COMPARISON OF THE OUTCOMES OF OPEN AND LAPAROSCOPIC RECTAL CANCER SURGERIES: RESULTS FROM A PORTUGUESE REGISTRY

COMPARAÇÃO DA CIRURGIA CONVENCIONAL COM A LAPAROSCÓPICA NO CANCRO DO RETO: RESULTADOS DO REGISTO PORTUGUÊS

J. S. LEITE[1], J. PIMENTEL[1], P. C. SILVA[2], J. GÍRIA[3], F. C. ALVES[1], L. SEMEDO[1], J. VENÂNCIO[4], L. GUIMARÃES[2], M. RUI[1], M. J. BRITO[5], R. FONSECA[4], J. LOPES[2], B. OLIVEIROS[6]

[1] Centro Hospitalar e Universitário de Coimbra; Faculdade de Medicina, Universidade de Coimbra. Portugal
[2] Centro Hospitalar Universitário de S. João, Porto. Portugal
[3] Hospital CUF-Tejo. Lisboa. Portugal
[4] Instituto Português de Oncologia. Lisboa. Portugal
[5] Hospital Garcia de Orta. Almada. Portugal
[6] Faculdade de Medicina, Universidade de Coimbra. Portugal

ABSTRACT

Introduction: This study aimed to compare the 3-year rates of local recurrence (LR) and overall survival (OS) for open (OPEN) and laparoscopic (LAP) surgeries in a Portuguese registry. **Material and Methods:** This observational study included patients who underwent rectal cancer resection performed in 16 hospitals between July 2014 and December 2019. The radiologic staging and the specimen images of the first three cases of any hospital were uploaded and audited by the scientific committee. Clinical and pathological characteristics and short and long-term outcomes of OPEN and LAP surgeries were analyzed. **Results:** The registry included 640 patients who underwent rectal cancer surgery: 562 (87.8%) underwent curative resection and 78 (12.2%) underwent palliative resection. In the curative cohort, OPEN surgery was performed in 269 cases whereas LAP surgery, which had a conversion rate of 17.5%, was performed in 266 cases. The pN staging showed that the LAP group had less advanced disease than the OPEN group. Anterior resection was performed in 57.8% of the cases whereas abdominoperineal resection was performed in 16.5%. Patients who underwent LAP surgery had shorter hospital stays. The 3-year LR rate was 3.0% (95% CI, 1.4%-6.3%) for LAP surgery and 8.3% (95% CI, 5.1%-13.1%) for OPEN surgery (P=0.02). The 3-year OS was 88.2% (95% CI, 83.1%-92.0%) for LAP surgery and 76.5% (95% CI, 69.1%-82.6%) for OPEN surgery (P=0.0061). **Discussion:** LAP surgery for patients with rectal cancer is associated with a decreased LR rate and improved OS, although in those with less advanced pN staging. **Conclusion:** The data support the view that the LAP approach is justified for rectal cancer when performed by surgeons with appropriate laparoscopic experience.

Keywords: *rectal cancer, clinical auditing, local recurrence, overall survival, laparoscopic surgery, open surgery.*

RESUMO

Introdução: O objetivo do estudo consistiu na avaliação da recidiva local (RL) e da sobrevivência global (SG) aos 3 anos, comparando cirurgia convencional (CONV) e laparoscópica (LAP) no registo Português do cancro do reto. **Material e Métodos:** Neste estudo observacional incluíram-se doentes com cirurgia por cancro do reto realizada em 16 hospitais, entre Julho 2014

e Dezembro 2019. O estadiamento imagiológico e as imagens anatomopatológicas foram registadas e auditadas pela comissão científica. Analisaram-se as características clinico-patológicas e os resultados pós-operatórios e à distância na cirurgia CONV e LAP. **Resultados:** O registo inclui 640 doentes que realizaram cirurgia por cancro do reto: 562 (87.8%) resseções curativas e 78 (12.2%) resseções paliativas. No grupo curativo foram realizadas 269 resseções CONV e 266 resseções LAP, que tiveram conversão em 17,5% dos casos. O grupo LAP tinha estadiamento pN menos avançado que o grupo CONV. A resseção anterior foi realizada em 57,8% dos casos e a amputação abdominoperineal em 16,5%. Os doentes com cirurgia LAP tiveram estadia pós-operatória mais curta. A taxa de RL aos 3 anos foi de 3,0% (95% CI, 1,4%-6,3%) na cirurgia LAP e 8,3% (95% CI, 5.1%-13,1%) na cirurgia CONV (P=0.02). A SG aos 3 anos foi 88,2% (95% CI, 83,1%-92,0%) na cirurgia LAP e 76,5% (95% CI, 69,1%-82,6%) na cirurgia CONV (P=0.0061). **Discussão:** Nos doentes com cancro do reto a cirurgia LAP associou-se a menor taxa de RL e melhor SG, embora em doentes com estadiamento pN menos avançado. **Conclusão:** Estes resultados confirmam que no cancro do reto a abordagem LAP é segura se for realizada por cirurgiões com adequada experiência laparoscópica.

Palavras-chave: *cancro do reto, auditoria clínica, recidiva local, sobrevivência global, cirurgia laparoscópica, cirurgia convencional.*

INTRODUCTION

The Portuguese Rectal Cancer Registry was established to improve the quality of rectal cancer treatment in hospitals under the National Health Service. The project was established in 2014 with the support of the Portuguese Society of Surgery and under a multidisciplinary team of surgeons, radiologists, and pathologists. This collaborative project was inspired by the Norwegian Rectal Cancer Project[1], with compulsory registration, and the Spanish Rectal Cancer Project[2], with voluntary entry database. In these projects live demonstrations were organized, and a central registry was created to provide feedback to participating institutions. In our project the quality of the rectal cancer surgery was evaluated using pathologic measurements[3]. The surgeons agreed that the pelvic magnetic resonance images (MRI) and the total mesorectal excision (TME) specimens should be audited by the steering committee, following a model inspired by the Belgian PROCARE project[4].

Laparoscopic (LAP) surgery has progressively replaced open (OPEN) colonic and rectal surgery in recent decades due to its favorable short-term outcomes, such as less pain, reduced blood loss, and improved recovery time[5,6]. However, evidence from large, randomized clinical trials indicating that the pathologic outcome after LAP resection of rectal cancer is not inferior to OPEN surgery is lacking[7,8]. Moreover, after a minimum follow-up duration of two years, the Z6051 trial and the ALaCaRT trial demonstrated that there are no significant differences between both approaches in terms of local recurrence (LR) and disease-free survival[9,10]. Notably, the findings of the ALaCaRT trial do not support the use of laparoscopic resection as a routine standard treatment[10].

