

## Retrospective Study

**Minimally invasive surgery for gastric cancer: A comparison between robotic, laparoscopic and open surgery**

Amilcare Parisi, Daniel Reim, Felice Borghi, Ninh T Nguyen, Feng Qi, Andrea Coratti, Fabio Cianchi, Maurizio Cesari, Francesca Bazzocchi, Orhan Alimoglu, Johan Gagnière, Graziano Pernazza, Simone D'Imporzano, Yan-Bing Zhou, Juan-Santiago Azagra, Olivier Facy, Steven T Brower, Zhi-Wei Jiang, Lu Zang, Arda Isik, Alessandro Gemini, Stefano Trastulli, Alexander Novotny, Alessandra Marano, Tong Liu, Mario Anecchiarico, Benedetta Badii, Giacomo Arcuri, Andrea Avanzolini, Metin Leblebici, Denis Pezet, Shou-Gen Cao, Martine Goergen, Shu Zhang, Giorgio Palazzini, Vito D'Andrea, Jacopo Desiderio

Amilcare Parisi, Alessandro Gemini, Stefano Trastulli, Jacopo Desiderio, Department of Digestive Surgery, St. Mary's Hospital, University of Perugia, 05100 Terni, Italy

Daniel Reim, Alexander Novotny, Klinik und Poliklinik fuer Chirurgie, Klinikum Rechts der Isar, Technical University Munich, 81675 Munich, Germany

Felice Borghi, Alessandra Marano, Department of Surgery, General and Oncologic Surgery Unit, Santa Croce e Carle Hospital, 12100 Cuneo, Italy

Ninh T Nguyen, Department of Surgery, Division of Gastrointestinal Surgery, University of California, Irvine Medical Center, Orange, CA 92868, United States

Feng Qi, Tong Liu, Gastrointestinal Surgery, Tianjin Medical University General Hospital, Tianjin 300052, China

Andrea Coratti, Mario Anecchiarico, Division of Oncological and Robotic Surgery, Department of Oncology, Careggi University Hospital, 50134 Florence, Italy

Fabio Cianchi, Benedetta Badii, Unit of general and endocrine surgery, Center of oncologic minimally invasive surgery (COMIS), Careggi University Hospital, 50134 Florence, Italy

Maurizio Cesari, Giacomo Arcuri, Department of General Surgery, Hospital of Città di Castello, USL1 Umbria, 06012 Città di Castello, Italy

Francesca Bazzocchi, Andrea Avanzolini, Department of General Surgery, Division of General, Gastroenterologic and Minimally Invasive Surgery, G.B. Morgagni Hospital, 47121 Forlì, Italy

Orhan Alimoglu, Metin Leblebici, Department of General Surgery, School of Medicine, Istanbul Medeniyet University, 34000 Istanbul, Turkey

Johan Gagnière, Denis Pezet, Department of Digestive and Hepatobiliary Surgery, Estaing University Hospital, 63000 Clermont-Ferrand, France

Graziano Pernazza, Department of Surgery, Robotic General Surgery Unit, San Giovanni Addolorata Hospital, 00184 Rome, Italy

Simone D'Imporzano, Esophageal Surgery Unit, Tuscany Regional Referral Center for the Diagnosis and Treatment of Esophageal Disease, Medical University of Pisa, 56124 Pisa, Italy

Yan-Bing Zhou, Shou-Gen Cao, Department of General Surgery, The Affiliated Hospital of Qingdao University, Qingdao 266003, Shandong Province, China

Juan-Santiago Azagra, Martine Goergen, Unité des Maladies de l'Appareil Digestif et Endocrine, Centre Hospitalier de Luxembourg, 1210 Luxembourg, Luxembourg

Olivier Facy, Service de Chirurgie Digestive et Cancérologique CHU Bocage, 21000 Dijon, France

Steven T Brower, Department of Surgical Oncology and HPB Surgery, Englewood Hospital and Medical Center, Englewood, NJ 07631, United States

