Robotic surgery for rectal cancer as a platform to build on: review of current evidence

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Abstract

Laparoscopy in colorectal surgery reduces the rate of postoperative complications, shortens the length of stay in hospital, and improves the quality of patient care. Despite these established benefits, the technical challenges of rectal resection for cancer have resulted in most operations being performed through open surgery in the USA. Moreover, controversy in the current literature questions the oncologic safety of a laparoscopic approach for rectal cancer. How then can surgeons innovate to overcome the technical challenges while preserving the critical oncological outcomes of high-quality rectal cancer surgery? Robotics may be a platform that allows us to overcome the technical challenges in the pelvis while maintaining both oncological outcomes and the benefits of a minimally invasive technique. Current evidence suggests that the quality of total mesorectal excision, the rates of circumferential margin involvement, and postoperative outcomes are comparable between robotic and laparoscopic surgery. While a robotic approach demonstrates lower conversion rates and reduced surgeon workload, the operative time is longer and initial costs are higher; however, time and future science will determine its true benefits. We review the current state of robotic surgery and its impact on rectal cancer surgery.

Keywords Rectal cancer · Total mesorectal excision · Minimally invasive surgery · Robotic surgery · Robotic platform

Introduction

Laparoscopy has expanded rapidly in the field of colon surgery and is now considered the standard of care for elective colonic resections in well-resourced countries [1]. The laparoscopic benefits of better postoperative short-term outcomes including functional recovery, pain and use of narcotics, complications, and shorter hospital stay have driven this change [2, 3]. Despite these obvious benefits, the use of laparoscopy for rectal cancer surgery is challenged. Technical difficulties, the need for extensive training, and cancer biology have contributed to stagnant implementation, with successful adoption only in high-volume centers in the USA [4]. Challenges related to the narrow anatomy of the pelvis and complex tumor morphologies, coupled with the limited nature of straight laparoscopic instruments, make tackling complex pelvic disease difficult.

Concerns about the oncologic safety of laparoscopic surgery (LS) for rectal cancer have been raised, according to several landmark randomized controlled trials (RCTs) comparing LS to open surgery (OS) (9, 10). The CLASICC trial demonstrated higher rates of circumferential resection margin (CRM) positivity (12%) in LS than in OS (6%) for anterior resection [5]. However, this difference has not impacted local recurrence or survival [6]. On a positive note, both the COLOR II and COREAN trials demonstrated no difference in CRM positivity and completeness of total mesorectal excision (TME) between the two groups and the long-term outcomes were comparable [7, 8]. All five RCTs demonstrated consistently good results for upper rectal cancer, although surgical outcomes for low rectal tumors need improvement [9]. Despite the apparent controversy, the basic facts for most surgeons in the field demonstrate a more rapid adoption of robotic approaches, which today seem to outpace LS [10]. Many surgeons, including the author group, believe that the proven short-term benefits of MIS and the long-term results of RCTs are proof enough to declare minimally invasive surgery (MIS) for rectal cancer safe and feasible in trained hands [11, 12]. This review outlines the limits and benefits, both potential and demonstrated, of robotic

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surgery over a laparoscopic approach in the treatment of rectal cancer.

Robotic surgery in the treatment of rectal cancer

The robotic platform has been developed in an attempt to overcome the limitations of LS, while maintaining the advantages of MIS. Surgeons can improve their technical skills in laparoscopy, but the opportunity to leap forward as a platform has remained unchanged since the early 90s. However, robotic surgery has innovated on its design providing potential new value in iterations of the platform since the FDA approved it in 2000. Today, the da Vinci Surgical System® (Intuitive Surgical, Sunnyvale, CA, USA) is the prevailing system although there are new entrants to this market. The surgeon sits at a console with the potential benefit of three-dimensional high-definition vision. From the console, the surgeon navigates four arms (typically three instrumental and one endoscope) without the physical limits of straight-lined instruments or the stress of retraction pressure experienced in laparoscopic surgery. The wristed instruments have seven degrees of motion, allowing fluidity of movements and accuracy of dissection, especially in a narrow pelvis [13].

The first robotic TME was described in 2006 by Pigazzi et al. [14]; since then, many other case series have been published on the safety and feasibility of RS in the treatment of rectal cancer. The interest within the scientific surgical community, as demonstrated by the progressively growing number of publications per year, highlights the widespread adoption of this new technology. Likewise, the number of robotic cases in the USA now exceeds that of LS for rectal cancer and it is the only technique growing in popularity [15]. The ROLARR study, which assigned 471 patients to undergo either conventional laparoscopic or robotic-assisted resection, remains the only adequately powered RCT on RS for rectal cancer published in the literature [16]. This trial was powered to investigate conversion rates as a potential beneficial effect of RS and revealed a lower conversion rate in the RS group, although it did not reach significance (8.1% vs. 12.2%). While male gender, high BMI, and low anterior resection were risk factors for conversion, the two approaches were comparable in terms of quality of resection, CRM positivity, and short-term postoperative outcomes. Although the ROLARR is considered the strongest available evidence comparing RS and LS, the results have been questioned because of the potentially confounding effect of the learning curve, which may have impacted the results [17].

