ORIGINAL ARTICLE

The "terminal line": a novel sign for the identification of distal mesorectum end during TME for rectal cancer

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Abstract

Background: Although the clinical importance of complete, intact total mesorectal excision (TME) is the widely accepted standard for decreasing local recurrence of rectal cancer, the residual mesorectum still represents a significant component of resection margin involvement. This study aimed to use a visible intraoperative sign to detect the distal mesorectal end to ensure complete inclusion of the mesorectum and avoid unnecessary over-dissection.
Methods: The distal mesorectum end was investigated retrospectively through a review of 124 operative videos at the Union Hospital of Fujian Medical University (Fujian, China) and Cleveland Clinic (Ohio, USA) by two independent surgeons who were blinded to each other. Furthermore, 28 cadavers and 44 post-operative specimens were prospectively examined by hematoxylin and eosin (H&E) staining and Masson's staining to validate and confirm the findings of the retrospective part. Univariate and multivariate analyses were carried out to detect the independent factors that can affect the visualization of the distal mesorectal end.
Results: The terminal line (TL) is the distal mesorectal end of the transabdominal and transanal TME (taTME) and appears as a remarkable pearly white fascial structure extending posteriorly from 2 to 10 o'clock. Histopathological examination revealed that the fascia propria of the rectum merges with the presacral fascia at the TL, beyond which the mesorectum ends, with no further downward extension. In the retrospective observation, the TL was seen in 56.6% of transabdominal TME and 56.0% of taTME operations. Surgical approach and tumor distance from the anal verge were the independent variables that directly influenced the detection of the TL ($P = 0.03$ and $P = 0.01$).

Conclusion: The TL is a visible sign where the transabdominal TME should end and the taTME should begin. Recognition of the mesorectal end may impact the certainty of complete mesorectum inclusion. Further clinical trials are needed to confirm the preliminary findings.

Key words: rectal cancer; total mesorectal excision; taTME; TAMIS; laparoscopy; robotic

Introduction

An intact and complete total mesorectal excision (TME) specimen is a reliable prognosticator of proper local control of the disease and, consequently, a lower risk of local and regional tumor recurrence [1–3]. Although the clinical importance of complete TME is the widely accepted standard for decreasing local recurrence of rectal cancer, the residual mesorectum still represents a significant component of resection margin involvement [4]. Thus, surgeons always emphasize the importance of understanding the relationship between the rectum, its mesentery, and the surrounding pelvic fascial layers to perform high-quality surgical resections [5, 6].

With the development of the "transanal" approach (taTME), the far distal mesorectal end is readily accessible [7]. taTME presumably provides better visualization to facilitate dissection in the distal pelvis, aiming to obtain better pathological surrogates to achieve R0 resection [8]. Recent reports of early multifocal pelvic recurrence have limited the implementation of this technique to clinical trials and high-volume centers [9–11]. It is of utmost importance to recognize the anatomical landmarks in the distal pelvis from the transanal approach to achieve complete TME; hence, it is necessary to recognize the termination of the mesorectum.

Our study aimed to define the distal end of the mesorectum within the far distal pelvic cone through a *visible* landmark. Histopathological examination was performed to confirm the gross findings for safe clinical practice to provide an anatomical basis for "*complete*" mesorectal dissection, regardless of whether the approach was transabdominal or transanal.

Patients and methods

Study design and settings

This was a combined retrospective–prospective study. A retrospective review of operative videos at the Union Hospital of Fujian Medical University (Fujian, China) and Cleveland Clinic (Ohio, USA) was performed and a prospective study of cadaveric, pathologically examined post-operative specimens was performed to confirm the retrospective findings. The cadaveric specimens were obtained from the Laboratory of Clinical Applied Anatomy, Fujian Medical University (Fujian, China) and the post-operative specimens were derived from the Union Hospital and the School of Basic Medical Science of Fujian Medical University (Fujian, China) between December 2017 and March 2020. The study was approved by the institutional review board committee of the Union Hospital, Fujian Medical University (No. 2020YK051) and Cleveland Clinic, Ohio (No. #21–589).

