Analysis of Early and Long-Term Oncologic Outcomes After Converted Laparoscopic Resection Compared to Primary Open Surgery for Rectal Cancer

Analysis of early and long-term oncologic outcomes after converted laparoscopic resection compared to primary open surgery for rectal cancer

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Abstract

Background: Laparoscopic rectal resection (LRR) for cancer is a challenging procedure, with conversion to open surgery being reported in up to 30% of cases. Since only a few studies with short follow-up have compared converted LRR and open RR (ORR), it is unclear if conversion to open surgery should be prevented by preferring an open approach in those patients with pre-operatively known risk factors for conversion. The aim of this study was to compare both early postoperative outcomes and long-term survival after converted LRR or ORR for non-metastatic rectal cancer.

Methods: A prospective database of consecutive curative LRRs and ORRs for rectal cancer was reviewed. Patients undergoing LRR who required conversion (CONV group) were compared with those who had primary open rectal surgery (OPEN group). Only patients with a minimum 5-year follow-up were included in the oncologic analysis. A multivariate analysis was performed to identify predictors of poor survival.

Results: A total of 265 patients were included in the study: 49 had a converted LRR (CONV group) and 216 had a ORR (OPEN group). There were no differences in perioperative morbidity, mortality and length of hospital stay between the two groups. Five-year overall survival and disease-free survival rates did not significantly differ between CONV and OPEN patients: 77.8% vs. 81% (P=0.930) and 62.9% vs. 72.7% (P=0.104), respectively. Similar 5-year OS and DFS rates were observed between patients who had converted LRR for locally advanced tumor or for non-tumor related reasons: 81.2% vs. 80.8% (P=0.839), and 62.5% vs. 63.7% (P=0.970), respectively. Poor grade of tumor differentiation, lympho-vascular invasion and a lymph node ratio of 0.25 or greater, but not conversion, were independently associated with poorer survival.

Conclusion: Conversion to open surgery does not impair short-term outcomes and does not jeopardize 5-year survival in patients with rectal cancer when compared to primary open surgery.

Keywords: converted - laparoscopy – open - total mesorectal excision - survival - rectal cancer

INTRODUCTION

Laparoscopic rectal resection (LRR) for rectal cancer is a technically demanding procedure, with conversion to open surgery being reported in up to 30% of cases [1]. During the last two decades, many efforts have been done to improve patient's selection for LRR. However, there are no scoring models including several patient-, disease-, procedure and surgeon-related variables that are able to accurately predict the chance of conversion of LRR to open surgery [2-6].

Several studies have focused on short-term outcomes and survival rates after laparoscopic resection converted to open surgery for colon cancer [7-17] and rectal cancer [18-26]; however, most of them compared patients who had converted or completed laparoscopic resection, reporting controversial results.

To date, it is unclear if conversion to open surgery causes additional postoperative morbidity and impairs survival, since only a few studies with a short follow-up have specifically compared patients undergoing converted LRR or open RR (ORR) for rectal cancer [22-26].

The aim of this study was to compare both early postoperative outcomes and long-term survival after converted LRR or ORR for non-metastatic rectal cancer.

MATERIALS AND METHODS

This study is a retrospective analysis of a prospective database including all patients undergoing rectal resection for rectal cancer at our Institution between January 1996 and December 2011. The localization of the tumor was categorized as lower rectum (distal tumor margin less than 5 cm from the anal verge), mid rectum (5 to 10 cm from the anal verge) and upper rectum (10 to 15 cm from the anal verge).

Exclusion criteria were: preoperative or intraoperative evidence of distant metastases, acute bowel obstruction, tumor perforation, synchronous colorectal cancers, T1-2 cancers treated

with transanal endoscopic microsurgery and previous rectal surgery. Patients with a preoperatively staged T4 rectal cancer were also not considered in this study, since they were treated only with an open approach.

The first LRR in our Institution was performed in April 1992. To avoid the bias related to the learning curve, the first 40 LRRs were excluded from the study.

