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Review

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Robotic surgery for gastric cancer

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Abstract

The number of robotic gastrectomy (RG) cases is increasing, especially in East Asia. The da Vinci Surgical System for RG allows surgeons to perform meticulous procedures using articulated devices and provides potential advantages over laparoscopic gastrectomy (LG). Meta-analyses including a large number of retrospective studies comparing RG and LG revealed only a limited advantage for RG over LG, such as lower blood loss, and the obvious disadvantage of longer operation times and higher medical cost. Specifically, a multicenter, prospective, single-arm study performed in Japan showed favorable short-term outcomes of RG over LG, while a non-randomized controlled trial in Korea showed similar postoperative complication rates for RG and LG, although the medical costs were significantly higher in RG. A well-designed randomized controlled trial is thus necessary to establish robust evidence comparing the two surgeries. In addition, further development of surgical robotics is expected for RG to be accepted more widely.

Keywords: Gastric cancer, robotic gastrectomy, surgery, minimum invasive surgery

INTRODUCTION

Gastric cancer is the third leading cause of cancer-related deaths and the fifth most common cancer worldwide[1]. Gastrectomy with radical lymphadenectomy is a mainstay of treatment on resectable gastric cancer; however, recent randomized controlled trials have demonstrated inferiorities of such expanded and invasive procedures[2-5]. In contrast, minimally invasive surgery including laparoscopic gastrectomy (LG) and robotic gastrectomy (RG) is attracting attention. LG was first introduced in 1991 in Japan[6], and since then, this procedure is used all over the world. The reported advantages of LG over radical open gastrectomy are faster recovery from the surgical stress, less bleeding, good cosmetic results, and shorter

Table 1. History of surgical robotics

Year	Event
1985	Puma 200 was used for neurosurgical biopsy
1986	ROBODOC was used for artificial joint replacement
1994	AESOP (Computer Motion Inc.) released and approved by the FDA
1998	ZEUS (Computer Motion Inc.) released
1999	da Vinci Surgical System (Intuitive Surgical Inc.) released
2000	da Vinci Surgical System approved by the FDA
2001	First case of intercontinental telesurgery (US-France)
2002	Hashizume performed robot-assisted distal gastrectomy
2003	Merger of Intuitive Surgical Inc. and Computer Motion Inc.

FDA: food and drug administration

hospital stays[7-9]. Nevertheless, this procedure has several drawbacks such as two-dimensional surgical view and the motion restriction using linear forceps. Surgical robotics has introduced in 1990s having the potential to overcome those limitations and is spreading rapidly in the world.

In this review, we provide an historical outline of the development of surgical robotics, and describe the advantages and disadvantages of robot gastrectomy for gastric cancer compared to LG.

HISTORY OF SURGICAL ROBOTICS

The history and development of surgical robotics [Table 1] goes back to the 1950s, with the development of so-called "telepresence robotic arms", although these were not intended for surgical applications, but rather for remotely controlled systems to handle hazardous substances or to perform tasks underwater or in space. In the 1980s, robotic arm development progressed rapidly with advances in computer technology, and in 1985, surgical robotics was first used in a clinical setting to perform a neurological biopsy[10]. A year later, researchers at the IBM Thomas J. Watson Research Center and University of California completed the development of ROBODOC, which became the first surgical robot approved by the USA Food and Drug Administration (FDA) for clinical use in humans[11]. In 1994, Computer Motion Inc. developed Automated Endoscopic System for Optimal Positioning (AESOP; Computer Motion Inc., USA) with the aim of solo-surgery using voice recognition to control the endoscope[12].

