Transanal Endoscopic Microsurgery

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Abstract

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Transanal endoscopic microsurgery (TEM) was developed by Professor Gerhard Buess 30 years ago at the dawn of minimally invasive surgery. TEM utilizes a closed proctoscopic system whereby endoluminal surgery is accomplished with high-definition magnification, constant CO₂ insufflation, and long-shafted instruments. The end result is a more precise excision and closure compared to conventional instrumentation. Virtually any benign lesion can be addressed with this technology; however, proper patient selection is paramount when using it for cancer.

Transanal endoscopic microsurgery (TEM) was first developed by Professor Gerhard Buess¹ almost 30 years ago. Several modifications have been made which are all based upon Buess's original vision of improving the visibility and reach of transanal surgery by employing superior optics, carbon dioxide-induced rectal distention, and longer instruments. The number of TEM manuscripts published since the 1980s has increased and training courses have become available at several centers across the globe. Most of the early publications were authored by Buess himself and in these he described his personal journey of first using the instruments on an animal model.² He then reported his clinical experience on an ever-increasing volume of human patients at a time when the concept of minimally invasive surgery, which he called "minimally aggressive but accurate," was capturing the attention of all surgeons.³ Buess's training courses were spread over several days; time was needed to master the technique since the initial participants had minimal experience in endoscopic or laparoscopic surgery. In contrast, today's TEM students learn the techniques and master the learning curve much more quickly because of laparoscopic and video skills acquired early during their surgical career.

TEM represents a unique blend of the old and the new. While transanal excision of rectal tumors has been part of the surgeon's armamentarium for almost a century, surgeons have been restricted by the suboptimal exposure and limited reach afforded by conventional instruments. TEM circumnavigates these restrictions. While virtually any adenoma can be removed with TEM, strict selection criteria must be used

when addressing malignant lesions to not compromise cure and adversely affect patient outcome. Some lesions in the mid and upper rectum which may have required a transabdominal radical resection for removal may now be addressed with a less invasive approach. As such, less postoperative pain, shorter recovery time, and a faster return to normal function are real and attainable goals. This is especially so when one considers the high morbidity associated with the Mason and Kraske procedures where wound infection and fecal fistulas can be disastrous for the patient.

Indications

As stated above, most adenomas regardless of size, location, and degree of circumferential involvement can be removed with TEM, provided the lesion can be reached with a rigid scope and is visible in its entirety. If the lesion extends around the rectosigmoid junction or if the curvature of the sacrum prohibits passage of a rigid scope up to the lesion, then perhaps TEM is not the best approach. Lesions which encompass 360 degrees of the wall circumference can be successfully removed with TEM and intestinal continuity reestablished with a hand-sewn end-to-end anastomosis performed transanally. Regarding removal of cancers, selection criteria require that the lesion have only superficial penetration of the rectal wall (preoperative staging with either endorectal ultrasound or magnetic resonance imaging [MRI] is essential), have well to moderately well differentiation, lack perineural and lymphovascular invasion, and

perhaps also lack a mucinous component (controversial).⁴ Budding tumor cells at the leading edge of the lesion have also been considered an ominous feature and a potential contraindication for transanal excision. If these criteria are not met, the risk of lymph node metastases is increased and such nodes would potentially go untreated by any method that does not incorporate mesorectal excision in its plan. It is generally felt that local recurrence following TEM is likely due to undetected nodal disease within the mesorectum. Large tumor size (greater than 3–4 cm) has been considered a relative contraindication primarily because difficult exposure with conventional instruments could lead to inadequate removal, positive resection margins, and higher recurrence rates. TEM, however, eliminates larger size as a contraindication. If one is contemplating TEM for a rectal cancer, previous endoscopic biopsies should be reviewed with an experienced pathologist for the above features and the lesion should be imaged (ultrasound or MRI) to determine depth of penetration and the presence of nodal metastases. If favorable histologic features are present, there is no evidence of enlarged lymph nodes, and the lesion does not penetrate beyond the submucosa, then one can consider TEM. Further therapy may be indicated after histologic review of the entire lesion has been performed. If, in fact, the lesion is a pT1 tumor, then many would consider TEM sufficient treatment; however, local excision alone is not appropriate treatment for any tumor that has penetrated into the muscularis propria or beyond.

Palliation of a tumor can be considered in instances where diffuse systemic metastases are present. Unfortunately, most primary tumors in these instances are large and may not be amenable to transanal excision. If the patient is medically unfit to undergo conventional surgery because of multiple comorbid factors, TEM may be considered if used in conjunction with radiation and chemotherapy. Experience in this regard is limited, therefore caution should be exercised. Adjuvant therapy combined with TEM may also be considered for those patients who are emotionally unwilling to undergo conventional surgery that may involve a stoma.

There are extended applications in the literature for TEM; however, for many of these conditions, experience is limited to anecdotal case reports or small series. Theoretically, TEM can be used to treat complex, suprasphincteric or extra-sphincteric fistulas with advancement flaps. TEM has been used to treat rectovaginal fistulas⁵ as well as rectourethral fistulas^{6–8} with varying success. Kanehira et al used TEM to treat 10 patients with rectourethral fistulas following radical prostatectomy. Success was achieved in seven and all had their colostomies reversed.⁹ The author has tried using TEM instrumentation to correct circular stapler-induced rectovaginal fistulas following low anterior resection. In this regard, all three cases so attempted failed primarily because diminished rectal capacity secondary to radiation and prior resection led to limited visibility and access. Strictureplasty can be performed with TEM instrumentation as well, the operation being done with single or multiple longitudinal incisions closed transversely or with a 180 or 270 degree transverse excision of the stricture followed by transverse closure of the

defect. Such efforts are best done in the lateral and posterior portions of the extraperitoneal rectum.^{10,11} TEM has been used to repair an anastomotic leak¹² and to excise retrorectal tumors.^{13,14}

TEM has been used in a hybrid manner with other minimally invasive technology. Buchs et al described using robotic instrumentation and TEM in three patients who were placed in the left lateral position with the robot being docked over the hip. An articulating cautery hook was used for the dissection and the defect was closed with barbed continuous sutures in each case. Mean operative time was 110 minutes which included 20 minutes of docking time.¹⁵ Efforts are underway at perfecting a transanal total mesorectal excision with TEM combined with laparoscopic mobilization of the proximal colon and control of the mesenteric vessels. Intestinal continuity is then established with either a coloanal anastomosis or a transanal colorectal anastomosis. In essence, aside from the trocar sites, an incisionless proctectomy with mesorectal excision is being performed.

