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Trends and outcomes of minimally invasive surgery for gastric cancer: 750 consecutive cases in seven years at a single center

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Gastric carcinoma;
Gastrectomy;
Minimally invasive surgery;
Intracorporeal anastomosis

Abstract

BACKGROUND: The aims of this study were to investigate trends in minimally invasive surgery (MIS) for gastric cancer through the experience of a single center and to predict the direction of the development of MIS.

METHODS: During a 7-year period, 2,160 patients underwent curative gastric cancer surgery. Changes in the proportion and pathologic features of a total of 750 cases that involved MIS, as well as the surgical methods and outcomes of MIS, were analyzed.

RESULTS: An analysis of the patient population treated by MIS revealed that the proportion of patients with T2 or greater tumors on the basis of pathologic findings was initially <5.0% but had recently increased to 24.3%. Although the proportions of intracorporeal anastomosis and robotic surgery had recently increased, the complication rate and operative time had stabilized 2 years after the 1st MIS.

CONCLUSIONS: Given these results, the application of MIS for gastric cancer is expected to become more frequent. In addition, new modalities will be preferred by both surgeons and patients to reduce the invasiveness of gastric cancer surgery.

Minimally invasive surgery (MIS), including laparoscopic surgery, is a popular surgical technique in the field of abdominal surgery because it carries several significant benefits.[1] These procedures can reduce postoperative pain, enhance bowel movement, and shorten the length of hospital stay. The development of laparoscopic instruments and other minimally invasive technologies, such as robotic devices, has led to changes in the procedures used in MIS. Notably, the development of minimally invasive techniques has resulted in less invasive surgery and reduced abdominal scarring.

Since the introduction of laparoscopy-assisted distal gastrectomy for early gastric cancer by Kitano et al,[2] this procedure has become a popular surgical procedures for gastric cancer. In this operation, anastomosis is performed by minilaparotomy after lymph node dissection in the laparoscopic view. This small incision in the epigastric area may cause postoperative pain, which may affect the postoperative outcome, but the pain associated with this procedure was significantly less than that associated with conventional

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laparotomy.[3,4] In addition, laparoscopic surgery has several limitations, including a necessary learning curve, the transmission of hand tremors to the laparoscopic instruments, and a limited angle of instrumental movement to meticulously dissect the lymph nodes. Therefore, the instruments and techniques in MIS have been changed to overcome the limitations encountered by surgeons and reduce patients' surgical stress.

Here, we present the experience with MIS for gastric cancer at a single center in Korea. These results shed light on the trends in MIS in the realm of gastric cancer surgery and highlight directions for its development in the future.

Methods

Between May 2003 and April 2010, a total of 2,160 patients with gastric cancer underwent curative surgical resection in the Department of Surgery at Ajou University School of Medicine. Of these patients, MIS was used in 750 patients (34.7%). Although the proportion of MIS was 14.2% of the total cases in the initial period, the proportion increased to 49.0% during the final year (Fig. 1). For preoperative staging, gastrofiberscopy, contrast-enhanced computed tomography, and chest x-ray were performed. Although endoscopic ultrasound was occasionally performed to clearly assess the depth of invasion, tumor invasion and lymph node metastasis were generally determined using computed tomography because of the inaccuracy of endoscopic ultrasound.[5] During the initial period of this study, the indications for MIS included gastric cancers confined to the submucosa with no clinical lymph node metastasis. In addition, the early gastric cancers that were absolute indications for endoscopic submucosal dissection were excluded from surgical resection. After >50 cases of MIS were performed at our institution, the indications for MIS were extended to include the muscularis propria, with or without perigastric lymph node metastasis, and extended (D2) lymph node dissection was performed on patients with locally advanced gastric cancer according to the Japanese gastric cancer treatment guide.[6]

