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Transanal Endoscopic Microsurgery in Small, Large, and Giant Rectal Adenomas

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Objective: To assess the outcomes of transanal endoscopic microsurgery in small (<3 cm), large (3-5 cm), and giant (>5 cm) lesions and compare these with reports of alternative techniques.

Design: Data from January 1998 to February 2010 were prospectively collected. Lesions were divided into 3 groups according to the maximum diameter (group A, <3 cm; group B, 3-5 cm; and group C, >5 cm) and outcomes were analyzed separately.

Setting: Colorectal unit in a single-district general hospital.

Patients: Patients diagnosed as having benign rectal adenomas.

Intervention: Transanal endoscopic microsurgery excision.

Main Outcome Measures: Completion of excision (R0), en bloc and full-thickness excisions, complication and local recurrence rates, and disease-free survival.

Results: A total of 320 lesions were analyzed. Overall en bloc and full-thickness excision rates were 99% and 80.7%, respectively. In the 279 benign lesions, the R0 rate was 90.3%. Outcomes for groups A, B, and C were, respectively: 9.3%, 12.8%, and 14.4% incidence of unexpected malignancy ($P=.64$); 95.9%, 92.2%, and 85.1% R0 resection for benign lesions ($P=.19$); and 7.4%, 14.9%, and 24.6% complication rates ($P<.05$). Overall operative mortality was 1 of 320 (0.3%). In group C, there was a higher estimated recurrence rate, therefore a lower disease-free survival than groups A and B; this difference was significant 40 months after surgery. Recurrences were associated with closeness to dentate line and advanced age (univariate analysis) and R1 resection (Cox regression).

Conclusions: Outcomes of transanal endoscopic microsurgery on large rectal lesions compared favorably with literature reports of alternative techniques. Postoperative complications and recurrences increased significantly with lesions larger than 5 cm.

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TRANSANAL ENDOSCOPIC MIcrosurgery (TEMS) is a minimally invasive technique for local excision of some rectal adenomas and other lesions not amenable to traditional endoscopic resection. It was first described by Buess et al[1] in 1984 and since then has gained popularity in view of its safety and ability to provide intact full-thickness specimens with low R1 resection and recurrence rates.[2-5] However, there is some debate as to the best technique for excision of large (>3 cm), and particularly giant, rectal adenomas in view of the increased risk for occult malignancy in large adenomas[5-9] combined with the significant incidence of R1 resections for traditional peranal techniques and piecemeal resection for endoscopic techniques such as endoscopic mucosal resection (EMR) in these lesions.[7,10-13]

See Invited Critique at end of article

Our study examined the R0 resection, en bloc and full-thickness excision, and recurrence and complication rates for TEMS in a consecutive series of large (3-5 cm) and giant (>5 cm) rectal adenomas and compared these with outcomes for small (<3 cm) lesions. We also reported outcomes for alternative techniques on lesions of equivalent size. The rationale for the division in 3 size groups is as follows. First, literature reports have suggested that EMR can provide en bloc excision for lesions less than 3 cm, therefore the study aimed to compare the outcomes of TEMS vs EMR in that group. Second, the literature has tended to

describe giant rectal lesions as being greater than 5 cm; our study aimed to compare outcomes of TEMS with the literature in this group. The residual 3-5 cm group was included for completeness.

METHODS

Data on all patients who underwent TEMS for benign rectal adenomas in St Richard's Hospital, Chichester, between January 1998 and February 2010 were collected in a prospective database. The anonymous analysis of the database was exempted from trust ethical committee (institutional review board equivalent) approval. Some of these patients have already been described elsewhere.[2,14,15] Preoperative staging included endoscopic assessment, biopsy sampling, pelvic magnetic resonance imaging (MRI), and endoanal ultrasound scan. However, radiologic assessment of the lesions was not uniform throughout the series, therefore these data were unsuitable for analysis. Lesions with a histologic proven diagnosis of invasive malignancy were excluded.

Patient demographics, complications, mortality, and recurrences were recorded. The resected lesions were analyzed for size, histology, thickness of excision, presence of unexpected cancer, and resection margin status. Low rectal lesions within 2 cm of the dentate line were excised with conservation of the underlying proximal internal sphincter; therefore, they were classified as partial-thickness excisions. Partial-thickness excision was also preferred on benign low anterior lesions in men to avoid nerve damage and, early in the series, on lesions above the peritoneal reflection to avoid a peritoneal defect. Late in the series, high anterior lesions were removed full thickness and the peritoneal defect sutured intraoperatively. Controlled recognized intraoperative breach of the peritoneum in high anterior lesions was not classified as perforation.[16] If there was evidence of incomplete resection of the muscularis propria in any part of the specimen either macroscopically or microscopically, the resection was classified as partial thickness. The specimens were pinned out on a corkboard in theater and the diameter of the lesion was recorded by the histopathologist in the fixed specimen. The 3 piecemeal specimens were resected in 2 to 3 large pieces and reconstructed when pinned out, allowing for measurement of the diameter (though not the margin status). Operative resection margins were 5 mm for benign lesions and 10 mm for adenomas suspected of containing foci of malignancy. Complete (R0) or incomplete (R1) resection margins were assessed by the pathologist. Lesions removed piecemeal were automatically classified as R1. Major complications were defined as sepsis, bleeding requiring transfusion, intraperitoneal perforation diagnosed postoperatively, pneumonia, rectovaginal fistula, pulmonary embolism, and myocardial infarction. Minor complications were defined as urinary tract infections/urinary retentions, temporary incontinence, rectal stenosis, fecal impaction, tenesmus, and minor bleeding.