The aim of this observational study was to report the results from a national audit program for multidisciplinary rectal cancer treatment, particularly the LR rate and overall survival (OS) of the LAP and OPEN surgical approaches.

MATERIAL AND METHODS

In Portugal, all hospitals that recorded more than 20 cases of multidisciplinary treatment of rectal cancer per year were invited to voluntarily participate in this study. Some regional scientific events were held in several hospitals to discuss the TME principles, the neoadjuvant treatment of rectal cancer, the pathology and the MRI reports proposed by the scientific committee. A specific rectal cancer online database, with pseudoanonimyzed data, was created in 2014 and maintained by the Portuguese Society of Surgery[11]. Each collaborative hospital

designated a surgeon coordinator and another surgeon responsible for data registration with user and password protected access to the online registry of the cases in his/her own hospital.

Tumors 15 cm or below the anal verge, measured using a rigid rectoscope, were included for assessment. Stage classification of the pathologic specimens followed the TNM classification and the Ryan regression grade (AJCC, 2010, 7th edition). The surgical approach was defined as OPEN surgery or LAP surgery, and those converted were included as LAP surgery with an intention-to-treat analysis.

The registered patient data included patient characteristics, Colorectal Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (CR-POSSUM) score[12], radiologic staging, neoadjuvant treatment, type of surgery, morbidity and mortality, pathological details, adjuvant treatment, and yearly follow-up.

Intraoperative bowel perforation was defined as any opening of the rectal lumen during dissection. The circumferential resection margin (CRM) was considered invaded if cancer cells were found <1 mm from the margin. Surgery was considered with a curative intent for those with a negative (R0) or positive (R1) microscopic invasion margin in the absence of distant metastases. Palliative resection was defined as resection with distant metastases or an operation associated with a macroscopic residual tumor (R2).

The pelvic MRI, the TME specimens, and the macroscopic and microscopic photos of the first three cases in any hospital were uploaded and audited by the scientific committee. Decisions on neoadjuvant treatment were made on an individual basis based on international guidelines. Decisions on individual follow-up planning were made at the discretion of surgeons, however based on the international recommendations. Follow-up information was reported yearly to the central database by the surgeon responsible for cancer registration in each hospital.

Morbidity was graded according to the Dindo-Clavien classification[13], and mortality was defined as any death that occurred during the first 30 days after surgery. LR and OS were the main outcome measures. LR was defined as recurrent disease in the pelvis, including the site of the anastomosis and the perineal wound.

Statistical analysis

Patient, treatment, and outcome data were determined separately for the OPEN and LAP approaches to analyze the influence of the methods on short-and long-term outcome measures. Categorical or dichotomous outcomes were presented as absolute numbers and percentages. The chi-squared test was used for intergroup analyses. Continuous outcomes were reported as medians with interquartile ranges (IQRs) or means with standard deviations, in accordance with their distribution. The Kaplan–Meier method was used to determine the actuarial 3-year LR and OS rates from the date of surgery. Comparisons of recurrence and survival in the subgroups were performed using the log-rank test and predictors of those were identified by a univariate and multivariate Cox regression. A two-sided P-value <0.05 was considered significant. All analyses were performed using IBM SPSS statistics, version 26 (IBM Corp., Armonk, New York, USA) or with the package survminer of R, version 4.0.3 (Vienna, Austria)

RESULTS

Sixteen hospitals participated in this project during the five-year inclusion period (July 2014 to December 2019). In the registry, all the cases of rectal resection with TNM staging were included. An overall missing data of 5% are signed in the Tables. All local rectal resections were excluded. Seven hospitals included more than 60 patients,

whereas eight had fewer than 20 cases. The rate of LAP surgery in the participating hospitals varied from 0 to 88%. These hospitals treated patients from all geographical areas of Portugal comprising approximately 10 million inhabitants. In each hospital, the procedures were performed by surgeons who specialized in colorectal surgery.

The registry included 640 patients who underwent rectal cancer surgery. In this rectal resection cohort, curative resection was performed for 562 (87.8%) patients and palliative resection for 78 (12.2%) patients. In the palliative group, 45 patients had hepatic metastasis, 19 had pulmonary metastasis, and 14 had R2 resections. Pelvic MRI was performed for 380 (76.2%) patients to determine staging, and restaging MRI was performed for 140 (37.8%) patients after chemoradiotherapy. The median follow-up duration in this study was 53 months (IQR, 38–65 months).

The entire cohort of patients who underwent curative and palliative surgery for rectal cancer showed 313 cases of OPEN surgery compared with 295 cases of LAP surgery (Table 1). The patients in the LAP surgery group were younger (P=0.002), had lower CR-POSSUM scores (P=0.036), and less advanced pathological T and N staging (P=0.023) than patients in the OPEN surgery group. Postoperative reoperation (10.3%, 10.5%) was similar in the OPEN and LAP surgery groups. Neoadjuvant treatment was administered to 51.4% of the patients, and 39 (11.8%) had complete pathologic regression (ypT0N0). Adjuvant treatment was administered to 46.1% of the patients. Macroscopic mesorectal excision was considered complete in 75.6% of the 541 analyzed cases, partially complete in 16.6%, and incomplete in 7.8%.

Table 2 shows the characteristics of the patients with only curative rectal surgery and the comparison of 269 cases of OPEN surgery with 266 cases of LAP surgery. Anterior resection (AR) was the most frequently performed procedure (57.8%), followed by abdominoperineal resection (APR) (16.5%), the Hartmann procedure (1.3%), and other procedures (12%). Sex distribution, tumor level, number of lymph node counts, type of resection, and neoadjuvant or adjuvant treatment were similar in both groups; however, age, multi-visceral resection, and pathologic N staging differed significantly (Table 2). A multi-visceral resection was rarely performed for patients in the LAP surgery group.

Regarding curative rectal surgery, the 30-day mortality was 1.5% in the OPEN and LAP surgery groups. The duration of postoperative stay was 2 days shorter in the LAP group than in the OPEN group, with a median of 7 days (IQR, 6–12) versus 9 days (IQR, 7–14), respectively.

Considering the TNM pathological staging, the LAP group did not show different pathologic T stages (P=0.13) but did show less lymph node invasion (P=0.015) compared to the OPEN group. The CRM involvement rates of the OPEN (3.7%) and LAP surgery groups (3.8%) were similar.

