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Complications of Minimal Invasive Surgery for Rectal Cancer - A Systematic Review

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Abstract

Background: Total Mesorectal Excision (TME) is widely accepted as the standard surgical treatment for mid and low rectal cancer. The Robotic (RoTME) and Laparoscopic (LaTME) approaches to treat rectal cancer are shown to be feasible. Transanal TME (TaTME) is the most recent minimal invasive approach with promising results. We aimed to review the peri and postoperative complications associated with the three approaches.

Methods: A systematic search in the PubMed and Embase databases was performed. Both authors assessed the studies for eligibility. Clinical randomized as well as non-randomized studies published during the last six years were included.

Results: In total 39 studies (8094 patients) met the inclusion criteria. The LaTME had low rates of urinary complications, high rates of wound infection and intraabdominal abscesses. The RoTME had high rates of anastomotic leakages, but low rates of several other complications like; ureter and bladder injuries, bleeding and thirty-day mortality. The anastomosis performed more efficiently after TaTME with lower rates of anastomotic leakages, but higher rates of bleeding and 30-days mortality.

Conclusion: The procedures each performed well in relation to the different complications however further research especially concerning TaTME and RoTME is needed. Focus on which procedure that best treats a specific tumor stage, tumor location and type of patient could possibly reduce complications and postoperative mortality in the future.

Keywords: Rectal cancer; Complications; Total mesorectal excision; Transanal; Robot-assisted surgery; Laparoscopic surgery

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Introduction

Rectal cancer is the fifth most common type of cancer in Denmark and less than 2 out of 3 will survive more than 5 years after diagnosis [1]. Significant advances have been achieved in the treatment of rectal cancer over the past three decades. The introduction of TME [2], and improved preoperative diagnostic work-up have improved the short- and long-term results [3,4]. TME is widely accepted as the standard surgical treatment for mid and low rectal cancer [3-5]. It is general acknowledged that the laparoscopic approach for the treatment of rectal cancer has more advantages than open surgery with faster recovery, shorter hospital stays, decreased blood loss, infection rates and multi-organ failure as well as comparable long-term outcomes [6-11]. However, LaTME is a technically difficult procedure in obese patients, males and patients with a narrow pelvis [12,13]. RoTME is a feasible approach with potential advantages compared with laparoscopy and open surgery [14-17], and is reported to be equivalent to laparoscopic surgery with respect to the short-term perioperative and oncologic outcomes [15,18,19]. However, the true cost-benefit advantages still are questionable [12,20,21], and results of a randomized trial are awaited [22]. As the newest approach, TaTME shows promising results as a safe and effective technique with acceptable short-term outcomes [23,24]. Perioperative complications play an important role in the adoption of the appropriate approach, like both the pathological outcomes and the complication rates do. The aim of this review is to highlight common and severe reported complications associated with LaTME, RoTME and TaTME.

Materials and Methods

A systematic search was conducted in PubMed and Embase databases on October 7, 2016 using the following words separately and in combination: “complication”, “surgery”, “rectal”, “cancer”,

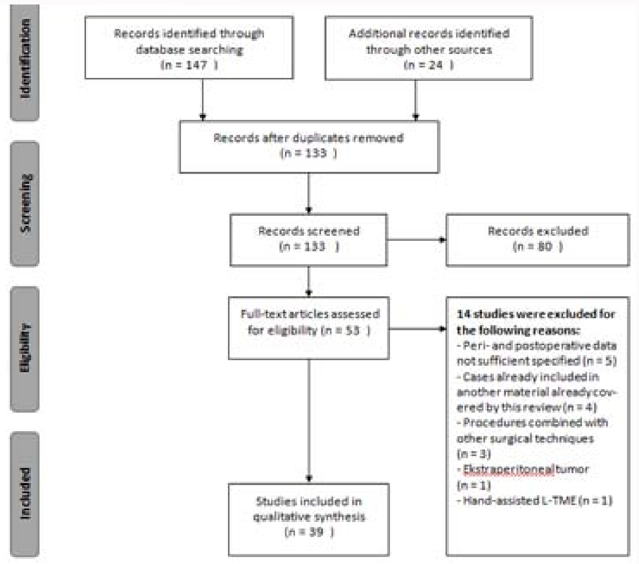

Figure 1: Flow diagram of article selection.

