



# Surgical treatment of locally recurrent rectal cancer: a narrative review

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**Objective:** To summarize the recent literature on surgical treatment of locally recurrent rectal cancer (LRRC).

**Background:** LRRC is a heterogeneous disease that requires a multidisciplinary treatment approach. The treatment and prognosis depend on the site and type of recurrence. Radical resection remains the primary method for achieving long-term survival and improving symptom control. Preoperative chemoradiotherapy can reduce tumor volume and improve the R0 resection rate. Surgeons must clearly understand pelvic anatomy, develop a detailed preoperative plan, adopt a multidisciplinary approach for the surgical resection of the tumor as well as any invaded soft tissues, vessels, and bones, and ensure proper reconstruction. However, extended radical surgery often leads to a higher risk of postoperative complications and a low quality of life.

**Methods:** We searched English-language articles with keywords “locally recurrent rectal cancer”, “surgery” and “multidisciplinary team” in PubMed published between January 2000 to October 2020.

**Conclusions:** LRRC is a complex problem. Long-term survival is not impossible following multidisciplinary treatment in appropriately selected LRRC patients. The management of LRRC relies on a specialist team that determines the biological behavior of the tumor and evaluates treatment options through multidisciplinary discussions, thereby balancing the surgical costs and benefits, alleviating postoperative complications, and improving patients’ quality of life.

**Keywords:** Locally recurrent rectal cancer (LRRC); surgery; multidisciplinary team (MDT)

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## Introduction

The treatment outcomes for patients with locally recurrent rectal cancer (LRRC) have improved significantly in the past 3 decades. With the introduction

of total mesorectal excision (TME), the application of neoadjuvant chemoradiotherapy, and the development of multidisciplinary treatment approaches, the incidence of local recurrence has decreased from 10–30% to 4–10% (1,2), a figure significantly lower than that of distant metastases

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(3-5). LRRC often presents with severe local symptoms, negatively affects patients' quality of life, and shortens patients' lifespan (6).

The complete resection of a recurrent tumor is a crucial factor for improving the quality of life and overall survival of rectal cancer patients with presacral recurrence. However, recurrent tumors often extend beyond the "sacral plane." The invasion of recurrent tumors in adjacent tissues, changes in the anatomical level, and fibrosis induced by radiotherapy substantially increase the difficulty of surgery. These complications often necessitate pelvic exenteration, which destroys the anatomical structures of the pelvic cavity and pelvic wall. Given that the patient population is difficult to manage, patients with LRRC require individualized multidisciplinary management to ensure the best outcome is achieved. At present, a comprehensive treatment approach, which includes surgery, is the best option for salvage treatment, and possibly even a cure.

We present the following article in accordance with the Narrative Review reporting checklist (available at <http://dx.doi.org/10.21037/atm-21-2298>).

## Methods

We searched English-language articles with keywords "locally recurrent rectal cancer", "surgery" and "multidisciplinary team" in PubMed published between January 2000 to October 2020.

## Timing and risk factors of local recurrence

Local recurrence of rectal cancer mostly occurs within 2 years of the initial surgery, and while more than 80% of cases are diagnosed within 5 years, some occur after 10 years (5,7,8). In the era of neoadjuvant chemoradiotherapy, a trend of delayed local recurrence has emerged (9,10). Early recurrence is defined as local recurrence within 12 months of the primary surgery for rectal cancer, and late recurrence is defined as local recurrence in  $\geq 12$  months after the primary surgery (10). From the time at which local recurrence is diagnosed, there is no difference in survival between patients with early local recurrence and those with late recurrence; thus, all patients with a local recurrence should be evaluated for curative surgery regardless of the timing of the local recurrence (11).

Risk factors for local recurrence can be divided into the following 2 categories: (I) risk factors related to the biological behaviors of tumors; and (II) factors related to

the surgical margins. Biological behaviors include more advanced tumor (T) and node (N) stages, poor tumor differentiation, vascular infiltration, lateral lymph node metastasis, extramural vascular invasion, perforation, and anastomotic fistula (12). Multiple studies have confirmed that a positive circumferential resection margin is a strong predictor of local recurrence (13,14). Surgery-related factors, such as the surgical approach, the surgical technique, and the surgeon's proficiency, can affect the surgical margin and lead to an increased risk of recurrence (15).

