Updates in Surgery (2019) 71:367–373
https://doi.org/10.1007/s13304-018-0533-5

ORIGINAL ARTICLE

Robotic assisted gastrectomy compared with open resection: a case-matched study

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Received: 4 December 2017 / Accepted: 26 April 2018 / Published online: 4 May 2018
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Abstract
In recent years, increasingly sophisticated tools have allowed for more complex robotic surgery. Robotic gastrectomy, however, is adopted in only a few selected centers. The goals of this study were to examine the adoption of robotic gastrectomy and to compare outcomes between open and robotic gastric resections. This is a case-matched analysis of patients who underwent robotic and open gastric resection performed at Sanchinarro University Hospital, Madrid from November 2011 to February 2017. Patient data were obtained retrospectively. Clinicopathologic characteristics and perioperative and postoperative outcomes were recorded and analyzed. Two groups of demographically similar patients were analyzed: the robotic group ($n=20$) and the open surgery group ($n=19$). The patient characteristics of the two groups have been compared. Robotic resection resulted in less blood loss, shorter postoperative hospital stay, and a longer operating time. The two groups had similar complication rates. Pathological data were similar for both procedures. Robotic gastrectomy for locally advanced gastric carcinoma is safe, and long-term outcomes are comparable to those patients who underwent open resection. Robotic gastrectomy resulted in a shorter hospital stay, less blood loss and morbidity comparable with the outcomes of open gastrectomy.

Keywords Robotic gastric cancer · Gastric cancer · Minimally invasive surgery · Reconstruction · Robotic gastrectomy · Total gastrectomy

Introduction

Total and subtotal gastrectomy with D2 lymph node dissection is the standard surgical procedure for most resectable gastric cancers [1]. Today, there are clearly important changes in the surgical approach of gastric cancer treatment due to an increased interest in the minimally invasive surgery (MIS) approach, as described by several authors in various fields [2]. MIS has progressively gained widespread interest for its important outcomes compared with the traditional open surgery approach [3, 4]. MIS may offer many advantages, including reduced postoperative pain, rapid recovery of gastrointestinal function and a shorter hospital stay. Nevertheless, laparoscopy gastrectomy (LG) has several notable limitations, especially the requirement for extensive D2 lymph node dissection which is performed in only a small number of medical centers that have extensive experience in esophagogastric surgery [5]. The robotic surgical system (RSS) was developed to overcome the current disadvantages of conventional laparoscopic surgery (LS). The potential advantages of robotic gastrectomy (RG) are related to the wristed instruments, 3D visualization, and improved ergonomics [6, 7].

In this series, we match open and robotic gastric resection. The safety and oncologic outcomes are compared between open and robotic resections.

Materials and methods

This study is a review of a prospectively collected database including patients undergoing robotic and open total gastrectomies for gastric cancer between November 2011 and February 2017. Patient demographics, operative data,

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pathology reports, and outcome data were obtained from a prospectively maintained gastric surgery database at Sanchinarro University Hospital, General Surgery Department, San Pablo University, CEU, Madrid, Spain.

Preoperative diagnosis, evaluation of tumor characteristics and staging were carried out by esophagogastroduodenoscopy with core-needle biopsy, computed tomography (CT), PET-CT and endoscopic ultrasonography (EUS). The pathological staging of the tumor was established according to the AJCC Cancer Staging Manual 7th Edition (2010) [8].