Zhi-Wei Jiang, Shu Zhang, Department of General Surgery, Jinling Hospital, Medical School, Nanjing University, Nanjing 210002, Jiangsu Province, China

Lu Zang, Department of Surgery, Ruijin Hospital, Shanghai Jiaotong University, School of Medicine, Shanghai 200020, China

Arda Isik, Department of General Surgery, Erzincan University, School of Medicine, 24100 Erzincan, Turkey

Giorgio Palazzini, Vito D'Andrea, Department of Surgical Science, "La Sapienza" University, 00161 Rome, Italy

Jacopo Desiderio, Department of Digestive Surgery, St. Mary's Hospital of Terni - University of Perugia, 05100 Terni, Italy

**Author contributions:** Parisi A and Desiderio J were involved in study conception and design; Parisi A, Reim D, Borghi F, Nguyen NT, Qi F, Coratti A, Cianchi F, Cesari M, Bazzocchi F, Alimoglu O, Gagnière J, Pernazza G, D'Imporzano S, Zhou YB, Azagra JS, Facy O, Brower ST, Jiang ZW, Zang L, Isik A, Gemini A, Trastulli S, Novotny A, Marano A, Liu T, Annetichiarico M, Badii B, Arcuri G, Avanzolini A, Leblebici M, Pezet D, Cao SG, Goergen M, Zhang S, Palazzini G, D'Andrea V and Desiderio J collected data and were involved in critical revision and drafting of the final manuscript.

Supported by CARIT Foundation (Fondazione Cassa di Risparmio di Terni e Narni), No. 0024137.

**Institutional review board statement:** The study was approved by the ethics Committee of CEAS Umbria.

**Conflict-of-interest statement:** 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.

**Data sharing statement:** Technical appendix, statistical code, and dataset available from the corresponding author at djdesi85@hotmail.it

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Manuscript source:** Invited manuscript

**Correspondence to:** Jacopo Desiderio, MD, Department of Digestive Surgery, St. Mary's Hospital of Terni - University of Perugia, Via Tristano di Joannuccio 1, 05100 Terni, Italy. [djdesi85@hotmail.it](mailto:djdesi85@hotmail.it)  
Telephone: +39-349-7531121  
Fax: +39-744-205078

Received: December 12, 2016

Peer-review started: December 26, 2016

First decision: January 10, 2017

Revised: January 23, 2017

Accepted: March 15, 2017

Article in press: March 15, 2017

Published online: April 7, 2017

## Abstract

### AIM

To investigate the role of minimally invasive surgery for gastric cancer and determine surgical, clinical, and oncological outcomes.

### METHODS

This is a propensity score-matched case-control study, comparing three treatment arms: robotic gastrectomy (RG), laparoscopic gastrectomy (LG), open gastrectomy (OG). Data collection started after sharing a specific study protocol. Data were recorded through a tailored and protected web-based system. Primary outcomes: harvested lymph nodes, estimated blood loss, hospital stay, complications rate. Among the secondary outcomes, there are: operative time, R0 resections, POD of mobilization, POD of starting liquid diet and soft solid diet. The analysis includes the evaluation of type and grade of postoperative complications. Detailed information of anastomotic leakages is also provided.

### RESULTS

The present analysis was carried out of 1026 gastrectomies. To guarantee homogenous distribution of cases, patients in the RG, LG and OG groups were 1:1:2 matched using a propensity score analysis with a caliper = 0.2. The successful matching resulted in a total sample of 604 patients (RG = 151; LG = 151; OG = 302). The three groups showed no differences in all baseline patients characteristics, type of surgery ( $P = 0.42$ ) and stage of the disease ( $P = 0.16$ ). Intraoperative blood loss was significantly lower in the LG ( $95.93 \pm 119.22$ ) and RG ( $117.91 \pm 68.11$ ) groups compared to the OG ( $127.26 \pm 79.50$ ,  $P = 0.002$ ). The mean number of retrieved lymph nodes was similar between the RG ( $27.78 \pm 11.45$ ), LG ( $24.58 \pm 13.56$ ) and OG ( $25.82 \pm 12.07$ ) approach. A benefit in favor of the minimally invasive approaches was found in the length of hospital stay ( $P < 0.0001$ ). A similar complications rate was found ( $P = 0.13$ ). The leakage rate was not different ( $P = 0.78$ ) between groups.

