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REVIEW ARTICLE

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Robotic-assisted surgery for rectal cancer: Current state and future perspective

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Abstract

Interest in minimally invasive surgery has increased in recent decades. Robotic-assisted laparoscopic surgery (RALS) was introduced as the latest advance in minimally invasive surgery. RALS has the potential to provide better clinical outcomes in rectal cancer surgery, allowing for precise dissection in the narrow pelvic space. In addition, RALS represents an important advancement in surgical education with respect to use of the dual-console robotic surgery system. Because the public health insurance systems in Japan have covered the cost of RALS for rectal cancer since April 2018, RALS has been attracting increasingly more attention. Although no overall robust evidence has yet shown that RALS is superior to laparoscopic or open surgery, the current evidence supports the notion that technically demanding subgroups (patients with obesity, male patients, and patients treated by extended procedures) may benefit from RALS. Technological innovation is a constantly evolving field. Several companies have been developing new robotic systems that incorporate new technology. This competition among companies in the development of such systems is anticipated to lead to further improvements in patient outcomes as well as drive down the cost of RALS, which is one main concern of this new technique.

KEYWORDS

clinical outcome, minimally invasive surgery, rectal cancer, robotic surgery, technical advancement

1 | INTRODUCTION

Interest in minimally invasive surgery has increased in recent decades. Laparoscopic surgery has been extensively used in various types of surgery, including colorectal surgery. Several randomized controlled trials (RCTs) have been conducted to investigate the comparative oncological safety of laparoscopic surgery for colorectal cancer versus open surgery (OS).[1–3] These studies have suggested that laparoscopic surgery is associated with little blood loss, fast bowel recovery, and a short length of hospital stay compared with OS.[4,5] However, laparoscopic surgery has several drawbacks, including the requirement for straight and inflexible devices, unstable intraoperative views associated with holding of the scope and application of countertraction by assistants, and uncomfortable ergonomic positions. In addition, hand–eye coordination is difficult because of the fulcrum effect,[6] especially at sites distal to the abdominal wall. Two recent large, multicenter RCTs revealed higher rates of a circumferential resection margin (CRM) in laparoscopic surgery for rectal cancer than in OS,[7,8] which might be related to the high degree of technical difficulty in accurate performance of surgery within the narrow pelvic space.

Robotic-assisted laparoscopic surgery (RALS) was introduced as the latest advancement in minimally invasive surgery to overcome some of the disadvantages of conventional laparoscopic surgery (CLS). The advantages of robotic assistance include providing an immersive three-dimensional view, better ergonomics and enhanced dexterity with tremor filtration and motion scaling, instrument articulation, and a stable endoscope platform. Due to these advantages, RALS has the potential to provide better clinical, oncological, and functional outcomes in rectal cancer surgery and allow for precise dissection in the narrow pelvic space. In this review article, we state an overview of the history, current evidence from clinical studies, and future perspective of RALS for rectal cancer.

2 | RALS: A NOVEL FRONTIER IN MINIMALLY INVASIVE SURGERY FOR RECTAL CANCER

The most commonly used system for robotic surgery is the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA, USA). This system obtained FDA approval in 2000; since then, da Vinci models have been modified regularly. The current model, da Vinci Xi, was introduced in 2014 to ensure easier docking; a wider range of motion with its smaller, thinner arms; and better access to different anatomical regions. In addition, use of the da Vinci Table Motion with the da Vinci Xi allows surgeons to reposition patients with instruments in place within the abdomen and without undocking the robot. Other current features of the robotic system are the EndoWrist Stapler, the EndoWrist Vessel Sealer, and the integration of Firefly fluorescence imaging to assess blood perfusion and identify lymphatic vessels and other structures such as the bile duct or ureter. As of December 2017, the number of installed da Vinci series was 4409 throughout the world, including 579 in Asia.[9] Several new robotic systems have focused on improving current systems and incorporating new technology. The Telelap ALF-X by TransEnterix (Morrisville, NC, USA) provides direct force feedback that allows the surgeons to sense the applied force to the organ.[10] The Flex Robotic System by Medrobotics (Raynham, MA, USA) is intended for transluminal surgery and obtained FDA approval in 2018.[11] The SPORT Surgical System by Titan Medical (Toronto, Canada) has been developed for single-port access robotic surgery.

