Chemoradiation and local excision versus total mesorectal excision for T2N0 rectal cancer: comparison of short- and long-term outcomes from 2 prospective studies

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Chemoradiation and Local Excision Versus Total Mesorectal Excision for T2N0 Rectal Cancer

Comparison of Short- and Long-Term Outcomes From 2 Prospective Studies

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Objective: Compare oncological long-term and short-term outcomes between patients with distal cT2NO rectal cancer treated with chemo-radio-therapy and local excision (CRT + LE) and patients treated with total mesorectal excision (TME).

Summary Background Data: Previous studies showed that CRT + LE is equivalent to TME in local tumor control and survival for T2N0 rectal cancer.

Methods: Seventy-nine patients with cT2N0 rectal adenocarcinoma treated with CRT + LE in the ACOSOG z6041 trial were compared to a cohort of 79 patients with pT2N0 tumors treated with upfront TME in the Dutch TME trial. Survival, short-term outcomes, and health-related quality of life (HRQOL) were compared between groups.

Results: Three patients (4%) in the CRT + LE group required abdominoperineal resection, compared with 31 (40%) in the TME group. Forty TME patients (51%) required a permanent stoma. CRT-related toxicity occurred in 43% of the CRT + LE patients; however, TME patients had a higher rate of complications requiring reoperation (1 vs 9%; $P = 0.03$). Five-year disease-free survival {88.2% [confidence interval (CI), 77.7%–93.9%] vs 88.3% [CI, 78.7%–93.7%]; $P = 0.88$} and overall survival [90.3% (CI, 80.8%–95.3%) vs 88.4% (CI, 78.9%–93.8%); $P = 0.82$] were similar in the 2 groups. Compared to baseline, overall HRQOL decreased in the CRT + LE group and improved in the TME group. In both groups, patients with sphincter preservation had worse HRQOL scores 1 year after surgery. **Conclusions:** In patients who underwent CRT + LE, oncological outcomes were similar to those of patients who underwent TME, with fewer complications requiring reoperation but significant CRT toxicity. Although overall HRQOL decreased in the CRT + LE group and improved in TME patients, when considering anorectal function, results were worse in both groups.

Keywords: local excision, neoadjuvant chemoradiation, rectal cancer, total mesorectal excision

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Surgical treatment of distal rectal cancer limited to the muscularis propria without lymph node metastasis (cT2NO) is challenging. Most guidelines recommend total mesorectal excision (TME).[1–3] Unfortunately, TME is a morbid operation that results in significant sexual, urinary, and defecatory dysfunction requiring in some cases a permanent stoma.[4–6]

Local excision (LE), although less morbid, is associated with very high rates of local recurrence (19%–47%).[7,8] The addition of chemoradiotherapy (CRT) either before or after LE is one approach to decrease this risk. The American College of Surgeons Oncology Group (ACOSOG) phase II trial Z6O41 explored the use of an oxaliplatin-based neoadjuvant CRT regimen followed by LE. The results showed disease-free and overall survival results comparable to those of TME series, with acceptable morbidity and good quality of life.[9,10] This single-arm study was powered using retrospective data from the National Cancer Database, in which the quality of the TME and the distance of the tumors from the anal verge are not reported.[11] The ultimate comparison between this new approach and TME would be a randomized controlled trial. Given the good prognosis of these patients, with local and distal recurrence rates in the single-digit range, the number of patients needed for each arm would be on the order of thousands. Furthermore, the significant cross-over seen in the recent GRECCAR II phase III trial, which compared LE versus TME in rectal tumors with good response to CRT, illustrates the difficulties that a trial like that would face.[12] In this sense, a comparison with a similar cohort of patients treated with TME for which information about staging and tumor height is available would provide a better assessment of the treatment effect.