### CONCLUSION

Laparoscopic and robotic surgery can be safely performed and proposed as possible alternative to open surgery. The main highlighted benefit is a faster postoperative functional recovery.

**Key words:** Gastric cancer; Gastrectomy; Minimally invasive surgery; Robotic; Robot-assisted; Laparoscopy

© **The Author(s) 2017.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** The IMIGASTRIC project is a multi-institutional study on gastric cancer developed to collect information on the surgical, clinical, and oncological features of patients undergoing gastrectomy with a robotic, laparoscopic, or open approach. A research group was

first established in 2014 and after sharing a specific study protocol, data collection officially started at the end of 2015. A tailored Web-based software was developed to standardize information, facilitate the process of data collection in a unified multi-institutional database, and guarantee the proper storage of patient's data. The purpose was to create an international registry with a high methodological quality.

Parisi A, Reim D, Borghi F, Nguyen NT, Qi F, Coratti A, Cianchi F, Cesari M, Bazzocchi F, Alimoglu O, Gagnière J, Pernazza G, D'Imporzano S, Zhou YB, Azagra JS, Facy O, Brower ST, Jiang ZW, Zang L, Isik A, Gemini A, Trastulli S, Novotny A, Marano A, Liu T, Annecchiarico M, Badii B, Arcuri G, Avanzolini A, Leblebici M, Pezet D, Cao SG, Goergen M, Zhang S, Palazzini G, D'Andrea V, Desiderio J. Minimally invasive surgery for gastric cancer: A comparison between robotic, laparoscopic and open surgery. *World J Gastroenterol* 2017; 23(13): 2376-2384 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v23/i13/2376.htm> DOI: <http://dx.doi.org/10.3748/wjg.v23.i13.2376>

## INTRODUCTION

The treatment of gastric cancer is in continuous development with the search for new therapeutic drugs, radiation therapy, endoscopy, surgery, and combined treatments. These modalities are used to try to give the patient the best possibility for a cure. Treatments are often tailored according to the characteristics and stage of the cancer and surgery remains one of the main stay treatment<sup>[1]</sup>. However, technologic advance has provided surgeons with minimally-invasive and even non-invasive procedures. Over the past two decades, gastrectomy has evolved toward the use of small surgical incisions with reduced trauma to the patient and a faster postoperative recovery. Laparoscopy has now spread globally and is within reach for most surgical centers. Researchers are now focusing on the application of even more sophisticated robotic technologies for gastrectomy. Robotic surgery, which until a few years ago seemed out of reach in many areas due to high costs, is now finding ever-increasing support among different oncologic surgical centers.

Gastric surgery is one of the most relevant and developed fields of minimally invasive surgery<sup>[2]</sup>. Although general international support has emerged in its application at dedicated centers, practitioners must still assess which patients would benefit most from these technologies. Other important questions include: What are the real benefits? Where do the limits lie? What kind of minimally invasive approach is preferable?

To date, no international guidelines exist to answer these questions, and the role of different minimally invasive techniques remains unclear. As a result, the institutes themselves, and sometimes the individual

surgeons, take their own direction.

In 2014, a research group was established<sup>[3]</sup> with the intent to further investigate these issues. So a first phase of data collection from the participating centers began with the entering of information into a well-planned registry.

This study aimed to report the findings that can be assessed from the data collected up to date, comparing minimally invasive techniques (laparoscopic and robotic) with traditional open surgery.

## MATERIALS AND METHODS

### Type of study

This is a multi-institutional propensity score-matched case-control study, comparing three treatment arms. Data collection started after sharing a specific study protocol<sup>[4]</sup>.