In the field of colorectal surgery, Weber et al.[12] performed the first robotic-assisted colectomy for benign disease in 2001, and Pigazzi et al.[13] reported the first robotic-assisted total mesorectal excision (TME) in 2006. The number of robotic colorectal procedures performed globally has rapidly increased. Because the public health insurance system in Japan has covered the cost of RALS for rectal cancer since April 2018, robotic-assisted rectal surgery has been attracting increasingly more attention.

3 | SHORT-TERM OUTCOMES

3.1 | Intraoperative outcomes

The use of RALS has been investigated in various colorectal procedures and compared with CLS and OS. Several studies have demonstrated that RALS is a safe and feasible approach in various colorectal procedures; however, robust clinical evidence supporting the benefit of robotic-assisted surgery for rectal cancer remains limited. The results from recent RCTs and meta-analyses of RALS vs CLS or OS for rectal cancer are summarized in Table 1.[14–20] Several recent meta-analyses have shown a significant difference in the outcomes between RALS and CLS for rectal cancer, including the rates of conversion to OS and positive CRM. Meanwhile, the recently published Robotic versus Laparoscopic Resection for Rectal Cancer (ROLARR) study, the first multicenter RCT comparing RALS versus CLS for rectal cancer, did not support the superiority of RALS over CLS. The ROLARR study showed no significant differences between RALS and CLS. These inconsistent conclusions may be caused by various differences in surgical procedures and proficiency among institutions. In addition, some meta-analyses showed a longer operation time for RALS. The docking and separation procedure for a robotic cart are time-consuming. The current robotic system, the da Vinci Xi, reduces repeated docking and makes docking easier and faster. These features are likely to further reduce the operative time for robotic rectal surgery.[21]

3.2 | Postoperative outcomes

Evaluating postoperative complications are essential for discussing the safety and adequacy of RALS. Recent meta-analyses have shown inconsistent conclusions in terms of postoperative complications. Several studies have shown no significant difference in the frequency of postoperative complications or length of hospital stay between RALS and CLS.[15,16,19] In contrast, two studies showed fewer postoperative complications and a shorter length of hospital stay in RALS than CLS.[17,18] In the ROLARR trial, there was no significant difference between RALS and CLS. No robust evidence of the benefit of RALS over CLS in terms of postoperative complications has yet been established. Anastomotic leakage reportedly occurred in 1.5%–12.2% of patients undergoing RALS and in 2.9%–10.8% of those undergoing CLS in a large cohort study including >200 RALS procedures.[14,22–28]

Although the ROLARR study could not demonstrate a lower conversion rate associated with RALS, the conversion rate was found to be lower in male patients, obese patients, and patients with distal cancer. This finding might reflect the technical difficulty in these patients. Because obesity is increasing globally, managing obese patients is clinically demanding. A recent systematic review showed that laparoscopic surgery for rectal cancer in obese patients is technically challenging because of the longer operative times, higher risk of postoperative complications, and higher rates of conversion to OS compared with non-obese patients.[29] Recent retrospective case-control studies that compared obese versus non-obese patients (body mass index of $\geq$30 vs <30 kg/m^2, respectively) undergoing robotic colorectal surgery consistently showed no difference in the conversion rate, rate of CRM, intraoperative or postoperative complications, or length of hospital stay.[30–34] Shiomi et al.[35] reported no significant difference in the operative times,

TABLE 1 Recent RCTs and meta-analyses comparing outcomes of robotic versus laparoscopic or open surgery for rectal cancer

