JGS

REVIEW ARTICLE

OPEN ACCESS

Robotic surgery for gastric cancer: a review of the literature

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To Cite
Di Nardo D, Palazzini A, Parisi A. Robotic surgery for gastric cancer: a review of thw literature. J Gastric Surg 2021; 3(2).

Publication history
Received: March 03, 2021
Accepted: March 15, 2021
Article in press: June 15, 2021
Published online: September 15, 2021

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ABSTRACT

Minimally invasive surgery is increasing attention worldwide as an effective treatment approach in gastric cancer.

In this context, several studies suggest that robotic technology may add some advantages over traditional laparoscopy, but the role of the robotic approach in the common surgical setting is still uncertain.

The objective of this study is to review the current evidences in the literature comparing robotic surgery to other surgical approaches.

Patients underwent robotic gastrectomy showed some benefits in terms of blood loss, postoperative morbidity, and length of hospital stay. No significant differences have been found in terms of survivals, while the number of lymph nodes retrieved with the robotic approach, expecially in the extraperigastric region, is generally higher than that of laparoscopy.

The current studies in the literature suggest that the robotic gastrectomy is not inferior to the laparoscopic procedure and provides some surgical and clinical benefits.

Keywords:
gastric cancer; robotic gastrectomy; minimally invasive surgery.

Background

Robotic surgery was born with the intention of overcoming the intrinsic technical limitations of the laparoscopic approach and of facilitating and making safer complex surgical maneuvers performed in traditional laparoscopy. In recent years, there has been a significant increase in the use of the robotic platform for the performance of gastrectomy for cancer and above all of total gastrectomy and extended lymphectomy (D2) in the treatment of advanced gastric cancer[1-3].

Performing D2 lymphectomy with removal of extraperigastric lymph nodes represents a technically demanding surgical maneuver to be performed laparoscopically. Along with intra-body anastomoses, D2 represents the limits of the application and diffusion of laparoscopic surgery for the treatment of gastric cancer[4]. These surgical steps of gastrectomy, in fact, require the execution of extremely delicate and fine surgical maneuvers that require high precision and excellent vision of the operating field.

Methods

Two authors (DDN, GP) performed an independent literature search. The PubMed/MEDLINE databases were queried with the following search: "robot-assisted surgery" and "laparoscopic" and "gastric cancer" and "gastrectomy". All article types were considered including case reports and case series. Reviews and meta-analyses were also included in the analysis.

The search was limited to the English language literature. The two authors evaluated and selected titles and abstracts of the relevant records. The included articles were fully revised and discussed among the authors and differences in opinion were solved with the opinion of a third author (AP).

The studies met the following criteria:

• Patients undergoing robotic total or distal gastrectomy for gastric cancer.

• Data on perioperative, post-operative, and oncological outcomes.

Continuous data are shown as mean ± standard deviation, whereas Categorical data are reported as numbers and percentages.

Robotic lymphadenectomy

SThe limited ergonomics and rigidity of laparoscopic instruments make the execution of D2 lymphectomy particularly difficult to perform, even for experienced laparoscopic surgeons. Specifically, the lymph node stations that are most difficult to remove with the laparoscopic technique appear to be numbers 4sa, 6, 9, 10, 11p, and 12a[5]. In addition to the technical complexity of the laparoscopic execution of a complete D2 lymphectomy (from the point of view of oncological principles), the technique brings with it the risk of iatrogenic haemorrhagic lesions of the large vessels along which some lymph node stations must be removed. These include the infrapyloric region, the inferior mesenteric vein (stations 6 and 14), and the lymph nodes of the supra-pancreatic region, including stations 7, 8, and 9[6].

The technical complexity of D2 lymphectomy, therefore, has the potential to result in the removal of a reduced number of lymph nodes, which in turn potentially implies a worsening of patient survival and an increase in intra-and postoperative morbidity. The guidelines of the U.S. National Comprehensive Cancer Network (NCCN) on the surgical treatment of gastric cancer not only indicate D2 lymphectomy as a standard curative treatment but also indicate the removal of at least 15 lymph nodes in order to achieve adequate staging of the disease. This guideline is based on a study that suggests that at least 15 lymph nodes be removed as the minimum necessary to obtain a survival benefit for the patient and to obtain a correct staging of the disease[7]. This study, like others[8], has shown that a continuous increase in survival is obtained with an increase in the number of lymph nodes removed, up to 40.