The starting point of follow-up was the date of the TEMS, while the terminating point was the date of local recurrence, the patient's death, or the patient's last visit available from records. Local recurrent lesions were defined as those manifesting on the previous surgical site during follow-up. Primary and recurrent benign lesions, independent from the resection margins status, had standard follow-up with sigmoidoscopy at 4, 12, and 24 months. Yearly follow-up with rigid sigmoidoscopy in the outpatient clinic was continued beyond 24 months when spontaneously requested by the patients. All malignant lesions treated by TEMS alone had standard follow-up, with flexible sigmoidoscopy and pelvic MRI every 6 months for 2 years, then annually to 5 years, and with computed tomographic chest/abdomen/pelvis scans at 1, 2, and 5 years. In addition, we used recorded longer-term data from routine subsequent colonoscopic follow-up on eligible patients according to national guidelines.[17] Excluded from the analysis of recurrence rates were patients who did not attend any follow-up visits and for which no data were available, those who died perioperatively, and those with unexpected malignant histology who underwent immediate radical resection after TEMS. The outcome data were analyzed in 3 subgroups according to the maximum diameter of the lesion recorded in the histopathologic report: group A, <3 cm; group B, 3-5 cm; and group C >5 cm. The analysis of recurrence rates at follow-up was reported as disease-free survival. Disease-free survival was the time from the TEMS procedure to the diagnosis of recurrence.

All data were initially entered into an ACCESS database (Microsoft), and the analysis was performed using the Statistical Package for the Social Sciences Windows version 13.0 (SPSS). Descriptive statistics consisted of the mean (SD) for parameters with Gaussian distributions (after confirmation with histograms and the Kolgomorov-Smirnov test), median (range) for non-Gaussian distributions, and frequencies for categorical parameters.

Comparisons among groups A vs B vs C were performed with the 1-way analysis of variance for continuous Gaussian variables and Kruskal-Wallis test for continuous non-Gaussian variables. Comparisons between groups A vs B+C were performed with the Mann-Whitney *U* test for continuous non-Gaussian variables. The χ^2 or Fisher exact tests were used for categorical variables (Fisher test, if cell counts were inferior to 5). The Kaplan-Meier method was used to perform the time-to-event analysis and evaluate the recurrence rates among the 3 groups, which were reported as disease-free survival. For this purpose, estimation of the rates was conducted up to 7 years of follow-up owing to the small number of patients available afterwards. The risks for recurrence among the 3 groups were compared with the log-rank Mantel-Cox method. Cox regression was used to study the influence of these covariates on recurrences. $P < .05$ was considered statistically significant. The Kaplan-Meier method was also used to perform the time-to-event analysis and evaluate the mortality rates among the 3 groups, which was reported as overall survival.

RESULTS

A total of 320 lesions with a preoperative diagnosis of benign adenoma were resected. Demographics as well as lesion areas and locations in relation to dentate line and rectal wall are summarized in **Table 1** (lesion diameter in Table 1 and **Figure 1**). Of 320 lesions, 124 lesions (38.7%) were 10 cm or greater from the dentate line and 31 lesions (9.6%) were 3 cm or less.

HISTOLOGIC ANALYSIS

The histologic findings are shown in Table 1. There were 49 adenomas in group A with a median maximum diameter of 2 cm (range, 0.6-2.8 cm) and a median lesion area of 3.6 cm^2 (range, 0.3-6.2 cm^2). In 5 of these (9.3%), there was an unexpected focus of adenocarcinoma. In group B, there were 129 adenomas with a median maximum diameter of 4 cm (range, 3.0-5.0 cm) and a median lesion area of 12.0 cm^2 (range, 4.5-25.5 cm^2). Nineteen of these (12.8%) contained unexpected malignancies. In group C, there were 101 adenomas with a median maximum diameter of 7 cm

Table 1. Demographics and Histopathologic Data of Patients Operated On[a]