The study was registered at clinical trials.gov with a registration number of NCT02325453.

### Groups and interventions

We defined the following groups of comparison: (1) Laparoscopic gastrectomy (LG): Patients underwent minimally invasive gastrectomy through traditional laparoscopic devices; (2) Robotic gastrectomy (RG): Patients underwent minimally invasive gastrectomy with the assistance of the "Da Vinci" robotic surgical system, which allows a surgeon to perform the procedure through a console and dedicated devices; and (3) Open gastrectomy (OG): Patients underwent gastrectomy with the traditional open approach.

### Time period and sites

Data entered into the IMIGASTRIC registry regarding procedures performed until data extraction (January 2016) were analyzed. All involved centers are referral institutions with a well-established gastric cancer program and experience in minimally invasive surgery. All diagnostic and surgical interventions at these centers were done according to international guidelines and information stored in institutional prospective data collection systems.

### Eligibility

Specific criteria were considered before starting data collection and reported in the study protocol.

**Inclusion criteria:** Gastric cancer reported in the biopsy report, upper endoscopy and CT scan for staging, both Early Gastric Cancer<sup>[5,6]</sup> and Advanced Gastric Cancer<sup>[5,6]</sup> were considered, curative surgery<sup>[7-9]</sup>.

**Exclusion criteria:** Evidence of metastatic disease, ASA score > 4, history of other surgery for gastric cancer, other malignancy, surgery with palliative intent.

**Reported information and outcomes:** This study

**Table 1** Characteristics of patients *n* (%)

	Open	Laparoscopy	Robotic	<i>P</i> value
Total	302	151	151	
Age	67.19 ± 13.1	65.82 ± 14.16	68.81 ± 12.12	0.14
BMI	24.33 ± 3.65	24.02 ± 2.22	24.58 ± 3.00	0.31
Sex				0.26
Female	117 (38.7)	66 (43.7)	70 (46.4)	
Man	185 (61.3)	85 (56.3)	81 (53.6)	
ASA				0.18
I	66 (21.9)	23 (15.2)	26 (17.2)	
II	139 (46.0)	64 (42.4)	73 (48.3)	
III	97 (32.1)	64 (42.4)	52 (34.4)	
Comorbidities	192 (63.6)	96 (63.6)	95 (62.9)	0.96

reported descriptive findings and outcomes among the three groups. The first part comprises three sections: basic patient characteristics, tumor findings, and surgical procedure details. The outcomes section offers a comparison regarding operative results, postoperative recovery, and complications:

**Primary outcomes:** No. of harvested lymph nodes (mean ± SD), estimated blood loss (EBL; mean ± SD), hospital stay (mean ± SD), and overall complications (no. patients, %).

**Secondary outcomes:** Operative time (mean ± SD), curative resection (R0; no. patients, %), intraoperative blood transfusion (no. patients, %), intraoperative complications (no. patients, %), intraoperative death (no. patients, %), post-operative day (POD) of patient mobilization (mean ± SD), POD of starting liquid diet (mean ± SD), POD of starting soft solid diet (mean ± SD), POD of resumption of peristalsis (mean ± SD), POD of first flatus (mean ± SD), length of intravenous antibiotic use (mean ± SD), length of intravenous analgesic use (mean ± SD), and post-operative transfusion (no. patients, %).

A deeper analysis of complications was reported, including the type of complications, the number related and not related to surgery, and the grade based on the Clavien-Dindo classification<sup>[10]</sup>. A specific analysis of anastomotic leakage was also reported.

#### Source of data analyzed

Investigators collected data through a web-based system (<https://imigastric.logix-software.it/>). Then data were extracted using pre-established IT tools.

#### Potential bias and study limitations

The retrospective approach is a major limitation for this study, but the propensity score case-matched analysis allowed us to determine a homogeneous distribution of cases.