The objective of this study was to compare the surgical and oncological outcomes, complication profiles, and quality of life between patients with cT2N0 tumors from the ACOSOG Z6041 study and a similar group of patients with low pT2N0 tumors treated only with TME from the Dutch TME trial.[13]

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MATERIALS AND METHODS

Patients

Patient consent was obtained by each of the trials, and institutional review board approval was obtained for this retrospective analysis. Patients in the ACOSOG Z6041 trial had clinical T2N0 rectal adenocarcinoma staged by endorectal ultrasound orendorectal-coil MRI, measuring < 4 cm in greatest diameter, involving < 40% of the circumference of the rectum, and located within 8 cm from the anal verge. The 79 patients who started the oxaliplatin-based neoadjuvant CRT were included in the present study; descriptions of the radiation protocol and chemotherapy regimen have been published previously.[14] LE was performed 4 to 8 weeks after completion of neoadjuvant CRT, as either conventional transanal excision or transanal endoscopic microsurgery (TEM). Full-thickness excision of the tumor with a 1-cm surrounding margin of normal tissue was required. According to the protocol, patients subsequently underwent TME if the surgical specimen had a positive margin or showed that the tumor category was ypT3.

The Dutch TME trial is a randomized controlled study that was designed to determine whether the addition of preoperative radiotherapy increased the benefit of TME.[13] Patients enrolled in the trial had a histologically confirmed adenocarcinoma of the rectum without evidence of distant metastasis, with the inferior margin of the tumor located not farther than 15 cm from the anal verge and below the level of S1–2. Patients were randomized to either short-course radiotherapy followed by TME or TME alone. Of the 1861 patients enrolled, 207 in the TME-only arm had pT2N0M0 tumors, and 146 of these had tumors situated up to 8 cm from the anal verge. This number was considered too small to perform propensity score matching, so 79 patients from this latter group were randomly selected as the comparison group and were included in the study.

Demographic data including sex, age, and Eastern Cooperative Oncology Group (ECOG) performance status, as well as information regarding the procedures performed, were collected. Pathology data were interpreted according to the criteria of the AJCC Cancer Staging Manual, 7th ed.[15]

Surgery Quality Control

Both trials required surgeons to document proficiency in performing the relevant surgical procedure to participate. Participating surgeons in the CRT + LE group were required to have performed at least 3 transanal excisions of rectal tumors with negative margins and to have completed a surgical skill verification program.[14] Surgeons in the Dutch TME trial attended symposia and workshops, viewed instructional videotapes, and were monitored by instructors to ensure that a proper TME was performed. Also, an instructor surgeon directly supervised the first five TME resections for each surgeon.[13]

Complications

Complications that occurred during the course of CRT were classified according to the National Cancer Institute's Common Terminology Criteria for Adverse Events. For patients who underwent CRT þ LE, information regarding surgical complications was available for the period of up to 60 days from the surgical intervention, and for patients who underwent TME, information regarding surgical complications was available for the period of the index admission. Surgical complications were classified as minor (no therapeutic intervention needed), moderate (intervention other than surgery needed to address complications), or severe (reoperation required).

HRQOL and Anorectal Function

For CRT + LE patients, health-related quality of life (HRQOL) was evaluated using the Functional Assessment of Cancer Therapy-General (FACT-G), a validated questionnaire containing 27 items corresponding to four subscales: physical well-being (7 items), social/family well-being (7 items), emotional well-being (6 items), and functional well-being (7 items). To address specific colorectal issues, a colorectal cancer concerns subscale (CCS), consisting of 7 items was also included. A FACT-Colorectal (FACT-C) score was calculated by adding the CCS score to the FACT-G score (34 items in total).[16]

For patients in the Dutch TME trial, the Rotterdam Symptom Checklist (RSCL) was used. RSCL is a self-report measure designed to cover 4 domains: physical symptom distress (23 items), psychological distress (7 items), activity level (8 items), and overall quality of life (1 item). The RSCL score was combined with a 9-item defecation scale created for the original study, to better reflect the impact of the treatment on anorectal function.[17]

HRQOL was assessed with the above questionnaires at enrollment and at 12 months after surgery in both studies. Given that different tools were used, analysis consisted of a comparison of trends over this 1-year period. Results were converted to a 0 to 100 scale, with higher scores indicating a higher HRQOL.[18,19] For overall HRQOL, FACT-G scores were compared with RSCL scores. For patients who underwent sphincter-preserving treatment (CRT + LE and TME with sphincter preservation), FACT-C scores were compared with RSCL scores combined with scores on the self-created defecation scale.

