Transanal Endoscopic Surgery for Rectal Cancer: Indications, Staging, and Perioperative Considerations

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Introduction and Rationale

The primary goal in the treatment of rectal cancer is curative therapy, best obtained through multidisciplinary care and the stage-appropriate use of three complementary modalities: total mesorectal excision surgery (TME), radiation therapy, and chemotherapy. Through en bloc resection of the rectal tumor and mesorectal lymph nodes, TME affords the highest chance of cure. However, TME is also associated with significant morbidity including a weeklong hospital stay, prolonged postoperative convalescence, risks of infections, and urinary, sexual, and defecatory dysfunction. TME is also accompanied by a temporary and occasionally permanent ostomy. Morbidity following TME in recent randomized trials ranges from 37 to 58%, and 30-day mortality is around 1% [1, 2].

It is from these concerns that surgeons have sought to identify patients that could be candidates for rectal sparing transanal local excision. Preservation of the rectum can avoid the significant morbidity and mortality of radical surgery and better maintain defecatory function. Unfortunately there is no single modality, histologic feature, radiographic study, and size and location of tumor that can predict with consistent accuracy whether the tumor extends beyond the rectal or has spread to regional lymph nodes.

In an ideal world, if we could accurately predict that there was no tumor in the lymph nodes and that complete local excision could be achieved, then local excision surgery would be curative. Conventional transanal excision (TAE) relies upon self-retaining and handheld retractors, stay sutures used to prolapse the rectal tissue into view, and extracorporeal lighting and viewing. In theory, transanal excision sounds straightforward; however, in practice, the surgeon faces significant challenges such

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as limited reach and retraction, poor lighting, and suboptimal exposure. Because of these physical limitations, TAE has been limited to benign lesions and malignant lesions less than 4 cm in maximum diameter and within 8 cm of the anal verge. Lesions exceeding these criteria were felt to require radical surgery.

Indications and Contraindications

The most common indication for transanal endoscopic surgery (TES) is for submucosal and full-thickness resection of benign lesions not otherwise resectable using standard colonoscopy. For more details, please refer to the Chap. 38 on TES for benign rectal lesions. With respect to rectal cancer, TES does not remove the at-risk mesorectal lymph nodes and, therefore, should be limited to selected early cancers with no evidence of local regional disease on imaging and have a low risk of occult lymph node metastasis. TES for rectal cancer might also be appropriate for more advanced tumors in patients who are unfit or unwilling to undergo radical surgery. The primary mode of determining increased risk of nodal metastasis remains in the domain of standard histologic evaluation. Unfortunately, this remains an imprecise science. No single histologic characteristic can predict lymph node metastasis in isolation; however, histologic factors that are associated with an increased chance of lymph node metastasis and local recurrence include T1SM3 and T2 depth of invasion, grade 3 histology, lymphovascular invasion, and positive margin status [3]. There are also not any currently available genetic, molecular, or immunologic markers that have increased diagnostic accuracy.

Principles and Quality Benchmarks

For malignant rectal lesions, the goal of transanal excision is complete en bloc resection without fragmentation of the specimen and negative margins. For rectal cancer, a 10 mm margin should be marked out prior to beginning dissection to ensure a negative margin. Submucosal dissection is not recommended for lesions harboring a known focus of invasive carcinoma.

Histologic Factors for Predicting Risk of Lymph Node Metastasis

Following full-thickness excisional biopsy via TES, histology slides should be reviewed, ideally at a multidisciplinary tumor board, to assess depth of invasion, margin status, and tumor histology. Patients that are identified as having adverse histologic features or have positive or indeterminate margins are at higher risk for local recurrence and should be treated with TME to ensure adequate staging and treatment (Table 39.1). There is also an additive relationship between increased number of adverse risk factors and incidence of lymph node metastasis [4, 5]. Figure 39.1 illustrates the odds ratios for the individual histologic risk factors [6].