Transabdominal and transanal TME operative video review

A cohort of 124 rectal cancer patients who underwent transabdominal TME or taTME were blindly reviewed by two expert surgeons (P.C. and S.S.) who have experience in video analysis techniques and surgery. The distal mesorectal end was meticulously examined for a potentially visible sign to act as a guide for sufficient distal dissection. For taTME, cases in which the proctotomy started within the levator hiatus were included to ensure complete tracking of the distal mesorectal end after initiating the proctotomy incision. The posterior dissection was initially performed below the endopelvic fascia exposing the levator muscle fibers to ensure complete inclusion of the ultra-distal mesorectum and avoid disrupting any TME integrity with proper circumferential resection margins (CRM). Subsequently, the endopelvic fascia was incised to enter the right TME plane. This step was meticulously examined during the intraoperative review process.

Cadaveric specimen observation

Dissection was performed on 28 cadavers (14 males and 14 females) aged between 65 and 85 years within 1 month postmortem to lower possible bias related to postmortem-related tissue damage. The cadaveric specimens were treated according to the university ethical rules that were mentioned in the informed donation consents to be used only for educational and research purposes. Any cadavers known to have a previous pelvic operation or pelvic disease that could disturb the normal pelvic anatomy were excluded. All specimens were hemipelvis at the mid-sagittal view. Different levels of dissection were captured using high-definition camera (Samsung S4 Zoom camera 4.3–43 mm 1:3.1–6.3, Samsung Electronics Company, Seoul, South Korea).

Post-operative specimen observations

A total of 44 post extra-levator abdominoperineal excision specimens with an equal male-to-female ratio were included. This kind of specimen was selected because it can demonstrate the distal end of the mesorectum with the puborectalis muscle (the levator hiatus). Specimens with locally advanced tumors invading the full thickness of the puborectalis muscle that disturbed the histological examination or measurements were excluded. We included all patients with mid- or low-seated rectal tumors who underwent TME through five transabdominal ports.

The mesorectum was examined at the level of the levator hiatus to identify its far-most distal extension. Samples were picked from three directions: anterior (12 o'clock), lateral (3 or 9 o'clock), and posterior (6 o'clock). These specimens were embedded into paraffin blocks and then sectioned into a coronal view (10- to 20-μm thickness) and stained with hematoxylin and eosin (H&E) and Masson's stain.

Outcomes

The primary outcome of the present study was to define a visible sign [terminal line (TL)] that denotes the distal end of the mesorectum during transabdominal and transanal TME. This sign was obtained after gross and histological examination of the distal mesorectum.

Statistical analysis

The visualization rates of the transabdominal TL were compared among patients according to the available post-operative data. Categorical variables were presented as numbers (percentage) and compared using the chi-square test or Fisher's exact test. Continuous variables were presented as mean ± standard deviation and compared using Student's t-tests or Mann–Whitney tests, as appropriate. Univariate analysis was performed and the variables that showed P-value < 0.1 were considered to have potential candidacy for the multivariate analysis. Using the multivariate analysis, the variables that showed P-value < 0.05 were considered to affect the visualization of the TL. All statistical analyses were performed using IBM SPSS software (Version 25.0, Armonk, NY: IBM Corp.). A P-value < 0.05 was considered significant.

Results

Intraoperative identification of TLs in the transabdominal and transanal TMEs

The cohort included 124 patients with rectal cancer who underwent surgery without a prospective search for any visible sign that may denote the distal end of the mesorectum but with the intent of achieving complete mesorectal excision.

Videos of 99 patients who underwent transabdominal TME were reviewed retrospectively and the patients' demographics are shown in Table 1. The TL, used as a marker of the distal end of the mesorectum, appeared as a remarkable pearly white semi-circumferential fascial structure extending posteriorly between 2 and 10 o'clock and was identifiable in 56.6% (56 of 99) of patients (Figure 1A).

Videos of 25 patients with low rectal cancer who underwent taTME were reviewed. A white line, similar to the transabdominal "terminal" line, was observed in 14 of 25 cases (56.0%) from the transanal view (Figure 1B and Supplementary Video).