Follow-Up and Survival

CRT þ LE patients were clinically evaluated every 4 months for 3 years and subsequently every 6 months for the following 2 years. Proctoscopy and endorectal ultrasonography were performed at the physician's discretion. Colonoscopy was performed 3 years after the initial surgery.

TME patients underwent clinical evaluation every 3 months during the first year and yearly thereafter for at least 2 more years. Yearly liver imaging and endoscopic evaluation were mandatory.

Local recurrence was defined as evidence of a tumor within the pelvis or the perineal wound. Distant recurrence was defined as evidence of a tumor in any other area. The starting point for the analyses of survival and recurrence was the day of surgery. Data were censored at the last disease evaluation with confirmation of no recurrence or at 60 months. To account for the difference in the study periods (TME, 1996–1999; CRT + LE, 2006–2009) and the differences in demographics (Europe vs the United States), relative survival analyses were performed (overall survival in the study group relative to overall survival in the general population for that period in the specified country).

Statistical Analyses

Statistical analyses were performed with SPSS version 20 software (IBM). Univariable analysis was performed with the chi-square test to compare proportions and with the Mann-Whitney test to compare continuous variables. Survival data were analyzed by the Kaplan-Meier method, and differences between groups were evaluated with the log-rank test. A Cox proportional-hazards model was used to calculate hazard ratios and 95% confidence intervals (CI). Statistical significance was set at 0.05.

TABLE 1. Patient and Tumor Characteristics

Characteristic	TME (n = 79)	CRT + LE (n = 79)	*P*
Mean age, y	64.4 ± 11.25	62.7 ± 11.24	0.3
Male, n (%)	51 (65)	53 (67)	0.7
ECOG, n*			
0	69	68	
1	9	10	
2	0	1	0.6
Tumor			
Mean size, cm	3.28 ± 0.71	2.84 ± 0.69	< 0.001
Mean distance from AV, cm	4.94 ± 2.3	5.02 ± 1.93	0.96

AV indicates anal verge.
*Data available in 78 patients in TME group.

RESULTS

Group Characteristics

The CRT + LE group and the TME group were similar in age, sex distribution, ECOG performance scores, and mean tumor distance from the anal verge. In the CRT + LE group, tumors were smaller (median, 3 vs 4cm; $P < 0.001$) (Table 1).

Of the 79 patients in the CRT + LE group, there were 2 who did not undergo surgery and one who underwent TME (per the decision of the treating team). The remaining 76 patients (96%) underwent LE after CRT. Three of the 76 patients subsequently underwent TME by abdominoperineal resection (APR) per-protocol (2/3 patients had ypT3 tumors, and 1 patient had a positive margin).

Of the 79 patients in the TME group, 46 (58%) underwent low anterior resection, 31 (39%) underwent APR, and 2 (3%) underwent

Hartmann's operation. Protective stomas were created for 30 (65%) of the 46 patients who underwent low anterior resection, and in 23 (77%) of the 30 patients, the stomas were reversed. At the end of follow-up, 40 (51%) of the 79 patients in the TME cohort had a stoma. The resection was categorized as R0 in 75 (98.6%) CRT + LE patients and 77 (97%) TME patients (Table 2).

TABLE 2. Surgical Procedures and Pathological Tumor Stages

	No. (%) of Patients	
Procedure or Stage	TME (n = 79)	CRT + LE (n = 76)
Procedures		
LAR	46 (58)	0
APR	31 (39)	3 (5)*
Hartmann's	2(3)	0
LE	0	47 (62)
TEM	0	29 (38)
Stoma	61 (77)	3 (4)
Diverting	30 (39)	0
Reversed	23 (77)	
Permanent	40 (51)	3 (4)
Resection		
R0	77 (97)	75 (98)
R1	2 (3)	1 (2)
R2	0	0
Stages		
T0/in situ		38 (50)
T1		11 (14)
T2	79	23 (30)
T3		3 (4)
Tx		1 (1)
N0	79	

Tx indicates T stage not determined.
*One patient had a positive margin, and 2 patients had ypT3 tumors.