Following total abdominal colectomy with ileostomy, patients may experience bleeding, tenesmus, and discharge from the remaining rectal stump. Completion proctectomy may be difficult if performed through a transabdominal approach, and if the stump is long, removal through a perineal approach may not be possible. Liyanage et al described using TEM in 12 patients to perform a completion proctectomy. The approach begins with an initial intersphincteric dissection after which the TEM rectoscope is inserted and close rectal dissection is performed until the top of the rectal stump is reached. Mean stump length was 18 cm, the peritoneal cavity was entered in nine patients without any small bowel injuries, and mean hospital stay was 5.5 days.¹⁶

Preoperative Assessment and Patient Preparation

If the goal of treatment is cure, then accurate preoperative staging is paramount. Assessment begins with a digital rectal examination which may reveal fixation or bulky extramural adenopathy. To determine local extent of disease (depth of penetration, lymph nodes), as previously stated, endorectal ultrasound or MRI can be used. A meta-analysis by Bipat et al analyzed 90 studies comparing ultrasound, computed tomography (CT), and MRI from 1985 to 2002. Ultrasound was found to be the most accurate for determining depth of penetration, being over 90% sensitive. MRI frequently over-staged T1 lesions.¹⁷ Ultrasound accuracy may decrease when used to evaluate more advanced and circumferential tumors.¹⁸ Ultrasound, CT, and MRI have comparably low sensitivities when ruling out perirectal lymph node metastases (67, 55, and 66%, respectively).¹⁷ The definition of what constitutes a metastatic lymph node has varied; one study considered any oval or circular structure greater than 5 mm to be malignant, while others use 10 mm as the threshold; others have stated that any detectable node should be considered metastatic regardless of size.¹⁸ The positive predictive value of a hypo-echoic node detected within the mesorectum increases with increasing size. Abdominal CT scans are usually not necessary

for early, superficial cancers or adenomatous lesions, as the likelihood for distant metastases is low.¹⁹

If a patient is referred to a surgeon for possible TEM, rigid proctosigmoidoscopy must be performed by the surgeon to determine the level of the lesion in the rectum and whether a rigid scope can access the lesion and reveal it in its entirety. Also, the exact spatial orientation of the lesion (anterior vs. posterior, right lateral vs. left lateral) must be determined as this will dictate patient position on the operating table. Although bowel cleansing is not required for colectomy, it is still essential for TEM to ensure visibility and reduce the risk of infection. Also, if the effects of general anesthesia decline midway during the operation and the patient strains or coughs, residual stool, if present, may appear at a most inopportune time. General or regional anesthesia is required. Patients are positioned on the operating room table in such a way that the lesion is at the bottom of the optical field, for example, lithotomy for a posterior lesion. Most cases can be done on an outpatient basis or with a single overnight stay.

Equipment

TEM utilizes a closed endoscopic system that allows for the instillation and retention of carbon dioxide gas; this creates constant rectal distention which facilitates exposure and visualization of the lesion, excision of the tumor, control of bleeding, and subsequent closure of the wound defect. Other distinguishing features of TEM are the long reach of the instruments and the unique stereoscopic magnified image. A combined multifunctional endosurgical unit regulates suction, irrigation, intrarectal pressure, and gas insufflation. Suction removes fluid, blood, waste, and smoke. Irrigation helps to maintain a relatively clean operative field and can rinse the end of the scope. CO₂ insufflation maintains distention of the rectum throughout the procedure and flow can be increased as high as 6 L/min. The intrarectal pressure is set at a desired level (usually 10–15 cm H₂O) and the four functions mentioned above are regulated to achieve a constant steady state at that level. The surgeon may choose at various times during the operation to increase the suction; when this occurs, the endosurgical unit will increase flow of CO₂ to maintain a steady state. If intrarectal pressure does not rise or if the rectum does not distend, there is likely a leak in the system and the surgeon should be able to systematically check the setup for air leaks.

The operating rectoscopes are beveled and are ~4 cm in diameter. A straight, nonbeveled rectoscope is also available and may be preferable for the very distal lesions where the lower lip of a beveled scope could slip exterior to the patient allowing for the escape of CO₂ and collapse of the operative field. If a patient has an anterior lesion, he or she should be placed in the prone position and the legs spread apart to permit close access to the perineum. For a posterior lesion, the patient is placed in the lithotomy position, and if the lesion is laterally located, the patient is placed in the appropriate lateral decubitus position. The end of the rectoscope is covered with a sealed facepiece which has airtight rubber seals and sealed working ports through which are inserted

the long-shafted instruments necessary for the dissection. The suction catheter can be electrified and in this way a bleeding vessel can be coagulated while the blood is being aspirated. In a similar way, the tissue graspers can be electrified for control of a bleeding vessel. The binocular eyepiece provides ×6 magnification and has a 50 degree downward view and a 75 degree lateral field of view. In contrast, the accessory scope has a 40 degree downward view and a reduced lateral view.

Most of the bleeding occurring during full-thickness TEM dissections is encountered when one traverses the mesorectum. The standard TEM cautery may be insufficient in stemming the flow of brisk bleeding; the surgeon may choose to use an alternative energy device for hemostasis such as a harmonic scalpel.²⁰ Studies have shown that a harmonic scalpel reduces operative time and bleeding. Ayodeji et al compared harmonic dissection with the standard TEM cautery unit in a nonrandomized fashion, correcting for differences in tumor size between the two groups. The harmonic dissector reduced operative time by 26%; however, in 50% of the harmonic group, the surgeon used a hybrid approach and used cautery for portions of the case.²¹ Hermesen et al showed that when the long harmonic shears are used, a further reduction in operative time can be achieved as well as a significant reduction in blood loss.²² Caution should be exercised. In rare instances, pelvic sepsis has occurred following cases that used the harmonic dissectors possibly as a result of prolonged application of energy to the tissue. When cautery is used to traverse the mesentery, the energy is imparted in short bursts at very focal and precise areas. In contrast, when a harmonic dissector is used, tissue is grasped and energy imparted over a longer period of time until the tissue separates.

The TEM needle holder is self-righting. The needle can be grasped in an inverted position, yet the needle holder will automatically place it in the upright position when the locking mechanism is activated. Sutures are started and finished with silver shots applied to the thread with a specially designed applicator. Traditional instrument knot tying is too tedious to perform on a constant basis. Laparoscopic suturing devices that automatically transfer the needle back and forth can be used as well.

Technique

The rectoscope is inserted up to the lesion under direct vision aided by the manual insufflations of air. The scope is then secured to the operating room table with the adjustable, double-jointed Martin arm and the facepiece is locked into place on the end of the scope. The Martin arm is moved multiple times during the procedure to keep the lesion and the area of dissection in the center of the optical field. Rubber sleeves, covered by rubber caps with a hole in their center, are placed onto the working ports of the facepiece. The long-shafted instruments are inserted and the tubing necessary for CO₂ insufflation, saline irrigation, and pressure monitoring is connected. The binocular eyepiece and the accessory scope are inserted.

The technique of excision will vary according to preoperative histology, suspicion that a “benign” lesion may contain an occult cancer, and the location of the lesion within the rectum. Small adenomas may be removed by dissecting within the submucosal plane; this is especially appropriate for an anterior lesion in a woman where the anterior peritoneal reflection is unpredictable in its location and a full-thickness excision may be hazardous. For a submucosal excision of a small adenoma, a 5-mm margin of normal-appearing mucosa is marked around the lesion, the mucosal edge is lifted with the tissue grasper, and the lesion is excised without entering the muscularis. Larger adenomas may contain invasive cancer and are excised using a full-thickness technique whereby the dissection is taken down into the mesorectal fat. If the peritoneum is violated, it should be repaired promptly and the operation completed as planned; conversion to laparotomy is not necessary. Before the endotracheal tube is removed, the abdomen should be examined in the event a large pneumoperitoneum needs needle decompression. Cancers are removed with a full-thickness excision after a 1-cm margin has been marked around the lesion. To help orient the pathologist to the deep and lateral margins, the specimen should be sutured or pinned to a flat surface such as cork board or a piece of telfa paper. Wounds are closed transversely with a 3–0 running monofilament suture and SH needle. TEM surgeons frequently debate whether or not the wound needs to be closed. Small submucosal excisions can certainly be left open; however, larger open wounds are more likely to cause a longer period of tenesmus, bleeding, and mucous discharge during the following days or weeks. Ramirez et al prospectively randomized TEM patients into a group that underwent wound closure and a group that did not. Wound closure extended surgery by 16 minutes but this was not significantly significant. In fact, no significant differences were noted with respect to intraoperative bleeding, length of stay, and early or late complications.²³ This author’s belief is that closure should be attempted in all, mainly to maintain one’s skills in suturing. There will be instances where suturing is mandatory such as in cases of peritoneal entry or following excision of circumferential lesions, and if one has become facile in wound closure, these difficult circumstances can be easily handled.