The TL was similarly identified in laparoscopic and robotic surgery (55.9% vs 58.1%, $P = 0.84$). Gender, surgical approach, and tumor distance from the anal verge showed a potential candidacy for further analysis. Using the multivariate analysis, while the surgical approach and tumor distance from the anal verge directly affected the recognition of the TL ($P = 0.03$ and $P = 0.01$), the gender did not significantly affect the visualization of the TL ($P = 0.07$) (Table 1).

Cadaveric examination

The TL was identified in all cadaveric specimens. It lies precisely at the upper border of the levator hiatus (Figure 2A and B) and is formed by the semi-circumferential attachment of the presacral fascia (endopelvic fascia) to the fascia propria of the rectum between 2 and 10 o'clock posteriorly. The TL could not be recognized anteriorly in all dissected specimens where the presacral fascia does not exist and the puborectalis muscle is relatively deficient (Figure 2C and D).

Post-operative specimen examination

Histological confirmation for the grossly described TL was performed to confirm the observed results. All specimens showed that the mesorectal end level lies at the upper border of the levator hiatus in all positions, with no mesorectal tissue extending underneath that level. It is worth mentioning that the mesorectum on the anterior side was remarkably thinner than that on the lateral or posterior side.

Table 1. Univariate and multivariate analysis of preoperative data

Variable	"Visualized" terminal line ($n = 56$)	"Non-visualized" terminal line ($n = 43$)	P-value for univariate analysis[a]	Multivariate analysis	
				Odds ratio (95% CI)	P-value
Age, years, mean ± SD	58.34 ± 12.1	58.23 ± 11.8	0.96		
BMI, kg/m², mean ± SD	22.26 ± 2.44	22.54 ± 2.58	0.57		
Gender, n (%)			0.07		
Male	29 (51.8)	30 (69.8)		2.4 (0.99–5.70)	0.07
Female	27 (48.2)	13 (30.2)		Reference	–
Neoadjuvant CRT, n (%)			0.21		
Yes	31 (55.4)	26 (60.5)			
No	19 (33.9)	9 (20.9)			
Missing data	6 (10.7)	8 (18.6)			
Type of operation, n (%)			0.84		
Laparoscopic	38 (67.9)	30 (69.8)			
Robotic	18 (32.1)	13 (30.2)			
Surgical approach, n (%)			0.08		
LAR	4 (7.1)	8 (18.6)		Reference	–
ULAR	36 (64.3)	29 (67.4)		2.48 (0.68–9.07)	0.17
ISR	16 (28.6)	6 (14.0)		5.33 (1.17–24.47)	0.03
Surgical instruments, n (%)			0.59		
Ultrasonic knife	38 (67.9)	27 (62.8)			
Electrocautery hook	18 (32.1)	16 (37.2)			
Tumor height, cm, mean ± SD	5.76 ± 1.01	6.64 ± 2.24	0.01	0.71 (0.53–0.95)[b]	0.01

BMI, body mass index; CRT, chemoradiotherapy; LAR, low anterior resection; ULAR, ultra-low anterior resection; ISR, intersphincteric resection; SD, standard deviation; CI, confidence interval.