TABLE 3. Postoperative Complications

Complications*	TME (n = 79)	CRT + LE (n = 79)	*P*
No. of patients with a complication	**45 (57%)**	**39 (51%)**	**0.3**
No. of patients with minor complications	**22 (28%)**	**23 (30%)**	**0.9**
Urinary retention	10	4	
UTI	8	0	
Pulmonary	4	0	
Bleeding	0	4	
Urinary symptoms	0	3	
GI disorder	0	4	
Cardiac	1	0	
Stoma related	1	0	
Neurological	1	2	
Anorectal infection	0	3	
Suture line dehiscence	0	1	
Rectal stenosis	0	2	
Other	3	5	
No. of patients with moderate complications	**8 (10%)**	**10 (13%)**	**0.6**
Bleeding	2	3	
Perineal wound complication	2	0	
Abdominal wound complication	1	1	
Ileus	1	1	
UTI	1	0	
Leak	1	0	
Neurological	1	1	
Line sepsis	1	0	
Anal ulcer	0	1	
Leukopenia	0	1	
Anorectal infection	0	2	
Stoma related	1	0	
No. of patients with severe complications	**7 (9%)**	**1 (1%)**	**0.03**
Pelvic abscess	2	0	
Bleeding	2	1	
Leak	1	0	
Necrosed stoma	1	0	
Abdominal dehiscence	1	0	

GI disorder indicates gastrointestinal disorder such as diarrhea or constipation; UTI, urinary tract infection.
*Minor, no therapeutic intervention needed; moderate, intervention other than surgery needed; severe, reoperation needed.

Complications

The CRT þ LE group and the TME group had similar overall surgical complication rates (51 vs 57%; $P = 0.34$), but TME patients had a higher rate of severe surgical complications that required reoperation (1 vs 9%; $P = 0.03$)

TABLE 4. Chemoradiotherapy-Specific Complications

Complication	No. (%) of Patients (n = 79)
≥1 Adverse event	57 (72)
≥1 Grade 3–4 adverse event	34 (43)
Gastrointestinal	14 (18)
Dermatologic	13 (17)
Hematologic	57 (72)
Pain	15 (19)
Metabolic	7 (9)
Infection/febrile neutropenia	5(6)

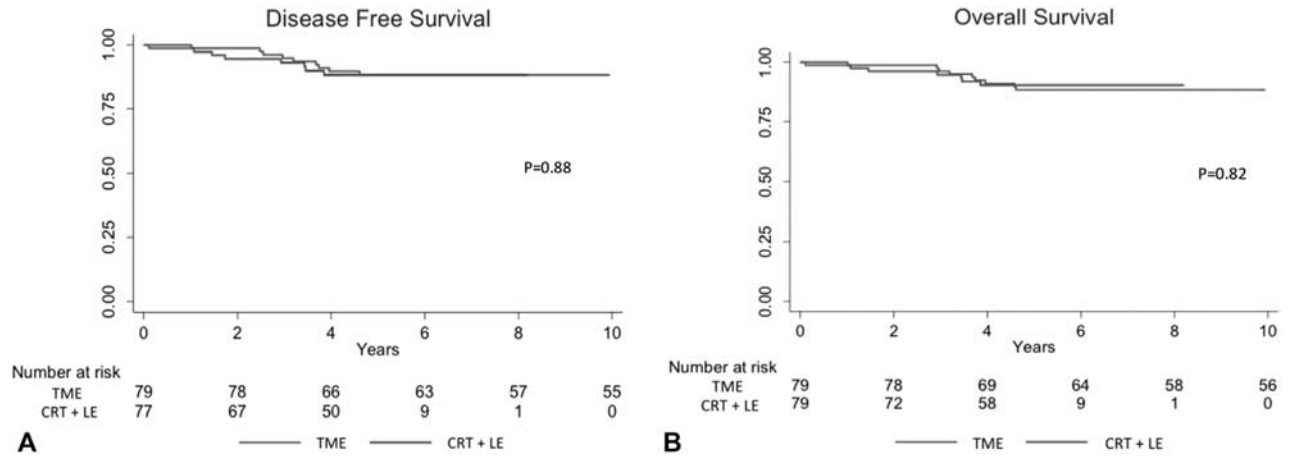

FIGURE 1. Disease-free survival and overall survival in patients who underwent TME and patients who underwent CRT þ LE.