A separate analysis of the curative surgery cohort included 217 patients who underwent LAP surgeries versus 46 (17.5%) with converted LAP surgeries and showed no differences in LR or OS; however, an increase in postoperative complications (P=0.06) was noted in the converted LAP group. LR occurred more frequently in the 100 cases of APR (8.0%) and in the multi-visceral resections (13.2%) than in the 347 cases of AR (3.7%; p=0.018).

In the curative cohort, the univariate analysis for LR revealed that advanced pT stage (HR 5.42; 95% CI, 1.87-15.74) and the involvement of the CRM (HR 3.56; 95% CI, 1.05-12.04) was significantly related to LR and the OPEN approach had some influence on LR (HR 2.17; 95% CI, 0.92-5.12) (Table 3). The variables age, sex, and the tumor level were not determinants of LR. In a multivariate analysis no clinical or pathological characteristics influenced LR.

The cumulative incidence of LR in the 465 cases of curative resections is shown in Figure 1. The estimated 3-year LR in the entire cohort of patients who underwent curative surgery was 5.1% (95% CI,

Table 1 – **Clinical and pathological characteristics of the entire cohort and the differences between the surgical approaches**

	All, n (%)	OPEN, n (%)	LAP, n (%)	p overall
	640	313*	295*	
Age, y, mean (SD)	68.7 (11.7)	70.2 (11.2)	67.3 (11.6)	0.002
Sex				
Female	238 (37.2)	114 (36.4)	112 (38.0)	0.737
Male	402 (62.8)	199 (63.6)	183 (62.0)	
CR-POSSUM, mean(SD)	7.3 (5.3)	8.0 (5.2)	7.0 (5.3)	0.036
Tumor level*				
0-5	158 (24.7)	63 (20.1)	92 (31.2)	0.259
6-10	204 (31.9)	95 (30.4)	106 (35.9)	
11-15	173 (27.0)	85 (27.2)	87 (29.5)	
Lymph node counts, mean(SD)	13.8 (9.6)	14.4 (10.0)	13.3 (9.3)	0.325
Metastasis*				
No	467 (73.0)	198 (63.3)	265 (89.8)	< 0.001
Yes	52 (8.1)	32 (10.2)	17 (5.8)	
Neoajuvant treatment*				
No	229 (35.8)	109 (34.8)	117 (39.7)	0.486
Yes	329 (51.4)	144 (46.0)	176 (59.7)	
Postoperative stay, days, mean (SD)	11.2 (7.9)	12.2 (8.2)	10.1 (7.4)	
median[P25,P75]	8 [6,13]	9 [7,15]	8 [6,12]	← 0.001
Type of resection*				
APR	107 (16.7)	50 (16.0)	56 (19.0)	0.013
Hartmann	8 (1.3)	7 (2.2)	0 (0.0)	
AR	363 (56.7)	159 (51.0)	203 (68.8)	
other	77 (12.0)	40 (12.8)	36 (12.2)	
Postoperative reoperations*				
No	469 (73.3)	212 (67.9)	254 (86.1)	0.501
Yes	63 (9.8)	32 (10.3)	31 (10.5)	
30-day mortality*				
No	509 (79.5)	234 (74.8)	274 (92.9)	0.361
Yes	11 (1.7)	7 (2.2)	4 (1.4)	
Operative complications*				
No	356 (55.6)	155 (49.5)	201 (68.1)	0.080
Yes	178 (27.9)	91 (29.1)	85 (28.8)	
Clavien class.*				
0 + I +II	54 (60.7)	54 (60.7)	48 (58.5)	0,407
III + IV	59 (34.5)	28 (31.5)	31 (37.8)	
V	10 (5.8)	7 (7.9)	3 (3.7)	
pT				
T0	59 (9.2)	22 (7.0)	35 (11.9)	0.023
T1	51 (8.0)	22 (7.0)	25 (8.2)	
T2	169 (26.4)	74 (23.6)	82 (27.8)	
T3	303 (47.3)	167 (53.4)	125 (42.4)	
T4	40 (6.3)	25 (8.0)	14 (4.7)	
pN*				
N0	388 (60.6)	174 (55.8)	198 (67.1)	0.002
N1	165 (25.8)	87 (27.8)	68 (23.1)	
N2	73 (11.4)	47 (15.0)	22 (7.5)	
Residual tumor*				
R0	555 (86.7)	269 (85.9)	260 (88.1)	0.003
R1	52 (8.1)	27 (8.6)	22 (7.5)	
R2	14 (2.0)	12 (3.8)	0 (0.0)	

AR – anterior resection. APR – abdominal perineal resection. CRM - circumferential resection margin. OPEN – open surgery. LAP – laparoscopic surgery

* Some data are missing

Table 2 – **Clinical and pathological characteristics of the curative surgery cohort and outcomes and differences in the surgical approaches**