The use of neoadjuvant chemoradiation therapy (CRT, 45 Gy over 4 weeks in association with systemic 5-fluouracil intravenous infusion) was discussed in an interdisciplinary tumor meeting and proposed to patients with T3-4N0-2M0 mid-lower rectal cancer. Surgery was planned 6 to 8 weeks after the completion of long-course neoadjuvant CRT. Both LRR and ORR with total mesorectal excision (TME) was performed for the treatment of mid and lower rectal cancers, while patients with a upper rectal cancer underwent a partial mesorectal excision (PME). All patients with a rectal cancer invading the anal sphincter underwent abdominoperineal resection (APR). LRR or ORR was performed depending on the operating colorectal surgeon's preference.

Conversion to open surgery was defined as an unplanned laparotomy or as a wound incision larger than the incision needed to remove the specimen.

The following variables were prospectively collected in the database: patient's characteristics (age, gender, ASA score, comorbidities), operative variables (operative time from skin incision to the application of dressings, complications, and conversion rate to open surgery in case of LRR), use of neoadjuvant treatment, pathologic examination, short-term outcomes (resumption of gastrointestinal functions, morbidity classified according to the Clavien Dindo classification [27], and length of postoperative hospital stay) and long-term oncologic results.

The following pathologic parameters were considered: tumor stage according to the TNM classification [28], number of lymph node harvested, lymph node ratio (LNR = number of posi-

tive nodes divided by total nodes harvested) and resection margins (longitudinal and circumferential).

Adjuvant chemotherapy was proposed within 8 weeks after surgery to all patients who had neoadjuvant CRT and to those patients with a postoperative diagnosis of stage 2-3 rectal cancer.

Follow-up protocol consisted of clinical examination, proctoscopy, serum carcinoembrionyc antigen assay every 3 months, and liver ultrasound every 6 months for the first 2 years, then annually. A CT scan of chest, abdomen and pelvis was obtained every year. A colonoscopy was performed at 1 year after surgery, then every 3 years.

Oncologic outcomes were overall survival (OS), disease-free survival (DFS), local recurrence (LR) and distant metastases rates.

Statistics

Quantitative data are provided as median and range, while categorical data are given as percentages. Proportions are compared using the χ^2 test or the Fisher exact test, where appropriate. Student's t test was used to compare normally distributed variables. Univariable OS and DFS rate analyses were performed using the Kaplan–Meier method and the differences between the groups were assessed with the log-rank test. OS and DFS were calculated from the date of surgery to the date of death from any cause or to the date of recurrence, respectively. Patients alive with or without recurrence were censored at the date of last examination. Time to LR or distant metastases was calculated from the time of surgery to date of evidence of relapse. We also performed a multivariable Cox regression analysis to identify predictors of poor OS and poor DFS. The included variables were: age, gender, surgical approach (CONV vs. OPEN), type of surgical procedure (AR vs. APR), grade of tumor differentiation, pT staging, number of lymph node harvested, LNR, lymphovascular invasion, and adjuvant chemotherapy. Explanatory variables with

univariable P≤0.200 were included in the multivariable analysis in order to evaluate all potential predictors in the final modeling process.

A level of 5% was set as the criterion for statistical significance. The data were collected in an Excel spreadsheet. The statistical analysis was performed using SYSTAT Version 10 (Copyright © SPSS Inc., 2000).

RESULTS

Between January 1996 and December 2011, a total of 537 patients underwent elective rectal resection for non-metastatic rectal cancer: 216 patients were treated with an open approach (OPEN group) and 321 patients had a laparoscopic resection. In 49 (15.3%) patients, LRR was converted to open surgery (CONV group).

Table 1 summarizes baseline patients' characteristics, showing no significant differences in sex, age, body mass index, ASA score, number of comorbidities, Charlson Comorbidity Index, tumor location and use of neoadjuvant CRT between the two groups.

