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REVIEW

The impact of transanal local excision of early rectal cancer on completion rectal resection without neoadjuvant chemoradiotherapy: a systematic review

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Abstract

Background The impact of transanal local excision (TAE) of early rectal cancer (ERC) on subsequent completion rectal resection (CRR) for unfavorable histology or margin involvement is unclear. The aim of this study was to provide a comprehensive review of the literature on the impact of TAE on CRR in patients without neoadjuvant chemoradiotherapy (CRT).

Methods We performed a systematic review of the literature up to March 2020. Medline and Cochrane libraries were searched for studies reporting outcomes of CRR after TAE for ERC. We excluded patients who had neoadjuvant CRT and endoscopic local excision. Surgical, functional, pathological and oncological outcomes were assessed. The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines were followed.

Results Sixteen studies involving 353 patients were included. Pathology following TAE was as follows T0 = 2 (0.5%); T1 = 154 (44.7%); T2 = 142 (41.2%); T3 = 43 (12.5%); Tx = 3 (0.8%); T not reported = 9. Fifty-three percent were > T1. Abdominoperineal resection (APR) was performed in 80 (23.2%) patients. Postoperative major morbidity and mortality occurred in 22 (11.4%) and 3 (1.1%), patients, respectively. An incomplete mesorectal fascia resulting in defects of the mesorectum was reported in 30 (24.6%) cases. Thirteen (12%) patients developed recurrence: 8 (3.1%) local, 19 (7.3%) distant, 4 (1.5%) local and distant. The 5-year cancer-specific survival was 92%. Only 1 study assessed anal function reporting no continence disorders in 11 patients. In the meta-analysis, CRR after TAE showed an increased APR rate (OR 5.25; 95% CI 1.27–21.8; *p* 0.020) and incomplete mesorectum rate (OR 3.48; 95% CI 1.32–9.19; *p* 0.010) compared to primary total mesorectal excision (TME)**.** Two case matched studies reported no difference in recurrence rate and disease free survival respectively.

Conclusions The data are incomplete and of low quality. There was a tendency towards an increased risk of APR and poor specimen quality. It is necessary to improve the accuracy of preoperative staging of malignant rectal tumors in patients scheduled for TAE.

Keywords Early rectal cancer · Transanal endoscopic microsurgery · Surgical transanal excision · Completion proctectomy · Completion rectal resection · Early salvage proctectomy · Early anterior resection

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Introduction

Transanal local excision (TAE) is the current standard treatment for T1 low-risk rectal cancers. TAE provides similar oncological outcomes but lower morbidity compared to anterior resection (AR) [1]. Completion rectal resection (CRR) is required following local excision if the histology shows any high-risk features or involved margins [1]. It is unknown to what extent TAE damages the anatomical planes of subsequent pelvic radical dissection and whether it affects the rate of abdominoperineal resection (APR), morbidity, and functional and oncological results of CRR. Two systematic reviews focused on the outcomes of CRR following TAE for early rectal cancer. The first showed that CRR after TAE was significantly associated with increased reintervention ($p \leq 0.04$) and a higher incomplete mesorectal excision rate ($p \leq 0.0003$) compared to primary total mesorectal excision (TME) [2]. The second reported an increased rate (40%) of APR [3]. Both reviews concluded that good quality data are lacking and the effects of TAE on CRR may be underestimated [2, 3]. However, both studies included patients who had endoscopic local excision of malignant polyps prior to CRR or CRR after TAE. CRR after endoscopic polypectomy is similar to primary AR because usually the mesorectal fascia and anal sphincter are not affected by the endoscopic procedure. On the other hand, neoadjuvant CRT could make CRR more challenging and lead to an increased rate of complications including effects on anal function.

The aim of this study was to provide a comprehensive review of the literature on the specific impact of TAE on CRR without neoadjuvant CRT and after excluding endoscopic polypectomy.

Materials and methods

A systematic search of the literature was performed on PubMed, Scopus and Web of Science up to March 2020. The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines were followed [4]. We considered both comparative and non-comparative studies, irrespectively of their size, publication status, and language. We included only patients who had CRR following TAE for early rectal cancer without neoadjuvant CRT. The primary endpoints included surgical (APR rate, postoperative major morbidity: Clavien–Dindo grade III–IV), functional (anal incontinence) and pathological (specimen quality-margin involvement) outcomes. The secondary endpoints included oncological outcomes (disease recurrence, 5-year cancer-specific survival).

Exclusion criteria were: CRR for local recurrence after TAE, neoadjuvant treatment before TAE or CRR, and local excision performed by endoscopic procedure. Case reports, conference abstracts, letters, and editorials.

The following search criteria were used in PubMed: ("proctectomy" [MeSH Terms] or "proctectomy" [All Fields]) or ("rectal" [All Fields] and "resection" [All Fields]) or "rectal resection" (All Fields) and "transanal excision" (All Fields) or "transanally excision" (All Fields) and "T1 rectal cancer local excision" or "Early rectal cancer local excision" and "salvage proctectomy" or "salvage anterior resection" and "completion proctectomy" or "completion anterior resection" and "TEM for early rectal cancer". Two investigators (ZR and GM) independently assessed all titles and abstracts to select studies reporting data on patients with early rectal cancer having CRR after TAE without neoadjuvant CRT. They analyzed full texts and selected the papers that fulfilled the inclusion criteria. The reference lists of the included studies were also searched with Google Scholar to identify additional studies. The final data extraction was performed using a standard data form. We included the first author's name, year of publication, country, sample size, intervention, tumor location, study design, tumor stage and relevant outcomes. The values (mean and standard deviation, median and inter-quartile range) were extracted from each study and recorded in a Microsoft Excel database. The methodological quality of the included studies was assessed according to the methodological index for non-randomized studies (MINORS) [5]. Comparative data were aggregated and the results were expressed as OR and 95% CI.