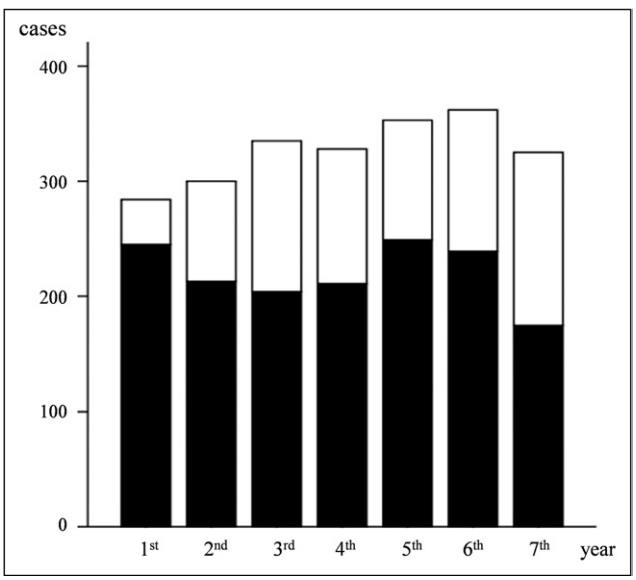

Figure 1 Number of patients who underwent gastrectomy with lymphadenectomy for gastric cancer. The open bar represents patients undergoing MIS, and the filled bar represents patients undergoing open conventional surgery. During the 1st year after the initial case, the proportion of MIS was 14.2% of the total cases. However, the proportion increased to 49.0% during the final year.

At our institution, a video laparoscopic system (CV-165; Olympus Corporation, Tokyo, Japan) was 1st introduced in 2003. Lymph nodes were dissected using laparoscopic ultrasonic devices (Harmonic Scalpel; Johnson & Johnson, New Brunswick, NJ). The range of lymph node dissection was performed according to the guidelines of the Japanese Gastric Cancer Association.[6]

Until February 2008, specimens were extracted, and all reconstructions were extracorporeally completed through 4-cm to 7-cm laparotomies in the epigastric area of the abdomen (Fig. 2A). During the final 2 years of the study, gastroduodenostomy, gastrojejunostomy after distal subtotal gastrectomy, and esophagojejunostomy after total gastrectomy were intracorporeally performed with staplers in the laparoscopic view (Fig. 2B). The specimen was extracted through a 3-cm umbilical trocar site.

To localize the tumor and determine the resection margin, the clips around the tumor were endoscopically applied on the day before the operation. During extracorporeal anastomosis, the resection margin was determined by palpating the applied clips. For intracorporeal anastomosis, portable plain radiography was performed to detect the location of the clips. As soon as the stomach was resected, the proximal resection margin was evaluated by intraoperative frozen section to determine whether tumor was involved. In patients diagnosed with positive tumor involvement in the proximal margin, additional resection was performed using a laparoscopic procedure as soon as possible. The range of gastric resection depended on the tumor's location, size, and morphologic features, and total or distal subtotal gastrectomies were performed on most patients. For <1.5% of patients with early gastric cancer, proximal gastrectomy or pylorus-preserving gastrectomy was performed.

A robotic operating system (da Vinci Surgical System; Intuitive Surgical, Sunnyvale, CA) was introduced at our institution in the 6th year of the study. Robotic procedures were performed using 5-port systems. The indications and procedures for robotic surgery followed the principles of laparoscopic surgery. However, robotic surgery was applied for patients who agreed to the high cost of robotic procedure not covered by the health insurance system. Intracorporeal or extracorporeal anastomosis was performed for reconstruction during robotic surgery. In the past 2 years, reconstructions were completed by intracorporeal gastroduodenostomy, gastrojejunostomy, and esophagojejunostomy and included robotic sewing techniques in most cases.[7]

Figure 2 Reconstruction methods after laparoscopic gastrectomy with lymph node dissection. (A) The anvil of the circular stapler was inserted for gastroduodenostomy through a minilaparotomy in the epigastric area. (B, C) Gastrojejunostomy using linear and circular staplers through a minilaparotomy. (D) Insertion of stapler for gastroduodenostomy in intracorporeal anastomosis. (E) The site for stapler insertion was closed using a linear stapler. (F) Intracorporeal gastroduodenostomy was completed. (G) The anvil was inserted into abdominal esophagus for esophagojejunostomy in the intracorporeal anastomosis. (H) The anvil and the body were connected for intracorporeal esophagojejunostomy. (I) Intracorporeal esophagojejunostomy was completed.