	Curative surgery	OPEN, n (%)	LAP n (%)	p overall
	562	269*	266*	
Age, y, mean (SD)	68.8 (11.6)	70.5 (10.7)	67.3 (11.7)	0,001
Sex				
Female	211 (37.5)	95 (35.3)	106 (39.8)	0,285
Male	351 (62.5)	174 (64.7)	160 (60.2)	
CR-POSSUM, mean(SD)	7.4 (5.2)	8.2 (5.0)	7.2 (5.3)	0,045
Tumour level*				
0-5	137 (24.4)	52 (19.3)	82 (30.8)	0,294
6-10	181 (32.2)	84 (31.2)	97 (36.5)	
11-15	147 (22.2)	69 (25.7)	77 (28.9)	
Number of nodes analyzed, mean(SD)	14.0 (9.7)	14.5 (10.3)	13.5 (9.2)	0,766
Postoperative stay, days, mean (SD)	10.9 (7.8)	11.9 (7.9)	10.2 (7.3)	
median[P25,P75]	8 [6,13]	9 [7,14]	7 [6,12]	< 0.001
Neoajuvant treatment*				
No	198 (35.2)	88 (32.7)	107 (40.2)	0.851
Yes	287 (51.1)	123 (45.7)	157 (59.0)	
Type of resection*				
APR	93 (16.5)	44 (16.4)	48 (18.0)	0,566
AR	325 (57.8)	139 (51.7)	185 (69.5)	
Other	65 (11.6)	31 (11.5)	33 (12.4)	
multivisceral resection*				
No	436 (77.6)	181 (67.3)	252 (94.7)	0,004
Yes	30 (5.3)	21 (7.8)	9 (3.4)	
Mortality, 30d*				
No	441 (78.5)	195 (72.5)	246 (92.5)	0,737
Yes	8 (1.4)	4 (1.5)	4 (1.5)	
Operative complications*				
No	315 (56.0)	131 (48.7)	184 (69.2)	0,109
Yes	148 (26.3)	73 (27.1)	74 (27.8)	
Clavien class.*				
0 + I +II	54 (60.4)	45 (61.6)	42 (50.2)	0,7
III + IV	49 (34.0)	23 (31.5)	26 (36.6)	
V	8 (5.6)	5 (6.9)	3 (4.2)	
Intraoperative bowel perforation*				
No	459 (81.7)	200 (74.3)	259 (97.4)	0,037
Yes	4 (0.7)	4 (1.5)	0 (0.0)	
pT				
T0	55 (9.8)	20 (7.5)	33 (12.4)	0,137
T1	51 (9.1)	22 (8.2)	25 (9.4)	
T2	159 (28.3)	71 (26.5)	75 (28.2)	
T3	257 (45.7)	140 (52.2)	110 (41,4)	
T4	25 (4.4)	13 (4.8)	11 (4.1)	
pN*				
N0	354 (63.0)	157 (58.6)	183 (68.8)	0,015
N1	144 (25.8)	74 (27.5)	61 (22.9)	
N2	53 (9.4)	33 (12.3)	17 (6.4)	
Stage*				
I	188 (36.5)	84 (32.1)	104 (41.1)	0.039
II	142 (27.6%)	71 (27.1)	71 (28.1)	
III	185 (35.9%)	107 (40.8)	78 (30.8)	
CRM assessment*				
No	457 (81.3)	225 (83.6)	209 (78.6)	1.000
Yes	21 (3.7)	10 (3.7)	10 (3.8)	
Regression grade*				
0	41 (7.3)	11 (4.1)	29 (10.9)	0,066
1	60 (10.7)	19 (7.1)	36 (13.5)	
2	96 (17.1)	45 (16.7)	46 (17.3)	
3	54 (9.6)	25 (9.3)	29 (10.9)	
Residual tumor*				
R0	520 (92.5)	248 (92.2)	247 (92.9)	0,87
R1	42 (7.5)	21 (7.8)	19 (7.1)	
Local recurrence*				
No	495 (88.1)	242 (90.0)	249 (93.6)	0,068
Yes	26 (4.6)	18 (6.7)	8 (3.0)	
Death all causes*				
No	395 (70.3)	175 (65.1)	217 (81.6)	< 0.001
Yes	119 (21.2)	81 (30.1)	37 (13.9)	

AR – anterior resection. APR – abdominal perineal resection. CRM - circumferential resection margin. OPEN – open surgery. LAP – laparoscopic surgery.

* Some data are missing

Table 3 – **Cox proportional hazard regression analysis for local recurrence in the curative surgery cohort**

Local recurrence	No event	Event	Univariate HR (95%CI)	p	Multivariate HR (95%CI)	p
	495	26				
Age, y, mean (SD)	69.0 (11.2)	66.1 (13.1)	0.99 (0.96 - 1.03)	0,627	0.96 (0.92 - 1.01)	0,085
Sex						
Female	188 (38.0)	6 (23.1)	Ref		Ref	
Male	307 (62.0)	20 (76.9)	2.40 (0.90 - 6.44)	0,081	2.50 (0.70 - 8.96)	0,16
Tumour level*						
0-5	125 (25.3)	7 (26.9)	Ref		Ref	
6-10	166 (33.5)	4 (15.4)	0.42 (0.12 - 1.44)	0,169	1.20 (0.20 - 7.06)	0,839
11-15	135 (27.3)	10 (38.5)	1.28 (0.49 - 3.37)	0,614	3.98 (0.54 - 29.34)	0,176
Neoajuvant treatment*						
No	177 (35.8)	10 (38.5)	Ref		Ref	
Yes	262 (52.9)	12 (46.2)	0.85 (0.37 - 1.97)	0,705	1.15 (0.35 - 3.78)	0,813
Adjuvant treatment*						
No	160 (32.3)	6 (23.1)	Ref		Ref	
Yes	229 (46.3)	15 (57.7)	1.76 (0.68 - 4.52)	0,244	0.92 (0.26 - 3.21)	0,454
Surgical approach*						
Laparoscopic	249 (50.3)	8 (30.8)	Ref		Ref	
Open	242 (48.9)	17 (65.4)	2.17 (0.92 - 5.12)	0,078	1.49 (0.53 - 4.18)	0,454
Type of resection*						
APR	82 (16.6)	7 (26.9)	Ref		Ref	
AR	304 (61.4)	12 (46.2)	0.44 (0.17 - 1.13)	0,087	0.30 (0.05 - 1.83)	0,19
Other	54 (10.9)	6 (23.1)	1.25 (0.42 - 3.71)	0,693	0.62 (0.09 - 4.54)	0,638
Intraoperative bowel perforation*						
No	423 (85.5)	19 (73.1)	Ref		Ref	
Yes	3 (0.6)	1 (3.8)	6.32 (0.85 - 47.25)	0,073	7.91 (0.80 - 78,17)	0,077
pT						
T0	51 (10.3)	0 (0.0)	Ref		Ref	
T1	47 (9.5)	1 (3.8)				
T2	141 (28.5)	3 (11.5)				
T3	224 (45.3)	18 (69.2)	5.42 (1.87 - 15.74)	0,017	5.60 (0.86 - 36.54)	0,072
T4	19 (3.8)	4 (15.4)				
pN						
N0	318 (64.2)	14 (53.8)	Ref			
N1	130 (26.3)	4 (15.4)	0.75 (0.24 - 2.29)	0,607	0.69 (0.17 - 2.74)	0,598
N2	41 (8.3)	7 (26.9)	3.55 (1.35 - 9.34)	0,01	2.36 (0.69 - 8.09)	
CRM assessment*						
No	401 (81.0)	21 (80.8)	Ref		Ref	
Yes	17 (3.4)	3 (11.5)	3.56 (1.05 - 12.04)	0,041	3.06 (0.62 - 15.20)	0,171
Regression grade*						
0	39 (7.9)	3 (11.5)	Ref		Ref	
1	52 (10.5)	4 (15.4)				
2	86 (17.4)	2 (7.7)				
3	49 (9.9)	9 (34.6)	1.05 (0.22 - 5.05)	0,953	1.86 (0.27 - 12.83)	0,53