There are studies in the literature that have shown the removal of a significantly lower number of lymph nodes in D2 lymphectomy performed with the laparoscopic approach compared to the open approach. In particular, in the study by Miura and colleagues, a reduced number of lymph nodes removed with the laparoscopic approach compared to the open approach was detected at the level of the lymph node stations along the great gastric curvature (stations 4 and 6), at the level of the celiac axis (station 9), and along the splenic artery (stations 11), resulting in an incomplete D2 lymphectomy[5]. Other authors found a significant reduction in the number of lymph nodes removed by laparoscopy compared to the open approach, even in the lymph node stations located along the common hepatic artery during laparoscopic distal gastrectomy[9].

Another surgical maneuver that is particularly difficult to perform laparoscopically in the context of D2 lymphectomy is that required when, based on the location of the neoplasm along the great gastric curve, it is necessary to remove the lymph nodes of the splenic hilum (station 10) to avoid the removal of the spleen and pancreatic tail. The removal of this organ and partial organ has been shown to have the potential to significantly increase perioperative morbidity and reduce survival[10, 11]. The lymph node dissection of the splenic hilum (station 10), with preservation of the spleen, is, in fact, particularly complex due to the depth inside the abdomen of the location of the splenic hilum and the wide anatomical variability of the terminal branches of the splenic artery along which the lymph nodes to be removed are located[12]. In this case, the possibility of causing uncontrollable bleeding or damage to the pancreas or spleen is very high, especially when using rigid and poorly ergonomic laparoscopic instruments.

The technical advantages offered by the robotic platform compared to laparoscopy are particularly important in oncological gastric surgery. In fact, the robotic approach makes it possible to perform lymph node dissection with greater precision and safety of the stations most difficult to remove laparoscopically, also reducing the risk of bleeding and iatrogenic damage to organs[13]. Robots can accomplish this because their articulated instruments make it is possible to perform finer and

more delicate surgical maneuvers that avoid tractions and excessive pressure on the tissues. Robots perform a more precise dissection compared to their laparoscopic counterparts, giving them the potential to reduce blood loss and to reduce trauma to organs and tissues[14].
The use of the robot also allows the elimination of the physiological tremor of the operator as well as that of the laparoscopic instruments, resulting in high-definition three-dimensional images of the operating field taken by robotic video-optics. Moreover, because robotic instruments are articulated, and being provided with "endowrist" (which allows the tip of the robotic instruments to rotate like the human wrist), they also allow for increased dexterity of movements inside the abdomen.
These features make it easier to carry out complete lymph node dissections even in areas that are difficult to access and "uncomfortable" to reach with rigid laparoscopic instruments. These areas include the region of the splenic hilum and the dorsal region of the pancreas, along which lies part of the D2 lymphectomy[13]. In fact, using laparoscopic instruments, it is difficult to reach this superior-posterior part of the pancreatic back, on which the splenic artery and the relative lymph node stations run, without applying excessive pressure on the pancreatic gland. This poses the risk of haemorrhagic lesions or of causing lesions of the gland with the ensuing onset of pancreatitis and pancreatic fistulas.
In these cases, and for all the other extra-perigastric lymph node stations in general, having the technical advantages of robotic surgery allows these surgical steps to be performed with greater comfort, precision, and ease, and therefore, theoretically, with greater efficacy and safety than the laparoscopic approach.

Reconstruction possibilities
It should be emphasized that the potential benefits of using the robot in gastric cancer surgery also lie in the advantages that this approach offers in the execution of intracorporeal anastomoses. Intracorporeal intestinal anastomoses represent another major technical limitation of traditional laparoscopy due to the difficulty of performing intracorporeal sutures with laparoscopic instruments[15].
This is particularly evident after performing a total gastrectomy, which requires the preparation of an esophagus-jejunal anastomosis and a jejuno-jejunal anastomosis, in the case of reconstruction with a Roux-en-Y technique. In this case, robotic surgery is particularly useful because of the technical advantages previously described. In fact, in the event that an intracorporeal esophagus-jejunal anastomosis is to be performed with a circular mechanical suturing device, as often happens in open surgery, the greater capacity of intracorporeal manipulation of the robot allows the placement and fixation of the head of the circular suturing device with greater dexterity and ease at the level of the esophageal stump, compared to the laparoscopic approach[13]. If an intracorporeal esophagus-jejunal anastomosis is planned with total manual suturing, the robot also offers, in this case, the possibility of performing sutures with greater ease and precision than laparoscopy, in particular in narrow and difficult-to-reach spaces such as the area of the esophageal hiatus[16, 17]. The intracorporeal performance of the anastomoses, facilitated by robotic surgery, allows us to avoid the creation of large incisions often necessary in laparoscopy to perform intestinal anastomoses. Therefore, robots allow us to respect even more the principles of minimal invasiveness, potentially increasing the rate of totally intracorporeal procedures.

