REVIEW ARTICLE
Journal of Digestive Cancer Reports 4(2):99-106, 2016

ISSN 2288-1581
http://www.gicancer.or.kr

Current Status of Robotic-assisted Surgery in Gastric Cancer

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Minimally invasive surgery for gastric cancer has increased in popularity during the last two decades mainly in the Asia for patients with early-stage cancer. Nevertheless, the development of laparoscopic surgery for gastric cancers in the Western world has been slow because of the advanced stage at diagnosis for which LG is not yet considered an acceptable alternative to standard open surgery. RAG has been reported as a safe alternative to conventional surgery for treating of early gastric carcinoma.
We assess the current status of robotic surgery in the treatment of gastric cancer focusing on the technical details, postoperative outcome, oncological considerations and future perspectives.
In gastrectomy the biggest advantage of the robotic approach is the ease and reproducibility of lymphadenectomy. Reports also show that even the intra corporeal digestive restoration is facilitated by use of the robotic approach, particularly following TG. Additionally, the accuracy of robotic dissection is confirmed by decreased blood loss in comparison to conventional laparoscopy. The learning curve and technical reproducibility also appear to be shorter with robotic surgery and, consequently, robotics can help to standardize and diffuse minimally invasive surgery in the treatment of gastric cancer. While published reports have shown no significant differences in surgical morbidity, mortality, or oncological adequacy between robot-assisted and conventional gastrectomy. There are some advantages in terms of postoperative recovery of patients after robotic surgery. More studies are needed to assess the true indications and oncological effectiveness of robotic use in the treatment of gastric carcinoma.

INTRODUCTION

The overall incidence of gastric cancer has rapidly declined over the past fifty years but unfortunately gastric cancer still remains the third most common cause of cancer-related death in the world.[1]

Introduction of a screening program for gastric cancer has enabled to increase the 5-year survival rate to almost 60% in Japan and many other Asian countries (Korea, China…)[2-4] but the remainder of the world still has a very poor 5-year survival rate for stage two and beyond disease (less than 25%).[5-9]

Currently, complete surgical resection is the only modality that may offer a cure for patients suffering from gastric cancer. For several years, laparoscopic gastrectomy (LG) has been reported a valid alternative to traditional open surgery in treatment for patients suffering from early stage gastric cancer, particularly in high endemic zones such as Asian countries.[10-15] A number of non-randomized and randomized controlled trials and also meta-analyses have confirmed that laparoscopic surgery for early gastric cancer can improve short-term results and the patients' quality of life when compared to open surgery.[16-20] However, In Western countries due to the decreased incidence of gastric cancer, the long and very complicated learning curve (40-50 cases) of the technique and also diagnosis at advanced stage, LG has not found popularization and still considered as a technically demanding procedure.[21,22]

Robotic assisted surgery has been introduced since late 1990 in order to overcome some technical limitations of lapa roscopic surgery, such as two-dimensional visualization, amplified physiologic tremor and restricted range of motion, ergonomic discomfort and the uncomfortable position forced upon surgeons.[23,24] The da Vinci surgical platform offers today greater surgical precision and ergonomic comfort, increasing the range of motion, improves dexterity, enhances visualization and finally improves access to the operation field. It was believed that all these technical advantages of robotic-assisted technique could assist the surgeons' minimal invasively to perform more complex procedures, that required

Received: November 24, 2016
Accepted: December 23, 2016
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precise surgical dissection and reconstruction, as well as in radical gastrectomy for cancer.[25]

In this review paper, we will discuss the current status of robotic assisted gastrectomy (RAG), including indications, perioperative outcomes, benefits, limitations and future perspectives, when it is used for the treatment of gastric cancer.

History of Robotic assisted Gastrectomy

The first experience of RAG was published in 2003 by Giulianotti, Hashizume and Sugimachi.[26,27] Following these reports, several retrospective studies and also meta-analysis have confirmed the feasibility, efficiency and oncological adequacy of RAG in the treatment of gastric adenocarcinoma.[28-35] The problem is that all those reports did not provide any significant evidence regarding long term survival rates of the patients who underwent RAG. Up to this date there is no significant data available about long term oncologic outcomes and survival of the patients that were treated by this technique. To our understanding, the longest follow up to date was reported by Puglies et al.[36] with a main observation time of 53 months. In this paper authors have compared the 3 year survival rate between RAG and conventional LG groups and found that the 3-year overall survival rate was 85% vs 78% respectively.

