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Review

ROBOTIC-ASSISTED LAPAROSCOPIC SURGERY FOR RECTAL CANCER (RALS): A REVIEW OF THE LITERATURE

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Summary

Surgical treatment of rectal cancer is still difficult even in big centers. The limited pelvic space, problematic operative exposure, complex surgeries with more common anastomotic complications make the results unsatisfying. After the concept of total mesorectal excision (TME) was introduced by Heald, the results have improved dramatically. Advances in technology added further excitement about awaited promising results. Surgeons tried to apply all new methods to search for the best treatment: – atraumatic, painless, safe, with low recurrence rates, fast recovery, with an acceptable price, and easy to learn or teach. Robotic-assisted laparoscopic surgery (RALS) was introduced to overcome the limitations of conventional laparoscopic and open surgery and improve on their main advantages.

A non-systematic literature review on the articles on RALS in the PubMed and Scopus database was performed. RALS, robotic-assisted laparoscopic surgery, and rectal cancer keywords were used. The search was restricted to articles in English, with main endpoints of interest on short-term and long-term surgical results and oncological outcomes. Fifty-seven articles from Europe, the USA, and Asia were identified. RALS was tried in large series in patients with different pathology and showed its values. However, there are still many controversies on its superiority, cost, and advantages. RALS is safe and efficient in experienced hands. It could be superior to conventional laparoscopic surgery (CLS). Its advantages in oncological outcomes over CLS are to be proven in structured randomized clinical trials (RCTs).

Keywords: rectal cancer, robotic-assisted laparoscopic surgery, RALS, literature review

Introduction

Robotic surgery is a novel technique introduced and primarily employed to overcome the limitations of conventional laparoscopic and open surgery and improve on their main advantages [1]. Robotic surgery has been successfully used in different pathologies and has shown its values. Surgical treatment of rectal cancer is one of the most challenging fields for surgeons. Conventional laparoscopic surgery for rectal cancer is still challenging, even for experienced centers. Surgical teams worldwide attempt to find solutions to this problem. Since the concept of total mesorectal excision (TME) was introduced by Heald, rectal cancer surgery results have improved significantly [2]. With the advancement of technology, surgeons are trying to implement novel techniques to provide the best surgical and oncological results for patients and easy to learn and teach. The best surgical method for treating rectal cancer has not been established yet. Open surgery is accessible and safe but is more traumatic and painful.

Laparoscopy is atraumatic and painless for patients but has a steep learning curve and can be associated with a high conversion rate or higher positive resection margins when applied for rectal cancer. In RCT, laparoscopic rectal surgery (LRS) has failed to prove its non-inferiority compared to open rectal surgery (ORS). However, the COREAN study revealed favorable results for the laparoscopic modality. Similar findings were reported from the COLOR II trial and by other authors [3–6]. On the other hand, two other big RCTs - ALaCaRT and ACOSOG Z6051 have demonstrated the non-inferiority of LRS as compared with ORS [7, 8]. Robotic surgery provides an atraumatic approach with better ergonomics, a three-dimensional stable view controlled by the operator, improved articulation of instruments, physiologic tremor filtering that all promise better clinical, oncologic, and functional outcomes. Based on the robotic systems' technical advantages, many authors believe that this approach can overcome conventional laparoscopic surgery limitations for rectal cancer patients.

The history of robotic rectal surgery started with the first robotic-assisted surgery for benign pathology reported in 2001 by Weber. Five years later, Pigazzi et al. performed total mesorectal excision for malignancy using RALS [9]. After that, the number of robotic colorectal surgeries worldwide increased very fast. In Japan, the health care system covers the cost of robotic surgery and attracts more attention [10].

The role of robotic surgery for rectal cancer treatment has not been clarified, and the value of this technique is subject to debate. Most data are based on retrospective studies, case studies, and non-randomized trials, making analyses difficult.

Aim

The present article aimed to make a comprehensive review of the current literature on the role of robotic surgery in treating rectal cancer, also focusing on surgical and oncological results and the learning curve.

