



Perspective

# The quality of total mesorectal excision specimen: A review of its macroscopic assessment and prognostic significance

Shi-Bo Song<sup>a,b</sup>, Guo-Ju Wu<sup>a</sup>, Hong-Da Pan<sup>a</sup>, Hua Yang<sup>a</sup>, Mao-Lin Hu<sup>a,b</sup>,  
Qiang Li<sup>a,b</sup>, Qiu-Xia Yan<sup>a,b</sup>, Gang Xiao<sup>a,\*</sup>

<sup>a</sup> Department of Gastrointestinal Surgery, Beijing Hospital, National Center of Gerontology, Beijing 100730, China

<sup>b</sup> Peking University Fifth School of Clinical Medicine, Beijing 100730, China

Received 20 September 2017

Available online 12 March 2018

## Abstract

As a surgical procedure which could significantly lower the recurrence rate of cancers, total mesorectal excision (TME) has been the gold standard for middle and lower rectal cancer treatment. However, previous studies have shown that the procedure did not achieve the ideal theoretical local recurrence rates of rectal cancers. Some researchers pointed out it was very likely that not all so-called TME treatments completely removed the mesorectum, implying that some of these TME surgical treatments failed to meet oncological quality standards. Therefore, a suitable assessment tool for the surgical quality of TME is necessary. The notion of “macroscopic assessment of mesorectal excision (MAME)” was put forward by some researchers as a better assessment tool for the surgical quality of TME and has been confirmed by a series of studies. Besides providing rapid and accurate surgical quality feedbacks for surgeons, MAME also effectively assesses the prognosis of patients with rectal cancer. However, as a new assessment tool used for TME surgical quality, MAME has an only limited influence on the current guidelines and is yet to be widely applied in most countries. The aims of this review are to provide a detailed introduction to MAME for clinical practice and to summarize the current prognostic significance of MAME.

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**Keywords:** Macroscopic assessment of mesorectal excision (MAME); Quality control; Total mesorectal excision (TME); Coning

## Introduction

In 1982, Heald et al<sup>1</sup> proposed the notion of total mesorectal excision (TME) from the perspective of embryological anatomy; this led to a deeper understanding of the rectal anatomic structure and made scientific and standardized assessments and control of the rectal cancer surgery possible. The local recurrence rates (LRRs) have been reduced from 20%–45% using traditional surgical treatments to less than 10% using

\* Corresponding author.

E-mail address: [xgbj@sina.com](mailto:xgbj@sina.com) (G. Xiao).

Peer review under responsibility of Chinese Medical Association.



TME.<sup>2,3</sup> For patients receiving neoadjuvant radiotherapy together with TME, the LRRs could be further reduced to 5%.<sup>4</sup> As a surgical procedure which could significantly lower the recurrence rate of cancers, TME has been the gold standard for middle and lower rectal cancer surgical treatment.

However, not all reported LRRs after TME were lower than 10%; in some studies,<sup>5,6</sup> the LRRs were 11%–19%. Some researchers pointed out it was very likely that not all so-called TME procedures completely removed the mesorectum, which means that some of these TME surgical treatments failed to meet oncological quality standards.<sup>7</sup>

García-Granero et al<sup>8</sup> suggested that the TME quality could be assessed in terms of two aspects: (1) involvement of the circumferential resection margin (CRM) and (2) integrity of the TME specimen. Although the importance of CRM involvement on the prognosis requires no more emphasis, it is very easy for CRM to be affected by the depth of tumor invasion or tumor-node-metastasis (TNM) stage when used for reflecting the surgical quality.<sup>9</sup> Furthermore, if the integrity of the mesorectum cannot be guaranteed even if the CRM was negative for tumor cells, there still may be some micro tumor deposits or positive lymph nodes in the residual mesorectum, which might increase the risk of cancer recurrence. Numerous studies have confirmed the correlation between the prognosis of patients with tumors and the integrity of mesorectal specimens evaluated macroscopically.<sup>6,8,10–15</sup> Therefore, some researchers put forward the “macroscopic assessment of mesorectal excision (MAME)” as a suitable assessment tool for the integrity of mesorectum, which could reflect the quality of TME.<sup>8</sup>