Comparison of outcomes
The first report in the literature describing a robotic gastrectomy was published in 2003 by Hashizume and colleagues[18].
Over the last decade, many studies have confirmed the feasibility of the robotic approach for performing gastrectomies for cancer. However, while the current literature presents three RCTs, only one of them, from the Department of Gastric Surgery at Fujian Medical University Union Hospital (Fuzhou), headed by Prof. Chang-Ming Huang, uses a high-quality methodology[19].
The RCT from this high-volume Gastric Cancer Center evaluated the short-term outcomes of patients who underwent robotic distal gastrectomy and compared them with those patients who underwent laparoscopic distal gastrectomy.
This is a relevant study, because despite the increasing use of robotic technology in gastric cancer patients, its safety and efficacy have not yet been delineated in a randomized controlled trial. This study represents the first RCT in this setting.
Three hundred patients with cT1-4a and N0/+ (between September 2017and January 2020) were enrolled.
The robotic group showed a faster postoperative recovery, milder inflammatory responses, and reduced postoperative morbidity (9.2% vs. 17.6%; respectively, p=0.039). Higher extraperigastric lymph nodes were retrieved in favor of the robotic group (17.6 ± 5.8 vs. 15.8 ± 6.6, p=0.018), with a lower noncompliance rate (7.7% vs. 16.9%; respectively, p = 0.006). Moreover, patients in the robotic group were more likely to start adjuvant chemotherapy earlier (median postoperative days: 28 [24-32] vs. 32 [26-42], p=0.003).
The direct cost was lower for the robotic approach than for laparoscopy (p<0.001). Therefore, the authors concluded that robotic surgery is associated with a lower morbidity rate, faster recovery, milder inflammatory responses, and improved lymphadenectomy.
In this context, another landmark study is a prospective study from the same Department of Gastric Surgery at Fujian Medical University Union Hospital (Fuzhou), headed by Prof. Chang-Ming Huang[20]. This compares the short-term outcomes, surgery burden, and technical performance of robotic total gastrectomy and laparoscopic total gastrectomy.
The study included 50 patients with advanced gastric cancer who underwent robotic gastrectomy combined with spleen-preserving splenic hilar lymphadenectomy between March 2018 and February 2020.
The robotic group had a lower volume of intraoperative blood loss than the laparoscopy group (38.7 vs. 66.4 mL, P = 0.042). The robotic approach also allowed the retrieval of more extraperigastric lymph nodes (20.2 vs.

