## Current Endoluminal Approaches: Transanal Endoscopic Microsurgery, Transanal Minimally Invasive Surgery and Transanal Total Mesorectal Excision

Cici Zhang and Patricia Sylla

## **Key Points**

- Current practice in rigid TES (TEM and TEO) is built on over 30 years of experience performing submucosal and full-thickness endoscopic resection of rectal lesions through rigid platforms, where improved visualization and exposure of rectal lesions have resulted in superior local control relative to conventional transanal excision.
- Extensive published data on the long-term oncologic results of local excision for rectal adenocarcinoma including TES has demonstrated that TES with curative intent should only be offered to carefully selected T1 rectal adenocarcinoma with no adverse histopathological features and local recurrence rates equivalent to that of TME, but with substantially lower morbidity.
- TAMIS, which incorporates standard laparoscopic instruments inserted through disposable single ports, has enabled wider adoption of TES and reduced setup and operative time, but has probably not shortened the learning curve for overcoming difficulties of operating within the confined transanal working place, particularly with suturing full-thickness rectal defects associated with peritoneal entry.
- Given the technical and operational challenges of open, laparoscopic, and robotic TME, taTME which combines abdominal and transanal bottoms-up dissection of the rectum and mesorectum has facilitated completion of these complex procedures, particularly for low rectal tumors in obese males.

C. Zhang, M.D.

P. Sylla, M.D., F.A.C.S., F.A.S.C.R.S. (⊠)
Department of Surgery, Division of Colon and Rectal Surgery, Icahn School of Medicine at Mount Sinai Hospital,
5 East 98th Street, Box 1259, New York, NY 10029, USA
e-mail: patricia.sylla@mountsinai.org • The cumulative published experience with taTME based on the largest published series with cohort size ranging from 16 to 140 patients has demonstrated an 89% rate of TME completion with 0–13% incidence of positive circumferential resection margin (CRM). Current ongoing trials are exploring the possibility that taTME might represent a new standard in the surgical management of mid and low rectal cancer.

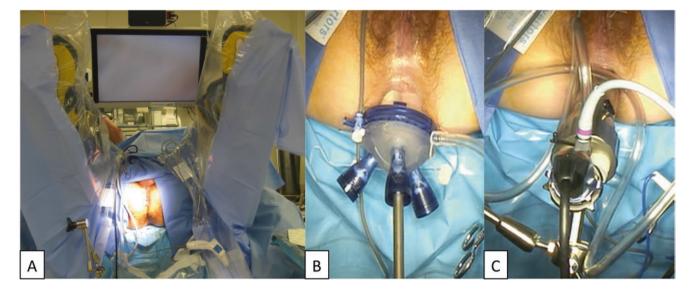
## The Evolution of Transanal Endoscopic Surgery and Transanal Total Mesorectal Excision

## **TEM and TEO**

Contemporary management of rectal lesions has been transformed by innovation and technology over the past few decades. Until recently, abdominoperineal resection (APR) and low anterior resection (LAR) were considered the standard definitive procedures for benign rectal lesions too large for conventional polypectomy and too proximal for transanal excision (TAE). These radical oncologic resections result in significant and costly morbidity, non-negligible mortality, significant functional disorders including the low anterior rectal syndrome, and the psychologic repercussions of temporary or permanent ostomies. Even when foregoing anastomotic complications and defecatory disturbances, APR still results in a substantial incidence of sexual and urinary dysfunction, as well as abdominal and perineal wound-related complications [1, 2].

Transanal endoscopic microsurgery (TEM, Richard Wolf Company, Tubingen, Germany) was pioneered by Buess in 1983 to perform endoscopic local resection of proximal rectal tumors inaccessible to endoluminal or transanal modalities [3]. TEM and transanal endoscopic operations (TEO, Karl Storz GmbH, Tuttlingen, Germany, Fig. 22.1a, b) are the two rigid metal TES platforms currently commercially available. Both consist in a 4-cm diameter meter beveled

Department of Surgery, Lenox Hill Hospital, 100 East 77th St, New York, NY 10075, USA



**Fig. 22.1** Patient positioning for TES and operative setup. Patients are most commonly placed in high lithotomy position (**a**). The TEO platform is inserted and secured to the operating table using an articulating arm.

TEO procedures are performed by a single operator (b). Alternatively, a TAMIS platform is inserted which requires an operator and dedicated camera assistant (c)

proctoscope sealed by a faceplate that provides multiport access and an airtight seal. The rectoscopes come in a variety of lengths (12, 13.7, and 20 cm for TEM and 7.5, 15, and 20 cm for TEO) to accommodate the location of the pathology with the 20 cm proctoscope providing access to the upper rectum and even the rectosigmoid. TEM and TEO sets include specialized instruments with angled tips, which are designed to improve ergonomics, minimize instrument collision, negotiate difficult angles, and allow for full-thickness dissection and suture closure of rectal defects. The rigid proctoscopes are equipped with a telescope (TEO) and stereoscope (TEM) that are affixed to the platform and provide HD and 3D (TEM) optics. The proctoscopes are in turn mounted onto the operating table by an articulating arm, providing stability of the operative field, and easily piloted by a single operator. TEM and TEO telescopes are compatible with standard laparoscopic cameras which offer the benefits of laparoscopy including HD and even 3D visualization (TEM). The TEM tower is also equipped with an automatic pressure-controlled CO<sub>2</sub> insufflation system that evacuates the smoke generated during dissections while maintaining a stable pneumorectum during transanal dissection.

Relative to radical rectal resections, TEM and TEO are associated with shorter OR time, shorter length of hospital stay and faster recovery, negligible morbidity, and negligible mortality. The cumulative incidence of bleeding, urinary retention, wound dehiscence, and infection ranges from 3 to 23% in the largest TEM series [4–8], with a 4.3–13.3% [6, 9] incidence of peritoneal entry. In a recent meta-analysis by Clancy, six studies encompassing 927 local excisions were compared for oncologic outcomes and postoperative complications [10]. There was no difference between postoperative complication rates (OR, 1.018; 95% CI, 0.658–1.575; p = 0.937). TEM had a higher rate of negative microscopic margins in comparison with transanal excision (OR, 5.281; 95% CI, 3.201–8.712; p < 0.001). TEM had a reduced rate of specimen fragmentation (OR, 0.096; 95% CI, 0.044– 0.209; p < 0.001) and lesion recurrence (OR, 0.248; 95% CI, 0.154–0.401; p < 0.001) compared with transanal excision [10]. Despite significant heterogeneity in surgeon experience, pathology, and follow-up, the data clearly demonstrated that improvement in visualization and technical precision facilitated by the stable endoscopic TEM and TEO platforms resulted in superior oncologic outcomes when compared to TAE.

#### TAMIS

Until recently, the utilization of TES has remained largely confined to high-volume and specialized centers. For several decades, widespread adoption of TEM and TEO was hindered by prohibitively high costs of the rigid platforms, scarcity of training, and steep learning curve associated with mastering of techniques. In 2009, during the height of enthusiasm for single-incision laparoscopy, an alternate transanal endoscopic setup using single-incision laparoscopic disposable ports was described named transanal minimally invasive surgery (TAMIS) [11, 12]. TAMIS has rapidly broadened adoption and application of TES for a variety of indications without compromising the benefits of TEM or TEO. Because TAMIS ports are not anchored to the operating table, it requires the operating surgeon to work side by side with an assistant who holds the bariatric length laparoscope that is recommended for use during these cases. TAMIS can be performed using standard laparoscopic equipment through a variety of single-incision platforms at much lower per-case costs relative to the cost of capital investment in rigid platforms and specialized TEM/TEO equipment [7]. Several commercially available devices have been described for TAMIS, but in the USA, the commercially available devices include the SILS Port (Medtronic, Mansfield, MA, USA) and the GelPOINT Path Transanal Access Platform (Applied Medical, Rancho Santa Margarita, CA, USA, Fig. 22.1c). The Triport (Olympus, Center Valley, PA) and the SSL (single-site laparoscopic access system, Ethicon Endo-Surgery, Cincinnati, OH, USA) have been reported in small series with comparable results mostly outside the USA [13, 14]. Flexible laparoscopes such as the Endoeye Flex (Olympus) and standard colonoscopes have been used through TAMIS platforms in order to reach higher up in the rectum and overcome the instrument collision. Interestingly, the use of automated suturing devices and self-retained barbed sutures, as well as specialized high flow insufflation and smoke evacuation systems to maintain a stable pneumorectum and a clear surgical field, has increased the per-case costs of TAMIS. High-flow CO<sub>2</sub> insufflation units such as the UHI-4 (intra-abdominal Insufflation Unit, Olympus) and the Airseal Insufflation System (SurgiQuestInc, Milford, CT, USA) have been used in conjunction with TES platforms. The Airseal in particular provides a continuous flow circuit that evacuates CO<sub>2</sub> and smoke and quickly recirculates filtered and high-pressure CO<sub>2</sub>, thereby maintaining a stable pneumorectum at all times. The Airseal insufflation system is reminiscent of the TEM automatic pressure-controlled CO<sub>2</sub> insufflation system, but it requires the use of disposable specialized cannulas inserted through the transanal platform. Finally, the use of TAMIS has also been described in conjunction with robotic platforms, harnessing the advantage of magnified 3D optics and greater dexterity of the robotic EndoWrist movements [15].

While the use of conventional laparoscopic equipment with TAMIS can be versatile and cost-saving, it poses significant limitations as well. The maneuverability of straight instruments through a small transanal workspace remains limited, and overcoming instrument collision makes for a steep learning curve in TAMIS [16]. In addition, the shorter TAMIS platforms provide limited access to the proximal rectum, and rectal lesions located behind haustral valves in upper rectum may be more difficult to reach, resect, and rectal defects more difficult to close using TAMIS platforms relative to the longer TEM or TEO platform [17]. The longer rigid platforms facilitate successful transanal closure of these defects by maintaining patency of the rectal lumen, particularly in the event of leakage of CO<sub>2</sub> following peritoneal entry. This is reflected in the relatively low conversion rates to laparoscopy or laparotomy in large TEM and TEO series which range from 0 to 41.6%, but average 10% [4, 5]. On the other hand, peritoneal entry during TAMIS appears to result in high rates of conversion to laparoscopic closure of rectal defects, ranging from 0 to 86%, which likely reflects the difficulties stenting the rectum adequately enough to permit closure of the rectal defects [18–20].

#### **Transanal TME**

Recent improvements in the treatment of rectal cancer can be attributed to the standardization of TME technique and the selective use of chemotherapy and radiation therapy [21]. Local recurrence rates have decreased from as high as 45% using traditional techniques to <10% after TME alone, and <6% after TME if performed with negative circumferential radial (CRM) and distal margins, in conjunction with radiation therapy [22, 23]. The introduction of minimally invasive techniques including laparoscopy and robotics has not altered the morbidity or negative impact of open TME on quality of life following sphincter-sparing and non-sphincter sparing TME. Among the largest randomized controlled trials comparing open versus laparoscopic TME such as the COLOR II, ACOSOG, and COREAN trials, wound infection rates have ranged from 5 to 6.5% and anastomotic leaks from 1.2 to 10%, without statistically significant differences between the groups [24-26]. Oncologic equivalence or noninferiority of laparoscopic TME was demonstrated across all the above trials except for the ACOSOG Z6051and AlaCart trials [24, 27]. The 30–40% incidence of sexual, urinary, and defecatory dysfunction are compounded by the addition of neoadjuvant radiation and have not been lowered with the use of laparoscopic or robotic surgery, despite improved visualization of pelvic nerves during pelvic dissection [25, 26]. However laparoscopic TME is significantly more technically challenging and is associated with a steep learning curve. Laparoscopic TME is particularly challenging during dissection of the lowermost part of the mesorectum, especially in male patients with high body mass index (BMI) and narrow pelvis. While conversion rates have progressively decreased from 30% early on in the laparoscopic TME experience to 16% and 11% in the COLOR II and ACOSOG Z6051 trials, respectively [24, 25, 28], overall adoption of laparoscopic TME has remained at 30% or less.

The recent increase adoption of robotic surgery during TME reflects the superior 3D visualization and enhanced dexterity and ergonomics provided by the da Vinci<sup>TM</sup> system (Intuitive Surgical, Sunnyvale, CA, USA), which may help overcome some of the challenges of deep pelvic dissection and reduce the steep learning curve [29]. Despite the suggestion that robotic surgery may reduce conversion rate during

TME across several large-case series and comparative studies, the recent ROLARR trial, a prospective, randomizedcontrolled of robotic-assisted versus laparoscopic TME, has not shown any statistically significant difference in conversion rates or other perioperative outcomes between laparoscopic and robotic TME [30].

In light of the ongoing anatomic and technical challenges of achieving sphincter-preserving TME while achieving a complete mesorectal specimen and negative margins, the concept of transanal Natural Orifice Transluminal Endoscopic Surgery (NOTES) colorectal surgery rapidly evolved from the experimental setting to clinical application [31, 32]. By accessing the rectum and mesorectum from a primarily transanal endoscopic approach, taTME aims to overcome these limitations and facilitate completion of these complex procedures. Since the report of the first case of hybrid laparoscopic-assisted transanal TME in a female patient with a T2 N1 mid-rectal cancer in 2009 using a TEO platform, several small pilot studies subsequently demonstrated the feasibility and safety of this approach [33-35]. These pilot studies were quickly followed by medium-sized series of taTME with the largest cohort size ranging from 16 to 140 patients with taTME performed for benign and malignant indications, in combination with LAR or APR, using a variety of transanal platforms and types of transabdominal assistance (open, multiport, single port and hand-assisted laparoscopy, and robotic). Cumulatively, the series have reported 98% rate of complete and near-complete TME specimens and a CRM-positive CRM ranging 0-13%, which is comparable to historical open and laparoscopic TME outcomes with the benefit of exceedingly low conversion rates

Although the experience with taTME remains preliminary with no long-term oncologic or functional outcomes and no randomized trials, these preliminary results strongly support taTME as an attractive alternative and potential new standard in the surgical treatment of resectable low and midrectal cancer.

## TES: Indications, Contraindications, and Patient Selection

TEM was initially intended for the management of large adenomas deemed unresectable by standard polypectomy or conventional transanal excision (TAE). Since its inception, TES has become an attractive alternative to standard LAR and APR with data supporting its safety profile, significantly lower postoperative pain, and reduced recovery time [36, 37]. Most importantly, TES provides a much more suitable choice for benign lesions that would otherwise be overtreated with LAR or APR. Indications for local excision using TES have expanded to include large adenomas, incompletely resected adenomas with high-grade dysplasia, small low-risk carcinoids, other benign rectal pathologies, as well as carefully selected T1 rectal tumors and more advanced rectal tumors in the palliative setting.

## **Rectal Adenoma**

#### **TES Versus TAE and EMR**

In the largest TEM and TEO retrospective series published to date with cohort size ranging from 91 to 353 patients, resection of  $\leq 3$  cm rectal adenomas using either submucosal dissection or full-thickness excision resulted in excellent long-term local control with local recurrence rates (LR) ranging 4–10%, mortality under 1%, and morbidity ranging 3-8% [37-40]. With respect to local control, as with TAE, several large TEM series have shown that the strongest predictor for LR following TEM was margin positivity [37, 38]. Several TEM and TAE comparative series have demonstrated superior local control with TEM, which is likely related to the benefits of rectal distention with CO<sub>2</sub>, magnified high definition laparoscopic visualization, and more precise dissection through transanal endoscopic platforms. Clancy et al. recently demonstrated in a meta-analysis of TAE and TEM/ TEO series (N = 927) that TEM was associated with higher rate of negative margins (OR, 5.281; 95% CI, 3.201-8.712; p < 0.001), lower rate of specimen fragmentation (OR, 0.096; 95% CI, 0.044–0.209; p < 0.001), and lower recurrence rate (OR, 0.248; 95% CI, 0.154–0.401; p < 0.001) compared to TAE for benign and malignant rectal pathologies comparing TEM and TAE [10].