Characteristic	No. (%) All Patients (N = 320)	Group A (n = 54)	Group B (n = 148)	Group C (n = 118)	*P* Value, χ^2	
Male	158 (49.4)	25 (46.3)	75 (50.7)	58 (49.2)	.86[c]	.62[d]
Age, mean (SD), y	70.5 (11.3)	69.6 (13.5)	69.2 (10.9)	72.5 (10.6)	A, .08[c]	A .55[d]
Lesion diameter, median (range), cm	4.5 (0.6-27.0)	2.0 (0.6-2.8)	4.0 (3.0-5.0)	7.0 (5.2-27.0)	K<.001[c]	M<.001[d]
Lesion area, median (range), cm^2	16.0 (0.3-196.0)	3.6 (0.3-6.2)	12.0 (4.5-25.5)	33.4 (0.5-196.0)	K<.001[c]	M<.001[d]
Distance from dentate line, mean (SD), cm	7.4 (4.4)	8.6 (4.1)	8.2 (4.0)	5.9 (4.7)	A<.001[c]	A<.001[d]
Anterior wall involvement	166 (51.9)	22 (40.7)	75 (50.7)	69 (58.5)	.09[c]	.07[d]
En bloc excision	317 (99.0)	54 (100.0)	148 (100.0)	115 (97.5)	.12[c]	>.99[d]
Full-thickness excision, no./No. (%)	243/301 (80.7)	29/52 (55.8)	123/143 (86.0)	91/106 (85.8)	<.001[c]	<.001[d]
Histology and T category						
Adenoma	279 (87.2)	49 (90.7)	129 (87.2)	101 (85.6)	.64[c]	.39)[d]
Severe dysplasia	94 (33.7)	19 (35.2)	38 (25.7)	37 (31.4)	.35[c]	.30[d]
Adenocarcinoma	41 (12.8)	5 (9.3)	19 (12.8)	17 (14.4)	.64[c]	.39[d]
T1, no./No. (%)	29/41 (70.7)	4/5 (80.0)	13/19 (68.4)	12/17 (70.6)		
Sm1, no./No. (%)[b]	10/29 (34.5)	1/4 (25.0)	4/13 (30.8)	5/12 (41.7)		
Sm2, no./No. (%)	10/29 (34.5)	1/4 (25.0)	6/13 (46.2)	3/12 (25.0)		
Sm3, no./No. (%)	6/29 (20.7)	2/4 (50.0)	1/13 (7.6)	3/12 (25.0)		
Smx, no./No. (%)	3/29 (10.3)	0/4 (0.0)	2/13 (15.4)	1/12 (8.3)		
T2, no./No. (%)	10/41 (24.4)	1/5 (20.0)	5/19 (26.3)	4/17 (23.5)		
T3, no./No. (%)	2/41 (4.9)	0/5 (0.0)	1/19 (5.3)	1/17 (5.9)		

Abbreviations: A, analysis of variance 1-way+Bonferroni test; K, Kruskal-Wallis test; M, Mann-Whitney *U* test; Sm, submucosal.
[a] In 19 patients, thickness of excision was unrecorded.
[b] Kikuchi subclassification for T1 carcinomas within sessile lesions.
[c] Comparison among groups A vs B vs C. No significant differences in the T category (T1, T2, and T3) were found when comparing groups A vs B vs C (Fisher exact test; *P* = .70) or groups A vs B+C (Fisher exact test; *P* = .65).
[d] Comparison between group A vs (B+C).

(range, 5.2-27.0 cm) and a median lesion area of 33.4 cm^2 (range, 3.5-196.0 cm^2). Unexpected malignancies were found in 17 cases (14.4%). T category and Kikuchi subclassification are shown in Table 1. There was no statistically significant difference among the 3 groups in the incidence of severe dysplasia or unexpected malignancy (*P* = .64). Two patients with T3 cancers were not identified preoperatively. One was treated in 2000 before endoanal ultrasound scan and MRI were available. The second was understaged preoperatively.

UNEXPECTED MALIGNANCY

Of the 41 patients with unexpected malignancy, no significant differences in the T category (T1, T2, and T3) were found when comparing groups, A vs B vs C (Fisher exact test; *P* = .70) or group A vs B+C (Fisher exact test; *P* = .65). Ten patients underwent immediate radical resection because of unfavorable histology including 4 patients with involved margins. The remaining 31 patients had no immediate radical resection (10 patients because of favorable histology [T1 submucosal stage 1, well differentiated with no lymphovascular invasion] and 21 patients owing to informed patient choice or unfitness for surgery in the presence of unfavorable histology).

RESECTION MARGINS AND TECHNIQUE OF EXCISION

The en bloc excision rate was 99% overall and 100% for lesions less than 5 cm (Table 1). Only 3 of 118 giant lesions (2.5%) were excised piecemeal. The thickness of excision was recorded in 301 of 320 lesions (94.1%). Of these 301 lesions, 243 (80.7%) were excised full thickness and 58 (19.3%) were excised partial thickness. The rate of full-thickness excision was significantly lower in group A (*P* < .001). No significant differences were observed for the resection margin involvement (R1) rate when the procedures were classified according to the be-

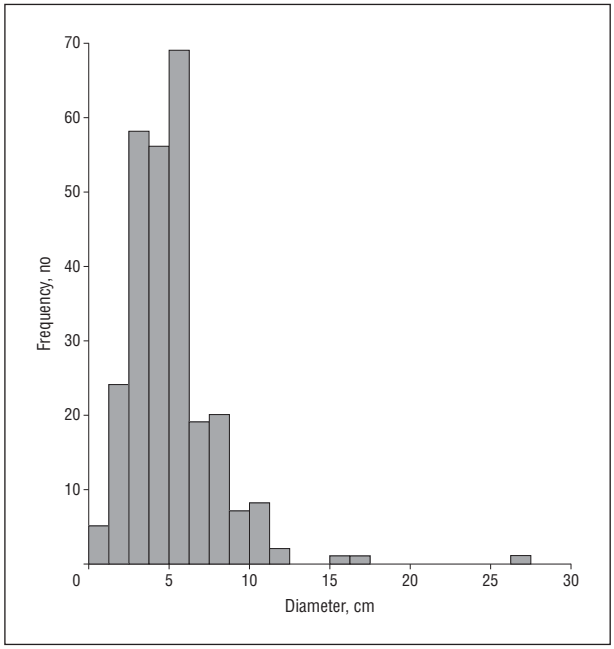

Figure 1. Histogram showing frequencies of lesion diameter.

