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*Editorial Update*

# Total Mesorectal Excision for Rectal Cancer: The Truth Lies Underneath

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**Abstract. The surgical technique itself has emerged as a crucial factor for local recurrence since the popularization of total mesorectal excision for the treatment of rectal cancer. This procedure is associated with lower local recurrence rates after "curative" surgery compared to traditional dissection of the rectum. The aim is to remove an intact mesorectal envelope from the promontorium down to the pelvic floor by sharp dissection with tumor-free margins and without causing injury to the pelvic nerves. However, the description of total mesorectal excision has been confusing. Moreover, the implication that total excision of all the perirectal fat contained within the perirectal fascia en bloc in all patients with rectal cancer can minimize local recurrence remains contentious. Therefore a critical appraisal of the procedure is required. Nonrandomized clinical studies have shown that total mesorectal excision reduces the local recurrence rate and increases disease-free survival in patients with adenocarcinoma of the middle and distal third of the rectum. Circumferential resection margins of 2 mm or more are associated with a lower local recurrence rate. Additional benefits in local control can be obtained with neoadjuvant treatment. Thus the modern treatment of rectal cancer combining total mesorectal excision with neoadjuvant chemoradiation results in excellent local tumor control. However, it is achieved at the cost of significant functional sequelae and impaired quality of life. The development of therapeutic alternatives that can achieve similar rates of local and distant tumor control without the mortality, morbidity, and functional consequences of radical surgery is a major challenge for colorectal surgeons.**

Local control of malignant solid neoplasms is based on removal of the primary tumor and its vascular and lymphatic drainage. This surgical principle constitutes the rationale for radical surgical resection of gastrointestinal malignancies. Radical proctectomy has been the standard of care for patients with rectal adenocarcinoma for decades. The primary goal is to "cure" the patient and secondarily keep the local recurrence rate low even if systemic failure occurs. Unfortunately, there is a wide variability in the reported local recurrence rate after rectal cancer surgery, but it may occur in as many as 35% to 45% of patients [1]. This is maybe due to both tumor-related and technique-related factors. Among the former, the tumor grade, histologic type, tumor border configuration, tumor budding, host lymphoid response, and extent of extramural penetration by tumor, neural, venous, or lymphatic invasion are beyond surgeon's control. The technique-related factor refers to the macroscopic quality of the mesorectum in the resection specimen and the proximity of the tumor to the circumferential resection margin. Here is where surgeons may make a difference. However, the concept that extensive and mutilating surgery is the best means to achieve local control in patients with rectal adenocarcinomas has given rise to some criticism.

The true impact of the surgical technique on local recurrence after radical proctectomy for rectal adenocarcinoma has been difficult to assess because of multiple confounding issues such as variability in tumor stage, tumor location, the use of adjuvant therapy, the variability in the extent of the follow-up, and the different techniques employed among studies. In recent years, the surgical technique has emerged as a crucial factor for local recurrence, ever since the popularization of total mesorectal excision (TME), a concept introduced by Heald et al. [2]. In the hands of its proponents, this procedure was initially associated with lower local recurrence rates after "curative" rectal cancer surgery compared to traditional dissection of the rectum. The aim of a TME is to remove an intact mesorectal envelope from the promontorium down to the pelvic floor by sharp dissection, with tumor-free margins and without causing injury to the pelvic nerves. The technique has been recently popularized, and some surgeons think it should be carried out routinely. Simultaneously, however, questions about the true value of TME have been raised [3, 4]. Many issues regarding the benefits of TME remain controversial, and unfortunately they cannot be worked out because well-controlled randomized trials are practically impossible to carry out [5].

The rectum with cancer can be mobilized along anatomic planes with minimal blood loss, preserving the pelvic autonomic nerves and maintaining a low prevalence of local recurrence [6]. Various techniques, including total mesorectal excision, are based on the same anatomic principles [6]; however, popular words have been used to replace well-established terminology. In particular, the description of total mesorectal excision has been confusing because of its emphasis on the words "total" and "mesorectum." Moreover, the implication that total excision of all the perirectal fat contained within the perirectal fascia en bloc in all patients with rectal cancer can minimize local recurrence remains contentious. Therefore a critical appraisal of TME is required, bearing in mind that overall

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survival and neither local recurrence nor disease-free survival is the most important goal when treating cancer patients.