Materials and Methods

A non-systematic review of current literature via PubMed and Scopus search engines was performed to identify relevant articles. The keywords used were "robotic rectal cancer surgery" and "robotic-assisted laparoscopic surgery". We reviewed the current clinical, pathological, short, and long-term oncological outcomes after robotic surgery for rectal cancer. Conversion rates, functional outcomes, and the learning curve of robotic rectal cancer surgery were also analyzed. The eligibility of the studies was determined according to the following criteria: studies including data on patients above 18 years of age with proved rectal cancer (up to 15cm from the anal verge), who underwent robotic surgery with treatment intent – low rectal resection, abdominoperineal resection, and intersphincteric resection. All the studies, which met the inclusion criteria and included results from robotic surgery vs. laparoscopic and open surgery for rectal cancer, were reviewed and analyzed. Researches reporting data about colorectal cancer were included only if the data for rectal cancer only could be separated. An additional search was done in the reference list of the identified studies, restricted to articles written in English. Studies were included for analysis if their outcomes of interest were reported. Only full-text articles were included.

Results

Fifty-seven articles were identified from Europe, Asia, and the USA. Of these, 24 were original studies, 7 were review articles, and 11 were systematic reviews with meta-analyses. Included and reviewed were 9 RCTs. The included studies and extracted data are shown in Table 1.

Short term outcomes

Learning curve

The learning curve for robotic rectal surgery was assessed by using the cumulative sum (CUSUM) technique[11–14]. Most of the authors reported

Table 1. Clinical and pathological outcomes of robotic-assisted vs. conventional laparoscopic vs. open surgery for rectal cancer

First author/ Year	Study design	Number of patients RALS/CLS	CRM involvement (P-value)	Harvested Lymph nodes	Conversion rate (P-value)	Operative time
			RALS vs. LS			
1. Jayne/ 2017[17]	RCT	237/234	No difference (n.s.)		No difference (n.s.)	Longer in RALS
2. Prete/ 2017[20]	Meta-analysis	334/337	No difference (n.s.)	No difference	Lower in RALS (0.04)	Longer in RALS
3. Li/ 2017[34]	Meta-analysis	1726/1875	No difference (n.s.)	No difference	Lower in RALS (<0.01)	Longer in RALS
4. Cui/ 2017[21]	Meta-analysis	473/476	No difference (n.s.)	Not reported	Lower in RALS (0.02)	Longer in RALS
5. Sun/ 2016[23]	Meta-analysis	324/268	Lower in RALS (0.05)	No difference (P = 0.38)	Lower in RALS (<0.01)	No difference
6. Xiong/ 2015[24]	Meta-analysis	554/675	Lower in RALS (0.04)	No difference	Lower in RALS (<0.01)	No difference
7.Ohtani/ 2018 [1]	Meta-analysis	2068/ 2280	No difference	No difference	Lower in RALS	Longer in RALS
			RALS vs. OS			
8. Liao/ 2016[57]	Meta-analysis	498/576	No difference		Not stated	Longer in RALS

	LHS	Recurrence	Cost	Anastomotic leak	Complications	EBL	Overall survival
				RALS vs. LS			
1.	No difference	U	No benefit for RALS		No difference		
2.	No difference	U	U	No difference	No difference	Not reported	
3.	No difference	No difference	Not reported	U	No difference	Lower in RALS	No difference
4.	Shorter in RALS	Not reported	Not reported	Not reported	Lower in RALS	Lower in RALS	Not reported
5.	Shorter in RALS	Not reported	Not reported	Not reported	Lower in RALS	Not reported	Not reported
6.	No difference	Not reported	Not reported	No difference	No difference	No significant difference	Not reported (insufficient data)
7.	Not stated	No difference	Not reported	No difference	No difference	No difference	No significant difference
				RALS vs. OS			
8.	Shorter in RALS				No difference		

LHS – length of hospital stay, EBL - estimated blood loss, NS – not significant, U – unknown, RALS – robotic-assisted surgery, CLS – conventional laparoscopic surgery, RCT – randomized control trial that robotics' learning curve was shorter than in conventional laparoscopic surgery for rectal cancer.