Potential bias and study limitations reflect those related to this type of study, particularly the potential lack of information in medical records analyzed and errors in filling in the clinical diary or the description

of the surgical procedure. Errors related to the transmission of data in a single registry were minimized by the creation of a dedicated IT tool with standardized fields by which information was collected and analyzed. International classifications and guidelines and shared measurement units were considered before starting the data collection phase to avoid heterogeneity.

The present study was reported in accordance with the STROBE guidelines and statement<sup>[11]</sup>.

#### Propensity score matching

Propensity score matching analysis was carried out using SPSS software version 23 and R software version 3.1, through the Custom Dialog "PS Matching". A value for each patient was calculated based on the covariates of sex, age, comorbidities, BMI, stage of disease, type of gastrectomy. Then, patients in the RG, LG and OG group were 1:1:2 matched considering a caliper = 0.2.

#### Statistical analysis

IBM SPSS Statistics V.23 was used to carry out the statistical analysis. An intention to treat analysis was performed.

Numbers and percentages were used to report dichotomous variables. Continuous variables were expressed as mean ± SD and median with IQR.

One-way ANOVA analysis of variance with post hoc multiple comparison adopting the Tukey's procedure was used to allow the comparison among the three groups for continuous variables. Values from categorical variables were compared between groups through the Pearson's  $\chi^2$  and the Fisher's exact test. Then, the Z test with the Bonferroni correction was used to evaluate statistical significance among the Robotic, Laparoscopic and Open approaches. Statistical significance was set at a *P* value < 0.05.

## RESULTS

#### Patients and group characteristics

At the time of this analysis, 1026 patients had been entered in the IMIGASTRIC registry. Among them, 44% underwent minimally invasive procedures, of which 227 patients (22%) had their procedure performed by laparoscopy and 222 (22%) by the robotic system.

The matching analysis resulted in a total sample of 604 patients, 151 from RG group, 151 from LG group, 302 patients from OG group. The successful matching permitted to obtain a homogeneous distribution of all patient's characteristics, surgeries performed and stage of the disease (Tables 1 and 2).

Particularly, the three groups exhibited similar distribution of baseline patient characteristics (Table 1) with regard to age (*P* = 0.14), gender (*P* = 0.26), BMI (*P* = 0.31), ASA (*P* = 0.18), comorbidities (*P* = 0.96).

The details of the surgical procedures performed and the tumor features are shown in Table 2. The groups showed no significant differences in the distribution of cases regarding type of gastrectomy (*P* = 0.42),

**Table 2 Details of surgical procedures and tumour pathology *n* (%)**

	Open	Laparoscopy	Robotic	<i>P</i> value
Type of gastrectomy				0.42
Distal	205 (67.9)	102 (67.5)	111 (73.5)	
Total	97 (32.1)	49 (32.5)	40 (26.5)	
Type of reconstruction				0.10
Billroth I / II	88 (29.1)	31 (20.5)	51 (33.8)	
Roux-en-Y G-J	117 (38.7)	70 (46.4)	60 (39.7)	
Roux-en-Y E-J	97 (32.1)	50 (33.1)	40 (26.5)	
D2 Lymphadenectomy	294 (97.4)	144 (95.4)	143 (94.7)	0.32
Position				0.57
Lower third	153 (50.7)	76 (50.3)	84 (55.6)	
Middle third	108 (35.8)	54 (35.8)	54 (35.8)	
Upper third	41 (13.6)	21 (13.9)	13 (8.6)	
Pathologic stage				0.16
0	19 (6.3)	4 (2.6)	4 (2.6)	
I A	76 (25.2)	54 (35.8)	54 (35.8)	
I B	48 (15.9)	27 (17.9)	27 (17.9)	
II A	55 (18.2)	14 (9.3)	14 (9.3)	
II B	28 (9.3)	14 (9.3)	14 (9.3)	
III A	24 (7.9)	12 (7.9)	12 (7.9)	
III B	34 (11.3)	17 (11.3)	17 (11.3)	
III C	18 (6)	9 (6)	9 (6)	
Undifferentiated carcinoma	115 (38.1)	65 (43.0)	55 (36.4)	0.46