Nagtegaal et al<sup>12</sup> found that in the subgroup of patients with a negative resection margin, patients with incomplete mesorectal resection had a higher overall recurrence rate (ORR) than those with complete mesorectal resection (28.6% vs. 14.9%,  $P = 0.03$ ); further, the overall survival (OS) rate was lower in the group of patients with incomplete mesorectal resection (76.9% vs. 90.5%,  $P < 0.05$ ). Quirke et al<sup>11</sup> also conducted an analysis on a subgroup of patients with negative CRMs and found that the LRR remarkably increased in the group of patients with incomplete mesorectal resection compared with that in the group of patients with complete mesorectal resection (12% vs. 4%). Therefore, the integrity of the mesorectal specimen can be regarded as an independent prognostic factor for patients who received rectal cancer resection. Moreover, MAME is not affected by the T stage, N stage, TNM

stage, or Dukes stage, making MAME a better tool than the CRM for TME quality assessment.<sup>8,11,12,14,16–18</sup>

## Relevant definitions

### MAME

MAME is a method of assessment, by which we can describe the integrity of the mesorectal specimen and assess the quality of TME via visual inspection and use of cross-sectional slices of the segment with tumor (3–5 mm in thick).<sup>6,8,11,12,19</sup> The visual inspection can provide a very clear indication of the quality of the mesorectal specimens, and the cross-sectional slices of the segment with tumor can provide further assessment of the regularity of the CRM, an indicator of the adequacy of the resection.<sup>19</sup>

According to the definitions by the CR07 protocol,<sup>11,15</sup> the quality of mesorectal specimens can be described as follows.

Mesorectal resection (MRR)/good/complete: intact mesorectum and smooth mesorectal surface with only minor irregularities; no defects deeper than 5 mm; no coning of the specimen towards the distal margin; and smooth macro-CRM on slicing.

Intramesorectal resection (IMR)/intermediate/nearly complete: intermediate bulk of the mesorectum with an irregular surface; a defect deeper than 5 mm, and no visible muscularis propria other than inserted levator; intermediate coning; intermediate irregularity of macro-CRM on slicing.

Muscularis propria resection (MPR)/poor/incomplete: small bulk of the mesorectum with a very irregular surface; defect down to the muscularis propria; severe coning; severe irregularity of macro-CRM on slicing.

### Coning

A “coning” (Fig. 1) would form if a surgeon cuts towards the tubular rectum during distal dissection instead of operating outside the visceral mesorectal fascia, leaving the specimen with a tapered, conical appearance. In the clinical practice, such a tendency during operation is not rare, and consequently, the surgical quality is undoubtedly suboptimal. Meanwhile, it is also unacceptable if the surgeon removes the distal mesorectum excessively, i.e., far beyond 5 cm from the distal tumor margin, which would not only have little help in improving the prognosis of patients, but also increase the incidence rate of post-operative complications.<sup>20</sup> Therefore, only when the

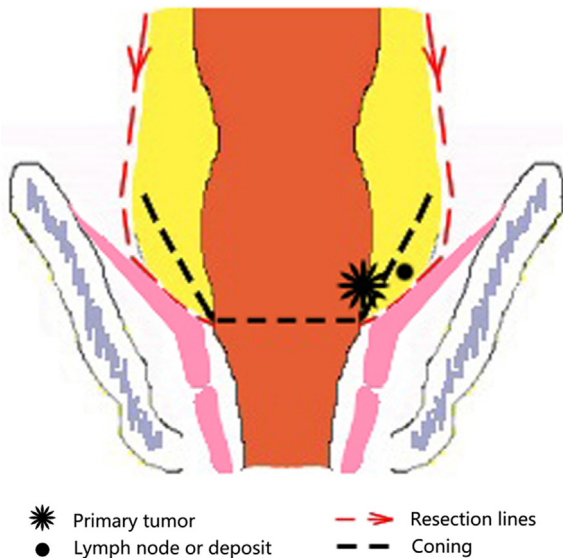


Fig. 1. “Coning”: the tendency to cut towards the tubular rectum during distal dissection. If the integrity of the mesorectum cannot be guaranteed, even though the mrCRM and pCRM are negative, there may still be some micro tumor deposits or positive lymph nodes in the residual mesorectum, which would increase the risk of local recurrence in patients who received TME. mrCRM: magnetic resonance imaging-assessed circumferential resection margin; pCRM: pathological circumferential resection margin; TME: total mesorectal excision.