With the implementation of high-quality TME, there has been a gradual shift from central recurrence (in the anastomosis site and perineum) to non-central recurrence; an increased proportion of recurrences have been found to be occurring in the presacral area and the lateral pelvic wall (16-18). The presacral plane is the most easily dissected plane during surgery and is almost always included in radiotherapy. Positive margins can lead to the spillage of tumor cells, which gravitate into the presacral space and develop into local recurrence in the presacral area (19). The metastasis rate of middle and low rectal cancer to the lateral lymph nodes is approximately 7-24% (20). Failing to surgically remove metastatic lateral lymph nodes can lead to lateral recurrence. Using three-dimensional reconstruction and histological sections, anatomical studies have shown that there is an alternative lymphatic drainage pathway from the rectal mesenteric lymphatic system to the lateral lymphatic system (21). During rectal resection, lymph and tumor cells can gain access to the lateral lymph node system. As lateral lymphatic tissue is not removed during standard TME and is partially damaged during lateral ligament dissection, lateral lymph leakage, and tumor implantation in the presacral space can occur after surgery (19). In a multicenter retrospective study of lateral lymph nodes with a short-axis diameter of  $>7$  mm, the lateral recurrence rate remained as high as 19.5%, even with neoadjuvant therapy and TME (22). Neoadjuvant chemoradiotherapy combined with TME and lateral lymph node dissection achieved reasonable local control.

## Preoperative assessment

Preoperative assessment is crucial for treating LRRC. As it is impossible to enter the normal anatomical level during the second operation, individualized surgical plans can only be formulated according to the patient's imaging examination. The preoperative assessment of LRRC

includes tumor markers, including chest, abdominal, and pelvic computed tomography (CT) to rule out distant metastasis, and pelvic magnetic resonance imaging (MRI) to clarify the status of local lesions, which can reveal vascular and sciatic nerve invasion and help differentiate between a tumor and post-radiotherapy fibrosis. High-quality pelvic MRI is critical for accurate local staging to determine local resectability (23). In addition, colonoscopy is used to exclude metachronous colorectal tumors. Pathologic diagnosis can be obtained using colonoscopy or CT-guided puncture. It is recommended that genetic testing and microsatellite instability testing supplement puncture pathology. If the pathological biopsy result is negative, the test should be repeated. If the CT or MRI diagnosis of local recurrence is uncertain, a positron emission tomography (PET)-CT can be performed to assist in the diagnosis of tumor recurrence, as the sensitivity, specificity, and accuracy of PET-CT are all above 90% (24). However, attention should be paid to false-negative and false-positive PET-CT diagnoses, such as false-negative diagnoses of mucinous adenocarcinoma due to low tumor cell density and the suppression of tumor tissue metabolism after chemoradiotherapy, and false-positive diagnoses due to sepsis, an anastomotic leak, a postoperative inflammatory response, radiotherapy, and physiological fluorodeoxyglucose uptake. PET-MRI combines the advantages of both PET-CT and pelvic MRI; thus, it has diagnostic value in the local staging of LRRC. Preliminary studies have shown that PET-MRI has a sensitivity, specificity, positive predictive value, and negative predictive value of 94%, 94%, 97%, and 90%, respectively, for the diagnosis of rectal cancer recurrence (25). When there is clinical evidence of tumor recurrence, such as an enlarged mass on imaging and an elevated carcinoembryonic antigen level, but the pathological diagnosis cannot be confirmed, the case should be submitted for multidisciplinary discussion (26).

Currently, several classification systems, mainly based on the anatomical separation of the pelvis, have been used to describe LRRC to aid in the surgical decision-making process and surgical approach (see *Table 1* for details on these classification systems). Unfortunately, there is no universally accepted classification system, and the use of classification systems varies from person to person. In fact, most staging systems are based on patients diagnosed with recurrence before the routine use of TME, neoadjuvant radiotherapy, and chemotherapy, which differs from the current treatment setting for rectal cancer. A unified classification system for recurrence will facilitate

academic exchange and data integration, thus enabling the standardization of treatment regimens and assisting in the comparison of treatment outcomes.