TES is also an important adjunct in centers that do not routinely perform endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD). Relative to conventional polypectomy and EMR, TES is associated with a lower early adenoma recurrence rate [41]. In addition, TES facilitates en bloc resection of complex adenomas including flat, large, prolapsing adenomatous lesions, or particularly in the setting of extensive mucosal scarring. In a retrospective review of 292 patients undergoing excision of adenomas larger than 2 cm via either TEM or EMR, a higher incidence of incomplete resection after a single EMR intervention resulted in a higher incidence of early recurrences relative to the TEM group (31.0 versus 10.2%, p <0.001) [42]. Of note, when additional endoscopic EMR procedures were performed within 6 months from the original procedure, the long-term efficacy of EMR was equivalent to that of TEM.

#### **Complex Adenomas**

Traditionally, adenoma size greater than 3 cm, referred to as giant adenomas, has been considered a relative contraindication for TES due to the higher incidence of positive margins and LR. Other relative contraindications to TES include circumferential and near-completely circumferential adenomas,

where, in addition to the increased risk of R1 resection, there is an increased risk of an underlying malignancy, and fullthickness closure of near-circumferential rectal wall defects can be exceedingly difficult, with a high risk for conversion, particularly early during the operator's learning curve. Several groups with extensive TEM experience and expertise have reported their results with TEM performed for rectal tumors larger than 5 cm. In a retrospective review of 233 rectal adenomas with median diameter of 5 cm (1-12 cm) resected full-thickness using TEM, Allaix et al. reported an 11.1% positive margin rate and a 5.6% overall LR rate at a median follow-up of 110 months [38]. However, the rate of positive margins was 8.9% for lesions <5 cm versus 20.9% for lesions > 5 cm (p = 0.047). Overall these findings support the use of TES to resect large rectal adenomas as an alternative minimally invasive strategy to avoid proctectomy; however, this is at the cost of an increased risk of an underlying invasive cancer, increased LR, and higher chance of conversion due to the technical difficulty of closing large fullthickness rectal wall defects associated with large rectal lesions [38, 43, 44].

To date, the published TAMIS experience with rectal adenomas is still limited but growing quickly. Among a total of 350 cases from 15 TAMIS series published between 2010 and 2015, 163 consisted in adenomas (Table 22.1) [7, 11, 12, 16, 17, 19, 20, 45-53]. The overall R1 resection rate for benign and malignant lesions ranged 0-17%, but was below 10% among the largest TAMIS series. Morbidity was similar to historical TEM/TEO rates and ranged from 0 to 25%. Noticeable among TAMIS series is the fact that there is limited to no data on resection of larger rectal lesions (>3 cm) and limited data on resection of lesions in the upper third rectum [7, 11, 12, 16, 17, 19, 20, 45-53]. The scant TAMIS experience with full-thickness resection of larger and upper third rectal lesions may reflect the intrinsic limitations of shorter disposable transanal platforms to safely reach, expose, and permit dissection of lesions that lie behind rectal folds and maintain rectal distention in the face of critical loss of pneumorectum during peritoneal entry [54].

## **T1 Rectal Cancer**

The use of TES alone in the curative treatment of rectal cancer remains controversial. Although earlier TEM cohort studies demonstrated unacceptably high rates of LR for unselected T1 (range, 0–26%) relative to a  $\leq 6\%$  LR rate for T1 tumors treated with radical proctectomy [55], more contemporary series have demonstrated its curative potential for carefully selected T1 rectal cancers with low-risk histopathological features [56]. The risk of locoregional recurrence following local excision of T1 rectal cancer is directly correlated to the risk of associated lymph node metastasis, which is not addressed by any of the local excision techniques. While standard preoperative staging of rectal cancer with CEA, stating CT scans and pelvic MRI and/or endorectal ultrasound (ERUS) can exclude patients with T2 and more advanced rectal tumors, the challenge resides in selecting T1 tumors associated with the lowest risk of lymph node metastasis and that will likely be cured with R0 local resection alone.

Histopathologic factors associated with increased risk for local recurrence following local excision of T1 rectal tumors include depth of submucosal involvement, poor differentiation grade, lymphovascular invasion (LVI), positive resection margins (R1 resection), large tumor size, and the presence of tumor budding [57–59]. One of the most important independent predictor for local recurrence following local excision of T1 rectal cancer is the extent of submucosal invasion. In a longitudinal cohort study of 182 patients with adenocarcinoma, Kikuchi et al. determined that the level of tumor invasion into the submucosa is predictive of LR following TEM for T1 tumors. Submucosal invasion was further classified as sm1, sm2, and sm3 representing invasion into the upper, middle, and deepest third, respectively, with deeper submucosal invasion correlating with increased risk of LVI and lymph node metastasis [60]. Kikuchi and Nascimbeni independently determined from large cohorts of T1 colorectal cancers undergoing radical resection that sm1, sm2, and sm3 depth of tumor invasion was associated with a 0-3%, 8-10%, and 23-25% risk of lymph node metastasis, respectively [59, 60]. As a result, local excision alone for sm3 and high-risk sm2 lesions is associated with higher risk of lymph node metastasis and local recurrence.

Another adverse prognostic factor associated with local recurrence and metastases, as well as significantly worse overall and disease-free survival in colorectal cancer, is the presence of tumor budding [55, 61, 62]. Tumor budding refers to the presence of single malignant cells or a small clusters of tumor cells (less than 5 cells) at the invasive tumor margin [63]. Ueno et al. demonstrated that in T1 colorectal carcinoma, high tumor grade, LVI, and tumor budding are all independently associated with lymph node metastases. Patients without any of these three features showed low rates of lymph node metastases (1%, 1/138); in the presence of one risk factor, the rate of nodal metastases increased to 21% (12/58), and when two or three factors were present, the risk was 36% (20/55), suggesting that local excision with TEM with negative resection margins would be sufficient treatment for early T1 colorectal carcinoma [64].

Based on the National Comprehensive Cancer Network (NCCN) guidelines, indications for transanal excision of rectal cancer include T1 tumors less than 3 cm in size, with no radiographic evidence of lymphovascular or perineural invasion. Unfavorable histopathologic features include >3 cm in size, LVI, positive margin, or sm3 depth of tumor invasion (Table 22.2).

Series Atallah [12] Van den Boezen [45]	Sex (M F)					_		-		
Atallah [12] Van den Boezen [45]		Ν	BMI	OR time (min)	Port	Conversion	Final cancer stage	Positive margin	Distance from anal verge (cm)	Morbidity (%)
Van den Boezen [45]	6.0	9	1	86	SIIS	0	Adenoma (3)	17	1	0
Van den Boezen [45]	5	>				>	pTis (1)	;		>
Van den Boezen [45]							pT1 (1)			
Van den Boezen [45]							Carcinoid (1)			
	5,7	12	28	55	SILS	2	Adenoma (9)	0	7 (3–20)	8.3 (2 converted
							pT1 (1)			to TAE)
							pT2 (2)			
Barendse [7]	7,8	15	1	57	SSL	2 (TEM)	Adenoma (7)	13	6 ± 4.5	7.7
							pT1 (1)			
							pT2 (3)			
							Carcinoid (1)			
							Fibrosis (1)			
Lim [46]	12, 4	16	24	86	SILS	0	pT1 (3)	0	7.5	0
							pT2-3 (8)			
							Mucocele (1)			
							Carcinoid (4)			
Ragupathi [47]	10, 10	20	28.2	79.8	SILS	0	Adenoma (14)	5	10.6	5
1 1 1							Unspecified			
							malignant (6)			
Albert [11]	33, 17	50	27.4	74.9	SILS/Gelpoint	0	Adenoma (25)	9	8.2 (3-14)	9
							Hyperplastic (2)			
							pTis (1)			
							pT1 (16)	1		
							pT2 (3)			
							pT3 (3)			
Seva-Periera [20]	4,1	5	I	52	SSL	1	pTis (2)	0	4	25 (1 converted
							pT2 1)			to LAR)
							Fibrosis (1)			
Bridoux [48]	8, 6	14	25	09	Endorec	0	Adenoma (10)	7.1	10 (5-17)	21
							pT1 (3)			
							pT2 (1)			
Lee [16]	17, 8	25	22.7	45	SILS	0	Adenoma (6)	0	9 (6–17)	0
							pT1 (9)			
							Carcinoid (9)			
							GIST (1)			
Schiphorst [19]	18, 19	37	I	64	SILS	1	Adenoma (23)	16	7 (from dentate)	8 (1 converted
							pTis (7)			to LAR)
							pT1 (4)			
							pT2-3 (2)			

222

McLemore [17]	18, 14	32	28	132	Gelpoint/SILS	0	Adenoma (10)	3	4 +/- 3	25
							pTis (1)			
							pT1 (6)			
							pT2 (4)			
							Carcinoid (2)			
							Fibrosis (9)			
Gorgun [49]	10, 2	12	28.8	79	Gelpoint	0	Adenoma (10) (	0	8 (5–12)	25
							pT2 (1)			
							Carcinoid (1)			
Hompes [18]	8,8	16	26	108	Transanal	1	Adenoma (6)	13	8 (3-10)	13 (1
					glove port,		pT1 (2)			conversion to
			-		Davinci robot		pT2 (1)			Hartman's)
							pT3 (1)			
							Fibrosis (5)			
Hahnloser [51]	51, 24	75	I	77	SILS	0	Adenoma (35)	4	$6.4 \pm 3$	19
							pTis (11)			
							pT1 (13)			
							pT2 (9)			
							pT3 (1)			
							Carcinoid (1)			
							Hamartoma (1)			
Mendes [13]	5,6	11	I	53.73	aSSL	0	Adenoma (4) (	0	5.3 (3–9)	6
							Carcinoid (3)			
							pT1 (2)			
							Melanoma (1)			
							Fibrosis (1)			
Maglio [52]	6, 9	15	28	86	Gelpoint	0	Adenoma (5) (	0	7	0
							pT0 (10) <sup>b</sup>			
"SSL Single-site laparoscopic (SSL <sup>TM</sup> ) access system, Ethicon Endo-Surgery, Cincinnati, OH, USA, min (minutes) "Patient had total regression after neoaditivant chemoradiation therapy	sopic (SSL <sup>TM</sup> ) avion after neoadiv	ccess sy uvant ch	/stem, Eth	nicon Endo-Surgery, C ttion therapy	Zincinnati, OH, US	A, min (minutes)				
	[			C Jacob and the second						

Criteria	<30% Circumference of bowel				
	< 3 cm in size				
	Margin clear (>3 mm)				
	Mobile, non-fixed				
	Within 8 cm of anal verge				
	T1 only				
	Endoscopically removed polyp with cancer or indeterminate pathology				
	No lymphovascular invasion or PNI <sup>a</sup>				
	Well to moderately differentiated				
	No evidence of lymphadenopathy on pretreatment imaging				

Table 22.2 NCCN guidelines for transanal excision

<sup>a</sup>Perineural invasion

As described earlier, while LR rates following local excision of unselected T1 rectal cancer were reported to range from 0 to 26%, these outcomes from older series reflected the heterogeneity of cohorts with respect to the type of local excision (TAE or TEM, submucosal dissection or fullthickness), variations in preoperative tumor staging, completeness of resection (R0 or R1, en bloc or fragmented), treatment with neoadjuvant or adjuvant therapy, tumor size, and detailed histopathologic analysis to stratify outcomes based on risk for occult nodal disease [65, 66]. This is contrast to more contemporary TES for T1 rectal cancer series that have demonstrated that with careful preoperative staging and risk stratification based on detailed histopathologic review, local recurrence following TES rates range from 0 to 10%, which is in line with oncologic outcomes from radical proctectomy [67, 68].

## **T2 and More Advanced Rectal Cancer**

It has been established in previous studies that local excision alone with TEM and TEO for T2 and more invasive rectal cancers with curative intent results in unacceptably high rates of LR [67]. Across early TEM series, the reported LR rates for T2 tumors not treated with neoadjuvant therapy ranged from 20 to as high as 36%, reflecting the associated high incidence of lymph node metastasis [69, 70]. In a systematic comparison of TEM versus radical resection with TME for T1 and T2 rectal tumors of performed by Mellgren et al., the 5-year LR rate for T2 tumors was 47% versus 6% after radical resection (p = 0.001). While there was no statistical difference in the overall 5-year survival between local resection and radical surgery groups for T1 tumors (72% versus 80%, p = 0.5), there was a statistical difference for patients with T2 tumors (65% versus 81%, p = 0.03) [69].

Although the standard of care for locally invasive rectal cancer remains radical surgery with TME, there has been an increasing trend towards organ preservation based on evidence

that clinically staged T2 and T3 rectal tumors downstaged with neoadjuvant chemoradiation therapy (CRT) may be cured with local excision or observation alone. Several small retrospective cohorts of patients with locally invasive rectal tumors treated primarily with CRT because they either declined radical surgery or were deemed poor surgical candidates demonstrated acceptable long-term oncologic data. A small randomized trial comparing preoperative CRT followed by TEM alone versus laparoscopic TME in patients with T2 rectal tumors found no difference in overall survival between the two groups (72% in CRT + TEM versus 80% in laparoscopic TME, p = 0.609). LR rates were also similar between the groups (12% with TEM versus 10% with TME, p = 0.686 [71]. With improvement in preoperative staging and more intensive chemoradiation regimens therapy, complete pathologic response rates greater than 20% have been documented with sustained good local control using either local excision or observation alone. The recent prospective multicenter ACOSOG Z6041 phase II trial reported the 3-year oncologic outcomes in 72 T2N0 tumors located in the distal 8 cm of the rectum, treated with capecitabine, oxaliplatin, and 54 Gy of radiation followed by local excision using TAE or TES [72]. The 3-year DFS for the intention-to-treat group was 88.2% and 86.9% for the per-protocol group. Overall, organ preservation could be achieved in 66% of patients, and the authors concluded that neoadjuvant therapy followed by local excision should be reserved for those with clinically staged T2N0 lesions that are not otherwise amenable to TME [72].

Most recently, advocates of organ-preserving strategies have investigated the outcomes of nonoperative management for rectal tumors that have demonstrated complete clinical regression following neoadjuvant therapy. The Habr-Gama group has the largest clinical experience to date with the "watch-and-wait" approach for locally advanced rectal cancer. Their findings in a cohort of 70 patients with preoperatively staged T2-T4, N0-N2 tumors treated with intensive CRT regimens demonstrated a 68% rate of complete clinical response based on reevaluation with imaging, endoscopy, and digital rectal examination (DRE) 10-12 weeks later to confirm the absence of residual tumor or other mucosal irregularity [73]. These 47 patients were subsequently observed, and a sustained complete clinical response was observed in 51% of the entire cohort at 3 years follow-up. The remaining 49% with evidence of recurrent disease underwent immediate or salvage surgery with either TEM or radical surgery. Based on these data, although the possibility of definitive, nonsurgical treatment of rectal cancer with CRT alone remains limited to a subset of biologically responsive tumors, advances in neoadjuvant chemoradiation therapy may potentially spare 50% of patients with T2 rectal tumors from radical surgery. Several European series have corroborated the findings from the Habr-Gama group [74, 75]

and demonstrated that with more aggressive CRT regimens, the rates of complete clinical response can exceed the historical 20–30% rate, although this may be at the cost of increase toxicity, possible overtreatment of early rectal tumors, and delayed local recurrence that may not be surgically salvageable.