“coning” is located within 5 cm from the distal tumor margin will the clinical benefits become significant.

### Macro-CRM

Macro-CRM can be defined as the general circumferential state of the TME specimen under visual inspection, which is different from the counterpart of pathological circumferential resection margin (pCRM) under a microscope.<sup>6,9,21,22</sup> In MAME, macro-CRMs are macroscopically grouped into margins with a smooth surface, intermediate irregularity, and severe irregularity. Furthermore, pathologists can slice through the site of tumors at 3–5-mm intervals to examine the circumferential margin macroscopically.<sup>21,22</sup> Additionally, Nagtegaal and van Krieken<sup>22</sup> believed that if the distance between the tumor and macroscopic CRM under visual inspection is no less than 1 cm, the pCRM could be considered to show a negativity.

### Evolution of MAME

As early as 1998, Quirke et al<sup>11</sup> first introduced three grades of mesorectal surgical quality that assess the quality of TME in the international multicenter CR07 and National Cancer Institute of Canada Clinical

Trials Group (NCIC-CTG) CO16 trial, i.e., good, intermediate, and poor; they also analyzed the prognostic differences among these patients with different MAME grades and reported a significant correlation between the LRR and MAME grade.

Subsequently, Nagtegaal et al<sup>12</sup> systematically described the macroscopic quality of the mesorectal specimens by classifying them into three groups: complete, nearly complete, and incomplete according to the definitions by the CR07 protocol; they further confirmed a significant correlation between the quality of the TME specimens and the prognosis of patients after rectal cancer resection.<sup>11,12</sup>

In recent years, some researchers proposed the concept of “TME scores”<sup>14</sup> or “MAME.”<sup>8</sup> They preferred the more descriptive and objective evaluation of the mesorectal quality based on the surgical plane of resection in which three grades of TME had been defined, including mesorectal plane of resection, intramesorectal plane of resection and muscularis propria plane of resection.<sup>8,10,11,13,15</sup>

In addition, Leonard et al<sup>15</sup> found that for prediction, both two-grade (grade of MRR vs. combined grade of IMR and MPR) and three-grade scoring systems functioned well; however, the former was more significantly associated with the OS and the risk of distant metastasis. Although the names of grades are different, the contents are consistent. Moreover, MAME based on the surgical plane of resection is more objective and widespread; therefore, MAME was used as follows.<sup>10</sup>

### Method of MAME

According to the National Comprehensive Cancer Network (NCCN) Guidelines Version 3.2017,<sup>23</sup> the status of the proximal and distal circumferential (radial) and mesenteric margins should be reported, and the pathologists should evaluate the quality (completeness) of the mesorectum. Although increasing attention has been paid to MAME, there is no international consensus on its assessment methods and criteria.<sup>21,22,24,25</sup> Therefore, it is necessary to develop an objective and repeatable standard of MAME and standardize the method of MAME, which is important for the prognosis assessment, postoperative decision-making, and early feedback provision on the surgical quality for surgeons. The method and process of MAME combined with the surgical principles of TME from a pathology perspective are listed below. Further, the detailed process of MAME is summarized in Fig. 2.

To start with, it should be clear that the TME specimens for optimal macroscopic evaluation should

