Lymph Node Dissection in Rectal Carcinoma: TME and What Else?

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Key Words

Rectal carcinoma · Total mesorectal excision · TME · Radical surgical therapy

Summary

Total mesorectal excision (TME) has been established as a standardized radical surgical procedure in malignant tumors of the middle and lower rectal third. In carcinomas of the upper rectal third, TME is seen as controversial. The aims of TME are low rates of locoregional recurrences and good functional results. Total mesorectal excision in the radical surgical treatment of lower and middle third rectal carcinomas is the essential part of lymphatic dissection in these tumors. It will be discussed if additional procedures are relevant for lymph node dissection, and how far they are established and approved. As yet, the results of laparoscopic TME show no advantage over conventional TME. The quality of TME should be assessed by a pathologist according to predefined criteria. In multimodal treatment regimens, TME is also essential.

Schlüsselwörter

Rektumkarzinom · Totale mesorektale Exzision · TME · Chirurgische radikale Therapie

Zusammenfassung

Die totale mesorektale Exzision (TME) hat sich als standardisiertes radikales Operationsverfahren bei malignen Tumoren im mittleren und unteren Rektumdrittel etabliert. Bei Karzinomen des oberen Rektumdrittels wird die totale mesorektale Exzision kontrovers diskutiert. Ziele der TME sind niedrige Raten lokoregionärer Rezidive und gute funktionelle Ergebnisse. Die totale mesorektale Exzision bei der radikalen operativen Therapie von Rektumkarzinomen im unteren und mittleren Rektumdrittel ist die essentielle Komponente hinsichtlich der Lymphknotendissection bei diesen Tumoren. Inwieweit weitere Maßnahmen bezüglich der Lymphknotenresektion bei Rektumkarzinomen von Bedeutung sind und inwieweit sie etabliert und standardisiert empfohlen werden können, soll im Weiteren geklärt werden. Die Ergebnisse der laparoskopischen TME zeigen bisher keine Vorteile gegenüber der konventionellen TME. Die Qualität der TME sollte vom Pathologen nach definierten Kriterien bewertet werden. Auch in multimodalen Behandlungskonzepten hat die TME einen zentralen Stellenwert.

Introduction

During the last 15–20 years, proven progress could be achieved in the staging [1] and treatment of rectal carcinoma by the es-

tablishment and implementation of quality criteria into surgical treatment and by incorporating multimodal treatment protocols.

Fig. 1. The 'Holy Plane' [2].

Total Mesorectal Excision (TME)

Background and Indication

Total mesorectal excision (TME) within the covering fascia of the rectum, the so-called 'holy plane' (fig. 1) [2], is the prerequisite for minimizing the rates of locoregional recurrence after radical surgical treatment (low anterior resection, intersphincteric resection, abdominoperineal rectal excision). Especially in advanced tumors with invasion beyond the rectal wall into perirectal fat and/or metastasis in the regional lymphatic system inside the mesorectal fascia, this method is the only possibility to surgically remove potentially tumorous tissue en bloc with the primary tumor.

Deposits like metastasis or satellites within the mesorectum, meaning discontinuous tumor spread of microscopic size in the surroundings of the primary tumor, justify the particular importance of the excision of the mesorectum by radical surgery. These deposits are found inside of the perirectal tissue, not only on the level of the primary but also distally [3]. Therefore, TME is the procedure of first choice in carcinoma of the middle and lower rectal third and is recommended by the German S3 guidelines for colorectal carcinomas, including preservation of the superior hypogastric plexus, hypogastric nerves, and inferior hypogastric plexus on both sides (grade of recommendation A, grade of evidence I-b, strong consensus [4]).

In carcinomas of the lower rectal third, radical surgery comprises 3 surgical procedures: Standardized low anterior resection with stapled anastomosis – with or without pouch – is recommended when sphincter preservation is possible. Otherwise, abdominoperineal rectal excision with a terminal colostomy is the procedure of choice. During the last years, cylindric excision of the pelvic floor has appeared to be beneficial [5]. Oncological benefit by this modification was recently discussed [6], but has to be proven in the long-term follow-up. The last option for sphincter preservation is the so-called intersphincteric or abdominoperineal resection with a peranal hand-sutured anastomosis. This procedure is limited to special tumor criteria and requires particular experience of the surgeon [7, 8].

In tumors of the upper rectal third, the current German S3 guidelines recommend partial mesorectal excision (PME) with transection of the rectum in a distance of 5 cm beyond the distal margin of the tumor (measured in situ) avoiding proximal thinning (no coning). This approach is based on the fact that in T3 and T4 tumors in rare cases satellites and lymph node metastases are found up to 4 cm from the distal tumor margin (measured on the fixed resection specimen stretched to in vivo length) [9]. In this context, controversy again exists over whether carcinomas of the upper rectal third should be assigned to rectal carcinoma or to colon carcinoma. A prospective randomized trial (Gast 5 [10]) is currently recruiting patients comparing PME versus TME in tumors of the upper third.