Robotic approach was used for T1, T2 and T3 tumor without involvement of other organs or vessels. Patients with cases of suspected advanced disease underwent a diagnostic laparoscopy prior to intervention. For all T3 and positive lymph node cancers, perioperative chemotherapy (PC) was planned, and previous workup assessments were repeated to assess the pathological response. Complications were graded using the Clavien–Dindo classification [9]. All patients were prospectively followed up with routine visits, initially 15 days after hospital discharge, and subsequently considering the clinical development. The main objective was to analyze the two groups in terms of intraoperative outcomes (operative time, blood loss, conversion to open surgery), short-term outcomes (complications, hospital stay, reoperation) and pathological data (resection margins, retrieved lymphonodes). Two surgeons—both experts in digestive surgery—performed all of the procedures with D1 or D2 lymphadenectomies following the Japanese Classification of Gastric Cancer (JCGC) [10]. The robotic procedures were performed using the Da Vinci® Si Surgical System (Intuitive Surgical, Inc., Sunnyvale; CA, USA) for the first procedures and then from 2014 we used the last Da Vinci® Xi generation. Both surgeons had extensive advanced laparoscopic experience and had completed an obligatory national training program at a certified robotic center (Santander, Spain).

Perioperative chemotherapy

Patients with T3 or N-positive tumors underwent PC in accordance with the EOX protocol (Epirubicin, Oxaliplatin, Xeloda) [11]. Chemotherapy was administered for three cycles preoperatively and three cycles postoperatively. Each three-week cycle consisted of epirubicin (epirubicin 50 mg/m^2 day 1) by intravenous bolus on day 1, oxaliplatin (130 mg/m^2 day 1) intravenously with hydration on day 1 and Xeloda (Capecitabine 625 mg/m^2/12 h) by oral administration. After the first cycle and in the absence of progression, deterioration of performance status, unacceptable toxicity or patient refusal, a second and third cycle of chemotherapy was administered. Before each cycle of chemotherapy, a complete blood count was obtained, and blood, urea, nitrogen, electrolyte and serum creatinine levels and liver function were determined. Dose modifications were defined for patients with toxicities (other than alopecia and vomiting) higher than grade 2. Restaging by endoscopy and CT scan was performed at the end of third cycle. Resection of the gastric tumor was performed at 4 weeks after the last day of chemotherapy. Three cycles of the same chemotherapy regimen were repeated as adjuvant treatment. Postoperative chemotherapy was to be initiated 6–12 weeks after surgery.

Surgical robotic techniques

Pneumoperitoneum induction is carried out through the left upper quadrant using a Veress needle with an intra-abdominal pressure of 13 mmHg. An 8 mm robotic port is placed just in the right lateral side of the umbilicus for 30º optics. Under direct vision, three 8 mm robotic trocars are inserted: two in the upper abdomen at the midclavicular line on the left and on the right, and one at the right anterior axillary line for liver retraction as shown in Fig. 1. After placement of the ports, the patient is positioned in a reverse Trendelenburg's position at approximately 15°. The Da Vinci Surgical System is moved to the operative table above the patient's head and the operative arms are connected to the ports. During the procedure, a 12 mm port is used by the assistant

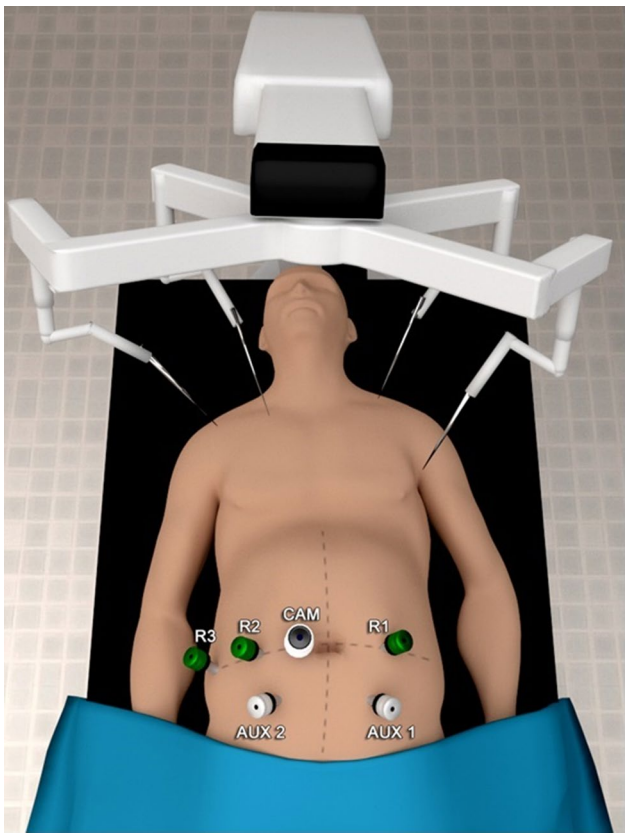

Fig. 1 Trocar placement scheme

surgeon between the left robotic port and the camera port. The 12 mm port is used for the introduction of aspiration, clip applier, sutures and staple.