In a report by Barrie et al., the learning curve for LRS ranged between 60 and 80 cases. In the RRS group, proficiency was achieved in 15 to 30 cases [14]. Huang et al. investigated patients with rectal cancer with more advanced disease after neoadjuvant chemoradiation and showed a shorter learning curve for RALS [15].

Corrigan et al. indicated another aspect of the learning curve. They showed that CRM was 2.9% for the learning curve and 4.6% after achieving surgical competence. They found that the CRM-positive rate was not influenced by the learning curve [16, 17].

Operative times

A longer operative time was a common short-term outcome in different reports [1, 15, 17–22]. Jayne et al. reported a mean operative time of 261.0 min for CLS (SD - 83.24) and 298.5 min (SD - 88.71) for RALS [17]. In a systematic review, Mak et al. reported mean operative time 37.5 min longer with RALS than with CLS [22].

Sun et al. reported no difference in the operative time (MD = 28.4; 95% CI = −3.48, 60.27; P = 0.08), based on a meta-analysis. Xiong et al. analyzed the pooled data of eight RCTs and NRCTs and found out that there was no difference between the operative time in the two groups (WMD 17.34, 95% CI [−18.11, 52.79], P=0.34)) [23, 24].

The longer operative times could be attributed to the docking time and changing of the robotic instruments. The various outcomes could be due to differences between operative procedures and proficiency in different institutions.

Estimated blood loss (EBL)

In a meta-analysis, Simillis C and al. reported that the robotic technique resulted in significantly lower operative blood loss compared with laparoscopic (29 mL vs. 58 mL) and open surgery (87 mL) techniques [18]. In a meta-analysis including 7 RCTs, Laiyuan Li reported data from 3 studies, including 250 patients: a smaller blood loss in RRS than the LRS. The difference, however, was not statistically significant −7.47; 95% CI: − 95.19 to 80.24; p = 0.87 [25] . A systematic review and meta-analysis reported by Lee SH found a lower blood loss in robotic intersphincteric resection (ISR) group (n - 273 (53.5%) than in the laparoscopic ISR group (n - 237 (46.5%) , (MD − 19.50, 95% CI − 33.51 to − 5.49, p = 0.006) [19].

Shiomi et al. evaluated robotic surgery in challenging situations, including lower rectal cancer cases in obese and non-obese patients. They reported no difference in operative times but significant advantages for EBL and other outcomes. In the group treated by RALS, there was no significant difference between blood loss in obese and non-obese patients (10.5 mL and 10.0 mL respectively, P=0.83, whereas a significant difference between obese and non-obese patients was found in the laparoscopy group (34.0 mL vs. 13.0 mL respectively, P= 0.02). These findings suggest promising results in the future if selected patients are operated on by better-specialized teams [26].

Conversion rate

Laparoscopy converted to open laparotomy bears an increased risk for complications. Although the results are better than in open surgery, the postoperative morbidity and mortality are higher than in laparoscopic groups without conversion [27, 28]. In a large retrospective cohort study, the conversion rates for the RALS were reported to be lower than for CLS, and the difference between the rates was statistically significant [29].

In a meta-analysis of 23 studies, Ohtani et al. showed conversion rates from RS to OS and LS to OS that ranged from 0 to 9.1% and 0 to 32%, respectively [1]. The conversion rate in RAS was significantly lower as compared to that in LS. The influence of conversion on both short-term and long-term survival outcomes in colorectal cancer patients is still unclear [30].

