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Transanal total mesorectal excision: pathological results of 186 patients with mid and low rectal cancer

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Abstract

Background Transanal total mesorectal excision (TaTME) seems to be a valid alternative to the open or laparoscopic TME. Quality of the TME specimen is the most important prognostic factor in rectal cancer. This study shows the pathological results of the largest single-institution series published on TaTME in patients with mid and low rectal cancer.

Methods We conducted a retrospective cohort study of all consecutive patients with rectal cancer, treated by TaTME between November 2011 and June 2016. Patient data were prospectively included in a standardized database. Patients with all TNM stages of mid (5–10 cm from the anal verge) and low (0–5 cm from the anal verge) rectal cancer were included.

Results A total of 186 patients were included. Tumor was in the mid and low rectum in, respectively, 62.9 and 37.1%. Neoadjuvant chemoradiotherapy was given in 62.4%, only radiotherapy in 3.2%, and only chemotherapy in 2.2%. Preoperative staging showed T1 in 3.2%, T2 in 20.4%, T3 in 67.7%, and T4 in 7.5%. Mesorectal resection quality was complete in 95.7% ($n=178$), almost complete in 1.6% ($n=3$), and incomplete in 1.1% ($n=2$). Overall positive CRM (≤ 1 mm) and DRM (≤ 1 mm) were 8.1% ($n=15$) and 3.2% ($n=6$), respectively. The composite of complete mesorectal excision, negative CRM, and negative DRM was achieved in 88.1% ($n=155$) of the patients. The median number of lymph nodes found per specimen was 14.0 (IQR 11–18).

Conclusions The present study showed good rates regarding total mesorectal excision, negative circumferential, and distal resection margins. As the specimen quality is a surrogate marker for survival, TaTME can be regarded as a safe method to treat patients with rectal cancer, from an oncological point of view.

Keywords Rectal cancer · Total mesorectal excision · Transanal TME · Circumferential resection margin · Mesorectal resection quality

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Total mesorectal excision (TME) has been the standard surgical treatment for rectal cancer since its introduction by Heald et al. [1] The quality of the TME specimen is a prognostic factor on both locoregional recurrence rate and long-term survival [2, 3]. Optimal pathological results can reduce locoregional recurrence rates by approximately 60–70% and increase 5-year survival by approximately 20% [4]. Additionally, adjuvant therapy further improves these figures [4, 5].

An increasing number of rectal surgeons worldwide are incorporating transanal TME (TaTME) in the treatment of patients with rectal cancer [6, 7]. However, published results of large series of patients treated by this technique

on pathological, oncological, and functional outcomes are scarce [7, 8].

It has been shown that the most important features for the evaluation of the quality of the specimen are the integrity of the mesorectum, the status of the resected margins, and the number of dissected lymph nodes. TaTME provides a better view of the plane of surgery and direct sight of the tumor, improving control over circumferential and distal resection margins. Our hypothesis is that the transanal approach may therefore provide improved pathological outcomes. In 2015, our research group published the initial results on operative and postoperative outcomes of patients with (high, mid, and low) rectal cancer treated by TaTME. The present analysis focuses on the pathological results of resection specimens retrieved by TaTME in a relatively large series of patients with mid and low rectal cancer, over a 5-year period.

Materials and methods

We conducted a retrospective cohort study of all consecutive patients with rectal cancer treated by TaTME between November 2011 and June 2016. Patient data were prospectively included in a standardized database. Patients with all TNM stages of mid (5–10 cm from the anal verge) and low (0–5 cm from the anal verge) rectal cancer were included. Patients with T4 tumors and/or threatened circumferential resection margin (CRM) on preoperative imaging were also included. Exclusion criteria for this analysis were patients requiring abdominoperineal resection or pelvic exenteration.

