pelvic organs or connective tissue without contact with or invasion into bone	
		Sacral	Tumor present in the presacral space and abuts onto or invades into the sacrum	
		Side wall	Tumor involving the structures on the lateral pelvic side wall, including the greater sciatic foramen and sciatic nerve through to the piriformis and gluteal region	
		Composite	Sacral and side-wall recurrence combined	
Royal Marsden Hospital	MRI; planes of dissection	C	Rectum or neorectum, intraluminal recurrence, perirectal fat or mesorectum, extraluminal recurrence	MRI diagnosis of tumor invasion within the lateral, posterior, or more than two compartments associated with reduced disease-free survival
		PR	Rectovesical pouch or rectouterine pouch of Douglas	
		AA PR	Ureters and iliac vessels above the peritoneal reflection, sigmoid colon, small bowel, and lateral side wall fascia	
		AB PR	Genitourinary system	
		L	Ureters, external and internal iliac vessels, lateral pelvic lymph nodes, sciatic nerve, sciatic notch, S1 and S2 nerve roots, piriformis, or obturator internus muscle	
		P	Coccyx, presacral fascia, retrosacral space, sacrum up to the upper level of S1	
		I	Levator ani muscles, external sphincter complex, perineal scar (APER), ischioanal fossa	

Abbreviation: MRI, magnetic resonance imaging.

Fig. 3 Pelvic compartments: sagittal view (blue, rectovesical pouch; green, posterior; brown, central; purple, inferior).

Fig. 4 Pelvic compartments: coronal view (yellow, lateral; green, posterior; brown, central).

(LRFS) for R0 resection was 86% for LAP cancer and 84% for RRC ($p = 0.817$). On multivariate analysis, only a positive resection margin was a significant predictor of reduced LRFS (hazard ratio: 5.48; $p = 0.002$) (► **Figs. 5–8**).

Contraindications of Pelvic Exenteration Surgery

Contraindications of pelvic exenteration include anatomical, surgical, medical, and psychological factors. The agreed contraindications include the following:

- **Absolute:**
 - Patient preference to not proceed with surgery.
 - Inoperable metastatic disease.
 - Tumor involving bone above S1 surgical landmark.
 - Patient not medically fit enough to withstand the surgery.

Patients at risk:

	0	12	24	36
R0	78	45	28	19
R1	15	6	5	3
R2	7	2	1	0

Fig. 5 Three-year disease-free survival for R0, R1, and R2 resection ($p < 0.001$).

Patients at risk:

	0	12	24	36
LAP	50	29	15	9
RRC	28	16	13	10

Fig. 6 Three-year disease-free survival for locally advanced primary cancer and recurrent rectal cancer after R0 resection ($p = 0.212$).

- **Relative:**
 - Distant metastases.
 - Metastases to para-aortic lymph nodes.
 - Tumor fixed to multiple sites in the pelvis.

Fig. 7 Three-year local recurrence free survival after R0 and R1 resection ($p = 0.001$).

Fig. 8 Three-year local recurrence free survival for locally advanced primary cancer and recurrent rectal cancer after R0 resection ($p = 0.780$).

- Tumor unable to be resected with margins that are surgically clear, that is, R0 resection.
- Tumor involving the lateral pelvic wall.
- Tumor involving the high sacrum (particularly if S1 and S2 nerve roots are involved).

Perioperative Management

Involved surgical compartments will determine the perioperative management. The operative procedure can take up to 22 hours especially when lateral compartment or neuro-

vascular excisions are involved. Colorectal surgeons are the lead surgeons working closely with other specialties such as urologists, and plastic and vascular surgeons. Orthopaedic surgeons may be required in selective cases. An experienced anesthetic consultant provides anesthetic management. A radiographer may be required for a period of the procedure. Two teams of surgical nursing staff are required. Where indicated, the anterior, axial, and lateral compartments are resected through an abdominal combined with a perineal lithotomy approach. Resection of the posterior compartment may require a posterior or abdominal approach. Involvement of the third sacral vertebrae (S3) and above because of the nature of the sacroiliac joint attachment requires a prone approach unless only the anterior cortex of the midline bones of the fifth lumbar vertebrae (L5) and upper sacrum need to be resected. Lateral higher sacrum and full vertebral excision of S2 and S3 requires the posterior prone approach.