#### **Other Indications**

TES has also been demonstrated to be effective at treating a variety of other rectal tumors and benign conditions. Local resection using TES has been well established in the management of low-risk rectal carcinoid tumors, particularly when incompletely resected endoscopically. In the absence of histopathological risk factors for lymph node metastasis including size <10 mm and absence of LVI, and early stage confirmed by ERUS and CT scans, rectal carcinoids are amenable to local excision [76]. TES may be better suited than EMR, ESD, and TAE for definitive treatment of rectal carcinoids due to the ability to perform full-thickness rectal excision. Two large series on rectal carcinoids treated with TEM either as initial modality or for completion of incomplete endoscopic excision included 24 and 27 patients, respectively, with lesion size ranging from 7.5 to 10.1 mm and located within 9 cm from the anal verge (AV). These studies demonstrated a 100% R0 resection rate with 100% OS and DFS at a 30–70.6 months follow-up [77, 78]. TES has also been described in small case series of carefully selected GIST tumors and benign retrorectal tumors including tail gut cysts and rectal duplication cysts tumors, as a minimally invasive alternative to transcoccygeal resection or radical proctectomy [79, 80]. There have also been a number of recent case reports and case series on the successful use of TES in the management of complex benign conditions such as recurrent rectourethral [81], rectovesical [82], and rectovaginal fistulas [83] that had failed traditional repair. In addition, other miscellaneous use of a transanal endoscopic approach has included stricture plasty and transanal repair of colorectal anastomotic complications including leaks and abscesses [39]. Finally, TES can be used for palliation of bleeding rectal tumors in patients who are medically unfit to undergo other palliative procedures including fecal diversion, stenting, surgical debulking, cryosurgery, embolization, and palliative radiation [84].

## **Patient Selection for TES**

Historically, a relative contraindication for TES included rectal lesions located higher than 8–10 cm from the AV, particularly if anterior, due to the high chance of full-thickness excision resulting in peritoneal entry. That is because peritoneal entry during full-thickness TEM excision was previously considered to be a complication requiring immediate conversion to laparotomy with low anterior resection or fecal diversion in order to mitigate the risk of leak and infection [85]. However, recent publications from experienced centers have demonstrated the feasibility and safety of transanal suture closure of upper rectal full-thickness defects without increased morbidity or adverse oncologic outcomes [86–88]. Based on this experience, it is generally recommended that only lesions within the reach of the 12–20 cm rigid proctoscope, and otherwise amenable to local excision, should be considered for full-thickness TES resection.

At the other extreme end of the rectum, due to their design and location in the anal canal following deployment, TAMIS does not permit access to rectal polyps located within 4 cm of the AV [16]. For lesions partially or entirely located within the distal 4 cm of the anorectal canal, the TEM and TEO platforms can often be pulled back maximally to permit exposure without losing excessive pneumorectum. This is in contrast to TAMIS where resection must be combined with a standard TAE approach for the distal part of the dissection.

With respect to rectal tumor size, nearly obstructing, nearcircumferential, and circumferential tumors constitute a contraindication for TES. This is due to the anticipated difficulty in achieving R0 resection and safely closing giant rectal defects using a purely transanal approach, without resulting in rectal stenosis or incomplete closure [89].

With respect to patient safety, TES can be safely performed in the large majority of patients, including high-risk surgical patients, provided they are acceptable candidates for general anesthesia. TES can also be safely performed in patients with morbid obesity (BMI ranging from 35 to 66) as reported in a recent case series, without an increase in adverse events [90, 91].

## taTME: Indications, Contraindications, and Patient Selection

Although firm consensus is building that sphincter-preserving LAR for low rectal tumors is the sweet spot for transanal TME, any type of proctectomy, including completion proctectomy, total proctocolectomy, APR, extralevator abdominoperineal excision (ELAPE), restorative proctectomy, or proctocolectomy (RPC) with ileoanal J pouch (IPAA) reconstruction, can be performed using taTME for a variety of benign and malignant etiologies. Based on the preliminary procedural, perioperative, and short-term oncologic data published to date, specific indications and contraindications of taTME with respect to specific pathology and anatomic factors have been described.

#### **Benign Conditions**

Completion proctectomy using a primarily transanal endoscopic approach has been described for benign indications including ulcerative colitis (UC) and Crohn's disease (CD), unsalvageable anastomotic complications, refractory fecal incontinence, diversion or radiation proctitis, and large carpeting unresectable distal rectal polyps [92–95]. Transanal endoscopic completion proctectomy can be performed using a pure transanal endoscopic approach when the rectum is short and mostly extraperitoneal, or using a hybrid approach with laparoscopic or robotic assistance. Distally, transanal proctectomy can proceed along the intersphincteric plane and, posteriorly, along the rectal wall, through the mesorectum, or along the TME plane. In restorative cases, transanal proctectomy or proctocolectomy can be combined with rectal mucosectomy followed by hand-sewn IPAA reconstruction as opposed to stapled pouch-to-anal anastomosis. In a total of four published case series reporting on the outcomes of a total of 35 patients who underwent pure or hybrid transanal endoscopic completion proctectomy, there was no mortality, and conversion to open proctectomy was required in one case [95]. The cumulative morbidity rate was 40% (14/35) including delayed perineal wound healing or dehiscence, colocutaneous fistula to the perineum requiring reoperation, incarcerated parastomal hernia, urinary tract infection, and bleeding [92-95]. In addition, three groups have recently reported their experience with transanal endoscopic proctectomy and IPAA, either as part of a 2-stage or 3-stage RPC for refractory UC in a total of 48 patients [96-98]. Abdominal proctectomy or proctocolectomy was performed using single-incision or multiport laparoscopy. Transanally, the proctectomy was performed following (1) rectal mucosectomy in 2 patients with preoperatively identified dysplasia, followed by hand-sewn anastomosis, and (2) without mucosectomy in 46 patients with subsequent stapled pouch-to-anal anastomosis. Conversion to open proctectomy occurred in three cases, and the overall morbidity rate was 29% and included one anastomotic leak, bleeding, hematoma requiring drainage, and pneumonia [96, 98]. These preliminary reports have demonstrated the feasibility and procedural safety of a primarily transanal endoscopic approach to facilitate distal rectal transection in UC, but data on even short-term pouch function is lacking.

## **Rectal Cancer**

The first 2009 report of a laparoscopic-assisted transanal taTME procedure in a female patient with a T2N1 midrectal adenocarcinoma using a TEO platform was rapidly followed by a series of small pilot series and case series that confirmed the feasibility and preliminary oncologic

safety of this approach for rectal cancer based on the adequacy of the TME specimen, lymph node harvest, and surgical margin clearance [32, 34, 35]. This early experience supported the subsequent rapid adoption of this technique worldwide, with an increasing number of midsize series on preliminary outcomes of this approach for rectal cancer. The major drive behind wide adoption of taTME has been the unanimously agreed upon benefits provided by transanal endoscopic access including (1) improved selection of the distal resection margin through transanal access, which eliminates the need for multiple stapler firings to transect the rectum transabdominally; (2) enhanced exposure of the perirectal and mesorectal dissection planes which facilitates TME completion, particularly in the narrow male pelvis where transabdominal exposure of the distal-most rectum is typically severely impeded; and (3) transanal extraction when feasible, which eliminates the need for an abdominal extraction incision.

Current indications and contraindications for transanal TME are consistent with indications for laparoscopic or robotic TME and based on standard tumor staging and include resectable T1 tumors with high-risk histological features, T2 and T3 tumors. Although early IRB-approved taTME protocols excluded node-positive disease and metastatic disease, indications for taTME have expanded to include node-positive patients and metastatic disease when taTME if performed with curative intent. Current indications for taTME also highlight specific tumor and patient characteristics that are particularly well suited for a primarily transanal approach. While there is no specified upper BMI limit for this approach, taTME has becoming the preferred approach in morbidly obese male patients with resectable rectal tumors. For very low rectal tumors located at or below the dentate line, when not invading the external anal sphincter, taTME can be performed in continuity with rectal mucosectomy and partial or total intersphincteric resection in order to achieve negative distal resection margins, followed by hand-sewn anastomosis. For mid-rectal tumors located >5 cm above the AV and at least 1 cm above the top of the anorectal ring, full-thickness rectal transection can be performed starting just below a purse-string suture placed to occlude the rectum below the tumor, with preservation of the anal sphincters, and followed by stapled colorectal anastomosis. For upper rectal tumors, located  $\geq 10$  cm from the AV, taTME is not unanimously believed to confer added benefits to a laparoscopic or robotic approach, with the obvious exception of the obese male. For these tumors, in an effort to preserve rectal function, transanal rectal transection is performed well above the anorectal ring followed by transanal tumor-specific mesorectal excision (TSME) and stapled colorectal anastomosis.

Currently, taTME is contraindicated for T4 disease, and tumors with predicted involved CRM, unless there is evidence of significant downstaging on restaging MRI following neoadjuvant treatment. Transanal TME is also contraindicated for completely or near-completely obstructing rectal tumors. Another relative contraindication includes prior prostatectomy or other complex pelvic resections, prior pelvic radiation for gynecologic or urologic malignancies, and recurrent rectal cancer, particularly by less experienced operators, which substantially complicate identification of the correct dissection planes from the perineal approach and increase the risk of organ injury, particularly of the bladder and urethra [91].

The published experience of taTME to date demonstrates heterogeneity in taTME approach and setups currently used around the world. The same experience however highlights adherence to the same basic principles of TME dissection with high ligation of the IMA and IMV, sharp dissection along the plane between the presacral fascia and the mesorectum, autonomic nerve preservation, and integrity of the mesorectum during transanal, abdominal, hybrid dissection, and during transanal specimen extraction. Variations in taTME approach include differences in operative setup (1-team versus 2-team simultaneous or sequential approach), operative approach (hybrid versus pure taTME), type of abdominal approach if utilized (open, multiport versus hand-assisted versus single-incision laparoscopic or robotic), transanal platform used (rigid reusable versus disposable), and various types of coloanal reconstruction when utilized (hand-sewn or stapled end-end, side-end, coloanal J ouch, or IPAA).

Among 13 taTME series that included a minimum of 15 patients (N = 16-140 patients per series), a total of 574 patients underwent taTME for rectal cancer with 6% performed with APR and 94% with LAR [99–111]. The majority of cases were performed for carefully selected nonobstructing resectable tumors preoperatively staged as T1–T3, N0–N1 tumors and located average of 4–7.6 cm from the AV. The average BMI ranged from 22 to 28. With a few exceptions, the large majority of authors only used taTME for resection of low and mid-rectal tumors, with preferential use of laparoscopic or robotic techniques for upper rectal tumors.

Cumulatively, across all 13 studies, the mesorectum quality was described complete in 89%, near complete in 9%, and incomplete in 2%, with a rate of positive CRM ranging 0–13% (Table 22.3) and an average lymph node harvest ranging from 10 to 23. In addition, conversion rates were <5% (N = 16-140) [99–111]. These results (Table 22.4) demonstrated oncologic outcomes that are preliminarily comparable to historical open and laparoscopic TME outcomes with the benefit of exceedingly low conversion rates [24, 25, 27]. Intraoperative complications were noted in 7% and the conversion rate to laparotomy was 3%. Intraoperative complications were described by authors as occurring early

during their learning curve. It was noted that laparoscopic assistance, preferably when combined with transanal TME dissection (i.e., a 2-team approach), helped identify and avoid critical anatomical structures and may reduce operative time. In a cohort of 20 patients undergoing laparoscopicassisted taTME, Chen et al. reported that a 2-team approach in 8/12 patients significantly shortened the operative time of the 1-team approach (157.5 versus 226 min) [111]. Of note, to date, after Leroy and Zhang described the first two cases of a pure taTME with LAR in 2013 [112, 113], three small series including a total of 23 patients have described pure transanal TME for rectal cancer, which routine attempt is associated with a high conversion rate to abdominal assistance [107, 110, 114]. Across the 13 largest taTME series, the average length of hospital stay (LOS) was 8.1 days (range 4.5-14), with a 30-40% 30-day complication rate. At an average follow-up ranging 5-32 months, 8 of the 13 studies reported local and distal recurrences occurring 5-24 months postoperatively.

The international experience with taTME does not yet include a phase II or III clinical trial comparing taTME with laparoscopic TME. However, five retrospective studies compare outcomes of matched cohorts of patients who underwent transanal versus laparoscopic TME [104, 105, 115–117]. Fernandez-Hevia et al. performed a case-matched comparison of 37 cases of laparoscopic-assisted TME using a 2-team approach, and 37 cases of transanal TME and demonstrated no significant differences with respect to quality of the mesorectal specimen, lymph node harvest, resection margins, or intraoperative complications [116]. Of note, 2-team taTME was associated with significantly shorter mean operative time than laparoscopic TME (215 versus 252 min). A comparable 30-day postoperative complication rate was also observed, but a statistically significant lower readmission rate was noted in the taTME group (2% versus 6%) [116]. Velthuis et al. retrospectively matched 25 cases of laparoscopic-assisted taTME with 25 cases of laparoscopic TME and found that taTME was associated with a significantly higher rate of complete mesorectum than laparoscopic TME (92% versus 72%) [117]. The studies by de'Angelis, Perdawood, and Chen each retrospectively compared laparoscopic-assisted taTME with laparoscopic TME demonstrating shorter operative times and hospital stays with no differences in intraoperative and postoperative complications and oncologic outcomes [104, 105, 115].