Intraoperative results

Table 2 reports the type of procedures performed in the two groups. Among patients undergoing anterior resection, a protective stoma was constructed in a similar rate of patients in the two groups.

Among the 49 patients who had LRR converted to ORR, conversion to open surgery was due to locally advanced rectal cancer in 16 (32.7%) cases. Obesity and adhesions secondary to previous abdominal operations were the reason of conversion in 15 (30.6%) and 5 (10.2%) patients, respectively (**Table 2**). A pre-emptive conversion to open surgery was performed in 46 (93.9%) patients, while a reactive conversion to an intraoperative complication occurred in only 3 cases

(6.1%), due to bleeding (1 case) or small bowel injury (2 cases). No rectal perforation occurred in both groups.

Median operative time and median estimated blood losses were similar between OPEN and CONV group (**Table 2**).

Early postoperative outcomes

No significant differences were observed in terms of return of bowel function and resumption of solid diet between the two groups.

Overall 30-day postoperative morbidity rates did not differ significantly between CONV and OPEN group, with similar rates of blood transfusion (4.1% vs. 2.3%, P=0.839), wound infection (4.1% vs. 0.9%, P=0.324), cardiac complications (0% vs. 2.8%, P=0.517), chest infection (0% vs. 1.4%, P=0.935), anastomotic leakage (7.5% vs. 8.1%, P=0.850) and need for reoperation (4.1% vs. 4.6%, P=0.831). Mortality rate was 0% in the CONV group and 1.4% in the OPEN group (**Table 3**).

Median length of postoperative hospital stay was similar in the two groups of patients.

Pathologic results

The number of lymph nodes resected, the positive margin rates and the TNM stage distribution did not differ between CONV and OPEN group (**Table 4**).

Long-term oncologic results

Median follow-up was 75 (range, 12−233) months for all CONV patients and 84 (range, 12-240) months for all OPEN patients (P=0.174). Median follow-up for patients alive at the time of analysis was 102 (range, 60-233) months for CONV patients and 123 (range, 60-240) months for ORR (P=0.288). A total of 18 (6.8%) patients were lost to follow-up. As a consequence, 247

patients were considered for the long-term oncologic analysis: 46 CONV patients and 201 OPEN patients.

Adjuvant chemotherapy was administered in 29 (63%) CONV patients and in 103 (51.2%) OPEN patients (P=0.199).

LR developed in 5 (10.9%) CONV patients and in 13 (6.5%) OPEN patients (P=0.470). Distant metastases rate was 30.4% in the CONV group (14 patients) and 21.4% in the OPEN group (43 patients; P=0.263). There were no significant differences in median time for local recurrence [20 (range, 13-54) months in the CONV group and 19 (range, 6-58) months in the OPEN group (p=0.958)] and distant metastases [17 (range, 4-83) months in the CONV group and 18 (range, 3-58) months in the OPEN group (P=0.374)] between the two groups.

Both 5-year OS and DFS rates did not significantly differ between the CONV group patients and the OPEN group patients: 77.8% vs. 81.0% (P=0.930) (**Figure 1A**), and 62.9% vs. 72.7% (P=0.104) (**Figure 1B**), respectively.

Survival rates were similar among CONV patients regardless of the cause of conversion. No significant differences in 5-year OS and DFS were observed between patients who had converted LRR for a locally advanced tumor or non-tumor related reasons: 81.2% vs. 80.8% (P=0.839) and 62.5% vs. 63.7% (P=0.970), respectively.

On univariate analysis, G3, pT3-4 rectal cancer, LNR ≥0.25 and lymphovascular invasion were significant risk factors for OS and DFS (**Table 5** and **Table 6**).

On multivariate analysis, G3, LNR≥0.25 and lymphovascular invasion were the only independent predictors of OS and DFS (**Table 5** and **Table 6**).