Anterior Recurrence

Involvement of the uterus and/or vagina requires bilateral salpingo-oophorectomy, radical hysterectomy, and posterior or radical vaginectomy performed as an en bloc excision with tumor and rectum. Involvement of the bladder dome or above can be treated by partial cystectomy en bloc with the recurrent tumor and rectum, performed with primary closure of the bladder. If the lower bladder (below the trigone) and/or prostate are involved, then radical cystectomy or cystoprostatectomy with ileal or colonic conduit formation is required.³⁴ For anterior compartment tumors abutting or infiltrating the pubic bone, a more radical margin becomes necessary for the excision of the anterior compartment. Resection of muscular and bony structures, including the pubic bone, may be required.

Central Recurrence

Central recurrence may include an extended resection of the axial compartment and surrounding tissues to ensure complete resection margins. Recurrent central rectal cancers can involve the uterus, fallopian tubes and ovaries, vagina, bladder, seminal vesicles, and/or prostate. All involved structures are included in the resection.⁴²

Lateral Recurrence

Some surgical centers consider lateral recurrence a contraindication to pelvic exenteration surgery. Where surgery is undertaken, en bloc excision of the lateral pelvic structures (obturator internus and piriformis muscles, sacrotuberous and sacrospinous ligaments, sacral nerve roots, and, where involved, bone that comprises the sacrum, ileum, or ischium) may be performed.⁴³

Posterior Recurrence

Surgical management of posterior recurrence usually involves abdominoperineal resection with sacrectomy. If the posterior recurrence only involves the sacral fascia, it can be resected by periosteal elevation en bloc with the tumor and posterior structures involved. Bony involvement requires sacral resection with the level of resection dependent on

Fig. 9 Double-barreled colostomy.

the level of sacrum involved. Low posterior tumors require wide excision of the entire posterior pelvic floor from the level of the ischial spine laterally to the junction of the S3–S4 vertebra medially (defined by the sacrospinous ligament more deeply).⁴⁴

Bladder Reconstruction

If the urethra and its sphincters can be preserved, an intestinal neobladder can be formed. However, the risk of fistulation is very high, especially if a low rectal anastomosis is performed at the same time. An alternative to reconstruction in the pelvis where the tissues are likely to have been irradiated is to make a continent catheterizable reservoir within the upper abdomen. Several techniques are available using varying combinations of large and small bowel with or without the appendix. In a series of total pelvic exenterations for gynecological malignancy, 40 patients had 26 complications related to the urological reconstruction and 24 had nonpouch-related complications.⁴⁵ An alternative is the formation of double-barreled colostomy first described in 1989 by Carter (→ **Fig. 9**). A series of 30 patients at the Royal Marsden Hospital has shown low morbidity rates. Complications involve urinary tract infections, with two patients with severe kidney injury due to urosepsis.

Abdominal Wall and Reconstruction of the Perineum

After resection of the involved pelvic compartments, a surgical reconstruction of the involved pelvic area is required, including reconstruction of the perineum. The type and extent of reconstruction performed varies according to a range of factors, including the extent of the resection, the patient's age and gender, prognosis, and patient preferences. The main procedures involved in reconstruction are filling of the pelvic dead space, reconstruction of the vagina, and

urinary diversion.³³ If the empty space is not reconstructed, the patient is at increased risk of abscesses, fistula formation, perineal wound problems, and intestinal obstruction. To prevent these complications, pelvic floor reconstruction can be performed using the following:

- Synthetic mesh.
- Omentum or other autologous tissue.
- Myocutaneous grafts, including rectus and gracilis muscle flaps, can be brought into the pelvis and perineum to create pelvic support and a neovagina. Split-thickness skin grafts have also been used to create neovaginas. The vertical rectus abdominis myocutaneous flap is commonly used as it provides good tissue bulk for the perineal or sacral defects, is able to be moved into the perineal or sacral space, and provides nonirradiated vascularized tissue into a region prone to healing problems.^{34,46}