### Surgical Anatomy

Anatomically, the word "mesorectum" is incorrect. In the surgical literature this term is currently used to name a cushion of fatty tissue derived from the hindgut that surrounds the rectum posterolaterally and is covered by a thin membrane called the fascia propria. It contains the terminal branches of the superior rectal vessels and the lymphatic drainage of the rectum and extends from the promontory to Waldeyer's fascia. The posterior aspect of the mesorectum is separated from the presacral fascia by an avascular plane of areolar tissue. This plane between the mesorectum and the presacral fascia is the natural plane of dissection during radical proctectomy. The hypogastric nerves cross this plane and can be easily visualized and dissected off the fascia propria of the rectum by sharp dissection. Laterally, the mesorectum intermingles with a bilateral condensation of connective tissue that surrounds the autonomic nerves passing from the pelvic plexus to the rectum. These structures are known as the lateral ligaments and connect the pelvic side wall with the mesorectum. Inconstantly, the lateral ligaments contain accessory middle rectal vessels, whereas the middle rectal artery usually runs immediately above the levators. During TME, the lateral ligaments should be sharply divided while avoiding clamping and ligating these structures to preserve the integrity of the mesorectum. The pelvic plexus lies outside the fascia propria of the rectum at the level of the lateral ligaments. They are rarely seen during extrafascial mesorectal excision but can be injured during the process of ligating the lateral ligaments or controlling bleeding in this area.

In its posterior aspect, the mesorectum is thick and bilobular in appearance. Anteriorly, it is either absent in the upper intraperitoneal portion of the rectum or reduced to a thin layer of areolar tissue in the middle and distal rectum. The fascia propria of the rectum is also thinner anteriorly than posteriorly. In addition to the mesorectum and the fascia propria of the rectum, the anterior rectal wall is separated from the genital organs by a remnant of the fusion of the two layers of the embryologic peritoneal cul-de-sac known as Denonvilliers' fascia. Whereas there is almost uniform agreement about the posterior plane of dissection during radical proctectomy, there is no consensus about the plane of dissection in relation to Denonvilliers' fascia in rectal cancer patients. The disagreement is in part the result of the considerable variation in the anatomic appearance of Denonvilliers' fascia, from a barely visible translucent membrane to a tough leathery membrane. Most surgeons follow the plane between the fascia propria of the rectum and Denonvilliers' fascia.

### Outcomes after Radical Rectal Surgery with TME

In patients with locoregional disease, complete removal of a rectal tumor with sufficient disease-free margins and its local vascular and lymphatic drainage should ideally yield a local recurrence rate close to zero. Depending on the location of the rectal tumor, the resection margins required to gain adequate local control may influence the surgical technique considerably. Although local control can be easily obtained for neoplasms in the upper third of the rectum, more distal tumors may be difficult to remove with disease-free margins, compromising preservation of the anal sphincters in many cases. Thus, the relative contribution of distal and circumferential margins to local recurrence has been studied extensively.

**Table 1.** Local recurrence after total mesorectal excision alone.

| Series | Local recurrence | % |
|---|---|---|
| Aitken et al. [8] | 1/64 | 1.6 |
| Belli et al. [9] | 3/72 | 4.2 |
| Cawthorn et al. [10] | 9/122 | 7.3 |
| Colombo et al. [11] | 10/89 | 11.2 |
| Dixon et al. [12] | 9/227 | 4.0 |
| Eu et al. [13] | 26/278 | 9.4 |
| Hainsworth et al. [14] | 8/45 | 17.8 |
| Heald et al. [15] | 4/152 | 2.6 |
| Jatzko et al. [16] | 25/187 | 13.4 |
| Kapiteijn et al. [17] | 57/661 | 8.6 |
| Kirwan et al. [18] | 3/67 | 4.5 |
| Maas et al. [19] | 3/42 | 7.1 |
| Moran et al. [20] | 4/55 | 7.3 |
| Tagliacozzo et al. [21] | 41/248 | 16.5 |
| Tocchi et al. [22] | 5/53 | 9.4 |
| Total | 233/2460 | 9.5 |