We investigated operative time and postoperative complications as measures of surgical outcomes. Operative time was measured from skin incision to closure. Surgical complications were noted if these events resulted in a longer hospital stay than expected.

Final staging was determined according to the 6th edition of the stage classification criteria from the Union for International Cancer Control. For patients diagnosed, on the basis of pathology, with stage II or higher advanced disease, adjuvant chemotherapy with a 5-fluorouracil-based regimen was administered for 1 year. Prospective follow-up was performed on all patients every 3 or 6 months; at each follow-up visit, a physical examination, tumor marker (carcinoembryonic antigen and carbohydrate antigen 19–9) analysis, computed tomography, and gastrofiberscopy were performed. Recurrence was determined on the basis of the radiologic findings. In case of recurrence in a region amenable to a surgical biopsy or radiologic supplementary biopsy, recurrence was confirmed via biopsy collection. Patient survival was calculated using Kaplan-Meier method with SPSS version 13.0 (SPSS, Inc, Chicago, IL).

Results

The clinical and pathologic features of the patients who underwent MIS for gastric cancer are listed in Table 1. Patients who were pathologically diagnosed with early gastric cancer were common (78.4%), and D1+ lymphadenectomy was performed in 61.7% of the patients. Total gastrectomy using MIS was performed in 9.3%, and the proportion undergoing robotic surgery was 11.2%.

Table 1 Clinicopathologic features of patients who underwent MIS for gastric cancer

Variable	n	%
Age (y)		
<65	490	65.4
≥65	260	34.6
Gender		
Male	485	64.7
Female	265	35.3
Approach		
Laparoscopic	680	90.6
Robotic	70	9.3
Resection		
Total gastrectomy	84	11.2
Subtotal gastrectomy	657	87.6
Proximal gastrectomy	4	.5
Pylorus-preserving gastrectomy	5	.7
Reconstruction		
Billroth I	392	52.3
Billroth II	230	30.6
Roux-en-Y	115	15.3
Other	13	1.8
Lymphadenectomy		
D1	7	.9
D1+	462	61.7
D2	264	35.2
D2+	7	.9
Unknown	10	1.4
Tumor invasion		
T1	588	78.4
T2/T3/T4	129	17.2
Unknown	33	4.4
Lymph node metastasis		
N0	610	81.3
N1/N2/N3	140	18.7

Initially, during the study period, most patients who underwent MIS (89.7%) were diagnosed with early gastric cancer. However, the proportion of advanced gastric cancer has gradually increased. In the final year of this study, 24.3% of patients who underwent MIS for gastric cancer were pathologically diagnosed with advanced gastric cancer (Fig. 3A). During the 1st year, only 5.1% of MIS cases were total gastrectomies. The proportion of total gastrectomies gradually increased to >12.0% in the final year (Fig. 3B). For reconstruction after gastric resection, extracorporeal anastomosis via minilaparotomy was performed on all patients during the 1st 5 years. After intracorporeal anastomosis was adopted in the final 2 years of the study, its use increased to >50% of all MIS cases (Fig. 3C). Robotic surgery for gastric cancer was also introduced at our institution in the final 2 years of the study, and 34.7% of MIS cases were performed using robotic surgery (Fig. 3D).