Results

Study selection

The PRISMA flow diagram is shown in Fig. 1. From the initial 787 potentially relevant articles, 122 remaining articles were further assessed for eligibility and 106 were excluded. Six relevant articles were excluded, because some patients did not meet the inclusion criteria [6–11] (Table 1). Sixteen studies were included [12–27] (Table 2).

Among the included studies, 3 also reported data from patients having neoadjuvant treatment: in these, it was possible to analyze the outcomes of the patients not undergoing CRT [14, 16, 26]. Four studies were case-matched analyses comparing CRR with primary AR [13, 15, 19, 20]: comparative data were aggregated assessing the OR, 95% CI and p value according to Fisher's exact test. The mean MINORS score was 12.8 and 5.9 in observational comparative and non-comparative studies, respectively.

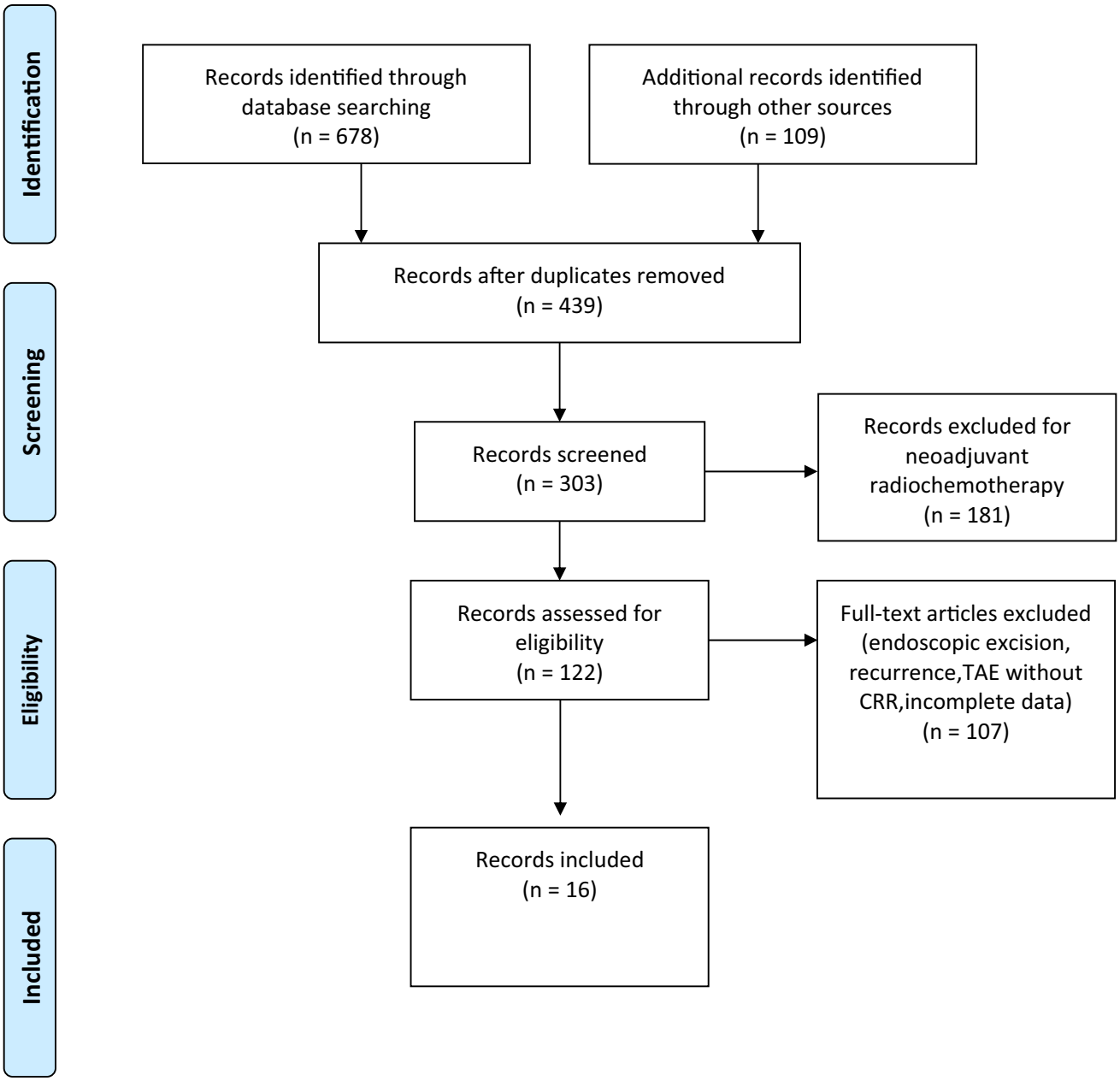

Fig. 1 PRISMA flow diagram. *TAE* transanal local excision, *CRR* completion rectal resection

Table 1 Relevant studies excluded

References	Reason for exclusion
Asayama et al. [6]	Endoscopic polypectomy
Gagliardi et al. [7]	Neoadjuvant CRT
Hahnloser et al. [8]	Endoscopic polypectomy
Baron et al. [9]	Endoscopic polypectomy
Piessen et al. [10]	Neoadjuvant CRT
Baatrup et al. [11]	Neoadjuvant CRT; incomplete data