AR – anterior resection. APR – abdominal perineal resection. CRM - circumferential resection margin
* Some data are missing

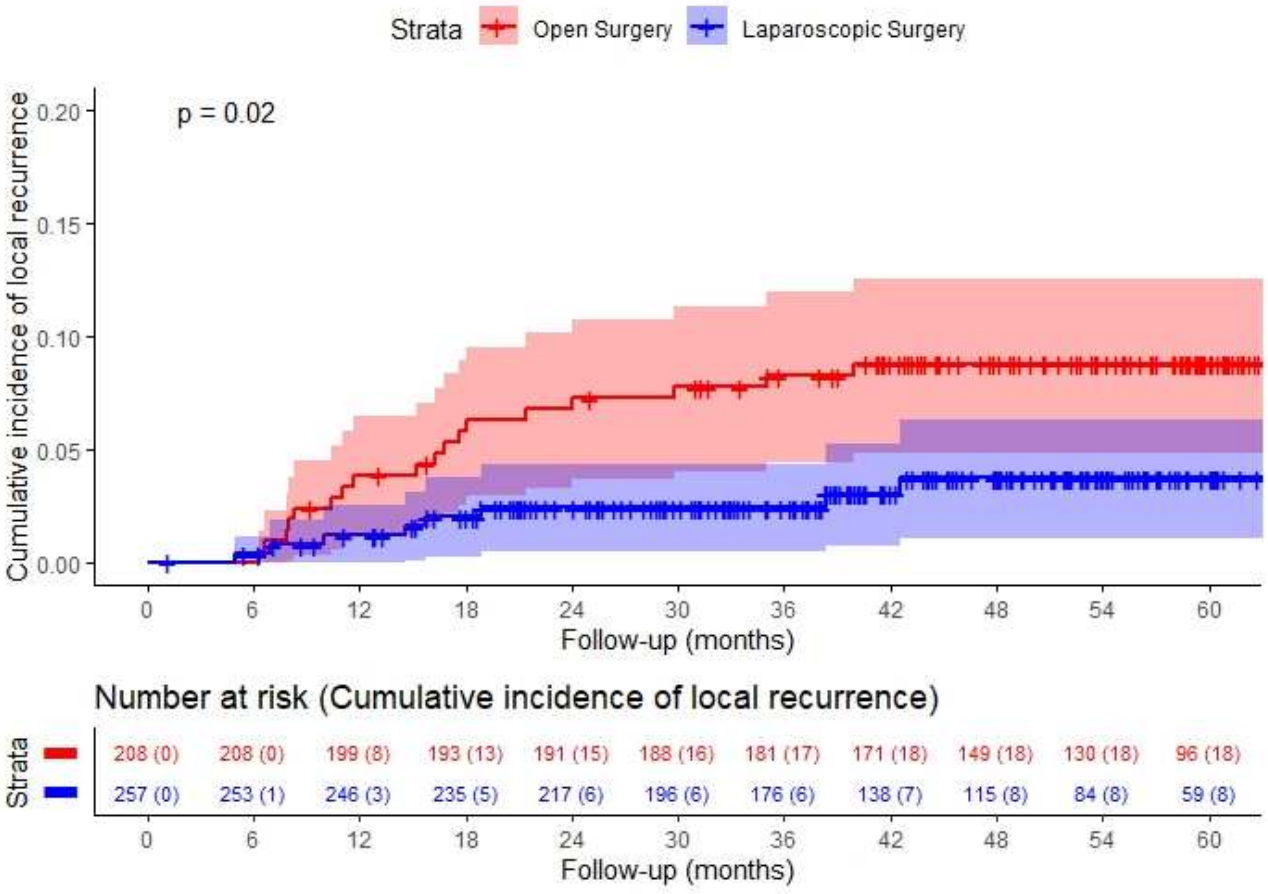

FIGURE 1 – **Cumulative incidences of local recurrence in relation to the surgical approach in the curative cohort**

3.4.-7.5%). The estimated 3-year LR rate was 8.3% (95% CI, 5.1.-13.1%) after OPEN surgery and 2.4% (95% CI, 1.1%-5.3%) after LAP surgery (log-rank test, P=0.020). In patients with stage I or III the rectal cancer rates of LR in OPEN and LAP surgery were similar, whereas in patients with stage II the LR was 15.8% (95% CI, 7.6%-29.9%) in the OPEN group, and 4.7% (95% CI, 1.5%-13.7%) in the LAP group (log-rank test, P=0.062).

In the curative cohort, the univariate analysis for OS showed that older age (HR 1.04; 95% CI, 1.02-1.06), open surgery (HR 1.74; 95% CI, 1.15-2.64), advanced pathologic staging (HR 3.09; 95% CI, 1.81-5.25) and CRM involvement (HR 3.56; 95% CI, 1.05-12.04) were related in a reduced OS (Table 4). A multivariate analysis demonstrated that only age (HR 1.04; 95% CI, 1.01-1.08), and stage (HR 2.99; 95% CI, 1.22-7.30) influenced OS.

The cumulative incidence of OS rate in the 456 curative resections is shown in Figure 2. The estimated 3-year OS of the entire cohort of patients who underwent curative surgery was 82.4% (95% CI, 78.2%-86.0%). The cumulative 3-year OS was 76.5% (95% CI, 69.1%-82.6%) for the OPEN surgery group and 88.2% (95% CI, 83.1.-92.0%) for the LAP surgery group (log-rank test, P=0.0061). The 3-year OS rate according to disease stages I and II were similar in the two groups, whereas in stage III group the OS rate was 61.4% (95% CI, 42.2%-73.9%) in the OPEN group and a higher rate of 84.1% (95% CI, 72.3%-91.4%) in the LAP group (log-rank test, P=0.005).