Tumors were staged using the 7th edition TNM classification [9]. The pretreatment work-up included blood analysis of carcinoembryonic antigen (CEA) and a total colonoscopy in which biopsies of the tumor were obtained. Oncological staging was done by transanal ultrasonography, thoracic and abdominal computed tomography (CT), and magnetic resonance imaging (MRI) of the pelvis. In patients in whom the tumor was not palpable by digital rectal examination, a rigid rectoscopy was also performed. All patients were discussed in a multidisciplinary oncological board which provided advice on further treatment. Patients were eligible for neoadjuvant chemoradiotherapy in the case of T3–T4/N0 or T1–T4/N1-2 tumors [10]. The same dedicated surgical team treated all patients. Patients were either operated on by one surgical team or by two surgical teams (the hybrid Cecil procedure) [11]. In the one-team procedure, the abdominal part was performed first because of the pneumoretroperitoneum that could develop after creating the pneumorectum in the transanal phase. This could result in difficult visualization of the dissection plane [11]. In the two-team hybrid procedure, the abdominal and the transanal dissections were performed simultaneously. The two-team hybrid procedure is a standardized procedure performed by two experienced oncologic gastroenterology surgeons and has been described elsewhere [11–13].

The same pathological team processed all the specimens [13]. The quality of the specimen was defined by the composite endpoint of (1) mesorectal quality and (2) status of the resected margins. The quality of the mesorectum was graded as described by Nagtegaal et al. [14]: (1) complete, in which the mesorectum is intact with only minor irregularities of a smooth mesorectal surface. No defect is deeper than 5 mm and there is no coning toward the distal margin of the specimen. There is a smooth circumferential resection margin on slicing. (2) Nearly complete, in which there is irregularity of the mesorectal surface. Moderate coning of the specimen is allowed. At no site, the muscularis propria is visible with exception of the insertion of the levator muscles. (3) Incomplete, little bulk to the mesorectum with defects down onto muscularis propria and/or very irregular circumferential resection margin. The CRM was considered positive in case of tumor growth ≤ 1 mm (continuous or discontinuous) and in case of a positive lymph node at ≤ 1 mm of the radical (non-peritoneal) dissection plane [3, 9]. The distal resection margin (DRM) was considered positive if microscopically involved by or ≤ 1 mm from the tumor margins. Tumor response to chemoradiotherapy was scored by a modification of the Ryan tumor regression grade, based on the volume of residual primary tumor cells: Grade 0: complete response (no viable cancer cells), Grade 1: moderate response (single cells or small groups of cancer cells), Grade 2: minimal response (residual cancer outgrown by fibrosis), and Grade 3: poor response (minimal or no tumor response; extensive residual cancer) [15].

Statistical analysis

Parametric data were reported as means with standard deviation (SD), and non-parametric data were reported as medians with the corresponding interquartile range (IQR). Data were analyzed with IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, NY, USA).

Results

A total of 186 patients were included in this analysis. Demographics are stated in Table 1. Surgery was performed by the one-team approach in 21.0% ($n = 39$) of the patients and by the two-team approach in 79.0% ($n = 147$) of the patients. Mean operative time was 147.8 min (SD 51.2), and anastomosis was performed in 98.3% ($n = 183$) of the patients. There were two intraoperative perforations of the rectum: one patient had a cT3N1 tumor, neoadjuvant treatment included only radiotherapy, and intraoperatively the tumor was found to infiltrate the pelvis. The

Table 1 Baseline characteristics of patients with mid or low rectal cancer treated by TaTME at Hospital Clinic Barcelona

		Transanal TME ($n=186$)
Age (years)	Median (IQR)	65.0 (56.0–75.0)
Gender	M/F (%)	118/68 (63.4/36.6)
BMI (kg/m^2)	Mean (±SD, range)	25.1 (±3.9, 17.7–36.2)
≥ 25	*N* (%)	71 (38.2)
≥ 30	*N* (%)	22 (11.8)
ASA classification[a]		
1	*N* (%)	7 (3.8)
2	*N* (%)	150 (80.6)
3	*N* (%)	25 (13.4)
4	*N* (%)	1 (0.5)
Unknown	*N* (%)	3 (1.6)
Tumor location		
Mid rectum	*N* (%)	117 (62.9)
Low rectum	*N* (%)	69 (37.1)
Tumor height[b]		
Mid rectum	Mean (±SD)	7.9 (±1.5)
Low rectum	Mean (±SD)	3.5 (±1.3)
Distance to MRF (mm)	Mean (±SD)	7.39 (9.0)
>1 mm	*N* (%)	118 (63.4)
≤1 mm	*N* (%)	45 (24.2)
Unknown	*N* (%)	23 (12.4)
≤1 mm excl. T4	*N* (%)	35 (20.8)
Neoadjuvant chemoradiation		
Yes	*N* (%)	116 (62.4)
No	*N* (%)	58 (31.2)
Only radiotherapy	*N* (%)	6 (3.2)
Only chemotherapy	*N* (%)	4 (2.2)
Unknown	*N* (%)	2 (1.1)
T stage		
T1	*N* (%)	6 (3.2)
T2	*N* (%)	38 (20.4)
T3	*N* (%)	126 (67.7)
T4	*N* (%)	14 (7.5)
N stage[c]		
N0	*N* (%)	102 (54.8)
N1	*N* (%)	63 (33.9)
N2	*N* (%)	19 (10.2)
Nx	*N* (%)	1 (0.5)
N-location		
Mesorectal	*N* (%)	77 (96.3)
Extramesorectal	*N* (%)	3 (3.8)
M stage		
M0	*N* (%)	167 (89.8)
M1	*N* (%)	19 (10.2)