CRT chemoradiotherapy

Preoperative staging and TAE

Sixteen retrospective studies including 353 patients were identified (Table 2). Endorectal ultrasound (ERUS) was performed routinely before TAE in 4 [12, 14, 22, 26], magnetic resonance imaging (MRI) in 2 [16, 24] and both ERUS and MRI in 3 studies [18, 19, 26]. In the other studies, these imaging methods were not routinely used or not reported. Two studies reported that preoperative T stage: cT1 cancers were underestimated in 59% and 20% of cases, respectively [15, 19]. The macroscopic morphology of polyps (polypoid,

Table 2 Features of TAE

Author	Patients	Tumor size mean mm (range)	Distance from anal verge mm (range)	TEM (%)	TAEP^ (%)	Full-thickness excision (%)	Defect closure (%)
Junginger et al. (2019) [12]	46	28 (7–60)	LR 8; MR22; UR16	38 (83)	8 (17)	29 (63)	46 (100)
Dulskas et al. (2019) [13]	9	28 (1.5–5)	< 30:3; 60–100: 4; > 100:2	NR	NR	NR	NR
Issa et al. (2018) [14]	12	NR	NR	12 (100)	–	12 (100)	12 (100)
Coton et al. (2018) [15]	41	20 ± 13	LR 28; MR 13	14 (34.1)	27 (65.9)	0 (0)	0 (0)
Gudbrand et al. (2018) [16]	2	NR	5.5 (5–6)	2 (100)	0	NR	NR
Osman et al. (2015) [17]	12	NR	NR	12 (100%)	0	12 (100)	12 (100)
Hompes et al. (2013) [18]	36	[a]72 (5–57) cm^2	LR6; MR 24; UR5	36 (100)	–	29 (81)	12 (33)
Morino et al. (2013) [19]	17	37 ± 12	54 ± 22	17 (100)	–	17 (100)	17 (100)
Levic et al. (2013) [20]	25	NR	90 (10–140)	25 (100)	–	23 (88)	NR
Bach et al. (2009) [21]	63	NR	NR	63 (100)	–	NR	NR
Nash et al. (2009) [22]	14	22 ± 11	60 ± 19	–	14 (100)	NR	NR
Borschitz et al. (2008) [23]	39	31 (5–100)	90 (40–160)	NR	NR	NR	NR
Bretagnol et al. (2007) [24]	7	NR	NR	7 (100%)	0	NR	NR
Lee et al. (2007) [25]	12	26 (6–60)	57 (10–120)	12 (100)	–	12 (100)	12 (100)
Min et al. (2007) [26]	7	NR	NR	–	7 (100)	7 (100)	NR
Nakagoe et al. (2004) [27]	11	18 (8–28)	70 (20–140)	11 (100)	–	6 (55)	NR
Total	353	–	–	249/305 (81.6)	56/305 (18.4)	147/ 219 (67)	111/ 176 (63)

TAE transanal local excision, *LR* low rectum, *M* middle rectum, *UR* upper rectum, *TAEP* transanal excision according to Parks**,** *TEM* transanal endoscopic microsurgery

[a]Tumor area

^transanal excision according to Parks

flat, depressed, and ulcerated) was reported in 3 studies [15, 21, 27] and the mobility (freely mobile, mobile, tethered, and fixed) in 2 studies [24, 26]. Data on pit pattern by chromoendoscopy or on the lifting sign were not reported in any studies.

Features of TAE (full-thickness rectal wall excision, rectal wall defect closure, pathology)

The features of TAE are listed in Table 2. There was lack of detailed data on full-thickness versus partial rectal wall excision and on closure versus not closure of the rectal wall defect. For this reason, we were not able to analyze the influence of these factors on the outcome of CRR. Nevertheless, Hompes reported a higher rate of poor specimen quality in patients having full-thickness excision than in those with partial excision of rectal wall (44% vs 0% p 0.03) (18). Pathology following TAE was as follows: T0 = 2 (0.5%); T1 = 154 (44.7%); T2 = 142 (41.2%); 3 = 43 (12.5%); Tx = 3 (0.8%); T not reported = 9. The rate of "positive margin" was 42.7% (Table 3). Other high-risk features such as poor differentiation and lympho vascular invasion were missing in the majority of studies.

Table 3 Pathology following TAE

Author (year)	Patients	Tx (%)	T0 (%)	T1 (%)	T2 (%)	T3 (%)	Positive margins (%)
Junginger et al. (2019) [12]	46	0	0 (0)	16 (35)	23 (50)	7 (15)	32 (69.5) "positive margin R1 or ≤ 1 mm"
Dulskas et al. (2019) [13]	9	NR	NR	NR	NR	NR	NR
Issa et al. (2018) [14]	12	0	0	2 (16.6)	5 (41.6)	5 (41.6)	5 (41.6) "involved"
Coton et al. (2018) [15]	41	0	[b]1 (2.4)	29 (70.7)	11 (26.8)	0 (0)	12 (29.2) " ≤ 1 mm"
Gudbrand et al. (2018) [16]	2	0	0	0	1 (50)	1 (50)	2 (100) "involved"
Osman et al. (2015) [17]	12	0	0	7 (58.3)	4 (33.3)	1 (8.3)	1 (8.3) "R1"
Hompes et al. (2013) [18]	36	0	[c]1 (2.7)	16 (44.4)	12 (33.3)	7 (19.4)	NR
Morino et al. (2013) [19]	17	0	0	3 (17.6)	10 (58.8)	4 (23.5)	3 (17.6) "positive"
Levic et al. (2013) [20]	25	3	–	11(44)	6 (24)	5 (20)	17 (68) "positive or unclear"
Bach et al. (2009) [21]	63	0	0	23 (36.5)	31 (49.2)	9 (14.2)	NR
Nash et al. (2009) [22]	14	0	0	14 (100)	0 (0)	0 (0)	8 (57) "positive. < 2 mm. not assessable"
Borschitz et al. (2008) [23]	39	0	0	19 (48.7)	20 (51.3)	0 (0)	13 (33.3) 5R1; "4Rx; 4 ≤ 1 mm"
Bretagnol 2007 [24]	7	0	0	3(43)	3(43)	1 (14)	NR
Lee et al. (2007) [25]	12	0	0	3 (25)	6 (50)	3 (25)	1 (8.3) "positive"
Min et al. (2007) [26]	7	0	0	0 (0)	7 (100)	0 (0)	NR
Nakagoe et al. (2004) [27]	11	0	0	8 (72.7)	3 (27.2)	0 (0)	NR margin clearance: T1: mean 0.8 mm (0–1 mm) T2: mean 0.7 mm (0.6–0.9)
Total	353[a]	3 (0.8)	2 (0.5)	154 (44.7)	142 (41.2)	43 (12.5)	94/220 (42.7)