17.5, P = 0.039).
The number of errors was lower in the robotic group than in the laparoscopic group (43.2 vs. 53.8 times/case, P < 0.001). A higher technical skill score (30.2 vs. 28.4, P < 0.001) and a lower surgery task load index (33.2 vs. 39.8, P <0.001) was shown in favor of the robotic surgery. There were no significant differences in terms of postoperative morbidity (14.6% vs. 16.7%, P = 0.748).
The authors of the final report on this high-level research concluded that robotic technology could provide experienced surgeons at high-volume, specialized institutions with a more precise operating environment and reduced surgical burden.
We believe that when robotic surgery is popularized to a certain, the urgent high-level evidence is warranted for its spreading. The two studies conducted by Fujian Medical University Union Hospital firstly confirmed the better short-term efficacy of robotic gastrectomy than laparoscopic gastrectomy and provided high-level evidence for the application of robotic surgery for patients with GC. These evidences play an important role in promoting the development and popularization of robotic gastrectomy for gastric cancer, which also provides more high-quality options for surgical treatment for patients with gastric cancer. In addition, these findings are of great significance to guide the Western surgeons to carry out minimally invasive gastric cancer surgery due to the low incidence rate of GC in Western regions.
Another study[21] compared the number of lymph nodes removed in 586 open, 64 laparoscopic, and 39 robotic gastrectomies. The authors of the study emphasized that they have encountered technical difficulties in performing D2 lymphectomy with a laparoscopic approach and to have performed a D2 lymphectomy only in 19% of patients treated with a laparoscopic approach compared to 88% of patients in the open group and 87% of patients in the robotic group. They also emphasized that with the help of robotic instrumentation, the execution of the D2 lymphectomy is considerably facilitated compared to the laparoscopic approach, in particular for the removal of infrapyloric and suprapancreatic lymph node stations[21].
Yoon and colleagues[22] specifically compared laparoscopic total gastrectomy with D2 lymphectomy performed in 65 patients versus a robotic procedure performed on a total of 36 patients. In particular, the authors claim that the robotic group removed a higher number of lymph nodes in the extraperigastric stations (stations 7–14) and, in particular, the suprapancreatic ones (stations 7–12a) in the splenic hilum and along the splenic artery. This suggests that robotic surgery actually facilitates the removal of lymph node stations that are more difficult to remove by laparoscopy.
Junfeng[23] found a significantly higher mean number of lymph nodes removed with the robotic approach (mean of 34.6 lymph nodes removed) compared to laparoscopy (mean of 32.7 lymph nodes removed). Specifically, the authors found a significantly higher number of lymph nodes removed with the robotic approach in the extraperigastric stations, explaining that this could be linked to the fact that the robotic approach facilitates exposure and dissection of some lymph node stations of the second level (such as stations 7, 8a, 9, and 11p), whose removal is notoriously more complex with the laparoscopic approach. This study is also one of few to report data on the 3-year survival of the patients included in the study. The 3-year overall survival rates were 67.8% in the robotic group and 69.9% in the laparoscopic group, and, therefore, substantially overlapping.
The authors of the study, Son and colleagues[24], found no significant difference in terms of the overall number of lymph nodes removed (mean of 47.2 lymph nodes removed with the robotic approach and 42.8 with the laparoscopic approach), but confirmed that the robotic approach allowed the removal of a significantly greater number of lymph nodes located in notoriously difficult-to-remove stations, such as the splenic hilum and along the splenic artery.
In another study, Wang and colleagues[25] compared the execution of robotic gastrectomy with the open approach. The authors randomized a total of 145 patients to an open surgery treatment group and 151 patients to a robotic treatment group. The results of the study did not reveal significant differences in terms of the number of lymph nodes removed between the open and robotic approaches (mean of 30.9 versus 29.3 lymph nodes removed with the open and robotic approaches, respectively), or in terms of postoperative complication rates. However, robotic surgery has made it possible to obtain a significant advantage in terms of reducing the amount of intraoperative blood loss, the length of hospital stay, and the time necessary for intestinal function to resume. The robotic approach, however, is burdened by significantly longer operating times than the open approach.

Discussion

In sum, current studies regarding the execution of gastrectomy with robotic D2 lymphectomy for cancer report conflicting results in terms of short-term oncological outcomes (number of lymph nodes removed) compared to the open and laparoscopic methods. Few studies have evaluated long-term survival (3 years) after performing a gastrectomy with robotic D2 lymphectomy. The number of lymph nodes removed is typically considered only as a surrogate measure of survival, which instead represents the best endpoint for evaluating the oncological efficacy of a surgical procedure. However, in the case of gastric cancer, numerous studies, including some so-called population studies, performed in both high- and low-volume centers, show that survival improves with the increase in the number of lymph nodes removed[26-29]. It remains difficult to ascertain whether this is linked to a real therapeutic beneficial effect or to the so-called phenomenon of "stage migration" [30].
In this regard, as already pointed out, there are currently few studies in the literature that have described survival after gastrectomy with robotic D2 lymphectomy compared to the laparoscopic counterpart, and no study has performed a comparison, in terms of survival, between robotic and open approaches.
A study by Li and colleagues[31] included patient survival at follow-up among the endpoints. The

researchers compared 112 patients who underwent robotic gastrectomy versus 112 patients who underwent laparoscopic gastrectomy with D2 lymphectomy. The authors found no significant difference in terms of the number of lymph nodes removed between the two groups or in terms of 3-year overall survival (78.6% vs 74.1% respectively in the robotic and laparoscopic groups). Eighteen percent of the robotic group and 21% of the laparoscopic group had a recurrence of disease at the 3-year follow-up.