[a]American Society of Anaesthesiologists classification: (1) healthy, (2) mild systemic disease, (3) severe systemic disease, (4) severe life-threatening systemic disease

Table 1 (continued)

[b]Height of distal edge of the tumor (cm) from the anal verge

[c]Assessed by magnetic resonance imaging

mesorectum was incomplete and with a positive CRM. The other patient had a rectal perforation at the anterior side, with a past medical history of radiotherapy and prostatectomy, and was staged as pT4.

As stated in Table 2, the overall mesorectal quality was complete in 95.7% ($n=178$) of the patients, almost complete in 1.6% ($n=3$), and incomplete in 1.1% ($n=2$). Both patients with an incomplete mesorectal resection had a mid rectal (cT3) tumor in which the pathologist reported a pT4 tumor, both patients were male and had a BMI > 25 kg/m2 (one of the patients was treated with radiotherapy before because of another malignancy). In the patients with a low rectal tumor, the mesorectal specimen was complete in 95.6% ($n=66$), almost complete in 2.8% ($n=2$), and unknown in 1.4% ($n=1$).

Overall positive CRM (≤ 1 mm) ratio (including T4 tumors) was 8.1% ($n=15$). Of the 15 patients with positive CRM: four patients (25%) had a T4 tumor, of whom one patient had tumor growth in the surrounding organs (vagina); in three patients (all with a low T3 rectal tumor), the specimen showed focal tumor contact at the CRM in the distal part of the specimen but had a complete mesorectal resection. Of these 15 patients with positive CRM, 10 patients received neoadjuvant chemoradiotherapy (80.0% had minimal or poor response) and five patients did not receive neoadjuvant chemoradiotherapy (previous radiotherapy, advanced age, and chronic renal failure).

The DRM was positive in six patients (3.2%), five of whom were treated with neoadjuvant chemoradiotherapy and three of whom had a tumor within 3 cm from the anal verge (type II according to Rullier classification [16]) and required partial intersphincteric resection. The tumor stage in patients with a positive DRM was T2 in one patient, T3 in four patients, and Tis in one patient (giant 8-cm circumferential polyp for which the pathology report confirmed a positive DRM with low-grade dysplasia). In patients with mid rectal cancer, the mean distal margin in cm was 2.7 (SD 1.6), with a positive DRM rate of 0.9% ($n=1$). In patients with low rectal cancer, the mean distal margin in cm was 1.1 (SD 1.0), with a positive DRM rate of 7.8% ($n=5$). From the five patients with low rectal cancer and a positive DRM, three patients had a positive CRM.

Complete mesorectal excision, negative CRM, and negative DRM were achieved in 91.1% ($n=102$) of the patients with mid rectal cancer and in 82.8% ($n=53$) of the patients with low rectal cancer.