Technical pearls are as follows:

- Sutures of short length are preferable to be able to pull the suture tight yet stay within the narrow confines of the rectoscope.
- Crossover of instruments should be avoided; rather, they should be manipulated in parallel.
- One should avoid dropping the needle. It is far better to pass it from instrument to instrument.
- One should avoid high-power settings on the cautery unit as excessive heat will fog the lens and create unnecessary smoke and splatter. Also the end of the scope should be kept at a distance from the lesion to keep debris from hitting the lens.
- The surgeon should become adept at knowing where air leaks in the system are likely to occur and how to fix them.

- The scope should be repositioned several times during the course of the dissection to keep the operative field in the center of the optical field.
- All of the instruments including the shaft of the eyepiece should be lubricated with mineral oil to facilitate passage and reduce wear and tear on the rubber seals of the facepiece.
- For large wound defects, one should use multiple sutures of short length. When closure is complete, one should be sure that the rectal lumen has not been inadvertently closed by passing a rigid proctoscope through the area. This last point cannot be overemphasized.

Complications

TEM complications occur less frequently compared with other resection methods. Buess reported a minor complication rate of 16% and a major complication rate of 9%.²⁴ Complications occurring intraoperatively include conversion to open or laparoscopic surgery because of technical difficulty, equipment failure, difficulty in ventilating the patient, hypercarbia, bleeding, and entry into the peritoneal cavity. Emphysema into the retroperitoneal, intraperitoneal, and subcutaneous tissues has been described.²⁵ Postoperative complications include urinary retention (5%), abdominal or rectal pain (1%), bleeding (1%), fluid overload (1%), suture line dehiscence (1%), perirectal abscess (<1%), and stricture (1%).²⁶ Bignell et al reported on 262 consecutive TEM cases and noted that pelvic sepsis occurred in 3% of patients and was more common when the lesion was located within 2 cm of the dentate line. Hemorrhage was noted in another 3% but occurred less often when the harmonic scalpel was used.²⁷ Rectovaginal fistulas have also been noted.²⁸ Flexer et al noted a stricture rate of 6% in a series of 164 patients; dilatation was performed either endoscopically or under anesthesia in all cases.²⁹

Wound dehiscence probably occurs more commonly than is thought; the exact incidence is not known because most surgeons do not routinely inspect the wound during the first 2 weeks after TEM. The addition of neoadjuvant radiation therapy does impair wound healing. Marks et al found that radiation significantly increased the incidence of wound complications; 26% of patients so treated experienced varying degrees of wound separation. Although most instances were successfully treated with outpatient antibiotics, one patient did require a diverting stoma.³⁰ Paganini et al specifically studied suture line disruption and noted that the incidence dropped from 12% to nil if the wound cavity was packed with hemostatic agents followed by packing the rectal ampulla with gauze.³¹

Peritoneal entry does not mandate conversion to an open approach and is not associated with an increase in postoperative complications.^{32–34} The defect can be repaired immediately and the operation completed as planned. If there are concerns about the adequacy of closure, the wound can be inspected laparoscopically and additional sutures placed. The incidence of peritoneal entry varies in the literature, ranging from 2 to 10%^{32–34}; in the author’s experience (unpublished data), it has occurred in 1.2%. Baatrup et al pooled data from

several TEM databases from the United Kingdom, Germany, Denmark, and Norway and found 22 instances of perforation into the peritoneal cavity in 888 cases (2%). All perforations were treated endoscopically; there were no deaths or severe complications noted in this group.³³ Intraperitoneal entry rarely requires fecal diversion.

Incontinence to feces and flatus are concerns because of the wide diameter of the scope, the long duration of many of the TEM cases, and the frequent need to reposition the scope during surgery. Gracia Solanas et al studied anal manometry in 40 TEM patients. Patients who had previous anal surgery and preoperative defects were excluded from evaluation. There was a global fall in anal resting pressure and maximal squeeze pressure; however, at 6 months, patients remained continent. Fifteen percent had rupture of their internal sphincter, producing variable degrees of incontinence which resolved after 6 months in 67% of patients so affected.³⁵ Operative time, tumor size, age, and gender did not seem to influence outcome,³⁶ although Herman et al have postulated that a resection of more than 50% of the circumference might contribute to persistent anal dysfunction.³⁷ Wang et al studied patients with manometry at 2 weeks, 6 weeks, 3 months, and 1 year after TEM. Lower resting pressures, squeeze pressures, and maximum tolerable volumes were noted early after surgery but normal values were recovered by the 1 year time point.³⁸ Jin et al used manometry and an incontinence survey to study patients at 2 weeks, 3 months, and 6 months after TEM. Squeeze pressures were depressed at 2 weeks but returned to normal by 3 months. Resting pressures and maximum tolerable volumes were significantly depressed at 3 months but returned to normal by 6 months. Ultrasound of the sphincter muscle was used to determine whether injuries to the muscle were sustained. No patients had an injury to the external sphincter; however, 14% of patients were found to have defects in the internal sphincter; 80% of these were incontinent to flatus.³⁹ Incontinence after TEM has been shown to be mild and self-limiting. Cataldo et al focused less on the changes in sphincter physiology and more on the quality of life as assessed using scores measuring lifestyle, coping, depression, and embarrassment. No change was noted between preoperative and postoperative scores. TEM did not produce any deterioration in the ability to defer defecation or the number of bowel movements in a 24-hour period.⁴⁰

Comparing Transanal Endoscopic Microsurgery with Endoscopic Mucosal Resection and Endoscopic Submucosal Dissection

Jeon et al reported on 66 patients with small rectal neuroendocrine tumors removed with either endoscopic mucosal resection (EMR), or endoscopic submucosal dissection (ESD), or TEM. TEM achieved a complete resection in 100% of patients (EMR 66%, ESD 83%). Complications were noted in 18% of the EMR patients and in 48% of the ESD patients. No recurrences were noted in any of the groups, although the follow-up period was short (21.5 ± 13.5 months).⁴¹ In a

retrospective study of patients with early rectal cancers, Kawaguti et al compared ESD ($n = 11$) and TEM ($n = 13$). No differences were noted with respect to ability to achieve negative margins, size of the tumor, local recurrence rates, and duration of the procedure.⁴² Arezzo et al performed a meta-analysis of the medical literature published between 1984 and 2010, looking at 11 ESD series and 10 TEM series describing the removal of large benign rectal lesions. TEM was more likely to remove the specimen intact (98.7 vs. 87.8%, $p < 0.001$) and achieve negative margins (88.5 vs. 74.6%, $p < 0.001$).⁴³ Barendse et al compared anorectal function following TEM and EMR excision of large rectal adenomas. Colorectal Functional Outcome questionnaires, the Wexner Incontinence Grading Scale, and manometry were performed preoperatively and again at 6 months after treatment. Anal resting pressures were lower after TEM than EMR but none of the other variables or quality of life parameters differed between treatment groups.⁴⁴