Due to the shortfall of studies, that have been published so far, presently the real benefits (including oncologic) of robotic assisted surgery for the treatment of gastric adenocarcinoma still remain inadequately investigated.

Especially, the "hot issue" that often arises, during the debate against this technique is cost-effectiveness of the robotic approach. Unlike the evolution of the use of LG compared to conventional open surgery, the definite advantages and cost-effectiveness of RAG has not been proven using well-designed randomized controlled trials.[37]

What affect has the perioperative outcome of robotic assisted surgery in gastric cancer had in comparison to laparoscopic and conventional open surgery? Well, two non-randomized trials have tried to compare the long-term survival rate between RAG and open gastrectomy. In a study published by Caruso et al.[38] which collected 149 cases after 24 months of follow up no difference in overall survival rate was reported between the two groups. However, in a study published by Pernazza et al.[39] which included 90 cases, after a mean follow up of 26 months, it was observed more long-term benefits of survival in the robotic versus the open group.

The meta-analysis, which included almost all articles published regarding this issue between 1990 and 2011, Xiong et al.[40] tried to compare RAG to LG in terms of perioperative outcomes. This meta-analysis collected 918 patients (268 in robotic arm vs. 650 in laparoscopic arm). The main findings of this paper have showed that while RAG was associated with a significantly longer operative room time (ORT) (OR/WMD 68.7 min for RG vs LG, $p<0.0001$) it also was associated with a significantly less intraoperative blood loss (OR/WMD 41.8 ml for RG vs LG, $p<0.006$). There was no difference between the two groups in terms of number of retrieved lymph nodes (LN), overall morbidity, perioperative mortality, or length of hospital stay (LHS). Whereas some other reports[33,41] showed results in favor of RAG but none of them were with significant statistical differences.

Overall it appears that presently robotic assisted gastrectomy is a feasible and safe method for treatment of early stage adenocarcinoma of the stomach, but the cost-effectiveness has yet to be verified.

Indications for Robotic-assisted Approach

The initial indication for the use of robotic assist approach in gastric cancer surgery was similar to those of laparoscopic surgery, which is clinical diagnosis of early stage gastric cancer without evidence of LN metastasis, except for lesions for which endoscopic submucosal dissection is indicated.[42-44] For this reason, RAG mostly expanded to the clinical stage T1 cancer with perigastric LN involvement and also serosa-negative gastric cancer without LN metastasis. Due to the possibility of peritoneal seeding and port site metastasis, neither robotic or LG is indicated for treatment of serosa-involved gastric cancer, especially in the Asian world.[43,45]

It is also a well known fact today that due to the trends of gastric cancer incidence in the east and west and also due to the governments' screening program in Asian countries there is a higher prevalence of early stage gastric cancer. The largest cohort of early-stage gastric cancer to date was published by Woo et al.[33] A total of 827 patients were included in this nonrandomized comparative study of robotic (236 patients) and laparoscopic surgery (591 patients) for stage Ia and Ib gastric carcinomas. The total ORT was significantly increased for the robotic procedures compared with laparoscopy (219.5 min vs 170.7 min, $p<0.001$), but the robotic group also showed a lower estimated blood loss (91.6 mL vs 147.8 mL, $p=0.02$). The LHS was slightly in favor of the robotic group (7 d vs 7.7 d, $p=0.004$) and there were no differences regarding morbidity and mortality. In terms of oncological principles, the number of retrieved LN was not different and all patients in the robotic group had negative resection margins.