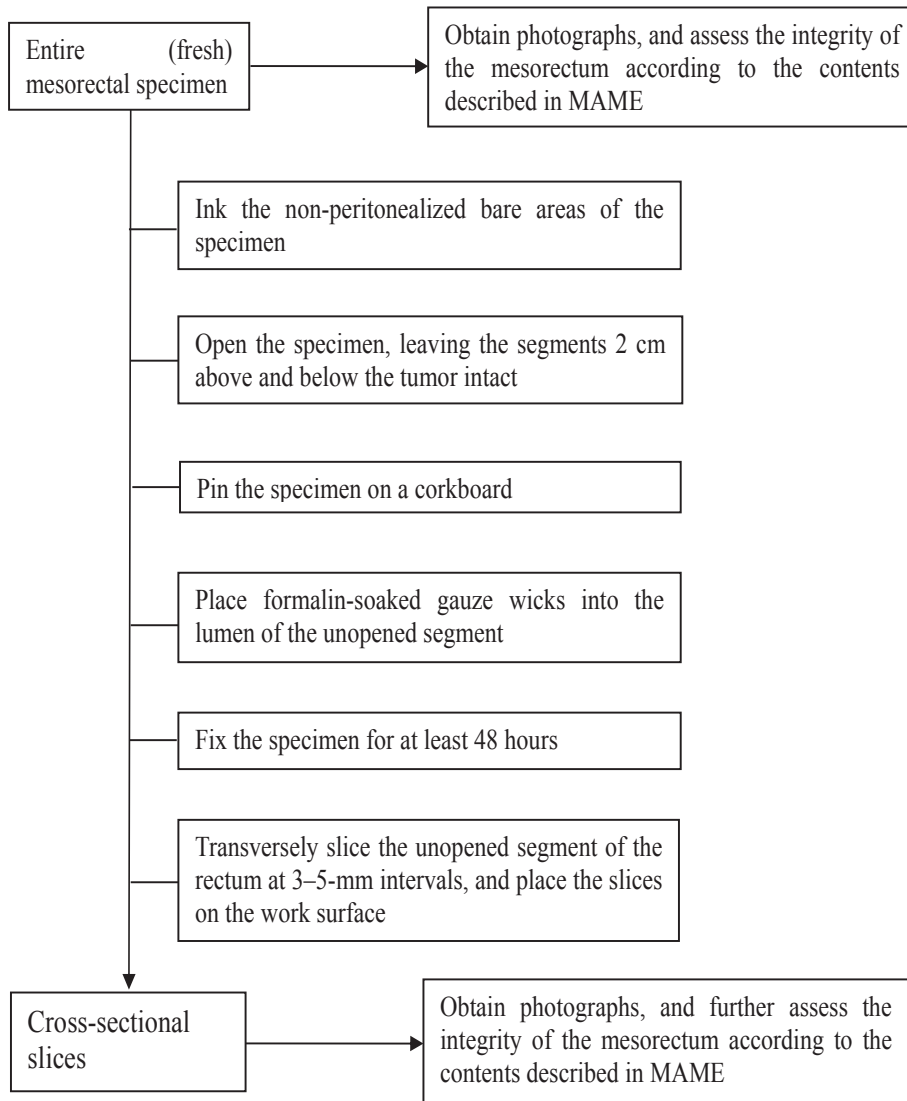


Fig. 2. Summary of the process for macroscopic pathological assessment. MAME: macroscopic assessment of mesorectal excision.

be received instantly after surgical removal, while unfixed and unopened.<sup>21,22</sup> Prior to the assessment, photographic documentation of the circumferential and distal margins of a fresh mesorectal specimen is desirable, which would serve as the evidence for macroscopic evaluation and review in the future.<sup>6,21,22</sup>

The integrity of the mesorectum will be assessed in accordance with the contents described in MAME. The macroscopic state of the mesorectal specimen should be evaluated first. It is necessary to carefully record whether the mesorectum is complete and smooth and whether there are any defects. If the specimen surface is not smooth or has any defects, the depth of defects should be measured. An optimal mesorectum specimen

should have a smooth and intact surface, while a poor-quality specimen has a small bulk in the mesorectum, deep defects reaching the muscularis propria, or even a perforation.<sup>21,22</sup> Thereafter, the degree of coning in the distal end of the mesorectum will be assessed. In partial mesorectal excision (PME), whether the distal transection is in a plane of 90° to the rectal wall should be assessed. The distal transection must be performed at the same distance (over 5 cm) from the gross distal tumor margin on the rectal wall and both inner and outer mesorectum, which could avoid the formation of coning.<sup>6</sup>

The circumferential margin in a gross mesorectal specimen is painted using ink, including all non-

peritonealized surfaces anteriorly and posteriorly.<sup>26</sup> It should be kept in mind that the serosal surfaces should not be inked, especially for the anterior part, because it might be difficult to identify the serosal involvement.<sup>26</sup>