The relative importance of circumferential margins was highlighted by Quirke et al. [7], who reported that most local recurrences were the direct result of inadequate mesorectal resection, a factor that might explain variations in local recurrence rates among surgeons. Heald et al. [2] should be credited with introducing the concept of removing the entire mesorectum in every rectal cancer patient. In a series of 100 patients treated by total mesorectal excision, they found tumor deposits in the mesorectum as far as 4 cm distal to the main tumor. Based on this information, they recommended that the entire mesorectum be removed from every rectal cancer patient. Heald et al. [2] also reported no local recurrence in 50 patients treated with total mesorectal excision with curative intent. Subsequent reports by the same authors and others in the United States and Europe have confirmed the low local recurrence rates obtained with total mesorectal excision (Table 1).

Hall et al. [23] studied the prognostic value of circumferential margin involvement in a series of 153 rectal cancer patients treated by mesorectal excision with curative intent by a single surgeon. Disease-free survival and overall survival were significantly lower in patients with positive margins, but the local recurrence rate was not different between groups. This study suggested that in rectal cancer patients, treated by curative-intent mesorectal excision, circumferential margin involvement is more an indicator of advanced disease than inadequate local surgery.

More recently, Nagtegaal et al. [24] have shown that involvement of the circumferential resection margin is a strong predictor for local recurrence after TME. A disease-free margin of less than 2 mm was associated with a statistically significant increase in the risk of local recurrence compared to wider margins (16.0% vs. 5.8%). In fact, margins of 1 mm or less were positively associated with a higher risk for distant metastases (37.6% vs. 12.7%) and shortened survival. Furthermore, the prognostic value of circumferential resection margin involvement is independent of the TNM classification. The authors concluded that accurate determination of circumferential resection margins in patients with rectal cancer is important for determining the local recurrence risk, which might subsequently be prevented by additional therapy. In contrast to earlier studies, they showed that an increased risk is present when margins from the tumor are 2 mm or less.

All these reports have confirmed the importance of excising the

rectum outside its fascia propria for preventing local tumor recurrence. For tumors located in the lower third of the rectum, a proctectomy performed in this plane inevitably results in excision of the entire mesorectum. The question that has been the subject of a heated debate is whether the entire mesorectum should be removed for cancers located in the upper or middle third of the rectum. Presently, it is clear that TME does not produce better results in patients with tumors in the upper third of the rectum [25].

Total mesorectal excision with negative circumferential margins does not guarantee local tumor control in rectal cancer; a small but not insignificant proportion of these patients ultimately develop local recurrence. The control arm of the Dutch study [26] on preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer contains the only prospective data on the local recurrence after total mesorectal excision. In that series, the local recurrence rate after a median follow-up of more than 2 years was 8.2%; it was 0.7% for stage I, 5.7% for stage II, and 15.0% for stage III. That same study demonstrated that preoperative irradiation improves local control compared with total mesorectal excision alone. Therefore, further investigation of the effects of neoadjuvant therapy is needed.

Additional concerns about TME are related to the functional costs, increased blood loss, higher anastomotic leak rates, and increased need for diversion [3]. A prospective analysis by Carlsen et al. [27] showed that the rate of anastomotic failure increases from 8% in patients who did not have TME to 16% in patients in whom the procedure was carried out. Moreover, the need for reoperation after anastomotic dehiscence was 100% for patients with TME in contrast to 25% among patients without TME. Therefore, the routine use of intestinal diversion has been proposed. Again, this policy brings additional problems to patients. Quality of life after radical proctectomy with TME is impaired by the routine formation of a temporary nonfunctioning stoma [28]. These negative aspects must be weighed against potential reduced local recurrence rates in patients with middle and upper rectal cancers.