The mean operative time for all patients who underwent MIS for gastric cancer was 177.6 minutes. The median operative time was >200 minutes during the 1st year. Two years after the 1st MIS, operative time had stabilized to approximately 180 minutes (Fig. 4A). The postoperative complication rate was 16.5% (124 of 751), and the mortality rate was .8% (6 of 751). The complication rate changed over time; 16 of 39 patients (41.0%) who underwent MIS during the 1st year had complications. Thirty-nine and 87 patients underwent MIS for gastric cancer during the 1st and 2nd years, respectively. The complication rate then stabilized to approximately 10% since the 3rd year after initial MIS (Fig. 4B). The most common complication was wound problems (29 patients [3.9%]), followed by intra-abdominal bleeding (9 patients [1.2%]) and anastomosis leakage (9 patients [1.2%]). Conversion of MIS to open surgery occurred in 3 patients (.4%): 1 patient had a tumor with serosa exposure on laparoscopy, and 2 patients required conversion to control bleeding and to perform additional resection for proximal margin tumor involvement.

The long-term oncologic outcomes were evaluated for the 257 patients who underwent laparoscopic surgery during the initial 3 years. The mean follow-up period was 56 months. The mean survival time of these 257 patients was 72.35 months. The overall 5-year survival rates were 92.3% for stage I, 69.8% for stage II, 42.2% for stage III, and 33.8% for stage IV. The differences in overall survival among the stages were significant ($P < .001$; Fig. 5A). The disease-free survival rates were 97.1% for stage I, 75.1% for stage II, 47.6% for stage III, and 28.8% for stage IV. The differences in disease-free survival among the stages were also significant ($P < .001$; Fig. 5B).

Comments

During the course of this study, the proportion of surgical gastric cancer cases involving MIS gradually increased from 13.7% to nearly 50%. The indications for laparoscopic surgery were initially restricted to early-stage disease but have broadened to include more advanced stages because of technical advancements in extended lymph node dissection. The treatment guidelines from the Japanese Gastric Cancer Association state that D2 lymphadenectomy is the standard procedure for locally advanced gastric cancer.[6] The accurate and safe application of laparoscopic D2 lymphadenectomy is crucial for its use as a treatment for advanced gastric cancer. To date, several studies have reported that laparoscopic D2 lymphadenectomy can be performed with technical safety.[8–11] These studies have suggested that experienced surgeons who have performed ≥50 cases of laparoscopic surgery for gastric cancer can perform extended D2 lymphadenectomy. The surgeons at our institution started performing D2 lymphadenectomy after performing >100 laparoscopic surgeries for gastric cancer, and our indications for laparoscopic surgery were expanded to include advanced gastric cancer. However, during preoperative staging, extremely advanced gastric cancers, such as cases with serosa-exposed tumors, were not included in our indications for laparoscopic surgery, because the possibility of unexpected metastasis and port-site metastasis resulting from the laparoscopic procedure could be not excluded.