(Table 3). However, 43% of CRT + LE patients experienced at least 1 adverse event of grade 3 or 4 related to CRT (Table 4)

Survival

Median follow-up was 1774 (IQR 1405–1980) days for the CRT þ LE group and 4440 (IQR 2874–5100) days for the TME group. The 5-year rate of local recurrence was 4.2% (CI, 1.4%–12.5%) in the CRT + LE group and 1.3% (CI, 0.2%– 6.7%) in the TME group [hazard ratio, 5.42 (CI, 0.59–49.64); $P = 0.14$]. We found no significant difference between groups in 5-year disease-free survival (DFS) [CRT + LE, 88.2% (CI, 77.7%-93.9%); TME, 88.3% (CI, 78.7%–93.7%); hazard ratio, 1.07 (CI, 0.41%–2.79%); $P = 0.88$], 5-year overall survival [CRT þ LE, 90.3% (CI, 80.8%–95.3%); TME, 88.4% (CI, 78.9%–93.8%); $P = 0.82$], or 5-year relative survival [CRT + LE, 99.8% (CI, 88.9%–100%); TME, 100% (CI, 92.7%–100%); $P = 0.99$] (Fig. 1).

HRQOL and Anorectal Function

In the CRT + LE group, the overall HRQOL minimally decreased at 1 year (the mean FACT-G score was 1.71 points lower), whereas in the TME group it increased at 1 year (the mean RSCL score was 8.12 points higher) (Fig. 2A). Patients who had undergone an APR had on average a higher HRQOL score at 1 year compared to patients who had undergone low anterior resection or CRT + LE (Fig. 2B).

In patients who had undergone sphincter-preserving treatment [CRT þ LE vs low anterior resection (LAR) from the TME group], HRQOL incorporating anorectal function (assessed by FACT-C orby RSCL in combination with the defecation scale) decreased in both groups at 1 year (Fig. 2C).

DISCUSSION

In our study, patients with clinically staged T2N0 distal rectal adenocarcinoma treated with CRT followed by LE had oncological outcomes that were similar to those of patients with pathologically staged T2N0 rectal cancer treated with TME. The rate of complications requiring reoperation was higher in patients who underwent TME, and more than half of the patients in the TME group required a permanent stoma. Despite this, patients who underwent TME had higher HRQOL scores than CRT + LE 1 year after treatment.

The results of our study are consistent with those of previous studies that investigated CRT þ LE for early-stage rectal can-cer.[12,20–23] One retrospective study of patients with T2N0 rectal cancers reported similar 5-year survival rates for patients who underwent CRT + LE and patients who underwent trans-abdominal surgery (77.7% vs 75.1%).[20] Another retrospective study of patients with T2N0 rectal cancer found no significant difference in 5-year overall survival between patients who underwent radical surgery (77.4%), patients who underwent CRT þ LE (76.1%), and patients who underwent LE plus adjuvant CRT (79.7%) ($P = 0.786$).[21] These studies did not report the size or height of the tumors or the type of chemo-radiation, and LE and TME were not standardized.

A prospective study of patients with cT2N0 rectal cancer in Italy (with a mean follow-up of 84 months) determined that the probability of local recurrence was 9% for LE patients and 6% for TME patients. The probability of DFS at the end of follow-up was 94% for both groups.[22] More recently, the GRECCAR 2 phase III study of patients with T2 or T3 rectal cancer reported similar 3-year oncologic outcomes (local recurrence, DFS, and overall survival) for patients who underwent LE after CRT and patients who underwent TME after CRT.[12] Finally, the CARTS phase II study of 55 patients with cT1-3 N0 rectal cancer (including 29 patients with cT2N0 cancer) treated with neoadjuvant CRT followed by LE (and, in case of poor response, completion TME) reported an actuarial 5-year local recurrence rate of 7.7% and 5-year DFS and overall survival rates of 81.6% and 82.8%, respectively.[23] The results from these studies are in line with our finding that for early rectal cancer, LE after CRT seems to be oncologically equivalent to radical surgery.