First author	Year	Study design	Number of Patients		CRM involvement			Conversion rate		
			RALS	CLS	Result	P value	Difference	Result	P value	Difference
RALS vs CLS										
Jayne	2017	RCT	237	234	Odds ratio 0.78	N.S.	No difference	Odds ratio 0.61	N.S.	No Difference
Prete	2017	Meta-analysis	334	337	Risk ratio 0.82	N.S.	No difference	Risk ratio 0.58	0.04	Lower in RALS
Li	2017	Meta-analysis	1726	1875	Odds ratio 0.80	N.S.	No difference	Odds ratio 0.35	<0.01	Lower in RALS
Cui	2017	Meta-analysis	473	476	Risk difference −0.02	N.S.	No difference	Risk difference −0.05	0.02	Lower in RALS
Sun	2016	Meta-analysis	324	268	Odds ratio 0.50	0.05	Lower in RALS	Odds ratio 0.07	<0.01	Lower in RALS
Xiong	2015	Meta-analysis	554	675	Odds ratio 0.44	0.04	Lower in RALS	Odds ratio 0.23	<0.01	Lower in RALS
RALS vs OS			RALS	OS						
Liao	2016	Meta-analysis	498	576	Mean difference −0.22	N.S.	No Difference	Not Stated		

First author	Operative time			Length of hospital stay			Complication		
	Result (min)	P-value	Difference	Result (d)	P-value	Difference	Result	P value	Difference
Jayne	Mean difference 37.5	Not stated	Longer in RALS	Mean difference −0.2	N.S.	No difference	Odds ratio 1.04	N.S.	No difference
Prete	Mean difference 38.43	<0.01	Longer in RALS	Mean difference −0.61	N.S.	No difference	RALS 27.3%, CLS 26.7%	N.S.	No difference
Li	Weighted mean difference 57.43	<0.01	Longer in RALS	Weighted mean difference −0.69	N.S.	No difference	Odds ratio 1.02	N.S.	No difference
Cui	Mean difference 33.73	<0.01	Longer in RALS	Mean difference −1.07	<0.01	Shorter in RALS	Odds ratio 0.58	<0.01	Lower in RALS
Sun	Mean difference 28.4	N.S.	No Difference	Mean difference −1.03	<0.01	Shorter in RALS	Mean difference 0.65	0.04	Lower in RALS
Xiong	Weighted mean difference 17.34	N.S.	No Difference	Weighted mean difference −0.37	N.S.	No difference	Odds ratio 0.95	N.S.	No difference
Liao	Mean difference 55.76	<0.01	longer in RALS	Mean difference −2.10	<0.01	Shorter in RALS	Odds ratio 1.00	N.S.	No difference

CLS, conventional laparoscopic surgery; N.S., not significant; RALS, robotic-assisted laparoscopic surgery; RCT, randomized control trial.

conversion to laparotomy, estimated blood loss, or length of stay between patients with visceral obesity and non-obese patients treated by RALS, whereas the operative time, estimated blood loss, and length of hospital stay were significantly worse in the patients with visceral obesity treated by CLS. RALS and its advantages in dexterity, visualization, and surgeon ergonomics may help to overcome the challenges of CLS in obese patients.

4 | LONG-TERM OUTCOMES

Only a few studies have reported on long-term outcomes because of the comparatively short history of RALS for rectal cancer. RALS was compared with CLS in four studies and with OS in two studies.[23,24,36–39] Kim et al. reported that RALS was a good prognostic factor compared with CLS in terms of overall survival and cancer-specific survival. The potential benefits with respect to long-term outcomes will be addressed in phase 3 prospective RCTs currently in progress, such as the ROLARR trial and the comparison of laparoscopic vs robot-assisted for rectal cancer (COLRAR trial).

5 | UROGENITAL FUNCTION

In the current treatment of rectal cancer, surgeons focus on preserving the postoperative urinary and sexual function as well as achieving complete resection of the tumor because these functions are major factors associated with quality of life for patients treated with rectal cancer surgery. Intraoperative injury to the pelvic splanchnic nerves and inferior hypogastric plexus is the most important cause of urinary and sexual dysfunction. However, few studies have addressed the urogenital complications after RALS for rectal cancer. Luca et al. first reported the utility of RALS for preserving urinary and sexual function after TME.[40] They concluded that the benefits of RALS were probably due to the superior movements of the wristed instruments as well as the high-quality three-dimensional vision, both of which were helpful for identification and precise preservation of the neural component. Recent large cohort studies have shown that the rate of urinary retention after rectal cancer surgery is significantly lower in RALS than CLS.[22,23,28]