After inking of the gross specimen, the rectal tube and mesorectum should be opened anteriorly, leaving the flanking region extending 2 cm beyond the tumor margin (where the specimen would be preserved intact), together with the tumor mass, untouched.<sup>21</sup> The tumor size should also be recorded as an element in tumor documentation.<sup>21</sup> The specimen should be pinned on a corkboard to prevent shrinkage artefacts, and a loose, formalin-soaked gauze wick should be placed within the lumen of the unopened segment to optimize fixation.<sup>27</sup> Subsequently, the specimen should be fixed for at least 48 hours. Although the duration is longer than that in fixation in many hospitals, this is vital for the serial cross-sectional slicing of the unopened segment.<sup>21,22,27</sup>

Finally, the unopened segment of the fixed specimen will be transversely sliced into thin sections (3–5 mm).<sup>21,22</sup> All the cross-sectional rings should be laid out to assess the mesorectal quality and macro-CRM further.<sup>21,22</sup> These thin sections will also lay the foundation for the subsequent microscopic examination. Photographic documents are necessary, especially in cases of a poor TME or positive macro-CRM. After the macroscopic assessment, the slices showing the closest relationship of tumor or a positive node to the circumferential margin should be further made into microscopic slices to examine the pCRM. Nagtegaal and van Krieken<sup>22</sup> believed that if the distance between the tumor and resection margin under visual inspection was over 1 cm as per the macroscopic pathological assessment, MAME would be enough to support the judgement of a negative pCRM. In sum, both the whole specimen (fresh) and cross-sectional slices (after fixing) should be examined for an adequate assessment.

## Prognostic significance of MAME

### *Local recurrence*

TME reduces the LRR for patients with rectal cancer. Primarily being employed to assess the local surgical quality, the prognostic value of MAME is mainly manifested in the relationship between different mesorectal grades and the LRR.

Quirke et al<sup>11</sup> were the first to group the mesorectal specimens into groups using three different grades in the CR07 trial, and they found that the 3-year LRRs in

the three groups were 4% for good, 7% for intermediate, and 13% for poor ( $P = 0.0039$ ), which suggested a significant correlation between the LRR and MAME grade. Nagtegaal et al<sup>12</sup> analyzed the data of 180 non-irradiated patients with detailed descriptions of the specimens in their pathology reports in the Dutch multicenter trial. In the group with an incomplete mesorectum, the LRR after 25.8 months of follow-up was 15.0% compared with 8.7% in the group with a nearly complete mesorectum ( $P = 0.01$ ).<sup>12</sup> Nagtegaal et al<sup>10,12,22</sup> believed that the integrity of the mesorectal specimens is not only an important predictor of local recurrence of rectal cancer but also provides reliable feedback on the surgeon's performance.

Maslekar et al<sup>16</sup> revealed significant differences among the LRRs of MRR, IMR, and MPR (1.6%, 5.7%, and 41%, respectively;  $P < 0.0001$ ), which strongly confirmed the prognostic value of the grades of the mesorectum. Although Jeyarajah et al<sup>14</sup> failed to reveal the correlation between the LRR and the grade of MRR, they found that the pCRM-negative patients were more likely to have a higher TME score ( $P = 0.0001$ ). Leite et al<sup>17</sup> ( $P < 0.01$ ) and García-Granero et al<sup>8</sup> ( $P = 0.003$ ) also reported a significant impact of the grades of the mesorectum on the LRR.

Most of these studies, pooled in a meta-analysis by Bosch and Nagtegaal<sup>10</sup> and including over 2174 patients, found that patients with an MPR had a significantly higher LRR than patients with the other two grades (either IMR or MRR) ( $P = 0.005$ ); moreover, the LRR in patients with either an MPR or an IMR was significantly higher than that in patients with an MRR ( $P = 0.04$ ). Therefore, it could be practical to employ the grades of the mesorectum as an indicator for the risk of local recurrence among patients who received rectal cancer resection.

Furthermore, in the pCRM-negative subgroup based on the data of Quirke et al,<sup>11</sup> the statistical difference in the 3-year LRR was significant (12% for MPR vs. 4% for MRR), while that in the 3-year disease-free survival (DFS) rate was subtle (74% for MPR vs. 81% for MRR); this indicated MAME as an independent prognostic factor for the LRR.