The oncological follow-up of two groups of patients undergoing robotic or laparoscopic gastrectomy was also analyzed in a retrospective observational study by Pugliese and colleagues[32]. However, in this study, there are a number of patients in both groups (about half) affected by early gastric cancer and therefore not subjected to D2 lymphectomy. The robotic group had a follow-up of only 28 months, and therefore, only the three-year survival was reported, which is not significantly different between the two groups of patients (85% versus 78% in the robotic and laparoscopic groups, respectively).

Junfeng and colleagues[23] compared 120 robotic versus 394 laparoscopic gastrectomies and found no significant difference in terms of 3-year survival between the two groups (the robotic group and the laparoscopic group had 1-year survival rates of 90.2% and 78.1, respectively). % at 2 years and 67.8% at 3 years, while in the laparoscopic group 87.3% at 1 year, 77.1% at 2 years and 69.9% at 3 years). In this study, however, a significant proportion of patients underwent D1 lymphectomy.

Finally, the study by Son and colleagues[24] currently reports the longest follow-up after robotic gastrectomy, with an average follow-up duration of 70 months. From the comparison between robotic and laparoscopic gastrectomy with D2 lymphectomy, the authors found no statistically significant difference either in terms of 5-year overall survival (89.5% in the robotic group versus 91.1% in the laparoscopic group) or in terms of disease-free survival (90.2% in the robotic group versus 91.2% in the laparoscopic group).

Ultimately, analyzing the literature available to date, it is impossible not to see the growing attention of the international scientific community with respect to the use of both laparoscopic and robotic minimally invasive surgical techniques for the treatment of gastric cancer due to their ability to produce better perioperative outcomes compared to surgery. Open (including pain relief, faster postoperative functional recovery, and reduced hospital stay). However, with regard to the use of the laparoscopic approach in the execution of D2 lymphectomy during gastrectomy for cancer, as mentioned, a substantially skeptical attitude of the international community currently persists, linked to the scarcity and controversy of the evidence available in the literature that does not make it possible to definitively sanction its non-inferiority in terms of oncological outcomes and survival rates compared to traditional open surgery[33]. In this scenario, the robotic system offers technical advantages that make the execution of technically more complex surgical maneuvers, such as D2 lymphectomy, easier and safer to perform than the laparoscopic counterpart.

Despite this, the evidence supporting the superiority of the robotic approach over the laparoscopic approach in gastrectomy with D2 lymphectomy is scarce and contradictory, as previously emphasized and reiterated by many authors and by the absence at the moment of guidelines that regulate its use[14, 34]. As evidence of this, almost all studies published in the field of laparoscopic and robotic surgery for the treatment of advanced gastric cancer, or concerning the execution of a D2 lymphectomy, call for the conduct of new multicenter randomized studies on this specific topic. However, this type of study is notoriously difficult to carry out due to the high costs and the fact that not all centers are able to offer patients both the laparoscopic and robotic approaches. Moreover, in many Asian countries, in which the incidence of gastric cancer is higher, it is the patient himself who decides whether or not to carry out the intervention with a robotic approach since he has to pay for the use of robotic technology, making randomization impossible.

An ideal study to investigate the role of minimally invasive surgery in gastrectomy with D2 lymphectomy requires not only many patients to obtain adequate statistical power but also to be able to investigate many clinical, surgical, and oncological variables, which could affect the results. From this perspective, despite a large multicenter randomized study, the creation and use of a multicenter registry, like that of our international study group on Minimally Invasive Surgery for Gastric Cancer (IMIGASTRIC), represents a valid alternative tool for the collection and analysis of data deriving from multiple institutions in the world[35].

Acknowledgements
None

Contributors
DDN, GP, AP conceptualized and designed the study, acquired, and analyzed data, interpreted the study results, drafted and revised the manuscript.

Funding
No funding was received for this study.

Competing interests
No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

Availability of data and materials
Further information is available from the corresponding author on reasonable request.

Ethics approval
Not applicable.

Provenance and peer review
Not commissioned; externally peer reviewed.

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