In our study, CRT + LE patients and TME patients had similar rates of surgical complications, but TME patients had a significantly higher rate of surgical complications requiring reoperation. Furthermore, surgical complications may be underestimated in the TME group, since this information was available only for the index admission, whereas in the CRT + LE group data was available up to 60 days from surgery. However, > 70% of the patients in the CRT + LE group experienced CRT-associated toxicity, and 43% had at least 1 grade 3 or 4 event. This study included oxaliplatin in addition to 5%-FU as a radiosensitizer. Based on subsequent experience from several prospective randomized trials, it is likely that oxaliplatin may have increased toxicity without improving oncologic outcomes.[24] In light of these findings, the CRT + LE approach may represent

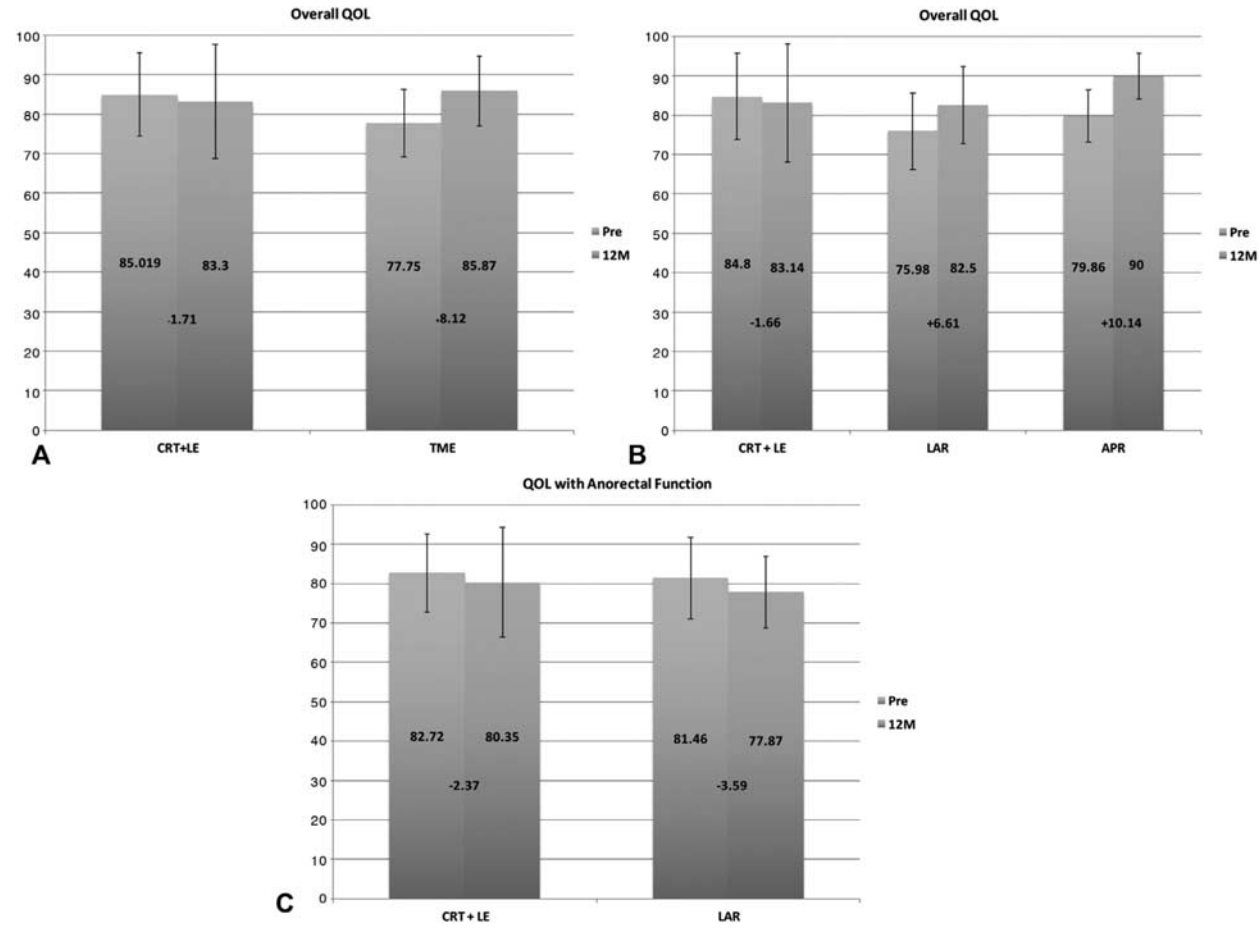

FIGURE 2. HRQOL. A, Overall HRQOL in CRT + LE vs TME patients (FACT-G vs RSCL). B, Overall HRQOL according to surgical intervention: CRT + LE vs LAR vs APR (FACT-G vs RSCL). C, Overall HRQOL considering anorectal function: CRT + LE vs LAR (FACT-C vs RSCL + self-created defecation scale). 12M indicates 12 months after surgery;Pre, before surgery.

a trade-off between a lower likelihood of surgical complications compared with TME and a relatively high likelihood of CRT toxicity.

Our study found that at 12 months after surgery, the overall HRQOL minimally decreased compared to baseline in CRT + LE patients (2 points on a 0-100 scale). In TME patients, HRQOL increased by 8 points in that time frame. However, when considering only patients that underwent sphincter-preserving treatment, the HRQOL scores incorporating anorectal function declined slightly in both the CRT + LE group (–2.4 points) and the TME group (–3.6 points) in the same time interval.