Although the published evidence is incomplete, it seems that serosa involvement would not be a clear and definitive contraindication for either of these approaches.[46] Due to a lack of screening programs for gastric cancer in the western world there is a high prevalence of advanced stage gastric cancer. In the largest study to date (5,839 patients) comparing robotic (436 patients), laparoscopic (861 patients) and open surgery (4,542 patients) performed for stage I, II and III gastric cancer by Kim KM et al,[47] overall safety of these three types of surgery was the main focus. The overall complication rate was the same between the three groups (OG 10.7% LG 9.4% and RG 10.1%, $p=0.494$) and so was their severity ($p=0.424$). However, robotic surgery was prone to complications related to leaks ($p=0.017$), whereas ileus and abscesses were more prevalent in open surgery ($p=0.001$, $p=0.013$ respectively). The robotic group showed a faster recovery with a shorter time to start the soft diet and a shorter LHS ($p<0.001$ for both parameters). This study also showed an increased duration of the procedure compared to laparoscopic and open surgery (224 min vs 176 min vs 158 min, $p<0.001$) combined with a lower estimated blood loss for the robotic group ($p<0.001$). The number of harvested LN was no different between open and robotic surgery. In a study published by Procopiuc et al,[48] enrolled 47 patients, where all patients suffered from exclusively advanced gastric cancer, patients were treated by either open ($n=29$) or robotic ($n=18$) surgery. Significantly longer mean ORT (320.83 min vs 243.36 min), but significantly lower blood loss (208.26 mL vs 546.62 mL) and shorter LHS (11.04 d vs 8.1 d) were obtained for the robotic group. They also found no difference in the number of retrieved LN or the rate of complications. After a mean follow up time of 31.66 month for the open surgery group and a 24.72 for the robotic surgery group, the Kaplan-Meier analysis of the survival data revealed no statistically significant difference between the two cohorts ($p=0.177$).

Our (unpublished) data includes 107 patients who mostly suffered from advanced stage gastric cancer. 62 patients underwent total gastrectomy (TG) (14 of them robotic, 20 laparoscopic and 28 open approaches) and 45 patients were treated by partial gastrectomy (PG) (26 of them robotic, 4 laparoscopic and 15 open technique). Age, gender and body mass index (BMI) were almost similar amongst patients who underwent all types of procedure.

Median LHS for robotic total gastrectomy is 4.5 days and it is significantly shorter than both laparoscopic total gastrectomy 7.0 days ($p=0.003$) and open TG 9.0 days ($p<0.001$). Similar significant differences in LHS between the robotic, laparoscopic and open gastrectomy group is observed amongst patients who underwent partial gastrectomy (median 4 vs 5.5 vs 10 days respectively), but the comparison between robotic and laparoscopic procedures is limited due to small numbers of laparoscopic PG.

Median ORT is significantly longer among robotic gastrectomy compared to open, the difference was 64 min in total gastrectomy group and 145 min in partial gastrectomy group ($p<0.001$ for both differences), but the difference in ORT between laparoscopic and robotic procedures is smaller and not significant. The number of dissected LN is similar between the 3 procedures in total gastrectomy group. In partial gastrectomy group, the number of harvested LN was even higher among both laparoscopic and robotic gastrectomy's compared to open ($p<0.001$).

We believe that robotic assisted surgery has a place in the management of selected patients with advanced gastric cancer but we also realize that there are still specific limitations and contraindications for the minimally invasive approach in those patients such as bulky tumors or tumors that require multi-visceral resection.

Surgical Technique

The operative procedure of RAG is not different from those of LG and open gastrectomy except of the use of robotic ports and articulating robotic instruments. Under general anesthesia, a patient is placed in supine, reverse Trendelenburg position with legs abducted. In the robotic technique, a camera port is inserted by the open method through an umbilical vertical incision with a 12-mm trocar. For all our procedures we used 30 degree robotic scope. After establishing pneumoperitoneum, three 8-mm trocars for the robotic arms are inserted under direct vision: one in the upper right quadrant, one in the lower right quadrant, and one in the upper left quadrant. A final fourth 12-mm trocar is inserted in the lower left quadrant for the assistant (Fig. 1). Either a hook or a monopolar shear is held in the first robotic arm located at the patient's left side. A Maryland bipolar forceps and a Cadiere forceps were held in the second and third arm, respectively, at the patient's right side.