[a]Variables with P-value < 0.1 by univariate analysis were recommended to multivariate analysis.
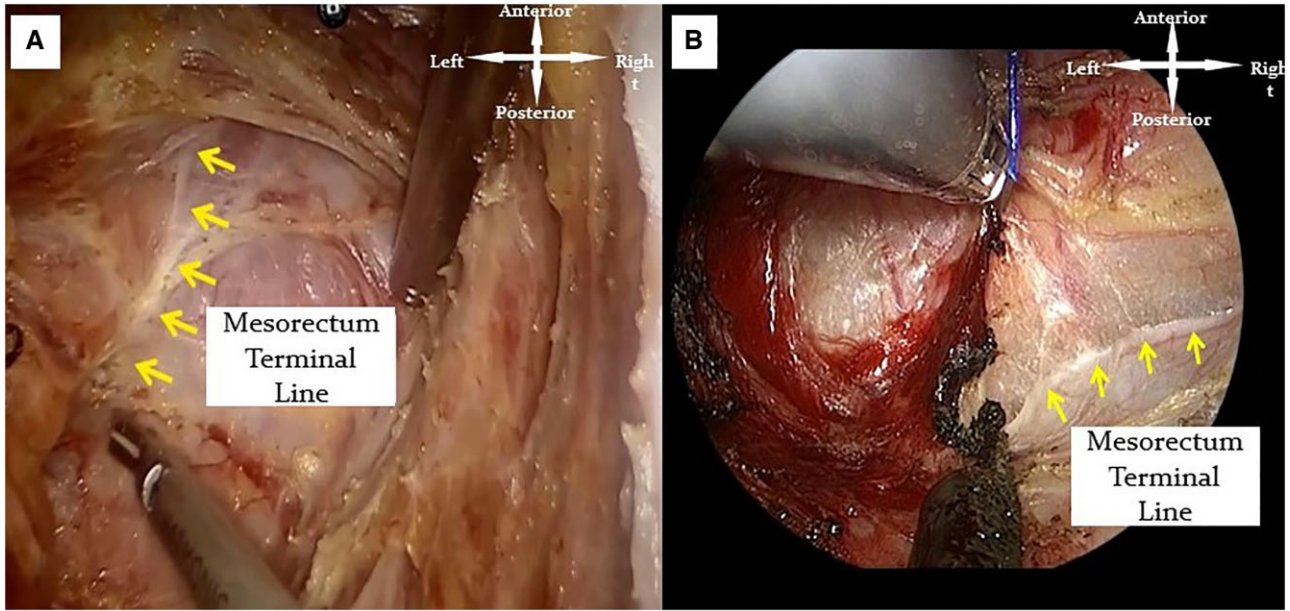
[b]Tumor distance from the anal verge increase by 1 cm.

Figure 1. The pearly white appearance of the "terminal line". (A) transabdominal view; (B) transanal view.
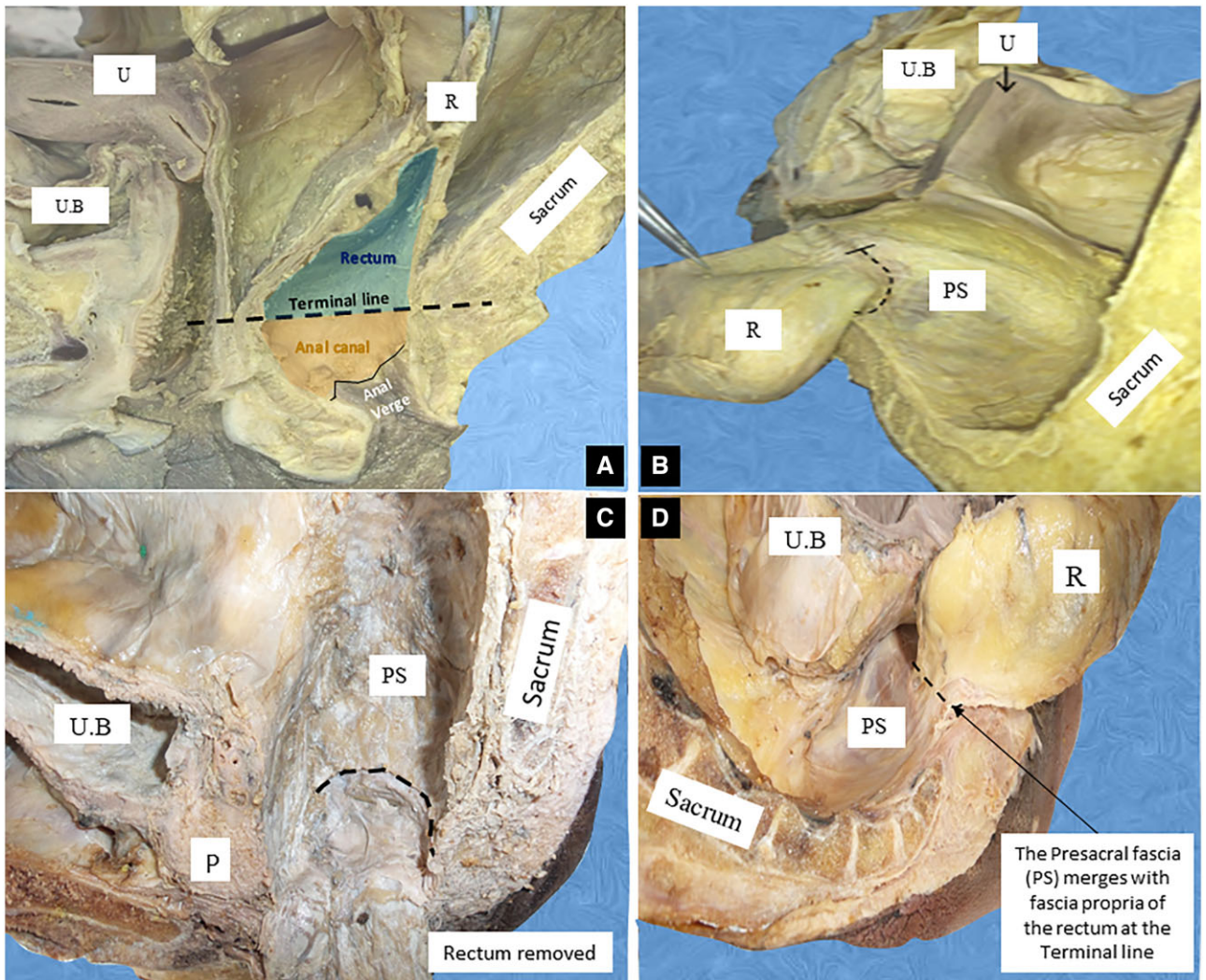