Current studies (large retrospective series, smaller case series, and single-center reviews and meta-analyses) on RS for rectal cancer focus on a variety of endpoints including

CRM positivity, quality of TME, operative time, conversion rates, postoperative morbidity, length of stay, urologic and sexual functional recovery, surgeon workload, learning curve, and costs.

Circumferential resection margin, quality of TME, and long-term outcomes

The plane of surgery achieved during TME [graded as good (mesorectal), intermediate (intramesorectal) and poor (muscularis propria plane)] and CRM involvement (< 1 mm between the deepest extent of tumor invasion into the mesorectal fat and the inked surface on the fixed specimen) are established surgical quality metrics and prognostic factors for local recurrence [18, 19]. The ROLARR trial reported no significant difference in TME completion (poor TME: 9.3% for RS and 5.2% for LS) and CRM involvement (12% for RS; 14% for LS) [16]. A recently published RCT from Korea comparing RS and LS showed comparable results for both outcomes (80.3% vs. 78.1% complete TME and 6.1% vs. 5.5% CRM positivity) [20]. Slightly better results favoring RS in reducing CRM involvement were found in four recent large retrospective cohort studies [21–24] and in one prospective cohort study [25]; however, none achieved significance (Table 1). Completeness of TME was comparable between the two techniques in most series [26–30] (Fig. 1). Two recent meta-analyses confirm these findings [31, 32]. Because of the limited history of RS for rectal cancer, there are few studies that report long-term outcomes. Two retrospective studies compared 3-year and 5-year overall survival and found similar rates in the RS and LS cohorts [33, 34].

Operative time and conversion rate

In the three largest single-center cohort studies comparing the operative times for RS and LS TME, two [23, 35] reported longer operative times for RS, while one showed no difference [24]. In two systematic reviews and meta-analyses including 2224 and 1074 patients, respectively, undergoing rectal resections, RS was associated with significantly longer operative times [31, 32]. Operative times for RS are affected by the time-consuming procedure of docking and instrument positioning. Our series evaluating the increased operative time required for RS, including our own learning curve of 260 robotic cases, demonstrated no increase in postoperative morbidity [36]. With time, experience, and innovations in the platform design (da Vinci Xi®), the operative times are likely to decrease further [37, 38].

Conversion to OS has a strong impact on both short- and long-term outcomes [39]. Hence, reducing conversion rates is of critical importance in MIS for rectal cancer.

Table 1 Circumferential resection margin involvement and conversion rates

References	Year	Study design	Number of patients (RS/LS)	Positive CRM, <i>n</i> (%)		Conversion rates, <i>n</i> (%)	
				RS	LS	RS	LS
Kang [37]	2013	Prospective cohort study	165/165	7 (4.2)	11 (6.7)	1 (0.6)	3 (1.8)
Speicher [52]	2015	National cancer database review	956 /5447	45 (5.5)	231 (4.9)	91 (9.5)	951 (17.5)*
Kim [35]	2017	Retrospective cohort study	224/224	9 (4.0)	11 (4.9)	0 (0.0)	2 (0.9)
Valverde [33]	2017	Retrospective cohort study	65/65	4 (6)	7 (11)	3 (5)	11 (17)*
Jayne [28]	2017	RCT	235/224 230/236	12 (5.1)	14 (6.3)	28 (12.2)	19 (8.1)
Rouanet [36]	2018	Retrospective cohort study	200/200	16 (8)	21 (11)	4 (2.0)	19 (9.5)*
Kim [32]	2018	RCT	66/73	4 (6.1)	4 (5.5)	1 (1.5)	0 (0.0)
Crolla [47]	2018	Retrospective cohort study	168/184	8 (4.8)	4 (2.2)	3 (1.8)	23 (12.5)*
Liu [34]	2019	Retrospective cohort study	80/116	0 (0.0)	1 (1.0)	1 (0.8)	4 (3.5)

Recent RCTs and large cohort studies (> 50 patients per group) comparing robotic versus laparoscopic surgery for rectal cancer

CRM circumferential resection margin, RCT randomized controlled trial, RS robotic surgery, LS laparoscopic surgery

*Significant difference between RS and LS ($p < 0.05$)

Fig. 1 Completeness of total mesorectal excision

Although the ROLARR trial failed to demonstrate a reduced risk of overall conversion for RS, significantly lower conversion rates were revealed in several subgroups, such as obese patients, men, and patients with low rectal cancer [16]. These results were confirmed by our institutional analysis, which revealed lower conversion rates in both obese and non-obese patients [40]. A National Cancer Database review of 16,275 patients undergoing robotic, laparoscopic, or open low anterior resection reported significantly lower conversion rates in the RS group [41]. The majority of large retrospective cohort series [20–24, 35, 41] and two recent meta-analyses [31, 32] confirmed these results (Table 1). Thus, RS seems to be associated with lower conversion rates than LS for rectal cancer.