Table 2. Postoperative Results of Patients Operated On[a]

	No. (%)					
	All patients (N = 320)	Group A (n = 54)	Group B (n = 148)	Group C (n = 118)	*P* Value, χ^2	
Resection Margins Status						
Overall R1 resection	31 (9.7)	2 (3.7)	14 (9.5)	15 (12.7)	.30[b]	.26[c]
Adenomas R1 resection, no./No. (%)	27/279 (9.7)	2/49 (4.1)	10/129 (7.8)	15/101 (14.9)	.19[b]	.34[c]
Adenocarcinomas R1 resection, no./No. (%)	4/41 (9.8)	0/5 (0.0)	4/19 (21.1)	0/17 (0.0)	.16[b]	.67[c]
Perioperative Complications						
Minor complications	29 (9.1)	1 (1.9)	10 (6.8)	18 (15.3)	<.01[b]	<.05[c]
UTI/urinary retention	16 (5.0)	0 (0.0)	5 (3.4)	11 (9.3)		
Temporary incontinence	4 (1.3)	1 (1.9)	2 (1.4)	1 (0.8)		
Rectal stenosis	4 (1.3)	0 (0.0)	1 (0.7)	3 (2.5)		
Tenesmus	3 (0.9)	0 (0.0)	1 (0.7)	2 (1.7)		
Minor bleeding	1 (0.3)	0 (0.0)	1 (0.7)	0 (0.0)		
Fecal impaction	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.8)		
Major complications	26 (8.1)	3 (5.6)	12 (8.1)	11 (9.3)	.7[b]	.45[c]
Sepsis	11 (3.4)	1 (1.9)	3 (2.0)	7 (5.9)		
Significant bleeding	10 (3.1)	2 (3.7)	6 (4.1)	2 (1.7)		
Pneumonia	2 (0.6)	0 (0.0)	1 (0.7)	1 (0.8)		
Perforation	1 (0.3)	0 (0.0)	1 (0.7)	0 (0.0)		
Rectovaginal fistula	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.8)		
PE/MI	1 (0.3)	0 (0.0)	1 (0.7)	0 (0.0)		
Total complications	55 (17.2)	4 (7.4)	22 (14.9)	29 (24.6)	<.05[b]	<.05[c]
Mortality						
Postoperative mortality	1 (0.3)	0 (0.0)	1 (0.7)	0 (0.0)	.56[b]	.65[c]
Cancer-related mortality	2 (0.6)	1 (1.9)	0 (0.0)	1 (0.8)	.31[b]	.21[c]
Other mortality	20 (6.3)	7 (13.0)	9 (6.1)	4 (3.4)	.06[b]	<.05[c]
Overall mortality	23 (7.2)	8 (14.8)	10 (6.8)	5 (4.2)	.05[b]	<.05[c]

Abbreviations: MI, myocardial infarction; PE; pulmonary embolism; UTI, urinary tract infection.

[a] Twenty-three patients were excluded from analysis of local recurrence: 9 were lost on follow-up, 1 died perioperatively, 3 died early after hospital discharge of causes unrelated to surgery, and 10 patients had unexpected malignant histology and underwent immediate radical resection after transanal endoscopic microsurgery.

[b] Comparison among groups A vs B vs C.

[c] Comparison between groups A vs B+C.

nign vs malignant lesions status and group of diameter (**Table 2**). The R1 resection rates for lesions excised full thickness and for lesions excised partial thickness were 23 of 243 (9.5%) and 6 of 58 (10.3%), respectively. Even in this case, there was no statistically significant difference in the R1 rates between the 2 techniques ($P = .84$).

PERIOPERATIVE MORBIDITY AND MORTALITY

There was 1 perioperative death in group B only. This patient had a delayed intraperitoneal perforation on the first postoperative day, was treated with a primary closure of the perforation and defunctioning loop colostomy, and died 9 days later of multiorgan failure. Data on minor and major postoperative complications are summarized in Table 2. In 19 patients who underwent full-thickness excision of high anterior lesions, the peritoneum was breached and sutured intraoperatively with no added morbidity. The incidence of complications was significantly greater after excision of larger lesions (Table 2).

FOLLOW-UP RESULTS

Twenty-three patients (12 with benign and 11 with malignant lesions) were excluded from the follow-up analysis: 12 did not attend follow-up, 1 died perioperatively, and 10 patients had unexpected malignant histology that underwent immediate radical resection after TEMS. The excluded patients were equally represented among groups: group A = 4 (8%), group B = 12 (8%), and group C = 7 (6%; χ^2 test; $P = .41$).

MALIGNANT LESIONS

Of the 31 malignant lesions treated by TEMS local excision alone, 1 patient declined further treatment and did not attend follow-up, 2 patients died within 6 months of surgery for causes unrelated to surgery, and 7 patients developed a malignant recurrence (all intraluminal), although all had R0 resection margins and full-thickness en bloc excision. None of the 31 patients had neo-adjuvant or adjuvant chemotherapy with or without or radiotherapy. The original histology from the previous TEMS in the 7 recurrences was pT1sm1 in 3 patients, pT1sm3 in 2, and pT2 in 2. At the time of the primary excision, 3 patients opted consciously for conservative management and 4 patients were unfit for radical surgery. The recurrences were treated with chemoradiotherapy and salvage radical surgery in 2 cases, with 1 further recurrence. One patient was successfully treated by repeat TEMS. Another underwent palliative radiotherapy. The remaining 3 patients had no further treatment because of advanced age and comorbidities.