TAE transanal local excision, *Tx* undefined

[a]T not reported in 9 pts

[b]High-grade dysplasia with MUTYH mutation and synchronous right colon cancer

[c]Large high-grade dysplasia with suspect of malignant invasion

Surgical outcome of CRR (APR rate, morbidity, timing of CRR)

AR, APR and Hartmann's procedure (HP) were performed in 75.7%, 23.2% and 1.1% of patients, respectively (Table 4). The laparoscopic approach was used in 41.8% of cases. The analysis of 2 case-matched studies showed increased risk of APR in patients having CRR compared to those having primary AR (OR = 5.25; 95% CI 1.27–21.8; $p = 0.020$) (13; 19) (Fig. 2). Morino et al. found that the previous TAE was the only significant risk factor for APR [19].

Overall postoperative major morbidity and mortality were 11.4% and 1.1%. The meta-analysis showed no differences in major morbidity in patients having CRR and primary TME (OR 1.07; 95% CI 0.45–2.52; $p = 0.880$) (13, 15, 19, 20) (Fig. 3). Three studies reported an intraoperative perforation rate of 20%, highlighting the risk of microscopic tumor dissemination during CRR [12, 13, 20]. In 1 series, rectal perforation with residual cancer was the main risk factor for recurrence [12] . The time interval (≤ 30 days versus > 30 days) between TAE and CRR did not affect the outcome of CRR (Table 5).

Pathology following CRR (specimen quality, positive m argins)

Overall, residual intramural cancer was present in 30% (range 7–52%) (Table 6). Ten studies reported the rate of margin involvement (mean 3.3%; range 0–50%). Metastatic lymph nodes were detected in 27.3% of specimens. The

Table 4 Surgical outcomes of CRR

Author (year)	N° patients	Timing days, mean (range)	AR (%)	APR (%)	Hartmann (%)	Laparoscopy (%)	Conversion (%)	Intraoperative perforation (%)	[a]Major morbidity (%)	Mortality (%)
Junginger et al. (2019) [12]	46	21 (7–86)	35 (76)	11 (24)	0 (0)	0 (0)	NR	10 (22)	NR	0 (0)
Dulskas et al. (2019) [13]	9	NR	9 (100)	0	0	NR	NR	2 (22.2)	2 (22.2)	0
Issa et al. (2018) [14]	12	47 (32–70)	9 (75)	3 (25)	0 (0)	8 (66.6)	0 (0)	1 (8.3)	2 (16.6)	0 (0)
Coton et al. (2018) [15]	41	25 (2–161)	37[b] (90.2)	4 (9.75)	0(0)	19 (46.3)	3 (15.7)	NR	5 (12.2)	0 (0)
Gudbrand et al. (2018) [16]	2	24 (22–27)	2 (100)	0	0	2 (100)	0	0	1 (50)	0
Osman et al. (2015) [17]	12	NR	7 (58.3)	5 (41.7)	0	12 (100)	O	NR	NR	0
Hompes et al. (2013) [18]	36	>47 days(21) <47 days(15)	31 (86.1)	4 (11.1)	1 (2.7)	16 (44.4)	1 (6.2)	NR	6 (16.6)	1 (2.7)
Morino et al. (2013) [19]	17	40 (20–56)	10 (58.8)	7 (41.1)	0 (0)	17 (100)	1 (5.9)	0 (0)	1 (5.8)	0 (0)
Levic et al. (2013) [20]	25	39 (14–183)	11 (44)	11 (44)	3 (12)	6 (24)	0 (0)	5 (20)	3 (12)	2 (8)
Bach et al. (2009) [21]	63	NR	53 (84.1)	10 (15.8)	0 (0)	NR	NR	NR	NR	NR
Nash et al. (2009) [22]	14	NR	9 (64.2)	5 (35.7)	0 (0)	NR	NR	NR	NR	NR
Borschitz et al. (2008) [23]	39	Within 28	27 (69.2)	12 (30.7)	0 (0)	NR	NR	NR	2 (5)	0 (0)
Bretagnol et al. (2007) [24]	7	NR	7 (100)	0	0	NR	NR	NR	NR	0
Lee et al. (2007) [25]	12	NR	5 (41.6)	7 (58.3)	0 (0)	NR	NR	NR	NR	NR
Min et al. (2007) [26]	7	NR	NR	NR	NR	NR	NR	NR	NR	NR
Nakagoe et al. (2004) [27]	11	35 (7–113)	10 (90.9)	1 (9.1)	–	–	NR	NR	0 (0)	0 (0)
Total	353		262/346 (75.7)	80/346 (23.2)	4/346 (1.1)	80/191 (41.8)	5/145 (3.4%)	18/111 (16.2)	22/192 (11.4)	3/257 (1.1%)