In the CARTS study, patients were selected to undergo LE (TEM) or TME according to response to CRT. HRQOL was evaluated with the EORTC QLQ 30 and 38. Authors found that with at least 1 year of follow-up, HRQOL was statistically worse in more domains for TME patients (physical functioning, fatigue, nausea and vomiting, and appetite loss) compared to patients who underwent TEM, who also had better scores in emotional function and mucus discharge/bleeding but worse anxiety scores.[23] In contrast, we found that HRQOL scores were better for our TME patients.

It has been suggested that having a stoma has a negative effect on body image and sexual function.[25] Our study did not find a negative effect of having a stoma on the overall HRQOL. In fact, APR patients had the biggest improvement in scores for overall HRQOL > 12 months. As reported in a previous publication from the Dutch TME trial, APR patients had increased scores in physical and psychological dimensions on the RSCL.[17] Furthermore, a recent study of patients with low rectal cancer found that APR patients had a better overall HRQOL and significantly less bowel dysfunction (as measured with an EORTC questionnaire) than patients who had undergone low anterior resection.[26] Further research is needed to determine the relative contribution of sphincter preservation to overall HRQOL in patients with low rectal cancers, as the negative effect of a permanent stoma may be less significant than commonly thought. Moreover, the fact that HRQOL seems to be worse after CRT + LE raises questions about the fundamentals of LE. We now know that more than 50% of these patients will have a pathological complete response to CRT, which makes them ideal candidates for organ-preserving strategies with no immediate surgery.[27] In the context of adjuvant CRT, LE (especially TEM) is not benign. Compared to a "watch and wait" approach, LE patients have worse resting and squeeze pressures, worse Cleveland Clinic incontinence index scores, and worse HRQOL as measured by the FIQL (fecal incontinence quality of life) questionnaire.[28]