Advantages and Disadvantages of Robotic-assisted Surgery in Gastric Cancer

As we mentioned above, a several technical issues have limited the application and diffusion of laparoscopy in major abdominal surgical procedures, which require special ability and advanced skills of the surgeons. Robotic technology can overcome most of the drawbacks of conventional laparoscopy

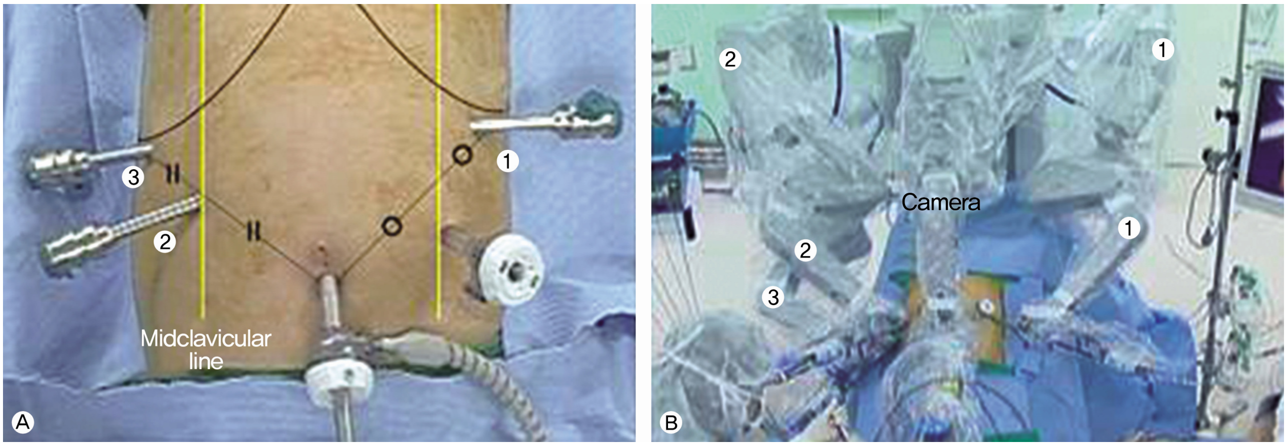

Fig. 1.

and provides the surgeon with an advanced system for viewing and manipulation, and the physiologic tremor is eliminated using a computerized mechanical interface. Additionally, the reticulated tools provide seven degrees of freedom (Endo-Wrist™ System) and can reproduce the movements of the human hand inside the abdominal cavity, thus facilitating manipulation. In fact, some clinical trials have shown that the robotic system can enhance the skill of surgeons in performing difficult dissections and suturing techniques.[49]

Improved view and less traumatic approach

With the robotic surgical system, the surgeon can access to a magnified, high-definition, three-dimensional vision. The images at the console are very sharp and similar to those of a surgical microscope, and the surgeon can easily identify smaller anatomical structures that cannot be visualized in conventional open and laparoscopic surgery. Another benefit of the view system in the robotic platform is the stability of the camera, which is held by a robotic arm and controlled directly by the operator surgeon. In addition, the robotic system is able to obtain a good view of all areas of the operating field. For example, during a radical gastrectomy, the operating field ranges from the first jejunal loop to the celiac trunk, or esophageal hiatus in cases of total gastrectomy. The nature of this operating field requires a compromise in port positioning and conventional laparoscopy does not allow adequate viewing in all cases (particularly in obese or long-limbed patients). For this reason, more accessory ports and a switch between camera and surgical tools are necessary to optimize the working conditions.

Without doubt, another major advantage of robotic assist techniques is the less traumatic effect on the tissue. Hiki et al.[53] asserted that manual handling of organs during gastrectomy is an important contributor to the inflammatory response after surgery. The small and reticulated robotic instruments may induce less conflict with tissue during surgery and respectively less inflammation than the instruments used for the laparoscopic or open surgery. Hence, postoperative bowel recovery in the robotic group may occur sooner and patients start to get diet faster. In addition, due to a low rate of postoperative pain there is less need of pain medications, they start to be mobile much faster which itself decreases significantly postoperative complications (pneumonia, thrombosis…) and patients can be discharged home faster.