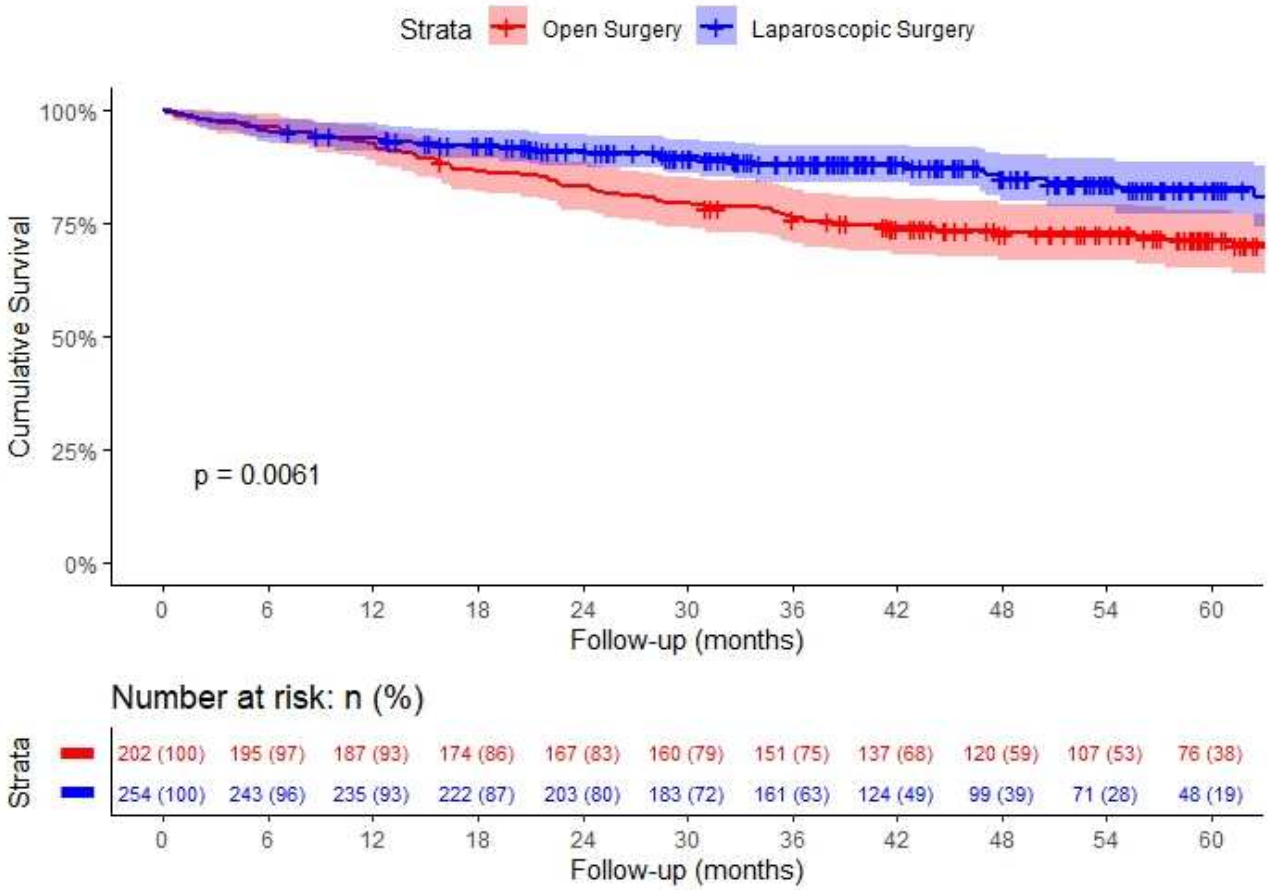

FIGURE 2 – **Cumulative overall survival in relation to the surgical approach in the curative cohort**

DISCUSSION

This study examined the recent practices and outcomes of rectal cancer surgery in Portugal and highlighted the comparison of the outcomes of OPEN and LAP rectal cancer surgeries. Half of the patients had LAP surgery with better oncologic outcomes than those who had OPEN surgery, although those who underwent LAP had tumors with less advanced pN stages, which may affect long-term oncologic outcomes.

The TNM stage, tumor level, and type of resection of our study cohort can be compared with those reported by the Norwegian Project in 2002[1], the Spanish Project in 2013[2,14], the Dutch Snapshot[15], the COLOR II trial[16], and the COREAN trial[17]. The incidence of APR in the present study (16.5%) was lower than those reported in the Spanish Project (23%), the Dutch Snapshot (30.5%), and the COLOR II trial (26.5%). Despite observing a higher frequency of LR in APR (8%) than in AR (3.7%), the multivariate analysis showed that APR was not an independent prognostic factor of the 3-year LR. This finding can be justified by the practice in recent years with a better understanding of the pelvic anatomy using MRI as a road map. Instead of "conventional" APR, which may waste specimens with CRM invasion, surgeons can perform a more precise radical procedure, such as extralevator abdominoperineal excision.

LAP surgery was performed more frequently in the Portuguese Project (49%) than in the Spanish

Table 4 – **Cox proportional hazard regression analysis for death in the curative surgery cohort**

Death all causes	No event	Event	Univariate HR (95%CI)	p	Multivariate HR (95%CI)	p
	395	119				
Age, y, mean (SD)	67.7 (14.3)	72.3 (10.6)	1.04 (1.02 - 1.06)	< 0.001	1.04 (1.01 - 1.08)	0.022
Sex						
Female	147 (37.2)	44 (37.0)	Ref		Ref	
Male	248 (62.8)	75 (63.0)	0.97 (0.88 - 0.97)	0.884	2.72 (1.28 - 5.81)	0.010
Tumor level*						
0-5	103 (26.1)	26 (21.8)	Ref		Ref	
6-10	131 (33.2)	28 (31.9)	1.09 (0.66 - 1.79)	0.745	1.42 (0.53 - 3.79)	0.490
11-15	115 (29.1)	27 (22.7)	0.91 (0.53 - 1.56)	0.733	2.07 (0.61 - 7.00)	0.241
Neoajuvant treatment*						
No	152 (38.5)	33 (27.7)	Ref		Ref	
Yes	208 (52.7)	62 (52.1)	1.42 (0.93 - 2.17)	0.105	3.06 (0.41 - 22.98)	0.277
Adjuvant treatment*						
No	132 (33.4)	32 (26.8)	Ref		Ref	
Yes	186 (47.1)	53 (44.5)	1.13 (0.73 - 1.76)	0.578	0.73 (0.33 - 1.62)	0.609
Surgical approach*						
Laparoscopic	217 (54.9)	37 (31.1)	Ref		Ref	
Open	175 (44.3)	80 (67.2)	1.74 (1.15 - 2.64)	0.009	0.84 (0.44 - 1.62)	0.609
Type of resection*						
APR	64 (16.2)	23 (19.3)	Ref		Ref	
AR	249 (63.0)	61 (51.3)	0.23 (0.46 - 1.21)	0.232	0.84 (0.33 - 2.16)	0.716
Other	48 (12.2)	13 (10.8)	1.82 (0.46 - 1.21)	0.232	0.16 (0.02 - 1.33)	0.089
Intraoperative bowel perforation*						
No	345 (87.3)	90 (75.6)	Ref		Ref	
Yes	3 (0.8)	0 (0.0)	0.05 (0.00 - 3059.35)	0.593	0.00 (0.00 - inf)	0.977
Stage*						
I	159 (40.3)	24 (20.2)	Ref		Ref	
II	104 (26.3)	33 (27.7)	2.32 (1.29 - 4.16)	0.005	2.64 (1.02 - 6.81)	0.045
III	119 (30.1)	59 (49.6)	3.09 (1.81 - 5.25)	< 0.001	2.99 (1.22 - 7.30)	0.016
CRM assessment*						
No	313(79.2)	105 (88.2)	Ref		Ref	
Yes	10 (2.5)	10 (8.4)	2.67 (1.34 - 5.32)	0.005	2.33 (0.82 - 6.59)	0.112
Regression grade*						
0	35 (8.9)	3 (2.5)	Ref		Ref	
1	44 (11.1)	11 (9.2)	2.49 (0.69 - 8.92)	0.163	1.36 (0.26 - 6.99)	0.716
2	70 (17.7)	18 (15.1)	2.62 (0.77 - 8.91)	0.122	0.99 (0.19 - 5.04)	0.987
3	33 (8.4)	17 (15.3)	4.71 (1.38 - 16.12)	0.013	2.30 (0.45 - 11.77)	0.318