Another sub-analysis performed by Quirke et al<sup>11</sup> showed that short-course preoperative radiotherapy reduced the 3-year LRR ( $P < 0.0001$ ) and improved the 3-year DFS rate ( $P = 0.013$ ) for all three grades; however, the benefit of short-course preoperative radiotherapy did not differ among the three grades ( $P = 0.30$  for trend). Leonard et al<sup>18</sup> found that patients who did not show downstaging after long-course chemoradiotherapy (CRT) had a higher incidence of MPR



than patients who showed downstaging ( $P = 0.0005$ ). Kiehlmann et al<sup>28</sup> analyzed the prognosis of patients who underwent preoperative long-term CRT and TME and found that the 5-year LRR was 6.7% in patients with either an MRR or an IMR compared with the LRR of 50% in the patients with an MPR ( $P = 0.015$ ). Therefore, neoadjuvant radiotherapy could improve the local prognosis of patients planned to undergo resection. However, even after neoadjuvant CRT, it should not be ignored that the quality (completeness) of the mesorectum still has a strong influence on local recurrence in patients with rectal carcinoma.<sup>28</sup>

### Overall recurrence

Nagtegaal et al<sup>12</sup> showed that the ORR also significantly increased in the MPR group compared with that in the MRR group (35.5% vs. 21.5%,  $P = 0.01$ ). Moreover, pCRM-negative patients showed an ORR of 14.9% in the MRR and IMR groups compared with the ORR of 28.6% in the MPR group ( $P = 0.03$ ), which was statistically different and indicated MAME as a reflection of the risk of overall recurrence among patients with rectal cancer, especially for pCRM-negative patients.

Maslekar et al<sup>16</sup> showed remarkable differences in the ORR (1.6% for MRR, 17% for IMR, and 59% for MPR;  $P < 0.0001$ ). García-Granero et al<sup>8</sup> also showed a statistical difference (1.6% for MRR, 17% for IMR, 59% for MPR;  $P = 0.032$ ). Moreover, the patients with rectal cancer and MPR in the meta-analysis by Bosch and Nagtegaal<sup>10</sup> had higher ORRs than the patients in the other two groups ( $P = 0.01$ ); however, there was no significant difference between the groups of patients with either an MPR or an IMR and the group of patients with an MRR ( $P = 0.07$ ).

However, in a recent prospective study with a long-term follow-up (5 years,  $n = 121$ ) by Madbouly et al,<sup>29</sup> no remarkable difference among different mesorectal grades in terms of the LRR or ORR was found in either all patients or in pCRM-negative patients only.

Although there is still a lack of sufficient evidence for the correlation between the grades of the mesorectum and the risk of overall recurrence, it is still of some practical significance in the clinical practice and could somehow be considered as a parameter of prognosis for patients after rectal cancer resection.

### Survival

Nagtegaal et al<sup>12</sup> demonstrated an association between MPR and a lower OS (76% for MPR and 86%

for MRR,  $P < 0.05$ ) and a similar result in their pCRM-negative group (76.9% for MPR and 90.5% for MRR,  $P < 0.05$ ). Leite et al<sup>17</sup> found that the 5-year cancer-free survival rate was 65% in their MRR group and 47% in their MPR group ( $P < 0.05$ ). However, neither did Quirke et al<sup>11</sup> find any correlation between mesorectal grading and 3-year DFS rate (79% in MRR patients, 75% in IMR patients, and 70% in MPR patients,  $P = 0.14$ ), nor did Maslekar et al<sup>16</sup> find any correlation with the survival rates ( $P = 0.17$ ).

Most of the studies consistently showed that avoiding MPR could significantly reduce the recurrence risk after TME surgery, and an optimal plane (MRR) of TME also could significantly improve the LRR and ORR compared with a poor plane (IMR or MPR).<sup>10</sup> However, owing to the lack of sufficient data to validate the prognostic value, there was seemingly a trend that a better survival was associated with an optimal plane (MRR).<sup>10,11,16,17</sup>