Comparing Transanal Endoscopic Microsurgery with Conventional Local Excision

It is not likely that there will ever be a randomized prospective study comparing TEM with conventional transanal excision which requires that surgeons enroll their own patients to either technique. Once the TEM technique is learned, it will be difficult for a surgeon to revert to a method accompanied by poor visibility, difficult reach, and doubt about the adequacy of the margins. Furthermore, TEM and transanal excision using conventional instruments are not the same operation, so a direct comparison is faulted. There are several published retrospective reports comparing TEM with other methods of local excision within a given institution. Moore et al studied 171 patients, 89 of which underwent conventional transanal excision and 82 of which underwent TEM. The number of postoperative complications was similar (15 and 17% for TEM and conventional excision, respectively); however, the conventional group had more major complications that included fistula, anastomotic leak, and bleeding. TEM was more likely to produce a specimen with clear margins, cause less specimen fragmentation, and yield lower recurrence rates.⁴⁵

Lin et al compared TEM patients treated at their institution with a group of patients who underwent a posterior trans-sphincteric approach (Mason operation) at another institution. In this study, 31 patients underwent TEM between 1995 and 2003 and were compared with patients who underwent Mason operation between 1995 and 2004. There were no differences noted in operative time or blood loss. The median hospital stay and time until resumption of food intake were shorter in the TEM group. In the Mason group, wound infections and fecal fistulas developed in 3.9% of patients. One patient required a transverse colostomy for the fistula to heal. Incontinence to flatus or liquid stool occurred in 31.4% of the Mason group, while 6.5% of the TEM group had incontinence to flatus only. Both groups showed complete recovery of continence, although the Mason group took almost a week longer to recover. There were no recurrences noted in the

TEM group, whereas a 3.9% recurrence rate was noted in the Mason group at 30-month follow-up.⁴⁶

In a study of excision of adenomas alone, de Graaf et al compared transanal excision ($n = 43$) with TEM ($n = 216$). Although the study was not randomized, the lesions were matched for tumor size and distance from the anal verge. Significant differences were noted in favor of TEM with respect to operative time (35 vs. 47 minutes), complication rates (5 vs. 10%), ability to achieve negative margins (88 vs. 50%), less tissue fragmentation (1.4 vs. 24%), and recurrence rates (6 vs. 29%). The authors concluded that TEM is superior to conventional transanal excision for rectal adenomas.⁴⁷ Christoforidis et al retrospectively studied only early rectal adenocarcinomas excised with either TEM ($n = 42$) or conventional instruments ($n = 129$) between 1997 and 2006. Metastatic, recurrent, previously irradiated, and snare excised tumors were excluded from the analysis. TEM was more likely to achieve clear margins (2 vs. 16%, $p = 0.017$). In this study, tumor margin status was an independent predictor of local recurrence and disease-free survival.⁴⁸ These studies underscore the distinct differences between TEM and other methods of locally excising rectal neoplasms; they are not the same operation and the differences suggest that TEM is the preferred approach. Because of the constant rectal distention, the magnified image, and longer reach, a more precise excision and wound closure is possible. This leads to better specimen handling, namely, less tissue fragmentation and a higher likelihood of obtaining negative margins; these, in turn, will lead to lower recurrence rates.

Follow-up and Treatment of Cancer Recurrence

Most experts agree that properly selected, favorable pT1 cancers do not require additional treatment after TEM. Favorable histologic features include well or moderately well differentiation, lack of lymphovascular invasion, lack of tumor budding at the leading edge, and lack of a mucinous component (controversial). The presence of unfavorable features should lead one to consider additional treatment even if the lesion is confined to the submucosa. Borschitz et al studied the influence of histopathologic criteria on long-term prognosis following TEM excision of pT1 rectal cancers. Low-risk tumors, that is, those with favorable features, had a local recurrence rate of 6%. In contrast, high-risk pT1 cancers had a local recurrence rate of 39%. In this study, some patients with high-risk pT1 cancers underwent immediate radical surgery; a local recurrence rate of 6% was noted in this subgroup and the 10-year cancer-free survival was 93%.⁴⁹ These data suggest that performing TEM prior to radical surgery does not adversely affect outcome, a finding confirmed on reviewing outcome in the United Kingdom database from 21 regional centers.⁵⁰ Also, the submucosa has been divided into three layers by thickness and are classified as SM1, 2, and 3. Penetration into the deepest submucosal layer has been considered an indication for additional treatment; however, not all pathologists espouse this subdivision, citing concerns about tangential cuts through the tumor

yielding misleading information. In a study of a national database from the United Kingdom, the outcomes of 487 patients treated with TEM for cancer were evaluated. TEM was found to produce long-term outcomes comparable to those published for radical total mesorectal excision when TEM was applied for properly selected, favorable tumors. Prompt radical surgery for those with adverse features appears safe for certain pT1 and pT2 cancers, that is, cure is not compromised by the patient having undergone TEM prior to radical surgery.⁵⁰ If radical surgery is deemed necessary, one should allow sufficient time for the wound and cavity to heal (at least 1 month) following TEM.

There has been concern about the effect of an initial TEM on the quality of the resected specimen when prompt radical surgery is subsequently performed. This was addressed in a retrospective review of the English national TEM database; 36 such cases were identified between 1992 and 2008. The quality of the resected specimen was good in 64%, moderate in 17%, and poor in 20%. Risk factors for an inferior specimen were a full-thickness TEM excision ($p = 0.03$), an interval greater than 7 weeks before radical surgery ($p = 0.05$), and distal lesions ($p = 0.04$). Patients with a good total mesorectal excision specimen had better disease-free survival (100 vs 51%, $p = 0.001$). Survival after radical surgery was 91% at 1 year and 83% at 5 years.⁵¹

TEM alone, or any method of local excision, is not appropriate treatment of a cancer that penetrates into the muscularis propria or beyond because of unacceptably high recurrence rates, probably from untreated nodal metastases within the mesentery. Borschitz et al showed that even for low-risk pT2 lesions (completely excised with negative margins, well differentiation, no lymphovascular invasion), recurrence rates of 29% were noted.⁵²

Follow-up after TEM should include frequent proctoscopic examinations (every 3 months for the first 2 years) and, in the case of cancer, ultrasound to inspect for enlarging adenopathy. Since the anatomy may be distorted by TEM, one should refrain from making any conclusions based on a single ultrasound examination. Rather, one should look for changes on serial ultrasounds performed over time. A colonoscopy should be performed at 1 year. Recurrence of an adenoma may be treated with endoscopic fulguration or with repeat TEM, but the recurrence rate should be 10% or less. Recurrence rates following TEM excision of pT1 cancers vary in the literature; most range from 0 to 12.5%, with an occasional report citing rates from 20 to 25%.^{19,53} Assuming negative margins were obtained, recurrence of a pT1 cancer occurs by one of two mechanisms, either the tumor was incorrectly staged at the onset and nodal metastases were present at the initial diagnosis or exfoliated cancer cells were implanted and grew in the wound defect. In either case, if there is recurrence, the mesorectum is at risk and should be treated accordingly with neoadjuvant chemotherapy and radiation prior to radical surgery.