Figure 2. The fascial composition of the distal mesorectal end in cadaveric specimens. Black dashed line: terminal line (attachment of the presacral fascia to the fascia propria of the rectum); P, prostate; PS, presacral fascia; R, rectum; U, uterus; UB, urinary bladder.

At the posterior and lateral positions, the pearly white structure that gives rise to the TL and denotes the mesorectal distal termination in gross findings consists of the attachment of the presacral fascia to the fascia propria of the rectum at the levator hiatus (Figure 3C–F). However, this fascial layer could not be found in the anteriorly taken specimens (Figure 3A and B). This explains why the white color sign of the terminal could not be found anteriorly in either the intraoperative video reviews or cadaveric examinations.

Masson's stain was used as a special stain for fascia to confirm the results of the H&E stain (posterior and lateral specimens). Similarly, it was confirmed that the presacral fascia was intervening between the fascia propria of the rectum and the fascia investing the levator ani muscle. It ends by attaching to the fascia propria of the rectum, while the levator fascia merges downward to invest the levator muscle inside the hiatus (Figure 4). These histological findings support and are compatible with the previously described gross findings of the intraoperative video reviews and cadaveric specimens.

Discussion

The TL represents the distal mesorectal end where the transabdominal dissection should end and the transanal proctotomy should start. The current study outlined the clinical value of identification of the TL in transanal and transabdominal TMEs.

Clinical value of TL identification in transabdominal TME

In the original description of TME, distal dissection should be advanced until the anorectal junction; however, there was no gross anatomical description for identification of the distal limit [12]. The present study described the TL sign to help identify the end of the distal mesorectum. Since the TL is formed by attachment of the presacral fascia to the fascia of the rectum, this part of the presacral fascia is pulled up when the rectum is retracted upward and thus has its pearly white color.