### TME-quality assessment instrument

Although MAME has been classified as a routine part of the pathological review in some countries, a convenient and united method of evaluation is still not globally available. To utilize the tool conveniently and uniformly, Simunovic et al<sup>30</sup> designed an assessment instrument TME-Quality Assessment (TME-QA) based on the Quirke classification system. After they compared the average scores for macroscopic specimen quality evaluated by different pathological professionals with TME-QA, including gold standard assessors, pathologists, and pathology assistants, the results showed an acceptable internal consistency (0.75 for the gold standard assessors, 0.63 for the pathologists, and 0.60 for the pathology assistants). However, the interrater reliability for macroscopic specimen quality among these three pathological professions was not sufficient (0.45 for the pathology assistants, 0.80 for the pathologists, and 0.86 for the gold standard assessors), which limits its popularization and application. By combining the instrument with the above-mentioned assessment methods, we may be able to design a direct, rapid, and reliable evaluation for specimens to assess the quality of TME for surgeons and the prognosis of patients.

### Conclusion

Most of the current studies showed that complete resection of the mesorectum can significantly reduce the risk of recurrence. Both MAME and CRM are key

prognostic factors for patients after rectal cancer resection. Furthermore, MAME can provide rapid and accurate feedback on surgical quality to guide surgeons and improve surgical techniques, which is vital for the quality control of TME. Although the TME-QA was good for MAME to some extent, it was not very easy to be handled by pathology assistants. We believe that MAME could be a direct, rapid, and reliable method of assessment for TME quality if we put more effort into designing a practical assessment instrument.

With MAME, we can rapidly identify the quality of TME, predict the outcomes of patients, and take further actions to manage a poor prognosis. However, techniques to prevent or manage the poor prognosis of an incomplete mesorectum need further investigation. The measures may include neoadjuvant radiochemotherapy, adjuvant radiochemotherapy, improvement of operation, or other treatments; however, relevant data are insufficient, and further studies and joint efforts of surgeons, pathologists, oncologists, and other medical professionals are needed.

### Conflicts of interest

None.