DISCUSSION

Both early and long-term oncologic outcomes in rectal cancer patients who have a converted LRR are poorly investigated. Most studies have been designed aiming at evaluating if converted patients have worse early and oncologic outcomes than patients undergoing a laparoscopic completed rectal resection [18-21]. However, the most clinically relevant question that should be raised in order to better select rectal cancer patients for LRR or ORR and improve their outcomes is: *"Are the patient's postoperative outcomes different if he undergoes a converted LRR or a planned ORR?"*. Unfortunately, there are very few and heterogeneous studies [22-26] that have attempted to answer this question comparing converted LRR to primary ORR, and the results are controversial. As a consequence, it is unclear if conversion leads to worse outcomes than primary ORR and therefore it should be prevented by preferring an open approach in those patients with preoperatively known risk factors for conversion.

We herein report a conversion rate of LRR to ORR of 15.3%, with a locally advanced rectal cancer being the most common reason of conversion (32.7%), followed by obesity and adhesions. These results are consistent with those reported in previous non-randomized comparative studies [21,29] and randomized controlled trials [22,30]. In the present study, the conversion to ORR was pre-emptive in most cases, while it was reactive to a complication in only 6% of patients (3 cases). We observed no significant differences in operative time and intraoperative blood loss between CONV and OPEN patients, suggesting that a pre-emptive conversion does not lead to adverse intraoperative outcomes. To date, the impact of pre-emptive and reactive conversion and the best timing for conversion of a laparoscopic colorectal resection are poorly investigated. For instance, Yang et al. [31] found in a retrospective case-match study that 60 patients after a pre-emptive had lower morbidity, earlier resumption of a regular diet and a shorter postoperative hospital stay than 30 patients who had a reactive conversion. However, Aytac et al. [32] did not confirm these results, reporting no statistically significant differences in rates of

overall morbidity and readmission between 30 patients who had a reactive conversion and 240 patients who had a pre-emptive conversion. The same authors investigated the potential impact of timing of conversion on postoperative outcomes. They failed to find a threshold for conversion, reporting similar complication rates after early or late conversion. Further large studies are needed to identify a threshold for conversion in technically challenging operations and shed more light on the possible short-term effects of a late conversion occurring after a prolonged laparoscopic dissection in rectal cancer patients.

There are very limited and conflicting data in the literature about the occurrence of intraoperative complications, such as lesion to intraabdominal organs and rectal perforation in patients who have a converted LRR. The results of a national registry study [23] showed significantly higher rates of intraoperative complications such as bleeding, ureteral and splenic injury among 201 CONV patients than among 16308 OPEN rectal cancer patients and the conversion rate was almost doubled in LRR lasting more than 180 minutes. Our strategy is to avoid any prolonged laparoscopic tissue dissection and any protracted manipulation of the tumor with the laparoscopic tools in order to minimize the risk of injury to intraabdominal organs and tumor spillage. In the present study, no intraoperative rectal perforation occurred, even in the presence of a locally advanced rectal tumor in more than 70% of CONV patients. This finding does not confirm the alarming results reported by Penninckx et al. in 2013, analysing the PROCARE database [25]. They found a significantly higher incidence of this feared complication among CONV patients: 21% vs. 9.4% (P=0.001). However, the interpretation of these results is challenged by the fact that, even though the experience with TME and laparoscopic TME was assessed per each centre, the level of training in laparoscopic TME of each surgeon participating in the PROCARE project was not known.

Some studies [22,23] reported significantly higher rates of postoperative complications, including wound infections, pneumonia, anastomotic leakages and 30-day mortality after con-

verted LRR than ORR for rectal cancer. For instance, among the CONV and OPEN patients enrolled in the CLASICC trial, the wound infection rate was 20% vs. 12%, the chest infection rate was 15% vs. 5%, while an anastomotic leak occurred in 15% vs. 7%, respectively. Conversely, other series [24,25] failed to find impaired short-term outcomes in patients who had a converted LRR when compared to OPEN patients. In the present series, overall morbidity rate was 16.3% among CONV patients and 18.9% after ORR. Minor and major complication rates according to the Clavien Dindo classification were similar (Clavien-Dindo 1-2 10.2 vs. 10.6%, and Clavien Dindo 3-5 6% vs. 6%, respectively) and compare favourably with the literature data [24].

