

Review Article

## Robotic-assisted Surgery: Expanding Indication to Colon Cancer in Japan

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### Abstract

In recent years, robotic-assisted surgery has demonstrated remarkable progress as a minimally invasive procedure for colorectal cancer. While there have been fewer studies investigating robotic-assisted surgery for the treatment of colon cancer than rectal cancer, evidence regarding robotic-assisted colectomy has been accumulating due to increasing use of the procedure. Robotic-assisted colectomy generally requires a long operative time and involves high costs. However, as evidence is increasingly supportive of its higher accuracy and less invasive nature compared to laparoscopic colectomy, the procedure is anticipated to improve the ratio of conversion to laparotomy and accelerate postoperative recovery. Robotic-assisted surgery has also been suggested for a specific level of effectiveness in manipulative procedures, such as intracorporeal anastomosis, and is increasingly indicated as a less problematic procedure compared to conventional laparoscopy and open surgery in terms of long-term oncological outcomes. Although robotic-assisted colectomy has been widely adopted abroad, only a limited number of institutions have been using this procedure in Japan. Further accumulation of experience and studies investigating surgical outcomes using this approach are required in Japan.

### Keywords

colon cancer, minimally invasive surgery, robotic-assisted surgery, robotic-assisted colectomy, laparoscopic colectomy, intracorporeal anastomosis

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### 1. Introduction

Surgical treatment for gastrointestinal disease has changed over the years, from the extended surgery in pursuit of curative treatment, which has attracted much attention in the past, to a focus on the development of surgical techniques that are both curative and function preserving, as well as on the standardization of surgical procedures. In recent years, remarkable progress has been made in minimally invasive surgery (MIS).

For many decades, studies comparing laparotomy and laparoscopic surgery (LS) for various diseases-especially malignant tumors-have been conducted, and the superiority and non-inferiority of LS versus laparotomy in terms of safety,

tolerability, and curability have been examined.

As a result, the equivalence of LS (i.e., MIS) and laparotomy (i.e., conventional surgery) has been demonstrated in many diseases; as such, LS has become widely performed. However, some diseases have shown non-inferiority in large randomized controlled trials, suggesting that LS is a surgical technique that has much room for improvement[1,2].

Robotic-assisted surgery (RAS) using a surgical robot has features not available in conventional LS, such as forceps with a wide range of motion, an anti-shake mechanism, high-resolution three-dimensional imaging, and functions including image stabilization and motion scaling, which are anticipated to overcome the problems of LS by enabling accurate and precise surgery with less invasiveness and more

**Table 1.** Clinical Outcomes between Robotic-assisted and Laparoscopic Colectomy.

Author	Ref	Year of publication	Year of registration	Type of study	Number of cases	Operation time (min) **	Blood loss (ml) **	Conversion rate	Postoperative complications (C-D, all grade)	Postoperative hospital stay (days) **	
Park	14	2019	2009–2011	Prospective randomized	RC	35	195	36	0%	17%	7.9
					LC	35	130*	47	0%	20%	8.3
Kulaylat	17	2018	2013–2015	Retrospective	RC	3864	203	NA	6%	15%	4.6
					LC	40063***	162*	NA	12%*	17%*	5.3*
Schootman	18	2017	2013–2015	Retrospective	RC	2233	236	NA	6%	24%	5.1
					LC	10844***	167*	NA	19%*	22%	5.3*
Ma	21	2019	1973–2018	Meta-analysis	RC	674	201	77	2%	21%	4.7
					LC	7095	134*	78*	6%*	26%*	4.2*
Solaini	22	2018	2000–2017	Meta-analysis	RC	869	206	69	4.0%	21%	5.8
					LC	7388	159*	80	5%*	23%*	6.1

C-D: Clavien–Dindo, LC: laparoscopic colectomy, NA: not available, RC: robotic-assisted colectomy, Ref: number of reference

\*: P<0.05, \*\*: mean, \*\*\*: propensity score-unadjusted cohort

freedom in the form required by the surgeon[3]. Against this background, the use of RAS has been spreading worldwide since the first report of robot-assisted total prostatectomy in 2001, and, in the field of colorectal cancer, both surgeries for colon and rectal cancers are rapidly becoming popular[4,5].

Colorectal cancer has been identified as the third most frequently diagnosed malignant disease in men and the second most in women worldwide; moreover, it is associated with a high mortality rate[6,7]. In Japan, the incidence of colorectal cancer is increasing. In fact, in recent years, it has become the third most common cause of cancer mortality and the most common cause of morbidity, thus making it a serious disease[8,9].