Robot-assisted total gastrectomy is performed according to the following standardized operative criteria: depending on the tumor stage, either a total or subtotal gastrectomy is performed and either a D1 or D2 lymphadenectomy. During the robot-assisted subtotal gastrectomy, the greater omentum is first divided and then dissected using robotic Ultracision™ (Ethicon Endo-Surgery) in the direction of the lower pole of the spleen. The dissection of the gastrocolic ligament is continued distally toward the pylorus. The lesser omentum is then opened from pars flaccida to the hepatic pedicle. With this dissection, the lymph nodes near the small gastric curve (station no. 3) are removed. Next, the proper hepatic artery is cleaned to identify the right gastric artery. This maneuver allows us to achieve the lymph nodes of station no. 5. Then, the release of the first part of the duodenum is completed and its transection can be performed. The superior mesenteric vein adipose tissue is also removed. Lymphadenectomy of major vessels is carried out starting from the hepatic hilum toward the celiac trunk, removing stations no. 12 and no. 8. Once the celiac trunk is released, the left gastric artery can be easily identified and cut, and the lymph nodes of station no. 7 are dissected. At this time, the left gastric vein is also sectioned. The lymphadenectomy of the splenic artery can be performed according to the tumor characteristic, achieving stations no. 10 and no. 11. Next, the abdominal esophagus is prepared depending on the surgical strategy. If this is necessary, the esophagus is prepared for a length of 4–5 cm to perform a safe anastomosis. The esophagus is divided using an Endo GIA stapler by the assistant surgeon.

The reconstruction phase

The reconstruction method is performed using an intracorporeal antecolic reconstruction using a Roux-en-Y esophagojejunostomy completed with a jejunojenostomy 40 cm distally to the esophagojejunostomy. For the esophagojejunostomy, an end to side robot-sewn anastomosis is carried out performing the first posterior layer with a continuous suture taking the jejunal serosa and the esophagus muscle fibers. The small intestine and the esophagus are then opened. A running suture of Maxon 3/0 (Maxon™, Polyglyconate, Monofilament Synthetic Absorbable Sutures, Covidien-Medtronic, Minneapolis) is used for both the external and the internal posterior layer. The small intestine and the esophagus are then opened. The jejunum and the esophagus are now well closed, and the last anterior continuous suture is carried out with a continuous suture of Prolene 3/0 (Prolene™, Ethicon US, LLC). A jejunojenostomy is performed to complete the reconstruction phase. This anastomosis is achieved 40 cm distally to the esophagojejunostomy following the same procedure described previously.

Surgical open techniques

Open total gastrectomy is performed according to the following standardized operative criteria: depending on the tumor location, either a total or subtotal gastrectomy is performed and either a D1 or D2 lymphadenectomy. The technique was achieved according to the conventional method described in the literature [12].

Matching process

A case-matched study design was used. Comparisons were performed between 20 patients who underwent robotic gastrectomy and a matched group extracted from a retrospective cohort of 19 patients who underwent open gastrectomy. The two groups have similar demographic characteristics. The distribution of continuous variables was reported as median and range. Categorical variables are presented as numbers and percentages. Student's t test and the Chi-square test were used to compare variables between patient groups. Significance was set to p value < 0.05. Analysis was performed using SPSS statistical software (SPSS Inc. Chicago, IL, USA). For construction of the patient control group, the data were collected either for continuous (age, BMI, etc.) and categorical (gender, tumour stage, etc.) variables according to the individually matched case–control design. Statistical computations of the matching algorithm were performed using SAS System for Windows (release 8.2/2001). The algorithm sorted the cases and controls randomly and matched the first case with the closest (according to the settings) control, repeating the process until all cases from the pool of available controls were matched.