### **Multidisciplinary management**

The complete resection of recurrent lesions is essential for improving local control and long-term survival. However, extensive surgery is accompanied by substantial complication and mortality rates, rendering this approach suitable only for certain patients. Radiotherapy, either alone or as part of concurrent radiotherapy and chemotherapy, can improve symptoms in most patients; however, it is not curative and may have considerable side effects (33).

The treatment of rectal cancer has developed into a multidisciplinary team (MDT) approach, whereby MDT discuss tumor diagnosis and staging to create optimal treatment strategies (2). This approach brings together the strengths of the disciplines related to colorectal cancer, including imaging, radiology, surgery, and oncology. Opinions from various experts significantly improve surgical quality, reduce local recurrence, improve overall survival, and promote the standardized treatment of tumors (34). The treatment of LRRC requires a MDT approach, which is beneficial for improving the R0 resection rate and the survival of patients with LRRC (35).

It is very important to establish an exenteration-specific multidisciplinary team (esMDT) for LRRC because the surgery often involves the surrounding organs. The performance of complex multi-organ resection on a regular basis can reduce the operation time and postoperative complication rate. In addition to urologists, gynecologists, orthopedic surgeons, vascular surgeons, and plastic surgeons, colorectal surgeons with experience in pelvic exenteration are responsible for preoperative and intraoperative decision making (36). As a multi-organ excision has a significant effect on physical appearance, physical function, and mental health, the esMDT also requires the participation of psychotherapists and specialist cancer care nurses.

### ***Multi-organ excision***

Fifty percent of patients with LRRC have isolated local recurrence without distant metastases (37). Surgical resection can benefit the long-term survival of this patient group, which has a 10-year disease-free survival rate of 38% (38). However, therapeutic surgery can only be

**Table 1** Classification systems in use for LRRC

Study Group	Country	Time	Number of patients	Definitions
Mayo Clinic (27)	USA	1995	224	F0: no fixation F1: fixation to 1 point F2: fixation to 2 points F3: fixation to more than 2 points
Yamada (28)	Japan	2001	60	Localized: invasion to the adjacent pelvic organs or tissue Sacral invasive: invasion to lower sacrum (S3, S4, S5), coccyx, periosteum Lateral invasive: invasion to sciatic nerve, greater sciatic foramen, lateral pelvic wall, upper sacrum (S1, S2)
Memorial Sloan Kettering Cancer Center (29)	USA	2003	55	Axial: anastomotic, mesorectal, perirectal soft tissue, perineum Anterior: genitourinary tract Posterior: sacrum and presacral fascia Lateral: soft tissues of the pelvic side wall and the lateral bony pelvis
Leeds (30)	UK	2005	64	Central: pelvic organs or connective tissue without contact with or invasion into bone Sacral: presacral space and abuts onto or invades into the sacrum Side wall: 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
Park (31)	Korea	2009	62	Central: anastomotic or perirectal soft tissue without fixed intrapelvic organ involvement Anterior: bladder, prostate, seminal vesicles, and vagina Posterior: presacral area and/or involved sacral bone invasion Lateral: iliac vessels, pelvic ureter, lateral pelvic lymph node, and/or internal iliac lymph nodes Perineal: perineal skin
Belli (32)	Italy	2020	280	S1: central/anterior (I) Totally inside rectal wall (II) Pararectal without infiltration of regional organs (III) Pararectal with infiltration of regional organs (vagina, uterus, bladder, ureter) S2: posterior (I) Pararectal with sacral infiltration below the second sacral vertebra (II) Pararectal with sacral infiltration of the first or second sacral vertebra S3: lateral (I) Pararectal with infiltration of lateral pelvic compartment

LRRC, locally recurrent rectal cancer.

performed in approximately 40% of patients with local recurrence (39). Due to the bony border of the pelvis, initial surgery, and radiotherapy, it is extremely difficult to distinguish the tumor boundary, and challenging to achieve a negative margin. There is a more than 2-fold increase in survival after pelvic resection for both R0 over R1 and R1 over R2 resection (40). To achieve R0 resection, surgeons need to perform a combined pelvic exenteration.