Table 39.1 Local recurrence rates (percentage) at 36 months following TEM excision of rectal cancer

		Maximum tumor diameter (cm)					
Depth of invasion	Lymphatic invasion	≤1	1.1–2	2.1–3	3.1–4	4.1–5	≥5.1
pT1 SM1	No	3.0	3.6	4.4	5.4	6.6	8.1
	Yes	5.2	6.4	7.7	9.4	11.4	13.7
pT1 SM2–3	No	10.5	12.7	15.3	18.5	22.1	26.4
	Yes	17.8	21.4	25.5	30.3	35.7	41.8
pT2	No	9.8	11.9	14.3	17.3	20.7	24.7
	Yes	16.7	20.0	23.9	28.5	33.7	39.5
pT3	No	19.7	23.6	28.0	33.2	39.0	45.4
	Yes	32.2	37.9	44.1	51.0	58.3	65.7

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pT pathological tumor stage, *SM1 and SM2–3* Kikuchi submucosal stage

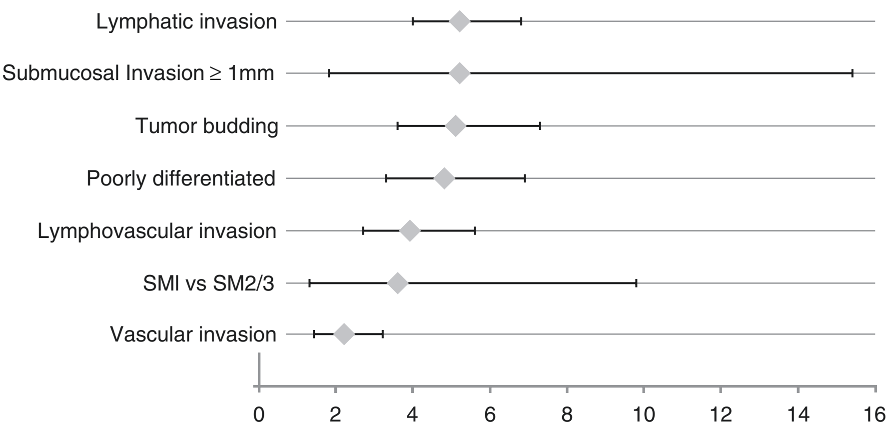

Fig. 39.1 Relative risk (95% confidence intervals) of lymph node metastasis in pT1 rectal cancers. SM1, invasion into superficial third of submucosa. SM2/SM3, invasion into middle and deep third of the submucosa. (Used with permission of Georg Thieme Verlag KG from Bosch et al. [6])

Depth of Invasion

When considering adverse histologic features for early rectal cancer, depth of tumor invasion is the most familiar and commonly referenced factor. T1 cancers are associated with a 10–15% incidence of occult lymph node metastases, and T2 cancers are associated with a 20–28% risk of lymph node metastasis [7–10]. Kikuchi and coauthors demonstrated the importance of depth of invasion within subclasses of submucosa invasion on the node metastasis and local recurrence in T1 cancers. By dividing submucosal invasion in the upper, middle, and lower thirds of the submucosa (SM1, SM2, SM3), an incremental increase in the risk of nodal metastases with a deeper depth of invasion is observed. SM3 level of invasion conferred a similar risk of nodal metastases as did a T2 cancer [11, 12]. Ding and coauthors described a similar phenomenon for T2 cancers whereby risk of lymph node metastasis increases with deeper penetration of the tumor into the muscularis propria [13].

Colonoscopic polypectomy specimens are usually partial thickness, so without the complete submucosal layer to visualize, the Kikuchi submucosal level of invasion cannot be determined. Under these circumstances, another predictive measurement system for depth submucosal invasion is needed. A Japanese collaborative study led by Kitajima reported that sessile polyps with depth of invasion <1 mm, as measured from the muscularis propria, and pedunculated polyps with <3 mm submucosal invasion into the polyp neck predicted for a very low risk of lymph node metastasis [14, 15].

Tumor Budding

There is increased recognition that tumor budding, defined as small nests of five or more cancer cells along the invasive front of the tumor, is a strong predictor of lymph node metastasis in colon and rectal cancer. Tumor budding is present in 16–25% of T1 cancers [16–18] and has an odds ratio of 5.1–5.8 at predicting lymph node metastases [6, 8].