**Table 3 Surgical and post-operative clinical outcomes *n* (%)**

	Open	Laparoscopy	Robotic	<i>P</i> value
Operative time (min)	198.67 ± 59.66	220.37 ± 91.89	365.44 ± 80.92	< 0.0001
EBL (mL)	127.26 ± 79.50	95.93 ± 119.22	117.91 ± 68.11	0.002
LN retrieved	25.82 ± 12.07	24.58 ± 13.56	27.78 ± 11.45	0.07
R0 resections	287 (95.0)	145 (96.0)	148 (98.0)	0.59
Intraoperative blood transfusion	9 (3)	7 (4.6)	4 (2.6)	0.56
Intraoperative complications	5 (1.7)	3 (2)	2 (1.3)	0.9
Hospital stay (d)	12.68 ± 5.88	9.07 ± 9.16	8.85 ± 5.82	< 0.0001
Mobilization (d)	2.36 ± 1.34	2.7 ± 1.51	1.42 ± 1.27	< 0.0001
Liquid diet (d)	5.79 ± 3.30	4.12 ± 3.37	3.21 ± 2.49	< 0.0001
Soft solid diet (d)	8.36 ± 5.45	5.73 ± 7.00	4.23 ± 3.79	< 0.0001
Resumption of peristalsis (d)	2.64 ± 0.67	2.52 ± 0.68	2.35 ± 1.16	0.003
First flatus (d)	4.01 ± 1.05	3.75 ± 0.76	3.23 ± 1.33	< 0.0001
Drain removal (d)	8.5 ± 3.55	6.44 ± 4.61	6.05 ± 8.69	< 0.0001
NG removal (d)	4.92 ± 1.88	3.98 ± 1.74	2.82 ± 2.01	< 0.0001
Intravenous antibiotic use (d)	6.13 ± 3.84	4.58 ± 3.52	3.92 ± 4.27	< 0.0001
Intravenous analgesic use (d)	3.79 ± 1.48	2.9 ± 0.91	3.44 ± 1.78	< 0.0001
Post-operative transfusion	19 (6.3)	13 (8.6)	13 (8.6)	0.56
Complications (patients)	59 (19.5)	18 (11.9)	27 (17.9)	0.13

EBL: Estimated blood loss; LN: Lymph nodes; NG: Nasogastric tube.

reconstruction performed (*P* = 0.1), lymphadenectomy (*P* = 0.32), tumor location (0.57), stage of the disease (*P* = 0.16) and rate of undifferentiated tumors (*P* = 0.46).

**Operative outcomes**

The operative time was significantly longer in the RG than the other two groups (*P* < 0.0001). A statistical difference in favor of the OG was also observed when compared with the LG (*P* = 0.01) (Table 3).

A reduction in the Estimated Blood Loss (EBL) resulted in favor of both of the minimally invasive approaches vs the OG (*P* = 0.002) and particularly slightly in favor of the LG when compared with the RG (*P* = 0.04). However, the need for intraoperative blood

transfusion did not differ among the groups (*P* = 0.56).

Regarding the number of harvested lymph nodes, each group confirmed to guarantee an adequate number of harvested lymph nodes for pathological assessment and no statistical significant differences were found in the comparison among groups (*P* = 0.07).

The conversion rate was 5.3% (*n* = 8) in the LG and 4.6% (*n* = 7) in the RG with no significant difference (*P* = 0.5).