"total mesorectal excision", "transanal", "TaTME", "laparoscopic" and "robotic". Only full text articles in English were included. The search and the review processes were undertaken by the two authors using the PRISMA guidelines [25]. The search identified 147 clinical trials. After crosschecking the reference lists 24 additional articles were retrieved. After removing duplicates 133 articles remained and abstracts were read systematically for eligibility. Only articles published during the last six years were included, as all these three approaches have been practiced during this period. All prospective and retrospective randomized and non-randomized studies concerning TME were included. Articles not sufficiently specifying data about complications and studies combining the procedure with other surgical techniques were excluded. We focused on the following intraoperative and postoperative complications; bleeding, Estimated Blood Loss (EBL), need for blood transfusion, anastomosed leakage, urine retention and complication, bladder and urethral injury, urinary tract infection, wound infection, bowel injury, intraabdominal and pelvic abscess and 30-days mortality. In total, we included 39 studies corresponding to 8094 patients. See the PRISMA flow diagram for detail (Figure 1).

Results

The included studies were single center as well as multicenter clinical studies, prospective or retrospective, including several randomized studies. Numerous studies were comparative or case-matched studies, where data originally were compared with open surgery [7-10,13,26-30]. In six studies, LaTME was compared with RoTME while four studies compared LaTME and TaTME [5,12,15,31-37]. The rest focused on a single procedure.

The extracted data are presented systematically in Table 1.

Indications

The pathology was cancer in all studies except Penna et al. [23], who included 86 (out of 720) benign cases. All cancer stages were included though Yamamoto et al. [38] and Fujii et al. [39] only included stage Tis-T2 tumors, Fleshman et al. [29] included T2-T3 and Baik et al. [28] included T1-T3. Rouanet et al. [40] selected men with narrow pelvis, fatty mesorectum, high BMI, large prostate and presence of fibrosis. Neither if the operation had to be converted into open surgery nor the experience of the surgeon effected if a study was included or not. Five studies only reported patients treated with neoadjuvant therapy while several studies included both cases with and without neoadjuvant treatment [7,28,29,31,35,36,41-43].

Peri and postoperative data

Bleeding and estimated blood loss (EBL): Fernandez-Hevia et al. [37] reported one readmission in the LaTME group because of hemorrhage, while Cho et al. [12] reported two conversions to open surgery in the LaTME group due to intractable major vessel bleeding. Van der Pas et al. [9] reported conversion in six out of 22 cases because of bleeding. Hellan et al. [16] reported three cases of bleeding after RoTME. Chen et al. [35] subdivided bleeding into presacral bleedings and other bleedings. Another two studies subdivided as intraabdominal or anastomotic bleeding [24,38]. Two studies found no significant difference in EBL between TaTME and LaTME [35,36] and three studies found no significant difference between RoTME and LaTME in bleeding or EBL [31,32,44]. Perdawood reported a lower blood loss for TaTME than LaTME [5]. Penna et al. [23] reported an intraoperative blood loss during TaTME of less than 100ml in 61% of the cases, and furthermore reported six cases (1%) of bleeding more than one liter. Serra-Aracil et al. [45] reported 158 ml in EBL after TaTME, and proclaimed it lower than the laparoscopic group of the COLOR II trail. Ielpo et al. [33] reported the highest EBL=280 ml for RoTME (range 0 ml to 4000 ml) while Park et al. [34] reported the lowest EBL=77.6 ml (range 0 ml to 700 ml). Two LaTME studies reported EBL of 28 ml and 20 ml respectively [38,39]. Overall, 2.9% of the patients had perioperative bleeding during TaTME and a general average EBL at 107.9 ml for every case 1.1% of the patients had perioperative bleeding during RoTME and an average EBL at 143.7 ml. The LaTME studies reported 1.4% of patients with bleeding and an average EBL at 115.1 ml. See Table 2 for calculations of the percentage and an overview.

