

TITLE PAGE**Comparison of perioperative outcomes between three techniques during transition from open to laparoscopic to robotic surgery for rectal cancer in a single academic hospital**

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Abstract

Background

The aim was to compare early outcomes of rectal cancer surgery during transition from open (OS) to laparoscopic (LS) to robotic-assisted surgery (RS) in a single institution.

Method

This retrospective study included consecutive patients who underwent elective surgery for rectal cancer. OS approach was used between 2011–2014, LS between 2013–2016 and RS between 2016–2019. The studied outcomes included 30-day/in-hospital mortality, complications, conversions, operation time, blood loss, length of stay and adequacy of excision.

Results

Fifty-three patients were treated by OS, 101 by LS and 166 by RS. There were no significant differences in early mortality between the groups; 1.9% in OS, 2.0% in LS and 1.2% in RS. Major complications occurred in 23%, 14% and 13%, respectively, with no significant differences between the groups. Three patients (1.8%) required conversion from RS to OS compared to 11 patients (12%) in the LS group ($P=0.001$). Operation times were 197 ± 63 minutes in OS, 221 ± 63 in LS and 258 ± 62 in RS, with statistically significant differences between OS and LS/RS groups ($P<0.001$). Blood loss was 655 ± 484 ml in OS, 347 ± 315 in LS and 237 ± 287 in RS, with statistically significant reduction between every group. Length of hospitalization was shorter in RS (8.7 ± 7.0) and LS (9.2 ± 6.1) groups compared to OS (13.7 ± 8.2 days, $P<0.001$). There were no differences in resection margins or number of harvested lymph nodes between the groups.

Conclusions

RS replaced OS and LS without compromising outcomes. RS was associated with reduction in blood loss, length of stay and lower conversion rate.

Introduction

Colorectal cancer is the most common gastrointestinal malignancy worldwide and one third of colorectal cancer is located in the rectum.[1] Before the development of minimally invasive techniques, open surgery (OS) was the mainstay of treatment for rectal cancer. Tumors located high in the rectum were operated using the anterior approach and those located low using abdominoperineal excision.[2,3] Laparoscopic surgery (LS) offers advantages compared to OS such as shorter postoperative length of stay and faster recovery of bowel function.[4] However, LS for rectal cancer is demanding because of the two-dimensional view and limited accuracy of laparoscopic instruments in the narrow pelvic space.[4,5] Even though the use of LS in rectal cancer has increased over the past two decades, more than 50% of patients with rectal cancer were still treated with OS between years 2010 and 2015 in the United States.[6] Robotic-assisted laparoscopic surgery (RS) for rectal cancer was first reported in 2006.[7] RS offers a solution to the ergonomic and optical limitations of LS by giving surgeon more space to perform with articular instruments and three-dimensional view.[5,8]

A recent meta-analysis which included five randomized controlled trials and 544 pooled patients provided evidence that RS produces similar perioperative outcomes with lower conversion rates to OS compared with LS approach.[9] However, randomized trials do not consider the learning curve in the transition between these surgical approaches, and LS and RS have rarely been compared against the traditional OS. A recent registry-based multicenter study by Asklid and colleagues which compared OS, LS and RS demonstrated lower conversion rate in RS approach compared to LS and the length of stay was shorter in patients treated with RS compared to LS or OS.[10] However, it should be noted that this study included also benign lesions.

The aim of the present study was to compare the perioperative outcomes of the three different techniques of rectal cancer surgery during transition from OS to LS, and further, to RS over one decade in a single academic teaching hospital.

Materials and methods

This was a retrospective study approved by the local institutional review board. Informed consent was not required. All consecutive patients who underwent elective curative resection for rectal cancer in a single academic teaching hospital between year 2011 and 2019 were included in the study. Patients treated in an emergency setting and those who underwent palliative non-curative surgery were excluded. All data were collected from the electronic medical records and a local prospectively maintained database for rectal cancer. Patients were divided into three groups based on the operative approach: LS, OS and RS. During the first trimester of the study period, OS was the main operative approach for rectal cancer. LS replaced OS during the second trimester. RS for rectal cancer was started in our institution in 2016, and since then, all patients, who were eligible for LS, has been treated with RS (DaVinci Xi, Intuitive, California, USA). In general, OS approach was used between 2011–2014, LS between 2013–2016 and RS between 2016–2019 (Figure 1).