Doornebosch et al evaluated the management and outcome of local recurrence after TEM for pT1 rectal cancers. Of 88 patients treated in this fashion, recurrences were noted in 18 (20.5%); the time to detection of the recurrence was

10 months. Of the 18 patients, 2 did not undergo surgery because of systemic metastases, and the remaining 16 underwent salvage surgery. A complete, margin-free excision was possible in 15 patients; 1 patient subsequently experienced local recurrence, whereas 7 developed distant recurrence. At 3 years, cancer-related survival was 58%.⁵⁴ It is arguable that distant recurrence may or may not be a consequence of the original treatment. Furthermore, none of the patients received neoadjuvant radiation or chemotherapy prior to salvage surgery, a point of contention in light of the potential mechanisms proposed to explain recurrence of a pT1 lesion mentioned above. That local recurrence (without systemic disease) can be successfully salvaged was shown in a study by Paty et al. Thirty-four patients developed recurrence after TEM, of whom 17 were considered surgical candidates. The remainder were either unfit for surgery or had systemic disease and died at a mean of 1.1 years. Of the patients undergoing salvage for local recurrence, 82% were successfully treated.⁵⁵

Transanal Endoscopic Microsurgery Followed by Adjuvant Radiation Therapy

Occasionally, TEM excision of a suspected adenoma or T1 cancer yields a pathology report showing the tumor was more advanced than originally thought. While most clinicians would advise radical surgery in these instances, a patient may be medically unfit or unwilling to do so. Ramirez et al removed a series of rectal carcinomas with TEM and then enrolled 28 patients in a study of postoperative radiation if a pT1 cancer had unfavorable features or if the lesion was staged pT2. Local recurrence was noted in three (11%) of these patients. Five-year overall survival was 94%, and cancer-specific survival was 96%.⁵⁶ Duek et al reported a series of 12 patients with pT2 cancers removed with TEM who then underwent radiation therapy. At a median follow-up of 3 years, there were no local recurrences. In contrast, local recurrence was noted in 50% of the patients who did not receive radiation.⁵⁷

Radiation Therapy Followed by Transanal Endoscopic Microsurgery

Lezoche et al treated 35 patients with a full course of pelvic radiation (5,040 Gy) followed by full-thickness TEM excision of lesions which were pT2 after histologic assessment. After a median follow-up of 38 months, there was one local recurrence. The probability of surviving 8 years was 83%.⁵⁸ In another study by Lezoche et al, 100 patients with rectal cancer underwent preoperative imaging with ultrasound; there were 54 uT2 and 46 uT3 cancers. All patients underwent preoperative radiation followed by TEM excision. Definitive histologic examination revealed 9 pT1, 54 pT2, and 19 pT3 cancers. A complete pathologic response was noted in 3 patients, and microscopic tumor confined to the mucosa and submucosa was noted in another 15 patients. At a median follow-up of 55 months, local recurrence was noted in 5% and distant metastases were noted in 2%. At 90 months, the

cancer-specific survival was 89%.⁵⁹ In a study of 137 patients with rectal cancer treated with preoperative radiation followed by TEM, Guerrieri et al found a local recurrence rate of 5%; almost half of these patients succumbed to systemic metastases at a median follow-up of 46 months. A disease-free survival rate of 100% was noted in 55 patients with either pT0 or pT1 cancers, 81% in 59 patients with pT2 cancers, and 59% in 23 patients with pT3 cancers.⁶⁰

Neoadjuvant Chemotherapy and Radiation Followed by Transanal Endoscopic Microsurgery

Significant downstaging can be achieved with preoperative chemotherapy and radiation. Although the standard of care is to proceed with radical surgery regardless of response to treatment, there is growing interest in either less radical surgery or watchful waiting for certain patients. There is no reliable imaging or endoscopic test capable of selecting such patients, however. Tulchinsky et al reported on 97 consecutive patients treated with neoadjuvant chemoradiation followed by radical surgery. Seventeen (18%) patients had no residual tumor at the primary site in the rectal wall; of these, only 1 had positive lymph nodes.⁶¹ The results would suggest that the vast majority of patients without mural disease do not need radical surgery and lymphadenectomy. Kim et al performed full-thickness local excisions on 22 patients who were apparent complete *clinical* responders to neoadjuvant therapy. Seventeen (65%) had no residual disease within the rectal wall; no further surgery was done and none developed local recurrence after a short mean follow-up of 24 months.⁶² Mohiuddin et al also achieved a very low recurrence rate in a similar group of patients.⁶³ Schell et al reported on 11 patients downstaged with neoadjuvant therapy who underwent transanal excision and were followed for a median of 48 months. None developed local recurrence; however, one patient had systemic metastases.⁶⁴ Bonnen et al performed local excision on 26 patients; 54% had a complete local pathologic response and 35% had microscopic residual disease. Two patients developed local recurrence at a mean follow-up of 46 months. Five-year actuarial overall survival rate was 86%.⁶⁵

Lezoche et al staged 135 patients with rectal cancer with endorectal ultrasound, MRI, or CT. Patients with T2N0 lesions ($n = 84$) received neoadjuvant therapy and then underwent TEM, whereas those with T1N0 lesions ($n = 51$) underwent TEM alone. For the former group, local recurrence developed in 5% and at a median follow-up of 97 months, and disease-free survival was 93%. For the patients with T1N0 cancers, local recurrence was 0% and disease-free survival was 100%. Final pathology revealed that there were 24 (18%) complete pathologic responders, 66 (49%) pT1 cancers, and 45 (33%) pT2 cancers. All of the recurrences occurred in the patients who had been staged as having T2 cancers and were still ypT2 after neoadjuvant therapy.⁶⁶ Caricato et al treated 30 patients with neoadjuvant chemoradiation followed by TEM for the patients ($n = 8$) who had a good clinical response and open surgery for those ($n = 22$) with evident residual disease

noted endoscopically or with imaging studies. After a mean follow-up of 47 months, the TEM group had a disease-free survival rate of 100%, whereas the open group had a disease-free survival rate of 77%.⁶⁷

Guerrieri et al described their TEM utilization with a series of 425 patients with rectal cancer. Tumors with a clinical stage of T1 underwent TEM alone. Patients with T2 or T3 cancers were treated with neoadjuvant therapy followed by TEM 40 to 50 days later. Recurrence rate was 9.4% for patients with pT2 or pT3 tumors. Survival rates were as follows: 100% for pT1 at 253 months, 93% for pT2 tumors at 255 months, and 89% for pT3 tumors at 239 months.⁶⁸

Marks et al reported his experience with tumors located less than 3 cm from the anus who underwent neoadjuvant therapy followed by sphincter-preserving surgery. Forty-nine patients had TEM; at a mean follow-up of 36.3 months, the local recurrence rate was 6% and the 5-year survival rate was 88%.⁶⁹

Borschitz et al performed an online search and accumulated data from seven different studies on 237 patients with clinical T2 and T3 cancers who underwent neoadjuvant chemoradiation followed by local excision. None of the patients with ypT0 cancers developed local recurrence. Recurrence rates were as follows: 0 to 6% for ypT1 cancers, 6 to 20% for ypT2 cancers, and up to 42% for ypT3 cancers.⁷⁰