Need for blood transfusion: Approximately 20% required blood transfusion after TaTME in Rouanet et al. [40]. Lacy et al. [24] reported three blood transfusions because of anemia and one due to hemorrhage after TaTME. Another study reported 1.6 % of cases requiring blood transfusion after LaTME [38]. Overall, 5% of patients undergoing TaTME, 2% of patients after RoTME and 2.3% after LaTME had peri or postoperative blood transfusion.

Anastomotic leakage: Five studies reported the diagnosis as a clinical suspicion where different criteria were reported; fever and pain, pus, gas or fecal discharge from the drain, pelvic abscess and peritonitis [9,10,31,33,46]. After TaTME, Penna et al. [23] reported 32 cases identified early and eight cases identified after 30 days. Perdawood reported four patients readmitted after TaTME and one after LaTME because of anastomotic leakage [5]. Penninckx et al. [26] subdivided leakage as: minor (14 cases) and major (30 cases) leaks after LaTME. Schiphorst et al. [30] reported four out of 46 cases leading to reoperation or fistula as Hu et al. [7] reported 3.1% of leakage and concluded that LaTME after neoadjuvant CRT is a safe procedure. Cho et al. [12] reported no early postoperative difference between LaTME vs. RoTME while Chen et al. [47] reported no statistically significant difference in leakage rates between the TaTME and LaTME groups. As for postoperative pelvic abscess formation overall 5.8% of the patients after TaTME, 8.0% after RoTME and 6.9% after LaTME had anastomotic leakage.

Urine retention and complications: Kang et al. [48] defined

Table 1: The extracted data are presented systematically.

Author	Study design	Pub. year	Procedure	No. of patients	Bleed	aEBL (ml)	Trans	Leak	Urin	Blad	UTI	W inf	Bowel	I abs	P abs	30-d
Lujan et al. [11]	Prospective	2013	LaTME	1387	14			81			36	92		85		16
Penninckx et al. [26]	Retrospective	2013	LaTME	764				44[a]								11
Van der Pas et al. [10]	Randomized	2013	LaTME	699	22			58*		9		28	6	51		8
Penna et al. [23]	Retrospective	2016	TaTME	634				35		7				15		17[aa]
Cho et al. [12]	Retrospective	2015	RoTME	278	3	179		32	5			2	1	3	1	0
Yamamoto et al. [38]	Prospective	2013	LaTME	490	3	28	8	40	5		11	36		3		0
Fujii et al. [39]	Prospective	2012	LaTME	400	2	20	1	33	4		8					0
Hellan et al. [16]	Retrospective	2015	RoTME	425	3	119	5	37	30	5		16	7			1
Kang et al. [48]	Prospective	2011	RoTME	389	3		8	27				2			12	0
Fleshman et al. [29]	Randomized	2015	LaTME	240	8	256		5		2						2
Park et al. [34]	Prospective	2015	RoTME	133		78	1	6	2	1		2		0		0
Liang et al. [9]	Randomized	2011	LaTME	169			4	4			1	9		2		0
Chen et al. [12]	Prospective	2015	TaTME	50	1	68		3	0	0	1				3	
Ielpo et al. [33]	Retrospective	2014	RoTME	56		280		4				3		4		0
Lacy et al. [24]	Prospective	2015	TaTME	140	5		4	12	3			0				
Saklini et al. [31]	Prospective	2013	RoTME	74		180		4				1		0		0
D'Annibel et al. [15]	Retrospective	2013	RoTME	50				5								0
Kim et al. [59]	Prospective	2012	RoTME	100			3	2								0
Schiphorst et al. [30]	Prospective	2014	LaTME	86		200	10	4	2		1	1		4		1
Fernández-Hevia et al. [37]	Prospective	2015	TaTME	37	1			2	1							
Yoo et al. [32]	Prospective	2015	RoTME	44	2	240		5	4					1		0
Gong et al. [13]	Randomized	2012	LaTME	67		86		1		1		1				
Levic et al. [17]	Retrospective	2015	RoTME	56		50		6	1		0				0	0
Tuech et al. [46]	Prospective	2015	TaTME	56			2	3	5							0
Baik et al. [28]	Prospective	2011	LaTME	54	0	313		4			3	3		0	3	0
Hu et al. [8]	Prospective	2014	LaTME	51	0	204	2	1	1		1	2			0	0
Burke et al. [42]	Retrospective	2016	TaTME	50		150		3	2	1					4	0
Perdawood. Khefagie [5]	Prospective	2015	TaTME	25		50		2	4				0			
Marks et al. [36]	Prospective	2016	TaTME	17		282								0		0
Serra-Aracil et al. [45]	Prospective	2016	TaTME	32		158	0	3								0
Rouanet et al. [40]	Prospective	2013	TaTME	30			6	0		2						0
Leong et al. [52]	Prospective	2011	RoTME	29	1		4	3	1						1	0
Muratore et al. [53]	Retrospective	2015	TaTME	26				2	1							1
Rasulov et al. [43]	Prospective	2015	TaTME	22		30			2	1		1				0
Atallah et al. [58]	Retrospective	2014	TaTME	20		153		1**				2			4	0
Kang et al. [49]	Prospective	2016	TaTME	20		50	2	1	2	1						0
Lacy et al. [51]	Prospective	2013	TaTME	20		45										0
Wang et al. [50]	Retrospective	2013	TaTME	16	0			0								0
Fernandez et al. [44]	Retrospective	2013	RoTME	13		157		1	5							0