Complications

The complication rate associated with pelvic exenteration surgery for recurrences is generally higher than that associated with resection of the primary malignancy.⁴⁷ The major complication rate is between 25 and 50%.⁴⁸ This excludes the perioperative mortality associated with the procedure, which is up to 12% in some case series.⁴⁹ Complications are more common in patients with lateral pelvic wall involvement and in those who have undergone sacrectomy.^{50,51} Hospital readmission rates of approximately 45% and reoperation rates of approximately 32% have been reported due to complications.⁴⁷

Early major complications (defined as complications that cause the need for reintervention or are the cause of prolonged hospitalization) of pelvic exenteration surgery include the following^{52–54}:

- Prolonged intubation (20%).
- Sepsis (35%).
- Abscess formation (7%).
- Other significant wound infection (5–40%).
- Urostomy-related complications (5–42%).
- Wound dehiscence (5–40%).
- Hemorrhage.
- Anastomotic breakdown at the level of the bowel, urinary pouch, or ureteral sites.

The rate of late major complications is lower, but approximately one-third of patients experience fistulae, bowel obstruction, ureteral strictures, renal failure, pyelonephritis, or chronic bowel obstruction. Other complications include deep venous thrombosis and pulmonary emboli, flap necrosis, and stomal necrosis.⁵⁵

Follow-Up Regimens

Follow-up after locally advanced rectal cancer surgery aims to detect recurrence at an early stage, detect second primaries, patient reassurance, audit, and research. Follow-up after resection depends on stage, type of surgery, perioperative treatment, and amenability to resection of recurrent disease. Rising concentration of carcinoembryonic antigen may indicate the need for further investigation.⁵⁶ Until

further evidence emerges regarding the sensitivity, specificity, and cost-effectiveness of fluorine-18 fluorodeoxyglucose positron emission tomography in differentiation between scar tissue and postoperative infection/inflammation from malignant change, its routine use cannot be recommended. However, early results suggest that it is promising in accurate detection of recurrence and/or metastases.

Quality of Life

Young et al⁵⁷ demonstrated that quality of life and related patient-reported outcomes improve rapidly after pelvic exenteration surgery. For 9 months after surgery, these outcomes were comparable with patients who did not have surgery. Other studies have used various noncomparative designs with quality-of-life assessments performed using different instruments at different time points in each study.^{58,59} Zoucas et al⁴⁴ reported improvement in quality of life between 4 and 16 months postsurgery, and You et al⁶⁰ found that the quality-of-life outcomes are comparable in 105 patients who had curative exenterations, noncurative surgery, and nonsurgical treatment.