Table 3. Estimated Recurrence Rates With the Kaplan-Meier Method[a]

Follow-up, y	Group A			Group B			Group C		
	Patients, No.	Cumulative Recurrences, No.	Cumulative Recurrence Rate, %	Patients, No.	Cumulative Recurrences, No.	Cumulative Recurrence Rate, %	Patients, No.	Cumulative Recurrences, No.	Cumulative Recurrence Rate, %
0	50	0	0.0	136	0	0.0	111	0	0.0
1	38	0	0.0	130	2	1.5	109	2	1.8
2	32	0	0.0	100	5	4.5	83	5	5.4
3	31	1	3.2	60	8	9.5	55	7	9.1
4	11	2	12.3	55	8	9.5	20	11	29.1
5	7	2	12.3	13	8	9.5	10	11	29.1
6	6	2	12.3	10	8	9.5	3	13	95.8
7	3	2	12.3	7	9	23.8	3	13	95.8
8	2	2	12.3	3	9	23.8	3	13	95.8
9	1	2	12.3	1	9	23.8	3	13	95.8
10	1	2	12.3	1	9	23.8	2	13	95.8
>10	1	2	12.3	1	9	23.8	1	14	100.0

[a]Values were grouped per year. Although all results were reported, a reliable estimate could be performed only until the seventh year of follow-up owing to the paucity of patients afterwards.

RECURRENCES

The time-to-event analysis performed with the Kaplan-Meier method showed different trends of recurrence rates among the 3 groups (**Table 3**; **Figure 2**), while the log-rank Mantel-Cox test defined that group C was statistically different from the others ($P = .04$). In this group, the risk for recurrences was significantly higher 40 months after the operation compared with groups A and B. In other words, the disease-free survival was shorter in group C compared with groups A and B, and this difference was significant 40 months after surgery. The univariate analysis showed a significant association of age and distance from the dentate line with recurrences (**Table 4**). The Cox regression analysis showed that among the variables evaluated, only R1 margins and age were significantly associated with recurrences, with the former having a greater influence (Table 4).

The time-to-event analysis performed with the Kaplan-Meier method also showed that the overall survival for group A was better than groups B or C (log-rank Mantel-Cox test; $P < .01$); however, the cancer-related overall survival was not significantly different (log-rank Mantel-Cox test; $P = .05$). The significant difference in the overall survival relates to the other causes of mortality (noncancer and nonsurgical related) that were not equally distributed among the groups (Table 2).

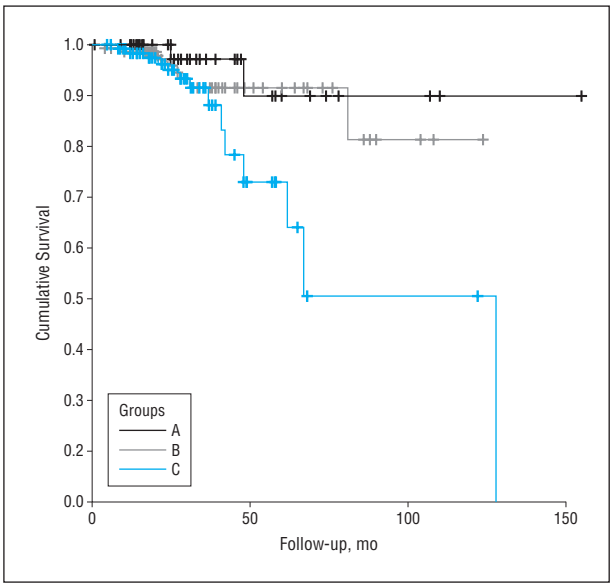

Figure 2. Disease-free survival among the 3 groups. Although all results are reported, a reliable estimate could be performed only until the seventh year of follow-up owing to the paucity of patients afterwards.

COMMENT

Large or recurrent rectal adenomas that are not amenable to standard colonoscopic polypectomy can be treated by a variety of methods. These include perianal or open rectal techniques, EMR, endoscopic submucosal dissection (ESD), TEMS, and open or laparoscopic transabdominal resection.[1,10,18,19] The ideal technique should be safe, cost-effective, have low R1 resection and recurrence rates, provide an intact en bloc full-thickness specimen for optimal histologic assessment, deal effectively with unexpected cancers, preserve the anorectal function, and be acceptable to patients. None of the currently available techniques fulfils all these criteria.

Our series showed that TEMS was able to achieve an overall R1 resection rate of 9.7%, an intact en bloc specimen in 99.0% of cases, and full-thickness excision in 80.7% of them. An intact en bloc specimen is important to allow definitive histologic analysis and reduce local recurrence.[11,20,21] Unexpectedly, the rate of full-thickness excision was significantly lower in the group with small lesions ($P < .001$). A possible explanation is that small lesions were more common early in the series as the excision of large lesions required a learning curve that coincided with an increased confidence of the authors in performing full-thickness resections, in particular on high lateral and anterior lesions. Nevertheless, partial-thickness excision did not translate into higher R1

Table 4. Univariate Analysis and Cox Regression Evaluating the Associations of Covariates With Recurrences