Surgical resection is the basis of colorectal cancer treatment, and the quality of surgery is an important factor. In Japan, surgical techniques for colorectal cancer have been well established and standardized since the days of laparotomy, and LS has also been widely performed. In this context, insurance programs have covered RAS for rectal cancer since April 2018, and the number of such procedures has rapidly increased. As a result, many studies supporting the utility of robot-assisted rectal resection have been published in Japan[10]. Among these published studies, a retrospective analysis of a large database in Japan by Matsuyama et al., which compared 2843 cases of robot-assisted low anterior resection, including 17,377 cases of laparoscopic low anterior resection for rectal cancer, found that the rate of conversion to laparotomy, the primary analysis endpoint, was significantly lower with RAS than with LS[11].

However, while the use of RAS to treat colon cancer is increasing along with rectal cancer treatment overseas, this procedure is not yet covered by insurance programs in Japan, and no comprehensive reports were found[12]. Currently, only a few medical institutions in Japan perform this

procedure as a private practice. Thus, in this present review, we discuss studies investigating the use of RAS to treat colon cancer published overseas and outline the introduction and expansion of indications for RAS for colon cancer in Japan.

## 2. Current Status of Robotic-assisted Colectomy Overseas

Since RAS for colon cancer was first reported in 2002, its safety and feasibility have been described in multiple studies conducted overseas[4,13-19]. In the United States, the Society of American Gastrointestinal and Endoscopic Surgeons guidelines state that, although the level of evidence for the recommendation is limited, RAS is recommended for proctectomy as well as colectomy procedures[20].

### Comparison of laparoscopic and robotic-assisted colectomy (Table 1)

At present, the majority of studies investigating robotic-assisted colectomy (RC) are retrospective in nature. In 2009, the results of one randomized comparative study were published. No differences between short- and long-term results for RC versus laparoscopic colectomy (LC) were identified, although the number of cases registered in the study was limited[14].

Comparative studies based on data from relatively large databases have recently commenced in addition to some ongoing prospective studies. Kulaylat et al. and Schootman et al. used data from the American College of Surgeons National Surgical Quality Improvement Program (2013-2015) to compare RC (3864 and 2233 cases, respectively) and LC (40,063 and 10,844 cases, respectively) using propensity scores to adjust for selection bias. The RC group demonstrated a lower conversion rate (6.0% versus [vs.] 11.5%, P

**Table 2.** Clinical Outcomes of Intracorporeal Anastomosis between Robotic-assisted and Laparoscopic Colectomy: Comparative Study.

Author	Ref	Year of publication	Year of registration	Type of study	Number of cases	Type of anastomosis	Operation time (min) **	Blood loss (ml) **	Conversion rate	Postoperative complications (C-D, all grade)	Postoperative hospital stay (days) **
Blumberg	15	2019	2003–2016	Retro-spective	RC 21 LC 101	ICA	330	100	0%	14%	3
Scotton	16	2018	NA	Retro-spective	RC 266 LC 160	ICA	253	NA	2%	0.5%***	NA
Lujan	13	2018	2009–2015	Retro-spective	RC 89 LC 135	ICA	190	38	2%	26%	4
Solaini	24	2019	2007–2017	Retro-spective	RC 305 LC 84	ICA	250	50	1%	23%	7
Sorgano	25	2021	2018–2019	Prospective	RC 48 LC 40	ICA	266	NA	0%	35.5%****	7.8
						ICA	254	NA	0%	30%****	7.4

C-D: Clavien–Dindo, ECA: extracorporeal anastomosis, ICA: intracorporeal anastomosis, LC: laparoscopic colectomy, NA: not available, RC: robotic-assisted colectomy, Ref: number of reference

\*:  $P < 0.05$ , \*\*: mean, \*\*\*: anastomotic leakage, \*\*\*\*: Clavien–Dindo more than grade II

$< 0.001$ ; and 5.7% vs. 18.8%,  $P = 0.050$ , respectively) and shorter postoperative length of hospital stay (4.6 days vs. 5.2 days;  $P < 0.001$ )[17,18].

