THE IMPACT OF ROBOTIC TOTAL MESORECTAL EXCISION ON SURVIVAL IN PATIENTS WITH RECTAL CANCER *– A PROPENSITY MATCHED ANALYSIS*

P Tejedor[1], F Sagias[1], K Flashman[1],
Yeh Han Lee[1], S Naqvi[1], N Kandala[2], J Khan[1]

1. Department of colorectal surgery, Queen Alexandra Hospital, Portsmouth, UK.
2. Faculty of Sciences, School of Health Sciences & Social Work, University of Portsmouth, UK.

Correspondence to:
Jim Khan
Queen Alexandra Hospital
Southwick Hill Road, Cosham.
PO6 3LY Portsmouth, UK.
Email: mkhan702@aol.com

Category: Original article
Shortlisted for Raven Prize session at BASO, November meeting 2018, Glasgow.
Abstract published: *European Journal of Surgical Oncology 44 (2018) 1837-1844*

Conflict of interest: None

WORD COUNT BODY TEXT: 2485 words
WORD COUNT ABSTRACT: 250 words
TABLES: 3
FIGURES: 2
Disclosures: None

AUTHOR'S CONTRIBUTION

All authors critically revised the paper for important intellectual content. All authors have contributed to the work and agreed on the final version. This manuscript is not being considered by any other journal.

KEY WORDS:

Robotic surgery; laparoscopic surgery; rectal cancer; oncologic outcome; total mesorectal excision; survival.

ABSTRACT

INTRODUCTION

Robotic surgery can overcome some limitations of Laparoscopic Total Mesorectal Excision (L-TME), improving the quality of the surgery. We aim to compare the medium-term oncological outcomes of L-TME vs. Robotic Total Mesorectal Excision (R-TME) for rectal cancer.

METHODS

A retrospective analysis was performed including patients who underwent L-TME or R-TME between 2011-2017. Patients presenting with metastatic disease or R1 resection were excluded. From a total of 680 patients, 136 cases of R-TME were matched based on age, gender, stage and time of follow-up with an equal number of patients who underwent L-TME. We compared 3-year disease free survival (DFS) and overall survival (OS).

RESULTS

Major complications were lower in the robotic group (13.2% vs. 22.8%, p=0.04), highlighting the anastomotic leakage rate (7.4% vs. 16.9%, p=0.01).

The 3-year DFS rate for all stages was 69% for L-TME and 84% for R-TME (p=0.02). For disease stage III, 3-year DFS was significantly higher in the R-TME group. OS was also significantly superior in the robotic group for every stage, reaching 86% in stage III.

In the multivariate analysis, R-TME was a significant positive prognostic factor for distant metastasis (OR 0.2 95%CI 0.1, 0.6, p=0.001) and OS (OR 0.2 95%CI 0.07, 0.4, p=0.000). Moreover, major complications were also found to have a negative impact on OS (OR 8.3 95% CI 3.2, 21.6, p=0.000).

CONCLUSION

R-TME for rectal cancer can achieve better oncological outcomes compared to L-TME, especially in stage III rectal cancers. However, a longer follow-up period is needed to confirm these findings.

INTRODUCTION

The fundamental principles of Total Mesorectal Excision (TME) surgery postulated by Bill Heald[1] were to perform surgery in the anatomical and embryological plane. This improved outcomes for rectal cancer patients in particular, reducing local recurrence. A few clinical trials across the globe have shown comparable outcomes between open and laparoscopic TME.[2,3] The minimally invasive approach has several advantages.[2,3] However, the adoption of L-TME worldwide remains low and varies between 15-45%. This is linked to a flat learning curve in L-TME.

Robotic surgery can offer some distinct advantages that can overcome some of these limitations of L-TME. The evolution of the technique has resulted in more advanced instruments for colorectal surgery, which make easier the dissection in a narrow pelvis, low rectal tumour and anatomical complexity. Thus, the true benefit of these advances will be the quality of the specimen resected which leads to reduced local recurrence and improved survival.

To date, there are only a few reports comparing oncologic outcomes of robotic and laparoscopic surgery.[4] None of them have demonstrated a significant difference between these 2 approaches, although there is a trend towards better oncological outcomes after a R-TME. Therefore, we aimed to compare the medium-term oncological results of L-TME vs. R-TME for rectal cancer.

METHODS

A retrospective analysis was performed based on a prospectively maintained database, including patients who had undergone L-TME or R-TME in a single centre over a 7-year period (January 2011- December 2017). A total of 680 patients were initially included for further analysis. Inclusion criteria were: Rectal tumor at baseline which would be considered to require complete TME and underwent either laparoscopic or robotic anterior resection with a stapled colorectal anastomosis. Patients presenting with metastatic disease or those whom underwent palliative resection were excluded from the study, leaving 639 patients for analysis.

Tumours were classified according to the distance between the tumour and the anal margin and the anatomical extent of the disease (TNM Classification of Malignant Tumours, 7th edition –employed in our centre untill December 2017-).

Patients were divided into 2 groups, based on the type of surgical intervention: L-TME or R-TME. Data recorded included patient demographics (sex, age, BMI, ASA), preoperative staging, postoperative complications (Dindo-Clavien), pathological report and oncological outcomes.

Primary endpoint was to compare 3-year disease free survival (DFS) and overall survival (OS). 3-year DFS was defined as the percentage of patients alive without recurrence of disease at 3 years measured from the date of surgery. 3-year OS was defined as the time from surgery to death from any cause. Secondary outcomes included postoperative complications (30-day) and pathological assessment of the quality of the specimen.

Local recurrence was defined as any clinical/radiological or histologic evidence of tumour relapse at the primary site. Distant metastases were diagnosed by CT scan.

The patient allocation to each arm was based on surgeon's preferred approach and access to a robotic theatre.

Statistical analysis

Descriptive statistics are presented with mean and standard deviation (SD) or median and interquartile range (IQR) for quantitative variables.

A case-control 1:1 design was applied to minimize baseline differences between the laparoscopic and the robotic group. Patients were propensity matched into those 2 groups. Confounding variables used to compute the propensity score were age, gender, BMI, tumour stage and duration of follow-up (less than 6 months, up to 1 year, between 1 and 2 years, 2 and 3 years, and more than 3 years). The rest of the analysis was performed using the matched patients by surgical approach.

Comparison of differences between groups was carried out using Chi-Squared analysis. Differences between median values of the groups were assessed using

Mann-Whitney U test. Odds ratios [OR] were computed for dichotomous and continuous risk factors between groups and logistic regression was performed, selecting those variables that showed a $p<0.25$ in the univariate analysis. A time-to-event analysis was performed using the Kaplan-Meier method and comparisons were analyzed by the log-rank test.

All statistical analyses were conducted using SPSS® version 22 software (SPSS, Inc., Chicago, IL) and *p*-values of <0.05 were considered statistically significant.

RESULTS

Between January 2011 and December 2017, 680 TME were performed in our centre. According to the inclusion criteria, 639 were included for analysis. The majority of patients were men (66%), with a median age of 68 (15) years. Median follow-up of the 639 patients was 37.4 (45) months. A total of 463 (73.5%) TME were performed laparoscopically and 176 (27.5%) robotically.