## Conclusions

The modern treatment of rectal cancer combining total mesorectal excision with neoadjuvant chemoradiation results in excellent local tumor control. Today, distant disease is the most common cause of death in rectal cancer patients. Successful local control, however, is achieved at the cost of significant functional sequelae and impaired quality of life. The development of therapeutic alternatives that can achieve similar rates of local and distant tumor control without the mortality, morbidity, and functional consequences of radical surgery is probably the main challenge for colorectal surgeons in the near future.

**Résumé. Depuis la popularisation de l'excision mésorectale totale (TME) pour le traitement du cancer rectal, la qualité de la technique chirurgicale tend à émerger comme facteur crucial dans la prévalence de récidive. Ce procédé est associé à un taux de récidive locale plus bas après chirurgie à visée "curative" comparé au taux de récidive après dissection traditionnelle du rectum. Le but de la TME est d'enlever par une dissection précise, instrumentale, l'enveloppe mésorectale intacte entre le niveau du promontoire jusqu'au plancher pelvien, en obtenant des marges de sécurité sans tissu tumoral, et sans provoquer de lésions nerveuses au niveau du pelvis. Cependant, la description de la TME n'est pas claire. De plus, l'implication que l'excision en bloc, de toute la graisse périrectale contenue dans le fascia périrectal, améliore le taux de récidive locale chez tous les patients reste discutée. Ainsi une évaluation critique du procédé est nécessaire. Les études cliniques non randomisées ont montré que la TME réduit le taux de récidive locale et augmente la survie sans maladie chez les patients atteints d'adénocarcinome du rectum moyen et distal. Des marges circonférentielles de 2 mm ou plus sont associées à un taux de récidive locale plus bas. On peut encore augmenter ces bénéfices dans le contrôle local du cancer du rectum par un traitement néoadjuvant. Ainsi le traitement moderne du cancer rectal associe la TME à une chimioradiothérapie adjuvante et donne un excellent contrôle local de la tumeur. Cependant, ce contrôle est obtenu grâce à d'importantes séquelles fonctionnelles et des conséquences néfastes pour la qualité de vie. Le développement d'alternatives thérapeutiques capables d'obtenir des résultats similaires en ce qui concerne la récidive locale et à distance mais sans la mortalité, la morbidité et les conséquences fonctionnelles de la chirurgie radicale, reste le principal challenge futur pour les chirurgiens colorectaux.**

**Resumen. La técnica quirúrgica ha surgido como un factor de importancia crucial en cuanto a recurrencia local desde la popularización de la resección mesorrectal total en el tratamiento del cáncer rectal. El procedimiento se asocia con menores tasas de recurrencia tras de cirugía "curativa" en comparación con la disección tradicional del recto. El propósito de la operación es resecar la envoltura mesorrectal desde el peritoneo hasta el piso pélvico, mediante disección no roma, con márgenes libres de tumor y evitando lesión de los nervios pélvicos. Sin embargo, la descripción de la resección mesorrectal total ha sido confusa. Además, la implicación de que la resección total en bloque de la grasa perirrectal contenida por la fascia perirrectal en todos los pacientes con cáncer rectal minimiza la tasa de recurrencia sigue siendo motivo de controversia, por lo cual se hace necesaria una evaluación crítica del procedimiento. Estudios clínicos no aleatorizados han demostrado que la resección mesorrectal total reduce la tasa de recurrencia local y aumenta la supervivencia libre de enfermedad en pacientes con adenocarcinomas de los tercios medio y distal del recto. La resección circunferencial con márgenes de 2 mm o más se asocia con menores tasas de recurrencia. Beneficios adicionales pertinentes al control local se pueden obtener con terapia neoadyuvante. Por consiguiente, el tratamiento moderno del cáncer rectal que combina la resección mesorrectal total con quimio-radiación neoadyuvante resulta en excelente control local del tumor. Sin embargo, esto se logra a costa de secuelas funcionales significativas y desmejoramiento de la calidad de vida. El desarrollo de modalidades terapéuticas alternativas que logren tasas similares de control local y distal del tumor sin la mortalidad, morbilidad y consecuencias funcionales de la cirugía radical, constituye el gran desafío que se plantea a los cirujanos colorrectales.**

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