In addition, Ma et al. and Solaini et al. reported a correlation between RC and reduced conversion risk, thus suggesting that RC is a superb tool for MIS[21,22]. Meanwhile, Ma et al. reported extended length of hospital stay in the LC group (mean difference [MD]  $-0.85$  days,  $P < 0.001$ ), low complication rates in the RC group (odds ratio [OR] 0.73%,  $P = 0.05$ ), reduced blood loss (MD  $-16.89$  mL,  $P < 0.001$ ), low conversion to open surgery rates (OR 0.34%,  $P = 0.008$ ), and shorter time to first flatus (MD  $-0.25$ ,  $P = 0.001$ )[21]. Similarly, an analysis by Solaini et al. identified a higher risk of conversion associated with LC (relative risk [RR] 1.7,  $P = 0.020$ ) and extended time to first flatus (standardized MD 0.85 days,  $P = 0.016$ )[22].

### **Intracorporeal anastomosis (Table 2)**

One of the major differences between RC and LC is the difficulty with intracorporeal operability. In particular, intracorporeal anastomosis (ICA) is deemed more difficult using LC than RC. Blumberg et al. retrospectively compared RC ( $n = 21$ ) and LC ( $n = 101$ ) procedures involving ICA. Although no significant difference was identified, the rates of complications and conversion rates were noted to be lower in the RC group than in the LC group (14% vs. 22% and 0% vs. 5%, respectively)[15].

In LC, postoperative recovery is quicker in ICA procedures than in extracorporeal anastomosis (ECA), and ICA is known to have low rates of postoperative complications, such as abdominal incisional hernia[23]. Similarly, the advantages of RC for ICA have also been reported[13,16,24,25]. Scotton et al. retrospectively compared the short-term results of robotic-assisted right hemicolectomy with ICA ( $n = 266$ )

and laparoscopic right hemicolectomy with ECA ( $n = 160$ ). Although surgical duration was longer in the RC group than in the ICA group (253 min vs. 210 min;  $P < 0.001$ ), time to first flatus (2.5 days vs. 3.1 days;  $P < 0.001$ ), time to first stool (3.2 days vs. 4.0 days;  $P < 0.001$ ), and oral intake of solid diet (4.0 days vs. 4.6 days;  $P < 0.001$ ) were determined to be shorter, and the rates of conversion (2.4% vs. 18.1%;  $P < 0.001$ ), anastomotic leakage (0.5% vs. 5%;  $P = 0.012$ ), and bleeding (0.5% vs. 4.4%;  $P = 0.024$ ) were lower[16].

Lujan et al. conducted a retrospective study comparing robot-assisted right hemicolectomy with ICA ( $n = 89$ ) and laparoscopic right hemicolectomy with ECA ( $n = 135$ ). For the RC group, surgical duration was longer, the incidence of abdominal incisional hernia was lower (0% vs. 7%;  $P = 0.155$ ), blood loss was reduced (38 mL vs. 61 mL;  $P = 0.004$ ), incision length was shorter (4.4 cm vs. 5.3 cm;  $P = 0.001$ ), and longer specimen length could be acquired (17.4 cm vs. 15.5 cm;  $P = 0.036$ )[13].

In a retrospective comparative study conducted by Solaini et al., which solely examined ICA in both RC and LC, RC ( $n = 305$ ) and LC ( $n = 84$ ) were compared. Although surgical duration was longer in the RC group (250 min vs. 160 min;  $P < 0.001$ ), the number of lymph nodes harvested was higher for RC (22 vs. 19;  $P = 0.028$ ), and re-admissions within 90 days were lower for RC (0.3% vs. 3.6%;  $P = 0.003$ ). No significant differences were noted between the groups in terms of time to first flatus, postoperative complications, and length of hospital stay[24].

Prospective research results have recently been reported. Sorgano et al. compared RC ( $n = 48$ ) with LC ( $n = 40$ ) and found no significant difference in terms of surgical duration (266 min vs. 254 min;  $P = 0.29$ ). The other short-term outcomes were comparable between standard LC and RC with

**Table 3.** Mid- and Long-term Oncologic Outcomes between Robotic-assisted and Laparoscopic Colectomy.

Author	Ref	Year of publication	Year of registration	Type of study	Number of cases	Operation time (min) **	Blood loss (ml) **	Conversion rate	Postoperative complications (C-D, all grade)	Postoperative hospital stay (days) **	DFS	OS
Park	14	2019	2009–2011	Prospective randomized	RC 35 LC 35	195	35.8	0%	17%	7.9	77%	91%
Spinoglio	28	2018	2005–2015	Retrospective	RC 101 LC 101	130*	46.8	0%	20%	8.3	84%	91%
Bae	30	2019	2008–2016	Retrospective, noncomparative	RC 43	279	NA	0%	28%	7.9	85%	77%
Siddiqi	31	2021	2015–2019	Retrospective, noncomparative	RC 77	236*	NA	7%*	34%	7.9	83%	73%
					RC 43	293	50	0%	26%	8	81%	94%
					RC 77	180	10	0%	12%	5	94%	94%

C-D: Clavien–Dindo, DFS: disease-free survival, LC: laparoscopic colectomy, NA: not available, OS: overall survival, RC: robotic-assisted colectomy, Ref: number of reference

\*: P < 0.05, \*\*: mean

ICA[25].