Our study had several limitations. First, 2 different populations from different countries and time periods were compared, and this was subject to differences in race, habits, life expectancy, cultural expectations, or another potential residual confounding. We tried to partly account for these time differences by analyzing relative survival; however, the effect of this time difference does not seem to be significantly impactful, since the relative 5-year survival of early rectal cancer (Stage I or localized) remained similar between the 1990s and 2000s in the United States and the Netherlands with numbers around 90%.[29,30] Second, follow-up schemes were different; CRT + LE patients were seen more frequently than TME patients, which potentially contributed to a different distribution of events. Third, the study compared tumors staged clinically to tumors staged pathologically. It is possible that some ypTO and ypTl tumors in the LE group might have been overstaged by ERUS. But there is also evidence that some tumors (ypT3) were understaged. Although overstaging tends to be more common than understaging with ERUS, the impact of overstaging (categorizing a tumor as cT2 when it is actually a cT1, still a stage I tumor) probably has a lower impact in oncologic outcomes compared to understaging (categorizing a tumor as cT2N0 when it is actually a T3, stage II). Overall 64% of the LE + CRT group were T0/T1 on pathology; unfortunately, it is not possible to estimate how many tumors were originally an over-staged cT1 or a donwstaged cT2. Considering the limited accuracy of ERUS in identifying mesorectal nodes, it is possible that some tumors considered cN0 in the LE group could have been also understaged regarding the nodal status. Unfortunately, patients in the Dutch trial were not clinically staged for cT and N status before randomization. Fourth, CRT + LE patients had smaller tumors on average than TME patients (mean 2.84 vs 3.28 cm). The clinical relevance of this difference is not likely to be high, however. Finally, the tools used to assess HRQOL and anorectal function differed between CRT + LE patients and TME patients, precluding any statistical analysis. The data is presented as trends between before and after the intervention assuming that the tools used measure (likely with different accuracies) similar aspects of HRQOL. We opted to convert the results of both questionnaires (FACT-C/FACT-G and RSCL) to a 0 to 100 scale following the instructions in the implementation manuals. To incorporate anorectal function evaluation into HRQOL of the TME patients who underwent sphincter preservation, a common score combining the RSCL and the self-created defecation scale was created for this purpose and then converted to a 0 to 100 scale. This conversion was done with a similar methodology as the one described in the RSCL manual. Although this tool was created for this study and was not validated beforehand, we think that this is the most approximate comparison that can be achieved with the data available in relation to the FACT-G score. The use of more accurate instruments, such as the LAR syndrome (LARS) score, would help clarify the real impact of these modalities on bowel function.[31] Unfortunately, the LARS score was not available when these trials were designed. Furthermore, the RSCL and FACT-C questionnaires include questions about satisfaction with sexual life but do not evaluate sexual function. This should also be considered in the morbidity burden when assessing low rectal cancer treatment.

The study's strengths include the availability of data on tumor size and height, allowing the analysis to focus on patients with early-stage distal rectal tumors, in contrast to retrospective studies based on data from the National Cancer Database. Additionally, the CRT regimen and surgery were standardized.

Definitive answers to the questions raised by the present study require a properly powered noninferiority randomized controlled trial hypothesizing that CRT + LE is not inferior to TME. With a hazard ratio for the noninferiority margin of 1.45, an alfa of 0.025 and a power of 90% the total sample size would be 980 patients (490 on each arm). Accruing 50 patients per year, twice the accrual ratio of the ACOSOG Z6041 trial, this hypothetical study would require a 20-year accrual period, plus 5 years of follow-up. Additionally, there is a legitimate concern that patients will not be willing to undergo randomization between these 2 interventions. In the meantime, retrospective studies, with all their limitations including potential for type II errors, and can provide physicians with a valuable perspective to have an honest discussion with patients about what to expect from surgical treatment of a T2N0 tumor in the lower rectum. An aspect not addressed by this study is the differences in costs between treatment modalities. As the patients were treated in different countries within different health care systems, a comprehensive cost-effectiveness analysis including direct and indirect costs was considered beyond the scope of this paper.

In conclusion, CRT + LE and TME have comparable oncological outcomes for distal T2N0 rectal cancers. TME is associated with more severe surgical complications, whereas a considerable proportion of CRT + LE patients experienced significant CRT toxicity. More than half of the TME patients had a permanent stoma at the end of follow-up. Despite this, when compared to baseline, TME patients presented better HRQOL scores 1 year after treatment; conversely, CRT + LE had worse scores. This information should be useful when discussing this alternative approach.

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