Fig. 2. The TME danger zones.

TME Technique

The TME procedure is described in detail in the publications of Heald [2]. Primarily 5 anatomical danger zones should be considered in TME with respect to functional postoperative results (fig. 2): i) protection of the superior hypogastric plexus; ii) protection of the hypogastric nerves; iii) protection of the inferior hypogastric plexus on both sides in the area of the so-called T-junction; iv) preparation behind Denonvilliers' fascia without violation of the capsule of the vesicles to avoid urogenital malfunction; v) protection of the dorsolateral region of the sacral nerves S2–S4. Overall, an exact preparation within the visceral and parietal fascia is essential to protect the structures of the autonomous nerves to avoid postoperative dysfunction [11].

TME – and What Else?

Conventional versus Laparoscopic TME

Controversy still exists regarding the benefit of laparoscopic TME. However, the results of laparoscopic TME have to match the results of conventional open surgery [7]. Within the hands of experienced laparoscopic surgeons, laparoscopic TME is associated with comparable peri- and postoperative complication rates. Conversion rates are low, and at least after short and intermediate follow-up intervals oncologic results in terms of locoregional recurrence rates and survival are comparable [12–17]. Long-term results are not available yet. According to current data, locoregional recurrence rates significantly increase after conversion from laparoscopic TME to conventional open procedure [18]. Regarding functional results, a prospectively randomized study demonstrates a higher rate of sexual dysfunctions in the laparoscopically treated arm [19].

TME and Prognosis

Without considering quality criteria of this operating procedure, the improvement in prognosis by consistent implementation of TME had been proved and published in numerous papers [20–23]. Although controlled trials have never been conducted, TME is an accepted surgical procedure in rectal carcinoma today. Noteworthy are the results of the quality assurance study [23] collecting prospectively multicenter data during the last years. According to the current results, a decrease in 5-year locoregional recurrence rates of 10% can be achieved by TME. A survey of locoregional recurrence rates in the newer literature shows a spread from 3 to 19% (table 1) [12–18, 24–34]. In a critical review of the literature presenting low recurrence rates, a very short follow-up period or a certain patient selection was noticed. In the non-selected collectives with primary curative resection, locoregional recurrence rates in the whole population amount to 10–15% after a median 5-year follow-up.

Table 1. Locoregional recurrence rates after conventional and laparoscopic total mesorectal excision (TME)

Authors [Ref.]	Conventional TME		
	Patients, n	LR rate, %	Median follow-up, months
Bülow et al. 2003 [26]	311	11.0	36
Wibe et al. 2004 [25]	1,315 (AR)	10.0	60
	821 (APE)	15.0	
	2,136 (total)	12.0	
Law et al. 2004 [27]	563	2 years: 6.0	39.6
		5 years: 9.7	
Piso et al 2004 [28]	337	8.6	73
Nagtegaal et al. 2005 [24]	392 (AR)	9.2	60
	146 (APE)	8.6	
Moore et al. 2005 [29]	422	4.0	116
Chiappa et al. 2006 [30]	264	3 years: 9.0	34
		5 years: 12	
Visser et al. 2007 [31]	632	11.0	60
Erlangen 1995–2000	373	8.8	52
Laparoscopic TME			
Hartley et al. 2001 [32]	21	5.0	38
Scheidbach et al. 2002 [13]	380	6.6	25
Yamamoto et al. 2002 [33]	70 (Tis, T1, T2)	3.0	23
Morino et al. 2003 [14]	87 ^a	4.2	46
Patankar et al. 2003 [34]	66	3.5	52
Braga et al. 2006 [17]	83	4.0	54
Lezoche et al. 2006 [12]	52	19.2	79
Ptok et al. 2006 [18]	237	3.3	30
	35	16.0	
Kim et al. 2006 [15]	273	2.9	27
Kitano et al. 2006 [16]	476	5.6	25

^aEvaluable malignancies.

LR = Locoregional recurrence; AR = anterior resection; APE = abdominoperineal excision.

Quality of TME – Is Every TME Really a TME?

Considerable differences in surgical quality of TME have been proved in several studies [24, 25, 35, 36]. Therefore, criteria for assessment of quality of TME have been established and reported in detail especially by Quirke and Nagtegaal [24, 37, 38]. Even perioperatively quality can be assessed by injection of ink or methylene blue solution into the inferior mesenteric or superior rectal artery. Postoperatively, the pathologist has to inspect and document the quality of the macroscopic surface due to exactly defined parameters, if it is smooth and intact or if there are irregularities or defects, prolapsed perirectal fat or visible rectal muscles, which forms the basis for valid classification [3]. Also, the status of the circumferential resection margin (CRM) is important.