Two groups, each of 136 patients (Fig. 1) were matched for age, gender, BMI, stage and duration of follow-up.

The rate of conversion was higher in the L–TME group (3.7% vs. 0%, p=0.03), and the LOS was significantly longer (7 vs. 6 days, p=0.001). Perioperative complications are shown in Table 1. Major complications were lower in the robotic group (13.2% vs. 22.8%, p=0.04), highlighting the anastomotic leakage rate, which was 7.4% in the R-TME vs. 16.9% in the L-TME group (p=0.01).

Pathological outcomes were similar in both groups. The median tumour size in both groups was similar (35 mm vs. 30 mm in the L-TME, p=0.373), as well as the percentage of Extramural Vascular Invasion (EMVI) positive for small or large vessel (23% in the L-TME vs. 19% in the R-TME, p=0.472), and the Circumferential Resection Margin (CRM) involvement (3.1% vs. 2.3% in the R-TME, p=0.518). Distal resection margin (DRM) was found affected in 1% of the patients in the L-TME group vs. none of them in the R-TME (Table 1).

The incidence of local recurrence was similar between groups (2.2% R-TME group vs. 2.9% L-TME). However, the development of distant metastasis is significantly higher in the L-TME (25.7% vs. 11.8% in the R-TME, p=0.003).

The 3-year DFS rate was 69% in the laparoscopic group and 84% in the robotic group (p=0.02). The 3-year OS rate was 70% in the L-TME groups and 97% in the R-TME group (p=0.000). The differences on DFS and OS according to each stage between groups are shown in Table 2. The 3-year DFS for disease stage III was significantly higher in the R-TME group (74% vs. 46% in L-TME, p=0.004). OS was also significantly superior in the robotic group for every stage, reaching 86% in the stage III (Fig. 2).

In the univariate analysis, common factors that influence both the 3-years DFS and 3-years OS are shown in Table 3. In the multivariate analysis we show the independent factors influencing local recurrence, distant metastasis and overall survival. The only independent factor influencing local recurrence were the major complications in the postoperative period (Dindo-Clavien ≥ III) (OR 6.3 95% CI 1.2, 33.3, p=0.03). Moreover, major complications were also found to have a negative impact on the overall survival (OR 8.3 95% CI 3.2, 21.6, p=0.000). The robotic approach was a significant positive prognostic factor for the development of distant metastasis (OR 0.2 95% CI 0.1, 0.6, p=0.001) and the improvement of the OS (OR 0.2 95% CI 0.07, 0.4, p=0.000). Also the presence of ExtraMural Vascular Invasion (EMVI) for small or large vessels is a prognostic risk factor of distant metastasis (OR 3 95% CI 1.3, 6.7, p=0.007) and decrease in OS (OR 3.7 95% CI 1.4, 9.6, p=0.007).

DISCUSSION

The aim of this study was to investigate the impact of the R-TME on medium-term oncological outcomes of rectal cancer. This is the first study that has demonstrated an improvement in 3-year DFS and OS with the robotic approach, reaching 74% and 86%, respectively, for disease stage III ($p<0.05$). There is a lower rate of postoperative complications, which could account for some of the survival improvement.

In the L-TME group, the 3-year DFS may appear lower than expected. However, our series included all stages patients and in comparison to COLOR II trial were T4 and T3b tumours were excluded, similar survival figures were reported (69% vs. 74.8%).[2] Similar results were obtained when analysing long-term results of the ALaCaRT trial[5] but, again, T4 tumours were not included in the study. A recent

propensity-matched analysis including T4 tumours showed a 2-year DFS of 64.9% for stage III patients in the laparoscopic group.[6]

Oncological outcomes of randomized control trials comparing R-TME vs. L-TME have not been published yet. However, previous descriptive studies showed equivalence in terms on DFS and OS.[4,7-9] Baek et. al[10] reported similar rates of 3-year DFS and OS (73.7% and 96.2%, respectively) for patients who underwent robotic surgery for stages I-III rectal cancer (84% and 93%, respectively, in our study). A multicentre study reported comparable short-term oncological outcomes with robotic rectal cancer surgery, reaching 97% 3-year OS.[11] Kim et al.[12] recently published a propensity score matched analysis showing a trend towards improved DFS and OS with a robotic resection. Moreover, they also demonstrated that the robotic approach was a significant positive prognostic factor for OS. Our study strongly supports these findings.

The main difference between previously mentioned reports and the present study is the surgical procedure. The surgery in this study is performed entirely robotically, according to the single-docking technique described before,[13] whilst a hybrid technique (robotic-assisted TME) is usually employed in other centres,[4,10] in which part of the procedure is performed laparoscopically. The advantages that the robot provides for this complex procedure are not reflected in a hybrid procedure.

Conversion to open surgery did not occur in the R-TME group whereas there were 5 cases in the L-TME group (3.7%), as previous studies noted.[14,15] In the ROLARR trial the rate of conversion to open surgery were lower than expected in both arms;[16] however, in a subgroup analysis of high-risk cases it suggests a trend of less conversion in the R-TME group.[17] The technological advances of the robotic system allow the surgeon to perform a more safely dissection in a narrow pelvis. It reduces the need of conversion to open surgery and it may thereby decrease the rate of postoperative complications.

In a review of recent literature, the rate of complications is similar between groups[14,18] even in obese patients, but the postoperative recovery is faster.[19] However, in the present study the outcomes of postoperative recovery were better in the R-TME group than in the L-TME group. These results are in accordance to the outcomes published in a recent meta-analysis.[20] Major complications occurred more frequently in the L-TME (Dindo-Clavien III-IV 22.8% vs. 13.2% in the R-TME, p=0.04). Among these patients, AL occurred in 16.9% in the L-TME compared to

7.4% in the R-TME (p=0.01). Previous studies have demonstrated that major complications such as AL influence both local recurrence and survival.[21,22] Consistent with these results, our study showed that the presence of complications Dindo-Clavien ≥ III was an independent prognostic factor for local recurrence (OR 6.3 95% CI 1.2, 33.3, p=0.03) and decreased overall survival in the multivariate analysis (OR 8.3 95% CI 3.2, 21.6, p=0.000). Consequently to the higher rate of major postoperative complications, a longer LOS was detected in the L-TME group (7 vs. 6 days, p=0.01), as published previously.[7,18,23,24] This phenomenon could be responsible for the delay in starting adjuvant treatment and result in poor survival.[25]

The rate of local recurrence at 3 years after surgery is very low after a robotic TME (2%), compared to previous robotic data that amount to 3.6%.[9] After laparoscopic or open surgery, outcomes reported a percentage near 5% in the COLOR II trial,[2] similar to the percentage shown in a database over 20000 patients.[26] The percentage of preoperative radiotherapy in our institution is low (20%), and the rate of complete response is only 3.8% in the R-TME group. However, it is not an independent prognostic factor for local recurrence in the multivariate analysis (p>0.05). With the higher use of preoperative radiotherapy we may see an increase in complete response but this may potentially increase the risk of postoperative complications.