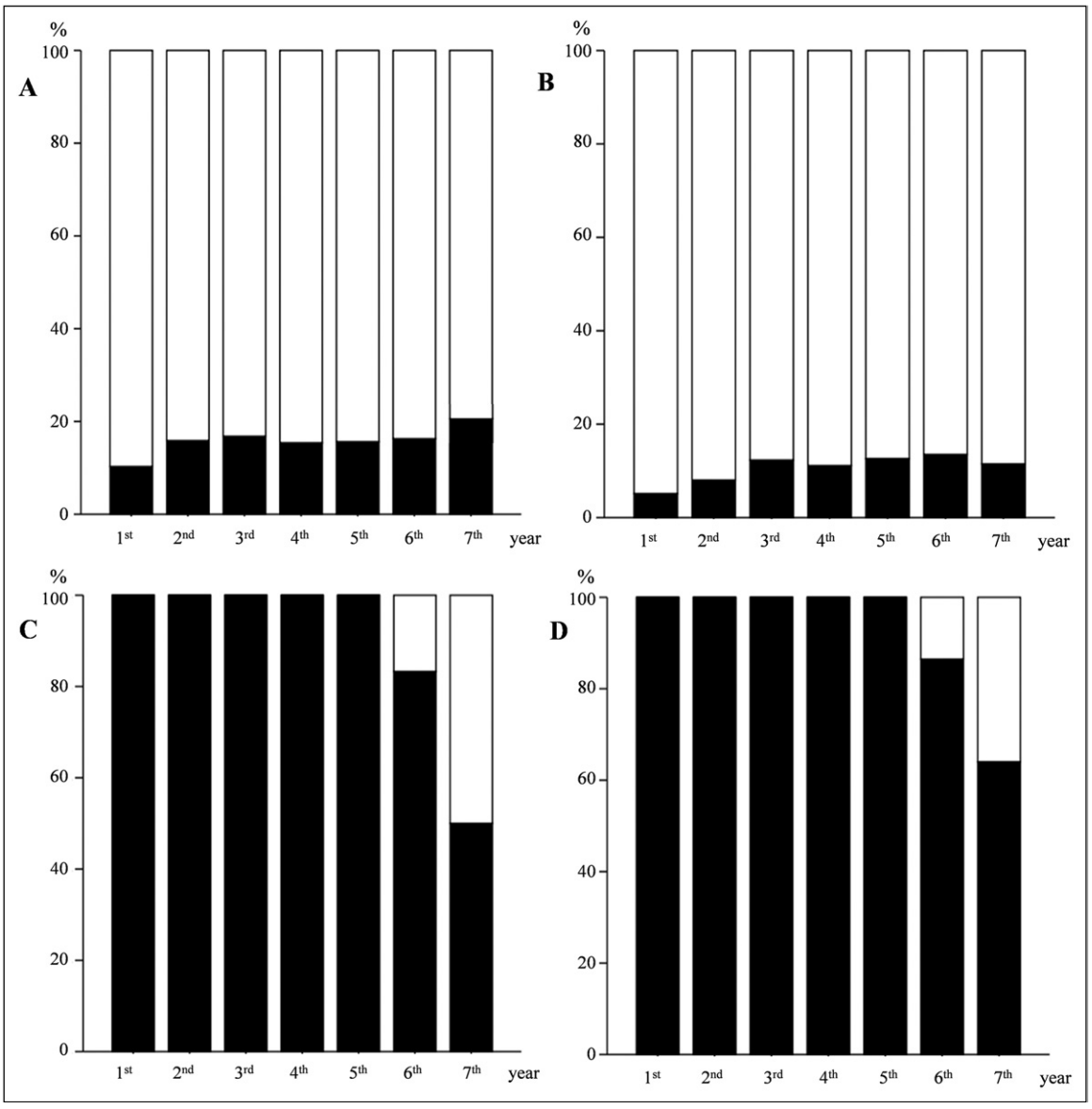

Figure 3 Changes in the pathologic results and surgical procedures in the cases of MIS for gastric cancer. (A) The filled bar shows the proportion of MIS patients who had advanced gastric cancer. This proportion increased to 24.3% in the final year of the study. (B) The open bar shows the proportion of MIS cases involving partial gastrectomy, and the filled bar shows the proportion of MIS cases involving total gastrectomy, which increased to 11.4% in the final year. (C) The filled bar shows the proportion of MIS cases involving extracorporeal reconstruction through minilaparotomy, and the open bar shows the proportion of MIS cases involving intracorporeal reconstruction. Intracorporeal reconstruction was performed only during the final 2 years. (D) The filled bar represents laparoscopic surgery, and the open bar represents robotic surgery.

Thus, the proportion of gastric cancer surgeries that involved laparoscopic surgery was <50%. If evidence supporting laparoscopic surgery for extremely advanced gastric cancers can be shown through clinical studies, the indications of laparoscopic surgery for gastric cancer will be adjusted accordingly.