It has been reported that conversion of a laparoscopic colorectal resection is associated with poor OS and DFS [13]. However, some recent studies have shown that several variables, such as tumor-related characteristics (T stage and LNR), but not conversion *per se* are independent predictors of survival, suggesting that poorer survival is more likely multifactorial [11]. The systemic inflammatory response in case of perioperative complications in these patients might also play a role in impairing long-term oncologic outcomes [13].

The evidence about oncologic outcomes after converted laparoscopic rectal resection for cancer is weak, being mainly based on studies with a short follow-up period. For instance, Rickert et al. [24] reported the oncologic outcomes in 38 CONV patients and 114 OPEN patients after a median follow-up of 34 months (range, 1-70). No significant differences were observed after CONV or OPEN rectal resection in LR rate (3% vs. 4.5%), distant metastases rate (9% vs. 10.1%) and in 3-year OS (84% vs. 85%). Similar results were reported by Penninckx et al. [25]: at 3 years after surgery, relative survival rate was 92.2% after CONV resection and 88.1% after OPEN resection. However, the evaluation of the oncologic outcomes in these patients was highly limited by the lack of follow-up data for too many patients that did not allow to assess both LR rate and DFS. The only study that reports long-term follow-up results is the CLASICC trial [33]. With a median overall follow-up of 62.9 months, Green et al. found no significant differences in

OS and DFS after CONV or OPEN rectal resection after adjustment for prognostic factors, age, sex and TNM stage, suggesting that conversion does not have adverse impact on survival.

To the best of our knowledge, our study comparing converted LLR and ORR for rectal cancer has the longest follow-up. We were able to include in the oncologic analysis 46 CONV patients and 201 OPEN patients with a median follow-up of 75 months in the CONV group and 84 months in the OPEN group. We observed slightly higher rates of LR and distant metastases in the CONV group, but the differences did not reach the statistical significance. As a consequence there was a trend towards a lower 5-year DFS in CONV patients (62.9% vs. 72.7%, P=0.104), while 5-year OS rates were very similar (77.8% vs. 81%). The multivariate analysis showed that G3, LNR≥0.25 and lymphovascular invasion, but not conversion, were the independent predictors of OS and DFS. However, the trend towards a lower 5-year DFS requires a careful consideration, and further studies are needed to confirm these data. Interestingly, survival rates were similar among CONV patients regardless of the cause of conversion. It might be argued that similar OS rates may be secondary to a shorter follow-up interval and more frequent postoperative outpatient evaluations of CONV patients who have higher postoperative morbidity rate than OPEN patients. However, in the present study there were no differences in postoperative morbidity among the two groups. We feel that the good results achieved after converted LRR in this study is related to our attitude to consider early conversion in locally advanced rectal cancers, thus reducing prolonged operative times, avoiding the risk of suboptimal oncologic dissection and reducing the rates of postoperative complications.

The present study has some limitations. First, this study was conducted at a single large academic institution; as a consequence, the results may not be generalized. Second, LRR and ORR were performed by different surgeons. However, the ORRs were performed by skilled surgeons in colorectal surgery and all LRRs were performed by a surgeon (M.M.) who was highly experienced in both colorectal and laparoscopic surgery; furthermore, the first 40 laparoscopic

resections were excluded to avoid the effect of the learning curve [34,35]. Third, it is a retrospective study. Nevertheless, this is an analysis of a prospectively collected database that included two homogeneous groups of patients followed up for a median period of time longer than 6 years. In addition, there were no missing data in both groups regarding intraoperative and both early and late postoperative outcomes.