The quality of the TME specimen remains a concern in L-TME. In the CLASICC trial, the patients on the laparoscopic group were found to have a higher rate of CRM involvement.[27] The ACOSOG Z6051[28] and the ALaCaRT[29] trials also failed trying to demonstrate the non-inferiority of the L-TME. Some of the inherent difficulties of laparoscopic surgery such as 2D image, a fulcrum effect, limited access to narrow pelvis, and amplification of tremor has been overcome by the increased use of robotic technology for TME surgery. Robots offer a 3D view, along with endowrist instruments and stability of the operating platform. It may also reduce operator fatigue, a potentially influential factor in major surgical procedures. Thus, this control allows surgeons to replicate the principles of open TME surgery in a minimal access fashion. Other recent studies have demonstrated at least non-inferiority of R-TME regarding pathological results.[30] Although the findings of the ROLARR trial[16] failed to show better pathological outcomes, the sample size was small. In addition, in Table 1 we show a lower rate of CRM involved in the robotic group, which is even

better than the results of the ROLARR trial[16] (CRM < 1 mm in 5.1% of cases) and lower than data out of Korea.[9] However, in our study the mesorectal grade was complete in a similar percentage of patients in both groups (95%), whilst previous findings suggested better results in the robotic approach.[14,31] The technological advantage of the robotic system leads to superior histopathological outcomes and hence an improvement in long-term survival.

The key question remains if long-term oncological outcomes are better in robotic rectal cancer surgery. This remains unanswered with the present evidence. Data from trials from Korea has shown no difference in outcomes between laparoscopic and robotic surgery.[4] However, rectal cancer surgery is very centralised in Korea, resulting in high volume surgeons performing over 300 cases per year and the positive patient profile with a low BMI allows successful undertaking of laparoscopic rectal cancer surgery. Higher conversion rates in L-TME are seen in the European population and the literature supports a reduced conversion rate with the use of robotic approach.[16,32]

This is a retrospective non-randomized study, so there are some inevitable biases. As most of the patients who underwent L-TME were operated earlier, it could be a bias regarding the learning curve. However, the 3 participating surgeons in this study had significant experience in TME surgery at the beginning of this study with over a hundred TME procedures performed individually. The good outcomes presented in this study can only be achieved by a specialized team of robotic surgery experts at a high-volume centre. Thus, the results in our single institutional study may not be generalized to all situations.

Comparison between these two groups may have been influenced by patient and tumour-related factors including age, gender, BMI, tumour stage or follow up. In order to minimise this, we undertook a comparison between two groups matched for these confounders. The propensity score matching is a useful method for reducing biases between groups. The propensity-matching methodology did not include neoadjuvant chemoradiotherapy and MRI risk factors (EMVI, tumour deposits), which may have led to heterogeneity or biases; however, the two groups were similar on these accounts.

CONCLUSIONS

R-TME for rectal cancer can achieve better oncological outcomes compared to L-TME, especially in stage III rectal cancers. The robotic approach has demonstrated to be a significant positive prognostic factor for local recurrence and overall survival, due to the better postoperative outcomes.

However, a longer follow-up period is needed to confirm the oncologic findings and to support the general adoption of the robotic system for rectal cancer surgery.

COMPLIANCE WITH ETHICAL STANDARDS

- No funding.
- Authors have no conflict of interest.
- All procedures performed in studies involving humans were in accordance with ethical standards of the institutional research committee and the 1964 Helsinki declaration and its later amendments.
- Informed consent was obtained from all participants.

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FIGURE LEGENDS AND FIGURES

Figure 1. Flowchart of patient selection.