**Oncological perspectives on RC (Table 3)**

In research investigating RC to date, the main focus of discussion has been on the safety and feasibility. Moreover, this trend was similar in comparative studies of RC and LC. Many oncological studies consider short-term outcomes, with little consideration for long-term prognosis.

Overseas, a strategy involving complete mesocolic excision (CME) has recently focused on the management of colon cancer. The concept of CME is similar to that of lymphadenectomy, also known as “Japanese D3 dissection.” Some studies have compared CME with RAS[26,27]. Spinoglio et al. reported no significant difference in the long-term prognosis in terms of 5-year overall survival (77% vs. 73%) and 5-year disease-free survival (85% vs. 83%) in comparing RC and LC with CME[28]. In a systematic review, Petz et al. suggested that surgical specimens in RC with CME were obtained appropriately with oncological adequacy and also reported the non-inferiority of RC compared with LC in terms of long-term prognosis[29]. A comparison of mid- and long-term oncological outcomes between RC and LC is summarized in Table 3[14,28,30,31].

**Disadvantages of RC**

Some reported disadvantages of RC include lengthened surgical duration and high costs[17,18]. For right hemicolectomy, re-docking of the robot cart may be necessary to secure an appropriate surgical field, and this has been indicated as a cause of increased operating times[32]. In addition, the restricted operating range of RAS within the abdominal cavity is the main drawback of extended colectomy, which requires a large surgical field[33]. Perhaps due to the impact of these disadvantages, the implementation of RAS for colon cancer has been slower than that for rectal cancer. It has been reported that 46% of certified colorectal cancer surgeons perform robot-assisted rectal surgery, and the proportion of RC is only 22% overseas[34].

**3. Current State of RC in Japan: Expectations for Clinical Research and Expanded Indications**

As discussed above, numerous reports addressing RC have been published overseas; in contrast, no comprehensive reports have been published in Japan. Robotic colectomy is not covered by health insurance programs in Japan, resulting in fewer operations and less evidence supporting colectomy than for resection of rectal cancer.

Prospective research investigating RC to treat colon cancer is currently being conducted based on information from overseas facilities using robotic surgery (Evaluation for the safety of robotic-assisted colectomy for resectable colon cancer: a multi-institutional, prospective, historical con-

trolled, feasibility study [JRCT1032190036]). Case registration is now progressing. Thus, in this study, we aim to evaluate the safety and feasibility of RC for radical resectable clinical stage I-III colon cancers. The primary endpoint is the rate of conversion to laparotomy, and the study aimed to verify the non-inferiority of RC compared with historical controls of LC and open surgery.

In Japan, RC is currently being performed in only a small number of facilities, despite the limited evidence supporting its effectiveness; in the same way that robotic-assisted lower rectal resection spread rapidly throughout the country after it was approved for insurance coverage in Japan, this procedure is also expected to be widely used once covered by insurance programs. To ensure that the dissemination of RC is performed safely, the generation of evidence supporting its safety, feasibility, and recoverability in Japan is also expected in the future, with a focus on current ongoing studies.

#### 4. Conclusion

Although RC involves longer operative times and higher costs, it is possible that this technique could be more precise and less invasive than LC. There are expectations that RC could improve the rates of conversion to laparotomy, which is an issue in LC, and promote more rapid postoperative recovery. In addition, it has demonstrated particular utility for specific procedures, such as ICA, and in terms of long-term prognosis from an oncological perspective. RAS appears to be a non-problematic procedure compared with traditional LS and laparotomy. While RC has become popular as a treatment option overseas, the procedure is currently performed in only a few facilities in Japan. Further accumulation of case experience and investigation of surgical outcomes in RC, therefore, is needed.

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#### Conflicts of Interest

There are no conflicts of interest.

#### Author Contributions

SY, MH, NI, TM, MT, and YK contributed to the concept, writing, and editing of this manuscript.

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