AR – anterior resection. APR – abdominal perineal resection. CRM - circumferential resection margin
* Some data are missing

Project (32%); although with a similar rate to the Dutch Snapshot (46.9%). The conversion rate observed in the present study (17.5%) was also comparable to that of the Dutch Snapshot (14.4%) and the COLOR II trial (17.4%). The duration of hospital stay in the curative cohort of the present study was two days shorter in the LAP surgery group than in the OPEN surgery group; a finding also noted in the short-term outcome of the COLOR II trial[18].

In the present curative cohort, the mean numbers of lymph nodes harvested during the LAP and OPEN surgeries (14.5 and 13.5) were similar to those reported in the COLOR II trial (13 and 14, respectively). Furthermore, the involvement of the CRM was recorded in 3.8% and 3.7% of the patients in the LAP and OPEN surgery groups, respectively; a finding which is lower than that observed in the Dutch Snapshot (7.8% and 16.6%) and in the COLOR II trial (10% and 10%), but similar to those recorded in the COREAN trial (2.9% and 4.1%).

There is a reasonable suggestion that the more distal and advanced cancer, the greater the uncertainty that LAP surgery will produce the same outcomes as OPEN[19]. However, in this study, the tumor level in the rectum was not related to differences in LR or OS, and LAP surgery was used more frequently in the lower third than OPEN surgery, as shown in Table 2. We can conclude that the LAP approach was not associated with worse results in tumors of the lower third. One explanation for this is the use of new minimally invasive alternatives for more distal tumors; several laparoscopic transanal TMEs have been performed and included in other resections.

Regardless of the technique used, rectal cancer surgery requires sufficient training to be performed safely. Laparoscopic surgical expertise is difficult to measure objectively; however, the expertise can be reflected in the duration and the conversion rate of the surgery[20]. The present study had considerable missing data regarding the duration of the operations; however, the conversion rate in our study did not exceed 16% throughout the study, just as reported in the COLOR II trial.

The overall 3-year LR rate in the present study was 5.1%, which is comparable with the values reported for the Spanish Project (7%), the Norwegian Project (8%), the Dutch Snapshot (5.9%), and the COLOR II trial (5%). In the present study, the rate of LR for LAP surgery (2.4%) was significantly lower than that for OPEN surgery (8.3%). The same comparison for the 3-year LR rate of LAP and OPEN surgeries in randomized controlled trials, such as the COLOR II trial showed 5% LR in both groups, 2.6% vs. 4.9% in the COREAN trial, 4.6% vs. 4.5% in the Z6051 trial, and 5.4% vs. 3.1% in the ALaCaRT trial, respectively. The 3-year OS rate in the present study was 88.2% after LAP surgery, a higher, clinically relevant value than the 76.5% after OPEN surgery; comparatively, the COLOR II trial showed the rates of 86.7% and 83.6%, respectively.

Our study found that better oncologic outcomes with a LAP approach is related to a cohort of younger patients, with lower CR-POSSUM score, tumors with less advanced pathologic N stages, and rare cases of multi-visceral resection, as shown in Table 2. However, the univariate analysis adjusted for the LAP approach showed a negative influence of this variable for LR (HR 2.17) and a positive influence for OS (HR 1.74) (Tables 3 and 4), in spite of having lost statistical value in the multivariate analysis. Furthermore, the influence of the LAP approach in the OS was more evident in the patients with stage III, with a significantly higher OS after LAP surgery (84.1%) than after OPEN surgery (61.4%). Interestingly, a similar finding was reported in the COLOR II trial, among patients stage III with a disease-free survival of 64.9% after LAP surgery and 52.0% after OPEN surgery. These data favor the interpretation that there is a trend toward better oncologic outcomes with LAP surgery in stage III, but the results might have been influenced by other residual confounding variables.

The main limitations of this study include the voluntary nature of the hospital registration in the

Portuguese Project and the reduced participation of several hospitals. It was not possible to evaluate the global results of the participating centers in the country. Another limitation is the overall 5% missing database and, for some of the analyzed variables, up to 22% of the data were missing, which may have led to potentially biased results.

This study suggests the need for mandatory clinical auditing to increase voluntary registration. The Netherland's experience with the Dutch Institute for Clinical Auditing[21], measuring the quality of care, giving benchmarking feedback, stimulating improvement initiatives, and enabling transparency, must be considered.

CONCLUSION

The current rectal cancer treatments of a large unselected Portuguese population were benchmarked against others with similar outcomes. The implementation of minimally invasive surgery in half of the patients in this study, particularly those with less advanced tumors, without invasion of adjacent tissues, was shown to be oncologically safe, with better short and long-term results for these patients than those in the OPEN cohort. The data support the view that the LAP approach is justified for rectal cancer when performed by surgeons with appropriate laparoscopic experience.

Acknowledgements

The authors thank all the Portuguese surgeons and 16 hospitals that performed rectal cancer surgeries and reported the data during the study period, the pathologists who examined the specimens, and the radiologists who analyzed the radiologic exams.

Protection of humans subjects

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration issued by World Medical Association. The ethical committee of all participating hospitals, as well as the council of national data protection, approved this study.

Confidentiality of data

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

Conflict of interest disclosure

The authors have no conflicts of interest.