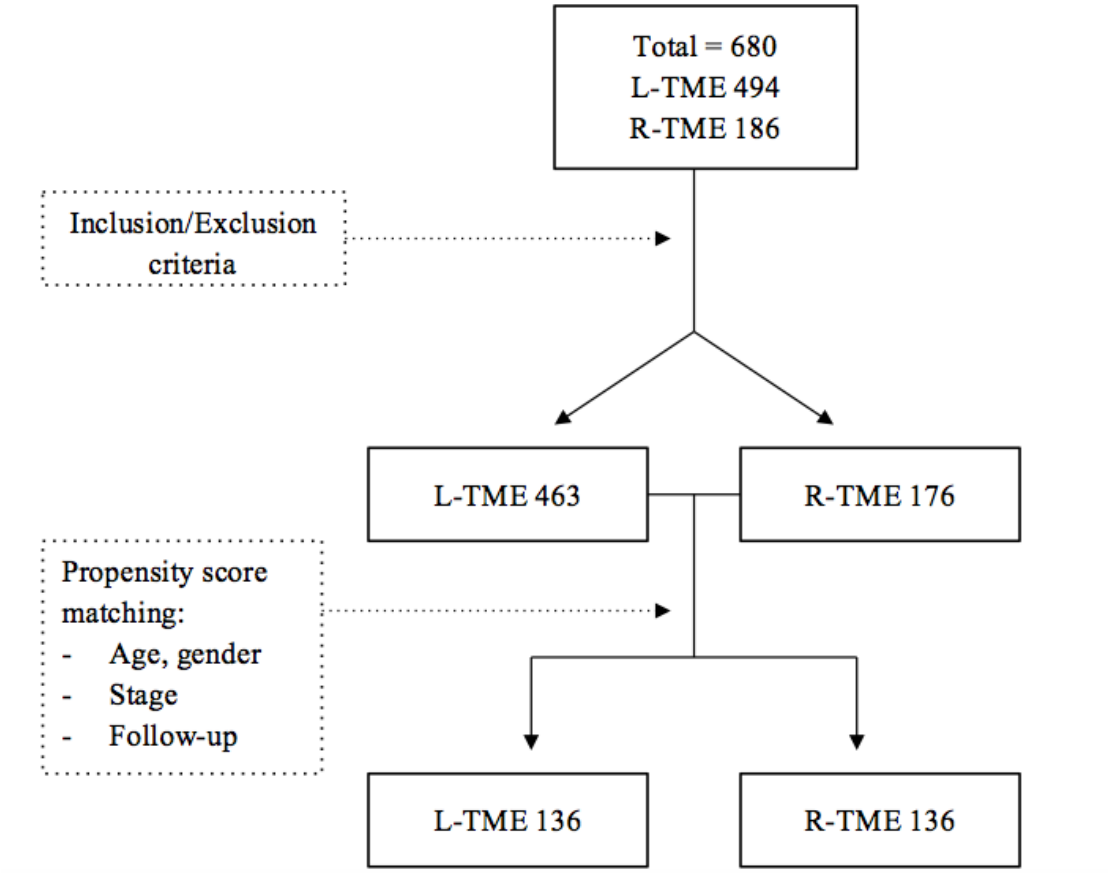
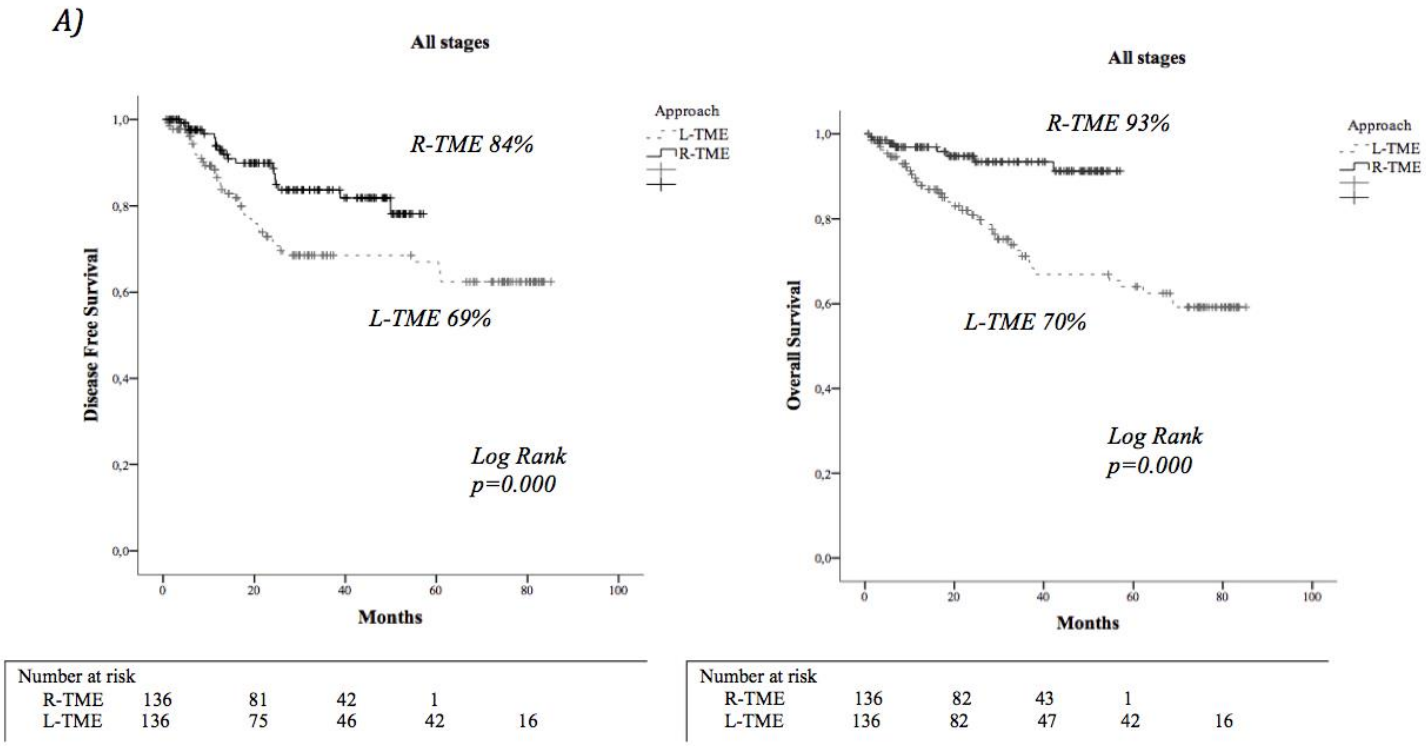
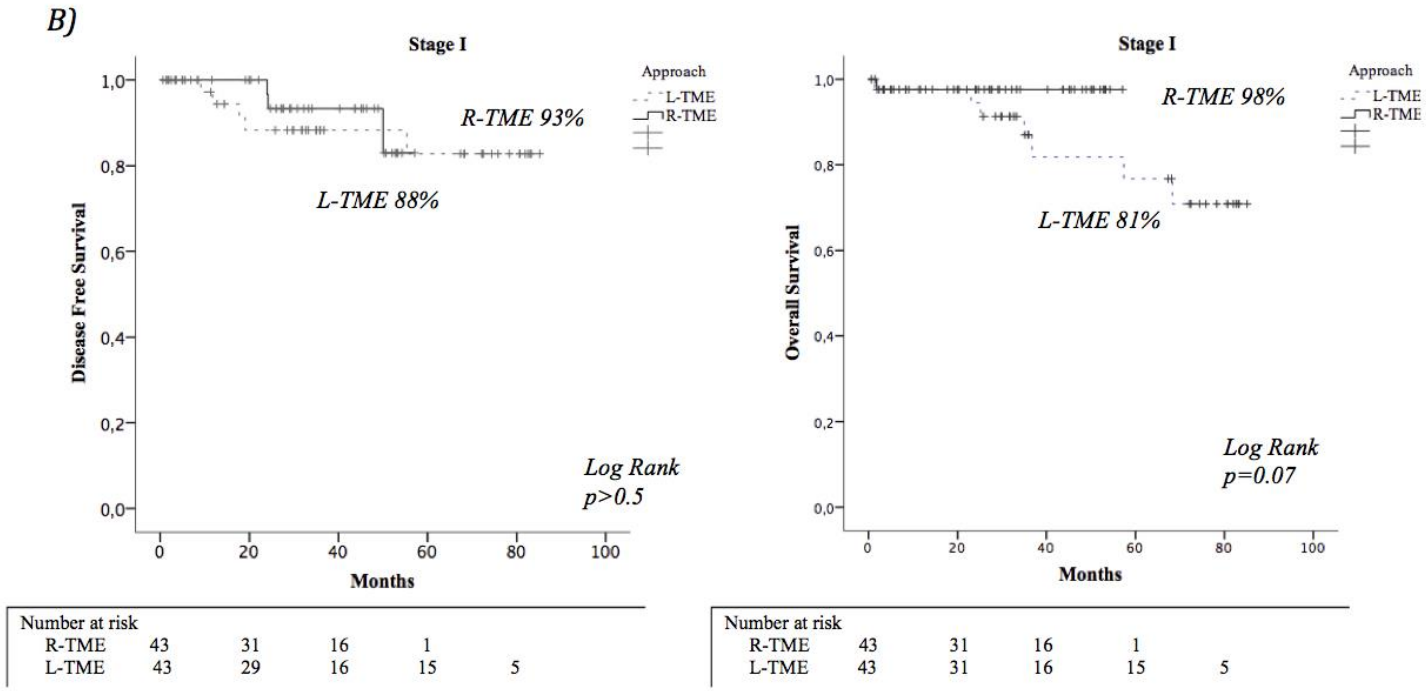


Figure 2. Comparison of 3-year DFS and OS between patients treated with L-TME and R-TME for rectal cancer. A) All stages, B) Stage I; C) Stage II; D) Stage III.