The US army also developed medical robotics for the use of telesurgery in the late 1980s with a master-slave manipulator system that was originally designed for battlefield surgery. This system was subsequently introduced into the clinical market as the da Vinci Surgical System (DVSS) by Intuitive Surgical Inc, and in 2000, DVSS became the first robot-assisted surgical system approved by the FDA for use in general laparoscopic surgery[13,14]. Computer Motion Inc. also developed ZEUS in 1998, adding a remote-control function to AESOP[15]. In the beginning, both systems were used only for cardiovascular surgery; however, they were gradually expanded to digestive surgery, urology, and gynecology. In 2001, ZEUS was used for the first case of telesurgery between New York and France to perform cholecystectomy[16]. This operation was called "Lindbergh operation" after the American aviator Charles Lindbergh who was the first person to fly solo across the Atlantic Ocean. The first RG [robotic distal gastrectomy (RDG)] for gastric cancer was reported in 2002 by Hashizume *et al.*[17] using DVSS.

In 2003, Computer Motion Inc merged with Intuitive Surgical Inc., and since then DVSS has been the only FDA-approved surgery-assisting robot, building a near-monopoly. In September 2018, there were 4,814 installed DVSS units worldwide, including 3,110 in the United States, 821 in Europe, and 629 in Asia[18] [Figure 1].

CURRENT STATUS OF RG FOR GASTRIC CANCER

The most apparent advantage of RG over LG is that articulated devices are available in RG. In addition, the motion scaling and tremor suppression functions in RG enable more precise movement, which is believed

Table 2. Summary of the meta-analyses comparing RG and LG with respect to short term outcomes

Author	Year	Country	Number of studies	Number of patients	Morbidity	Blood loss	Operation time	Retrieved LN	Hospital stay	Time to oral intake	Time to first flatus	Medical cost
Hyun et al.[26]*	2013	Korea	9	7,200	RG = LG	RG = LG	RG > LG	RG = LG	RG = LG	-	-	-
Shen et al.[19]	2014	China	8	1,875	RG = LG	RG < LG	RG > LG	RG = LG	RG = LG	-	-	-
Chuan et al.[20]	2015	China	5	1,796	RG = LG	RG < LG	RG > LG	RG = LG	RG = LG	-	-	-
Hu et al.[21]	2016	China	12	3,580	RG = LG	RG < LG	RG > LG	RG > LG	RG < LG	-	RG > LG	-
Wang et al.[23]	2017	China	3	562	RG = LG	RG = LG	RG > LG	RG = LG	RG = LG	-	-	-
Chen et al.[22]	2017	China	19	5,953	RG = LG	RG < LG	RG > LG	RG = LG	RG = LG	RG > LG	RG = LG	RG > LG
Guerra et al.[25]	2018	Italy	8	2,026	RG = LG**	-	RG > LG	RG > LG	RG = LG	-	-	-

*This study included open gastrectomy and compared among robotic, laparoscopic, and open gastrectomy; **only pancreatic complications were compared, including acute pancreatitis and pancreatic fistula. LN: lymph nodes; RG: robotic gastrectomy; LG: laparoscopic gastrectomy

to reduce tissue damage and blood loss. Another advantage of RG is a three-dimensional (3D) field of view that facilitates surgeons to recognize depth perception. Recently, 3D images also became available in LG; however, special glasses are necessary and the quality of imaging remains inferior to that in RG. Furthermore, the ergonomics-based surgery console used in RG can reduce the fatigue of operators. While the surgical devices for RG were limited at first, ultrasonically activated device (harmonic), vessel sealers, Endo Wrist staplers, and other instruments are now available.

Short-term outcomes

Retrospective studies

Numerous retrospective, case-control studies comparing RG and LG have been conducted, and several meta-analyses were performed using those studies [Table 2][19-26]. Shen *et al.*[19] conducted 8 studies with a total of 1,875 patients that showed approximately 40 mL lower blood loss in RG than LG; however, the operation time for RG was approximately 50 min longer. The duration of hospital stay, morbidity, and numbers of retrieved lymph nodes were comparable between RG and LG. Other meta-analysis indicated similar results, with the exception of a difference between RG over LG with morbidity. Guerra *et al.*[25] analyzed 8 studies, including 2026 patients, focusing on pancreatic complications. Pancreatic fistula occurred in 2.7% of patients receiving RG and 3.8% of patients receiving LG, for an odds ratio of 0.72. Although the difference was not statistically significant, the authors concluded that RG trended toward lower rates of postoperative pancreas-related events, despite more unfavorable baseline characteristics compared with LG.