Data systematically presented starting with the study counting the largest total number of patients			
Bleed: Bleeding	aEBL: average Estimated Blood Loss	Trans: Bloodtransfusion	Leak: Anastomose leak
Urin: Urine retention & complication	Blad: Bladder & urinary injury	UTI: Urinary tract infection	W inf: Wound infection
Bow: Bowel injury	I abs: Intraabdominal abscess	P abs: Pelvic abscess	30: 30-days mortality
*58 out of 461 patients	**1 out of 15 patients	[a]44 out of 524 patients	[aa]17 out of 548 patients

Table 2: Calculations of the percentage and an overview.

Complication		Ta-TME			R-TME			L-TME	
	cases	total	percent	cases	patients	percent	cases	patients	percent
Bleeding	7	243	2.9%	12	1136	1.1%	54	3839	1.4%
EBL average	-	256	107.9 ml	-	1079	143.7 ml	-	2146	115.1 ml
Need for blood transfusion	14	278	5.0%	21	1076	2.0%	31	1357	2.3%
Anastomotic leakage	67	1151	5.8%	132	1647	8.0%	346	4982	6.9%
Urine retention & complication	20	426	4.7%	48	978	4.9%	41	1654	2.5%
Bladder and urethral injury	12	806	1.5%	6	558	1.1%	14	1241	1.1%
Urinary tract infection	1	50	2.0%	0	56	0.0%	65	2814	2.3%
Wound infection	3	182	1.6%	26	1355	1.9%	178	3516	5.1%
Bowel Injury	0	25	0.0%	8	703	1.1%	8	1002	0.8%
Intraabdominal abscess	15	651	2.3%	8	585	1.4%	158	3642	4.3%
Pelvic abscess	11	120	9.2%	14	752	1.9%	7	223	3.1%
30-days mortality	18	857	2.1%	1	1414	0.1%	39	5044	0.8%

Cases: the number of patients reported with the complication
Total: the number of patients reported with or without the complication
Percent: the percent of cases among the total number of patients
EBL average in mililiter blood (not percent)

voiding difficulty as urinary retention or urinary incontinence requiring urological medication or reinsertion of a Foley catheter. Tuech et al. [46] reported five patients (8.9%) with postoperative urinary retention, all treated by temporary urethral catheterization. After three months, all patients reported normal urinary function. Kang et al. [49] reported two urinary retentions during TaTME and one reported three cases of urinary retention after removing the Foley catheter after LaTME and none after TaTME [47]. Five cases of neurogenic urinary retention were reported after LaTME in one study [38]. In summary, 4.7% after TaTME, 4.9% after RoTME and 2.5% after LaTME had urinary retention or complications.