Reference

- 1 Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. *Eur J Cancer* 2013;49(06):1374–1403
- 2 Meyer JE, Narang T, Schnoll-Sussman FH, Pochapin MB, Christos PJ, Sherr DL. Increasing incidence of rectal cancer in patients aged younger than 40 years: an analysis of the surveillance, epidemiology, and end results database. *Cancer* 2010;116(18):4354–4359
- 3 MERCURY Study Group. Diagnostic accuracy of preoperative magnetic resonance imaging in predicting curative resection of rectal cancer: prospective observational study. *BMJ* 2006;333(7572):779
- 4 Solum AM, Riffenburgh RH, Johnstone PA. Survival of patients with untreated rectal cancer. *J Surg Oncol* 2004;87(04):157–161
- 5 Carlsson U, Lasson A, Ekelund G. Recurrence rates after curative surgery for rectal carcinoma, with special reference to their accuracy. *Dis Colon Rectum* 1987;30(06):431–434
- 6 Arnott SJ. The value of combined 5-fluorouracil and x-ray therapy in the palliation of locally recurrent and inoperable rectal carcinoma. *Clin Radiol* 1975;26(02):177–182
- 7 MacFarlane JK, Ryall RD, Heald RJ. Mesorectal excision for rectal cancer. *Lancet* 1993;341(8843):457–460
- 8 van Gijn W, Marijnen CA, Nagtegaal ID, et al; Dutch Colorectal Cancer Group. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer: 12-year follow-up of the multicentre, randomised controlled TME trial. *Lancet Oncol* 2011;12(06):575–582
- 9 Sagar PM, Pemberton JH. Surgical management of locally recurrent rectal cancer. *Br J Surg* 1996;83(03):293–304
- 10 Ito Y, Ohtsu A, Ishikura S, et al. Efficacy of chemoradiotherapy on pain relief in patients with intrapelvic recurrence of rectal cancer. *Jpn J Clin Oncol* 2003;33(04):180–185
- 11 Nielsen MB, Rasmussen PC, Lindegaard JC, Laurberg S. A 10-year experience of total pelvic exenteration for primary advanced and locally recurrent rectal cancer based on a prospective database. *Colorectal Dis* 2012;14(09):1076–1083
- 12 Bhangu A, Ali SM, Darzi A, Brown G, Tekkis P. Meta-analysis of survival based on resection margin status following surgery for recurrent rectal cancer. *Colorectal Dis* 2012;14(12):1457–1466
- 13 Heriot AG, Byrne CM, Lee P, et al. Extended radical resection: the choice for locally recurrent rectal cancer. *Dis Colon Rectum* 2008;51(03):284–291
- 14 Beyond TME Collaborative. Consensus statement on the multidisciplinary management of patients with recurrent and primary rectal cancer beyond total mesorectal excision planes. *Br J Surg* 2013;100(08):E1–E33
- 15 Tepper JE, O'Connell M, Hollis D, Niedzwiecki D, Cooke E, Mayer RJ; Intergroup Study 0114. Analysis of surgical salvage after failure of primary therapy in rectal cancer: results from Intergroup Study 0114. *J Clin Oncol* 2003;21(19):3623–3628
- 16 Ngan SY, Fisher R, Burmeister BH, et al. Promising results of a cooperative group phase II trial of preoperative chemoradiation for locally advanced rectal cancer (TROC 9801). *Dis Colon Rectum* 2005;48(07):1389–1396