The ROLARR trial is a large multicentric randomized controlled trial comparing RS to LS. The authors aimed to compare robotic-assisted with conventional laparoscopic surgery for the risk of conversion to open surgery among patients undergoing resection for rectal cancer. A total of 471 patients (237 patients in CLS and 234 in RALS) with rectal adenocarcinoma, selected with intension for radical resection were enrolled and randomized for surgery at 29 centers across 10 countries, between January 7, 2011, and September 30, 2014. Surgeons with at least primary experience participated in the study. The overall conversion rate was 10.1 %, but no significant difference in the conversion rates between the groups was found. We must be aware of the results from subgroup analysis and the interactions between the treatment, on the one hand, and sex and BMI, on the other. The authors found obvious differences between the conversion rates for CLS and RALS groups in men with 25 conversions/156 patients (16.0%) in the CLS group and 14 conversions /161 patients (8.7%) in the RALS group (odds ratio and 95% CI – 0.455, p=0.0429). In female patients, they found 3 conversions /74 patients (4.1%) in the CLS group, 5 conversions/ 75 patients (6.7%) in the RALS group (odds ratio and 95% CI 2.022, p=0.3757). In obese patients, the interaction effects between treatment and BMI showed 10 conversions /54 patients (27.8%) for CLS group, and 10 conversions / 53 patients (18.9%) in the RALS patients (odds ratio and 95% CI - 0.583, p=0.2944). The authors concluded that the lower conversion rate than anticipated resulted in numbers of cases in almost all groups that were too small to produce statistically meaningful comparisons [17].

Anastomotic leak

AL is one of the major complications in oncological colorectal surgery. In the ROLARR trial, anastomotic leak incidence was 9.9% for the conventional laparoscopic group and 12.2% in the robotic-assisted laparoscopic group [17]. The range of anastomotic complications cited in the literature is wide [31]. In a series of 472 robotic and 8392 laparoscopic colorectal resections for malignant and benign pathology, Feinberg et al. found a 3.8% incidence of AL in the RS group [32] and 3.1% in laparoscopic patients (p = 0.34) [33].

Postoperative outcomes

The postoperative outcomes testified to the safety and feasibility of the method. Several meta-analyses showed no significant differences in the overall postoperative complication rates between RALS and CLS [1, 20, 34]. In the ROLARR trial, the intraoperative and postoperative complications 30 days after surgery showed no significant difference between the groups (OR = 1.02, 0.60 to 1.74, p = 0.94) [17]. At the same time, RALS was found beneficial in the analysis of Cui and Sun [21, 23].

The recovery outcomes do not distinctly point out an advantage of one of the operative methods. Li and al. analyzed 7 RCTs and reported shorter length of hospital stay (LOS) and first passing flatus shorter in the robotic group, but the difference was not statistically significant (95% CI: − 0.35 to 0.22; P = 0.66) [35, 25].

Pathological outcomes

Circumferential resection margin (CRM) positivity is well known as one of the main risk factors for local recurrence after rectal surgery. The mode of margin involvement is different, but in the presence of tumor cells less than 1 mm from the resection margin, the CRM is considered positive [32]. Jayne et al. reported a 5.7% CRM positivity (5.1% vs. 6.3% for RRS and LRS, respectively) but without a statistically significant difference between the groups [17]. A Korean RCT reported positive lateral margins in 6.1% in the robotic group compared with 5.5% for conventional laparoscopy [36].

As an essential factor for recurrence, the distal resection margin (DRM) was mainly investigated. Shirouzu et al. found an appropriate DRM of 1 cm for most patients with rectal cancer [37]. In patients with middle and low rectum cancers in stages II and III, after chemoradiation, Manegold found acceptable DRM less than 1cm with the necessity of high-quality TME dissection and R0 resection; consequently, the surgeon could be able to do more sphincter sparing procedure without compromising the oncologic results [38]. In a meta-analysis of seven, RCT Liao et al. found an advantage for robotic surgery over laparoscopy concerning DRM (0.29 vs. 1.37, p=0.003)[39].

Quality of mesorectal excision

Total mesorectal excision (TME) is a standard procedure nowadays, reflecting the surgical technique's quality. A good quality TME provides a low recurrence rate and increased overall survival [40, 41]. The quality of TME on the operative specimen is classified into complete, nearly complete, and incomplete according to the defects and irregularities of the mesorectal fascia and fat [42]. The surgical plane was also used for better description like mesorectal, intramesorectal, and muscularis propria plane [40].

Milone et al. conducted a meta-analysis of 12 studies comparing robotic and laparoscopic TME. [43].The analysis involving 1510 procedures showed a significant advantage of the robotic TME (OR=1.83, 95% CI 1.08-3.10, p= 0.03).