Patient consent statement

Informed consent was obtained from all patients included in the study.

Funding Sources

This project was supported by the Portuguese Society of Surgery without any grant from the government or industry.

Autors' contributions

Study concept and design: Leite, Pimentel, Silva, Gíria.
Analysis and interpretation of data: All authors
Drafting of the manuscript: Leite
Critical revision of the manuscript: All authors
Statistical analysis: Oliveiros

Appendix

Steering Commitee: J. S. Leite; J. Pimentel; P. C. Silva; J. Gíria; F. C. Alves; L. Semedo; J. Venâncio; L. Guimarães; M. Rui; R. Fonseca; M. J. Brito; J. Lopes; B. Oliveiros.

Collaborators included in the Portuguese Rectal Cancer Registry

CHBV Aveiro (Jorge Sousa, MD; Margarida Martins, MD)

H Braga (Mesquita Rodrigues, MD; Humberto Cristino, MD; Pedro Leão, MD; Costa Pereira, MD)

CHUC Coimbra (António Manso, MD; António Ribeiro, MD; Ana Oliveira, MD; Eva Santos, MD; Maria Koch)

H G. Orta (Corte Real, MD; Luís Galindo, MD)

HSM Guarda (José Rodrigues, MD; Liliana Cabral, MD; Adelaide Campos, MD)

Norte Alentejano (Eduardo Soeiro, MD; Carlos Figueiredo, MD; Hugo Capote, MD)

HS João (Alexandre Duarte, MD; Laura Barbosa, MD)

VN Gaia (Lurdes Gandra, MD; João Cardoso, MD)

ULS Alto Minho (Fernando Barbosa, MD; Paulo Passos, MD; Teresa Almeida, MD)

CHT Viseu (Carlos Casimiro, MD; Vitor Marques, MD; Fernando Valério, MD)

CH Trás-os-Montes AD (António Oliveira, MD; Paulo Sousa, MD)

H Santarém (Luís Ferreira, MD; Pedro Vasconcelos, MD; Luís Vilela, MD)

HD Setúbal (José Fontinha, MD; Sofia Rufino, MD; Marta Lemos, MD)

IPO Coimbra (Henrique Ferrão, MD; Teresa Silva, MD, Sheila Martins, MD)

CHU Porto (Marisa Santos, MD; Anabela Rocha, MD; Mónica Sampaio, MD)

HES Évora (Artur Silva, MD; José Travassos, MD; Raquel Sanchez, MD)

REFERENCES

1 Wibe A; Møller B, Norstein J, et al. A national strategic change in treatment policy for rectal cancer – Implementation of total mesorectal excision as routine treatment in Norway. A national audit. Dis Colon Rectum. 2002;45:857-866.

2 Ortiz H, Wibe A, Ciga MA et al. Impact of a multidisciplinary team training programme on rectal cancer outcomes in Spain. Colorectal Dis 2013;15:544-551.

3 Bosch SL, Nagtegaal ID. The importance of the pathologist's role in assessment of the quality of the mesorectum. Curr Colorectal Cancer Rep 2012;8:90-98.

4 Leonard D, Penninckx F, Fieuws S, et al. PROCARE, a multidisciplinary Belgian Project on Cancer of the Rectum. Factors Predicting the Quality of Total Mesorectal Excision for Rectal Cancer. Ann Surg 2010;252:982-988.

5 Veldkamp R, Kuhry E, Hop WC, et al. Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. Lancet Oncol 2005;6:477-484.

6 van der Pas MH, Haglind E, Cuesta MA, et al. Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. Lancet Oncol 2013;14:210-218.

7 Fleshman J, Branda M, Sargent DJ, et al. Effect of laparoscopic-assisted resection vs open resection of stage II or III rectal cancer on pathologic outcomes: the ACOSOG Z6051 randomized clinical trial. JAMA 2015;314:1346-1355.

8 Stevensen AR, Soloman MJ, Lumley JW, et al. Effect of laparoscopic-assisted reaction vs open resectionon pathological outcomes in rectal cancer: the ALaCaRT randomized clinical trial. JAMA 2015;314:1356-1363.

9 Fleshman J, Branda ME, Sargent DJ, et al. Disease-free survival and local recurrence for laparoscopic resection compared with open resection of stage II to III rectal cancer: follow-up results of the ACOSOG Z6051 randomized controlled trial. Ann Surg 2019;269:589-595.

10 Stevenson ARL, Soloman MJ, Brown CSB, et al. Disease-free survival and local recurrence after laparoscopic-assisted resection or open resection for rectal cancer: the Australasian laparoscopic cancer of the rectum randomized clinical trial. 2019;269:596-602.

11 www.spcir.com Cancro do Reto – Registo nacional

12 www.riskprediction.org.uk

13 Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-213.

14 Ortiz H, Wibe A, Ciga M, et al. on behalf of the Spanish Rectal Cancer Project. Multicenter study of outcome in relation to the type of resection in rectal cancer. Dis Colon Rectum 2014;57:811–822.

15 Dutch Snapshot Research Group. Benchmarking recent national practice in rectal cancer treatment with landmark randomized controlled trials. Colorectal Dis. 2017;19(6):O219-O231.
16 Bonjer HJ, Deijen CL, Abis GA et al. for the COLOR II study group. A randomized trial of laparoscopic versus open surgery for rectal cancer. N Engl J Med 2015; 372: 1324–1332.
17 Jeong SY, Park JW, Nam BH, et al. Open versus laparoscopic surgery for midrectal or low-rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): survival outcomes of an open-label, noninferiority, randomised controlled trial. Lancet Oncol 2014;15:767-774.
18 van der Pas MH, Haglind E, Cuesta MA, et al. Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. Lancet Oncol 2013;14:210-8.
19 Mathis KL, Nelson H. Laparoscopic proctectomy for cancer. Ann Surg 2019;269:603-604.
20 Harrysson IJ, Cook J, Sirimanna P, Feldman LS, Darzi A, Aggarwal R. Systematic review of learning curves for minimally invasive abdominal surgery: a review of the methodology of data collection, depiction of outcomes, and statistical analysis. Ann Surg 2014;260:37-45.
21 Beck N, van Bommel, Eddes E, et al. The Dutch Institute for Clinical Auditing. Achieving Codman's dream as a nationwide basis. Ann Surg 2020;271:627-631.

Correspondência:
JÚLIO SOARES LEITE
e-mail: julio.s.leite@gmail.com

Data de recepção do artigo:
22/02/2022

Data de aceitação do artigo:
04/11/2022