Overall, taTME for rectal cancer has thus far been demonstrated to be safe and effective as an alternative oncologic surgical approach in resectable rectal cancer and is particularly well-suited for tumors of the low and mid-rectum, particularly in the obese male patient. Preliminary oncologic data from taTME series, including the analysis of the quality of mesorectal excision, have shown that taTME is associated with a high rate of complete mesorec-

	Serra-Aracil				Perdawood			Muratore				Chouillard	
Series	([108])	Burke [109]	Kang [107]	Buchs [106]	[105]	de'Angelis [104] Veltcamp [103]	Veltcamp [103]	[102]	Lacy [100]	Chen [111]	Tuech [140]	[110]	Rouanet [99]
Sex (M,F)	24,8	30,20	12,8	12,5	19,6	21,11	48,32	16,10	89,51	38,12	41,15	6,10	30,0
N	32	50	20	17	25	32	80	26	140	50	56	16	30
BMI	25	26	22.3	27.1	28	25.1	27.5	26.2	25.2	24.2	27	27.9	26
OR time (min)	240	267	200	315	300	195	204	241	*166	182	270	265	04
Tumor location from anal verge	5-10	4.4	9	2	4-10	2.5-5	1-10	3-6	$30\% \le 550\%$ 5.1-10 20% > 10	5.8	0-5	Mid/Low	<5 (20) 5–10 (10)
CRT	Y(16)	Y(43)	Y(6)	Y(6)	Y(7)	Y(27)	Y(26)	Y(19)	Y(90)	Y(50)	Y(47)	1	Y(29)
Final cancer	T0(2),	Stage T0(12),	Tis(2), T1-2(9),	T0(4),	T2(8), T3(16),	T1(3), T2(12),	T0(6), T1(3),	T0(5),	T0 (15),		T0(11), T1(7),	T0(1), T1(3),	T1(1),T2(8),
stage	T1(7), T2(10), N+(12), M1(1)	T1(2), T2(11), T3(21), T4(4), N+(16)	T3(3), T3(5), N(+7)	T2(8), T3(5), N(+7)	T4(1), N+(11)	T3(11), T4(2), N+(5)	T2(29), T3(42), N0 (44), N+(36)	T1(7),T2(6), T3(8), N+(7)	stage I (34), stage II (43), stage III (39), stage IV (9)	T2(13), T3/ T4(12), N+(17)	T2(16), T3(21), T4(1), N+(15)	T2(3), T3(7), T4(1), N+(5)	T3(18),T4(3), N+(16)
Complete TME (%)	93.8	72	06	94.1	80	84.4	88.8	88.5	97.1	1	83.9	1	100
Intraoperative complications (n)	0	Conversion (1), urethral injury (1), iliac injury (1)	Conversion (4), urethral injury (1), bleed (1)	Conversion (3)	Bleeding (2)	Conversion (1)	Bleed (2), bowel perforation (1)	0	0	Conversion (1), bleed (2), vaginal injury (1)	Conversion (3)	0	Conversion (2), urethral injury (2), air embolism (1)
Positive margin	0	6	0	5.9	4	9.4	2.5	0	6.4	4	5.4	0	13.3
Morbidity	44	62	25	30	60	25	39	23	34.3	26	25	18.8	26.6
<i>CRT</i> chemoradiation therapy *Performed by 2 experienced	liation therap 2 experience	<i>CRT</i> chemoradiation therapy *Performed by 2 experienced rectal cancer surgeons, working simultaneously, intra-abdominally and transanally	geons, working	simultaneousl	y, intra-abdom	inally and transa	mally						

 Table 22.3
 Largest published taTME case series

	COREAN [26]	COLOR II [25]	ACOSOG [24]	AlaCaRT [27]	taTME (Table 22.1)
Ν	340	1044	462	473	574
Laparoscopy	170	699	240	238	
Open	170	345	222	235	
Conversion (%)	0	17	11.3	9	2.6 (0-20)
Laparoscopy mesorectal quality (%)					
Complete	72.4	88	73	87	89% (72-100)
Near complete	19.4	9	19	10	9%
Incomplete	4.7	3	8	3	2%
Positive CRM (%)					4.4 (0–13.3)
Open	4.1	10	7.7	3	
Laparoscopic	2.9	10	12.1	7	
Positive distal margin (cm)					
Open	2	3	9.8	3.0	
Laparoscopic	2	3	9.8	2.6	
Lymph node harvest (n)					(10–23)
Open	18	14	16.5	N/A	
Laparoscopic	17	13	17.9	N/A	

**Table 22.4** Comparison of taTME published data and international laparoscopic versus open TME trials

tal specimens, which may or may not surpass that achieved using laparoscopic TME. Currently, the GRECCAR 11 in France and the international COLOR III trial are underway and will compare standard laparoscopic TME versus transanal TME [118].

#### **Emerging Applications of taTME**

Novel indications for a primarily transanal endoscopic rather than a transabdominal approach have been described. Bravo et al. recently described the case of Hartmann's reversal performed using a transanal approach to dissect the rectum in combination with abdominal assistance to fully mobilize the rectal stump, extract the specimen, and perform a stapled colorectal anastomosis [119]. Although T4 rectal cancer and recurrent rectal tumors constitute a relative contraindication to taTME due to concerns about oncologic adequacy of any procedure that does not achieve en bloc resection of the tumor and involved structures, in experience hands, transanal endoscopic strategies have recently been explored in reoperative complex pelvic surgery. In their series of 17 patients with unsalvageable anastomotic complications following LAR for rectal cancer (N = 10) or IPAA for UC or familial polyposis coli (FAP, N = 7) despite a number of prior surgical interventions, Borstlap et al. described successful redo coloanal anastomosis or redo IPAA in 82% (14/17) using open or laparoscopic-assisted transanal endoscopic dissection through a TAMIS platform [91]. In this series, no mortality occurred, intraoperative organ injury was noted in 1 patient (right hypogastric vein injury), and the overall morbidity rate was 53%

(9/17) including 2 anastomotic leaks, 4 pelvic abscesses, and 1 urethral stenosis requiring urinary diversion. Despite the high morbidity rate noted following these complex transanal procedures, intestinal continuity could be ultimately achieved in 71% (10/14) of patients at 6 months following redo transanal coloanal reconstruction using TAMIS.

# Preoperative Staging, Assessment, and Preparation

#### **Preoperative Assessment and Staging**

Accurate preoperative assessment and staging of rectal tumors is essential to the appropriate selection of patients for local excision or TES versus TME regardless of the specific approach to radical proctectomy. Accurate staging is essential to achieve R0 resections, and potential candidates for TES or taTME must undergo a comprehensive evaluation to localize and stage tumors accurately.

In addition to a complete medical and surgical history, colonoscopy with biopsies should be performed with careful pathology review to locally stage malignant lesions and identify high-risk histopathological features that might preclude local excision. A comprehensive physical exam and rigid or flexible proctoscopy should also be performed to confirm the tumor size, orientation along the rectal wall, distance from the AV, and extent of rectal wall involvement, as well as a digital rectal exam (DRE) to assess baseline anal sphincter tone, tumor fixity, and relationship of the tumor to the anorectal ring and potential tumor invasion of the anal sphincters. For TES, this assessment is essential to determine the extent and feasibility of the planned resection, anticipate potential operative challenges, optimize patient positioning, obtain the relevant instrumentation, and mitigate intraoperative complications in order to complete TES procedures safely. For taTME, this assessment is also critical to confirm whether a primary transanal approach is indicated and requires partial or complete en bloc internal sphincter resection in order to achieve R0 resection.

Rectal cancer staging also includes assessment of the pretreatment carcinoembryonic antigen (CEA) level; CT scans of the chest, abdomen, and pelvis to rule out distant disease; pelvic MRI; and possibly an ERUS. Pelvic MRI has largely supplanted ERUS as the preferred modality for rectal cancer staging because it provides critical and objective assessment of the CRM, tumor location in relation to anal sphincters, prostate, vagina, and even the peritoneal reflection, all essential for accurate local staging [120]. Patients with locally advanced rectal cancer should undergo neoadjuvant treatment, although in some select cases, short-course radiation or chemotherapy alone may be selected. Assessment of tumor response by pelvic MRI following completion of neoadjuvant treatment may have an impact on the operative plan, i.e., watch and wait if complete clinical response by pelvic MRI, sigmoidoscopy, and DRE is demonstrated versus radical response, with or without sphincter preservation.

With regard to predicting perioperative as well as functional outcomes and quality of life following LAR and APR, preoperative assessment should include patients' baseline activity level, defecatory function, as well as urinary and sexual function. Patients who are candidates for taTME with sphincter preservation should be extensively counseled regarding the need for temporary fecal diversion, and the anticipated high incidence of functional disturbances and quality of life issues from the LAR syndrome, particularly following coloanal anastomoses for very low rectal tumors that require partial or complete intersphincteric resection (ISR).

#### **Preoperative Preparation for TES**

Patients typically undergo mechanical bowel preparation, and enemas are also administered to ensure clearance of the rectum. Adequate bowel preparation is important to reduce the risk of pelvic sepsis in the event of peritoneal entry during full-thickness dissection. Standard perioperative parenteral antibiotic and thromboembolic prophylaxis is provided. A Foley catheter is inserted if procedures are anticipated to require longer than 2 h. General anesthesia with paralytics is usually recommended in order to avoid leakage of  $CO_2$  during procedures; however, spinal anesthesia has been demonstrated to be feasible and safe during TAMIS procedures [72]. Regarding intraoperative positioning, patients are either placed in the lithotomy position, prone, or in lateral decubitus position depending on the platform used, distance of the tumor from the AV, and tumor location along the rectum (Fig. 22.1a). TEM and TEO platforms are beveled metal proctoscopes with a built-in 30° angled scope fixed at the superior aspect of the platform, and patients are positioned such that rectal lesions are directly opposite the scope for optimal access (Fig. 22.1b). The majority of experienced operators will perform TEM, TEO, and TAMIS noncomplex cases with patients in lithotomy position regardless of tumor location. TAMIS does require a dedicated assistant for camera control (Fig. 22.1c). One relative indication for placing patients in prone position includes anticipation of peritoneal entry during full-thickness excision of high-risk rectal lesions [4].

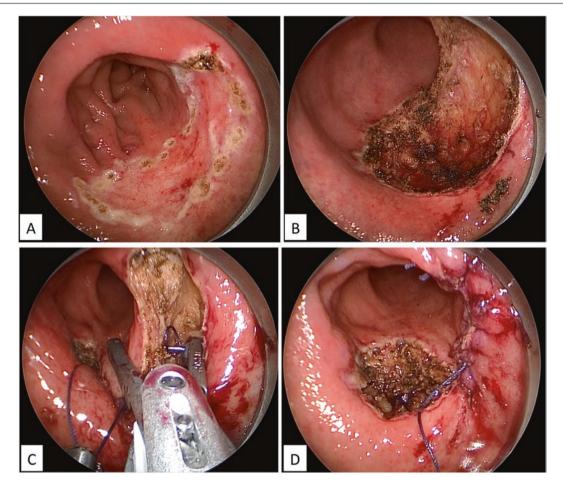
#### **Preoperative Preparation for taTME**

When performed for rectal cancer, as for any other TME approaches, taTME is typically deferred for 8-12 weeks following completion of neoadjuvant treatment. For restorative procedures including LAR and IPAA, patients undergo full mechanical bowel preparation with or without enemas, with or without oral antibiotic preparation, in addition to standard perioperative parenteral antibiotic and thromboembolic prophylaxis. A Foley catheter is inserted. As with other types of MIS TME, patients are placed in lithotomy position, although completion proctectomy using taTME has been described in cases with limited hip flexion [94]. Rectal lavage with dilute betadine is often performed either prior or immediately following occlusion of the rectum below the tumor with a rectal purse-string suture. The abdomen and perineum are both prepped and draped to allow for sequential or simultaneous abdominal and transanal procedures.

#### **Technical Considerations**

## **Procedural Steps for TES**

Prior to insertion of the TES platform, anal blockade with a local anesthetic is performed followed by gentle dilatation of the anus to prevent rectal trauma. The typical  $CO_2$  pressure needed to maintain an adequate pneumorectum ranges 10–15 mmHg, although high pressures might be needed to compensate for  $CO_2$  leakage [103, 108]. In TAMIS, depending on the port used, two or three 5-mm trocars can be inserted into the cannula of the port. In some cases, fixation sutures can be used for better secure the platform and prevent leakage or extrusion [12]. Regardless of the platform used, the same procedural steps are undertaken. The target lesion

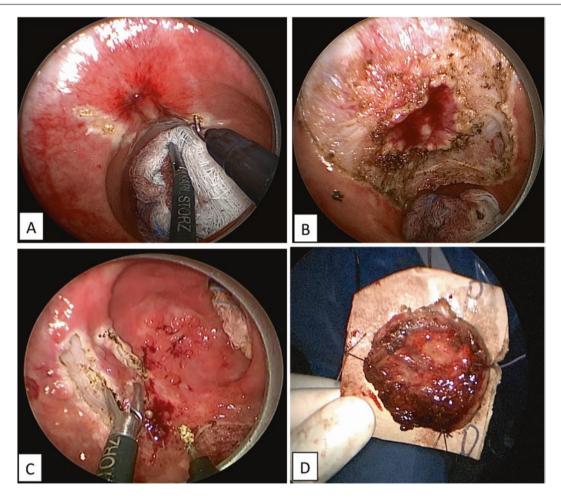


**Fig. 22.2** TES full-thickness excision of a residual posterior mid-rectal scar following neoadjuvant treatment of a locally invasive rectal cancer. The mid-rectal scar is scored circumferentially with monopolar cautery with 0.5–1 cm margins (**a**). Full-thickness dissection of the scar is carried

out with cautery until the mesorectum is reached (b). Following complete excision of the lesion and transanal specimen extraction, the rectal defect is closed using a suturing device (c). Full-thickness suture closure of the rectal defect proceeds until the defect is entirely closed (d)

is identified, and the rectal mucosa is scored circumferentially with monopolar energy with a 5-10 mm margin (Figs. 22.2a-d and 22.3a, b). Monopolar cautery and/or bipolar device is used for submucosal or full-thickness dissection of the lesion. Submucosal dissection can be used in conjunction with submucosal injection to elevate the pathology from the underlying muscular layer (Fig. 22.3c). Fullthickness dissection is carried out with an energy device through the transanal channel of the TEM/TEO platform or through a standard laparoscopic port in TAMIS. Dissection is continued perpendicular to the mucosal surface, through the entire thickness of the rectal wall, until the perirectal fat or mesorectum is reached (Figs. 22.2b and 22.3b). Of note, the use of CO<sub>2</sub> insufflation units that can evacuate cautery smoke while maintaining a constant high CO<sub>2</sub> flow to maintain a stable pneumorectum greatly enhances the image quality achieved during these procedures and the accuracy of the dissection [121]. Care must be taken if perirectal or mesorectal fat is excised in an attempt to acquire local lymphadenectomy. Wider rectal defects, although may be necessary, not only complicate closure but are also associated with high morbidity such as increase infection, bleeding, and suture line leak [122, 123]. In addition, wider rectal dissection which may be extended to include partial mesorectum may complicate or compromise the quality of salvage TME, if subsequently warranted. Detrimental residual inflammation and fibrosis along the mesorectal plane may be encountered during interval TME up to 3 months after TES [18]. Arolfo et al. also demonstrated that post-TEM perirectal histology demonstrated 62% (24/39) tissue fibrosis after extensive mesorectal dissection which may gravely impact subsequent LAR procedures [123].

Following complete dissection of the rectal lesion, the specimen is extracted through the platform and oriented for pathology as needed. Prior to rectal wall defect closure, particularly in the event of fecal spillage in the rectal wound, the area can be washed out with saline and irrigated with dilute iodine solution. The submucosal or full-thickness defect is



**Fig. 22.3** TES full-thickness excision of an anterior mid-rectal wall carcinoid tumor with the patient in lithotomy position (**a**). During full-thickness anterior wall dissection, care is taken not to injure the posterior vaginal wall (**b**). TES submucosal excision of clusters of rectal

polyps forms a retained rectal stump in a patient with FAP who underwent prior ileorectal anastomosis (c). Following complete TES excision of rectal lesions, the specimen is oriented (proximal and distal margins) for pathology

typically closed with running or interrupted absorbable monofilament sutures (Fig. 22.2c, d). A variety of suture materials are described including glycolide and trimethylene carbonate (Maxon, Codisan S.p.A.), polydioxanone (PDS, Ethicon Inc. Somerville, New Jersey, USA), polyglactin (Vicryl, Medtronic, Mansfield, MA, USA), and the V-loc barbed absorbable suture (Medtronic) which is a self-retaining suture that does not require a knot. In addition a variety of sutures and suturing devices are commercially available to overcome the technical challenges of laparoscopic suturing through transanal platforms. These include extracorporeal knot tiers and disposable automated suturing devices that facilitate knot tying such as the Endo Stitch<sup>TM</sup> device (Medtronic, Fig. 22.2c) and the Cor-Knot device (LSI Solutions, Victor, NY). In addition, the TEM instruments include an angled needle holder, and sutures can be secured with specialized silver bullets (Richard Wolf).

