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Transanal Endoscopic Microsurgery in Young Patients: A Retrospective Study

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1. Abstract

1.1. Introduction: Local excision of rectal lesions is considered an acceptable choice for elderly and high-risk patients, yet data is scarce regarding its application in young adults.

1.2. Materials and Methods: Records of all patients under the age of 50 who underwent TEM procedure at the Hasharon Hospital, Rabin Medical Center, 2005-2016, were reviewed retrospectively.

1.3. Results: A total of 24 patients under the age of 50 years underwent TEM during the study period. The mean age was 42.1 years. The mean tumor size was 2.4 cm with a mean distance from the anal verge of 8.4cm. The majority of the tumors were located in the lateral walls. No major intraoperative or postoperative complications were recorded. Median length of stay was 2 days. Surgical margins were free of tumor in all cases. In the mean follow up of 55 months, local recurrence of the rectal tumor was detected in one patient.

1.4. Conclusion: Local excision by TEM for benign rectal lesions has an excellent outcome in young adult patients. For rectal cancer, TEM may offer the balance between efficacy of complete oncologic resection and postoperative quality of life, and may be considered, in selected cases, as an alternative to radical surgery for young adults.

2. Introduction

Colorectal Cancer (CRC) is the most common gastrointestinal neoplasia. The incidence of colon and rectal cancer in young patients is increasing [1,2].

Evidence has demonstrated worse outcomes for young adults with CRC [3], as death rates have increased since 2004to 1.3% per year in patients younger than 50 years of age [4]. However, data on outcome specifically for young patients with rectal cancer are controversial [5]; Some studies have demonstrated comparable survival outcomes in young and late onset patients, other studies have suggested poorer survival outcomes in young patients [6,7] Little is known as to the reason for which young adults without predisposing genetic abnormalities develop rectal cancer [8]. Young patients tend to present with a more advanced stage disease compared with their older counterparts [5,9]. The American National Comprehensive Cancer Network (NCCN) guideline for CRC screening has been recently revised and now recommend to begin screening at 45 years of age [10]. Routine screening for patients in Israelis still recommended to begin at the age of 50 years [11].

Younger age may affect therapeutic decisions. For example, patients who present with colon cancer before the age of 50 years are usually considered for a more radical surgery and undergo an extended colectomy [12]. The standard treatment for rectal tumors is radical surgical treatment, either by Anterior Resection (AR) or Abdominoperineal Resection (APR) along with a Total Mesorectal Excision (TME). For early rectal cancers, this procedure is usually curative but can have a substantial impact on quality of life due to

its high morbidity and mortality rates. In fact, adverse events after colorectal radical resection range from 20 to 40 percent, including anastomotic leakage, urinary and sexual dysfunction, and permanent colostomy [13,14]. Given the morbidity associated with TME, alternative approaches to management of rectal cancer have been explored, including local excision via Transanal Excision (TAE) or Transanal Endoscopic Microsurgery (TEM).

Surgery for rectal tumors in young patients should strive to balance the efficacy of oncologic control and quality of life [15]. TEM is an endoscopic local excision technique, which enables high quality excision of certain rectal lesions [16].

For benign rectal lesions, this technique has proven its superiority over the traditional TAE [17], while for early rectal cancer TEM has demonstrated better functional outcomes, and appears to have comparable long term survival rates when compared to radical surgery [18].

TEM is considered by several authors [19,20] to be the technique of choice for rectal adenoma and an acceptable alternative to radical resection in patients with low-risk T1 rectal adenocarcinoma. While local excision of rectal lesions is considered an acceptable choice for elderly and high-risk patients [21,22], data is scarce regarding its application in young adults [23]. The objective of this study is to explore the outcomes in young patients undergoing TEM for rectal lesions.

3. Methods

Approval for this retrospective cohort study was obtained from the Institutional Review Board of the Rabin Medical Center with a waiver of informed consent. All patients who underwent TEM procedure at the Hasharon Hospital, Rabin Medical Center from January 2005 to December 2016 were quarried. Patients under the age of 50 were included in the study, older patients were excluded.

Demographic and clinical and pathological data were retrospectively collected from the medical electronic data files. Among variables collected were tumor location, dimensions, histology, and indications for surgery. Data regarding operative findings post-operative outcomes, and post-operative complications were also collected.

Prior to surgery, patients underwent a pre-operative evaluation for TEM, according to a protocol which included full colonoscopy with biopsy, rigid proctoscopy to assess the tumor size, location within the rectal wall and distance from the anal verge, and the number of lesions. Endo-rectal ultrasound was also performed.