Computer tomography and magnetic resonance imaging were used in the diagnostics. The European Society for Medical Oncology guidelines were followed when considering preoperative chemoradiotherapy (PO-CRT).[11] The tumors were graded as 1 (low grade), 2 (moderate grade) and 3 (high grade) based on the final pathology report. In addition, tumors were graded according to the TNM-classification. Resection margins and the number of harvested lymph nodes were also based on review of the pathology report.

The studied main outcomes were 30-day or in-hospital mortality, complications, conversion to open surgery, operation time, blood loss, length of stay at the hospital and the adequacy of excision, i.e., resection margins of the tumor. Clavien-Dindo classifications Grades 3, 4 and 5, were classified as major complications. Grades 1 and 2, were classified as minor complications.[12] Multiorgan resections were excluded from the operation time and blood loss analyses.

IBM SPSS Statistics software version 27 was used to analyze all data. χ^2 - or Fisher's exact test was used to compare nominal data. Continuous variables were presented as mean \pm standard deviation and Kruskal-Wallis one-way analysis of variance was used to compare these variables between the three groups. P-value below 0.05 was considered significant.

Results

Altogether, 321 patients underwent elective surgery for colorectal cancer during the ten-year study period; 53 patients were treated by OS, 101 by LS and 166 by RS. There were no significant differences in mean age, gender, Body mass index (BMI) or American Society of Anesthesiologists Classification (ASA) between the groups (Table 1). Over time, a slightly larger proportion of patients undergoing RS received PO-CRT (73 %) compared to those in OS (61 %) and LS (65 %) groups ($P < 0.001$). Tumors located in the rectosigmoid region were operated more often by OS, whereas there were no differences in the locations of lower rectum tumors between the groups.

Operative details are presented in Table 2. The rate of unplanned conversion from LS to OS was greater than from RS to OS; 12% versus 1.8% ($P < 0.001$). One procedure in both RS and LS groups were performed as a planned hybrid operation. The mean operation time in the OR group was approximately 20 minutes shorter than in the LS group ($P < 0.001$) and 60 minutes shorter than in the RS group ($P < 0.001$). The difference of operation time between LS and RS groups was not statistically significant. The blood loss volume was lower in the RS group compared to OS ($P < 0.001$) and LS ($P < 0.003$).

There were no statistically significant differences in 30-day or in hospital mortality rates; 1.9% in OS, 2.0% in LS and 1.2% in RS (OS/LS, $P = 1.000$; OS/RS, $P = 1.000$; LS/RS $P = 1.000$) (Table 3). There were no statistically significant differences in the distribution of complications between the groups either. Major complications (Clavien-Dindo 3-5) occurred in 23%, 14% and 13%, respectively. In patients who received PO-RCT, the rates of major complications were 26%,

12% and 15%, respectively. Length of hospital stay was nearly the same in LS and RS groups; however, it was significantly higher in the OS group. Up to 40% of patients in the RS group were discharged within five days whereas only 6% of patients in the OR group were discharged in five days or less. Out of 206 patients (64%) who received an intestinal anastomosis during the index procedure, 14 (7%) had leakage; there were no statistically significant differences in the rates of anastomotic leakage between the groups.

Final pathological assessment of grading and adequacy of the excision are presented in Table 4. There were no major differences in the spread of the cancer between the groups with grade 2 being most common in 80-90% of the patients. Significant differences in T-, N- or M- classifications between the groups did not occur. The resection margins did not vary significantly between the groups. However, at least 1 mm circumferential margin was reached in 85% in OS, 91% in LS and 95% of cases in RS groups; the differences between OS and RS groups was borderline significant in favor of the RS technique.