CRR completion rectal resection, *AR* anterior resection, *APR* abdominoperineal resection, *TAE* transanal local excision

Timing : time interval between TAE and CRR time between TAE and CRR

[a]Major morbidity: Clavien–Dindo III–IV

[b]One ileal pouch-anal anastomosis

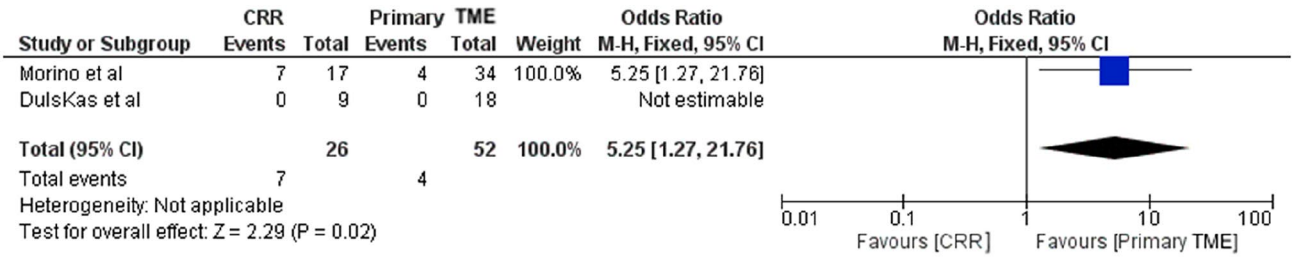

Fig. 2 APR rate in CRR and primary TME. *CRR* completion rectal resection, *APR* abdominoperinel resection, *TME* total mesorectal excision

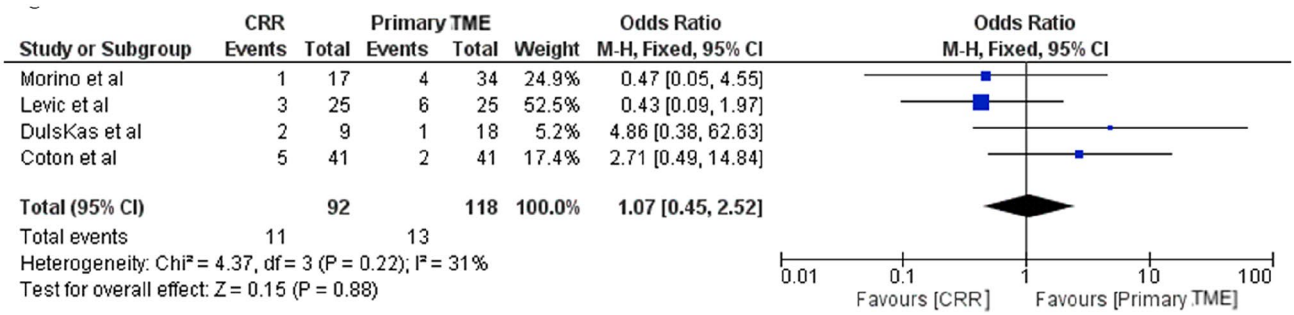

Fig. 3 Major morbidity in CRR and primary TME. *CRR* completion rectal resection, *TME* total mesorectal excision on

specimen quality was reported in 122 patients: 30 (24.6%) had an incomplete mesorectal fascia, resulting in defects of the mesorectum (Table7).

The meta-analysis showed no significant difference in margin involvement in patients undergoing primary TME vs. CRR (OR 3.46; 95% CI 0.67–17.9; $p=0.140$) [13, 15, 19, 20] (Fig. 4). We found a significantly increased risk of inadequate mesorectum in patients having CRR compared to those having primary TME (OR 3.48; 95% CI 1.32–9.19; $p=0.010$) [13, 15, 19, 20] (Fig. 5).

Oncological outcomes of CRR (recurrence, 5-year cancer-specific survival)

Ten studies (260 patients) reported recurrent disease in 31 patients (12%) after CRR. The recurrence was local in 8 (3.1%), distant in 19 (7.3%), both local and distal in 4 patients (1.5%) (Table 8). In T1 stage the overall recurrence was 7.8%. Eight studies (230 patients) reported 5-year cancer-specific survival mean of 92% (Table 8).

One case-matched study (20) reported no significant difference of overall recurrence in patients having primary TME and CRR (OR 0.167; $p=0.189$). Another case-matched study (13) showed similar 5-year disease-free survival rate in patients undergoing primary AR and CRR (OR not assessable, $p=1$).

Functional outcome of CRR (anal continence)

Only 1 study assessed anal function, reporting no incontinence in 11 patients undergoing completion AR [20].