Lymphovascular Invasion

Lymphovascular invasion (LVI) is present in 12–32% of T1 rectal cancers [7, 17]. LVI has long been recognized a predictor of lymph node metastasis with a reported odds ratio between 3.0 and 11.5 [6–8, 19].

Poor Differentiation

Poorly differentiated tumor histology has also long been a predictor of lymph node metastasis in early rectal cancer. However, this feature is seen rather infrequently and is only present in 2–4% of early rectal cancers [5, 6, 8, 20].

Preoperative Planning, Patient Workup, and Optimization

Once a patient has been diagnosed with rectal cancer, a standardized workup is initiated to exclude synchronous colorectal neoplasm and assess for locally advanced and metastatic disease [3]. Synchronous neoplasm is excluded via screening colonoscopy. Metastatic disease is evaluated using CT scan of the chest, abdomen, and pelvis. Local regional disease is evaluated using rectal cancer protocol MRI or endorectal ultrasound (EUS). EUS is useful in evaluating candidates for local excision, as it is better than MRI and CT in visualizing the individual layers of the bowel wall and differentiating superficial T1 and T2 rectal cancers [19]. Rectal cancer protocol MRI is a useful adjunct in assessment and surveillance of mesorectal lymph nodes [21].

For optimal surgical planning, preoperative rigid or flexible sigmoidoscopy is necessary to assess the location and extent of the rectal tumor, the tumor height from the anal verge, anterior/posterior/lateral location, tumor bulk, extent of circumferential involvement, or other features which might hinder access to the proximal border of the tumor. This can affect choice of patient positioning, planned complexity and length of surgery, risk of intraperitoneal entry, and plan for closure strategy.

Sometimes a "rectal" tumor is found up in the sigmoid, beyond the reach of transanal instruments.

Standard transanal excision has typically been restricted to tumors that are less than 40% of the circumference of the rectum and tumors within 8 cm of the anal verge. These limitations, however, arose not because these dimensions portend high risk of recurrence, but rather, they represented the restricted reach and visibility afforded through standard transanal instrumentation. TES – through improved lighting, visualization, advanced instrumentation, and the benefit of a stable pneumorectum – overcomes these size and location restrictions such that they are no longer considered a contraindication, provided the tumor can be removed en bloc with negative margins.

Operative Setup and Technique

The requisite equipment for transanal endoscopic surgery involves an operating transanal platform, laparoscopic or modified laparoscopic instruments, CO_2 insufflation unit, laparoscope and light source, suction device, and monopolar and/or bipolar energy sources and handpieces depending on the surgeons' preferences and a method to close the rectal wall defect such as suture or laparoscopic suture devices. Each TES platform will require a greater or lesser amount of disposable and reusable equipment. The initial TES platforms used rigid, reusable proctoscopes, transanal endoscopic microsurgery (TEM, Richard Wolf Medical Instruments, Knittlingen, Germany), and transanal endoscopic operating system (TEO®, Karl Storz, Tuttlingen, Germany). Transanal minimally invasive surgery (TAMIS), introduced in 2010, utilizes a disposable single-port platform placed transanally. The most common TAMIS platform is the GelPOINT® Path (Applied Medical, Rancho Santa Margarita, CA, USA).

As with all major surgeries, patient comorbidities and nutritional and smoking status should be optimized prior to elective surgery. Preoperative preparation involves a bowel preparation to ensure the rectal lumen and surgical field remain as clear as possible during the procedure. Most surgeons advocate for a full mechanical bowel preparation to achieve this goal, and some centers report clearance with enemas alone. Colorectal surgery prophylactic preprocedural intravenous antibiotics are administered in the operating room. Since spontaneous patient breathing can compromise adequate pneumorectum, general anesthesia with muscular relaxation is the preferred anesthetic modality.