Discussion

This study demonstrates that the transition of surgical technique in the treatment of rectal cancer from OS to LS to RS over a decade is feasible in a relatively small institution. Considering the learning curve, this can be done safely without compromising the adequacy of the excision. Moreover, the study demonstrates reduction in blood loss and length of hospital stay in patients treated with RS. In addition, conversion rate from endoscopic surgery to OS was notably lower in the RS group compared to the LS group. Overall, the combined 30-day and in-hospital mortality rate was low, less than 2%, and the rate of major complications was acceptable especially in the RS group (13%).

There are only few studies with analogous comparison of all three techniques. In the previously mentioned study by Asklid and colleagues, the conversion rate from LS to OS was 18% and from RS to OS 8%; the latter was notably higher than in our study (2%). Minor complications

were reported more often in our study. On the other hand, we had fewer major complications in RS group, whereas more in OS and LS groups. In the present study, data is from a single center whereas the data in the Asklid's study is collected from Swedish part of the international Enhanced Recovery After Surgery interactive audit system, where multiple centers feed their data, and possibly, the smallest complications may not be reported with accuracy similar to our study.[10]

The use of PO-CRT increased over time in our institution from OS to RS period. According to literature, PO-CRT could potentially increase tissue damage, and therefore, also tendency of blood loss and other complications.[13,14] However, in our study, there were no major differences in the rates of complications between those who received PO-CRT and those who did not. The blood loss was also lower in the RS group indicating that the increased use of PO-CRT has not been an issue. There are several reasons for the potential benefits of RS regarding the loss of blood during the operation. The three-dimensional view and 10-times magnification help the surgeon to observe the vascular structures more precisely compared to the naked eye. Also, the vision to the target is easy to hold. The multi-dimensional arms make it possible to approach the tissues from various directions that would be awkward in OS and LS. Furthermore, robotic technique allows the surgeon to take care of a good posture, which may help the operator to be more concentrated in a lengthy operation.

The length of hospital stay was lower in both RS and LS groups compared to those treated with OS. Postoperative ileus and infections were the main concerns in patients with prolonged hospitalization. Normal physiological time for the recovery of colon's motility after surgery is considered 3-5 days.[15] Minimal invasive and atraumatic surgery may reduce the incidence of POI, as seen in our data. This aspect, however, needs more research.

The conversion rate in our study was lower in the RS group than in the LS group. This is in accordance with previous studies as discussed earlier in this paper. Based on a previous study, the main risk factors for conversion to OS are age over 75, male sex, ASA score of III or more and

body mass index over 30.[16] Regarding these features, there were no differences between the groups in our study. Therefore, we conclude that the main reason for the decreased conversion rate in RS compared to LS may be the previously mentioned technical improvements in RS. Owing perhaps to this same reason, the resection margins in our study improved slightly after transition to RS, although there were no major statistically significant changes in the adequacy of excision over time. The effect of endoscopic techniques to the resection margins can be seen in previous studies as well.[17,18]

For those surgeons considering transition to RS in the treatment of rectal cancer, there are a few things to consider. Based on our observation, a sufficient experience in laparoscopic rectal surgery is a major advantage that allows shorter learning curve to robotic surgery. A fairly recent study comparing outcomes of two surgeons performing colorectal surgery, one with previous experience of more than 200 cases of LS and one with less than 100 cases, demonstrated no apparent learning curve for the surgeon with more experience with LS during transition to RS. In contrast, the other surgeon with less experience in LS achieved similar level after 15 cases of RS.[19] Our recommendation is, that before starting RS for rectal cancer the operators should observe these procedures in a high-volume institution and be accompanied by an experienced proctor during the first few cases.

The main limitation of this study is the minimal amount of missing data and the lack of standardized reporting regarding pathological findings. The second limitation is that there was no long-term follow up, and therefore, the study reported only early outcomes. However, all patients within the region are treated in the same hospital including those who develop complications after discharge; therefore, no complications went undetected. In this study, we did not evaluate functional outcomes after discharge. The potential advantage of RS to functional recovery after discharge should be evaluated in a prospective study.