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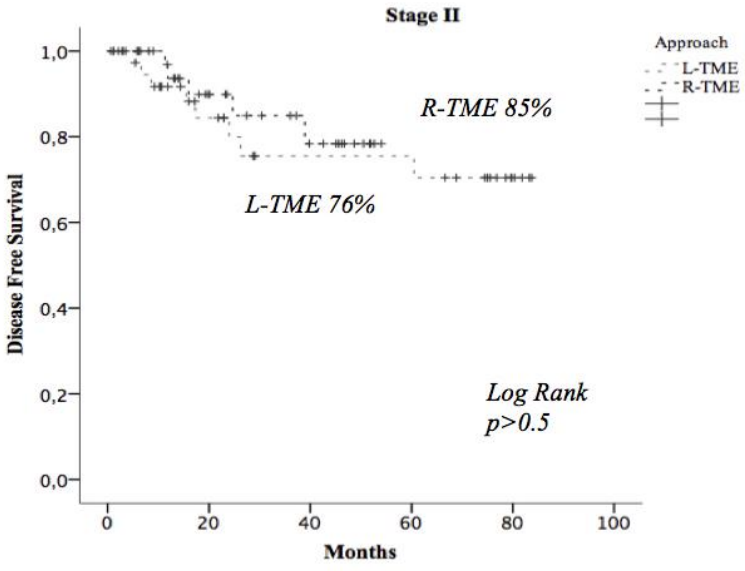
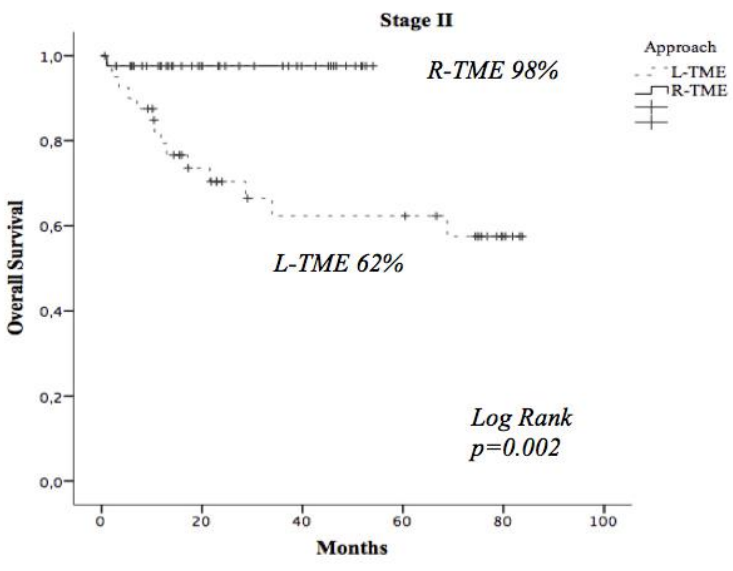
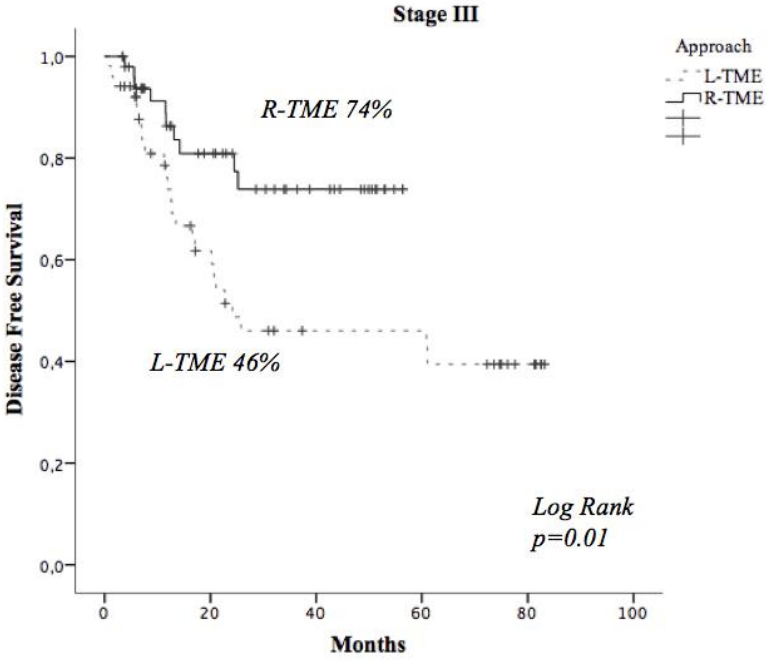


Number at risk					
R-TME	41	23	15	14	3
L-TME	41	20	15	14	3

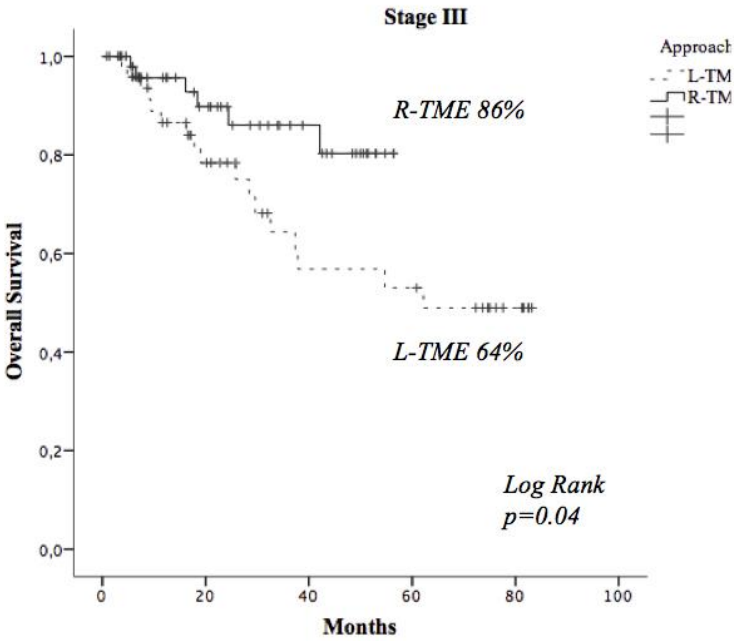


Number at risk					
R-TME	41	21	11	1	
L-TME	41	23	15	14	3

D)



Number at risk					
R-TME	51	23	27	14	1
L-TME	51	23	14	13	6



Number at risk					
R-TME	51	28	15	1	
L-TME	51	27	15	13	6

Table 1. Patients' characteristics and postoperative pathological outcomes after propensity score matching.

	L-TME n = 136	R-TME n = 136	p value
Age (median –IQR-) (year)	69 (14)	68 (16)	p=0.545
Sex (Male:Female) (%)	76:24	76:24	p=1
BMI	27 (6)	27 (5)	p=0.635
ASA			
I-II	74%	83%	p=0.096
III	26%	17%	
MRI			
Tumour distance from ARJ (median –IQR-) (cm)	6 (9)	6 (6)	p=0.160
CRM +	16.2%	21.1%	p=0.362
EMVI +	40.7%	38.8%	p=0.812
Neoadjuvant chemoradiotherapy	16.2%	20.6%	p=0.348
TRG (%)			
1	16.6%	3.8%	
2	44.5%	50%	p=0.267
3	27.8%	23.1%	
4	0	15.4%	
5	11.1%	7.7%	
Conversion to open	3.7%	0	p=0.03
Dindo-Clavien			
I-II	77.2%	86.8%	p=0.04
III-V	22.8%	13.2%	
Anastomotic leak (AL)	16.9%	7.4%	p=0.01
Radiological leak	12.7%	5.8%	
Reoperation due to AL	4.2%	1.6%	
LOS (median days)	7 (8)	6 (6)	p=0.02
Adjuvant chemotherapy			
Stage II	17%	13%	p=0.532
Stage III	65%	61%	p=0.682