	Univariate Analysis	Cox Regression				
					95% CI for Exp(B)	
	P Value	B	*P* Value	Exp(B)	Lower	Upper
Age, y	.006[a]	0.080	.04	1.083	1.004	1.168
Type of adenoma	.60[b]	0.427	.56	1.533	0.368	6.385
Full-thickness or partial-thickness excision	.69[b]	–0.489	.40	0.613	0.196	1.917
Residual margin R1	.37[b]	1.468	.02	4.339	1.299	14.497
Distance from dentate line	.02[a]	–0.048	.49	0.953	0.832	1.091
Type of dysplasia	.15[b]	–0.529	.22	0.589	0.252	1.377
Type of complications	.19[b]	–0.404	.52	0.668	0.196	2.272

Abbreviations: B, positive coefficient (B); Exp, expected.
[a] Univariate analysis of variance.
[b] Measured by χ^2.

rates when compared with full-thickness ones, and no association was found with local recurrence rates (Table 4).

Unexpected cancer is a problem in apparently benign rectal lesions. The preoperative assessment (including biopsy, pit-pattern analysis, endorectal ultrasonography, and MRI) does not always identify a small focus of carcinoma, which is otherwise found only at the final analysis of the complete specimen. In the present series, the preoperative staging included endoscopic assessment, biopsy sampling, pelvic MRI, and endoanal ultrasound scan. However, pelvic MRI and endorectal ultrasonography were not generally available in the early years of the study, while later on they produced results of variable quality because they originated from different machines and numerous referring hospitals. Therefore, the preoperative radiologic staging was not suitable in our series for a consistent analysis.

In view of the limitations of the current preoperative staging techniques, it can be argued that any therapeutic technique other than wide full-thickness excision biopsy of an intact specimen as provided by TEMS could lead to under treatment. In our series, the incidence of unexpected carcinoma in lesions greater than 3 cm was 13.5%, which compares with rates of 5% to 29% reported in other series of large rectal adenomas.[5-9] Interestingly, although there was a trend toward an increased incidence of unexpected malignancy in larger adenomas, this did not reach statistical significance. In the presence of unexpected cancer, accurate histopathologic analysis and assessment of resection margins is paramount to determine the risk for local recurrence and the need for more radical treatment. Pathologic parameters that have been identified as predictive factors for lymph nodes metastasis in early rectal cancers include depth of submucosal invasion, cell differentiation, tumor-cell dissociation, and lymphovascular invasion.[22-24] An intact en bloc full-thickness specimen as provided by TEMS allows accurate assessment of the depth of submucosal invasion and the resection margin status to inform decision making on further management. Transanal endoscopic microsurgery excision of small, early rectal cancers without adverse pathologic features is an accepted and successful treatment. For cancers with adverse pathologic features, outcomes of immediate radical resection after local excision are comparable with those of primary radical surgery.[25,26] However, delayed salvage surgery for local recurrence after local excision has less favorable results with a disease-free survival for immediate resection vs delayed salvage surgery of 94.1% vs 55.5%, respectively.[27]

Traditional peranal excision is a safe technique for lesions in the distal rectum but is associated with high R1 resection and recurrences in both benign and malignant lesions and cannot access the upper rectum.[10] When compared with peranal excision, TEMS provides lower R1 resection (10%-19% vs 29%-37%), lower local recurrences (5%-9% vs 27%), and better cost-effectiveness with similar complication rates.[9,28-30] The overall R1 and local recurrences in this TEMS series (9.7% and 8.4%, respectively) supported the findings from previous reports when compared with literature from perianal techniques.

Modern endoscopic techniques such as EMR and ESD perform dissection in the submucosal layer rather than full-thickness excision as with TEMS. Submucosal dissection is acceptable for benign lesions but if unexpected malignancy is found on definitive histologic examination, it can be argued that full-thickness dissection is better in providing accurate Kikuchi submucosal staging and greater tumor clearance.[31] Submucosal staging is a valuable predictive factor for mesorectal lymph node involvement. Together with good local clearance, this information allows the patient the informed option of not proceeding to radical resection.[22] Endoscopic mucosal resection can only provide an intact en bloc specimen in 24% to 63% of rectal adenomas greater than 2 cm as opposed to 98.9% of lesions 3 cm or greater by TEMS in the present series.[7,11-13] A piecemeal specimen precludes assessment of the circumferential and deep resection margins, which is a predictor of local recurrence in adenomas and is of particular importance when unexpected malignancy is found.[2] Recurrences after EMR for lesions 2 cm or greater is up to 46%, particularly following piecemeal excision,[32-36] as opposed to 9.5% for lesions 3 cm or greater in our series.

Endoscopic submucosal dissection involves dissection of the submucosal layer using an endoscopic knife and allows higher en bloc resection rates of larger lesions than EMR.[20] Reports on ESD of large rectal lesions greater than 3 cm have shown intact en bloc specimen in 79% to 93% of cases and R1 rates of 11% to 26%.[11,12,37,38] In our series, the outcomes of TEMS in similar lesions compared favorably with an intact en bloc specimen in 98.9% and R1 resection in 10.9%. Furthermore, unlike ESD and EMR, TEMS can be performed safely in recurrent lesions where the submucosal plane is obliterated and in lesions that do not lift with submucosal injection, indicating the possibility of invasive carcinoma.[36,39]

Overall, TEMS complications were already reported in our unit.[15] Our study demonstrated that their risk is strongly correlated with lesional size and significantly increased with the excision of lesions greater than 5 cm. Overall results were comparable with rates reported in literature (5%-26%).[28,40,41] Transanal endoscopic microsurgery can cause a mild transient anorectal dysfunction owing to the anal dilatation performed by the 4-cm operating proctoscope. However, the sphincter function, if affected, returned to normal after TEMS in all but 1 study. Indeed, rectal function often improves once the tumor had been removed.[42-45] This was confirmed in our series, where mild transient anorectal dysfunction subsided spontaneously at follow-up in all 4 patients who experienced it.