Patient positioning is based on surgeon preference and surgical platform. TAMIS, using the disposable platform with straight instruments, can universally be done in lithotomy position. This also permits easy access to the abdomen for laparoscopy in the event of intraperitoneal entry and need for laparoscopic closure. TEM and TEO reusable platforms have beveled proctoscopes and angled instruments that facilitate operating on tumors located in the down position. Hence, patients with anterior tumors can be positioned prone split leg, posterior tumors in lithotomy, and lateral tumors in decubitus hip flex position. Intraperitoneal entry with TEM and TEO can usually be repaired transanally. Since TES patients have minimal postoperative discomfort, they can be managed as an outpatient or a 23-hour overnight stay.

Technique for TEM and TEO

Following positioning, the anus is gently dilated to facilitate insertion of the 4-cm-diameter proctoscope. The proctoscope is secured to the table with a U-shaped mounting arm. An airtight faceplate is secured, and tubing is connected to the suction insufflator unit. Pneumorectum is established and the video laparoscope adjusted to view the target lesion. Three instrument ports are available for use of the modified angled TEM/TEO laparoscopic instruments.

Needle tip electrocautery is utilized to demarcate a 10 mm margin around a cancer. Full-thickness dissection is then initiated and carried into the mesorectal fat (Fig. 39.2). Partial en bloc resection of the adjacent mesorectum has also been described for T1 lesions with unfavorable histology and T2 lesions [22]. The risk of bleeding is higher when operating on larger lesions and in the mesorectum where larger vessels are encountered. Bipolar or ultrasonic energy devices should be used or on standby for these situations. Continuous suction functions to clear the cautery smoke during the procedure. The integrated suction-insufflation unit prevents loss of pneumorectum from suctioning.

Following specimen removal, the defect is closed transversely using a running absorbable suture. A metal clip is locked at each end of the suture in lieu of intracorporeal knot tying. Alternative closing techniques include use of barbed sutures or laparoscopic suturing device. Closure of large resection defects is facilitated by starting the closure with a bisecting suture in the middle of the defect, thereby converting one large defect into two small defects (Figs. 39.3 and 39.4). With the increased proximal reach of TEM/TEO, intraperitoneal entry occasionally occurs and, in experience hands, can safely be closed via the TEM/TEO instrumentation [23–25]. TEM/TEO suffers from technical limitations of the rigid proctoscope causing significant instrument conflict and has a longer learning curve for both technique and instrument troubleshooting compared to other transanal techniques.

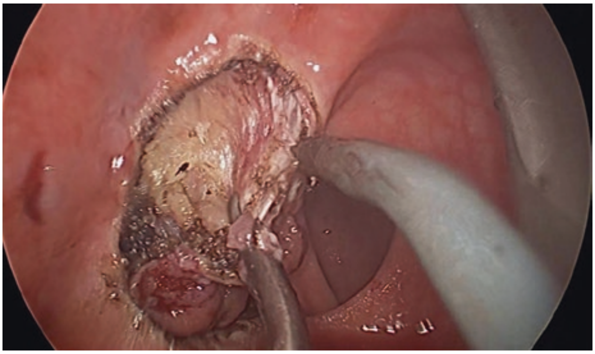

Fig. 39.2 Full-thickness resection into the mesorectal fat following dissection through the TEM platform. (Copyright retained by Mark H. Whiteford, MD)

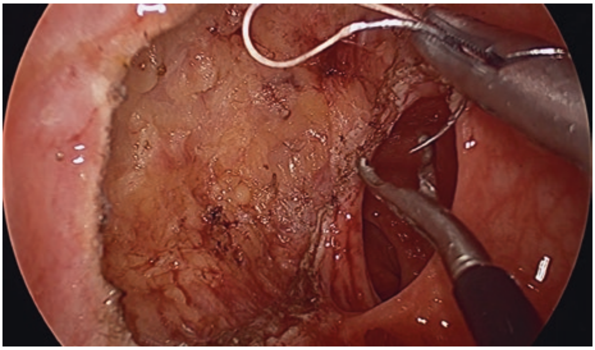

Fig. 39.3 Large full-thickness defect. (Copyright retained by Mark H. Whiteford, MD)