Follow-up (median months – IQR-)	28 (61)	25 (34)	p=0.067
Histopathology			
TNM stage (%)			
0	0.7%	0.7%	p=1
I	31.6%	31.6%	
II	30.1%	30.1%	
III	37.5%	37.5%	
T (%)			
0	0.7%	0.7%	p=0.067
1	12.5%	11%	
2	24.4%	36%	
3	52.9%	48.5%	
4	9.5%	3.8%	
N (%)			
1	23.5%	26.4%	p=0.658
2	14%	11%	
Grade of differentiation			
Well	3.8%	4.5%	p=0.752
Moderate	88.6%	90.3%	
Poor	4.8%	2.2%	
Mucinous	2.9%	3%	
Tumour size (median – IQR-) (mm)	30 (15)	35 (20.5)	p=0.373
EMVI + (%)	23.1%	19.3%	p=0.472
Lymph nodes harvested (median – IQR-) (%)	17 (10)	18 (10)	p=0.940
DRM < 2 mm (%)	1%	0	p=0.424
CRM + (%)	3.1%	2.3%	p=0.518
TME (%)			
Complete	96%	96.2%	p=0.635
Nearly complete	4%	3%	
Incomplete	0	0.8%	

*ASA = American Society of Anesthesiologists; BMI = Body Mass Index; CRM = Circumferential Rectal Margin; DRM = Distal Resection Margin; EMVI=ExtraMural

Vascular Invasion; LOS = Length Hospital Stay; NS = Non significant; TME = Total Mesorectal Excision; TRG = Tumour Regression Grade.

Table 2. 3-year Disease Free Survival (DFS) and overall survival (OS). Comparison between patients with laparoscopic and robotic TME.

	L-TME n = 136	R-TME n = 136	p value
Local recurrence	2.9%	2.2%	p=0.469
Distant metastasis	25.7%	11.8%	*p=0.003*
3-y DFS			
All stages	69%	84%	*p=0.000*
Stage I	88%	93%	p=0.722
Stage II	76%	85%	p=0.571
Stage III	46%	74%	*p=0.01*
3-y OS			
All stages	70%	93%	*p=0.000*
Stage I	81%	98%	*p=0.07*
Stage II	62%	98%	*p=0.002*
Stage III	64%	86%	*p=0.04*

Table 3. Univariate and multivariate analysis of factors influencing Disease Free Survival and overall survival.

	Local Recurrence			Distal Metastasis			Overall Survival		
	Univariate	Multivariate (95% CI)	p	Univariate	Multivariate (95% CI)	p	Univariate	Multivariate (95% CI)	p
R-TME	0.7			0.003	0.2 (0.1-0.6)	0.001	0.000	0.2 (0.07-0.4)	0.000
Age (≥75)	0.09	2.4 (0.3-7.3)	0.9	0.5			0.000	4.3 (1.7-10.8)	0.002
Sex (Male)	0.5			0.4			0.2	0.8 (0.2-2.8)	0.8
BMI (≥30)	0.1	1.5 (0.2-8.9)	0.6	0.8			0.8		
ASA (≥III)	0.6			0.3			0.003	1.8 (0.7-4.8)	0.2
Low rectum (<5cm ARJ)	0.4			0.4			0.6		
Preop radio	0.6			0.3			0.5		
Preop chemo	0.6			0.4			0.4		
Dindo ≥ III	0.1	6.3 (1.2-33.3)	0.03	0.25	1.3 (0.5-3.7)	0.6	0.000	8.3 (3.2-21.6)	0.000
LOS ≥ 8 days	0.5			0.01	1.8 (0.9-3.8)	0.1	0.005	0.8 (0.3-2.4)	0.7
Tumour size (≥ 3 cm)	0.1	3.2 (0.3-31.3)	0.3	0.6			0.07	1.3 (0.5-3.5)	0.6
TNM stage III	0.2	2.6 (0.4-14.9)	0.3	0.000	4.1 (1.9-8.9)	0.000	0.06	1.8 (0.7-4.7)	0.2
CRM < 1 mm	0.8			0.04	1.4 (0.2-13.9)	0.7	0.04	3.8 (0.4-42.2)	0.3
DRM < 2 mm	0.8			0.8			0.8		
EMVI +	0.6			0.000	3 (1.3-6.7)	0.007	0.006	3.7 (1.4-9.6)	0.007
TME Incompl	0.8			0.8			0.8		
Differentiation (grades 3-4)	0.6			0.1	1.9 (0.5-7.3)	0.3	0.4		
Chemotherapy	0.6			0.007	0.9 (0.3-2.3)	0.8	0.6		

ARJ=Anorectal Junction; ASA=American Society of Anesthesiologists; BMI=body mass index, CI=confidence interval, CRM=circumferential resection margin; DRM =

Distal Resection Margin; EMVI=ExtraMural Vascular Invasion; TME=Total Mesorectal Excision; L-TME=Laparoscopic TME; R-TME=Robotic TME.

Figure 1. Flowchart of patient selection.