There are ongoing questions about how a tumor regresses in response to neoadjuvant therapy. Does it recede in a symmetrical, concentric fashion? Is there always a mucosal component or is tumor buried in areas where the overlying bowel appears normal? These questions have implications regarding the use of transanal excision following neoadjuvant therapy and whether sphincter preservation is increased during TME. Regarding the former, a very important issue is whether the dimensions of the transanal specimen is determined by the size of the resultant scar/ulcer or should it be determined by the pretreatment size of the tumor. To answer this question, we took 75 specimens removed during low anterior resection or abdominoperineal resection and took serial radial clock-face biopsies from the epicenter of the scar. The mean number of biopsies taken per specimen was 14. Twenty-seven percent of specimens had no identifiable tumor; of the remaining 73%, tumor was confined to the ulcer in 51% and 49% had tumor in grossly normal areas. Of this latter group, tumor was present greater than 2 cm from the ulcer edge in 11%, and 3% had tumor present greater than 4 cm from the edge. On the basis of these data, it might be ill advised to perform a transanal excision following neoadjuvant therapy with only a 1-cm margin of normal-appearing mucosa. It might also appear ill advised to choose the distal margin during TME based on where there seems to be normal mucosa.⁷¹

Studies Comparing Transanal Endoscopic Microsurgery with Radical Surgery

In a nonrandomized study, De Graaf et al compared 80 patients treated with TEM to 75 treated with total mesorectal excision. All had pT1 cancers, and all had negative margins.

The TEM group had shorter operative times, less bleeding, shorter hospital stays, fewer complications, and lower reoperation rates. At 5 years, overall survival and cancer-specific survival rates were comparable. Local recurrence developed in 24% of the TEM group and 0% of the TME group, yet survival was not affected.⁷² Ptok et al reported a nonrandomized retrospective German multicenter trial involving 282 hospitals and 479 patients with low-risk pT1 cancers treated for cure. Eighty-five patients were treated with conventional transanal excision and 35 patients underwent TEM; collectively, local recurrence developed in 6% of this group at a mean follow-up of 44 months. Of the 359 patients treated with radical surgery, local recurrence developed in 2% ($p = 0.05$); however, tumor-free survival did not differ between the groups.⁷³ Lee et al compared TEM and radical surgery, also in a nonrandomized fashion, for patients with pT1 and pT2 cancers. No chemotherapy or radiation was administered. There was no significant difference in local recurrence rates for patients with pT1 cancers treated with TEM or radical surgery. For T2 cancers, however, local recurrence developed in 19.5% of the TEM patients and 9.4% of those undergoing radical surgery ($p = 0.04$). There were no significant differences between the two groups in terms of 5-year disease-free survival rates. The authors concluded that further treatment is warranted for a pT2 cancer removed by TEM.²⁸

In a randomized, prospective trial with a minimum of 3-year follow-up, Lezoche et al randomized 40 patients into a TEM group ($n = 20$) and a total mesorectal laparoscopic resection group ($n = 20$) following neoadjuvant therapy. Final pathology in the TEM group revealed that there were seven pT0 cancers, six pT1 cancers, and seven pT2 cancers. For the mesorectal excision group, there were seven pT0 cancers, four pT1 cancers, and seven pT2 cancers. Significant downstaging occurred in both groups. At a mean follow-up of 56 months, one local recurrence and one distant recurrence developed in each group. The probability of local or distant failure was 10% for TEM and 12% for laparoscopic resection, whereas the probability of survival was 95% for TEM and 83% for laparoscopic resection. The authors conclude that the results were comparable between the two study arms in terms of failure and survival.⁷⁴ Lezoche updated his series to include 35 patients in each arm and the results have held up; similar results were noted in each treatment arm with respect to local failure and probability of survival.⁷⁵

Conclusions

TEM is a safe technique with a broad range of applications including the excision of rectal neoplasms, treatment of complex rectal fistulas, and stricturoplasty. Virtually any adenoma can be removed with this technique; however, caution should be exercised regarding its use with rectal cancer. The standard against which it will be compared is level-appropriate mesorectal excision. Most would agree that TEM excision of favorable, low-risk pT1 cancers is acceptable. It should not be used as the sole form of therapy for pT2 or deeper cancers. There is considerable interest in combining TEM with

postoperative radiation or neoadjuvant chemotherapy and radiation for these locally advanced tumors. Publications investigating combined therapy all have small sample sizes and few prospectively randomize patients; nevertheless, the results are compelling.

We conclude the following: TEM excision of favorable pT1 cancers is safe as sole therapy, outcome is not necessarily compromised if prompt radical surgery is performed after TEM, TEM alone is not appropriate for T2 or greater lesions, and most patients who experience recurrence after TEM can be salvaged with radical surgery. Many patients do not require radical surgery and lymphadenectomy if neoadjuvant therapy produces a complete histologic response at the primary site in the rectal wall. The problem is how to reliably identify such patients. The phenomenon of tumor scatter, that is, the presence of buried tumor in normal-appearing areas remote from the tumor or scar epicenter, begs for caution in adopting the wholesale practice of treating patients with neoadjuvant therapy followed by either transanal excision or watchful waiting.

Future use of TEM may include transanal lymph node sampling or dissection with or without the use of sentinel lymph node technology. In fact, Buess himself had alluded to the potential for node retrieval in the 1980s. TEM may also be used in performing a transanal total mesorectal excision when combined with a laparoscopic mobilization. Efforts are underway at perfecting this technique. Technical modifications are likely in the future to make the equipment more affordable; as such, TEM will likely gain in popularity.