Causes of inadequate TME include defects in the mesorectum, irregularity of the mesorectal surface, coning of the specimen, irregular CRM on slicing, and poor identification of the mesorectum terminus. Thus, the concept of the TL, proposed in the present study, may improve the quality of the distal resection margin, which is one of the most critical factors that impact locoregional recurrence [13]. In previous reports, improper identification of the distal mesorectum during surgery resulted in mesorectal residue that had a negative impact on oncological outcomes [14, 15]. Syk *et al.* reported that mesorectal residue accounted for recurrence in 50 of 90 patients, rendering it the
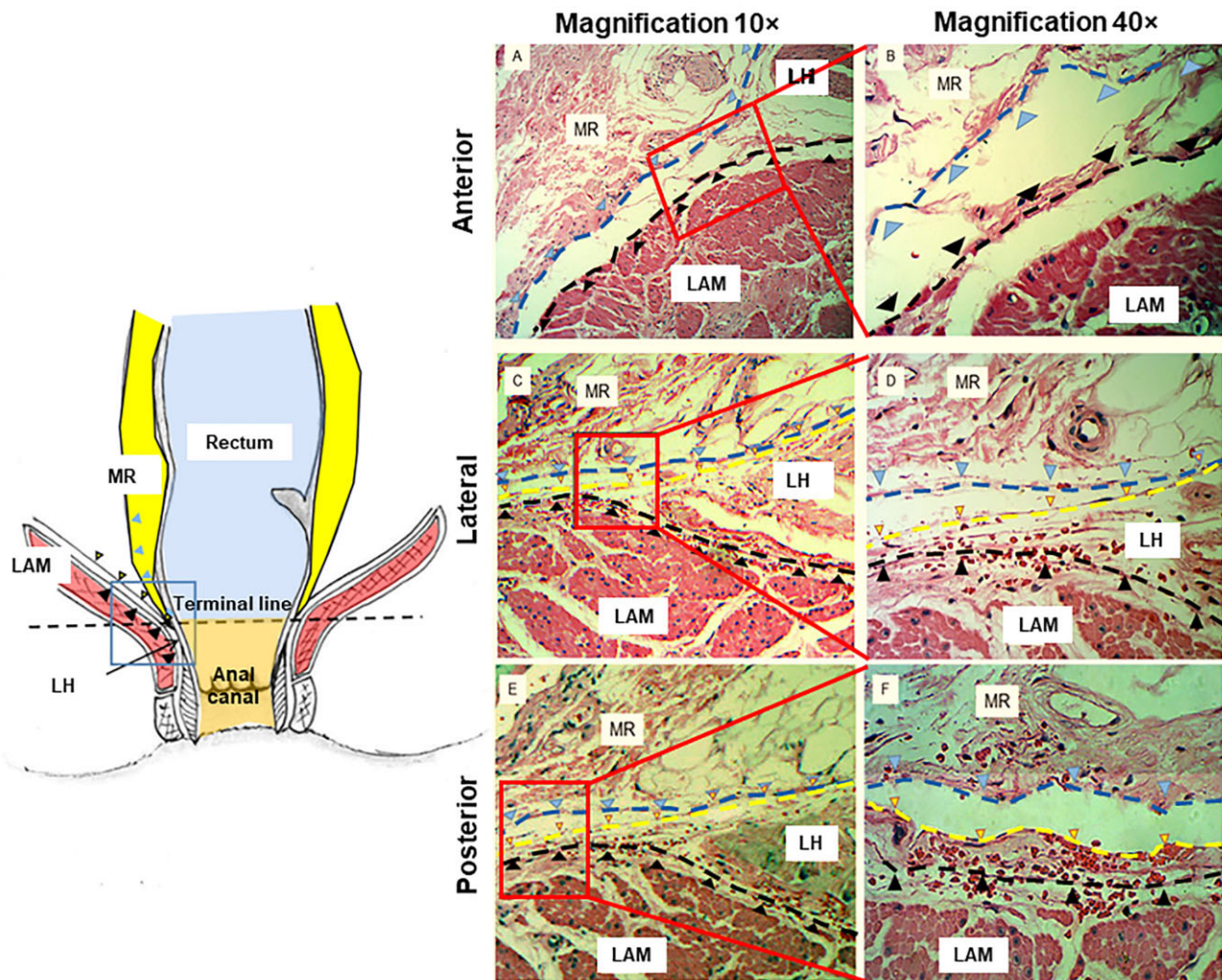