Ergonomic Approach and Need of Less learning Curve

Another important point related to the Robotic-assisted approach is the learning curve. Several authors have reported that it requires a shorter learning curve than conventional laparoscopy, particularly in cases of radical gastrectomy and lymphadenectomy for gastric cancer.[50-52] Our subjective opinion is that for a surgeon well trained in open and laparoscopic surgery, the shift to robotic techniques is very fast for two reasons. Firstly, most of the robotic general surgery procedures are laparoscopic assisted robotic procedure and secondly, during the robotic surgery we use same principles as in conventional laparoscopy (make pneumoperitoneum and at the same time to use a laparoscopic energy devise by an assistant surgeon….). However, we also assume and believe that although experience in laparoscopic surgery is helpful and important, it is not mandatory for every surgical procedure and thus a shorter learning curve would make it easier for inexperienced surgeons to adopt minimally invasive surgery, in general, for treatment of different surgical pathologies including gastric cancer.

Finally, the robotic console reduces ergonomic discomfort, enabling the surgeon to maintain a comfortable position for many hours if needed. We believe that all of these technical advantages are very important to improve the performance status of surgeons and the quality of minimally invasive surgery, particularly for longer and more complex surgical procedures.

Lymph Node Dissection

As we all know, one of the crucial steps in gastric cancer surgery is lymphadenectomy since the removal of an adequate number of LN has been shown to improve the accuracy of staging and regional disease control.[53] This procedure is typically considered to be technically difficult to perform in conventional laparoscopic surgery, especially when D2 lymphadenectomy is mandatory.[54] This is mainly due to the use of conventional straight forceps in laparoscopic surgery that do not allow the surgeon to reach deep-seated vessels and areas such as for example the supra pancreatic one. As previously discussed, stable exposure and use of wristed instruments with the robotic system may help the surgeon to efficiently perform very precise LN dissection in these complicated areas, in particular around the posterior aspect of the common hepatic artery and the splenic vessels, including the splenic hilum.

In addition, during LN dissection in cases of vascular injury the recovery from bleeding is easier than with conventional laparoscopy. In this situation, the surgeon has direct control of the vision and can use three surgical tools for clamping and suturing which is significantly easier to perform by wristed instruments. We believe that it is almost impossible to reproduce in same working conditions during a conventional laparoscopic procedure.

In a comparative study among open, laparoscopic and robotic gastrectomy, Kim et al.[55] it was reported that there were no differences in terms of number of harvested LN. However, the estimated blood loss in the robotic group was significantly lower than in the open and laparoscopic groups. The same result was reported in the meta-analysis from Xiong et al. 40 Our (unpublished) data also supports the literature. In Robotic total gastrectomy group the median number of dissected LN was 23.5 vs. 21 in laparoscopic group and in subtotal gastrectomy group 21.5 vs 20.5 respectively (not statistically significant different).

Finally, other reports have indicated that the robotic system can facilitate D2-lymphadenectomy in patients with high BMI compared with conventional laparoscopy.[56-59] Recently, Lee et al.[60] have shown that the benefits of a robotic approach were more evident in high versus normal BMI patients when performing distal gastrectomy with D2 lymphadenectomy, particularly in terms of achieving a consistent number of retrieved LN (>25). The authors concluded that robotic surgery may overcome the technical difficulties due to excessive intra-abdominal fat and thick abdominal walls during laparoscopic lymphadenectomy. In our (unpublished) data median BMI of patients underwent RAG was 29.4.

Digestive Reconstruction

One of the important technical drawbacks during conventional LG is digestive restoration particularly following total gastrectomy (TG). The anastomotic techniques reported for RAG procedures are very different for TG, ranging from a hybrid-open approach to a full robotic procedure. Previously it has been reported that digestive restoration was performed extra corporeally through the same mini laparotomy used for specimen removal.[65,66] This hybrid-open technique was used both in gastrojejunostomy and gastroduodenostomy following distal gastrectomy, as well as in esophagojejunostomy following TG. Song et al.[65] reported that this approach is possible for patients with a very low BMI. As a result, most of the Asian surgeons usually use extra corporeal anastomosis. In cases with high BMI, it is very difficult to perform an extracorporeal anastomosis, unless an incision larger than that for a mini laparotomy.[67-69] Another problem with extracorporeal anastomosis is the lack of appropriate vision, as well as the excessive traction put on the viscera, making the application of stapling devices under these conditions potentially difficult and dangerous. Other authors, particularly from the Western world, have reported performing an intra corporeal digestive restoration using a linear stapler for gastrojejunostomy and a circular stapler for esophagojejunostomy.[26,31,56] This technique is more commonly used in Western countries where higher BMI patients rarely consent to an extracorporeal anastomosis.