Prospective studies

Very limited prospective studies of RG have been conducted thus far. We conducted single-center early and late phase II studies in patients with cStage I gastric cancer to evaluate the safety of RG[27,28], involving 18 and 120 patients, respectively, in each study that found an incidence of intra-abdominal infectious complications of Clavien-Dindo classification grade ≥ II of 0% and 3.3%, respectively. Thus, the null hypotheses were rejected, and the studies concluded that RG can be safely used in cStage I gastric cancer.

In a prospective, multicenter, non-randomized, control study was conducted in Korea from May 2011 to December 2012 to compare the short-term surgical outcomes of RG (n = 223) and LG (n = 211)[29]. No significant difference was observed in the incidence of overall postoperative complications (RG 11.9%, LG 10.3%) and the mortality rate was 0% in both groups; however, the operation time was 40 min longer and the financial cost was 5,000 USD higher for RG than for LG. The authors concluded that RG was not superior to LG, and subsequent sub-group analysis showed a significantly lower amount of blood loss in RG when D2 lymph node dissection than that in LG[30].

A multicenter, prospective, single-arm study conducted in Japan evaluated the safety of RG in 330 patients with cStage I/II gastric cancer enrolled from October 2014 to January 2017, with the primary endpoint of

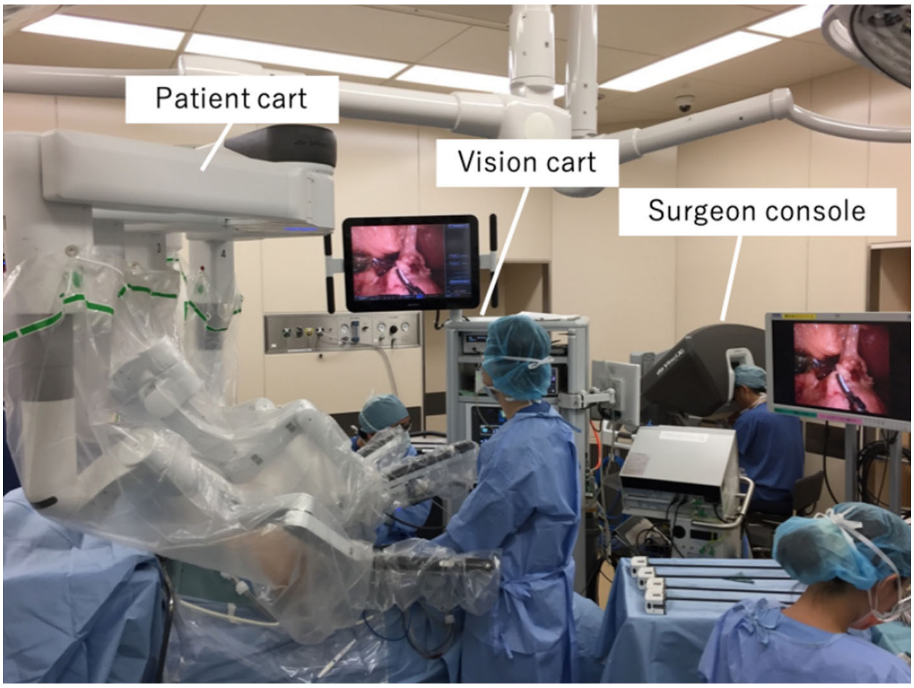

Figure 1. The da Vinci Surgical System comprises the patient cart, vision cart and surgeon console

postoperative complication[31]. The incidence of postoperative complications of Clavien-Dindo grade ≥ III was 2.45%, which was significantly lower than that in the historical control group (6.4%). Based on this result, RG for gastric cancer has been covered by national health insurance since April 2018 in Japan.