**Clinical recovery outcomes**

A significantly shorter hospital stay (*P* < 0.0001) was found in both of the minimally invasive groups vs the

**Table 4 Analysis of post-operative complications *n* (%)**

Type of complication	Open	Laparoscopy	Robotic	Total
Anastomotic stenosis	1	1	1	3
Arrhythmias	1	1	2	4
Cerebral vascular accident	0	0	1	1
Congestive heart failure	1	0	0	1
Delayed gastric emptying	3	0	0	3
Dumping syndrome	3	0	0	3
Fluid collection/abscess	4	1	0	5
Intestinal obstruction	2	3	0	5
Intra-abdominal bleeding	2	0	4	6
Intraluminal bleeding	3	2	3	8
Leak	11	4	4	19
Myocardial infarction	2	0	0	2
Pancreatic fistula	2	0	4	6
Peritonitis	1	0	0	0
Pleural effusion	3	0	0	3
Pneumonia	8	1	4	13
Pulmonary edema	1	0	0	1
Pulmonary embolism	0	0	1	1
Remnant stomach necrosis	0	1	0	1
Sepsis	4	0	1	5
Urinary	3	3	0	6
Wound infection	0	1	0	1
Other	13	1	2	16
Total no. of complications	68	19	30	117
Non-surgical related	32 (47.1)	6 (31.6)	10 (33.3)	48 (41.03)
Surgical-related	36 (52.9)	13 (68.4)	20 (66.7)	69 (58.97)
Clavien dindo grade				
I + II	50 (73.5)	12 (63.2)	28 (93.3)	90 (76.9)
IIIa	3 (4.4)	2 (10.5)	0 (0.0)	5 (4.3)
IIIb	11 (16.2)	5 (26.3)	2 (5.7)	18 (15.4)
IV	4 (5.9)	0 (0.0)	0 (0.0)	4 (3.4)
Leakage rate	11 (3.6)	4 (2.6)	4 (2.6)	
Reoperation	11 (3.6)	5 (3.3)	2 (1.3)	
Analysis of leakage				
Leakage rate	11 (3.6)	4 (2.6)	4 (2.6)	
Site of leak				
Duodenal stump	4	1	2	7
Esophagojejunostomy	4	3	0	7
Gastroduodenostomy	1	0	0	1
Gastrojejunostomy	2	0	2	4
Leak-related reoperation	5 (1.7)	2 (1.3)	0 (0.0)	

OG, without differences between the LG and RG ( $P = 0.97$ ).

All steps in the patients' recovery status happened faster in both of the minimally invasive approaches than the open surgery (Table 3). A small benefit was found to be significant in the minimally invasive groups vs the OG in intravenous antibiotic and analgesic discontinuation ( $P < 0.0001$ ). Data on post-operative blood transfusion did not differ among the groups ( $P = 0.56$ ).

### Analysis of complications

The number of patients experienced complications did not differ among the three groups ( $P = 0.13$ ), as well as no differences were found regarding the different types of complications ( $P = 0.052$ ). The most frequently observed complications included leakage, bleeding (intraluminal and intra-abdominal), and pancreatic fistula. Among the medical complications, pneumonia and urinary complications were most common (Table 4).

No differences with regard to the distribution of surgical and non-surgical complications ( $P = 0.29$ ) were assessed between the groups.

Overall, no differences were found when considering the grade of complications, based on the Clavien-Dindo scale (0.11). Most of the complications experienced by each group were grade I or II (76.9%, overall). The number of patients requiring reoperation did not differ among the three groups ( $P = 0.38$ ).

### Analysis of leakage

Anastomotic leakage was the most relevant complication reported. The leakage rate was not different ( $P = 0.78$ ) between LG (2.6%), RG (2.6%) and OG (3.6%). Therefore, further analysis is reported. The distribution of the leakage by different anastomotic sites was similar among the groups ( $P = 0.36$ ). In 36.84% of cases, a new surgery was required, while 63.16% of cases were managed with total parenteral nutrition and abdominal drainage. The leak-related reoperation rate did not differ

among the three groups ( $P = 0.29$ )(Table 4).

## DISCUSSION

The present study has analyzed data on gastrectomies coming from a large registry, after sharing a specific protocol and using a tailored web-based software. It represents the first attempt to establish an international project for gastric cancer on minimally invasive surgery. It includes both the robotic and laparoscopic surgery, and the open approach as control group.