Bladder and urethral injury: Penna et al. [23] reported five cases of urethral injuries (0.7%) and two bladder injuries (0.3%) during perineal dissection after TaTME while Kang et al. [49] reported one urethral injury as a result of dissecting too anteriorly into an enlarged prostate. Rasulov et al. [43] reported one bladder injury during TaTME, which was closed laparoscopically and the patient was discharged with a urinary catheter, removed one week later. Park et al. [34] reported one case of bladder injury because of tumor adhesion to the bladder as well responsible for conversion from RoTME to LaTME. One study reported five genitourinary injuries after RoTME as just one out of two RoTME studies mentioning ureter or bladder injuries [16]. Gong et al. [13] reported one conversation from LaTME to open surgery due to ureteric injury. Overall, five bladder injuries and seven urethral injuries (1.5%) among 806 patients after TaTME were reported. 1.1% of the patients undergoing RoTME and 1.1% of the patients undergoing LaTME had intraoperative urethral or bladder injuries.

Urinary tract infection: Chen et al. [35] reported as only TaTME-study one case among 50 patients and Levic et al. [17] as the only RoTME-study none cases of urinary infection among 52 patients. Baik et al. [28] reported two cases of grade three and one case of grade two urinary tract infections after LaTME. Concerning LaTME, 2.3% among 2814 patients suffered from postoperative urinary tract infection.

Wound infection: Several studies emphasized that the TaTME procedure frequently allows specimen exteriorization without an abdominal incision, eliminating abdominal site morbidity as wound infection and hernia during specimen extraction [37,42,50,51]. Yamamoto et al. [38] reported that wound infection was diagnosed within 30 days of the operation according to the criteria of the Centers for Disease Control and Prevention. 1.6% of the patients after TaTME, 1.9% after RoTME and 5.1% after LaTME suffered from wound infection.

Bowel injury: Perdawood reported none bowel injury after TaTME [5]. Two studies reported eight cases (1.1%) after RoTME, besides accentuated one patient that required conversation from RoTME to LaTME because of bowel perforation [12,16]. Three studies reported 0.8% of patients among 1002 patients after LaTME [5,9,12].

Intraabdominal abscess: Fifteen cases of pelvic or abdominal abscess without evidence of anastomotic leakage were reported by Penna et al. [23], listed under intraabdominal abscess in our tables. Van der Pas [9] reported just abscess, listed as intraabdominal. Saklani et al. [31] categorized intraabdominal abscess as a severe complication together with anastomotic leakage. Two studies reported no significant difference between RoTME and LaTME [32,34]. Overall 2.3% of patients after TaTME, 1.4% after RoTME and 4.3% after LaTME had intra-abdominal abscesses.

Pelvic abscess: Chen et al. [35] reported three cases of pelvic abscess (8%) in the TaTME group and four cases (6%) in the LaTME group, all treated with antibiotics. Burke et al. [42] reported four cases among 50 patients and two readmissions because of pelvic collection after TaTME. All leaks and pelvic collections were managed conservatively with antibiotics and prolonged drainage by Leong et al. [52]. Baik et al. [28] graded it as a serious condition since one patient was hospitalized for 167 days because of pelvic abscess. Kang et al. [48] reported no significant difference neither RoTME nor LaTME groups regarding pelvic abscess. Overall, 9.2% of the patients after TaTME, 1.9% after RoTME and 3.1% after LaTME had pelvic abscess.

30-days mortality: TaTME: Four studies concluded no postoperative mortality and two studies reported no surgery-associated deaths [36,42,43,50,51]. Penna et al. [23] reported 0.5%

30-days mortality and concluded to be similar according to previous rectal surgery trials. Muratore et al. [53] reported a patient that died of myocardial infarction three days after surgery. Three studies did not mention mortality while Serra-Aracil reported no 30-days mortality but a six percent median score on the CROPOSSUM scale [5,35,37,45]. Overall, 2.1% patients died during the first 30 days after surgery.

RoTME: Two studies reported none cases of postoperative death without mentioning the follow-up period, while ten studies reported no cases in a follow-up period between 30 days and 3 years [34,44]. Overall, one patient among 1414 (0.1%) died within the first 30 days.

LaTME: Van der Pas reported eight cases of death within 28 days [9]. Penninckx et al. [26] reported 11 cases among 764 patients (1.44%) while Yamamoto et al. [38] reported the lowest mortality; none cases among 490. Overall 0.8% of the patients died during the first month after surgery.