Recently, total laparoscopic surgery, including intracorporeal anastomosis in the laparoscopic view, has been developed for gastric cancer surgery because of the technical difficulty of performing reconstruction through a small incision.[12] In particular, an intracorporeal procedure can provide a superior visual field in obese patients with abundant intra-abdominal fat and thick abdominal walls. Several clinical studies have compared laparoscopy-assisted and totally laparoscopic surgery for gastric cancer.[12–14] In these studies, total laparoscopic surgery using intracorporeal anastomosis was superior in terms of postoperative recovery, length of hospital stay, and the occurrence of inflammatory reactions, although totally laparoscopic surgery was more expensive. At our institution, totally laparoscopic surgery was performed in the last 2 years of the study. In a previous report, we showed that linear gastroduodenostomy for intracorporeal Billroth I reconstruction was simple and feasible.[15] We have also performed Billroth II and Roux-en-Y

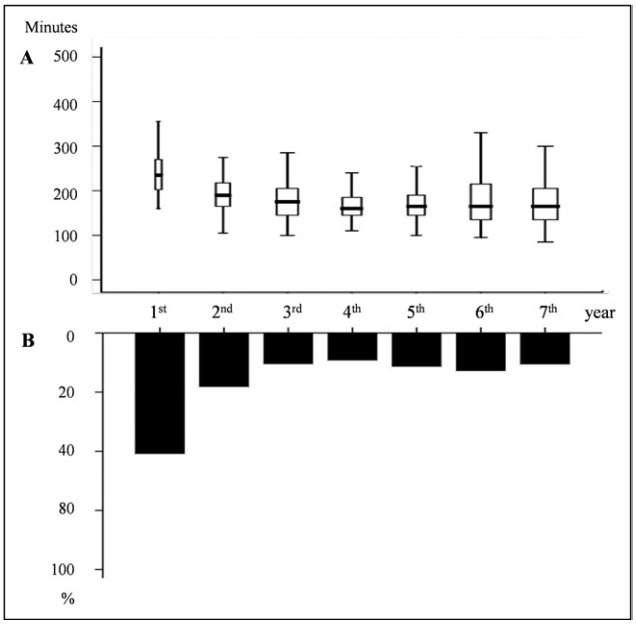

Figure 4 Yearly surgical outcomes of MIS for gastric cancer. (A) Box plot showing the operation time over 7 years. (B) The filled bar represents the postoperative complication rate.

procedures using intracorporeal anastomosis. Despite our use of intracorporeal reconstruction, the complication rate at our institution did not increase in the final 2 years. Thus, intracorporeal reconstruction, after overcoming the learning curve of laparoscopic surgery, can be readily performed.

The critical limitation of laparoscopic surgery was the learning curve for technical stabilization. We previously reported that the learning curve for laparoscopic surgery for gastric cancer, analyzed using the cumulative sum method, was overcome after 40 cases.[16] Another study reported that the experience of 50 laparoscopic procedures for gastric cancer was required to overcome the learning curve.[17] In this study, 39 such procedures were performed during the 1st year, and the complication rate was stable (approximately 10%) from the 2nd year. Retrospective multicenter studies in Korea and Japan reported complication rates of 12.9% to 13.1%,[18,19] which are comparable with our rate, starting 2 years after the initial case.

From the oncologic perspective of MIS for gastric cancer, only 1 clinical trial has compared survival rates after laparoscopic surgery versus open resection.[20] Although a small number of patients with various stages were enrolled in this trial at a single Western center, 5-year overall survival (55.7% vs 54.8%, respectively) and disease-free survival (58.7% and 57.3%, respectively) were not significantly different between the laparoscopic and open surgery groups. In Eastern societies, where laparoscopic surgery is usually used to treat early-stage gastric cancer, the long-term oncologic outcomes of laparoscopic surgery for gastric cancer have been evaluated.[21,22] These studies have shown that the 5-year disease-free survival rate was 89% to 94% for stage I, 63% to 83% for stage II, and 50% for stage III. The authors stated that laparoscopic surgery should be designated as the standard treatment for early gastric cancer. Compared with previous reports,[21,22] the long-term oncologic outcomes of the patients who had undergone laparoscopic surgery for gastric cancer in this study also indicate that this is a feasible treatment.