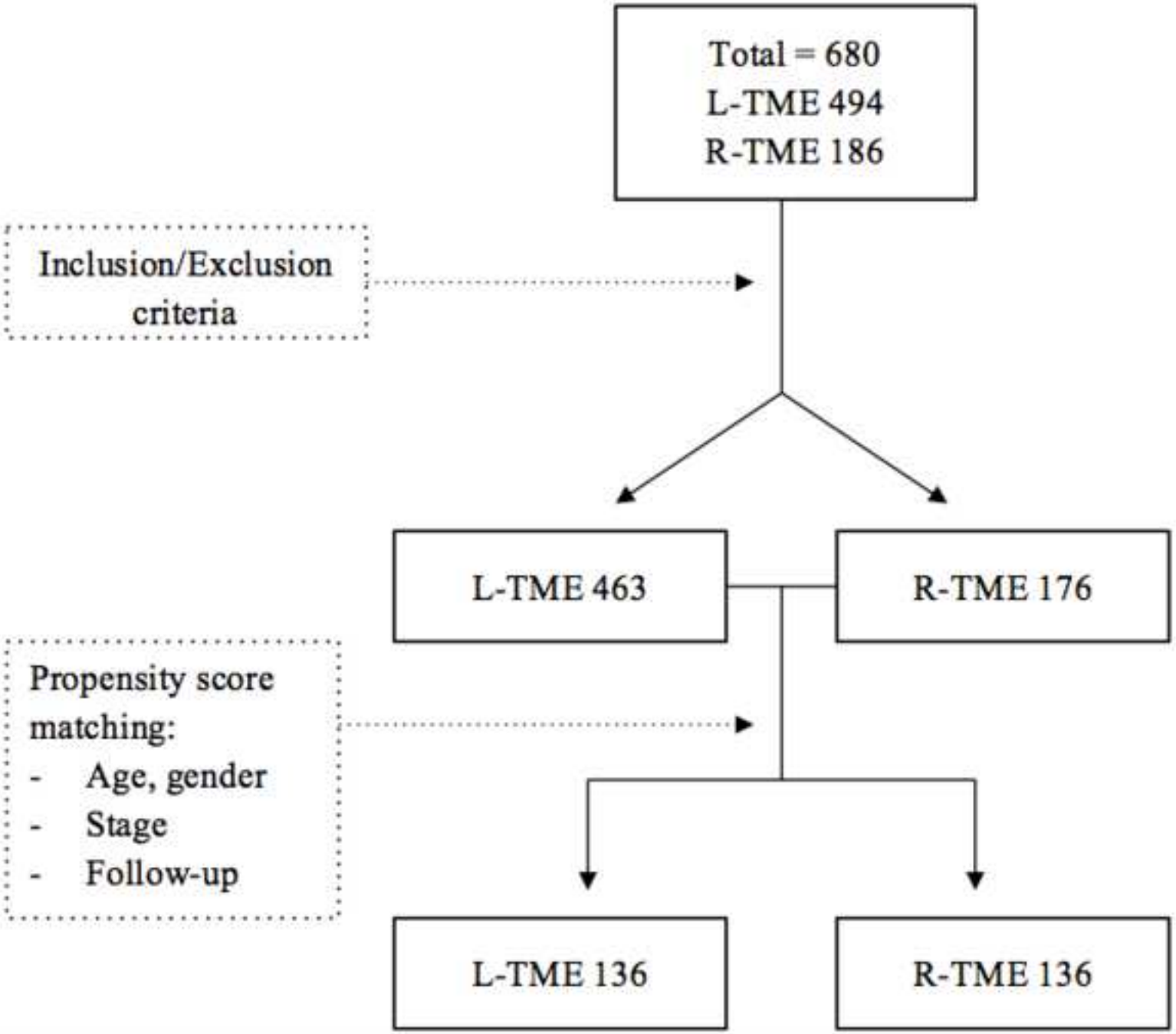


Figure 2. Comparison of 3-year DFS and OS between patients treated with L-TME and R-TME for rectal cancer. A) All stages, B)

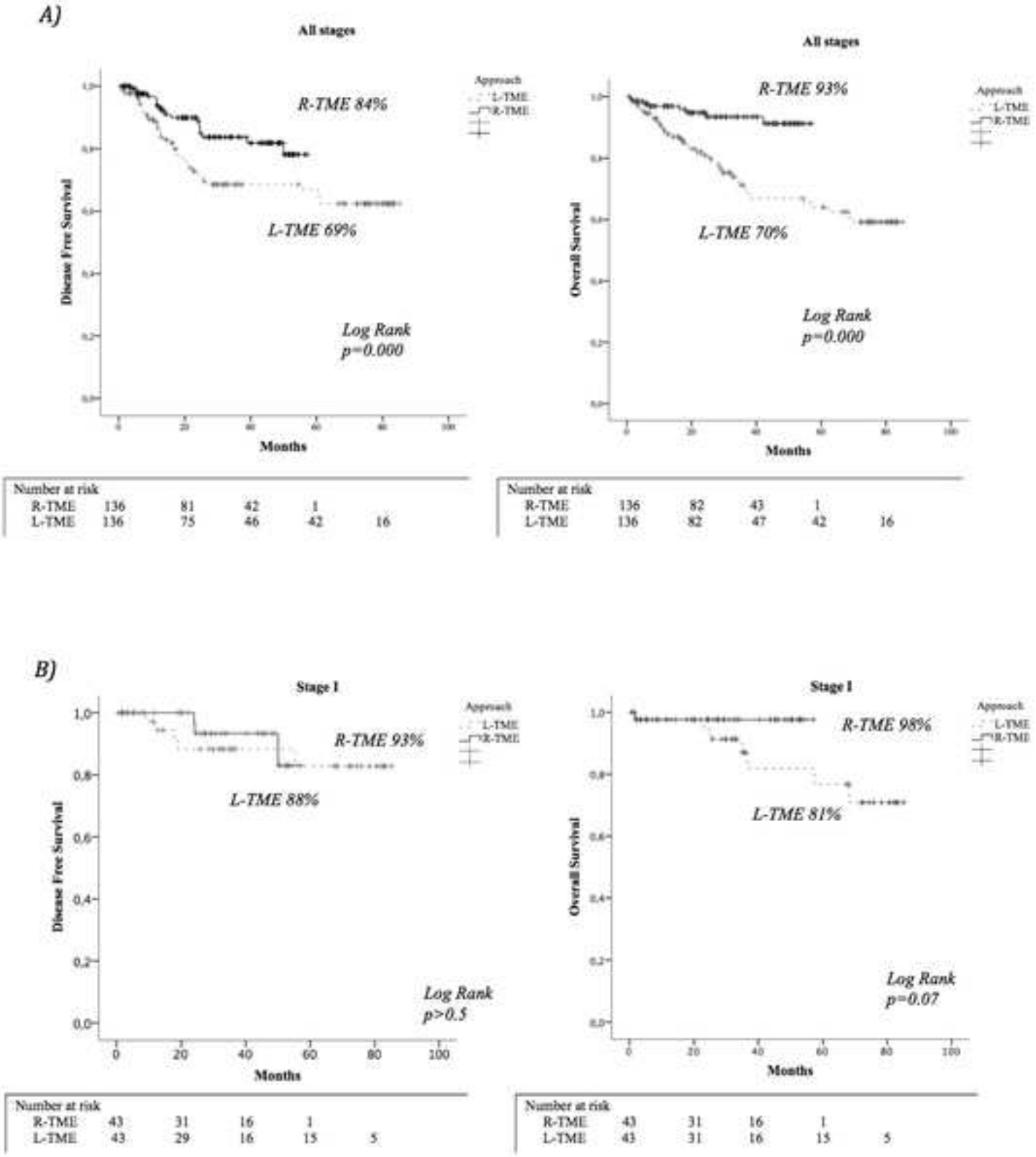
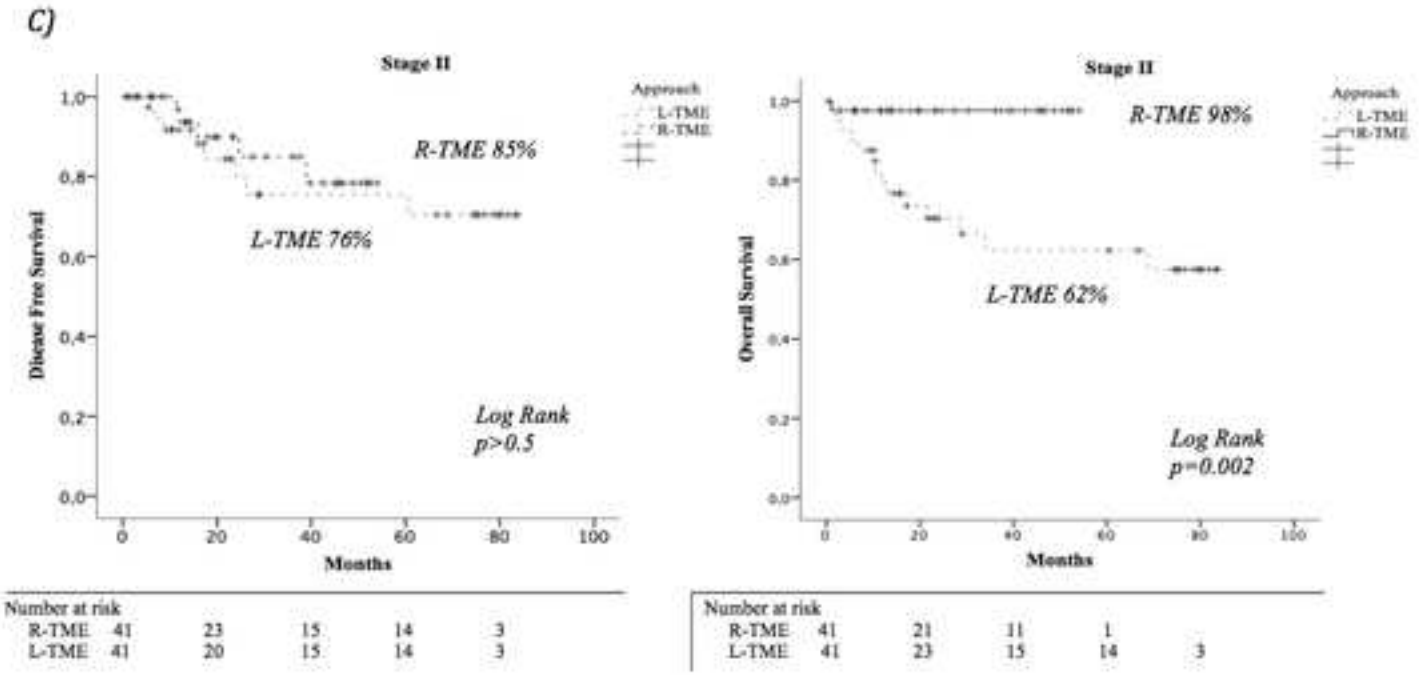