The superiority of one of the surgical approaches has not been clearly explained even in RCTs. Jayne et al. reported lower rates of complete TME in the robotic approach. In the ROLARR trial, complete TME was achieved in 75.4% of robotic cases and 80.3% of laparoscopic cases [17]. Kim et al. reported complete or nearly complete TME in 98.5% of patients treated robotic-assisted modality and 100% grade I and II in the laparoscopic modality (p = 0.599) [17, 36].

Urogenital Function

The urogenital function is crucial for the postoperative quality of life after rectal cancer surgery. The surgical damage to the pelvic autonomic nerves is considered a primary cause. TME has been established as a gold standard procedure for rectal cancer treatment since Heald et al. reported his results in 1982 [2]. Some studies [36, 44] have demonstrated favorable urogenital outcomes for robotic surgery vs. laparoscopic surgery in RCTs, while other studies did not show benefits [17, 45, 46].

Long-term outcomes

The versatility in difficult operative situations and the short learning curve for surgeons accustomed to open surgery made the robotic systems popular and most used, despite their short history. Therefore, only a few studies report long-term oncological outcomes. Cho et al. conducted a case-matched study comparing robotic and laparoscopic approaches and found no significant difference in the overall 5-year local and distal metastatic recurrence between the groups. The long-term tumor recurrence, oncologic and clinical outcomes, like overall survival and disease-free survival, are equivalent for five years in both groups [47]. In previous studies, the 3-year oncological outcomes are similar [48–50]. In a comparative study between laparoscopic and robotic surgery, Park et al. did not observe a significant difference between the groups for 5-year local recurrence rate (LRR), OS, and DFS rates [35].

Patriti et al. reported medium and short-term outcomes of a study enrolling 66 patients, with no differences observed in all categories [51]. Furthermore, long-term and oncological outcomes were investigated in several meta-analyses, and robotic surgery did not provide additional oncological advantages over conventional laparoscopic surgery. Both modalities could be used to treat rectal cancer with favorable outcomes [1, 19, 34]. Kim et al. reported the results from a retrospective study, including 732 patients: totally robotic - 272 and laparoscopic - 460). After propensity score matching (PSM) and multivariate analysis, they stated that the robotic approach had added some oncologic benefit and represented a significant favorable prognostic factor for OS and cancer-specific survival [52].

In Japan, Yamaguchi et al. and Katsuno et al. have recently reported beneficial long-term survival rates after treating a large group of patients. Despite some limitations of the study, the authors achieved better longevity at each stage than recorded in the national registry of patients with rectal cancer [53–56].

Thus, further prospective multi-center RCTs are essential for elucidating robotic surgery's role in terms of long term and oncologic outcomes. The results of the last phase of the ROLARR and COLLAR trials are expected.

Discussion

The robotic approach is feasible and ontologically safe, but there is no strong evidence for its superiority compared with conventional laparoscopy. There are a few randomized control trials reporting on this topic. The heterogeneity of endpoints, study designs, the inclusion of patients with heterogeneous pathology and comorbidities, non-standardized surgery render the interpretation of the results more challenging. One other thing to mention is that not all studies investigate all endpoints of interest. Data on treated patients and type of surgery is not reported, precise, or standardized.

Some studies include surgeons with varying degrees of experience, such as laparoscopy experts, but differing in their learning curve for robotics.

The robotic system provides significant advantages - improved operative view, articulating instruments, motion scaling, camera, and tree instruments controlled by the surgeon. This technique may be advantageous in the narrow pelvic space, but it still needs to be improved. The docking, undocking procedures, and changing of the instruments are time-consuming and make operative times and surgical procedures longer and more difficult.

Conclusion

Robotic surgery is a feasible and safe technique for rectal cancer patients. There is no substantial evidence supporting its superiority when compared with the conventional laparoscopic technique. The heterogeneity of the data makes its analysis complicated. Robotic surgery may benefit obese patients and male patients, who are at high risk for conversion. Further researches in this field are needed.

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