Extensive surgery compromises function. However, patients with unresected advanced pelvic malignancies may also experience severe pain as a result of bone, muscle, or nerve invasion. Due to an improved understanding of pelvic anatomy and the increasing precision of preoperative image evaluation, surgeons have gradually gained experience, enhanced their skills, and developed increasingly radical resection techniques (41,42), thereby expanding from central pelvic resection to lateral pelvic wall resection, high sacral resection, and pubic resection that includes muscle, nerve, vascular, and bony structures. Relative and absolute contraindications to pelvic exenteration are now defined by the ability to safely reach the R0 margin, rather than by historical anatomic or surgical technical limitations (43).

Presacral recurrence is a common type of local recurrence in rectal cancer, has an incidence of approximately 15–30% (7,16,17), and can only be cured by sacral resection. For patients in whom R0 resection is achieved, the 5-year survival rate can reach up to 35–46% (17,44). Without surgical resection, the median survival time for most patients is approximately 7 months (45). In cases of recurrent tumor invasion of the distal sacrum (S3 level or below), combined sacral resection has become a recognized practice for treating LRRC (26,46). However, invasion of the high sacrum increases the surgical difficulty, and high sacral resection and S1–3 sacral nerve resection can lead to neurological dysfunction of the bladder and bowel (47,48). Sacral involvement at or above the S2 level was previously considered a contraindication to surgical resection; however, it is now changing (44). High and low sacral resections have similar survival benefits, and the level of sacral resection does not affect the ability to achieve R0 resection (49,50). Bhangu *et al.* (51) found that combined abdominal-sacral resection improved overall survival, but that S1–2 resection was associated with a higher complication rate than S3 and S4–5 resections, which have complication rates of 60%, 27%, and 29%, respectively. To reduce postoperative complications, surgeons are beginning to explore limited osteotomies, such as the high cortical osteotomy (52) and unilateral sacral segmental resection (53). However, these

methods are only exploratory procedures; thus, surgical indications should be strictly adhered to, and individualized surgery should only be applied to patients with limited local sacral involvement and recurrence.

The surgical resection of the lateral pelvic invasion is difficult. The proximity to the pelvic bone and major neurovascular structures means that achieving a complete resection and negative margin is technically challenging. Thus, the lateral recurrence type has a poor prognosis (18). Austin *et al.* (54) reported a new approach for the *en-bloc* resection of pelvic sidewall structures, including the internal iliac vessels, piriformis and obturator internus muscles, ischium, sacrotuberous and sacrospinous ligaments. Long-term follow-up results of lateral pelvic wall resections showed that 62 of 100 patients who underwent surgery for LRRC achieved R0 resection, and had a median overall and disease-free survival time of 41 and 27 months, respectively, and 1-, 3-, and 5-year survival rates of 86%, 46%, and 35%, respectively. However, the morbidity of extensive lateral resection is very high, and 82% of patients experience postoperative complications, of which sepsis, which occurs in approximately 50% of cases, is the most common (55). More than 50% of patients who underwent combined iliac vessel resection reported vascular-related complications, of which 24% required reoperation (56).

Advanced pelvic tumors involving the sciatic or femoral nerve have traditionally been considered inoperable, primarily due to the low rate of R0 resection and concerns about impaired function and quality of life following nerve resection (26). However, Brown *et al.* (56) found that total sciatic and femoral nerve resection could be performed to treat extended pelvic exenteration, and that 65% of patients achieved R0 resection, had a 5-year survival rate of 55%, a complication rate of 63%, and returned to preoperative overall quality of life levels 1 year after surgery. As surgeons have a limited ability to perform lateral R0 resection because of the limitations imposed by the pelvic bone, patients with lateral recurrence have a poorer prognosis than those with recurrences at other sites. A more thorough total resection of the iliac vessels may improve outcomes of future lateral recurrences.