Table 2 Tumor characteristics and pathological results of patients with mid or low rectal cancer treated by TaTME at Hospital Clinic Barcelona

		Transanal TME ($n=186$)
Tumor size (cm)	Mean (±SD)	2.9 (±4.1)
CRM < 1 mm		15 (8.1)
CRM < 1 mm excl. T4 tumor		11 (6.4)
CRM mid rectal tumor		
≤1mm[a]	*N* (%)	8 (6.8)
≤1 mm excl. T4	*N* (%)	6 (5.5)
Unknown[b]	*N* (%)	2 (1.7)
CRM low rectal tumor		
≤1mm[a]	*N* (%)	7 (10.1)
≤1 mm excl. T4	*N* (%)	5 (8.1)
Unknown[b]	*N* (%)	1 (1.4)
CRM (mm)	Mean (±SD)	15.4 (15.5)
Mesorectal resection quality		
Complete	*N* (%)	178 (95.7)
Almost complete	*N* (%)	3 (1.6)
Incomplete	*N* (%)	2 (1.1)
Unknown[b]	*N* (%)	3 (1.6)
Evaluated lymph nodes		
Overall	Median (IQR)	14.0 (11–18)
Non-irradiated patients	Median (IQR)	15.0 (14–22)
Distal resection margin (cm)	Mean (±SD)	2.1 (1.6)
Mid rectal tumor	Mean (±SD)	2.7 (1.6)
Low rectal tumor	Mean (±SD)	1.1 (1.0)
Distal resection margin affected		
Mid rectal tumor	*N* (%)	1 (0.9)
Low rectal tumor	*N* (%)	5 (7.8)
Proximal margin (cm)	Mean (±SD)	13.9 (4.9)
Perineural invasion	*N* (%)	15 (8.1)
Vascular invasion	*N* (%)	31 (16.7)
Perforation	*N* (%)	2 (1.1)
Differentiation grade		
Good	*N* (%)	7 (4.5)
Moderate	*N* (%)	117 (75.5)
Poor	*N* (%)	11 (7.1)
Budding		
No	*N* (%)	150 (91.5)
Low grade	*N* (%)	12 (7.3)
Moderate grade	*N* (%)	1 (0.6)
High grade	*N* (%)	1 (0.6)
Histological subtype		
High-grade dysplasia	*N* (%)	1 (0.5)
Adenocarcinoma	*N* (%)	173 (93.5)
Mucinous adenocarcinoma	*N* (%)	11 (5.9)
Regression grade[c]		
Grade 0	*N* (%)	24 (12.9)
Grade 1	*N* (%)	35 (18.8)
Grade 2	*N* (%)	29 (15.6)
Grade 3	*N* (%)	12 (6.5)
Unknown	*N* (%)	33 (17.8)
No neoadjuvancy	*N* (%)	53 (28.5)
pT stage		
T0	*N* (%)	30 (16.1)
Tis	*N* (%)	3 (1.6)
T1	*N* (%)	12 (6.5)
T2	*N* (%)	55 (29.6)
T3	*N* (%)	78 (41.9)
T4	*N* (%)	5 (2.7)
Unknown	*N* (%)	3 (1.6)
pN stage		
N0	*N* (%)	121 (65.1)
N1	*N* (%)	39 (21.0)
N1c	*N* (%)	3 (1.6)
N2	*N* (%)	13 (7.0)
Nx	*N* (%)	7 (3.8)
Unknown	*N* (%)	3 (1.6)
Stage		
Complete pathological response	*N* (%)	21 (11.5)
Stage I	*N* (%)	37 (20.3)
Stage II	*N* (%)	54 (29.7)
Stage III	*N* (%)	50 (27.5)
Stage IV	*N* (%)	19 (10.4)

[a]CRM involvement: circumferential resection involvement margin ≤ 1 mm

[b]Patients treated at Hospital Clinic of Barcelona, referred from other hospitals and follow-up was done elsewhere

[c]Regression grade modified from Ryan

Discussion

This study presents the largest single-center cohort on pathological results of patients with mid and low rectal cancer treated with TaTME. Mesorectal quality was complete or nearly complete in 97.3% of the patients. Negative CRM was obtained in 91.9% of the patients—including T4 tumors—and negative DRM was obtained in 96.8% of the patients. A median of 14.0 lymph nodes was harvested per specimen.

The transanal technique could offer advantages in obtaining optimal pathological outcomes compared to open approach or laparoscopy. Various randomized controlled trials have been performed trying to establish which technique is superior in the treatment of patients with rectal cancer, comparing laparoscopy and open approach in TME [17–20]. Complete TME ranged between 74.7 and 95.1% for open surgery and between 72.4 and 92.1% for laparoscopic

surgery. Negative CRM ranged between 87.9 and 97.0% for open surgery and between 90.5 and 97.1% for laparoscopic surgery.