Discussion

In this review, after TAE 53% of the rectal tumors were staged as more advanced than pT1 and 12% as pT3, suggesting that preoperative staging was inaccurate and may have led to improper TAE. Clinical examination is the mainstay of the preoperative assessment for early rectal cancer [28–33], but few studies reported key features of the tumors, such as morphology and mobility and none of them reported the lifting sign as a deep submucosal neoplastic invasion parameter (sensitivity 61–100%; specificity 83–95%) [34–36]. Although endorectal ultrasound (ERUS) is the standard procedure to stage T1 rectal cancers [37], some studies have reported its low accuracy (50%) in staging T1 tumors and its understaging (44%) in T2 and T3 cancers [38–41]. Moreover, distinguishing T1 substages (sm1-sm2-sm3) using ERUS can be very challenging [42, 43], thus the current estimation of the submucosal invasion depth is still mainly based on the pathology report [42, 44–46]. One suggestion of the late Gerhard Buess is to perform biopsy prior to TAE using, when possible, a core needle which provides

Table 5 Influence of time interval between TAE and CRR on outcomes of CRR

	Short interval ≤ 30 days (2, 12, 15, 23)	Long interval > 30 days (14, 18, 19, 20, 27)	OR (95%-CI)	*p* value
APR rate	27/128	26/101	0.77 (0.42–1.43)	0.433
Major morbidity	8/82	12/101	0.80 (0.31–2.07)	0.812
Poor specimen	7/41	21/72	0.50 (0.19–1.30)	0.179
Margin positive	2/128	3/101	0.52 (0.09–3.16)	0.657

CRR completion rectal resection, *TAE* transanal local excision, *APR* abdominoperineal resection

the pathologist with enough tissue to be able to detect poor differentiation and lymphovascular invasion.

TAE may lead to rectal wall defects and fibrotic healing of the mesorectum that may compromise the mesorectal plane during pelvic dissection [47], increasing the risk of intraoperative perforation, septic complications and tumor dissemination [10, 18, 48]. Moreover, the fibrotic scars may make coloanal anastomosis extremely challenging and increase the risk of APR [18]. The "down-to up" transanal approach during CRR could facilitate pelvic dissection during AR [2, 16, 49–51]; however, only 1 study in our review reported this approach [16].

This is the first review on the impact of TAE on CRR in patients with early rectal cancer who did not have preoperative CRT which may act as a confounding factor. Even under these more stringent conditions, we noted a tendency towards an increased rate of APR and poor specimen quality. Nearly 25% of the patients had APR. In line with our results, the meta-analysis of Jones et al. reported that 40% of patients had APR following TAE [3]. Difficult pelvic dissection following TAE can lead to an incomplete mesorectal specimen, one of the most important prognostic factors for local recurrence [2, 52, 53]. Piessen et al. reported that the rate of incomplete mesorectal specimen is significantly higher in CRR than in primary AR (71% vs 4%, $p < 0.001$) [10]. The meta-analysis of Eid et al. showed that patients undergoing CRR had higher rate of incomplete mesorectal excision than those who had primary TME (32% vs 7%) [2]. In line with these results, in our review, the rate of "poor" specimen quality following CRR was 25%. Hompes et al. reported that patients with a "poor" specimen quality had a lower 5-year disease-free survival rate than those with a "good" specimen quality (51% vs 100%, $p < 0.0001$) [18]. Finally, Similarly to the meta-analysis of Eid [2], we found no difference in major morbidity between CRR and primary TME [2].

In our review, there are not comparative data on oncological outcomes. We reported recurrence rate following CRR (12%) similar to that described in the meta-analysis of Jones et al. (14%) (3). Gagliardi et al. and Hanloser et al. suggested that TAE does not affect the outcome of CRR reporting a 5-year cancer-free survival rate of 88% and 94%, respectively. However, these studies included patients who had endoscopic local excision or neoadjuvant CRT [7, 8]. In a nationwide population-based registry of 144 patients, the survival rate did not differ in patients undergoing CRR or primary AR, regardless of the pT stage (pT1: 85% vs 95%; pT2: 89.5% vs 92.9%; pT3/4: 73.4% vs 74.9%): an unspecified proportion of patients had CRT [55]. Clermonts et al. compared 20 patients having CRR with 40 patients having primary AR and no differences in local recurrence and in 5-year survival rate were found: neoadjuvant CRT was given to 20% and 38% of patients with AR and CRR, respectively [56]. Conversely, in a multivariate analysis of 95 patients

Table 6 Pathology features of residual cancer in the CRR specimen

Author year	*N*°	Mural residual cancer (%)	T1	T2	T3	AJCC stage
Junginger et al. (2019) [12]	46	6 (13)	–	3	3	–
Dulskas et al. (2019) [13]	9	NR	–	–	–	–
Issa et al. (2018) [14]	12	NR	–	–	–	–
Coton et al. (2018) [15]	41	14 (34)	4	5	5	I
Gudbrand et al. (2018) [16]	2	1 (50)	–	–	1	III:1
Osman et al. (2015) [17]	12	2 (17)	–	–	2	III:5
Hompes et al. (2013) [18]	36	12 (33,3)	–	–	–	I–II:5; III:12
Morino et al. (2013) [19]	17	7 (41,1)	–	5	2	I:3; II:1; IIIa:3; IIIb:1
Levic et al. (2013) [20]	25	13 (52)	–	–	–	I:4; II:3; IIIa:2; IIIb:1; IIIc:3
Bach et al. (2009) [21]	63	NR	–	–	–	NR
Nash et al. (2009) [22]	14	1 (7)	–	–	–	NR
Borschitz et al. (2008) [23]	39	NR	–	–	–	–
Bretagnol et al. (2007) [24]	7	NR	–	–	–	NR
Lee et al. (2007) [25]	12	1 (8,3)	–	–	1	NR
Min et al. (2007) [26]	7	NR	–	–	–	NR
Nakagoe et al. (2004) [27]	11	2 (18)	2	–	–	NR
Total	216	59 (27,3)	–	–	–	