In conclusion, during the 9-year study period, RS replaced OS and LS in the treatment of rectal cancer in our institution. This was achieved without compromising the early outcomes and adequacy of excision. RS was associated with reduction in blood loss and length of stay at the hospital. In addition, patients who underwent RS had lower conversion-to-open rate compared to those treated with LS.

Table 1. Preoperative characteristics stratified by operative technique; OS = open surgery, LS = laparoscopic surgery, RS = robotic surgery

Parameter	OS N = 53	LS N = 101	RS N = 166	P (OS vs. LS)	P (OS vs. RS)	P (LS vs. RS)
Sex, male	33 (62%)	60 (60%)	111 (67%)	0.730	0.539	0.218
Age, years	67 ± 10	66 ± 11	69 ± 9	0.492	0.455	0.059
BMI, kg/m ²	28 ± 5	26 ± 4	26 ± 5	0.059	0.025	0.589
ASA class				0.044	0.373	0.092
- Low risk (1-2)	19 (44%)	63 (62%)	86 (52%)			
- High risk (3-4)	24 (56%)	38 (38%)	80 (48%)			
- Missing	10					
Preoperative chemoradiotherapy	31 (61%)	65 (65%)	121 (73%)	0.403	0.048	0.192
Tumour location				0.018	<0.001	0.001
- Rectosigmoid	17 (32%)	18 (18%)	6 (4%)			
- Upper rectum	4 (8%)	26 (26%)	38 (23%)			
- Mid-rectum	7 (13%)	18 (18%)	51 (30%)			
- Lower rectum	25 (47%)	39 (39%)	71 (43%)			

Data are presented as n (%) or mean ± standard deviation.

ASA = American Society of Anesthesiologists, BMI = Body Mass Index

Table 2. Operative technique and surgical parameters; OS = open surgery, LS = laparoscopic surgery, RS = robotic surgery

Parameter	OS N = 53	LS N = 101	RS N = 166	P (OS vs. LS)	P (OS vs. RS)	P (LS vs. RS)
Procedure type						
- AR	33	68	105			
- APR	19	30	49			
- ELAPE			11			
- Hartmann's procedure	1	1				
- Panproctocolectomy		2	1			
- Multiorgan resection	11	5	7			
Conversion to OS		12 (12%)	3 (1.8%)			<0.001
Hybrid procedure		1 (1.0%)	1 (0.6%)			
Operation time*, min	197 ± 63	221 ± 63	258 ± 62	<0.001	<0.001	0.162
Blood loss volume*, ml	655 ± 484	347 ± 315	237 ± 287	<0.001	<0.001	0.003

Data are presented as n (%) or mean ± standard deviation.

* = Multiorgan resections are not included in the analyses.

AR = Anterior Resection, APR = Abdominoperineal Resection, ELAPE = Extralevator

Abdominoperineal Excision

Table 3. Complications and early outcomes; OS = open surgery, LS = laparoscopic surgery, RS = robotic surgery

Parameter	OS N = 53	LS N = 101	RS N = 166	P (OS vs LS)	P (OS vs RS)	P (LS vs RS)
All patients						
All complications	35 (66%)	58 (57%)	85 (51%)	0.302	0.109	0.593
Minor complications	23 (43%)	44 (44%)	63 (38%)	1.000	0.520	0.371
Major complications	12 (23%)	14 (14%)	22 (13%)	0.180	0.126	1.000
Patients who had PO-CRT	N = 31	N = 66	N = 121			
All complications	25 (81%)	43 (65%)	69 (57%)	0.126	0.047	0.373
Minor complications	17 (55%)	35 (53%)	51 (42%)	1.000	0.229	0.169
Major complications	8 (26%)	8 (12%)	18 (15%)	0.140	0.181	0.664
Length of hospital stay, d	13.7 ± 8.2	9.2 ± 6.1	8.7 ± 7.0	<0.001	<0.001	0.188
≤ 5 d	3 (6%)	27 (27%)	66 (40%)			
6 – 10 d	21 (40%)	42 (42%)	64 (39%)			
≥ 11 d	29 (55%)	32 (32%)	36 (22%)			
Anastomotic leakage*	2/33 (6%)	3/68 (4%)	9/105 (9%)	0.506	0.632	0.170
30-day or in-hospital mortality	1 (1.9%)	2 (2.0%)	2 (1.2%)	1.000	1.000	1.000

Data are presented as n (%) or mean ± standard deviation.