Robotic surgery was first introduced as an advanced technology for complex procedures, such as cardiac and prostate surgery.[23,24] Recently, several surgeons have applied robotic techniques to gastric cancer surgery using the da Vinci Surgical System.[25–27] These reports have shown that robotic surgery for gastric cancer is technically feasible,

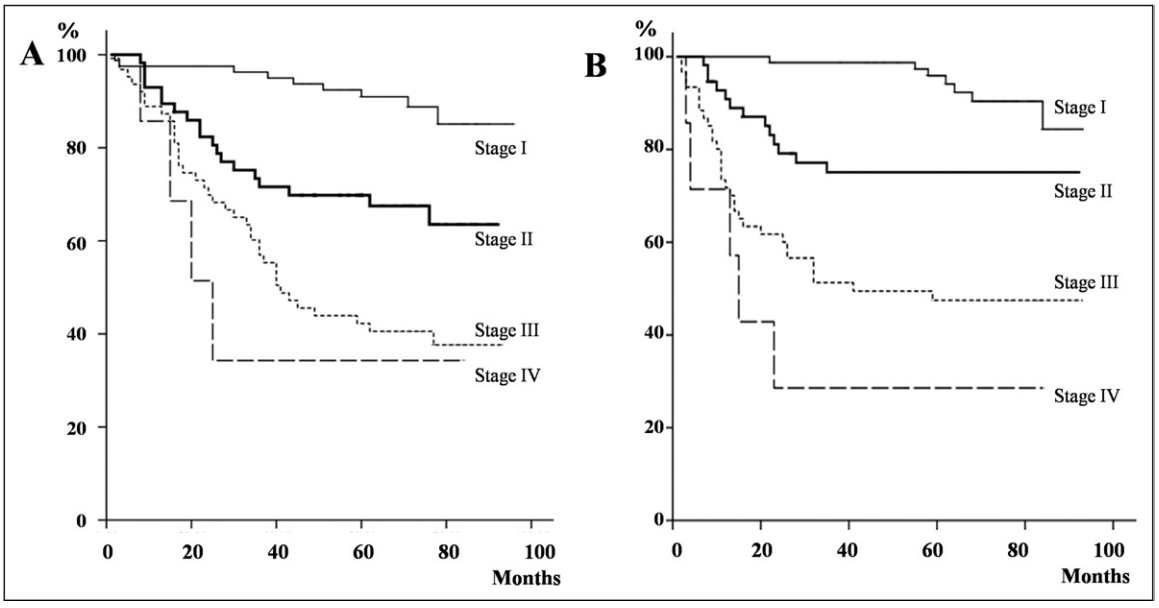

Figure 5 Long-term oncologic outcomes of patients who underwent MIS for gastric cancer. (A) Kaplan-Meier curve presenting the overall survival rate after curative resection. (B) Kaplan-Meier curve presenting the disease-free survival rate after curative resection.

and robotic procedures may be effective for patients with gastric cancer. The benefits of the robotic procedure, including 3-dimensional operation views and the wide-angle movement of the robotic arm without hand tremors, could be useful for the complex lymphadenectomy procedures involved in gastric cancer surgery. In particular, surgeons who are skilled in laparoscopic surgery for gastric cancer can easily overcome the learning curve for robotic surgery.[28] Although the proportion of robotic surgery reached 37% of all MIS for gastric cancer at our institution, it did not affect the complication rates and operation times. One reason for this favorable result is that the robotic surgery was performed by surgeons who had performed >500 laparoscopic surgeries for gastric cancer. However, it has limitation for popular use, because robotic surgery is not covered by the national insurance system in Korea. If clinical studies further demonstrate the efficacy of robotic procedures for gastric cancer and the cost problem is solved, its use will increase.

Conclusions

The proportion of patients with gastric cancer treated with MIS has increased relative to the proportion treated with conventional open surgery. Pathologic results showed that MIS was applied to more advanced cases, and the long-term oncologic outcomes of MIS are reasonable. Given these results, the application of MIS to gastric cancer is expected to increase. In addition, new modalities, such as robotic surgery, will be preferred by both surgeons and patients for reduced invasiveness.

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