- 17 Krook JE, Moertel CG, Gunderson LL, et al. Effective surgical adjuvant therapy for high-risk rectal carcinoma. *N Engl J Med* 1991;324(11):709–715
- 18 Salerno G, Daniels IR, Brown G. Magnetic resonance imaging of the low rectum: defining the radiological anatomy. *Colorectal Dis* 2006;8(Suppl 3):10–13
- 19 Siegel R, Burock S, Wernecke KD, et al. Preoperative short-course radiotherapy versus combined radiochemotherapy in locally advanced rectal cancer: a multi-centre prospectively randomised study of the Berlin Cancer Society. *BMC Cancer* 2009;9:50
- 20 Pilipshen SJ, Heilweil M, Quan SH, Sternberg SS, Enker WE. Patterns of pelvic recurrence following definitive resections of rectal cancer. *Cancer* 1984;53(06):1354–1362
- 21 Ogunbiyi OA, McKenna K, Birnbaum EH, Fleshman JW, Kodner IJ. Aggressive surgical management of recurrent rectal cancer—is it worthwhile? *Dis Colon Rectum* 1997;40(02):150–155
- 22 Sauer R, Liersch T, Merkel S, et al. Preoperative versus postoperative chemoradiotherapy for locally advanced rectal cancer: results of the German CAO/ARO/AIO-94 randomized phase III trial after a median follow-up of 11 years. *J Clin Oncol* 2012;30(16):1926–1933
- 23 Van Cutsem E, Dico M, Haustermans K, et al. The diagnosis and management of rectal cancer: expert discussion and recommendations derived from the 9th World Congress on Gastrointestinal Cancer, Barcelona, 2007. *Ann Oncol* 2008;19(Suppl 6):vi1–vi8
- 24 Denost Q, Kontovounisios C, Rasheed S, et al. Individualizing surgical treatment based on tumour response following neoadjuvant therapy in T4 primary rectal cancer. *Eur J Surg Oncol* 2017;43(01):92–99
- 25 Hashiguchi Y, Sekine T, Sakamoto H, et al. Intraoperative irradiation after surgery for locally recurrent rectal cancer. *Dis Colon Rectum* 1999;42(07):886–893, discussion 893–895
- 26 Kusters M, Valentini V, Calvo FA, et al. Results of European pooled analysis of IORT-containing multimodality treatment for locally advanced rectal cancer: adjuvant chemotherapy prevents local recurrence rather than distant metastases. *Ann Oncol* 2010;21(06):1279–1284
- 27 Dubois JB, Bussières E, Richaud P, et al. Intra-operative radiotherapy of rectal cancer: results of the French multi-institutional randomized study. *Radiother Oncol* 2011;98(03):298–303
- 28 van Stiphout RG, Lammering G, Buijsen J, et al. Development and external validation of a predictive model for pathological complete response of rectal cancer patients including sequential PET-CT imaging. *Radiother Oncol* 2011;98(01):126–133
- 29 Cammà C, Giunta M, Fiorica F, Pagliaro L, Craxi A, Cottone M. Preoperative radiotherapy for resectable rectal cancer: a meta-analysis. *JAMA* 2000;284(08):1008–1015
- 30 Genovesi D, Myerson RJ, Cêfaro GA, et al; G.I. A.I.R.O. Working Group. Postoperative 5-FU based radiochemotherapy in rectal cancer: retrospective long term results and prognostic factors of a