Several studies have assessed urinary and sexual function after RALS and CLS using the International Prostate Symptom Score (IPSS) and the International Index of Erectile Function questionnaire (Table 2).[14,41–45] Some of these studies showed significantly improved urinary continence at 3, 6, and 12 months after TME performed by RALS. In addition, most of them showed that RALS conferred significantly improved sexual function at 3, 6, and 12 months after TME compared with CLS. Kim et al. noted that markedly impaired urinary function was only found in male patients in both the RALS and CLS groups.[43] A significant difference in the IPSS between the RALS and CLS groups was only found in male patients at 6 months after TME. These results may indicate that preservation of pelvic autonomic nerves is more difficult in male patients because of their narrower and deeper pelvis. Male patients may benefit more from robotic surgery than female patients. Further large prospective studies with long-term follow-up are needed.

6 | LEARNING CURVE

It is essential to evaluate the impacts of the learning process when introducing new approach or technology in a clinical setting. Use of the cumulative sum methodology to evaluate the learning process of RALS for rectal cancer has been reported. To date, nine studies have reported the learning curve of RALS for rectal cancer using the cumulative sum method, providing a range of 15–44 cases for the learning period.[46–54] Conversely, previous studies that focused on the learning curve of laparoscopic rectal surgery estimated that approximately 40–90 cases are required to attain proficiency.[55–59] These results suggest that the learning curve for RALS may be shorter than that of CLS for rectal cancer.

Bege et al. reported that the learning process for laparoscopic mesorectal excision affects the first 50 cases most heavily in terms of postoperative complications. Improvements in surgical education are necessary for the patient's safety during the period of the surgical learning curve. The dual-console robotic surgery system represents a significant advancement in integrated teaching and supervising. In our experience, the major advantage of this system is the seamless transfer of control of instruments between the trainer and trainee. In addition, the trainer can provide virtual pointers to guide the trainee on the screen of the trainee's console. A recent study of urological surgery showed significant reductions in operating time, intraoperative complications, and postoperative complications when using a dual-console system than a single-console system.[60] Although studies evaluating dual-console robotic training systems are insufficient to date, they have the potential to change surgical training strategies in the near future.

7 | COSTS

One main disadvantage of RALS is the high cost of initial attainment and subsequent maintenance of the robotic system. Decreasing these costs for the widespread adoption of RALS is in demand. One study showed that increased proficiency in RALS shortens the operative time and lowers the overall costs.[61] Overall costs are also affected by the length of hospital stay, postoperative complication rates, and readmission rates. Hottenrott stated that the cost can be reduced by the accumulation of robotic cases in specialized centers as well as competition for machines or related instruments among companies.[62] To reduce the per-patient costs of RALS, hospitals need to raise the number of RALS; this can be accomplished by raising the number of surgeons. Moreover, several companies are trying to develop new robotic surgical systems, and this new competition will reduce the cost of RALS and lead to innovations of technology. With these improvements in clinical outcomes, the increasing expertise of surgeons in RALS, and the sustained efforts to reduce the costs of the robotic surgical system (attainment and maintenance costs), RALS may become the most cost-effective approach for rectal cancer.

8 | EXTENDED PROCEDURES

8.1 | Lateral lymph node dissection

Advanced lower rectal cancer metastasizes to the lateral lymph nodes of the pelvic wall with an incidence of 15.6%–20.1%.[63,64] A large multicenter RCT from Japan showed inferiority of mesorectal excision alone to mesorectal excision with lateral lymph node dissection (LLND). In that study, LLND reduced the incidence of local recurrence by 50% compared with mesorectal excision alone in patients with stage II and III rectal cancer.[65] According to the current Japanese guidelines, LLND is recommended for T3 and T4 tumors located distal to the peritoneal reflection.[64] LLND remains technically difficult because complete and thorough lymphadenectomy needs to be achieved while preserving the autonomic nerves to avoid urinary and sexual dysfunction in the complicated and narrow pelvic space. Because CLS for LLND is technically challenging and difficult, the standard approach to LLND is still OS. Yamaguchi et al. and Kim et al. reported that RALS was superior to OS and CLS for LLND because of the lower rate of urinary retention.[66,67] In addition, Yamaguchi et al. showed an excellent 5-year local relapse-free survival rate of 98.6% in robotic LLND compared with 90.9% in open LLND (P = 0.029).[39]