Figure 2. Comparison of 3-year DFS and OS between patients treated with L-TME and R-TME for rectal cancer. C) Stage II; D)



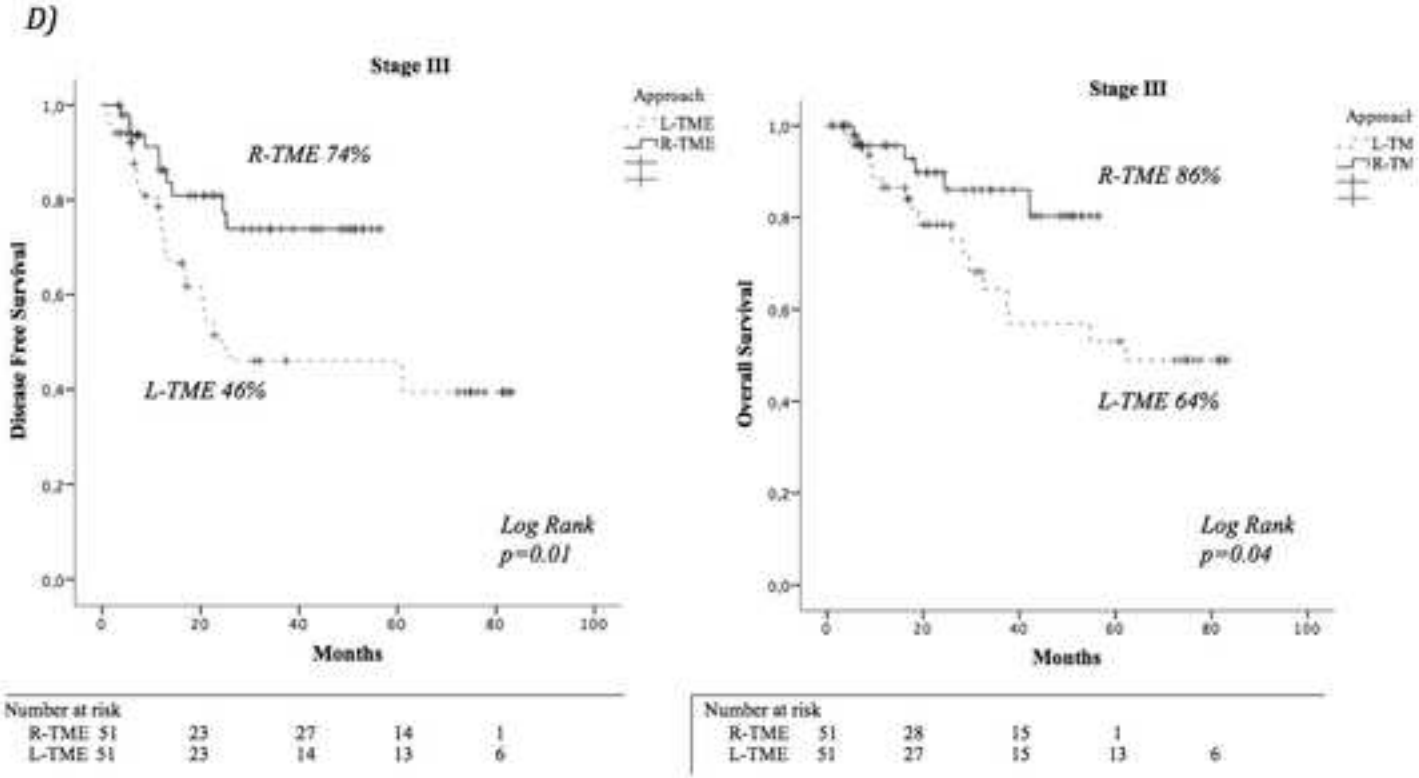


Table 1. Patients' characteristics and postoperative pathological outcomes after propensity score matching.

	L-TME n = 136	R-TME n = 136	p value
Age (median –IQR-) (year)	69 (14)	68 (16)	p=0.545
Sex (Male:Female) (%)	76:24	76:24	p=1
BMI	27 (6)	27 (5)	p=0.635
ASA			
I-II	74%	83%	p=0.096
III	26%	17%	
MRI			
Tumour distance from ARJ (median –IQR-) (cm)	6 (9)	6 (6)	p=0.160
CRM +	16.2%	21.1%	p=0.362
EMVI +	40.7%	38.8%	p=0.812
Neoadjuvant chemoradiotherapy	16.2%	20.6%	p=0.348
TRG (%)			
1	16.6%	3.8%	
2	44.5%	50%	p=0.267
3	27.8%	23.1%	
4	0	15.4%	
5	11.1%	7.7%	
Conversion to open	3.7%	0	p=0.03
Dindo-Clavien			
I-II	77.2%	86.8%	p=0.04
III-V	22.8%	13.2%	
Anastomotic leak (AL)	16.9%	7.4%	p=0.01
Radiological leak	12.7%	5.8%	
Reoperation due to AL	4.2%	1.6%	
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