In the event of peritoneal entry during full-thickness rectal wall dissection, when transanal closure of the rectal wall defect is not technically possible or suspected not to be airtight, diagnostic laparoscopy should be performed with closure of any residual intraperitoneal rectal defects (Fig. 22.2). The peritoneal cavity defect can also be closed by a combined transanal and laparoscopic approach [17, 51]. Postoperatively, a gastrografin enema can be performed if a leak at the rectal closure site is suspected.

It is worthy to note that there is evidence that leaving rectal wall defects open does not increase the incidence of wound-related complications, as long as the defect is not associated with peritoneal entry [51, 124]. In a recent TAMIS series of 75 patients who underwent partial or full-thickness resection for rectal lesions located an average  $6.4 \pm 2.3$  cm from the AV, the authors found no differences in postoperative complications between the 40 patients whose defects were left open versus the 35 patients whose defects were suture closed [51]. However, it should be noted that only 6% of the 35 open rectal wall defects were located anteriorly compared to 28% of 38 closed rectal wall defects. Clearly, for larger, full-thickness lesions, and in particular for highrisk lesions where peritoneal entry has occurred or is suspected, closure of rectal defects should be performed to minimize the risk of septic complications.

#### **Procedural Steps for taTME**

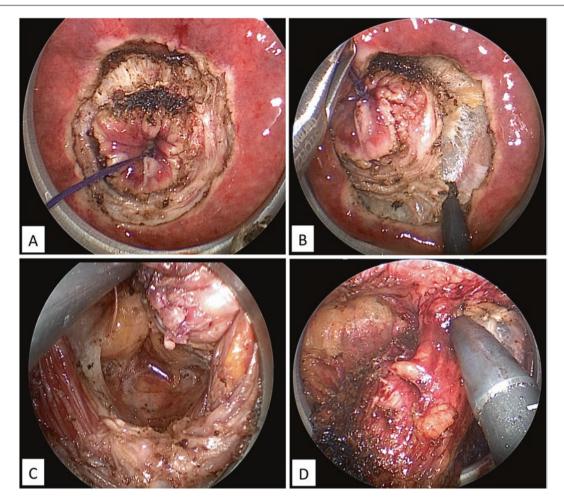
The large majority of taTME procedures are performed using a hybrid rather than pure transanal endoscopic approach. Abdominal assistance is provided using laparoscopic or open access (multiport, single port, hand-assisted, or robotic). Procedures can either be performed as a 1-team approach (with a single team performing the abdominal and transanal dissection sequentially), or a 2-team approach (with a transanal team and an abdominal team working simultaneously).

Most surgeons using a 1-team approach will start with the abdominal dissection first, with mobilization of the splenic flexure and high ligation of the inferior mesenteric artery and mobilization of the sigmoid and proximal rectum. The extent of subsequent pelvic dissection depends on the surgeon's preference, but is usually carried out until further rectal and mesorectal dissection becomes difficult, at which point the team will transition to transanal dissection. Occasionally, transanal dissection will be initiated first, followed by abdominal access and dissection. Whether a 1-team or 2-team approach is utilized, the steps of transanal dissection are dependent on the exact tumor level, i.e., distance from dentate line and anorectal ring. Following confirmation of the exact location of the tumor by digital and visual inspection with anoscopy, assessment of the required distal margin is made.

For tumors that are >2 cm above the dentate line, or  $\geq 1$  cm above the anorectal ring, a purse-string suture is placed at least 0.5 cm below from the rectal tumor either directly through a standard anoscope or endoscopically through the TES platform. In the latter case, the transanal platform is inserted first, followed by purse-string occlusion of the rectum. The purse-string usually consists of 2-0 Prolene or 2-0 Vicryl sutures (Fig. 22.4a). It is essential for the purse-string suture to be airtight to avoid distention of the proximal colon with CO<sub>2</sub> and spillage of fecal material or tumor cells on the operative field. Following insertion of the TES platform and purse-string occlusion of the rectum, pneumodistention with  $CO_2$  is achieved to a pressure of 10-15 mmHg. The rectal mucosa is scored circumferentially with monopolar cautery, followed by full-thickness incision of the rectal wall circumferentially (Fig. 22.4b). Fullthickness rectal and mesorectal mobilization is carried out

sequentially using monopolar cautery, with efforts to avoid the use of bipolar energy, which is not usually needed if dissection along the correct planes is carried out. Posterior mesorectal dissection is carried out along the avascular plane between the presacral fascia and the mesorectum (Fig. 22.4c), while anteriorly, dissection is carried between the rectovaginal fascia or rectoprostatic fascia (Fig. 22.4d). Laterally, care must be taken to avoid dissection of the pelvic sidewall during mesorectal mobilization, in order to preserve the nervi erigente. During the anterolateral dissection of the rectum and mesorectum, care must be taken to avoid injury to the neurovascular bundles bilaterally. It also serves as a landmark for the location of the prostate, if difficulties are encountered during anterior mobilization and identification of the posterior aspect of the prostate. Transanal TME dissection is carried out circumferentially and in a sequential pattern, and every effort is made to avoid dissecting too far along any given plan, in order to avoid plane distortion (Fig. 22.5a). Ultimately, anterior dissection is carried out cephalad until the peritoneal reflection is reached (Fig. 22.5b). Posteriorly, depending on the angulation of the sacral promontory, transanal dissection can usually be extended toward S1-S2 levels, and posterior dissection is completed using a combined abdominal and transanal approach in the 2-team approach. Even when using a 1-team approach, abdominal assistance during this step is critical, as it allows 2 teams to work simultaneously to complete mobilization of the rectum and merge the abdominal and transanal planes of dissection. Peritoneal entry is usually performed transanally and under laparoscopic visualization from above (Fig. 22.5b). Following complete mobilization of the TME specimen, the colon is either exteriorized transanally or through an abdominal incision, if the specimen is deemed too bulky to permit transanal extraction. Following transection of the specimen (Fig. 22.5c), colorectal stapled anastomosis can be usually carried out when the rectal transection was initiated well above the dentate line. Double purse-string circular stapled anastomosis technique is used, with either end-end, side-end, coloanal J pouch, or transverse coloplasty, depending on the surgeon's preference [125]. In the large majority of published taTME cases, a protective loop ileostomy is constructed, with the use of closed pelvic drains.

For tumors <2 cm from the dentate line or <1 cm from the top of the anorectal ring, intersphincteric resection, either partial or complete, is performed first in order to achieve negative distal resection margins. ISR is performed first through a Lone Star retractor (Lone Star Medical Products Inc., Houston, TX) and monopolar cautery, which is extended cephalad until the puborectalis muscle and bottom of the mesorectum are identified posteriorly, and the rectovaginal or rectoprostatic plane is visualized anteriorly. The anorectal stump is then closed with a purse-string suture, and the TES platform is inserted with  $CO_2$  insufflation. Further posterior



**Fig. 22.4** Transanal TME for a mid-rectal rectal cancer in a male patient treated with neoadjuvant treatment. Following purse-string occlusion of the rectal lumen below the tumor, the TEO platform is inserted, and the rectum is distended with  $CO_2$ . Full-thickness rectal dissection is carried out with monopolar cautery (**a**). Circumferential

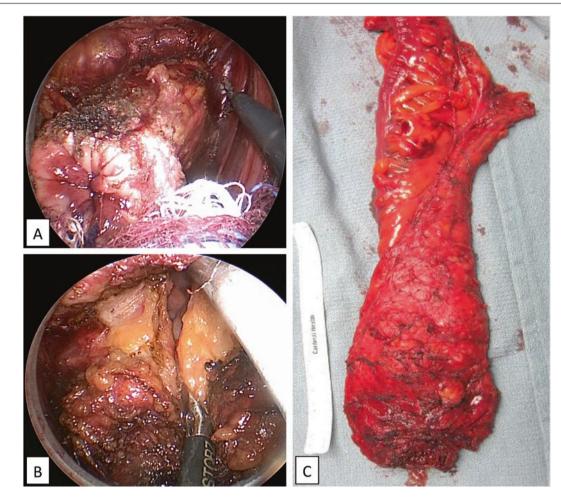
rectal and mesorectal dissection proceeds superiorly, until the puborectalis (**b**) and the plane between the presacral fascia and mesorectum (**c**) is identified posterolaterally. Anteriorly, dissection proceeds along the plane between the anterior rectum and the posterior aspect of the prostate (**d**)

dissection is needed posteriorly including division of the anococcygeal raphe in order to access the presacral space. Following identification of the inferior aspect of the mesorectum posteriorly, and the rectovaginal or rectoprostatic plane anteriorly, transanal TME can proceed as described above. Following specimen extraction, hand-sewn coloanal anastomosis is performed using either end-end, side-end, coloanal J pouch or transverse coloplasty with a protective ileostomy.

#### Alternative taTME Techniques

When transanal restorative proctocolectomy or proctectomy is performed with IPAA in ulcerative colitis of FAP, following laparoscopic mobilization of the colon and/or rectum, transanal procedures are initiated with placement of a Lone Star retractor and circumferential rectal mucosectomy starting at the level of the dentate line. Full-thickness rectal transection is then carried out at the level above the anorectal ring followed by rectal dissection either along the rectal wall or along the mesorectal plane [94]. Alternatively, a pursestring suture is placed transanally 3 cm above the dentate line followed by full-thickness incision of the rectal wall and close rectal dissection. Following specimen extraction, IPAA is performed with a single stapled technique [96].

With transanal endoscopic proctectomy or proctocolectomy with APR, if performed, the colon is mobilized followed by ligation of the inferior mesenteric vessels, and mobilization of the rectosigmoid colon and TME dissection are initiated using an open, laparoscopic, or robotic transabdominal approach. Intersphincteric or standard proctectomy is carried out either simultaneously (2-team) or sequentially with the abdominal dissection (1-team). The anus is suture closed followed by intersphincteric or extrasphincteric proctectomy using a standard perineal instruments. Transanal



**Fig. 22.5** Transanal TME for a mid-rectal rectal cancer in a male treated with neoadjuvant treatment. Circumferential rectal and meso-rectal dissection proceeds cephalad toward the peritoneal cavity (**a**). The anterior peritoneal reflection is incised anteriorly under visualization and assistance by the abdominal team in a 2-team approach (**b**).

Following completion of the TME using a combined transanal and abdominal approach, the specimen is exteriorized, transected, and sent to pathology for evaluation according to standard TME protocol assessment. Meanwhile, colorectal or coloanal anastomosis is completed

dissection is extended superiorly until the perineal body has been divided and the rectoprostatic or rectovaginal plane is identified. Posteriorly, dissection is carried out until the puborectalis is visualized. The TES platform is then inserted with CO<sub>2</sub> insufflation, and further rectal dissection is carried out endoscopically. Posteriorly, dissection can be carried out either close to the rectal wall, within the mesorectal plane, or along the plane between the mesorectum and presacral fascia, depending on the pathology and surgeon's preference. Following the proctectomy, the specimen is exteriorized followed by perineal wound closure in layers. Another alternative transanal completion proctectomy for benign disease consists in initiating transanal endoscopic full-thickness rectal transection through the TES platform starting well above the dentate line, followed by completion of the rectal dissection and mesorectal dissection, and exteriorization of the specimen. Intersphincteric dissection of the short anorectal

stump is then carried out, following by exteriorization of the specimen and perineal wound closure [92].

#### **Specimen Extraction**

The specimen can be extracted transanally or transabdominally depending on the size [99]. A wound protector is recommended by most to avoid implantation of tumor cells. Finally, a protective diverting loop ileostomy is recommended by most surgeons. Transanal extraction could result in untoward shearing of the mesentery, namely, the marginal artery with the potential, to seed exfoliated tumor cells. Furthermore, it can result in shear stress on proximal arterial inflow and may result in conduit ischemia compromising the anastomosis when restoring gastrointestinal continuity. To minimize marginal artery injuring during transanal specimen extraction, the mesentery at the level chosen for proximal division should be performed intracorporeally with division of the marginal artery [126].

## **Closure of Rectal Defect**

The submucosal or full-thickness defect is commonly closed with absorbable sutures. A variety of sutures and suturing devices are commercially available to overcome the technical challenges created by the narrow, rigid platform. A circular staple like the EEA (Medtronic) can be used in establishing the colorectal anastomosis in taTME. It is worthy to note that closing submucosal, posterior, or distal full thickness defects is not associated with increased morbidity [127].

### Postoperative Care and Surveillance

Following TES, patients are usually discharged on the same day of surgery, especially if transanal endoscopic resection was submucosal or full-thickness but well below the peritoneal reflection. In patients in whom more complex fullthickness TES was performed, overnight observation is usually recommended, especially if peritoneal entry was clearly visualized and repaired, or suspected based on evidence of pneumoperitoneum at the end of the case. A regular diet can be safely reinstated after surgery, and no additional antibiotics are typically given. Routine imaging is not recommended in the absence of clinical indication. The low postoperative morbidity following TES procedures is reflected in the short hospital stay and minimal postoperative pain requirement. Up to 50% of patients undergoing TEM for rectal cancer are safely discharged on the day of surgery as reported in several recent series [128]. When patients are admitted for observation, length of stay ranges 0-5 days due to management of major medical comorbidities or observation following cases of peritoneal entry [128].

Following routine postoperative follow-up, specific surveillance depends on the final pathology. Patients with completely resected adenomas and other benign pathologies are usually reassessed endoscopically within 6–12 months postoperative to confirm early recurrence. In patients who have undergone complete excision of T1 rectal tumors, in the absence of high-risk pathologic features, patients are observed, and surveillance follows NCCN guidelines with clinical evaluation, CEA, and flexible sigmoidoscopy every 3–4 months for the first 3 years and every 6 months for the following 2 years until year 5 [129]. In addition, yearly CT scans are performed at 1 year followed by 3 years postresection. Some physicians have also advocated yearly pelvic MRI for 5 years to assess for locoregional recurrence.

In patients who have undergone TES for T1 tumors with positive margins or high-risk histopathological features, completion TME is recommended. In patients who decline radical resection or are poor surgical candidates, adjuvant chemoradiation may be offered.

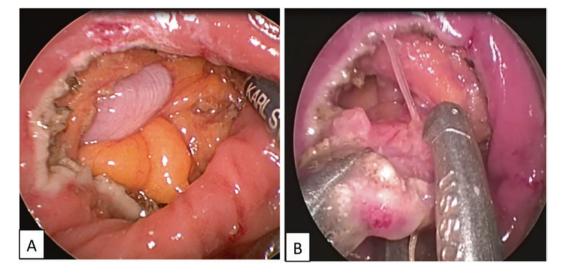
Patients undergoing taTME are managed using the same enhanced recovery protocols as with any other minimally invasive TME procedures. Removal of the Foley catheter is usually delayed beyond the standard 24–48 h protocols in patients with risk factors for urinary retention, including males with an enlarged prostate, benign prostatic hyperplasia (BPH), and patients who have undergone deep perineal dissection and very low LAR. Additional parenteral antibiotics are given as indicated, and patients are discharged home according to standard protocols once adequate pain control, oral fluid intake, and stoma function have been achieved.

Postoperative oncologic surveillance after taTME follows standard NCCN guidelines for rectal cancer, as outlined above. Ileostomy closure is deferred until completion of adjuvant treatment as indicated.