Similarly to the overall complications, the local recurrence rate also increased with the excision of lesions greater than 5 cm when compared with smaller lesions (Table 3). The difference became more significant 40 months after surgery and perhaps a prolonged follow-up on giant lesions would be advisable. To our knowledge, there are no prospective studies in the literature directly comparing the effectiveness and safety of TEMS vs endoscopic techniques on these giant lesions; therefore, we were not able to make recommendations concerning the way they are best managed.

The univariate analysis found that the distance from the dentate line was a significant factor associated with the recurrence in this series (Table 4). The proximity to the dentate line prevents full-thickness excisions owing to the need to preserve the sphincters. In view of the beneficial effect of a full-thickness excision in decreasing R1 resections and local recurrence rates in T1 cancer,[46] this could have translated into higher R1 rates and recurrence rates. However, thickness of excision (full or partial) was not found to be independently associated to recurrence in this series.

The Cox regression analysis also found that the R1 status, more than the distance from the dentate line, was associated with the recurrence rates. This confirms previous findings about the importance of an R0 resection on reducing recurrence rates where only 4% of R0 benign resections recurred compared with 29% of R1 resections,[2] and only 7% of R0 resections for T1 cancers compared with 46% of R1 resections.[26] In our series, there was a trend toward higher R1 rates for larger lesions and, although this association did not reach statistical significance, this could be the consequence of a sample size bias. The higher R1 rate in large lesions could indeed explain the increased recurrence rate we found for adenomas greater than 5 cm.

Our results confirmed that giant rectal adenomas close to the dentate line represent the most challenging subgroup of lesions to face.

In conclusion, TEMS on large rectal adenomas provides en bloc, full-thickness specimens, with R1 and recurrences comparable with or better than those reported in literature for perianal excision, EMR, or ESD. Although in this series there was a trend toward higher R1 resections and unexpected cancers in large and giant lesions when compared with small lesions, this did not reach statistical significance. However, the risk for postoperative complications and local recurrences significantly increased with lesions larger than 5 cm as well as incomplete resections (R1) and close distance to the dentate line. In view of the limitations of this study, future prospective studies on larger series will be welcome to confirm our findings and better delineate the best way of managing giant lesions.

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REFERENCES

1. Buess G, Hutterer F, Theiss J, Böbel M, Isselhard W, Pichlmaier H. A system for a transanal endoscopic rectum operation [in German]. *Chirurg*. 1984;55(10):677-680.
2. Whitehouse PA, Tilney HS, Armitage JN, Simson JN. Transanal endoscopic microsurgery: risk factors for local recurrence of benign rectal adenomas. *Colorectal Dis*. 2006;8(9):795-799.
3. Middleton PF, Sutherland LM, Maddern GJ. Transanal endoscopic microsurgery: a systematic review. *Dis Colon Rectum*. 2005;48(2):270-284.
4. 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.
5. Ramirez JM, Aguilella V, Gracia JA, et al. Local full-thickness excision as first line treatment for sessile rectal adenomas: long-term results. *Ann Surg*. 2009;249(2):225-228.
6. Nivatvongs S, Snover DC, Fang DT. Piecemeal snare excision of large sessile colon and rectal polyps: is it adequate? *Gastrointest Endosc*. 1984;30(1):18-20.
7. Ah Soune P, Ménard C, Salah E, Desjeux A, Grimaud JC, Barthet M. Large endoscopic mucosal resection for colorectal tumors exceeding 4 cm. *World J Gastroenterol*. 2010;16(5):588-595.
8. 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):533-537.
9. 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):1831-1836.