In Erlangen, the so-called M.E.R.C.U.R.Y. classification was introduced classifying the quality of TME in 3 grades (table 2, fig. 3). Approved quality criteria of TME are: i) complete resection; ii) no defects on mesorectal surface; iii) preservation of pelvic autonomous nerves; iv) adequate distal margin of clearance.

Quality of TME is of prognostic relevance. It is scientifically proven [24, 38] that quality of TME significantly influences the rates of locoregional recurrence and survival. There is a significant correlation between TME quality and CRM status. In CRM-positive findings, a significantly higher rate of incomplete mesorectal excisions was found. Table 3 shows the correlation between TME quality and prognosis.

Lateral Pelvic Lymph Node Dissection

The importance of lateral lymph node dissection in locoregional recurrence rates and prognosis in low rectal carcinoma is mainly emphasized

Table 2. M.E.R.C.U.R.Y. classification

Grade 1 (good)	mesorectum intact only minor irregularities smooth mesorectal surface no defects larger than 5 mm no coning
Grade 2 (moderate)	moderate bulk to mesorectum irregularity of the mesorectal surface moderate coning muscularis propria not visible
Grade 3 (poor)	little bulk of mesorectum defects down into muscularis propria

in the Far Eastern publications [39]. Havenga et al. [40] compared high-quality TME to additional lateral pelvic lymph node dissection (D3 dissection) and to a collective without TME. However, no difference in recurrence rates or any prognostic benefit was found after D3 dissection compared to TME alone. After high-quality TME, locoregional recurrence rates are lower than those in the Japanese literature with additional D3 dissection. When lymph node metastases were found in the lateral compartment beyond the parietal mesorectal fascia, a 5-year survival rate of only 40% was observed [41]. This demonstrates that in cases of lateral pelvic lymph node metastasis, the physiologic barrier has been exceeded by these advanced tumors and prognosis can be compared to distant

Fig. 3. M.E.R.C.U.R.Y. classification. Quality of TME in 3 resection specimens: 1 = optimal, 2 = suboptimal, 3 = poor.

metastasis. Therefore, a prognostic benefit of this extended radical procedure seems questionable.

TME and Multimodal Therapy

The results of the German prospective multicenter trial (CAO/ARO/AIO 94) demonstrate significant benefit in advanced rectal carcinoma (T3, T4 and/or N+) by neoadjuvant chemoradiotherapy in conventional long-term

application [42]. In the neoadjuvant treatment arm, a decrease in locoregional recurrence rate from 12 to 6% was noted compared to the adjuvant treatment arm. Additionally, a significant increase in preservation of the anal sphincter in low tumor sites was found after neoadjuvant chemoradiotherapy. This raises the question if neoadjuvant treatment can eclipse or compensate the quality of surgery, especially TME, in rectal carcinomas of the middle or lower third. However, the data from the Swedish and Dutch study groups definitely highlight that TME plays a central role in locoregional recurrence rates independent of preoperatively performed radiotherapy [35, 43]. This was proved by the effect of the surgical training programs. Surgery of suboptimal quality can not be compensated by multimodal treatment concepts.

Conclusion

Locoregional recurrence rates can be reduced by TME. The quality of TME determines the results of function and prognosis. TME is essential within multimodal treatment concepts. TME is an essential element and part of lymph node dissection in lower and middle third rectal carcinoma and is an accepted surgical standard of current radical rectal carcinoma surgery.

Table 3. Quality of TME assessed by the pathologist and prognosis

Authors [Ref.]	Locoregional recurrence			p
	Rates	Status	Patients	
Nagtegaal et al. 2002 ^a [24]	2-year	complete or nearly complete incomplete	5.5% (n = 114) 11.4% (n = 25)	0.09
Quirke et al. 2006 [38]	3-year	complete nearly complete incomplete	1% (n = 596) 6% (n = 382) 9% (n = 141)	n.a.
Maslekar et al. 2006 [44]	crude	complete nearly complete complete or nearly complete incomplete	1/61 (2%) 3/52 (6%) 4/113 (3.5%) 7/17 (41%)	0.332 <0.001 ^b
Distant metastases				
Nagtegaal et al. 2002 ^a [24]	2-year	complete or nearly complete incomplete	12.2% (n = 114) 19.2% (n = 25)	0.11
Maslekar et al. 2006 [44]	crude	complete nearly complete complete or nearly complete incomplete	0/61 (0%) 6/52 (12%) 6/52 (12%) 3/17 (18%)	0.008 0.095
Observed survival				
Nagtegaal et al. 2002 ^a [24]	2-year	complete or nearly complete incomplete	90.5% (n = 114) 76.9% (n = 25)	<0.05
Maslekar et al. 2006 [44]	crude	complete nearly complete complete or nearly complete incomplete		n.s. n.s.

^aOnly patients with negative circumferential margin.

^bIn multivariate analysis significant influence on locoregional recurrence ($p < 0.001$).

n.a. = Not available; n.s. = not significant (detailed numbers are missing).

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