Discussion

Complications and mortality due to surgery are of major importance and widespread adoption of new surgical methods depends among other things on complication rates and risk of postoperative death. Consequently, the studies management of data is important. One source of potential reporting bias is the retrospective nature of twelve studies in this review. Here the choice of outcomes reported can be influenced by the results, potentially making published results misleading [54]. Performance bias due to the experience among surgeons is another limiting factor as well as the number of surgeons performing the procedures vary from one to 65 different surgeons [13,29]. Several studies reported complications using the Clavien-Dindo classification, which impeded the use of data in relation to our study design [12,23,24,29,32,33,43,49,55]. Different diagnostic criteria and treatment options for the anastomotic leakage have been used throughout the studies [9,10,31,33,46]. However, more cases of leakage in the RoTME group compared to the TaTME and LaTME were reported. The anastomosis seemed to perform more efficiently after TaTME with lower number of leaks. The seriousness of the cases was however unclear. Unfortunately, only readmission or not after anastomotic leakage have been reported, while the length of hospitalization and death has not [5,23,30,42]. The LaTME-group advanced with well experienced surgeons because of the longer use of laparoscopic approach, though no superior data found as compared with TaTME [56]. Opposite, the LaTME performed better in relation to urine retention than RoTME and TaTME. Urine retention is a complication due to the operative procedure with iatrogenic injuries on the autonomic nerve in the narrow pelvic area [49], as well as the epidural analgesia which often is used during abdominal surgery [57]. Nevertheless, patients mostly recovered and gained previously bladder function during weeks after surgery and hospitalization, and it was further more deemed to constitute a mild complication [31,46]. Regarding wound infection, LaTME constituted a higher risk of post-operative wound infection, while TaTME possibly advantage from the fact that the specimen extraction were done transanal reducing intraabdominal wound related complications [37,42,50,51]. An almost equal percentage of urethral injuries among the three approaches were noted, as well as no higher percentage of injuries on nearby organs like bowel and bladder. Nevertheless, previous studies reported the TaTME procedure to cause more cases of urethral injuries [58]. Like injuries on organs, pelvic and intraabdominal abscess is a severe complication, which can lead to reoperation [23,37,42]. The reported cases in the TaTME varied from 2.4% to 20% what clearly underline the need for further research including big randomized trials [23,35,59]. As well the indication for blood transfusion varied among the studies, well-illustrated by Liang et al. [8] who transfused four patients out of 169 while Schiphorst et al. [30] transfused ten out of 86. The need for blood transfusion generally followed the bleedings and blood loss, but uniformed international evidence-based guidelines according to indication for blood transfusion might reduce bias. More bleeding and need for blood transfusion were reported among TaTME and presents a potential serious condition, with a need for acute conversion to open surgery [9,12,37]. We calculated an average EBL for each one of the approaches, which possible distorted the accuracy, though gave us an opportunity to make a comparison. The average EBL was higher among RoTME than TaTME and LaTME. Baik et al. [14] pointed, that prompt open conversion is impossible during RoTME because removing the robotic system is a time-consuming procedure, which is sometimes necessary for immediate control of serious bleeding. A fact that possible influences a higher blood loss during especially the most difficult RoTME operations ending up with conversion. The TaTME had a higher 30-days mortality rate than RoTME and LaTME, with poor evidence concerning cause of death. A recently published TaTME-study concluded no higher mortality according to previous rectal surgery trials [23]. However, research with longer follow-up period is needed since TaTME is a new technique meaning that surgeons improved in the studies and possibly reduced the complication rate in step with gaining higher level of experience [5,23,36,49].

Conclusion

We exposed an extract of complications in minimal invasive surgery for rectal cancer. The TaTME, as the newest procedure, had equal percentage of urethral injuries compared to LaTME and RoTME besides a low rate of anastomotic leakage. On the other hand, RoTME presented a lower percentage of bleeding and 30-days mortality in compare to especially TaTME. Further research is required, ideally randomized studies, to compare the three procedures regarding rates of serious intra and postoperative complications besides comparing their pathological results. Also, focus on which procedure that best treats a specific tumor stage, location and type of patient could possibly reduce complications and postoperative mortality in the future.

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