10. Parks AG. A technique for excising extensive villous papillomatous change in the lower rectum. *Proc R Soc Med*. 1968;61(5):441-442.
11. Saito Y, Fukuzawa M, Matsuda T, et al. Clinical outcome of endoscopic submucosal dissection versus endoscopic mucosal resection of large colorectal tumors as determined by curative resection. *Surg Endosc*. 2010;24(2):343-352.
12. Puli SR, Kakugawa Y, Gotoda T, Antillon D, Saito Y, Antillon MR. Meta-analysis and systematic review of colorectal endoscopic mucosal resection. *World J Gastroenterol*. 2009;15(34):4273-4277.
13. Iizuka H, Okamura S, Onozato Y, Ishihara H, Kakizaki S, Mori M. Endoscopic submucosal dissection for colorectal tumors. *Gastroenterol Clin Biol*. 2009;33 (10-11):1004-1011.
14. Whitehouse PA, Armitage JN, Tilney HS, Simson JN. Transanal endoscopic microsurgery: local recurrence rate following resection of rectal cancer. *Colorectal Dis*. 2008;10(2):187-193.
15. Bignell MB, Ramwell A, Evans JR, et al. Complications of transanal endoscopic microsurgery (TEMS): a prospective audit. *Colorectal Dis*. 2010;12(7 online): e99-e103.
16. 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):964-966.
17. Cairns SR, Scholefield JH, Steele RJ, et al; British Society of Gastroenterology; Association of Coloproctology for Great Britain and Ireland. Guidelines for colorectal cancer screening and surveillance in moderate and high risk groups (update from 2002). *Gut*. 2010;59(5):666-689.
18. Hargrove WC III, Gertner MH, Fitts WT Jr. The Kraske operation for carcinoma of the rectum. *Surg Gynecol Obstet*. 1979;148(6):931-933.
19. Harvey EH, Young MR, Flanigan TL, et al. Complications are increased with the need for an abdominal-assisted Kraske procedure. *Am Surg*. 2004;70(3):193-196, discussion 197.
20. Hotta K, Saito Y, Matsuda T, Shinohara T, Oyama T. Local recurrence and surveillance after endoscopic resection of large colorectal tumors. *Dig Endosc*. 2010; 22(suppl 1):S63-S68.
21. Cao Y, Liao C, Tan A, Gao Y, Mo Z, Gao F. Meta-analysis of endoscopic submucosal dissection versus endoscopic mucosal resection for tumors of the gastrointestinal tract. *Endoscopy*. 2009;41(9):751-757.
22. 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):200-206.
23. Choi PW, Yu CS, Jang SJ, Jung SH, Kim HC, Kim JC. Risk factors for lymph node metastasis in submucosal invasive colorectal cancer. *World J Surg*. 2008;32 (9):2089-2094.
24. Nakada I, Tabuchi T, Nakachi T, et al. Histological factors contributing to a high risk of recurrence of submucosal invasive cancer (pT1) of the colon and rectum after endoscopic therapy. *Surg Today*. 2008;38(8):675-678.
25. Hahnloser D, Wolff BG, Larson DW, Ping J, Nivatvongs S. Immediate radical resection after local excision of rectal cancer: an oncologic compromise? *Dis Colon Rectum*. 2005;48(3):429-437.
26. 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.
27. Weiser MR, Landmann RG, Wong WD, et al. Surgical salvage of recurrent rectal cancer after transanal excision. *Dis Colon Rectum*. 2005;48(6):1169-1175.
28. Doornebosch PG, Tollenaar RA, De Graaf EJ. Is the increasing role of transanal endoscopic microsurgery in curation for T1 rectal cancer justified? a systematic review. *Acta Oncol*. 2009;48(3):343-353.
29. 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.
30. Langer C, Liersch T, Süss M, et al. Surgical cure for early rectal carcinoma and large adenoma: transanal endoscopic microsurgery (using ultrasound or electrosurgery) compared to conventional local and radical resection. *Int J Colorectal Dis*. 2003;18(3):222-229.
31. Kikuchi R, Takano M, Takagi K, et al. Management of early invasive colorectal cancer: risk of recurrence and clinical guidelines. *Dis Colon Rectum*. 1995; 38(12):1286-1295.
32. Hurlstone DP, Sanders DS, Cross SS, et al. Colonoscopic resection of lateral spreading tumours: a prospective analysis of endoscopic mucosal resection. *Gut*. 2004; 53(9):1334-1339.
33. Seitz U, Bohnacker S, Seewald S, Thonke F, Soehendra N. Long-term results of endoscopic removal of large colorectal adenomas. *Endoscopy*. 2003;35(8): S41-S44.
34. Seo GJ, Sohn DK, Han KS, et al. Recurrence after endoscopic piecemeal mucosal resection for large sessile colorectal polyps. *World J Gastroenterol*. 2010; 16(22):2806-2811.
35. Higaki S, Hashimoto S, Harada K, et al. Long-term follow-up of large flat colorectal tumors resected endoscopically. *Endoscopy*. 2003;35(10):845-849.
36. Tanaka S, Haruma K, Oka S, et al. Clinicopathologic features and endoscopic treatment of superficially spreading colorectal neoplasms larger than 20 mm. *Gastrointest Endosc*. 2001;54(1):62-66.
37. Nishiyama H, Isomoto H, Yamaguchi N, et al. Endoscopic submucosal dissection for colorectal epithelial neoplasms. *Dis Colon Rectum*. 2010;53(2):161-168.
38. Hurlstone DP, Atkinson R, Sanders DS, Thomson M, Cross SS, Brown S. Achieving R0 resection in the colorectum using endoscopic submucosal dissection. *Br J Surg*. 2007;94(12):1536-1542.
39. Uno Y, Munakata A. The non-lifting sign of invasive colon cancer. *Gastrointest Endosc*. 1994;40(4):485-489.
40. Yoshida N, Yagi N, Naito Y, Yoshikawa T. Safe procedure in endoscopic submucosal dissection for colorectal tumors focused on preventing complications. *World J Gastroenterol*. 2010;16(14):1688-1695.
41. de Graaf EJ, Doornebosch PG, Tetteroo GW, Geldof H, Hop WC. Transanal endoscopic microsurgery is feasible for adenomas throughout the entire rectum: a prospective study. *Dis Colon Rectum*. 2009;52(6):1107-1113.
42. 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.
43. Cataldo PA, O'Brien S, Osler T. Transanal endoscopic microsurgery: a prospective evaluation of functional results. *Dis Colon Rectum*. 2005;48(7):1366-1371.
44. 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.
45. 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):1635-1643.
46. 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.