CRR completion rectal resection

Table 7 Pathology features of the CRR specimen

Author (year)	*N*°	Margin positive (%)	[b]Poor specimen (%)	LN harvest (%)	Patients with LN metastases (%)
Junginger et al. (2019) [12]	46	0 (0)	NR	NR	8 (17.3)
Dulskas et al. (2019) [13]	9	2 (22.2)[a] vs 0 *p* 0.135	2 (22.2)[a] vs 0 p = 0.135	12.44 (2–22)[a] vs 12.5 (0–38) *p* 0.986	NR
Issa et al. (2018) [14]	12	0 (0)	NR		–
Coton et al. (2018) [15]	41	1 (2.4)[a] vs 0 (0) p1	7 (17)[a] vs 2 (4.8) *p* 0.15	23.1 ± 10.9[a] vs 25.0 ± 11.1 p 0.430	14 (34.1)[a] vs 13 (31.7) *p* = 0.814
Gudbrand et al. (2018) [16]	2	1 (50)	NR	18 (12–24)	1 (50%)
Osma et al. (2015) [17]	12	0 (0)	NR	NR	5 (41.6)
Hompes et al. (2013) [18]	36	2 (5.5)	13 (36)	NR	12 (33)
Morino et al. (2013) [19]	17	0 (0)[a] vs 0 (0) p = 1	0[a]	10.8 ± 5.4[a] vs 12.4 ± 4.7	4 (23.5)
Levic et al. (2013) [20]	25	1 (4)[a] vs 1 (4) *p* = 0.99	8/19 (42)[a] vs 5/21 (23.8)	12 (3–25)[a] vs 10 (3–22) *p* 0.34	6 (24)[a]
Bach et al. (2009) [21]	63	NR	NR	–	–
Nash et al. (2009) [22]	14	NR	NR	–	6 (43)
Borschitz et al. (2008) [23]	39	NR	NR	–	–
Bretagnol et al. (2007) [24]	12	NR	NR	–	–
Lee et al. (2007) [25]	7	NR	NR	NR	2 (28)
Min et al. (2007) [26]	7	NR	NR	–	–
Nakagoe et al. (2004) [27]	11	0	NR	–	1 (10)
Total		7/211 (3.3)	30/122 (24.6)	–	59/216 (27.3)

[a]Comparison between CRR and primary AR

[b]Incomplete perirectal fascia resulting in mesorectal defects

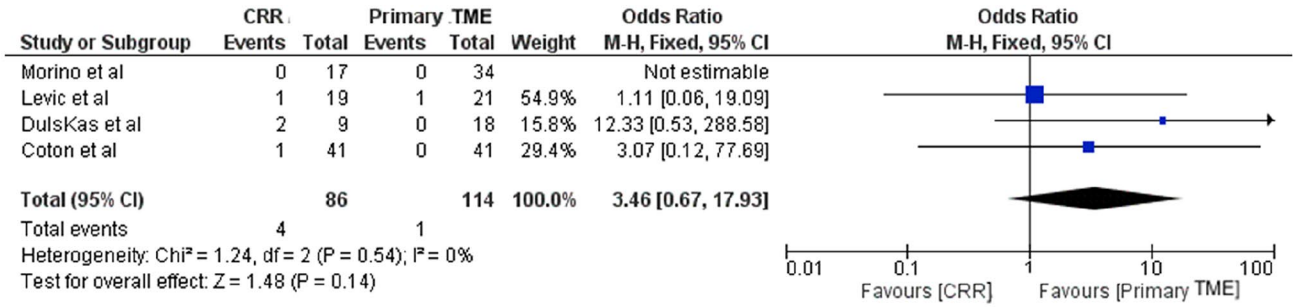

Fig. 4 Risk of positive margin after CRR and primary TME. *CRR* completion rectal resection, *TME* total mesorectal excision

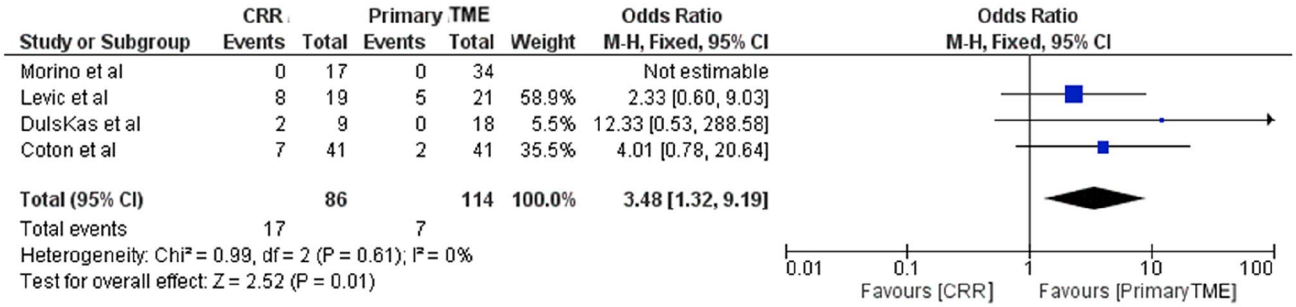

Fig. 5 Risk of poor specimen after CRR and primary TME. *CRR* completion rectal resection, *TME* total mesorectal excision