Combined urogenital resection is the only option for recurrent tumors that invade the urogenital organs anteriorly. Complete or partial resection of the pubic bone is required to treat tumor invasion of the pubic bone. Austin *et al.* (57) confirmed the feasibility of radical pubic bone excision in the context of extended pelvic exenteration in a study with 29 patients (11 of whom had LRRC) with pelvic

tumors. Of these patients, 62% underwent partial pubic bone excision, and 38% complete pubic bone excision. 76% achieved R0 resection, and there was an overall 5-year survival rate of 53%. The median operating time was 10.5 hours, the median blood loss was 2,971 mL, and the postoperative complication rate was 70%. Thus, radical pubic bone excision during resection may result in a high morbidity rate; however, it is a potential treatment option for patients with recurrent tumor invasion of the pubic bone.

Extended pelvic resections, such as total pelvic exenterations and sacral resections, result in a hollow pelvic cavity, leaving patients vulnerable to complications, such as pelvic abscess, fistula formation, bowel obstruction, and poor perineal wound healing. This is known as “empty pelvis syndrome” (58). Preoperative radiotherapy also increases the risk of poor perineal wound healing (59). The use of tissue with a vascular pedicle to eliminate dead space and close the perineal wound is currently considered a reasonable method for addressing this complication (60). Common musculocutaneous flaps used to close pelvic and perineal defects include the vertical rectus abdominis musculocutaneous flap and gluteal musculocutaneous flap (61). It is important to note that blood supply to the gluteus musculocutaneous flap may be affected because the internal iliac vessels are ligated during pelvic surgery, resulting in a partial disruption of blood flow. The use of artificial patches to close the pelvic inlet has also been reported, which can reduce pelvic effusion and perineal wound complications (59).

### **Perioperative treatment**

LRRC is characterized by invasive growth, venous infiltration, and the presence of isolated cancer cells (i.e., cancer cells that are isolated and located at least 1 mm beyond the tumor margin) (62). To improve tumor control, preoperative therapy may be introduced to better manage peri-tumoral cancer cells. However, as most patients with rectal cancer have previously undergone pelvic radiotherapy, radiation oncologists are often concerned that reirradiation may cause serious late adverse effects on normal tissues. However, a growing body of evidence from clinical studies suggests that reirradiation is safe and tolerable (63,64). Indeed, studies have indicated that irradiation of 30–45 Gy in patients with a history of radiotherapy is both safe and effective, provided that the interval between the 2 treatments is longer than 6 months, the irradiation is

delivered in a hyperfractionated regimen, and the delivery is combined with capecitabine administration (65,66). A retrospective study by Ogawa *et al.* (67) showed that when combined with preoperative chemoradiotherapy, the effectiveness of surgery increased. Specifically, the study showed a 5-year recurrence-free survival rate of 24.4% versus 0%, and a 5-year overall survival rate of 46.6% versus 29.3%. For patients who did not receive preoperative chemoradiotherapy, the R0 resection rate was 26%, while for patients who either received preoperative reirradiation (with chemotherapy) or full-course radiotherapy (with chemotherapy), the R0 resection rates were 43% and 50%, respectively (68).

In addition to the R0 resection rate, the pathological complete response (pCR) rate also indicates prognosis. The pCR rate in patients who received neoadjuvant chemoradiotherapy has been reported to be approximately 8.5–13% (65,66,69,70). Voogt *et al.* (71) reported that for patients who received induction chemotherapy combined with neoadjuvant radiotherapy and chemotherapy, the pCR rate was 17%, the 3-year survival rate was 92%, and the R0 resection rate was 63%. However, more than half of the complete responders relapsed within 3 years. Several other studies have also supported the application of preoperative chemoradiotherapy (for further details of these studies, see *Table 2*). It should be noted that preoperative radiotherapy and chemotherapy can increase complication rates (73). A study reported that patients with resectable LRRC who underwent surgery alone and patients who underwent surgery and received preoperative chemoradiotherapy developed postoperative complications of Clavien-Dindo grade >III at rates of 26.4% (29/153) and 62.2% (33/53), respectively (74). In addition, the incidences of incisional infection, bowel obstruction, pelvic abscess, and bleeding were consistently higher in patients who underwent surgery and also received preoperative radiotherapy and chemotherapy (74). Preoperative chemoradiotherapy may increase the postoperative complication rate; however, it remains the most effective method for improving R0 resection rates.