Postoperative morbidity and length of stay

Numerous prospective and retrospective cohort studies have found no significant difference in postoperative complication rates or length of hospital stay between RS and LS patients [20–22, 32–42] (Table 2). These findings were confirmed by the ROLARR trial, where 32.4% of patients experienced some complication within 30 days: 31.7% in the conventional LS group and 33.1% in the RS group [16]. Multiple meta-analyses have been conducted, but the results indicate no superiority of either technique in terms of postoperative short-term outcomes [31, 32, 42]. These results were challenged by our institutional series, which revealed significantly lower postoperative morbidity in the RS group (Crippa et al., Ann Surg 2020, in press).

Technical considerations of splenic flexure mobilization

Splenic iatrogenic injury during flexure mobilization occurs in approximately 0.4% of rectal resections and warrants total splenectomy in the majority of cases [43]. Given this non-negligible morbidity, the necessity to routinely mobilize the splenic flexure remains controversial. Although some authors believe that splenic flexure mobilization is necessary to ensure a tension-free and well-vascularized anastomosis [44], most studies suggest that routine splenic flexure takedown does not confer any advantages in terms of postoperative morbidity and oncological outcomes among rectal cancer patients [45–47]. When splenic flexure mobilization is necessary, LS appears to be associated with a lower rate of incidental splenic procedures than OS [48]. While forced traction for adequate exposure during open

Table 2 Postoperative morbidity and length of stay

References	Year	Study design	Number of patients (RS/LS)	Postoperative complications, n (%)		Length of stay, mean (sd/range)	
				RS	LS	RS	LS
Kang [37]	2013	Prospective cohort study	165/165	34 (20.6)	46 (27.9)	10.8 (5.5)	13.5 (9.2)
Speicher [52]	2015	National cancer database review	956 /5447	–	–	5 (4–7)	5 (4–7)
Kim [35]	2017	Retrospective cohort study	224/224	77 (34.3)	56 (25)	13.5 (14.1)	13.8 (10.9)
Valverde [33]	2017	Retrospective cohort study	65/65	27 (42)	32 (49)	11 ($\pm$ 8)	12 ($\pm$ 10)
Jayne [28]	2017	RCT	236/230 237/234	78 (33.1)	73 (31.7)	8.0 (5.85)	8.2 (6.03)
Rouanet [36]	2018	Retrospective cohort study	200/200	51 (25.5)	48 (24.0)	10 (4–69)	11 (2–60)*
Kim [32]	2018	RCT	66/73	23 (34.8)	17 (23.3)	10.3 (3.4)	10.8 (7.4)
Crolla [47]	2018	Retrospective cohort study	168/184	71 (42.2)	111 (60.3)	6 (2–67)	7 (3–104)
Liu [34]	2019	Retrospective cohort study	80/116	6 (7.5)	24 (20.6)	11.20 (5.80)	14.72 (6.90)*

Recent RCTs and large cohort studies (> 50 patients per group) comparing robotic versus laparoscopic surgery for rectal cancer

CRM circumferential resection margin RCT randomized controlled trial, RS robotic surgery, LS laparoscopic surgery

*Significant difference between RS and LS ($p < 0.05$)

procedures represents the most important reason for iatrogenic injury, better and magnified visualization of the spleen and its attachments provided by the laparoscopic approach helps the surgeon avoid unnecessary traction [49].

RS provides similar advantages in terms of improved anatomic visualization leading to controlled traction. Recent studies suggest that through improved maneuverability conferred by the fourth-generation robotic platform, takedown of the splenic flexure can be efficiently performed and standardized [50, 51]. In our institution, the splenic flexure is addressed in a medial to lateral fashion, taking the inferior mesenteric vein at the inferior border of the pancreas, mobilizing the colonic mesentery off Gerota's fascia, entering the lesser sac above the pancreas, and continuing the mesenteric dissection along the inferior border of the pancreas to the splenic hilum. Once the medial dissection is complete, the lateral attachments are taken along with the disconnection of the omentum from the transverse colon.