#### **TES Complications**

#### **Perioperative Morbidity and Mortality**

Over three decades of published short- and long-term outcomes from large clinical series have consistently demonstrated the exceedingly low mortality and low morbidity associated with TEM and TEO, especially relative to that associated with TME [8, 24, 25, 27, 28]. The largest TEM and TEO series that included 262-693 patients have reported a <1% mortality rate and 5-20% 30-day morbidity rates, with the most common complications including transient urinary retention (5-10%) and postoperative bleeding (1-13%), the latter rarely requiring reoperative intervention [8, 9, 130]. The majority of TES-related complications are relatively minor and transient, with major complications composed of less than 10% [8, 9, 37, 127]. Other reported complications of TES include conversion to TAE or abdominal procedures, suture line dehiscence, which range from minor defects managed conservatively with antibiotics and bowel rest, to major defects with intraperitoneal leakage and sepsis, requiring washout and fecal diversion. In a prospective multicenter study of 588 patients who underwent TEM resection, Guerrieri et al. reported a 5.9% incidence of partial disruption or leak of the suture line that were all successfully managed conservatively with antibiotics [131]. Additional adverse events include infectious complications (urinary tract infections and perirectal and presacral abscess), retrovisceral fistulas, and rectal stenosis. Rare complications include organ injury, with two cases of urethral injury reported following TEM resection of anterior rectal lesions



**Fig.22.6** Full-thickness transanal excision of an anterior upper rectal lesion is complicated by peritoneal entry with visualization of the sigmoid colon (**a**). The full-thickness rectal defect was closed transanally with absorbable sutures using a suturing device (**b**)

in a series of 402 TEM cases [132]. In the largest multicenter series published to date, among 693 combined who underwent TEM or TEO procedures, conversion rate to TAE or abdominal procedures was 4.3%, and the 30-day morbidity was 11.1%, with hemorrhage and suture dehiscence being the most common surgical complications [9].

In the more limited literature on TAMIS, the published incidence of postoperative complications ranges 0–25% across series, with bleeding and urinary retention reported as the most common complications (Table 22.1) [129]. A recent review of 16 TAMIS series across a total of 390 patients reported a 10.8% complication rate, including a 2.7% incidence of bleeding and 0.5% incidence of suture dehiscence [129]. There were no deaths, and the conversion rate to either TAE, TEM, or laparoscopy was 2.3%. In the absence of comparative studies evaluating TEM/TEO versus TAMIS approaches, no conclusions can be drawn regarding differences in morbidity, mortality, or length of stay between approaches.

## **Peritoneal Entry**

Peritoneal entry (PE) during TES, either unplanned or anticipated based on location and/or extent of the rectal lesion, often complicates TES procedures and requires careful management. Earlier TEM reports considered PE to be a major complication requiring conversion to laparotomy with lavage, radical resection with or without fecal diversion [85]. From an oncologic standpoint, PE was also thought to increase the risk of tumor cell spillage and peritoneal tumor implants during rectal cancer excision [86]. In TEM series by the most experienced centers with more than 300 included patients, that rate of PE ranges 5 to 10.7% [6]. The studies have demonstrated that PE occurred more commonly during full-thickness resection of lesions located in the upper rectum, anteriorly or laterally along the rectal wall, and during resection of circumferential or near-circumferential rectal lesions [133]. Several studies have reported no increased morbidity relative to TEM cases without PE and no adverse short- or long-term oncologic outcomes in patients in whom peritoneal entry occurred during TEM excision of rectal tumors [68, 88]. As a result, tumor location 10 cm or more from the AV is no longer considered a contraindication to TEM surgery, as long as full-thickness suture closure of rectal defects can be achieved transanally by experienced operators [86, 88]. Entry into the peritoneal cavity during TES procedures can be very challenging to close transanally as a result of collapse of the rectum with leakage of CO<sub>2</sub> into the abdominal cavity, especially if patients are in lithotomy position (Fig. 22.6a, b). Over time however, experienced centers with large TEM and TEO series have demonstrated that conversion rates following peritoneal entry have decreased, with conversion rates ranging from 0 to 40% but averaging 10% or less [68]. Even less has been published regarding the experience of PE during TAMIS. The systematic TAMIS review of 367 procedures reported inadvertent PE in only four cases (1.025%), and the average distance of rectal lesions from the AV was 7.6 cm [129]. All four cases of PE occurred during dissection of upper rectal lesions, and two (50%) could be closed transanally, while the others required abdominal conversion. Only three TAMIS series that include 32-75 patients have reported an incidence of PE ranging from 2 to 9.4% [11, 17, 51]. Among the seven cases of PE during TAMIS across all three studies, six (86%) required conversion to laparoscopy or laparotomy from inability to

effectively close the rectal wall defect. This may reflect the long learning curve required for managing these complex rectal lesions and the currently small experience with TAMIS to date. But it may also reflect technical limitations of shorter TAMIS platforms, which do not always permit adequate retraction and exposure of the proximal rectum [54].

#### **Functional Outcomes**

With respect to functional outcomes following TES, anorectal dysfunction ranges from <1 to 4% and is typically transient [5, 8, 130]. In patients with normal anal sphincter function at baseline, transient decrease in resting and squeeze anal sphincter pressures proportional to the duration of procedures have been documented, with complete resolution at 12 months postoperatively and no long-term impact on anorectal function [134, 135]. By virtue of the prolonged stretching of the anal sphincter by 4 cm wide rigid platforms, it has been hypothesized that more pliable disposable transanal platforms may have a less detrimental impact on anorectal function. On the other hand, there is also concern that functional outcomes might be worse as compared to traditional rigid platform TES because of more extreme movements and stretch allowed by the flexible platform. Thus far, although limited, published data on short-term functional outcomes following TAMIS have been comparable to historical TEM reports. One small prospective study conducted by Schiphorst et al. assessed functional outcomes in 37 patients following TAMIS using FISI score collected preoperatively and at 3, 6, 9, and 12 months postoperatively [19]. Among 18 patients with normal fecal continence at baseline, no change in Fecal Incontinence Severity Index (FISI) scores was found in 83%, suggesting preserved long-term anorectal function following TAMIS procedures, while several TEM series demonstrated no significant changes in the Fecal Incontinence Severity Index (FISI) or Fecal Incontinence Quality of Life (FIQL) scores at 6 weeks postoperatively and return to baseline of the colorectal functional outcome (COREFO) at 12 weeks postoperatively [136, 137]. However, two series reported persistent sphincter dysfunction following TEM based on long-term assessment using either St. Mark's or Wexner incontinence scores, with operative time, preoperative radiotherapy, and perioperative complications acting as independent risk factors [138, 139].

## **Complications of taTME**

Cumulatively, across 13 published taTME series with sample size ranging from 16 to 140 patients, conversion to open laparotomy was noted in 3% with an additional 7% incidence of intraoperative complications including hemor-

rhage, rectal and vaginal perforations, four cases of urethral injuries in males, and one ureteral injury, and prostatic injury, as well as cases of delayed anastomosis due to questionable viability of the colonic conduit (Table 22.3). In two of the four cases of urethral injuries, the injuries were described in taTME cases involving low, anterior, and/or bulky rectal and anterior tumors in males, with difficulties identifying the correct dissection plane and relatively early along the surgeon's learning curve [99]. In one case, the injury was treated nonoperatively, two were repaired intraoperatively, and one required urethroplasty 1 month postoperatively [99, 107, 109]. It was noted that laparoscopic assistance at this stage helped identify and avoid critical anatomical structures. The overall mortality rate across all large taTME series was less than 1%, and the 30-day morbidity rate was 33.7% with major complications including anastomotic leaks (8.6%), pelvic sepsis (<5%), and minor complications including transient urinary retention and urinary tract infection, ileus, obstruction, surgical site infection, and rectal stricture. Of note, transient urinary retention was noted at a rate ranging from 3 to 9% across series, with resolution within 3 months following taTME procedures [99, 102, 116, 140, 141].

Regarding functional outcomes, at a follow-up ranging from 5 to 32 months, 5 of the 13 studies reported fecal incontinence with average Wexner score of 6.9 (3–18). Rouanet and colleagues reported 60% incidence of fecal incontinence at 1-year follow-up with median Wexner score of 11 with gas incontinence of 35% and liquids of 15% [99]. In a series of 56 patients, Tuech reported a 5% incidence of severe incontinence with one patient converted to a colostomy 1 year postoperatively. The median Wexner score was 5 overall [140]. Regarding oncologic outcomes, eight out of the 13 studies reported local and distant recurrence with 45 cases of local or distant recurrences. The time to recurrence ranged from 5 to 24 months.

#### **Pearls and Pitfalls**

#### **Management of Peritoneal Entry During TES**

Rectal lesion that is particularly high risk for peritoneal entry during full-thickness resection includes anterior and lateral lesions located in the upper rectum or rectosigmoid, as well as circumferential or near-circumferential lesions [86–88]. Depending on the size of the peritoneal defect, rapid accumulation of  $CO_2$  into the abdominal cavity can result in the collapse of the pneumorectum. When patients are positioned in lithotomy, this can significantly complicate closure of the rectal wall defect. Several strategies can be used to mitigate the critical loss of pneumorectum such as placement of an abdominal Veress needle or trocar to decompress the pneu-

moperitoneum and increase in the transanal CO<sub>2</sub> insufflation pressure. Ideally, the rectal defect should be closed, at least partially, as rapidly as possible in order to minimize ongoing loss of pneumorectum (Fig. 22.6a, b). Some operators also recommend placement of stay sutures near high-risk lesions prior to full-thickness rectal dissection, in order to facilitate quick identification of the edges of the rectal defect for rapid closure. Most importantly, preemptive positioning of patients in prone position in anticipation of possible peritoneal entry helps mitigate the degree of CO<sub>2</sub> leakage into the abdominal cavity. The prone position helps tamponade the volume of CO<sub>2</sub> loss and helps maintain a stable pneumorectum to facilitate closure of the full-thickness rectal wall defect [68]. Following closure of the rectal defect, if there is concern that the rectal closure is not entirely airtight, laparoscopy should be performed to evaluate and/or reinforce the closure, and a leak test can also be performed at that time.

## taTME Dissection for Very Low Rectal Tumors in a Male Patient

It has been well established among taTME experts that although taTME is best suited for low rectal tumors in obese males in particular, these cases are the most complex cases with the longest learning curve, by virtue of the lack of familiarity of surgeons with the deep perineal anatomy from an endoscopic approach, and [2] variable expertise with rectal mucosectomy or intersphincteric resections, which is a necessary skillset during sphincter-preserving taTME when a negative distal margin must be achieved for very low tumors. When taTME is used for low rectal tumors that require ISR (tumors <2 cm from the dentate line or <1 cm from the top of the anorectal ring), it is recommended to initiate intersphincteric dissection using an open transanal approach using monopolar cautery, until critical structures have been clearly identified, including the puborectalis posteriorly with the inferior aspect of the mesorectum and the posterior aspect of the vagina or prostate anteriorly. Several authors have described having initiated intersphincteric dissection endoscopically, through the transanal platform. Endoscopic dissection is carried out for a few centimeters cephalad followed but purse-string closure of the anorectal stump and completion of endoscopic TME. Early in the operator's learning curve however, endoscopic ISR has been associated with a high risk of erroneous dissection into an incorrect plane anteriorly, where, as in the case of a difficult APR, dissection above the perineal body can result in dissection too close to the prostate, or worse, dissection above the prostate and into the membranous or prostatic urethra. This is primarily related to unfamiliarity of surgeons with this perineal approach and the periprostatic anatomy.

#### taTME Operative Setup

Based on the taTME reports published to date, procedures can be performed using as 1-team approach, whereby the same operative team performs transanal TME followed by abdominal mobilization of the splenic flexure, inferior mesenteric vessel transection, left colon and rectosigmoid colon mobilization and completion of the TME, or vice versa (abdominal mobilization first followed by transanal dissection). The alternative 2-team approach utilizes 2 surgical teams that work simultaneously from the start by combining abdominal and transanal dissection, or sequentially, where both teams work simultaneously only during the critical taTME portions which include peritoneal entry from the transanal side followed by completion of the TME followed by transanal or transabdominal specimen extraction. Several studies suggest potential advantages of a 2-team simultaneous approach including reduction in operative time [100, 107]. Another potential advantage is avoidance/reduction of intraoperative complications by improving visualization of deep pelvic structures by combining view from the abdominal and transanal sides, which may increase the accuracy of the dissection. A 2-team approach is difficult to organize in many hospitals, with logistical difficulties staffing cases with two attendings for the several hours required for taTME. When a simultaneous 2-team approach is not practical, it is recommended that at the very least, the transanal team employs a second team during the critical time needed for completion of the rectal and mesorectal mobilization following peritoneal entry by the transanal team and during specimen extraction and confirmation of the viability of the colonic conduit prior to anastomosis.

#### Conclusion

Since the first description of TEM over 30 years ago, the operative management of rectal diseases has evolved from radical proctectomy to minimally invasive abdominal techniques that most recently have incorporated transanal endoscopic approaches. Driven by the need for improved surgical outcomes in patients with rectal cancer, and steady technological and conceptual innovations in the field of minimally invasive surgery, TES had rapidly expanded the range and complexity of minimally invasive colorectal applications that can be performed using a primarily transanal endoscopic approach. The recent development of taTME and its rapid adoption worldwide based on favorable preliminary oncologic results is a reflection of ongoing efforts to facilitate the safe completion of otherwise exceedingly complex pelvic procedures and possibly move the field one step closer to NOTES in minimizing the trauma and limitations of transabdominal incisions and dissection. Several randomized trials

of taTME versus laparoscopic TME are underway to further evaluate the safety and efficacy of taTME, which may become the new standard of care in the surgical management of mid- and low rectal tumors.

### References

- Moghadamyeghaneh Z, Phelan M, Smith BR, Stamos MJ. Outcomes of open, laparoscopic, and robotic abdominoperineal resections in patients with rectal cancer. Dis Colon Rectum. 2015;58(12):1123–9.
- Reshef A, Lavery I, Kiran RP. Factors associated with oncologic outcomes after abdominoperineal resection compared with restorative resection for low rectal cancer. Dis Colon Rectum. 2012;55(1):51–8.
- Burghardt J, Buess G. Transanal endoscopic microsurgery (TEM): a new technique and development during a time period of 20 years. Surg Technol Int. 2005;14:131–7.
- Morino M, Arezzo A, Allaix ME. Transanal endoscopic microsurgery. Tech Coloproctol. 2013;17(S1):55–61.
- Bignell MB, Ramwell A, Evans JR, Dastur N, Simson JNL. Complications of transanal endoscopic microsurgery (TEMS). a prospective audit. Colorectal Dis. 2010;12:e99–103.
- Allaix ME, Arezzo A, Caldart M, Festa F, Morino M. Transanal Endoscopic microsurgery for rectal neoplasms: experience of 300 consecutive cases. Dis Colon Rectum. 2009;52(11):1831–6.
- Barendse RM, Doornebosch PG, Bemelman WA, Fockens P, Dekker E, de Graaf EJR. Transanal employment of single access ports is feasible for rectal surgery. Ann Surg. 2012;256(6):1030–3.
- Kumar AS, Coralic J, Kelleher DC, Sidani S, Kolli K, Smith LE. Complications of transanal endoscopic microsurgery are rare and minor. Dis Colon Rectum. 2013;56(3):295–300.
- Barendse RM, Dijkgraaf MG, Rolf UR, Bijnen AB, Consten ECJ, Hoff C, et al. Colorectal surgeons' learning curve of transanal endoscopic microsurgery. Surg Endosc. 2013;27(10):3591–602.
- Clancy C, Burke JP, Albert MR, O'Connell PR, Winter DC. Transanal endoscopic microsurgery versus standard transanal excision for the removal of rectal neoplasms. Dis Colon Rectum. 2015;58(2):254–61.
- Albert MR, Atallah SB, de Beche-Adams TC, Izfar S, Larach SW. Transanal minimally invasive surgery (TAMIS) for local excision of benign neoplasms and early-stage rectal cancer. Dis Colon Rectum. 2013;56(3):301–7.
- Atallah S, Albert M, Larach S. Transanal minimally invasive surgery: a giant leap forward. Surg Endosc. 2010;24(9):2200–5.
- Mendes CRS, de Miranda Ferreira LS, Sapucaia RA, Lima MA, Araujo SEA. Transanal minimally-invasive surgery (TAMIS): technique and results from an initial experience. J Coloproctol. 2013;33(4):191–5.
- Michalik M, Bobowicz M, Orlowski M. Transanal endoscopic microsurgery via triport access system with no general anesthesia and without sphincter damage. Surg Laparosc Endosc Percutan Tech. 2011;21(6):308–310.
- Atallah S, Parra-Davila E, de Beche-Adams T, Albert M, Larach S. Excision of a rectal neoplasm using robotic transanal surgery (RTS): a description of the technique. Tech Coloproctol. 2012;16(5):389–92.
- Lee T-G, Lee S-J. Transanal single-port microsurgery for rectal tumors: minimal invasive surgery under spinal anesthesia. Surg Endosc. 2013;28(1):271–80.
- 17. McLemore EC, Weston LA, Coker AM, Jacobsen GR, Talamini MA, Horgan S, et al. Transanal minimally invasive sur-

gery for benign and malignant rectal neoplasia. Am J Surg. 2014;208(3):372-81.