By achieving high accuracy through irradiation of the tumor and tumor bed during surgery, intraoperative radiotherapy (IORT) maximizes the dose to the tumor while sparing normal tissue. As a part of the MDT approach, IORT allows for increased local control. A systematic review showed that despite the significant heterogeneity of IORT studies, the technique could improve the 5-year local control, disease-free survival, and overall survival rates in

Table 2 Published report as to the efficacy of preCRT

Study	Country	Study design/study period	No. of patients		Outcome	Complication
			preCRT	None-preCRT		
Voogt (71)	Netherlands	Retrospective/2010–2018	132	NA	pCR 17% R0 63% 3-y OS 68% 3-y LRFS 72%	Major postoperative complications (Clavien-Dindo Grades III + IV + V) 31%
Ogawa (67)	Japan	Retrospective/2000–2014	25 <sup>a</sup>	16 <sup>a</sup>	R0 93% vs. 94% 5-y OS 46.6% vs. 29.3% (P=0.12) 5-y LRFS 24.4% vs. 0% (P=0.02)	Major complications (Clavien-Dindo Grades III + IV), 28% vs. 43.8% (P=0.33)
Sorrentino (72)	Italy	Retrospective/2009–2017	49	103	R0 51% vs. 47.6% (P=0.691) 5-y DFS 60.4% vs. 33.6% (P=0.089) 5-y OS 84.6% vs. 71.1% (P=0.196)	Postoperative complications rates, 36.7% vs. 30.1% (P=0.413)
Bosman (63)	Netherlands	Retrospective/1994–2013	113 <sup>b</sup> /135 <sup>c</sup>	24	R0 62.8%/55.6% vs. 42% 5-y OS 39.1%/34.1% vs. 23% (R0 + R1 + R2) (P=0.164) 5-y LRFS 59.7%/45.9% vs. 35% (P=0.003)	Major complications (Clavien-Dindo Grades III + IV + V), 39.7% vs. 34.8%
PelVEx Collaborative (73)	International	Retrospective/2004–2014	614	516	R0 59.9% vs. 56.4% 5-y OS 25.6% vs. 16.4% (R0 + R1 + R2) (P=0.008)	Major complication (Clavien-Dindo Grades III + IV) within 30 days, 61.3% vs. 38.7% (P<0.001)

<sup>a</sup>, patients with posterior invasive LRRC; <sup>b</sup>, the full-course group did not receive radiotherapy for the primary tumor, but received a full scheme of radiotherapy for recurrence; <sup>c</sup>, the reirradiation group received radiotherapy for the primary tumor and also for local recurrence. LRRC, locally recurrent rectal cancer; preCRT, preoperative chemoradiotherapy; pCR, pathological complete response; LRFS, local relapse-free survival; OS, overall survival; NA, not available.

patients with colorectal cancer (75,76). IORT is an adjuvant therapy rather than an alternative to aggressive surgical resection and is not considered a viable strategy after R2 resection.

Systemic therapy can be used both as a preoperative “test” of tumor biology and as an option for eliminating micrometastatic disease after surgery. Adjuvant treatment after pelvic resection varies among treatment centers (77,78), and the high incidence of complications after total pelvic exenteration often results in interruptions or delays of the planned adjuvant chemotherapy. Multicenter data have shown that most patients who relapsed after resection usually developed the metastatic disease (30–42%), but only 14–20% developed isolated local recurrence (17,79). Despite this pattern of recurrence, research has shown that adjuvant chemotherapy does not improve the 5-year disease-free survival rate (79). This finding also reveals existing challenges in the treatment of LRRC.

## Problem-solving approach

### *Patient selection*

Recurrence after multimodal treatment and TME usually requires extended resection and may be more biologically invasive than those after nonstandard treatment. Patients with local recurrence after failed TME are more likely to undergo salvage surgery than those with local recurrence after standard TME (80). In most cases, the failure of LRRC surgery is due to metastatic disease. The lung is the most common site of metastasis; however, some patients may develop an isolated second local recurrence (81). The introduction of systemic therapy to screen patients who have more promising tumor biology could help to identify candidates for aggressive surgical resection.