Urogenital function

Sexual dysfunction after rectal cancer surgery occurs in up to 80% of men and 60% of women as a consequence of nerve damage during TME with the additional effect of preoperative radiation and psychological impairment in the presence of a stoma [52–54]. The magnified vision combined with increased precision and steadiness of movements through the robotic platform may facilitate better dissection of small anatomical structures such as the inferior hypogastric plexus [55]. Several small prospective and retrospective comparative studies demonstrated earlier recovery of normal voiding

and sexual function after RS than after LS, particularly in men [56, 57]. These results were confirmed more recently by a RCT [20] and a prospective propensity score-matched survey study [57]. Although not powered to answer these questions, both the ROLARR trial and the largest retrospective series to date have found no significant differences between the two groups in these specific outcomes [58]. Potential advantages of the robotic approach regarding genito-urinary functional recovery need further investigation through well-designed studies and standardized functional assessments.

Surgeon workload

The surgeon must deal with the growing challenge of complex procedures in the setting of new treatment modalities, the need to master technical skills, and the economic pressure to achieve outstanding clinical results. Current evidence suggests a negative association between surgeon distress and clinical performance, potentially impacting the quality of care [59]. LS was introduced and promoted to improve patient care and less attention was paid to the impact of this new technology on surgeon workload and ergonomics [60]. In fact, both mental demand and physical effort experienced by surgeons are higher during LS than OS, especially when performing challenging procedures [61]. A recent study from Mayo evaluating a surgeon's perspective on open, laparoscopic, and robotic proctectomy demonstrated that robotic procedures required significantly less mental and physical effort, resulting in a reduced workload [62]. These results may be explained by the special design of the robotic platform, which combines both outstanding visuals and four arm

controls within a single comfortable console. Future studies should assess if these surgeon-related benefits will translate into better clinical outcomes.

Learning curve and costs

It has been hypothesized that the advantages of the robotic platform regarding ease of use, improved range of motion, and better visualization may have an impact on the learning curve to acquire adequate surgical competence (16). The learning curve for robotic colorectal procedures is recognized to be multiphasic, with an initial training phase, followed by a second more stable progression phase, and finally by a consolidated third phase [63]. In a recent large cohort of robotic rectal resections, Sng et al., recommended at least 35 cases in the first phase, 93 cases in the second phase, and 69 cases in the third phase, with a mean operative time of 4.6 h [64]. Other studies have explored the learning curve of RS for rectal resections, reporting a range of 25–35 cases for the learning period [28, 65], although at least 40 cases were required to obtain sufficient expertise in previous papers that focused on the learning curve of LS [65, 66]. Since laparoscopic experience plays an important role in proficiency in RS, comparing the learning curve between these two techniques could be difficult and the results should be interpreted with caution.

One of the prevailing arguments against acquisition of a robotic platform involves cost. Arguably, fixed costs related to the platform, including purchase and maintenance, inevitably demand an initial and sustained financial commitment [67]. However, several recent studies have revealed comparable expenses of OS, LS, and RS, taking into account intraoperative costs, costs of postoperative care, and duration of hospital stay. In particular, decreased conversion and postoperative complication rates, along with a shortened length of stay, may contribute to cost-efficacy [68, 69]. Furthermore, costs may decrease with surgical experience [70, 71]. In rectal cancer surgery, it is particularly important to put surgery-related costs into perspective considering that the most significant cost drivers are chemo- and radiotherapies. Surgeons may harm themselves and their patients by railing against surgical tool innovation when that represents less than 5% of the total cost of care for a patient with rectal cancer in the USA.

Conclusions

RS for the treatment of rectal cancer appears to be oncologically safe and feasible with equal outcomes to other modes of surgery in both short-term morbidity and pathological surrogate markers of quality. Further research on both

short- and long-term oncological outcomes is needed. The potential and demonstrated benefits of RS must be taken seriously as RS represents one of the few positively iterated platforms in surgery. Technical advantages over LS include improved three-dimensional vision, articulation of instruments, improved surgeon ergonomics, and better accessibility to narrow spaces such as the pelvis. Moreover, institutions like ours have demonstrated that these benefits lead to lower levels of mental and physical workload for the surgeon. As we view the landscape and trends in MIS surgery, surgeons are choosing Robotics as the “go-to” MIS approach for rectal cancer. These trends may be influenced by the findings of many institutional retrospective series, which demonstrate lower conversion rates and a shorter learning curve. While operative time and cost remain a challenge, one must remember the COST trial [72], in which the same arguments were made for LS. Today, those detracting voices for innovation have been drowned out by science and progress.

Future adequately designed and powered studies are needed to define the potential benefits of RS over LS. We are convinced that RS represents a platform to build on and one that is clearly demonstrating value for patients and surgeons.

Compliance with ethical standards

Conflict of interest Pietro Achilli and his co-authors have no conflicts of interest to declare.

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