The transanal technique provides a clear view of the plane of surgery, which could lead to easier deep pelvic dissection and a higher percentage of complete mesorectal specimens [21]. The most challenging patients (male, obese, and with narrow pelvis) could be the patients who benefit the most. The advantages of this technique allow even the patients with ultra-low rectal tumors to be treated by sphincter-saving surgery. Another possible advantage of TaTME is that during dissection there is no traction on the rectum and thereby no traction on the tumor [11]. Hypothetically, as the rectum is pushed forward, there is less risk of rupturing the tumor or damaging the mesorectal circumferential fascia.

TaTME provides a direct sight of the tumor and thus determination of the pure string placement, hypothetically improving the control of the DRM [11]. In the present cohort of patients, however, six patients had a positive DRM, which was remarkable. The DRM is decided just below the tumor to preserve as much length of the rectum as possible. One hypothesis for the positive DRM is the presence of tumor cells beyond the distal resection from the residual tumor after neoadjuvant therapy [22]. Another hypothesis is that the positive DRM is caused by the presence of occult tumor beneath the mucosal edge, although this is a rare event [23].

A total of 97.3% of the patients had a complete or nearly complete mesorectal resection quality. In contrast, 8.1% of the patients had a positive CRM. In the evaluation of the CRM, there is no difference in the definition of CRM involvement due to continuous tumorous tissue, discontinuous tumor "nests," or due to an invasion of lymph nodes aligned at the CRM [9]. In the case of advanced tumor growth, obtaining a negative CRM is not always possible. The risk of involved CRM is highest in stage T4 tumors, in T3 tumors with risk of an involved CRM on preoperative imaging, and when stage N2 is suspected. Furthermore, the mesorectum becomes thinner and less voluminous toward the pelvic floor, with tumor growth through the mesorectal fascia (MRF) occurring sooner in comparison to tumors in the mid or high rectum [24]. As a result, negative CRM is much harder to obtain in the low rectum, despite complete mesorectal excision. This was supported by the results of this study, in which a negative CRM was obtained in 93.2% of the patients with mid rectal tumors and in 89.9% of the patients with low rectal tumors. To clarify, 7.5% of the patients had a T4 tumor and 24.2% had a distance of less than 1 mm to the MRF, based on preoperative imaging.

Recently, outcomes from the international TaTME registry have been published [6]. A total of 66 units from 23 countries pooled their data, accounting for 720 patients. In 96.0% of the patients, a complete or nearly complete mesorectal quality was obtained, and positive CRM and DRM ratios were 2.4 and 0.3%, respectively. The mean number of lymph nodes harvested was 16.5 compared to 14.0 in this study. In both studies, the benchmark for lymph node yield of 12 lymph nodes was achieved. The international TaTME registry showed high-quality pathological results. Nevertheless, starting in November 2011, all consecutive patients with rectal cancer not requiring APR or pelvic exenteration were intended to treat by TaTME and included in the present analysis, limiting the inclusion bias.

At the Hospital Clínic of Barcelona, the experience with TaTME is extensive. This study evaluates a cohort of patients treated by TaTME in this single institution, which might be a limitation for the generalizability of our results. Much progress has been made since our first description of TaTME in 2010 [25]. Potential pitfalls are based on the differences in anatomy, especially in patients with previous pelvic surgery or radiotherapy. Although mid- and long-term oncological outcomes need to be evaluated, these outcomes suggest that the potential of TaTME is enormous. However, performance of an optimal TaTME requires training [7].

Conclusions

This study shows good rates regarding total mesorectal excision, negative circumferential, and distal resection margins. As the specimen quality is a surrogate marker for survival, TaTME can be regarded as a safe method to treat patients with rectal cancer, from an oncological point of view. Clinical oncological outcomes for this cohort of patients treated by TaTME will follow in the future.

Compliance with ethical standards

Disclosure Dr Antonio M. Lacy reports personal fees from Medtronic, Olympus, Applied Medical, and Conmed, outside the submitted work. Drs F. Borja de Lacy, Dr Jacqueline JEM van Laarhoven, Drs María Clara Arroyave, Drs Raquel Bravo, and Dr Miriam Cuatrecasas have no conflict of interest or financial ties to disclose.

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