Surgical resection with a therapeutic intent is the most relevant prognostic factor for LRRC. Despite their importance in prognosis, the traditional preoperative evaluations undertaken by surgeons cannot be used to accurately identify patients suitable for radical surgery. A systematic review indicated that the overall percentage of positive margins after pelvic resection for LRRC was 34.4% (40). This means that nearly one-third of patients bear the risk of surgical complications and do not benefit from the surgery. Thus, more accurate and individualized strategies are needed for the preoperative evaluation and treatment of LRRC.

### *Specialized management*

Complex major surgeries often induce serious complications. Pelvic exenteration presents a complication rate of 37–100% and a mortality rate of up to 24% (82,83); however, recent reports from specialist centers have shown improved postoperative complication rates of 30–70% and postoperative mortality rates of 0–3.5% (77,84). Due to the small number of patients eligible for surgery, it is exceptionally difficult for surgeons to gain surgical experience, and surgeons often need to complete dedicated training at specialist centers (85). A skilled colorectal surgeon needs at least 14 cases to accumulate sufficient experience to stabilize the incidence rate at an acceptable level (86). The adoption of a specialist approach has been effective in significantly boosting the R0 resection rate, maximizing surgical benefits, and minimizing trauma (18,87). Adequate preoperative cardiopulmonary assessment and exercise programs can improve patients’ surgical tolerance. Effective anesthesia management is beneficial in early postoperative rehabilitation. Specialist centers with centralized surgical management pathways, preoperative imaging assessment teams, and critical care teams are key to improving patient outcomes. Super-radical surgeries are now being commonly performed in some centers with the necessary capabilities, and these centers are achieving high R0 resection rates and low complication rates (42,44,84,88,89). The “growth” of specialist centers requires the mobilization of multidisciplinary resources, the accumulation of experience, and the exploration of different surgical approaches, which in turn can transform occasional involvement into sustained pathfinding.

### *Balancing the costs and benefits of surgery*

Selecting patients for LRRC resection remains a complex and highly individualized process. Patients are often carefully selected; however, such patient selection may have created the “false impression” that the treatment is always effective. It cannot be denied that super-radical surgery provides a chance of long-term survival to an increasing number of patients with local recurrence. The goal of surgical techniques should be to achieve optimal tumor control without compromising the patient’s function and quality of life. However, achieving a negative margin usually requires extended resection at the cost of musculoskeletal vascular nerve tissues and genitourinary



and gynecologic organs; thus, the surgery consequently results in an increased complication rate and has adverse effects on the patient's quality of life, as manifested by lower quality of life scores and the development of chronic pain symptoms (90). Low preoperative quality of life, being female, total pelvic exenteration, and positive margins were found to be associated with a poor postoperative quality of life. Patients' postoperative quality of life usually returns to the baseline level within 1 year of surgery (91,92). However, a high postoperative complication rate does not mean a high postoperative mortality rate. Indeed, research has shown that the 30-day mortality rate was significantly reduced (83,84). It should be noted that as surgical resection is the only treatment option for "palliative patients," the psychological benefits of surgery should not be neglected (93). Thus, surgeons should have frank discussions with their patients about the extent of surgical resection and the expected functional and tumor prognosis.

#### ***Combined treatment improves resection rates***

Due to its limited efficacy, surgery must be combined with other modalities to improve its scope. For example, preoperative radiotherapy and chemotherapy can convert unresectable tumors to resectable tumors, while postoperative adjuvant radiotherapy and chemotherapy can control local residual lesions or microscopic metastases and reduce the risk of distant metastases. Alternatively, immunotherapy has achieved good results in treating advanced colorectal cancer (94). For patients with LRRC, the application of immune-targeted therapy or immunotherapy combined with chemotherapy and radiotherapy can serve as an alternative to surgery.

#### **Conclusions**

LRRC is a potentially curable disease with substantial heterogeneity. Its treatment relies on an MDT approach rather than an individualized surgical approach. Patient screening and selection through a MDT approach and exenteration-specific surgical treatment at specialist centers are critical if treatment outcomes are to be improved in the future. The benefits of extended surgeries should be carefully balanced against their associated risks based on the biological behavior of the tumor, symptom control, and quality of life.

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