- Hompes R, McDonald R, Buskens C, Lindsey I, Armitage N, Hill J, et al. Completion surgery following transanal endoscopic microsurgery: assessment of quality and short- and long-term outcome. Colorectal Dis. 2013;15(10):e576–81.
- Schiphorst AHW, Langenhoff BS, Maring J, Pronk A, Zimmerman DDE. Transanal minimally invasive surgery. Dis Colon Rectum. 2014;57(8):927–32.
- Sevá-Pereira G, Trombeta VL, Capochim Romagnolo LG. Transanal minimally invasive surgery (TAMIS) using a new disposable device: our initial experience. Tech Coloproctol. 2013;18(4):393–7.
- Coco C, Valentini V, Manno A, Rizzo G, Gambacorta MA, Mattana C, et al. Functional results after radiochemotherapy and total mesorectal excision for rectal cancer. Int J Colorectal Dis. 2007;22(8):903–10.
- Peeters KCMJ, Marijnen CAM, Nagtegaal ID, Kranenbarg EK, Putter H, Wiggers T, et al. The TME trial after a median follow-up of 6 years. Ann Surg. 2007;246(5):693–701.
- Rickles AS, Dietz DW, Chang GJ, Wexner SD, Berho ME, Remzi FH, et al. High rate of positive circumferential resection margins following rectal cancer surgery. Ann Surg. 2015;262(6):891–8.
- Fleshman J, Branda M, Sargent DJ, Boller AM, George V, Abbas M, et al. Effect of laparoscopic-assisted resection vs open resection of stage II or III rectal cancer on pathologic outcomes. JAMA. 2015;314(13):1346–10.
- 25. van der Pas MH et al. Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. Lancet Oncol. 2013;14(3):210–8.
- 26. Kang S-B, Park JW, Jeong S-Y, Nam BH, Choi HS, Kim D-W, et al. Open versus laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): short-term outcomes of an open-label randomised controlled trial. Lancet Oncol. 2010;11(7):637–45.
- Stevenson ARL, Solomon MJ, Lumley JW, Hewett P, Clouston AD, Gebski VJ, et al. Effect of laparoscopic-assisted resection vs open resection on pathological outcomes in rectal cancer. JAMA. 2015;314(13):1356–8.
- Guillou PJ, Quirke P, Thorpe H, Walker J, Jayne DG, Smith AM, et al. Short-term endpoints of conventional versus laparoscopicassisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. Lancet. 2005;365(9472):1718–26.
- Corcione F, Esposito C, Cuccurullo D, Settembre A, Miranda N, Amato F, et al. Advantages and limits of robot-assisted laparoscopic surgery: preliminary experience. Surg Endosc. 2004;19(1):117–9.
- 30. Collinson FJ, Jayne DG, Pigazzi A, Tsang C, Barrie JM, Edlin R, et al. An international, multicentre, prospective, randomised, controlled, unblinded, parallel-group trial of robotic-assisted versus standard laparoscopic surgery for the curative treatment of rectal cancer. Int J Colorectal Dis. 2011;27(2):233–41.
- Emhoff IA, Lee GC, Sylla P. Transanal colorectal resection using natural orifice translumenal endoscopic surgery (NOTES). Dig Endosc. 2013;26:29–42.
- 32. Sylla P, Bordeianou LG, Berger D, Han KS, Lauwers GY, Sahani DV, et al. A pilot study of natural orifice transanal endoscopic total mesorectal excision with laparoscopic assistance for rectal cancer. Surg Endosc. 2013;27(9):3396–405.
- Sylla P, Rattner DW, Delgado S, Lacy AM. NOTES transanal rectal cancer resection using transanal endoscopic microsurgery and laparoscopic assistance. Surg Endosc. 2010;24(5):1205–10.
- de Lacy AM, Rattner DW, Adelsdorfer C, Tasende MM, Fernández M, Delgado S, et al. Transanal natural orifice transluminal endoscopic surgery (NOTES) rectal resection: "down-to-up" total

mesorectal excision (TME)—short-term outcomes in the first 20 cases. Surg Endosc. 2013;27(9):3165–72.

- Dumont F, Goéré D, Honoré C, Elias D. Transanal endoscopic total mesorectal excision combined with single-port laparoscopy. Dis Colon Rectum. 2012;55(9):996–1001.
- Heintz A, Mörschel M, Junginger T. Comparison of results after transanal endoscopic microsurgery and radical resection for T1 carcinoma of the rectum. Surg Endosc. 1998;12(9):1145–8.
- de Graaf EJR, Doornebosch PG, Tetteroo GWM, Geldof H, Hop WCJ. Transanal endoscopic microsurgery is feasible for adenomas throughout the entire rectum. Dis Colon Rectum. 2009;52(6):1107–13.
- Allaix ME, Arezzo A, Cassoni P, Famiglietti F, Morino M. Recurrence after transanal endoscopic microsurgery for large rectal adenomas. Surg Endosc. 2012;26(9):2594–600.
- Léonard D, Colin J-F, Remue C, Jamart J, Kartheuser A. Transanal endoscopic microsurgery: long-term experience, indication expansion, and technical improvements. Surg Endosc. 2011;26(2):312–22.
- 40. Guerrieri M, Baldarelli M, Organetti L, Grillo Ruggeri F, Mantello G, Bartolacci S, et al. Transanal endoscopic microsurgery for the treatment of selected patients with distal rectal cancer: 15 years experience. Surg Endosc. 2008;22(9):2030–5.
- 41. Barendse RM, van den Broek FJC, Dekker E, Bemelman WA, de Graaf EJR, Fockens P, et al. Systematic review of endoscopic mucosal resection versus transanal endoscopic microsurgery for large rectal adenomas. Endoscopy. 2011;43(11):941–9.
- 42. Barendse RM, van den Broek FJC, van Schooten J, Bemelman WA, Fockens P, de Graaf EJR, et al. Endoscopic mucosal resection vs transanal endoscopic microsurgery for the treatment of large rectal adenomas. Colorectal Dis. 2012;14(4):e191–6.
- 43. Serra-Aracil X, Caro-Tarrago A, Mora-López L, Casalots A, Rebasa P, Navarro-Soto S. Transanal endoscopic surgery with total wall excision is required with rectal adenomas due to the high frequency of adenocarcinoma. Dis Colon Rectum. 2014;57(7):823–9.
- Schäfer H, Baldus SE, Hölscher AH. Giant adenomas of the rectum: complete resection by transanal endoscopic microsurgery (TEM). Int J Colorectal Dis. 2006;21(6):533–7.
- 45. van den Boezem PB, Kruyt PM, Stommel MWJ, Tobon Morales R, Cuesta MA, Sietses C. Transanal single-port surgery for the resection of large polyps. Dig Surg. 2011;28(5–6):412–6.
- 46. Lim S-B, Seo S-I, Lee JL, Kwak JY, Jang TY, Kim CW, et al. Feasibility of transanal minimally invasive surgery for mid-rectal lesions. Surg Endosc. 2012;26(11):3127–32.
- Ragupathi M, Maele DV, Nieto J, Pickron TB, Haas EM. Transanal endoscopic video-assisted (TEVA) excision. Surg Endosc. 2012;26(12):3528–35.
- Bridoux V, Schwarz L, Suaud L, Dazza M, Michot F, Tuech J-J. Transanal minimal invasive surgery with the EndorecTM trocar: a low cost but effective technique. Int J Colorectal Dis. 2013;29(2):177–81.
- 49. Emre Gorgun I, Aytac E, Costedio MM, Erem HH, Valente MA, Stocchi L. Transanal endoscopic surgery using a single access port: a practical tool in the surgeon's toybox. Surg Endosc. 2013;28(3):1034–8.
- Hompes R, Rauh SM, Ris F, Tuynman JB, Mortensen NJ. Robotic transanal minimally invasive surgery for local excision of rectal neoplasms. Br J Surg. 2014;101(5):578–81.
- 51. Hahnloser D, Cantero R, Salgado G, Dindo D, Rega D, Delrio P. Transanal minimal invasive surgery for rectal lesions: should the defect be closed? Colorectal Dis. 2015;17(5):397–402.
- Maglio R, Muzi GM, Massimo MM, Masoni L. Transanal minimally invasive surgery (TAMIS): new treatment for early rectal cancer and large rectal polyps—experience of an Italian center. Am Surg. 2015;81(3):273–7.
- Haugvik S-P, Groven S, Bondi J, Vågan T, Brynhildsvoll SO, Olsen OC. A critical appraisal of transanal minimally invasive sur-

gery (TAMIS) in the treatment of rectal adenoma: a 4-year experience with 51 cases. Scand J Gastroenterol. 2016;51(7):855–9.

- Molina G, Bordeianou L, Shellito P, Sylla P. Transanal endoscopic resection with peritoneal entry: a word of caution. Surg Endosc. 2015;30(5):1816–25.
- Tytherleigh MG, Warren BF, McC Mortensen NJ. Management of early rectal cancer. Br J Surg. 2008;95(4):409–23.
- Doornebosch PG, Ferenschild FTJ, de Wilt JHW, Dawson I, Tetteroo GWM, de Graaf EJR. Treatment of recurrence after transanal endoscopic microsurgery (TEM) for T1 rectal cancer. Dis Colon Rectum. 2010;53(9):1234–9.
- Heafner TA, Glasgow SC. A critical review of the role of local excision in the treatment of early (T1 and T2) rectal tumors. J Gastrointest Oncol. 2014;5(5):345–52.
- 58. Suzuki A, Togashi K, Nokubi M, Koinuma K, Miyakura Y, Horie H, et al. Evaluation of venous invasion by Elastica van Gieson stain and tumor budding predicts local and distant metastases in patients with T1 stage colorectal cancer. Am J Surg Pathol. 2009;33(11):1601–7.
- Nascimbeni R, Burgart LJ, Nivatvongs S, Larson DR. Risk of lymph node metastasis in T1 carcinoma of the colon and rectum. Dis Colon Rectum. 2002;45(2):200–6.
- Kikuchi R, Takano M, Takagi K, Fujimoto N, Nozaki R, Fujiyoshi T, et al. Management of early invasive colorectal cancer. Dis Colon Rectum. 1995;38(12):1286–95.
- Syk E, Lenander C, Nilsson PJ, Rubio CA, Glimelius B. Tumour budding correlates with local recurrence of rectal cancer. Colorectal Dis. 2011;13(3):255–62.
- Prall F, Nizze H, Barten M. Tumour budding as prognostic factor in stage I/II colorectal carcinoma. Histopathology. 2005;47(1):17–24.
- 63. Ueno H, Murphy J, Jass JR, Mochizuki H, Talbot IC. Tumour "budding" as an index to estimate the potential of aggressiveness in rectal cancer. Histopathology. 2002;40(2):127–32.
- Miskovic D, Ni M, Wyles SM, Tekkis P, Hanna GB. Learning curve and case selection in laparoscopic colorectal surgery. Dis Colon Rectum. 2012;55(12):1300–10.
- 65. Borschitz T, Heintz A, Junginger T. The influence of histopathologic criteria on the long-term prognosis of locally excised pT1 rectal carcinomas: results of local excision (transanal endoscopic microsurgery) and immediate reoperation. Dis Colon Rectum. 2006;49(10):1492–506; discussion1500–5.
- Stipa F, Giaccaglia V, Burza A. Management and outcome of local recurrence following transanal endoscopic microsurgery for rectal cancer. Dis Colon Rectum. 2012;55(3):262–9.
- Bach SP, Hill J, Monson JRT, Simson JNL, Lane L, Merrie A, et al. A predictive model for local recurrence after transanal endoscopic microsurgery for rectal cancer. Br J Surg. 2009;96(3):280–90.
- Morino M, Allaix ME, Famiglietti F, Caldart M, Arezzo A. Does peritoneal perforation affect short- and long-term outcomes after transanal endoscopic microsurgery? Surg Endosc. 2012;27(1):181–8.
- Mellgren A, Sirivongs P, Rothenberger DA, Madoff RD, Garcia-Aguilar J. Is local excision adequate therapy for early rectal cancer? Dis Colon and Rectum. 2000;43(8):1064–71.
- Lee W, Lee D, Choi S, Chun H. Transanal endoscopic microsurgery and radical surgery for T1 and T2 rectal cancer. Surg Endosc. 2003;17(8):1283–7.
- Lezoche E, Baldarelli M, Lezoche G, Paganini AM, Gesuita R, Guerrieri M. Randomized clinical trial of endoluminal locoregional resection versus laparoscopic total mesorectal excision for T2 rectal cancer after neoadjuvant therapy. Br J Surg. 2012;99(9):1211–8.
- 72. Garcia-Aguilar J, Shi Q, Thomas CR, Chan E, Cataldo P, Marcet J, et al. A phase II trial of neoadjuvant chemoradiation and local excision for T2N0 rectal cancer: preliminary results of the ACOSOG Z6041 trial. Ann Surg Oncol. 2012;19(2):384–91.