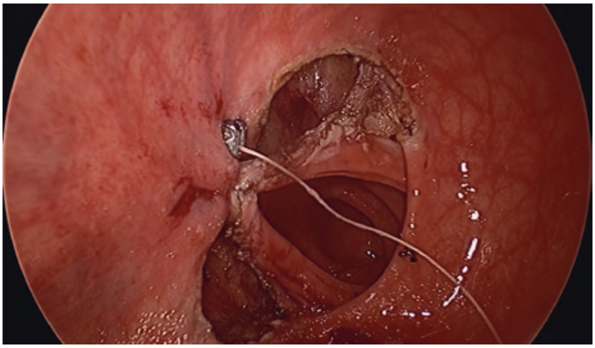

Fig. 39.4 Large defect bisected with suture closure. (Copyright retained by Mark H. Whiteford, MD)

Technique for TAMIS

TAMIS is a modification of TEM whereby the reusable rigid 4-cm-diameter operating proctoscope is replaced by a flexible, disposable single-port laparoscopic platform (Fig. 39.5). Standard laparoscopic instruments are utilized. Insufflation and smoke evacuation are accomplished using specialized high-flow insufflators such as the AirSeal® insufflator (ConMed, Utica, NY, USA), to avoid bellowing of the pneumorectum from standard laparoscopic insufflators. A 1 cm and full-thickness resection principles are identical to those mentioned above for TEM/TEO. Defect closure techniques vary among authors and include the use of different laparoscopic suturing devices or barbed sutures (Fig. 39.6) [26]. Intraperitoneal entry during TAMIS is more likely to require laparoscopic assistance for defect closure due to loss of rectum and visualization of the defect via the transanal device [27].

Oncologic Outcomes

The oncologic results following local excision of rectal cancer are mostly derived from case series and phase 2 trials. Many of these studies are subject to selection bias, include patients who had malignant polyps excised colonoscopically, or only

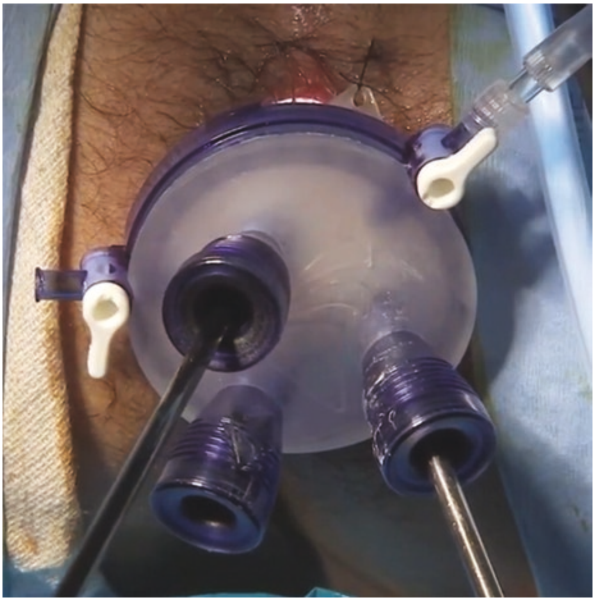

Fig. 39.5 TAMIS platform inserted transanally for TES. (Courtesy of Dr. Daniel Popowich)

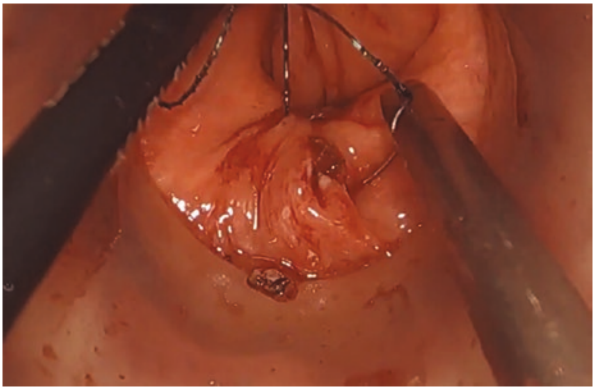

Fig. 39.6 Transanal endoscopic suturing of a full-thickness rectal defect through a TAMIS platform using a barbed suture. (Courtesy of Dr. Daniel Popowich)

track patients with favorable histology and negative margins. It is therefore difficult to make high-probability predictions for this heterogeneous disease process.