### References

- Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery—the clue to pelvic recurrence? *Br J Surg.* 1982;69:613–616.
- van Lingen CP, Zeebregts CJ, Gerritsen JJ, Mulder HJ, Mastboom WJ, Klaase JM. Local recurrence of rectal cancer after total mesorectal excision without preoperative radiotherapy. *Int J Gastrointest Cancer.* 2003;34:129–134.
- Bülow S, Christensen IJ, Harling H, et al. Recurrence and survival after mesorectal excision for rectal cancer. *Br J Surg.* 2003;90:974–980.
- van Gijn W, Marijnen C, Nagtegaal ID, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer: 12-year follow-up of the multicentre, randomised controlled TME trial. *Lancet Oncol.* 2011;12:575–582.
- Wiig JN, Carlsen E, Søreide O. Mesorectal excision for rectal cancer: a view from Europe. *Semin Surg Oncol.* 1998;15:78–86.
- Hermanek P, Hermanek P, Hohenberger W, Klimpfinger M, Köckerling F, Papadopoulos T. The pathological assessment of mesorectal excision: implications for further treatment and quality management. *Int J Colorectal Dis.* 2003;18:335–341.
- Schiebe M, Budach W, Hoffmann W. Stellenwert der prä- und postoperativen Strahlentherapie in der Primärbehandlung des Rektumkarzinoms [in German]. *Der Onkologe.* 2001;7:391–399.
- García-Granero E, Faiz O, Muñoz E, et al. Macroscopic assessment of mesorectal excision in rectal cancer: a useful tool for improving quality control in a multidisciplinary team. *Cancer.* 2009;115:3400–3411.
- Nagtegaal ID, Quirke P. What is the role for the circumferential margin in the modern treatment of rectal cancer? *J Clin Oncol.* 2008;26:303–312.
- Bosch SL, Nagtegaal ID. The importance of the pathologist's role in assessment of the quality of the mesorectum. *Curr Colorectal Cancer Rep.* 2012;8:90–98.
- Quirke P, Steele R, Monson J, et al. Effect of the plane of surgery achieved on local recurrence in patients with operable rectal cancer: a prospective study using data from the MRC CR07 and NCIC-CTG CO16 randomised clinical trial. *Lancet.* 2009;373:821–828.
- Nagtegaal ID, van de Velde CJ, van der Worp E, Kapiteijn E, Quirke P, van Krieken JH. Macroscopic evaluation of rectal cancer resection specimen: clinical significance of the pathologist in quality control. *J Clin Oncol.* 2002;20:1729–1734.
- Nagtegaal ID, van Krieken JH. The multidisciplinary treatment of rectal cancer: pathology. *Ann Oncol.* 2007;18 Suppl 9:ix122–126.
- Jeyarajah S, Sutton CD, Miller AS, Hemingway D; Leicester Colorectal Specialist Group. Factors that influence the adequacy of total mesorectal excision for rectal cancer. *Colorectal Dis.* 2007;9:808–815.
- Leonard D, Penninckx F, Laenen A, Kartheuser A; PROCARE. Scoring the quality of total mesorectal excision for the prediction of cancer-specific outcome. *Colorectal Dis.* 2015;17:O115–O122.
- Maslekar S, Sharma A, Macdonald A, Gunn J, Monson JR, Hartley JE. Mesorectal grades predict recurrences after curative resection for rectal cancer. *Dis Colon Rectum.* 2007;50:168–175.
- Leite JS, Martins SC, Oliveira J, Cunha MF, Castro-Sousa F. Clinical significance of macroscopic completeness of mesorectal resection in rectal cancer. *Colorectal Dis.* 2011;13:381–386.
- Leonard D, Penninckx F, Fieuw S, et al. Factors predicting the quality of total mesorectal excision for rectal cancer. *Ann Surg.* 2010;252:982–988.
- Quirke P. Limitations of existing systems of staging for rectal cancer: the forgotten margin. In: Søreide O, Norstein J, eds. *Rectal Cancer Surgery: Optimisation — Standardisation — Documentation.* Berlin, Germany: Springer-Verlag; 1997:63–81.
- Kanso F, Lefevre JH, Svrcek M, Chafai N, Parc Y, Turet E. Partial mesorectal excision for rectal adenocarcinoma: morbidity and oncological outcome. *Clin Colorectal Canc.* 2016;15:82–90. e1.
- Parfitt JR, Driman DK. The total mesorectal excision specimen for rectal cancer: a review of its pathological assessment. *J Clin Pathol.* 2007;60:849–855.
- Nagtegaal ID, van Krieken JH. The role of pathologists in the quality control of diagnosis and treatment of rectal cancer—an overview. *Eur J Cancer.* 2002;38:964–972.
- National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Rectal Cancer, Version 3*; 2017. [https://www.nccn.org/professionals/physician\\_gls/pdf/rectal.pdf](https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf). Accessed November 6, 2017.
- Sterk P, Opitz T, Kasperk R, Schubert F, Schumpelick V, Klein P. Studies of the vascular anatomy of the mesorectum support the concept of the total mesorectal excision. *Tech Coloproctol.* 2000;4:151–156.
- Compton CC. Updated protocol for the examination of specimens from patients with carcinomas of the colon and rectum, excluding carcinoid tumors, lymphomas, sarcomas, and tumors of the vermiform appendix: a basis for checklists. Cancer Committee. *Arch Pathol Lab Med.* 2000;124:1016–1025.

26. Ludeman L, Shepherd NA. Serosal involvement in gastrointestinal cancer: its assessment and significance. *Histopathology*. 2005;47:123–131.
27. Williams NS, Dixon MF, Johnston D. Reappraisal of the 5 centimetre rule of distal excision for carcinoma of the rectum: a study of distal intramural spread and of patients' survival. *Br J Surg*. 1983;70:150–154.
28. Kiehlmann M, Weber K, Göhl J, et al. The impact of surgical quality on prognosis in patients undergoing rectal carcinoma surgery after preoperative chemoradiation. *Int J Colorectal Dis*. 2016;31:247–255.
29. Madbouly KM, Hussein AM, Abdelzaher E. Long-term prognostic value of mesorectal grading after neoadjuvant chemoradiotherapy for rectal cancer. *Am J Surg*. 2014;208:332–341.
30. Simunovic MR, DeNardi FG, Coates AJ, Szalay DA, Eva KW. Product analysis and initial reliability testing of the total mesorectal excision-quality assessment instrument. *Ann Surg Oncol*. 2014;21:2274–2279.

Edited by Pei-Fang Wei