CONCLUSION

Conversion of LRR to ORR for non-metastatic rectal cancer does not seem to affect the short-term outcomes and jeopardize long-term survival. Based on these data and in the absence of validated models that predict the chance of a laparoscopic rectal resection to be converted to open surgery, we feel that the laparoscopic approach should be attempted even in those rectal cancer patients with preoperatively known risk factors for conversion.

Conflict of interest. None of the authors have any conflicts of interest associated with this study.

Table 1 Baseline patients'characteristics.

	CONV (n =49)	**OPEN (n =216)**	**P value**
Sex (Male), n (%)	 30 (67.3)	 133 (54.2)	0.907
Age (years)	68.5 (52-87)	67 (24-87)	0.087
Body Mass Index (Kg/m^2)	24 (20-36)	23 (21-38)	0.176
ASA score, n (%) 1 2 3	 21 (26.5) 16 (40.8) 12 (32.7)	 69 (31.9) 80 (37.1) 67 (31)	0.336
Charlson Comorbidity Index	2 (2-4)	2 (2-7)	0.809
Comorbidities, n	1 (0-3)	1(1-5)	0.448
Tumor site, n (%) Upper rectum Mid/lower rectum	 14 (28.6) 35 (71.4)	 45 (20.8) 171 (79.2)	0.324
Neoadjuvant CRT, n (%) Mid/lower rectum	 10 (28.5)	 80 (46.8)	0.193

CONV= converted laparoscopic rectal resection
OPEN = open rectal resection
ASA = American Society of Anesthesiologists
CRT = chemoradiation therapy

Table 2 Intraoperative results.

	CONV (n =49)	**OPEN (n =216)**	**P value**
Operative time (min)	200 (130-240)	150 (50-420)	0.410
Intraoperative blood loss (ml)	150 (50-1000)	100 (10-2800)	0.501
Reasons for conversion, n (%) Tumor related locally advanced tumor Non-tumor related Obesity Adhesions Others	 16 (32.7) 33 (67.3) 15 5 13		
Surgical procedure, n (%) AR APR	 40 (81.6) 9 (18.4)	 172 (77.3) 44 (20.4)	 0.906
Deverting stoma (in AR patients), n (%)	20 (64.5)	102 (59.3)	0.711

CONV= converted laparoscopic rectal resection
OPEN = open rectal resection
AR = anterior resection
APR = abdominoperineal resection

Table 3 Postoperative results.

	CONV (n =49)	**OPEN (n =216)**	**P value**
Flatus (days)	3 (2-5)	3 (1-13)	0.673
Stools (days)	4 (2-7)	4 (1-15)	0.365
Oral intake (days)	4 (2-7)	3 (2-14)	0.114
Length of hospital stay (days)	10 (6-25)	10 (6-78)	0.160
Complications, n (%)			
Overall	8 (16.3)	41 (18.9)	0.819
Grade 1	3	12	0.851
Grade 2	2	11	0.944
Grade 3	3	15	0.914
Grade 3a	1	5	
Grade 3b	2	10	
Grade 4	0	0	
Grade 5	0	3	0.935

CONV= converted laparoscopic rectal resection
OPEN = open rectal resection

Table 4 Pathology results.

	CONV (n =49)	**OPEN (n =216)**	**P value**
Positive CRM, n (%)	1 (2)	3 (1.4)	0.756
Number of lymph nodes, n	13 (1-35)	10 (1-40)	0.297
Pathology stage, n (%)			0.256
pCR	0	7 (3.2)	
1	7 (14.3)	54 (25)	
2	17 (34.7)	67 (31)	
3	25 (51)	88 (40.8)	
Tumor stage, n (%)			0.651
0	0	7 (3.2)	
1	3 (6.1)	12 (5.6)	
2	11 (22.4)	55 (25.5)	
3	31 (63.3)	131 (60.6)	
4	4 (8.2)	11 (5.1)	
N stage, n (%)			0.407
0	24 (48.9)	128 (59.3)	
1	21 (42.9)	72 (33.3)	
2	4 (8.2)	16 (7.4)	

CONV= converted laparoscopic rectal resection
OPEN = open rectal resection
CRM = circumferential margin
pCR = pathologic complete response

Table 5 Univariate and multivariate analysis of risk factors for overall survival.