Clinical T1Nx Cancer

CALGB 8984 was a multicenter phase 2 trial examining long-term outcomes of local excision for early rectal cancer. One hundred seventy-seven patients with early-stage low rectal cancer underwent transanal excision. T1 cancers with negative margins (n = 59) were followed with no further treatment. T2 cancers with negative margins (n = 51) underwent adjuvant long-course chemoradiotherapy

Table 39.2 Long-term oncologic results comparing transanal endoscopic surgery and radical total mesorectal excision for favorable T1 rectal cancer

Series (year)	Number of patients	Follow-up (months)	5-year local recurrence	5-year disease-free survival	5-year overall survival
Winde (1996) [33]	24 TEM	41	4.1%	–	96%
	26 TME	46	0%	–	96%
Heintz (1998) [34]	46 TEM	52	4.3%	–	79%
	34 TME	52	2.9%	–	81%
Lee (2003) [35]	52 TEM	–	4.1%	95%	100%
	17 TME	–	0%	94%	93%
Ptok (2007) [36]	105 TAE + TEM	43	6.0%	91%	84%
	312 TME	42	2.0%	92%	92%
De Graaf (2009) [37]	80 TEM	42	24%	90%	75%
	75 TME	84	0%	87%	77%

TEM transanal endoscopic microsurgery, *TME* total mesorectal excision, *TAE* transanal excision

(5400 cGy, 5-fluorouracil). The 6-year local failure-free survival was 83% for T1 [28]. These optimistic results, however, were tempered by multiple subsequent single-institution reports demonstrating recurrence rates from 7% to 18% following transanal excision for favorable T1 cancers [29–32].

There are limited quality data comparing oncologic outcomes between TES and radical surgery for favorable T1 rectal cancer. Five of the larger studies are summarized in Table 39.2 [33–37]. Winde and coauthors published the only randomized trial comparing TEM to low anterior resection; however, this study was underpowered by only including 50 patients. Taken together, these studies demonstrate that TEM has a higher incidence of local recurrence relative to radical surgery; however, because of salvage radical surgery, 5-year tumor-specific survival and overall survival between the two techniques are not statistically different.

There are no long-term oncologic data comparing TAMIS to radical surgery. There is one large multi-institution cohort study comparing medium-term (14 months) follow-up of TAMIS ($n = 181$) to long-term (42 months) follow-up for TEM ($n = 247$) for benign and malignant rectal neoplasms. All stage (Tis, T1, T2, T3) local recurrence and 5-year disease-free survival for TAMIS and TEM were similar at 7% and 78% vs 7% and 80%, respectively [38].

Clinical T2Nx Cancer

Local recurrence following transanal excision alone for T2 rectal cancer is several-fold higher than that following radical surgery. To compensate for this, radiation therapy has been added to local excision of T2 rectal cancer to reduce the rate of local recurrence. The abovementioned CALGB 8984 trial reported a 71% 6-year failure-free survival for T2 cancers treated with adjuvant radiation therapy [28]. Lezoche and coauthors enrolled 100 patients in a single-institution randomized trial comparing neoadjuvant chemoradiotherapy followed by TES vs neoadjuvant chemoradiotherapy followed by laparoscopic TME for favorable ultrasound-staged uT2 N0 low rectal tumors. There was no difference in the probability of local recurrence or cancer-related survival at 5 years [22].

The American College of Surgeons Oncology Group Z6041 phase 2 multicenter trial enrolled 90 patients with uT2 N0 rectal cancer to undergo preoperative chemoradiotherapy with capecitabine plus oxaliplatin followed by local excision. A total of 77 patients completed treatment of which 98% had a negative resection margin, and 64% of tumors were downstaged (ypT0–T1), of which 44% had a pathologic complete response. There was no treatment-related mortality, and at a median follow-up of 56 months, 3-year disease-free survival was 88%, and overall survival was 95%. Bowel function and quality of life returned to baseline by 12 months [39].