Currently, using intra corporeal techniques for digestive restoration appears to be the preferred solution for robot-assisted procedures and is applicable in every type of patient. The technical precision of the sutures is comparable to that of open surgery and the advantages of a minimally invasive procedure, including less pain and better aesthetics, remain. In fact, several Asian authors have reported a technical shift from extra corporeal to intra corporeal anastomosis.[70,71] It is expected that increased experience and confidence with the robotic system will enable the surgeon to perform high-precision intra corporeal sutures, thereby ensuring a safer method for patients undergoing digestive anastomoses.

Operating Room Time

A variety of studies that have been published about robotic assisted gastric surgery have reported that operating room time (ORT) is prolonged when compared with the laparoscopic approach.[61-63] There are a number of possible explanations for this: first, robotic surgery is associated with an increased set-up time needed to position the robotic platform before beginning surgery. However, according to several reports in the literature and also our own experience, docking times can be shortened after passing the learning curve. Secondly, the prolonged time may be due to camera motion interrupting the operative procedure. However, longer ORT never has been shown to translate into increased perioperative complications and thus should not discourage surgeons from investigating the further use of robotic assisted surgery.

Compared to many other studies in the literature, our (unpublished) data hasn't shown any significant difference in terms of ORT between robotic and laparoscopic groups. Median ORT for Robotic total gastrectomy group was 273 min vs 265 min for laparoscopic group (no statistically significant difference). Median ORT for Robotic subtotal gastrectomy group was 277 min vs. 256 min for laparoscopic group (no statistically significant difference).

Cost Efficiency

As it was mentioned above, one of the unresolved issues regarding robotic surgery is cost efficiency. Robotic assisted gastric surgery undoubtedly has higher costs than laparoscopic surgery[64] and the only way its use can be justified would be through improved patient survival achieved through more efficient surgery. So far, several studies have showed the potential relevant advantages of robotic technique that would justify the higher costs of robotic systems. However, a multicenter, randomized study is needed to confirm this clinical benefit and evaluate whether it may effectively translate into improvement of long-term patient survival and quality of life.

Future Direction

In the near future, perhaps the introduction of new systems for integrated and advanced imaging can include an aid for surgeons to better identify the position of the tumor, resection margin, and regional nodes needed to be removed. A current example of this is a newer version of the da Vinci Surgical System, which integrates indocyanine green (ICG) fluorescence via an infrared camera. For gastric cancer patients, a possible application may be the injection of ICG into the tumor following lymphatic diffusion, which would allow for easier identification of the regional nodes draining lymph from the tumor. Theoretically, it would also be possible to identify the sentinel nodes in cases of EGC treatable by local resection.

CONCLUSIONS

To date, RAG for gastric adenocarcinoma is associated with oncological adequate lymphadenectomy, faster patient recovery and longer operating time. The major technical advantages of the robot-assisted approach are the ability to perform very precise LN dissection and intra corporeal reconstruction. The accuracy of robotic surgical dissection results in decreased blood loss and need of intraoperative blood transfusion. The learning curve and reproducibility of RAG seems to be shorter and more feasible than with conventional laparoscopy and therefore robotics has the potential to contribute a standardization and major diffusion of minimally invasive surgery for the treatment of gastric cancer. Although more studies are necessary to assess adequately the indications and oncological effectiveness of robotic treatment of gastric carcinoma, the potential of this approach cannot be ignored. This is a reality today that RAG already appears a valid alternative to conventional open or laparoscopic resection of gastric cancer for the treatment of early stage gastric adenocarcinoma and we deeply believe that with a steep learning curve, reasonable oncological results and complications, da Vinci robotic gastrectomy can become the procedure of choice for any operable stage gastric cancer patient.

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