Figure 3. Histopathological examination (hematoxylin and eosin staining) of the distal mesorectal end. Specimens picked in the anterior (A and B), lateral (C and D), and posterior (E and F) directions. Magnification: 10× in A, C, and E, and 40× in B, D, and F. The blue dashed line (fascia propria of the rectum) merges with the yellow dashed line (presacral fascia) at the terminal line, beyond which the distal mesorectum ends. Blue arrowheads/blue dashed line: fascia propria of the rectum; yellow arrowheads/yellow dashed line: presacral fascia (terminal line); black arrowheads/black dashed line: levator ani fascia; LAM, levator ani muscle; LH, levator hiatus; MR, mesorectum.
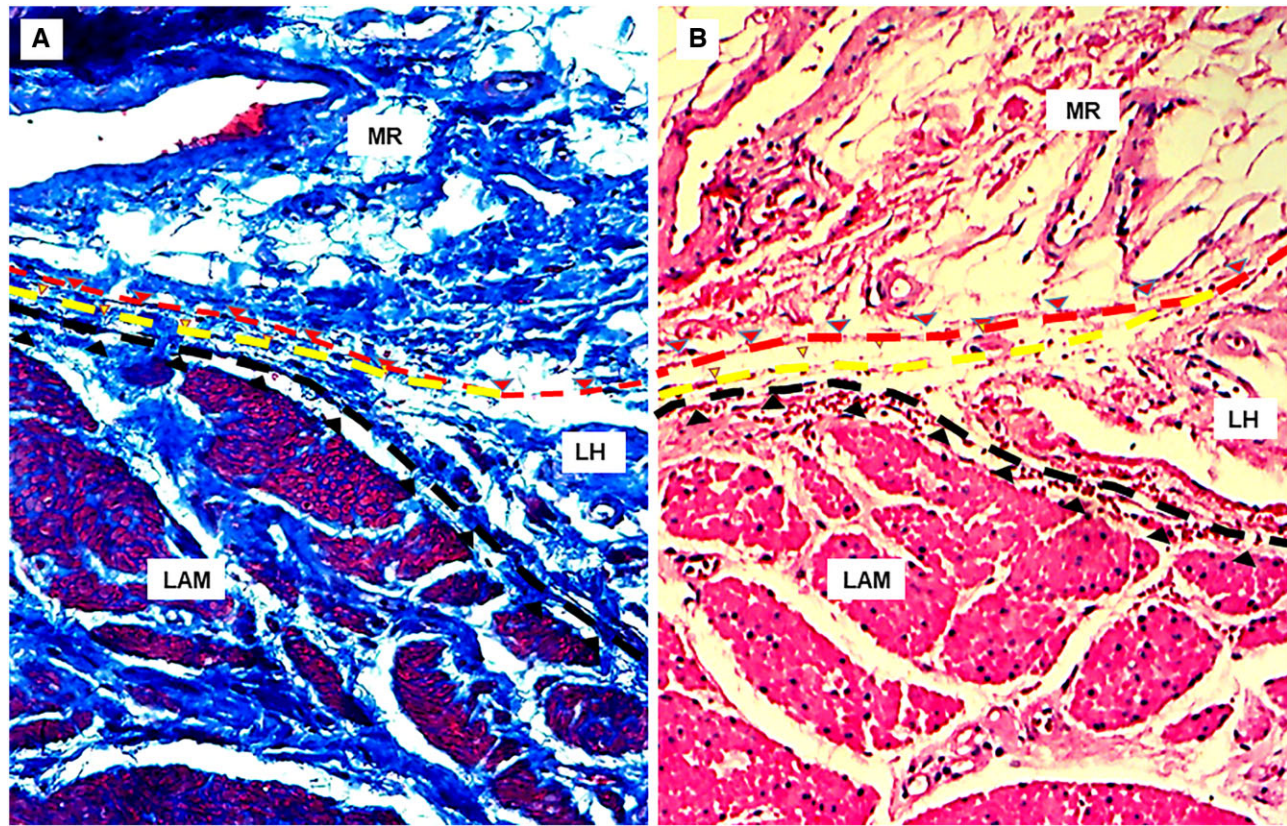
Figure 4. Histopathological examination of the distal mesorectal end. (A) Masson's staining (magnification 40×); (B) hematoxylin and eosin staining (magnification 40×). Red dashed line: fascia propria of the rectum; yellow dashed line: presacral fascia (terminal line); black dashed line: levator ani fascia; MR, mesorectum; LAM, levator ani muscle; LH, levator hiatus.

most common cause of local recurrence [16]. Heald *et al.* proposed that a "perfect" TME as the most effective treatment for rectal cancer; however, achieving a perfect TME can be difficult and challenging. It was hypothesized that achieving a "perfect" TME may help lower the dose/frequency of chemoradiotherapy cycles in patients requiring this kind of therapy after surgery [17]. Furthermore, the present study emphasized the role of the mesorectum TL, as it denotes the level at which dissection should stop to minimize the risk of unnecessary further dissection that may compromise the rectal stump and result in a higher rate of low anterior resection syndrome (LARS) [18].