TEM was routinely proposed for patients who had benign rectal lesions non-amenable for endoscopic excision or those with early rectal cancer without evidence of lymph node involvement on imaging. TEM was also suggested to patients with indeterminate margins after endoscopic polypectomies, and for selected retro-rectal or submucosal lesions.

The preparation for surgery in TEM patients was similar to the preparation of patients undergoing colon resection. It included mechanical bowel preparation on the day before the operation and administration of prophylactic antibiotics at the time of anesthesia induction. The original Richard Wolf equipment was used to perform the procedure, the detailed surgical technique of TEM is described elsewhere [24]. All rectal wall defects were closed. All patients had a urinary catheter in place at the time of surgery, which was removed on the first day after surgery. Patients resume oral intake of a liquid and soft diet on the first post-operative day and are subsequently advanced. Pain management included oral dipyrone or paracetamol, and narcotics as needed. Patients were discharged when diet was well tolerated and no complications were detected. Perioperative complications were defined as unexpected and untoward events occurring either during the procedure or on the postoperative period.

Patients were evaluated two weeks after surgery and re-examined at 3-month intervals for the first two postoperative years, and every 6 months thereafter. Clinical examination and rectoscopy were performed during each of the follow-up sessions.

Patients were referred to radical rectal resection whenever pathology specimen of the TEM showed rectal wall invasion; pT2, pT3 or high risk T1tumors as pT1 sm3, or lympho-vascular invasion.

Descriptive data analyses were performed by calculating frequencies and percentages for categorical variables and mean and range for continuous variables.

4. Results

A total of 165 patients underwent a TEM procedure in the study period. Of them, 24 patients (15%) were under the age of 50 years and underwent the procedure were included. Table 1 summarizes patients' demographic data and tumors' characteristics. The mean age was 42.1 years (range 21-49). Thirteen (54%) of the patients were male and eleven (46%) females. Most patients (n=15, 62%) had an American Society of Anesthesiology (ASA) score of 1. Six (26%) rectal lesions were adenomas with low grade dysplasia (LGD), five (21%) were adenomas with high grade dysplasia (HGD), four (17%) had involved margins after endoscopic polypectomy, and five (21%) had other pathologies (two suspected carcinoid, and three undetermined pathology). Four rectal lesions had carcinoma by the preoperative biopsies, the staging of all the tumors was T1 SM1 (17%), all were with favorable histological features; no lymphovascular invasion, nor perineural invasion. The mean tumor size was 2.4 cm (range 1- 4); with a mean distance from the anal verge of 8.4cm (range 5-13). Seven (29%) of the lesions were located in the posterior rectal wall, three (13%) in the anterior wall and fourteen (58%) in the lateral walls.

Table 1: Patient demographics and clinical variables

Variable		Patients (n=24)
Age, years (range)		42 (21-49)
Sex, male/female		13-Nov
BMI, kg/cm^2 (range)		21.4 (21-40)
ASA* score (%)	1	15 (62.5%)
	2	6 (25%)
	3	3 (12.5%)
Indication of surgery (%)	Adenoma LGD†	6 (25%)
	Adenoma HGD‡	5 (21%)
	Carcinoma	4 (17%)
	Indeterminate margins after polypectomy	4 (17%)
	Other	5 (21%)
Tumor Diameter, cm (range)		2.4 (1-4)
Distance from anal verge, cm (range)		8.4 (5-13)
Rectal wall location (%)	Posterior	7 (29%)
	Anterior	3 (13%)
	Right lateral	9 (37.5%)
	Left lateral	5 (21%)

*ASA – American Society of Anesthesiology

† LGD – Low Grade Dysplasia

‡ - HGD – High Grade Dysplasia

Perioperative variables are summarized in Table 2. Mean operative time was 68 minutes (range 46-108 minutes). No major intraoperative or postoperative complications were recorded. Estimated blood loss during surgery was minimal. The only minor complication documented was postoperative urinary retention which occurred in two patients. Median length of stay was 2 days (range 1-4). There was one re-admission in the postoperative period of a patient who experienced rectal bleeding four days after discharge; he was treated conservatively without need for blood transfusion or any invasive intervention. No other readmissions were recorded.

Table 2: Operative variables

Variable		Patients (n=24)
Operation time, minutes (range)		68 (46-108)
Hospital length of stay, days (range)		2 (1-4)
Perioperative complications (%)	Peritoneal entry	0
	Bleeding	0
	Urinary retention	2 (8.5%)

Observing the final pathological reports of the specimens (Table 3); adenocarcinoma was found in 6 patients; T1 carcinoma in four patients (17%) and T2 in two patients (8%). Adenomatous polyp was found in 12 patients; HGD in 6 patients (25%), LGD in 4 patients (17%), and no residual disease after endoscopic polypectomy in 2(8.5%) patients. Other pathologies include carcinoid tumor, neuroendocrine tumor, endometriosis, and a solitary rectal ulcer. Surgical margins were free of tumor in all cases.