Results

The main demographic and preoperative data comparison of the two groups are summarized in Table 1. The proportion of patients submitted to neo-adjuvant chemotherapy was also similar between the two groups (Table 1). Operative outcomes are summarized in Table 2. As shown in Table 2, the mean operative time was significantly longer in the RG group compared to the OG group (416 ± 90 vs 336 ± 96 min; $p = 0.001$). However, in the RG group, intraoperative blood loss was significantly lower (500 ml vs 176 ml; $p = 0.05$) and postoperative bowel recovery was faster than in the OG group but without statistical significance ($p = 0.306$).

Table 1 Demographic and Preoperative data

	Open group ($n=19$) n (%)	Robotic group ($n=20$) n (%)	p value
Age (years)[a]	68.92 ± 6.8	62 ± 14.5	0.22
Sex: M/F (%)	78.6/21.4	53.3/46.7	0.24
BMI (Kg/m^2)	22 ± 2.5	21.8 ± 2.3	
ASA			0.012
1	3 (15)	5 (25)	
2	13 (69)	13 (65)	
3	3 (15)	2 (10)	
Tumor location			
Upper	10 (53)	10 (50)	
Middle	4 (21)	6 (30)	
Lower	5 (26)	4 (20)	
cTNM stage			
Tis			
T0*		2 (10)	
I	4 (21)	3 (15)	
II	7 (37)	6 (30)	
III	8 (41)	7 (35)	
IV	0	2 (10)	
Perioperative CT: n (%)	13 (69)	12 (60)	0.39
SUV[b] Preoperatory	4.15 (2–8.9)	2 (0–6.48)	0.42

BMI body max index, *ASA* American Society of Anesthesiologist

*Patients with high genetic risk

[a]Means ± standard deviations

[b]Median (Interquartile rank)

Conversion to open laparotomy occurred in two patients (10%). In one case, this was the result of a complicated surgical dissection due to many visceral adhesions. The other case was the infiltration of the duodenal margin in an intraoperative pathological examination. For this reason, it was converted to complete the procedure. No significant differences in short-term surgical outcomes were appreciated between groups (Table 3). Overall postoperative complication rates were not statistically different between the two groups ($p=0.37$). Two cases of intestinal fistula occurred in the OG group and only one needed re-operation. The patient that was not reoperated was managed with digestive stent placement. The mean length of hospital stay was similar for both [RG: 15 (12–33) OP 14 (11–16) ($p=0.306$)].

Oncologic outcomes are summarized in Table 4. The adequacy of resection, expressed as the number of retrieved nodes and negative surgical margins, was similar for both groups (30 ± 12 28 ± 10 0.16). Negative resection margins were obtained in all patients of both groups. There was no difference in the adequacy of D2 dissection when an RG was performed with respect to the OG, as no statistically significant differences in terms of the number of retrieved lymph nodes were found. The mean (SD) number of lymph nodes harvested was comparable between the RG and OG groups, 26 ± 12 and 25 ± 10, respectively ($p=0.16$).

Discussion

In the last decade, more and more minimally invasive gastrectomies have been reported in the literature with the key-reported benefits comparing the open surgery approach with laparoscopic surgery [13].