Variable	Univariable analysis		Multivariable analysis	
	HR (95% CI)	**P value**	**HR (95% CI)**	**P value**
Age[a]				
>67	1			
≤67	1.33 (0.73-2.43)	0.365		
Gender				
Female	1			
Male	1.06 (0.58-1.95)	0.879		
Surgical approach				
CONV	1			
OPEN	1.10 (0.51-2.38)	0.812		
Type of surgery				
AR	1		1	
APR	1.58 (0.79-3.17)	0.194	1.99 (0.59-6.78)	0.270
Grade of tumor differentiation				
G1-2	1		1	
G3	4.23 (2.02-8.86)	<0.001	5.91 (1.77-19.76)	0.004
pT staging				
T0-T1-T2	1		1	
T3-T4	3.74 (1.68 – 8.34)	0.001	1.75 (0.51 -6.02)	0.375
Number of lymph nodes				
≥12	1			
<12	1.18 (0.47-1.54)	0.649		
Lymph node ratio				
0	1		1	
0.01-0.24	1.47 (0.65-3.31)	0.380		
≥0.25	11.35 (4.73-27.29)	<0.001	5.86 (1.67-20.53)	0.006
Lymphovascular invasion				
Absent	1		1	
Present	7.77 (3.20-18.86)	<0.001	4.03 (1.39-11.69)	0.010
Adjuvant CT				
No	1			
Yes	0.68 (0.37-1.25)	0.220		

[a] Median age of the study population
HR = Hazard Ratio
95% C.I. = 95% Confidence Interval
AR = anterior resection
APR = abdominoperineal resection

Table 6 Univariate and multivariate analysis of risk factors for disease-free survival.

Variable	Univariable analysis		Multivariable analysis	
	HR (95% CI)	**P value**	**HR (95% CI)**	**P value**
Age[a]				
>67	1			
≤67	1.08 (0.62-1.88)	0.887		
Gender				
Female	1			
Male	1.03 (0.58-1.82)	0.913		
Surgical approach				
CONV	1		1	
OPEN	0.59 (0.30-1.17)	0.146	0.86 (0.27-2.81)	0.807
Type of surgery				
AR	1		1	
APR	1.80 (0.94-3.47)	0.081	1.28 (0.52-4.17)	0.688
Grade of tumor differentiation				
G1-2	1		1	
G3	3.70(1.79-7.64)	<0.001	5.68 (1.77-18.24)	0.004
pT staging				
T0-T1-T2	1		1	
T3-T4	2.07 (1.08 – 3.96)	0.033	1.25 (0.36 -2.26)	0.674
Number of lymph nodes				
≥12	1			
<12	1.03 (0.59-1.80)	0.927		
Lymph node ratio				
0	1		1	
0.01-0.24	1.36 (0.64-2.92)	0.424		
≥0.25	13.35 (5.24-25.69)	<0.001	7.72 (2.31-25.79)	0.001
Lymphovascular invasion				
Absent	1		1	
Present	5.59 (2.45-12.75)	<0.001	2.72 (1.01-7.53)	0.048
Adjuvant CT				
No	1			
Yes	0.68 (0.38-1.22)	0.238		

[a] Median age of the study population
HR = Hazard Ratio
95% C.I. = 95% Confidence Interval
CONV = converted laparoscopic resection
OPEN = open resection
AR = anterior resection
APR = abdominoperineal resection

LEGENDS FOR FIGURES

Figure 1. A. Overall survival (P=0.930; Log rank test); **B**. Disease-free survival (P=0.104; Log rank test).

CONV = converted laparoscopic resection; OPEN = open rectal resection

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