Completion of rectal resection was required in two patients with T2 carcinoma on final pathology; both underwent laparoscopic AR 10 weeks after the TEM. No residual pathology was found in the AR specimen in the 2 cases.

In the mean follow up of 55 months (range 20 to 81 months; median 80 months) local recurrence of the rectal tumor was detected in one female patient at 33 months after TEM. The patient underwent radio-chemotherapy followed by laparoscopic APR. The final pathology was T3 without nodal involvement.

No cases of postoperative incontinence were reported.

Table 3: Pathology results:

Pathology (%)	Patients (n=24)
Adenoma LGD*	4 (17%)
Adenoma HGD†	6 (25%)
Carcinoma T1	4(17%)
Carcinoma T2	2 (8.5%)
Carcinoid	3 (13%)
NED‡	1 (4%)
SRU§	1(4%)
Endometriosis	1(4%)
No residual tumor	2 (8.5%)

* LGD – Low Grade Dysplasia

† HGD – High Grade Dysplasia

‡ NED – Neuroendocrine tumor

§ SRU – solitary rectal cancer

5. Discussion

Minimally invasive colorectal surgical techniques such as TEM, offers an effective treatment option with minimal morbidity. While traditionally local excision for rectal lesion was considered a more acceptable choice for elderly and high-risk patients [21.22], TEM is, in actual fact, considered by several authors [19,20] to be the technique of choice for rectal adenoma and an acceptable alternative to radical resection in patients with low-risk T1 rectal carcinoma.

Offering more radical resections for young patients with rectal lesions seems a reasonable oncological choice given the advantages of the radical surgery in patients with a longer life expectancy. On the other hand, radical rectal resection carries the risk of considerable postoperative morbidity, and consequently, when considering the balance between oncological resection of the rectal lesion and postoperative morbidity, it is reasonable to opt for TEM instead [25,26].

The overall complication rate for TEM for benign and malignant lesions has been reported to range from 6% to 31% [27]. Among possible perioperative complications are urinary retention, postoperative infection, suture line dehiscence, and bleeding. Tsai et al. [28] reported a 10.8% rate of urinary retention in their study cohort. The current study reports only 2 (8.5%) cases of urinary retention recorded in the perioperative course. Neither overall complications nor length of hospitalization were increased in the present study.

Another concern of morbidity is postoperative incontinence. Cataldo et al. [29] addressed this issue, founding no significant deleterious effects of TEM on fecal continence. Another study by Morino et al. [19] noted a temporary decrease in post procedure anal resting pressure, which returned to preoperative values at a mean time of 4 months postoperatively. In accordance with previously published reports, this study cohort reports no incidences of incontinence.

Undoubtedly, the treatment of rectal tumors in young patients presents a challenge for the surgeon in obtaining the optimal results combining both oncological outcome and quality of life. Some studies have suggested a more aggressive disease is at play in younger adults with rectal carcinoma [30,31]. Other series demonstrated no significant differences in oncologic outcomes when comparing patients aged under and over 50 years with rectal tumors when adjusting for tumor stage, suggesting that patients under the age of 50 years who present with rectal tumors do not necessarily have more aggressive disease [32].

Attempts of aggressive management, such as radical resection in young patients with colorectal tumors, have not resulted in improved outcome. Considering the increasing incidence of such tumors in young adults, it is suggested they be handled in the same manner as older patients [33]. When discussing benign lesions, retrospective evidence shows that TEM is more effective than transanal local excision in achieving clear margins and resulting in a less fragmented specimen, and is associated with lower recurrence rates [27]. When a benign rectal lesion is situated in the upper rectum, TEM represents an alternative to the transabdominal approach, especially considering the association of the latter with high morbidity and mortality in the all-age groups [34] possibly having more impact in young patients. Observing long term results, no incontinence was reported among the patients. In accordance of published reports. On the other hand, patients undergoing anterior resection of rectum experience anterior resection syndrome symptoms in 50-90% of cases [34].