Several authors have published their experiences so as to define the role of MIS for gastric cancer; however, the current evidence is far from definitive that this approach should become a common surgical practice [14, 15]. Although the robotic approach for the treatment of gastric cancer has grown rapidly in recent years, most patients with gastric cancer are still treated with open surgery. RG was introduced as an advanced platform that was studied to overcome the technical limitations of conventional laparoscopy. In the field of general surgery, the expansion of robotic surgery is still slow due to technical difficulties and time-consuming procedures [16]. The present study has analyzed data on gastrectomies from a single-center institute. It includes the gastric robotic surgery and the open approach as control group. To date, only two publications [17, 18] in the

Table 2 Patient operative data

	Open group ($n=19$) n (%)	Robotic group ($n=20$) n (%)	p value
Reconstruction (Roux-en-Y esophagojejunostomy anastomosis)	19	20	
Operative time (min)	336 ± 96	416 ± 90	0.0001
Conversion	–	2 (10)	
D1	8 (42)	8 (40)	
D2	11 (57)	12 (60)	
Blood loss (ml)[a] (range)	500 (0–1500)	176 (0–1500)	0.05

[a]Valore medio ± deviazione standard

Table 3 Postoperative data

	Open group ($n=19$) n (%)	Robotic group ($n=20$) n (%)	p value
Complications	7 (36)	2 (10)	0.37
Anastomotic leakage	2 (10)	0	
Pneumonia ab ingestis	1 (5)	0	
Wound infection	2 (10)	0	
Cardiac failure		1 (5)	
Stenosis of jenjuno-jejunal anastomosis		1 (5)	
Paralytic ileus		0	
SIRS	2 (10)		
Hospital stay (day)[b]	15 (12–33)	10 (09–13)	0.3
Reoperation rate n(%)	0	1 (5%)	
Post-operatory mortality (90 days)	1 (5)	0	

[a]Means ± standard deviations

[b]Median (Interquartile rank)

Table 4 Tumor characteristics

	Open group ($n=19$) n (%)	Robotic group ($n=20$) n (%)	p value
pTNM stage			
pT0			
pTis		2 (10)	
Stage I	6 (32)	6 (30)	
Stage II	8 (41)	8 (40)	
Stage III	5 (26)	4 (20)	
Lymph-node retrieved	30 ± 12	28 ± 10	0.16
Tumor size (cm)[b]	3.25 (1.88–6.13)	1 (0.2–1.7)	0.001
R1 resection	0	0	
Tumoral differentiation			NS
Well Differentiated	3 (16)	6 (30)	
Moderately	5 (26)	5 (25)	
Undifferentiated	11 (58)	9 (45)	

[a]Means ± standard deviations

[b]Median (Interquartile rank)

literature report a comparison between open surgery and robotic surgery. Among the intraoperative outcomes, these studies confirm lower blood loss in the minimally invasive approaches compared with the open approach. The general evidence among different studies is the advantage of robotic surgery over open surgery in reducing operative bleeding [19]. In our experience, the mean operative time in RG has long been compared with the open procedures ($p<0.0001$). This does not appear to be justifiable given the docking time and other factors likely come into play. The long operative time of RS procedures remains an issue of debate. It is our belief that the operative time decreases significantly after the initial learning curve [6]. When a robotic approach is used for the surgical treatment of gastric cancer, the same extent of lymph node dissection as in traditional surgery should be performed, and postoperative outcomes should also be favorable. Although overall survival is the prime oncologic parameter, wide margin resection and the number of retrieved lymph nodes reflect the adequacy of surgical resection. According to the Japanese and British guidelines, a complete surgical resection D2 lymph node dissection is recommended as the standard procedure for advanced gastric cancer [20, 21]. In the last few years, several studies have been published comparing laparoscopic surgery with the open approach for gastric cancer [22, 23]. They show similar survival outcomes with satisfactory long-term oncological results for laparoscopic gastrectomy in both early and advanced gastric cancer. MIS for advanced gastric cancer still remains technically complicated to ensure extended lymph node dissection. In fact, several randomized studies