8.2 | Multivisceral resection for rectal cancer

Dissection beyond the TME plane and multivisceral resection for rectal cancer are also technically challenging extended procedures. Only two studies to date have addressed this procedure as performed by RALS.[68,69] Both Hino et al. and Shin et al. reported that multivisceral resection by RALS for rectal cancer was safe and

TABLE 2 Recent studies comparing urogenital outcomes of RALS versus CLS for rectal cancer

Outcome First author	Year	Study design	Number of patients RALS	CLS	Results	P-value
IPSS at 3 mo after surgery						
Lee SH	2015	Meta-analysis	44	54	Better in RALS	0.02
Broholm M	2015	Meta-analysis	76	86	Better in RALS	0.04
Kim HJ	2018	Case-matched study	130	130		N.S.
IPSS at 6 months after surgery						
Lee SH	2015	Meta-analysis	44	54		N.S.
Broholm M	2015	Meta-analysis	76	86		N.S.
Jayne D	2017	Randomized controlled trial	175	176		N.S.
Kim HJ	2018	Case-matched study	130	130	Better in RALS	0.02
IPSS at 12 months after surgery						
D'Annibale A	2013	Prospective study	30	30		N.S.
Lee SH	2015	Meta-analysis	60	69	Better in RALS	0.09
Broholm M	2015	Meta-analysis	92	101	Better in RALS	0.05
Wang G	2017	Randomized prospective study	71	66	Better in RALS	<0.05
IIEF at 3 months after surgery						
Lee SH	2015	Meta-analysis	32	29	Better in RALS	0.005
Broholm M	2015	Meta-analysis	64	64	Better in RALS	0.002
IIEF at 6 months after surgery						
Lee SH	2015	Meta-analysis	32	29	Better in RALS	0.03
Broholm M	2015	Meta-analysis	64	61	Better in RALS	<0.0001
Jayne D	2017	Randomized controlled trial	97	84		N.S.
IIEF at 12 months after surgery						
D'Annibale A	2013	Prospective study	30	30	Better in RALS	0.045
Wang G	2017	Randomized prospective study	71	66	Better in RALS	0.034

CLS, conventional laparoscopic surgery; IIEF, International Index of Erectile Function questionnaire; IPSS, International Prostate Symptom Score; N.S., not significant; RALS, robotic-assisted laparoscopic surgery.

feasible; the conversion rate to OS was 0.0% and 2.8%, respectively, and the median blood loss was 41 and 200 mL, respectively. Both studies showed that the rate of CRM involvement was 0%.

9 | CONCLUSION AND FUTURE PERSPECTIVE

Robotic-assisted rectal surgery provides several advantages over CLS by advanced technologies including articulating instruments and motion scaling, especially when performing an operation in the narrow pelvic space. Current evidence shows the robotic approach has been proven technically and oncologically safe and feasible for rectal cancer. Robotic systems also have great advantages in terms of surgical education using a dual console.

Although the initial results are promising, no overall robust evidence that RALS is superior to CLS or OS has yet been established. The current evidence shows that compared with CLS, robotic-assisted rectal surgery for obese patients (body mass index of ≥30 kg/m^2) and male patients with a narrow pelvis is associated with lower conversion rates to OS, a shorter operative time, less blood loss, and a shorter length of hospital stay. Future multicenter prospective RCTs that include surgeons who are uniformly skilled in RALS are needed to evaluate the benefits of robotic-assisted rectal surgery.

The future of RALS for rectal cancer is constantly and rapidly evolving. Next-generation robotic surgical systems are anticipated to further improve patients' outcomes.

DISCLOSURES

Conflict of Interest: All authors declare no conflict of interests for this article.

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