Table 8 Oncological outcomes

Author (year)	*N*°	FU months mean (range)	LR (%)	DR (%)	LR and DR (%)	5-year cancer-specific survival (%)
Jungering et al. (2019) [12]	46	139.2	2 (4)	5 (10.8)	1 (2.1)	40 (88)
Dulksas et al. (2019) [13]	9	22.8 (8–80)	NR	NR	NR	9 (100)
Issa et al. (2018) [14]	12	NR	NR	NR	NR	NR
Coton et al. (2018) [15]	41	56 (0–178)	NR	NR	NR	NR
Gudbrand et al. (2018) [16]	2	NR	NR	NR	NR	NR
Osman et al. (2015) [17]	12	NR	NR	NR	NR0	NR
Hompes et al. (2013) [18]	36	49.2 (3–137)	1 (2.7)	5 (13.8)	0	30 (83) Inferior spec (51) Good spec (100) P0.001
Morino et al. (2013) [19]	17	NR	NR	NR	NR	NR
Levic et al. (2013) [20]	25	25 (3–126)	0	1 (4)	0	NR
Bach et al. (2009) [21]	63	36 (0–143)	1 (1.5)	4 (6.3)	0	62 (97)
Nash et al. (2009) [22]	14	67	0	0	0	14 (100)
Borschitz et al. (2008) [23]	39	61 (9–190)	0	2 (5.1)	3 (7.6)	35 (89)
Bretagnol et al. (2007) [24]	7	34 (1–102)	4 (57)	NR	NR	NR
Lee et al. (2007) [25]	12	48.5 (7.7–91.8)	0	1 (8.3)	0	11 (91.6)
Min et al. (2007) [26]	7	84.9 (39.9–155.7)	0	1 (14.3)	0	NR
Nakagoe et al. (2004) [27]*	11	86.5 (63.2–110.5)	0	0	0	10/10 (100)
Total	–	–	8/260 (3.1)	19/260 (7.3)	4/260 (1.5)	211/230 (91.7)

LR local recurrence, *DR* distant recurrence, *FU* follow-up

5-year cancer-specific survival comparison between patients with "inferior" (Grade 1–2) and "good specimen" (Grade 3)

*One patient died of cholangiocarcinoma after 87 months.

(41 of these with preoperative radiotherapy) van Gijn et al. found a higher local recurrence rate after CRR compared with primary AR (5.2% vs 10.2%, $p < 0.0001$).

Recently a meta-analysis focused on local recurrence after TAE for early rectal cancer followed by CRR, CRT or no additional treatment. CRT and CRR showed similar local recurrence rate for T1 high risk (4.1% vs 3.9%). Local recurrence was higher (13.6%) in patients with T1 high risk who did not receive additional treatment. Even in the T1 group with low-risk features local recurrence was zero if TAE was followed by CRT or CRR vs. 6.7% for TAE alone. CRR was associated with the lowest recurrence in T2 rectal cancer (4%) [54]. It, therefore, seems that TAE alone is no longer a safe option, whether for low-risk or high-risk early rectal cancers.

TAE includes anorectal stretching and partial organ resection that may worsen anorectal function in patients having CRR. Jakubaskaus et al. found that 29% of patients complained of fecal incontinence with impairment of the quality of life, 8 years after TEM [57]. A meta-analysis showed that significant deterioration of the anorectal manometry parameters did not affect the quality of life but the authors recommended that the worsening of anal function following TAE should not be underestimated [58]. Recently, van Heisenberg et al. found that 29% of patients treated with TEM had major low anterior resection syndrome with a significant negative impact on their quality of life [59]. We cannot draw any conclusions about the functional outcomes of CRR following TAE, because only one study assessed the anal function reporting no continence disorders. Future studies should address carefully the bowel function of these patients.

Future perspectives

To date, the preoperative tumor staging of early rectal cancer is not accurate enough to reliably predict the T stage and nodal status. The main rationale of CRR following TAE is to remove potential metastatic lymph nodes. Future efforts should focus on the following issues.

Preoperative T staging and high-risk features

It is essential to improve the accuracy of preoperative T staging and especially the degree of submucosal invasion. An accurate clinical examination should always be carried out. The endoscopic "lifting sign" test could be adopted by the colorectal surgeon before attempting a surgical transanal excision. New endoscopic techniques such as the high-frequency miniprobe ultrasound (HFMU), narrow-band imaging (NBI) and endocytoscopy (EC) with artificial intelligence have shown promising results in the estimation of submucosal invasion depth [42, 43, 60]. It is advisable to obtain a biopsy specimen of good size to avoid performing TAE in patients with poorly differentiated tumors or lymphovascular invasion.

Preoperative N staging

Endoscopic posterior mesorectal resection (EPMR) is an interesting rectum-preserving staging procedure which identifies patients with mesorectal lymph node metastasis [61]. However, the technique was never fully established and all the shortcomings of TAE highlighted in this review would also apply to EPMR.

Endoscopic tailored dissection

Emerging technologies and devices may provide endoscopic full-thickness resection [62]. It would be desirable to perform a tailored excision according to the different degree of wall invasion, guided by new promising diagnostic tools (HFMU, NBI, and EC). Furthermore, endoscopic mucosal dissection may cause less damage to anal sphincter function than TAE.

CRR is usually performed in early rectal cancer with an intermediate or high risk of lymph node metastasis (5–20%). In these cases, emerging data suggest that CRT may offer similar oncological outcomes (53). We are waiting for conclusive oncological results from the STAR-TREC and TESAR trials [63, 64]: CRT could make CRR an obsolete treatment.

Conclusions

The data are incomplete and of low quality. There was a tendency towards an increased rate of APR and poor specimen quality but no increase in complication rate. It is necessary to improve the accuracy of preoperative staging of malignant rectal tumors in patients scheduled for TAE.

Declarations

Conflict of interest The authors declare that they have not conflict of interest.

Ethical approval This article does not contain any studies with human or animal subjects performed by the any author.

Informed consent For this type of study, the informed consent is not required.

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