* = Includes only patients who received an anastomosis during the index procedure

PO-CRT = Preoperative chemoradiotherapy

Table 4. Summary of pathological findings; OS = open surgery, LS = laparoscopic surgery, RS = robotic surgery

Parameter	OS N = 53	LS N = 101	RS N = 166	P (OS vs LS)	P (OS vs RS)	P (LS vs RS)
Grade				0.414	0.024	0.257
- 1	6 (13%)	6 (7%)	7 (5%)			
- 2	37 (79%)	78 (87%)	139 (93%)			
- 3	4 (9%)	6 (7%)	4 (3%)			
- Missing	6	11	16			
Margins						
- Proximal \geq 10 cm	34 (74%)	70 (78%)	116 (77%)	0.671	0.692	1.000
Missing	7	11	16			
- Distal \geq 1 cm	42 (91%)	84 (93%)	147 (98%)	0.861	0.078	0.138
Missing	7	11	16			
- Circumferential \geq 1 mm	37 (84%)	80 (91%)	143 (95%)	0.529	0.045	0.417
Missing	9	12	16			
Number of lymph nodes	16 \pm 12	19 \pm 13	18 \pm 10	0.167	0.066	0.674
TNM classification						
T-class				0.197	0.202	0.450
- 0	7 (13%)	11 (11%)	16 (10%)			
- 1	6 (11%)	6 (6%)	20 (12%)			
- 2	12 (23%)	31 (31%)	50 (30%)			
- 3	25 (47%)	47 (47%)	68 (41%)			
- 4	3 (6%)	6 (6%)	8 (5%)			
- Tis			3 (2%)			
- Missing			1 (1%)			
N-class				0.063	0.166	0.722
- 0	32 (60%)	78 (78%)	122 (73%)			
- 1	16 (30%)	15 (15%)	31 (19%)			
- 2	5 (10%)	8 (8%)	13 (8%)			
M-class				0.075	0.127	0.603
- 0	46 (87%)	98 (98%)	159 (95%)			
- 1	5 (9%)	3 (3%)	7 (5%)			
- Missing	2 (4%)					

Data are presented as n (%) or mean \pm standard deviation.

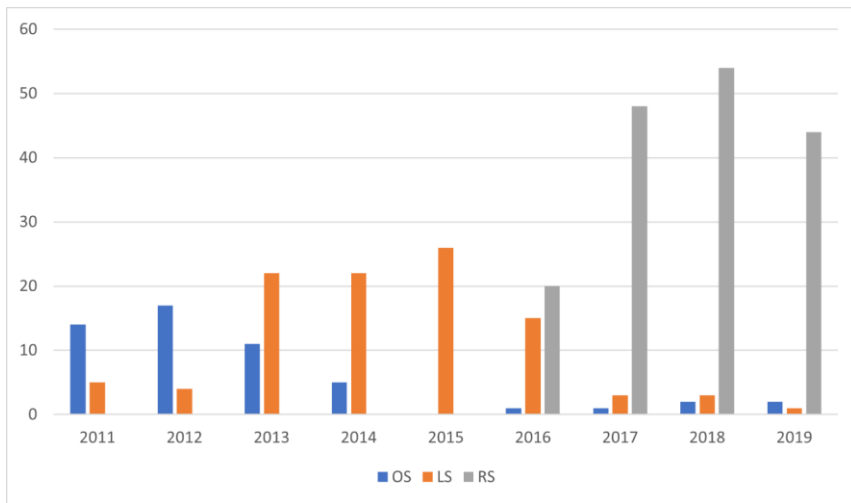


Figure 1. The numbers of procedures during the study period representing the transition from OS (open surgery) to LS (laparoscopic surgery) and to RS (robotic surgery).

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