Long-term outcomes

A few retrospective case-control studies have been conducted to compare long-term outcomes between RG and LG in Japan and Korea[32-34]. In a study conducted in Japan, data from 84 patients who underwent RG and 437 patients who underwent LG around the same time were retrospectively analyzed; the 3-year overall survival rates were 86.9% and 88.8%, respectively, and did not differ to a statistically significant extent (P = 0.636)[33]. A study conducted in Korea using propensity score matching found 5-year overall survival rates of 93.2% in RG and 94.2% in LG; again the difference was not statistically significant (P = 0.4112)[34]. Although not prospective findings, these results indicate that the long-term outcomes of RG are not inferior to those of LG.

Learning curve

The learning curve for RG is reportedly shorter for experienced surgeons who had performed LG, estimated to total between 10 and 25 cases[35-39], although 40-60 cases is the estimated number needed to reach stabilization in LG[40,41]. Thus, although the 3D imaging and instrument flexibility of RG may help to make the learning curve less steep, the fact that an expert in LG performed the RG in many cases could have affected the results. In contrast, a recent study showed that stabilization of the operation time occurred after 25 cases, even for surgeons without prior LG experience, suggesting that prior LG experience is not necessarily required[42].

Nevertheless, robotic surgery requires surgeons to attain some extent of specialized training. Intuitive Surgical Inc. provides a training program and surgeons have to pass this program and be certificated as a Console Surgeon of DVSS to perform RG using DVSS. Interestingly, this training program targets surgeons from various fields and it is not sufficient to perform RG independently. Therefore, we have developed three-step educational program targeted at qualified surgeons [Table 3], who should perform more than 10

Table 3. Educational Program in Shizuoka Cancer Center

Step	Target item	Purpose
1	Has taken the training courses led by Intuitive Surgical Inc. and acquired surgeon certification	Learn the basic operation of the da Vinci Surgical System and perform repetitive training of surgical techniques and surgical procedures
	Perform at least 10 h of offsite training using the da Vinci Surgical System	Learn the smooth operation of the da Vinci Surgical System
2	Under the guidance of the proctor, perform over 10 robotic gastrectomies (including total gastrectomies, cardia side gastrectomies)*[1-4] Do not cause other organ damage requiring repair, arterial injuries requiring reconstruction, or other intraoperative complications requiring an open conversion	Gain experience in robotic gastrectomy
	Perform one or more robotic total gastrectomies	Gain experience as a surgeon for robotic total gastrectomies to acquire esophagus jejunal anastomosis
3	Achieve a rating of B or higher from the proctor in all items of the surgical evaluation on robotic distal gastrectomy	The proctor evaluates whether or not the target surgeon is appropriate as a robotic surgeon, according to unified standards

*1: The proctor performs surgery mainly for the first case and the operator learns beside or performs part of the surgery; *2: at least the second case should be a case of distal gastrectomy, D1 + dissection, with BMI < 25, PS = 0, and ASA - PS 2 or less; *3: teaching by dual console is desirable until the third case; *4: in the case of a longer than 6 months absence during participation, 2 cases of experience will be added after receiving a retraining program provided by Intuitive Surgical Inc., regardless of the number of experienced cases

cases of RG including one or more cases of total or proximal gastrectomy[43]. A proctor scores the surgeon in accordance to the evaluation list, and when a high score is achieved, the surgeon will be allowed to perform RG independently.