- 73. Habr-Gama A, Sabbaga J, Gama-Rodrigues J, São Julião GP, Proscurshim I, Bailão Aguilar P, et al. Watch and wait approach following extended neoadjuvant chemoradiation for distal rectal cancer. Dis Colon Rectum. 2013;56(10):1109–17.
- 74. Maas M, Beets-Tan RGH, Lambregts DMJ, Lammering G, Nelemans PJ, Engelen SME, et al. Wait-and-see policy for clinical complete responders after chemoradiation for rectal cancer. J Clin Oncol. 2011;29(35):4633–40.
- 75. Dalton RSJ, Velineni R, Osborne ME, Thomas R, Harries S, Gee AS, et al. A single-centre experience of chemoradiotherapy for rectal cancer: is there potential for nonoperative management? Colorectal Dis. 2012;14(5):567–71.
- McDermott FD, Heeney A, Courtney D, Mohan H, Winter D. Rectal carcinoids: a systematic review. Surg Endosc. 2014;28(7):2020–6.
- 77. Kinoshita T, Kanehira E, Omura K, Tomori T, Yamada H. Transanal endoscopic microsurgery in the treatment of rectal carcinoid tumor. Surg Endosc. 2007;21(6):970–4.
- Kumar AS, Sidani SM, Kolli K, Stahl TJ, Ayscue JM, Fitzgerald JF, et al. Transanal endoscopic microsurgery for rectal carcinoids: the largest reported United States experience. Colorectal Dis. 2012;14(5):562–6.
- Serra Aracil X, Gómez Díaz C, Bombardó Junca J, Mora López L, Alcántara Moral M, Ayguavives Garnica I, et al. Surgical excision of retrorectal tumour using transanal endoscopic microsurgery. Colorectal Dis. 2010;12(6):594–5.
- 80. Tielen R, Bremer AJA, van der Graaf WTA, Flucke UE, de Wilt JHW. Transanal endoscopic microsurgery following treatment with imatinib: a case report of a patient with a rectal gastrointestinal stromal tumor. Acta Chir Belg. 2015;115(2):166–9.
- Andrews EJ, Royce P, Farmer KC. Transanal endoscopic microsurgery repair of rectourethral fistula after high-intensity focused ultrasound ablation of prostate cancer. Colorectal Dis. 2011;13(3):342–3.
- Kanehira E, Tanida T, Kamei A, Nakagi M, Iwasaki M, Shimizu H. Transanal endoscopic microsurgery for surgical repair of rectovesical fistula following radical prostatectomy. Surg Endosc. 2014;29(4):851–5.
- D'Ambrosio G, Paganini AM, Guerrieri M, Barchetti L, Lezoche G, Fabiani B, et al. Minimally invasive treatment of rectovaginal fistula. Surg Endosc. 2012;26(2):546–50.
- 84. Türler A, Schäfer H, Pichlmaier H. Role of transanal endoscopic microsurgery in the palliative treatment of rectal cancer. Scand J Gastroenterol. 1997;32(1):58–61.
- Lev-Chelouche D, Margel D, Goldman G, Rabau MJ. Transanal endoscopic microsurgery: experience with 75 rectal neoplasms. Dis Colon Rectum. 2000;43(5):662–7; discussion 667–8.
- 86. Baatrup G, Borschitz T, Cunningham C, Qvist N. Perforation into the peritoneal cavity during transanal endoscopic microsurgery for rectal cancer is not associated with major complications or oncological compromise. Surg Endosc. 2009;23(12):2680–3.
- Gavagan JA, Whiteford MH, Swanstrom LL. Full-thickness intraperitoneal excision by transanal endoscopic microsurgery does not increase short-term complications. Am J Surg. 2004;187(5):630–4.
- Marks JH, Frenkel JL, Greenleaf CE, D'Andrea AP. Transanal endoscopic microsurgery with entrance into the peritoneal cavity: is it safe? Dis Colon Rectum. 2014;57(10):1176–82.
- Lee GC, Sylla P. Shifting paradigms in minimally invasive surgery: applications of transanal natural orifice transluminal endoscopic surgery in colorectal surgery. Clin Colon Rectal Surg. 2015;28(3):181–93.
- Kumar AS, Chhitwal N, Coralic J, Stahl TJ, Ayscue JM, FitzGerald JF, et al. Transanal endoscopic microsurgery: safe for midrectal lesions in morbidly obese patients. Am J Surg. 2012;204(3):402–5.

- Borstlap WAA, Harran N, Tanis PJ, Bemelman WA. Feasibility of the TAMIS technique for redo pelvic surgery. Surg Endosc. 2016;30:5364–71.
- 92. Bremers AJ, van Laarhoven KJ, van der Kolk BM, de Wilt JH, van Goor H. Transanal endoscopic microsurgery approach for rectal stump resection as an alternative to transperitoneal stump resection. Br J Surg. 2013;100(4):568–71.
- Liyanage C, Ramwell A, Harris GJ, Levy BF, Simson JNL. Transanal endoscopic microsurgery: a new technique for completion proctectomy. Colorectal Dis. 2013;15(9):e542–7.
- McLemore EC, Coker A, Leland H, Yu PT. New disposable transanal endoscopic surgery platform: longer channel, longer reach. Gastroenterol Hepatol. 2013;1:46–50.
- Wolthuis AM, de Buck van Overstraeten A, D'Hoore A. Dynamic article: transanal rectal excision: a pilot study. Dis Colon Rectum. 2014;57(1):105–9.
- 96. Buck van Overstraeten A, Wolthuis AM, D'Hoore A. Transanal completion proctectomy after total colectomy and ileal pouchanal anastomosis for ulcerative colitis: a modified single stapled technique. Colorectal Dis. 2016;18(4):O141–4.
- Tasende MM, Delgado S, Jimenez M, del Gobbo GD, Fernandez-Hevia M, DeLacy B, et al. Minimal invasive surgery: NOSE and NOTES in ulcerative colitis. Surg endosc. 2015;29(11):3313–8.
- Leo CA, Samaranayake S, Perry Woodford ZL, Vitone L, Faiz O, Hodgkinson J, et al. Initial experience of restorative proctocolectomy for ulcerative colitis by transanal total mesorectal rectal excision and single-incision abdominal laparoscopic surgery. Colorectal Dis. 2016;18(12):1162–6.
- Rouanet P, Mourregot A, Azar CC, Carrere S, Gutowski M, Quenet F, et al. Transanal endoscopic proctectomy. Dis Colon Rectum. 2013;56(4):408–15.
- 100. Lacy MDB et al. Transanal total mesorectal excision for rectal cancer: outcomes after 140 patients. J Am Coll Surg. 2015;221(2):415–23.
- Tuech JJ, Bridoux V, Kianifard B, Schwarz L, Tsilividis B, Huet E, et al. Natural orifice total mesorectal excision using transanal port and laparoscopic assistance. Eur J Surg Oncol. 2011;37(4):334–5.
- 102. Muratore A, Mellano A, Marsanic P, De Simone M. Transanal total mesorectal excision (taTME) for cancer located in the lower rectum: short- and mid-term results. Eur J Surg Oncol. 2015;41(4):478–83.
- 103. Helbach MV, Deijen CL, Velthuis S, Bonjer HJ, Tuynman JB, Sietses C. Transanal total mesorectal excision for rectal carcinoma: short-term outcomes and experience after 80 cases. Surg Endosc. 2016;30:464–70.
- 104. de'Angelis N, Portigliotti L, Azoulay D, Brunetti F. Transanal total mesorectal excision for rectal cancer: a single center experience and systematic review of the literature. Langenbecks Arch Surg. 2015;400(8):945–59.
- 105. Perdawood SK, Khefagie Al GAA. Transanal vs laparoscopic total mesorectal excision for rectal cancer: initial experience from Denmark. Colorectal Dis. 2016;18(1):51–8.
- 106. Buchs NC, Nicholson GA, Yeung T, Mortensen NJ, Cunningham C, Jones OM, et al. Transanal rectal resection: an initial experience of 20 cases. Colorectal Dis. 2016;18(1):45–50.
- 107. Kang L, Chen W-H, Luo S-L, Luo Y-X, Liu Z-H, Huang M-J, et al. Transanal total mesorectal excision for rectal cancer: a preliminary report. Surg Endosc. 2016;30:2552–62.
- 108. Serra-Aracil X, Mora-López L, Casalots A, Pericay C, Guerrero R, Navarro-Soto S. Hybrid NOTES: TEO for transanal total mesorectal excision: intracorporeal resection and anastomosis. Surg Endosc. 2016;30:364–54.
- 109. Burke JP, Martin-Perez B, Khan A, Nassif G, de Beche-Adams T, Larach SW, et al. Transanal total mesorectal excision for rectal cancer: early outcomes in 50 consecutive patients. Colorectal Dis. 2016;18(6):570–7.

- 110. Chouillard E, Chahine E, Khoury G, Vinson-Bonnet B, Gumbs A, Azoulay D, et al. NOTES total mesorectal excision (TME) for patients with rectal neoplasia: a preliminary experience. Surg Endosc. 2014;28(11):3150–7.
- 111. Chen WH, Kang L, Luo SL, Zhang XW, Huang Y, Liu ZH, et al. Transanal total mesorectal excision assisted by single-port laparoscopic surgery for low rectal cancer. Tech Coloproctol. 2015;19(9):527–34.
- 112. Leroy J, Barry BD, Melani A, Mutter D, Marescaux J. No-scar transanal total mesorectal excision: the last step to pure NOTES for colorectal surgery. JAMA Surg. 2013;148(3):226–30; discussion 231.
- 113. Zhang H, Zhang Y-S, Jin X-W, Li M-Z, Fan J-S, Yang Z-H. Transanal single-port laparoscopic total mesorectal excision in the treatment of rectal cancer. Tech Coloproctol. 2013;17(1):117–23.
- 114. Marks JH, Huang R, McKeever D, Greenfield M. Outcomes in 132 patients following laparoscopic total mesorectal excision (TME) for rectal cancer with greater than 5-year follow-up. Surg Endosc. 2016;30(1):307–14.
- Chen C-C. Transanal total mesorectal excision versus laparoscopic surgery for rectal cancer receiving neoadjuvant chemoradiation: a matched case–control study. Ann Surg Oncol. 2015;23(4):1169–76.
- 116. Fernandez-Hevia M, Delgado S, Castells A, Tasende M, Momblan D, Díaz del Gobbo G, et al. Transanal total mesorectal excision in rectal cancer: short-term outcomes in comparison with laparoscopic surgery. Ann Surg. 2015;261(2):221–7.
- 117. Velthuis S, Nieuwenhuis DH, Ruijter TEG, Cuesta MA, Bonjer HJ, Sietses C. Transanal versus traditional laparoscopic total mesorectal excision for rectal carcinoma. Surg Endosc. 2014;28(12):3494–9.
- 118. Deijen CL, Velthuis S, Tsai A, Mavroveli S, de Lange-de Klerk ES, Sietses C, et al. COLOR III: a multicentre randomised clinical trial comparing transanal TME versus laparoscopic TME for mid and low rectal cancer. Surg Endosc. 2015;30:3210–5.
- 119. Bravo R, Fernández-Hevia M, Jiménez-Toscano M, Flores LF, de Lacy B, Quaresima S, et al. Transanal Hartmann reversal: a new technique. Surg Endosc. 2016;30(6):2628–31.
- 120. Bipat S, Glas AS, Slors FJM, Zwinderman AH, Bossuyt PMM, Stoker J. Rectal cancer: local staging and assessment of lymph node involvement with endoluminal US, CT, and MR imaging—a meta-analysis. Radiology. 2004;232(3):773–83.
- 121. Bislenghi G, Wolthuis AM, de Buck van Overstraeten A, D'Hoore A. AirSeal system insufflator to maintain a stable pneumorectum during TAMIS. Tech Coloproctol. 2015;19(1):43–5.
- 122. Paganini AM, Balla A, Quaresima S, D'Ambrosio G, Bruzzone P, Lezoche E. Tricks to decrease the suture line dehiscence rate during endoluminal loco-regional resection (ELRR) by transanal endoscopic microsurgery (TEM). Surg Endosc. 2014;29(5):1045–50.
- 123. Arolfo S, Allaix ME, Migliore M, Cravero F, Arezzo A, Morino M. Transanal endoscopic microsurgery after endoscopic resection of malignant rectal polyps: a useful technique for indication to radical treatment. Surg Endosc. 2013;28(4):1136–40.
- 124. Ramirez JM, Aguilella V, Arribas D, Martinez M. Transanal fullthickness excision of rectal tumours: should the defect be sutured? a randomized controlled trial. Colorectal Dis. 2002;4(1):51–5.

- 125. Penna M, Knol JJ, Tuynman JB, Tekkis PP, Mortensen NJ, Hompes R. Four anastomotic techniques following transanal total mesorectal excision (TaTME). Tech Coloproctol. 2016;20(3):185–91.
- 126. Atallah S, Albert M, Monson JRT. Critical concepts and important anatomic landmarks encountered during transanal total mesorectal excision (taTME): toward the mastery of a new operation for rectal cancer surgery. Tech Coloproctol. 2016;20:483–94.
- 127. Benson AB, Bekaii-Saab T, Chan E, Chen Y-J, Choti MA, Cooper HS, et al. Rectal cancer. J Natl Compr Canc Netw. 2012;10:1528–64.
- 128. Ford SJ, Wheeler JMD, Borley NR. Factors influencing selection for a day-case or 23-h stay procedure in transanal endoscopic microsurgery. Br J Surg. 2010;97(3):410–4.
- Martin-Perez B, Andrade-Ribeiro GD, Hunter L, Atallah S. A systematic review of transanal minimally invasive surgery (TAMIS) from 2010 to 2013. Tech Coloproctol. 2014;18(9):775–88.
- 130. Tsai BM, Finne CO, Nordenstam JF, Christoforidis D, Madoff RD, Mellgren A. Transanal endoscopic microsurgery resection of rectal tumors: outcomes and recommendations. Dis Colon Rectum. 2010;53(1):16–23.
- 131. Guerrieri M, Baldarelli M, Morino M, Trompetto M, Da Rold A, Selmi I, et al. Transanal endoscopic microsurgery in rectal adenomas: experience of six Italian centres. Dig Liver Dis. 2006;38(3):202–7.
- Guerrieri M, Baldarelli M, de Sanctis A, Campagnacci R, Rimini M, Lezoche E. Treatment of rectal adenomas by transanal endoscopic microsurgery: 15 years' experience. Surg Endosc. 2010;24(2):445–9.
- 133. Ramwell A, Evans J, Bignell M, Mathias J, Simson J. The creation of a peritoneal defect in transanal endoscopic microsurgery does not increase complications. Colorectal Dis. 2009;11(9):964–6.
- Kennedy ML, Lubowski DZ, King DW. Transanal endoscopic microsurgery excision. Dis Colon Rectum. 2002;45(5):601–4.
- 135. Allaix ME, Rebecchi F, Giaccone C, Mistrangelo M, Morino M. Long-term functional results and quality of life after transanal endoscopic microsurgery. Br J Surg. 2011;98(11):1635–43.
- Cataldo PA, O'Brien S, Osler T. Transanal endoscopic microsurgery: a prospective evaluation of functional results. Dis Colon Rectum. 2005;48(7):1366–71.
- 137. Hompes R, Ashraf SQ, Gosselink MP, van Dongen KW, Mortensen NJ, Lindsey I, et al. Evaluation of quality of life and function at 1 year after transanal endoscopic microsurgery. Colorectal Dis. 2015;17(2):O54–61.
- Dafnis G, Påhlman L, Raab Y, Gustafsson U-M, Graf W. Transanal endoscopic microsurgery: clinical and functional results. Colorectal Dis. 2004;6(5):336–42.
- 139. Restivo A, Zorcolo L, D'Alia G, Cocco F, Cossu A, Scintu F, et al. Risk of complications and long-term functional alterations after local excision of rectal tumors with transanal endoscopic microsurgery (TEM). Int J Colorectal Dis. 2015;31(2):257–66.
- 140. Tuech JJ, Karoui M, Lelong B, De Chaisemartin C, Bridoux V, Manceau G, et al. A step toward notes total mesorectal excision for rectal cancer. Ann Surg. 2015;261(2):228–33.
- 141. Rink AD, Kauff DW, Paschold M, Vestweber K-H, Lang H, Kneist W. [Hybrid TAMIS total mesorectal excision: a new perspective in treatment of distal rectal cancer—technique and results]. Chirurg. 2016;87(3):225–32.