TEM is more effective than traditional TAE for resection of benign rectal masses, in all ages [27]. When concerning malignant rectal lesions, TEM is considered safe and effective in treating certain T1 lesions with favorable features and without adverse pathologic findings. When compared to radical rectal resection via the transabdominal approach it has been shown to be associated with lower morbidity and mortality [35,36].

local recurrence of a rectal tumor was detected in one female patient at 33 months after TEM. A 49-year-old female, who had a flat polyp in the lower rectum, final pathology revealed a TVA HGD polyp with free margins. The patient developed a recurrence 33 months after the TEM. The patient underwent radiochemotherapy treatment followed by laparoscopic APR. The final pathology was T3 without nodal involvement.

In our series all T1 cancer were sm1. TEM currently is indicated as a curative treatment of malignant neoplasms that are histologically confirmed as pT1sm1 carcinomas. The optimal management of the T1sm2 tumors without any unfavorable criteria remains unclear due to lymph node positivity. In fact, node positivity increases for increasing level of infiltration of the submucosa, with 1-3% of nodes for T1sm1 lesions, 8-10% for T1sm2, and up to 25% in T1sm3 [37]. We suggest young patients withT1sm2 lesions be offered radical rectal surgery at this current time, with TEM limited to patients participating in prospective trials with adjuvant or neoadjuvant treatment [38].

Two patients in the present study had a T2 tumor in the final pathology, and subsequently underwent a radical rectal resection as a completion surgery. Completion of surgery after TEM procedure has been demonstrated to be safe and returns oncological outcome to that of primary radical TME surgery. This effect is also seen in series where immediate reoperation is performed [39,40]. In actual fact, laparoscopic rectal surgery following TEM is safe, and bears no negative impact on the completeness of the resection [41].

The standard of treatment for rectal T2 adenocarcinoma is TME via the transabdominal approach with or without adjuvant and neoadjuvant therapy [42]. Considering the high recurrence rate with probably of occult lymph node metastases [43]. An unexpected T2 excised by TEM can be safely managed by salvage radical surgery

with good oncological outcomes.

Local recurrence rates after TEM range from 0 to 33% for T1 rectal cancers [44]. In a study by Stipa et al. [45], 96% (26/27) of patients with local recurrence after TEM underwent subsequent salvage surgery, with 9 requiring repeat TEM, and 17 who underwent radical surgery. In patients who underwent radical salvage surgery, 5-year survival was 69%, which is comparable with previously reported data [46].

Previous data suggest that TEM for rectal cancer, even in cases of local recurrence followed by radical salvage surgery, offers overall long-term survival, comparable to that obtained with initial radical surgery [45]. Risk of recurrence is mitigated by the high repeatability of the procedure, as well as the good satisfactory outcomes seen with salvage radical resection.

A single case of local recurrence was recorded in this study, the patient had a low rectal polyp, final pathology after TEM was high grade dysplasia. Recurrence occurred 33 months after the TEM procedure, patient underwent a subsequent laparoscopic APR with permanent colostomy. According to some reports, patients requiring radical rectal resection after having undergone TEM for a distal rectal lesion are more likely to result in an APR rather than a low AR. This probable outcome is attributed to the more challenging nature of the radical rectal resection procedure in such circumstances, secondary to scar formation [47,48]. The transanal TME technique could probably overcome these technical difficulties and thus influence over the rate of permanent colostomy in these patients and avoid unnecessary APR [49]. While TEM may offer quality of life with non-inferior long term oncologic safety, it may necessitate a longer period of postoperative follow up. However, exact frequency and length of required follow-up period are yet to be defined, suggesting treatment of these patients as “high risk” until further data become available from larger randomized controlled trials.

This study is limited by its small sample size and retrospective nature. Long accrual periods contribute to variability in the perioperative care as it evolved over the years, and diagnostic modalities were not uniform for all patients, impacting the choice of surgical approach.

Local excision by TEM is considered a valid alternative to the traditional surgical treatment of adenomas and low risk (T1) rectal tumors [25], but it is certainly an oncologic compromise, in cases of more advanced and high-risk rectal lesions, for which rectal resection by TME is considered the standard of care [24]. Nonetheless, radical rectal resection carries a considerable postoperative morbidity when performed within a short period of time following TEM, and therefore, it is justifiable to opt for TEM instead [26].

TEM offers the benefits of providing quality of life without oncological compromise and without compromising oncological results. This surgical approach is likely not suitable for patients with ‘polypogenic rectums’ which have several lesions. These would likely benefit from an up-front radical resection of the rectum instead of repeat TEMs, due to the increased burden and cost of undergoing repeated surgical procedures.

6. Conclusion

Local excision by TEM for benign rectal lesions is safe and has an excellent outcome in young adult patients. For early rectal cancer, TEM may offer the balance between efficacy of complete oncologic resection and postoperative quality of life, and it may be considered, in selected cases, as an alternative to radical surgery in this group of patients.

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