Ergonomics

Robotic surgery provides surgeons with an ergonomically sound work environment because although LG is usually performed in the standing position, RG can be performed in a sitting position at an ergonomically designed surgeon console, which is expected to reduce operator fatigue. A survey study comprising 26 questions was performed to document the discomfort of robotic surgery compared with open and laparoscopic surgery, and to investigate the factors that affect the risk of physical symptoms, involving surgeons with various specialties and 1,215 who practiced all three approaches. This survey demonstrated that robot-assisted surgery was associated with the least physical discomfort and symptoms compared with open and laparoscopic surgery[44]. The breakdown of symptoms indicated that robotic surgery was less likely to lead to neck, back, hip, knee, ankle, foot, shoulder, elbow, and wrist pain than open or laparoscopic surgery, although the frequency of eye and finger pain was higher in robotic surgery. In another survey of 432 surgeons using robotic surgery in various fields, 56.1% complained of physical symptoms or discomfort, with the most frequent complaints being neck stiffness, finger pain, and eye fatigue[45]. Thus, although robotic surgery reduces the physical symptoms and discomfort of surgeons in comparison to open and laparoscopic surgery, more than 50% of surgeons have complained of a certain degree of physical stress, typically finger pain and eye strain.

Disadvantages of robotic compared to laparoscopic gastrectomy

The most critical disadvantage of RG is a lack of tactile perception, which can lead to incomplete ligature and tissue damage due to excessive stress. Visual information can compensate the lack of tactile perception; however, serious injury could still happen outside the field of view. Surgical robotics can potentially apply an unexpectedly strong force that never occurs in conventional surgery. Thus, even slight mishandling of the DVSS may lead to a fatal accident, even with a built-in system to prevent excessive compression to organs.

Requiring a long operation time is another disadvantage in RG. A retrospective study investigating factors contributing to prolongation of the operation time identified "junk time" as a cause of the prolongation[46]. In this study, the authors classified the overall operation time into two groups: the effective time (time required for actual surgical techniques such as port replacement, lymphadenectomy, and reconstruction) and the junk time (setup docking, and adjustment of surgical instruments). They found that junk time was significantly longer in RG, at 41.5 min, than in LG, though effective time was not statistically different between the groups. Although there was no difference in the number of instrument exchanges, the time required to exchange instruments was also significantly longer in RG than in LG. Additionally, the operation time was reduced by about 1 h when ultrasonically activated devices were used[47]. These studies suggest that a smarter and simpler system is needed for the setup and for instrument change, and development of new devices are warranted to reduce the operation time.

FUTURE PERSPECTIVES

A lack of robust evidence regarding RG use appears to be the most important future issue. Although RG has many theoretical advantages over LG, a definite and significant benefit of RG over LG has not been shown in a clinical setting due to the lack of randomized controlled trials (RCT). It cannot be denied that the high cost of RG affects the difficulty in conducting RCT, with some meta-analyses and a prospective study conducted in Korea indicating that RG is 4000-5000 USD more expensive than LG[22,29]. In Japan, RG has been covered by health insurance since April 2018; thus, patients can undergo RG without any extra cost. Thus, while the economic burden on medical institutions remains, the groundwork for RCT has been completed, and a well-designed RCT is needed to investigate the superiority of RG over LG.

Currently, several companies are developing surgical robots, with such market competition expected to decrease the price and further their use. Moreover, we anticipate the near future to bring development of new devices or miniaturization of existing surgical robots, together with innovative development, including concomitant use with 3D imaging[48], artificial intelligence, and virtual reality[49].

CONCLUSION

RG with DVSS facilitates meticulous surgical procedures with 3D imaging, instrument flexibility, tremor suppression, and improved ergonomics. Problems with RG remain including an unacceptable lack in tactile perception, longer operation times, and high medical costs. Moreover, although RG has theoretical advantages over LG, robust evidence is lacking. Well-designed, randomized controlled trials are therefore needed to establish stronger evidence and further develop the field of surgical robotics.

DECLARATIONS

Authors' contributions

Designed the study, reviewed literature, and wrote the manuscript: Makuuchi R
Critical revision of the manuscript and approval of the final version: Kamiya S, Tanizawa Y, Bando E
Writing the manuscript, drafting and critical revision and editing, and approval of the final version: Terashima M

Availability of data and materials

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Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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