Pitfalls and Troubleshooting

TES complications are similar to those of other anorectal surgeries and tend to be of low severity and of short duration. Mortality is rare [40, 41].

Intraoperative Complications

Intraoperative hemostasis is a surgical norm. TES is no different in this regard; however, the surgeon needs to develop the important balance between adequate suctioning to visualize the site of bleeding and excessive suctioning which results in loss of pneumorectum and needed exposure. Typical bleeding sites include the muscularis propria of the rectal wall and the mesorectal vessels. Bulky lesions also tend to have more robust blood supply and are more prone for brisk bleeding. Most bleeding can be controlled with monopolar cautery. Additional techniques include graspers connected to cautery, bipolar or ultrasonic energy devices, epinephrine injection, laparoscopic clips, suture ligation, and, rarely, packing.

Most of the rectum lies in an extraperitoneal location and is surrounded by a fatty mesorectum. TES excision into this extraperitoneal space rarely causes significant infection or morbidity. The anterior and lateral upper rectum, however, becomes an intraperitoneal organ whereby full-thickness transgression can result in intraperitoneal defect which mandates secure closure. Once considered a complication requiring laparoscopy/laparotomy and transabdominal repair, in the hands of experienced surgeons with a transanal laparoscopic suturing skill set, intraperitoneal entry and defect closure have been demonstrated to be safe using the rigid platforms [23–25]. At the time of intraperitoneal entry, CO_2 pneumorectum escapes into the abdominal cavity with resultant loss in pneumo-distention of the rectum and potential collapse of the working space. The rigid reusable TES platforms are able to maintain exposure to the intraperitoneal defect which permits transanal suturing to be completed. The TAMIS platform, however, does not stent the rectal lumen open, so complicated intraperitoneal entry using this device is often managed by converting to a laparoscopic approach for suture repair of the rectal defect [27]. Until a TES surgeon has acquired adequate endoluminal suturing skills to securely close an intraperitoneal entry, it is best to avoid upper rectal and anterior lesions early in their experience.

Postoperative Complications

Most common complication following TES surgery is urinary retention which occurs in 5–10% of cases [40, 41]. Like other anorectal surgeries, this is usually a self-limiting event which might require short-term urinary catheterization.

Small amounts of rectal bleeding and spotting are to be expected following transanal surgery. Major bleeding resulting in readmission or return to the operating room is infrequent. These events typically occur several days postoperatively related to a suture line disruption or later when patients restart their anticoagulation. Treatment is based on the severity and the clinical condition of the patient. Often the bleeding stops spontaneously; otherwise, a return to the operating room is necessary to obtain hemostasis using whatever combination of techniques deemed necessary, transanal endoscopic surgery, traditional transanal instrumentations, or flexible endoscopic techniques.

Suture line dehiscence is suspected when patients report increased bloody and mucous drainage, constant pelvic pain, and perhaps fevers and night sweats, usually several days to a week following surgery. It is more common following excision of low tumors and in patients that have received neoadjuvant radiation. True pelvic sepsis and fistulas are rare complications as is the need for urgent fecal diversion, but this must be considered where clinically appropriate.

Conclusion

The standard surgical treatment for early rectal cancer is total mesorectal excision. Oncologic equivalence between transanal endoscopic surgery and total mesorectal excision has not yet been demonstrated in the scientific literature so must still be considered a compromise. That said, many patients unfit for or unwilling to undergo radical surgery for early rectal cancer will choose organ sparing transanal endoscopic surgery for their treatment. Like all rectal cancer surgery, TES for early rectal cancer should be part of a multidisciplinary team to assure proper preoperative staging and interpretation, thoughtful patient selection, sound technical performance to obtain en bloc resection with negative margins, and careful histologic evaluation of the resection specimen. Tumors with unfavorable histology, including tumor budding, lymphovascular invasion, and deep submucosal invasion, have a high risk of occult lymph node metastasis and subsequent local recurrence. These patients should be steered toward radical surgery, be considered for adjuvant radiation, or be offered close surveillance follow-up.

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