show that an extended lymph node dissection is an important factor influencing long-term survival [24]. A recent study by Huang et al. confirms that there is a significant difference in the extent of lymphadenectomy among the robotic, laparoscopic and open techniques [25]. The number of retrieved lymph nodes in this paper was similar between open and robotic groups, but the laparoscopic group revealed fewer retrieved lymph nodes than both the open and robotic groups. The authors explained that they encountered technical difficulties in performing the laparoscopic D2 lymphadenectomies. A study by Caruso et al. [17] on patients who had undergone a gastrectomy with D2 lymph node dissection confirms no significant difference between the number of lymph nodes obtained using the robotic versus open procedures (28.0 ± 11.2 vs. 31.7 ± 15.6, respectively) [1]. Robotic surgery can facilitate better D2 dissection. RG reduces the limits of the laparoscopic approach allowing precise and more accurate dissections with improved suturing compared with the LG group. In our study, the mean (SD) number of lymph nodes harvested was comparable between the RG and OG groups, 30 ± 12 vs 28 ± 10, respectively ($p = 0.16$). The mean number of metastatic nodes was also similar between the groups. This is a favorable result compared with that of the most recent laparoscopic gastric resection series published according to the recommended standard for conventional open D2-lymphadenectomy [19, 25]. We strongly believe that RS can extend the real benefits of MIS.

RSS in our series has been shown to be a safe and feasible tool with results that are not inferior to those of open surgery. In our series, we performed robotic surgery in patients with both early and advanced gastric cancer. Advanced gastric cancer currently benefits from PC. The results of the MAGIC trial [11] showed a decreased tumor size and stage, and a significantly improved progression-free- and overall survival rate for patients receiving a perioperative regimen, composed of a perioperative regimen of EOX. About 64% of the patients enrolled in this trial completed PC and surgery, and most of them were unable to receive adjuvant treatment. In our clinical experience, patients operated on with RSS have a good performance status postoperatively. This enables them to receive the complete chemotherapy regimen, with a significantly improved overall rate of survival.

In the analysis of the postoperative course, the number of overall complications was lower in the RG than OG with no statistical differences ($p = 0.37$). Particularly, significant advantages were found in medical and minor surgical complications. However, no differences were seen for major surgical complications in this study. The overall complication rate of RG described in our study was 41%, which is consistent with that described in the literature, ranging from 29 to 68% [17, 18] of patients and being similar to the OG group.

Anastomotic leakage is a major complication after gastric cancer surgery. Digestive reconstruction remains a critical step of the gastrectomy with MIS. In the literature, several authors have reported the execution of mechanical anastomosis in most of the cases [26]. Only few authors describe intracorporeal sutures with a full robotic-sewn anastomosis [27–29]. In our series, intracorporeal anastomosis was performed in all patients who were not converted to open surgery. It is our opinion that the execution of extracorporeal anastomosis may eliminate the real advantages of MIS. The traditional Roux-en-Y reconstruction can be performed satisfactorily with the RSS without major complications. In our series, postoperative intestinal fistula resulted in being slightly higher in the OG group (10%). No case of anastomotic leakage was recorded in RG confirming the safety of this approach. MIS has demonstrated relevant advantages over open surgery with regard to postoperative hospital stay.

Our analysis shows the advantages in hospitalization with the minimally invasive approaches but without statistical significance between the RG and OG groups ($p = 0.306$). In addition, all resected margins in this study were free of tumors in both groups. This study has some limitations due to its retrospective nature, however, there is currently no prospective randomized clinical trial comparing robotic- versus open technique. The unicentric nature of our study guarantees the homogeneity of the surgical procedures performed in both robotic- and open groups.

Conclusion

RG with lymph node dissection is safe, technically feasible and oncologically effective in well-selected patients when compared to open resections. Further studies are needed to confirm our preliminary results. Robotic surgery can be safely performed and proposed as a possible alternative to open surgery.

Acknowledgements The authors thank Pablo Ruiz.

Author contributions EV and YQ proposed the study. RC performed the research and wrote the first draft. RC collected and analyzed the data. All authors contributed to the design and interpretation of the study and to further drafts. EV is the guarantor.

Funding No specific funding.

Compliance with ethical standards

Conflict of interest We wish to confirm that there are no known conflicts of interest associated with this publication for each authors. 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.

Research involving human participants and/or animals The study was approved by the institutional ethical committee of Sanchinarro University Hospital.

Informed consent All patients included were informed about the treatment and provided written informed consent.

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