References

- Buess G, Theiss R, Hutterer F, et al. Transanal endoscopic surgery of the rectum - testing a new method in animal experiments [in German]. *Leber Magen Darm* 1983;13(2):73-77
- Kipfmüller K, Buess G, Naruhn M, Junginger T. Training program for transanal endoscopic microsurgery. *Surg Endosc* 1988;2(1):24-27
- Buess G, Kipfmüller K, Ibal R, et al. Clinical results of transanal endoscopic microsurgery. *Surg Endosc* 1988;2(4):245-250
- Saclarides TJ, Bhattacharyya AK, Britton-Kuzel C, Szeluga D, Economou SG. Predicting lymph node metastases in rectal cancer. *Dis Colon Rectum* 1994;37(1):52-57
- Vavra P, Dostalík J, Vavrova M, et al. Transanal endoscopic microsurgery: a novel technique for the repair of benign rectovaginal fistula. *Surgeon* 2009;7(2):126-127
- Quinlan M, Cahill R, Keane F, Grainger R, Butler M. Transanal endoscopic microsurgical repair of iatrogenic recto-urethral fistula. *Surgeon* 2005;3(6):416-417
- 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):342-343
- Bochove-Overgaauw DM, Beerlage HP, Bosscha K, Gelderman WA. Transanal endoscopic microsurgery for correction of rectourethral fistulae. *J Endourol* 2006;20(12):1087-1090
- 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* 2015;29(4):851-855
- Baatrup G, Svensen R, Ellensen VS. Benign rectal strictures managed with transanal resection—a novel application for transanal endoscopic microsurgery. *Colorectal Dis* 2010;12(2):144-146
- Kato K, Saito T, Matsuda M, Imai M, Kasai S, Mito M. Successful treatment of a rectal anastomotic stenosis by transanal endoscopic microsurgery (TEM) using the contact Nd:YAG laser. *Surg Endosc* 1997;11(5):485-487
- Beunis A, Pauli S, Van Cleemput M. Anastomotic leakage of a colorectal anastomosis treated by transanal endoscopic microsurgery. *Acta Chir Belg* 2008;108(4):474-476
- Zoller S, Joos A, Dinter D, et al. Retrorectal tumors: excision by transanal endoscopic microsurgery. *Rev Esp Enferm Dig* 2007;99(9):547-550
- Serra Aracil X, Gómez Díaz C, Bombardó Junca J, et al. Surgical excision of retrorectal tumour using transanal endoscopic microsurgery. *Colorectal Dis* 2010;12(6):594-595
- Buchs NC, Pugin F, Volonte F, Hagen ME, Morel P, Ris F. Robotic transanal endoscopic microsurgery: technical details for the lateral approach. *Dis Colon Rectum* 2013;56(10):1194-1198
- Liyanage C, Ramwell A, Harris GJ, Levy BF, Simson JN. Transanal endoscopic microsurgery: a new technique for completion proctectomy. *Colorectal Dis* 2013;15(9):e542-e547
- Bipat S, Glas AS, Slors FJ, Zwiderman AH, Bossuyt PM, 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):773-783
- Huh JW, Park YA, Jung EJ, Lee KY, Sohn SK. Accuracy of endorectal ultrasonography and computed tomography for restaging rectal cancer after preoperative chemoradiation. *J Am Coll Surg* 2008;207(1):7-12
- Saclarides TJ. TEM/local excision: indications, techniques, outcomes, and the future. *J Surg Oncol* 2007;96(8):644-650
- Druzijanić N, Perko Z, Kraljević D, et al. Harmonic scalpel in transanal endoscopic microsurgery. *Hepatogastroenterology* 2008;55(82-83):356-358
- Ayodeji ID, Hop WC, Tetteroo GW, Bonjer HJ, de Graaf EJ. Ultra-cision Harmonic Scalpel and multifunctional tem400 instrument complement in transanal endoscopic microsurgery: a prospective study. *Surg Endosc* 2004;18(12):1730-1737
- Hermesen PE, Ayodeji ID, Hop WH, Tetteroo GW, de Graaf EJ. Harmonic long shears further reduce operation time in transanal endoscopic microsurgery. *Surg Endosc* 2009;23(9):2124-2130
- Ramirez JM, Aguilera V, Arribas D, Martinez M. Transanal full-thickness excision of rectal tumours: should the defect be sutured? a randomized controlled trial. *Colorectal Dis* 2002;4(1):51-55
- Buess G, Mentges B, Manncke K, Starlinger M, Becker HD. Technique and results of transanal endoscopic microsurgery in early rectal cancer. *Am J Surg* 1992;163(1):63-69, discussion 69-70
- Simkens GA, Nienhuijs SW, Luyer MD, de Hingh IH. Massive surgical emphysema following transanal endoscopic microsurgery. *World J Gastrointest Surg* 2014;6(8):160-163
- Ganai S, Kanumuri P, Rao RS, Alexander AI. Local recurrence after transanal endoscopic microsurgery for rectal polyps and early cancers. *Ann Surg Oncol* 2006;13(4):547-556
- Bignell MB, Ramwell A, Evans JR, Dastur N, Simson JN. Complications of transanal endoscopic microsurgery (TEMS): a prospective audit. *Colorectal Dis* 2010;12(7 Online):e99-e103
- 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):1283-1287
- Flexer SM, Durham-Hall AC, Steward MA, Robinson JM. TEMS: results of a specialist centre. *Surg Endosc* 2014;28(6):1874-1878
- Marks JH, Valsdottir EB, DeNittis A, et al. Transanal endoscopic microsurgery for the treatment of rectal cancer: comparison of wound complication rates with and without neoadjuvant radiation therapy. *Surg Endosc* 2009;23(5):1081-1087