- pooled analysis on 1,338 patients. *Anticancer Res* 2013;33(10):4557–4566
- 31 Brunschwig A. Complete excision of pelvic viscera for advanced carcinoma; a one-stage abdominoperineal operation with end colostomy and bilateral ureteral implantation into the colon above the colostomy. *Cancer* 1948;1(02):177–183
 - 32 Dresen RC, Gosens MJ, Martijn H, et al. Radical resection after IORT-containing multimodality treatment is the most important determinant for outcome in patients treated for locally recurrent rectal cancer. *Ann Surg Oncol* 2008;15(07):1937–1947
 - 33 Bouchard P, Efron J. Management of recurrent rectal cancer. *Ann Surg Oncol* 2010;17(05):1343–1356
 - 34 Pawlik TM, Skibber JM, Rodriguez-Bigas MA. Pelvic exenteration for advanced pelvic malignancies. *Ann Surg Oncol* 2006;13(05):612–623
 - 35 Suzuki K, Dozois RR, Devine RM, et al. Curative reoperations for locally recurrent rectal cancer. *Dis Colon Rectum* 1996;39(07):730–736
 - 36 Yamada K, Ishizawa T, Niwa K, Chuman Y, Akiba S, Aikou T. Patterns of pelvic invasion are prognostic in the treatment of locally recurrent rectal cancer. *Br J Surg* 2001;88(07):988–993
 - 37 Mohiuddin M, Marks GM, Lingareddy V, Marks J. Curative surgical resection following reirradiation for recurrent rectal cancer. *Int J Radiat Oncol Biol Phys* 1997;39(03):643–649
 - 38 Wasserman K. Diagnosing cardiovascular and lung pathophysiology from exercise gas exchange. *Chest* 1997;112(04):1091–1101
 - 39 Belardinelli R, Lacalaprice F, Carle F, et al. Exercise-induced myocardial ischaemia detected by cardiopulmonary exercise testing. *Eur Heart J* 2003;24(14):1304–1313
 - 40 Abbas SM, Hill AG. Systematic review of the literature for the use of oesophageal Doppler monitor for fluid replacement in major abdominal surgery. *Anaesthesia* 2008;63(01):44–51
 - 41 Bhangu A, Ali SM, Brown G, Nicholls RJ, Tekkis P. Indications and outcome of pelvic exenteration for locally advanced primary and recurrent rectal cancer. *Ann Surg* 2014;259(02):315–322
 - 42 Schneider A, Köhler C, Erdemoglu E. Current developments for pelvic exenteration in gynecologic oncology. *Curr Opin Obstet Gynecol* 2009;21(01):4–9
 - 43 Austin KK, Solomon MJ. Pelvic exenteration with en bloc iliac vessel resection for lateral pelvic wall involvement. *Dis Colon Rectum* 2009;52(07):1223–1233
 - 44 Zoucas E, Frederiksen S, Lydrup ML, Månsson W, Gustafson P, Alberius P. Pelvic exenteration for advanced and recurrent malignancy. *World J Surg* 2010;34(09):2177–2184
 - 45 Ramirez PT, Modesitt SC, Morris M, et al. Functional outcomes and complications of continent urinary diversions in patients with gynecologic malignancies. *Gynecol Oncol* 2002;85(02):285–291
 - 46 Buchel EW, Finical S, Johnson C. Pelvic reconstruction using vertical rectus abdominis musculocutaneous flaps. *Ann Plast Surg* 2004;52(01):22–26
 - 47 Kakuda JT, Lamont JP, Chu DZ, Paz IB. The role of pelvic exenteration in the management of recurrent rectal cancer. *Am J Surg* 2003;186(06):660–664
 - 48 Saito N, Koda K, Takiguchi N, et al. Curative surgery for local pelvic recurrence of rectal cancer. *Dig Surg* 2003;20(03):192–199, discussion 200
 - 49 Nishio M, Sakakura C, Nagata T, et al. Outcomes of total pelvic exenteration for colorectal cancer. *Hepatogastroenterology* 2009;56(96):1637–1641
 - 50 Wells BJ, Stotland P, Ko MA, et al. Results of an aggressive approach to resection of locally recurrent rectal cancer. *Ann Surg Oncol* 2007;14(02):390–395
 - 51 Boyle KM, Sagar PM, Chalmers AG, Sebag-Montefiore D, Cairns A, Eardley I. Surgery for locally recurrent rectal cancer. *Dis Colon Rectum* 2005;48(05):929–937
 - 52 Wanebo HJ, Antoniuk P, Koness RJ, et al. Pelvic resection of recurrent rectal cancer: technical considerations and outcomes. *Dis Colon Rectum* 1999;42(11):1438–1448
 - 53 Ferenschild FT, Vermaas M, Verhoef C, et al. Total pelvic exenteration for primary and recurrent malignancies. *World J Surg* 2009;33(07):1502–1508
 - 54 Houvenaeghel G, Moutardier V, Karsenty G, et al. Major complications of urinary diversion after pelvic exenteration for gynecologic malignancies: a 23-year mono-institutional experience in 124 patients. *Gynecol Oncol* 2004;92(02):680–683
 - 55 Jimenez RE, Shoup M, Cohen AM, Paty PB, Guillem J, Wong WD. Contemporary outcomes of total pelvic exenteration in the treatment of colorectal cancer. *Dis Colon Rectum* 2003;46(12):1619–1625
 - 56 Grossmann I, de Bock GH, Meershoek-Klein Kranenbarg WM, van de Velde CJ, Wiggers T. Carcinoembryonic antigen (CEA) measurement during follow-up for rectal carcinoma is useful even if normal levels exist before surgery. A retrospective study of CEA values in the TME trial. *Eur J Surg Oncol* 2007;33(02):183–187
 - 57 Young JM, Badgery-Parker T, Masya LM, et al. Quality of life and other patient-reported outcomes following exenteration for pelvic malignancy. *Br J Surg* 2014;101(03):277–287
 - 58 Yang TX, Morris DL, Chua TC. Pelvic exenteration for rectal cancer: a systematic review. *Dis Colon Rectum* 2013;56(04):519–531
 - 59 Thaysen HV, Jess P, Laurberg S. Health-related quality of life after surgery for primary advanced rectal cancer and recurrent rectal cancer: a review. *Colorectal Dis* 2012;14(07):797–803
 - 60 You YN, Habiba H, Chang GJ, Rodriguez-bigas MA, Skibber JM. Prognostic value of quality of life and pain in patients with locally recurrent rectal cancer. *Ann Surg Oncol* 2011;18(04):989–996