The anterior part of the mesorectum is a critical part when performing TME. It was found to be thinner than the posterior mesorectum, which was compatible with other studies [19]. A thinner anterior mesorectum has a strong correlation with higher rates of positive circumferential tumor margins and local recurrence [20].

Clinical value of TL identification in taTME

Needless to say, it is crucial to include all the mesentery packages during proctectomy for rectal cancer, especially in low and mid-rectal tumors, regardless of the approach [21]. Since the termination of the mesorectum is encountered earlier in the taTME, it is of immense importance to be appropriately identified. Therefore, intactness and completeness of the fascia propria of the rectum are crucial to avoid mesorectal residues.

Depending on body habitus, sex, length of the anal canal, and tumor location, the TL coincides with the landing zone for the transanal access channel used during taTME [22]. This means that a proctotomy incision will be made at, below, or above the TL. In the first two situations, extreme caution should be exercised by the taTME surgeon to ensure the inclusion of that tiny piece of terminal mesenteric fat during the initial dissection after proctotomy to avoid breaching the fascia propria of the rectum distally and leaving residual mesorectum behind. Distal mesorectal residue is commonly found with local recurrences after transabdominal TME [14] and after taTME [10].

Occasionally, proctotomy may take place in the levator hiatus below the "terminal line"; then, the plane is between the rectal wall and levator muscle (puborectalis). If one is not cautious and cognizant of that while dissecting cephalad, this may lead to disastrous dissection between the rectal wall and its intimate mesentery resulting in "*guttering*" deformity [as the taTME surgeon (S.S.) in this article called it].

In this deformity, the surgeon dissects between the rectal wall and its adjacent tiny tapered unrecognized end of mesenteric fat for a short distance before realizing that this is the wrong plane and the fat underneath is a mesentery that requires inclusion in the specimen. The specimen in this case will seem complete from the outside while there is a hidden "gutter" between the rectal wall and its mesentery just above the proctotomy. The pathologist may not recognize it and may consider the specimen complete [17], while it could potentially be incomplete at a zone close to the tumor location. In Norway, although the rate of free CRM and distal resection margin were reported within the standard range, the investigators

questioned the possible causes of the unpredictable local recurrence that occurred after taTME [10], so "guttering" should be strongly considered in such a situation, especially if the TL cannot be seen. Although our main aim was to anatomically define the distal mesorectal end (TL), the present study is limited by the retrospective nature and low number of surgeons involved in the blind observation process. A future prospective multicenter study would be necessary for further confirmation of our proposed TL sign.

Conclusions

The TL represents the distal mesorectal end where the transabdominal dissection should end and the transanal proctotomy should start. It looks like a semi-circumferential pearly white line that extends between 2 and 10 o'clock at the levator hiatus. To the best of our knowledge, this study is the first to set an anatomical definition of the distal mesorectal end through a visible landmark for intraoperative identification. In this study, based on clinical observation supported by cadaveric and histopathologic dissection, we described the TL visualized by the transabdominal and transanal approaches and reported its impact on potential *complete* TME for mid- and low rectal cancer.

Supplementary Data

Supplementary data is available at *Gastroenterology Report* online.

Authors' Contributions

W.M.G., X.W., S.S., and P.C. conceived and designed the project. W.M.G., X.W., and S.S. collected the data. W.M.G., X.W., and S.H.E. analysed and interpreted the data. W.M.G. drafted the manuscript. W.M.G. and X.Z. performed and supervised cadaveric dissection. W.M.G. and M.X. performed the histopathological examination. S.H.E. and S.S. revised the manuscript for intellectual content. All authors read and approved the final manuscript.

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Conflict of Interest

The authors declare that there is no conflict of interests in this study.

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