- 31 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* 2015;29(5):1045–1050
- 32 Gavagan JA, Whiteford MH, Swannstrom LL. Full-thickness intra-peritoneal excision by transanal endoscopic microsurgery does not increase short-term complications. *Am J Surg* 2004;187(5):630–634
- 33 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):2680–2683
- 34 Koebrugge B, Bosscha K, Ernst MF. Transanal endoscopic microsurgery for local excision of rectal lesions: is there a learning curve? *Dig Surg* 2009;26(5):372–377
- 35 Gracia Solanas JA, Ramírez Rodríguez JM, Aguilera Diago V, Elía Guede M, Martínez Díez M. A prospective study about functional and anatomic consequences of transanal endoscopic microsurgery. *Rev Esp Enferm Dig* 2006;98(4):234–240
- 36 Doornebosch PG, Gosselink MP, Neijenhuis PA, Schouten WR, Tollenaar RA, de Graaf EJ. Impact of transanal endoscopic microsurgery on functional outcome and quality of life. *Int J Colorectal Dis* 2008;23(7):709–713
- 37 Herman RM, Richter P, Walega P, Popiela T. Anorectal sphincter function and rectal barostat study in patients following transanal endoscopic microsurgery. *Int J Colorectal Dis* 2001;16(6):370–376
- 38 Wang HS, Lin JK, Yang SH, Jiang JK, Chen WS, Lin TC. Prospective study of the functional results of transanal endoscopic microsurgery. *Hepatogastroenterology* 2003;50(53):1376–1380
- 39 Jin Z, Yin L, Xue L, Lin M, Zheng Q. Anorectal functional results after transanal endoscopic microsurgery in benign and early malignant tumors. *World J Surg* 2010;34(5):1128–1132
- 40 Cataldo PA, O'Brien S, Osler T. Transanal endoscopic microsurgery: a prospective evaluation of functional results. *Dis Colon Rectum* 2005;48(7):1366–1371
- 41 Jeon JH, Cheung DY, Lee SJ, et al. Endoscopic resection yields reliable outcomes for small rectal neuroendocrine tumors. *Dig Endosc* 2014;26(4):556–563
- 42 Kawaguti FS, Nahas CS, Marques CF, et al. Endoscopic submucosal dissection versus transanal endoscopic microsurgery for the treatment of early rectal cancer. *Surg Endosc* 2014;28(4):1173–1179
- 43 Arezzo A, Passera R, Saito Y, et al. Systematic review and meta-analysis of endoscopic submucosal dissection versus transanal endoscopic microsurgery for large non-invasive rectal lesions. *Surg Endosc* 2014;28:427–438
- 44 Barendse RM, Oors JM, de Graaf EJ, et al. The effect of endoscopic mucosal resection and transanal endoscopic microsurgery on anorectal function. *Colorectal Dis* 2013;15(9):e534–e541
- 45 Moore JS, Cataldo PA, Osler T, Hyman NH. Transanal endoscopic microsurgery is more effective than traditional transanal excision for resection of rectal masses. *Dis Colon Rectum* 2008;51(7):1026–1030, discussion 1030–1031
- 46 Lin GL, Meng WC, Lau PY, Qiu HZ, Yip AW. Local resection for early rectal tumours: Comparative study of transanal endoscopic microsurgery (TEM) versus posterior trans-sphincteric approach (Mason's operation). *Asian J Surg* 2006;29(4):227–232
- 47 de Graaf EJ, Burger JW, van Ijsseldijk AL, Tettersoo GW, Dawson I, Hop WC. Transanal endoscopic microsurgery is superior to transanal excision of rectal adenomas. *Colorectal Dis* 2011;13(7):762–767
- 48 Christoforidis D, Cho HM, Dixon MR, Mellgren AF, Madoff RD, Finne CO. Transanal endoscopic microsurgery versus conventional transanal excision for patients with early rectal cancer. *Ann Surg* 2009;249(5):776–782
- 49 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):1492–1506, discussion 1500–1505
- 50 Hompes R, McDonald R, Buskens C, et al; Association of Coloproctology of Great Britain and Ireland Transanal Endoscopic Microsurgery Collaboration. Completion surgery following transanal endoscopic microsurgery: assessment of quality and short- and long-term outcome. *Colorectal Dis* 2013;15(10):e576–e581
- 51 Bach SP, Hill J, Monson JR, et al; Association of Coloproctology of Great Britain and Ireland Transanal Endoscopic Microsurgery (TEM) Collaboration. A predictive model for local recurrence after transanal endoscopic microsurgery for rectal cancer. *Br J Surg* 2009;96(3):280–290
- 52 Borschitz T, Heintz A, Junginger T. Transanal endoscopic microsurgical excision of pT2 rectal cancer: results and possible indications. *Dis Colon Rectum* 2007;50(3):292–301
- 53 Sengupta S, Tjandra JJ. Local excision of rectal cancer: what is the evidence? *Dis Colon Rectum* 2001;44(9):1345–1361
- 54 Doornebosch PG, Ferenschild FT, de Wilt JH, Dawson I, Tettersoo GW, de Graaf EJ. Treatment of recurrence after transanal endoscopic microsurgery (TEM) for T1 rectal cancer. *Dis Colon Rectum* 2010;53(9):1234–1239
- 55 Paty PB, Nash GM, Baron P, et al. Long-term results of local excision for rectal cancer. *Ann Surg* 2002;236(4):522–529, discussion 529–530
- 56 Ramirez JM, Aguilera V, Valencia J, et al. Transanal endoscopic microsurgery for rectal cancer. Long-term oncologic results. *Int J Colorectal Dis* 2011;26(4):437–443
- 57 Duek SD, Issa N, Hershko DD, Krausz MM. Outcome of transanal endoscopic microsurgery and adjuvant radiotherapy in patients with T2 rectal cancer. *Dis Colon Rectum* 2008;51(4):379–384, discussion 384
- 58 Lezoche E, Guerrieri M, Paganini AM, Feliciotti F. Long-term results of patients with pT2 rectal cancer treated with radiotherapy and transanal endoscopic microsurgical excision. *World J Surg* 2002;26(9):1170–1174
- 59 Lezoche E, Guerrieri M, Paganini AM, Baldarelli M, De Sanctis A, Lezoche G. Long-term results in patients with T2-3 N0 distal rectal cancer undergoing radiotherapy before transanal endoscopic microsurgery. *Br J Surg* 2005;92(12):1546–1552
- 60 Guerrieri M, Feliciotti F, Baldarelli M, et al. Sphincter-saving surgery in patients with rectal cancer treated by radiotherapy and transanal endoscopic microsurgery: 10 years' experience. *Dig Liver Dis* 2003;35(12):876–880
- 61 Tulchinsky H, Rabau M, Shacham-Shemueli E, et al. Can rectal cancers with pathologic T0 after neoadjuvant chemoradiation (ypT0) be treated by transanal excision alone? *Ann Surg Oncol* 2006;13(3):347–352
- 62 Kim CJ, Yeatman TJ, Coppola D, et al. Local excision of T2 and T3 rectal cancers after downstaging chemoradiation. *Ann Surg* 2001;234(3):352–358, discussion 358–359
- 63 Mohiuddin M, Marks G, Bannon J. High-dose preoperative radiation and full thickness local excision: a new option for selected T3 distal rectal cancers. *Int J Radiat Oncol Biol Phys* 1994;30(4):845–849
- 64 Schell SR, Zlotnick RA, Mendenhall WM, Marsh RW, Vauthey JN, Copeland EM III. Transanal excision of locally advanced rectal cancers downstaged using neoadjuvant chemoradiation. *J Am Coll Surg* 2002;194(5):584–590, discussion 590–591
- 65 Bonnen M, Crane C, Vauthey JN, et al. Long-term results using local excision after preoperative chemoradiation among selected T3 rectal cancer patients. *Int J Radiat Oncol Biol Phys* 2004;60(4):1098–1105
- 66 Lezoche G, Guerrieri M, Baldarelli M, et al. Transanal endoscopic microsurgery for 135 patients with small nonadvanced low rectal cancer (iT1-iT2, iN0): short- and long-term results. *Surg Endosc* 2011;25(4):1222–1229
- 67 Caricato M, Borzomati D, Ausania F, et al. Complementary use of local excision and transanal endoscopic microsurgery for rectal cancer after neoadjuvant chemoradiation. *Surg Endosc* 2006;20(8):1203–1207

- 68 Guerrieri M, Gesuita R, Ghiselli R, Lezoche G, Budassi A, Baldarelli M. Treatment of rectal cancer by transanal endoscopic microsurgery: experience with 425 patients. *World J Gastroenterol* 2014; 20(28):9556–9563
- 69 Marks J, Nassif G, Schoonyoung H, et al. Sphincter-sparing surgery for adenocarcinoma of the distal 3 cm of the true rectum: results after neoadjuvant therapy and minimally invasive radical surgery or local excision. *Surg Endosc* 2013;27(12):4469–4477
- 70 Borschitz T, Wachtlin D, Möhler M, Schmidberger H, Junginger T. Neoadjuvant chemoradiation and local excision for T2-3 rectal cancer. *Ann Surg Oncol* 2008;15(3):712–720
- 71 Hayden DM, Jakate S, Pinzon MC, et al. Tumor scatter after neoadjuvant therapy for rectal cancer: are we dealing with an invisible margin? *Dis Colon Rectum* 2012;55(12):1206–1212
- 72 De Graaf EJ, Doornebosch PG, Tollenaar RA, et al. Transanal endoscopic microsurgery versus total mesorectal excision of T1 rectal adenocarcinomas with curative intention. *Eur J Surg Oncol* 2009;35(12):1280–1285
- 73 Ptak H, Marusch F, Meyer F, et al. Colon/Rectal Cancer (Primary Tumor) Study Group. Oncological outcome of local vs radical resection of low-risk pT1 rectal cancer. *Arch Surg* 2007;142(7): 649–655, discussion 656
- 74 Lezoche E, Guerrieri M, Paganini AM, et al. Transanal endoscopic versus total mesorectal laparoscopic resections of T2-N0 low rectal cancers after neoadjuvant treatment: a prospective randomized trial with a 3-years minimum follow-up period. *Surg Endosc* 2005;19(6):751–756
- 75 Lezoche G, Baldarelli M, Guerrieri M, et al. A prospective randomized study with a 5-year minimum follow-up evaluation of transanal endoscopic microsurgery versus laparoscopic total mesorectal excision after neoadjuvant therapy. *Surg Endosc* 2008; 22(2):352–358