To date, only three publications<sup>[12-14]</sup> in the literature report a three-arms comparison among open surgery, laparoscopic, and robotic surgery. None of these reports feature Western patients, and two come from a Korean database<sup>[13-15]</sup>. All other existing studies show a series of robotic surgeries compared only with laparoscopy, except one study that compared the robotic with the open approach<sup>[16]</sup>. The current gold standard remains open surgery, so any comparison in the short and long term should consider a control group of open surgery. The potential benefits and differences between laparoscopic vs robotic techniques are unclear, and for robotic surgery, a gap exists in strong evidence and well-designed studies. Currently, the main international guidelines<sup>[1,7]</sup> of management of gastric cancer do not discuss the robotic technology, although many centers are utilizing robotic gastrectomy for the treatment of gastric cancer in the past decade.

Scientific evidence for the role of laparoscopic and robotic gastrectomy is not keeping pace with these technological developments. The current study includes information to gain an understanding on the use of minimally invasive surgical techniques and their impact on surgical practice<sup>[3,4]</sup>. The goal of this study was to gather data to examine the actual role of minimally invasive surgery.

Among the intraoperative outcomes, this study confirms lower blood loss in the minimally invasive approaches compared to the open approach ( $P = 0.002$ ). Within the minimally invasive techniques, there was lower blood loss in the LG. Viñuela *et al*<sup>[17]</sup>, in his meta-analysis, showed similar findings with a significantly lower blood loss in the LG vs OG. In Kang's study<sup>[18]</sup>, the RG had lesser EBL than the LG, especially for technically demanding lymph node stations (93.25 mL vs 173.45 mL,  $P < 0.001$ ). Junfeng *et al*<sup>[19]</sup> highlighted that the RG group had a smaller amount of EBL in elderly patients (101.4 mL vs 131.4 mL,  $P = 0.017$ ). The general consensus among different studies is the advantage of robotic surgery over laparoscopy and open surgery in reducing operative bleeding. However, researchers have not achieved full agreement on this aspect, as shown by Eom *et al*<sup>[20]</sup> (RG: 152.8 mL vs LG: 88.3 mL,  $P = 0.09$ ) and Son *et al*<sup>[21]</sup> (RG: 173.2 mL vs LG: 116.6 mL,  $P = 0.014$ ). The results of these two studies are closer to our reported analysis.

We observed a significantly high operative time with the robotic approach ( $P < 0.0001$ ). This appears

not entirely justifiable by the docking time and other factors likely come into play. The conversion rate to open surgery does not differ ( $P = 0.5$ ), demonstrating the substantial equivalence of both techniques in being able to complete the minimally invasive procedure. Studies<sup>[17,22]</sup> in the literature have widely discussed and reported results in terms of the safety and feasibility of minimally invasive procedures for gastrectomy. The present study confirms the overall low rate of intra-operative complications with no statistical differences vs open surgery ( $P = 0.9$ ).

The most relevant issue is definitely ensuring proper oncological surgery by performing an adequate lymphadenectomy with minimally invasive approaches. Researchers still regard nodal clearance as an important factor influencing long-term survival. Viñuela *et al*<sup>[17]</sup> showed a significant higher number of lymph nodes retrieved in the OG than in the LG by 3.9 nodes ( $P < 0.001$ ), while no significant difference was found in ensuring a proper number of lymph nodes ( $> 15$  Lns) for pathological stage assessment ( $P = 0.09$ ).

Laparoscopy has shown to require a long learning curve and experience to perform an extended lymphadenectomy, when required.

Robotic surgery can facilitate better D2 dissection. This advanced technology clearly possesses intrinsic advantages for this surgical step, but researchers have not yet proven and verified them through appropriate trials: Overall, only four studies<sup>[12-14,16]</sup> have compared robotic surgery with the open approach on this outcome. In particular, Kim MC's study<sup>[14]</sup> does not report a significant difference among the three surgical groups, in contrast with Huang<sup>[12]</sup> and Kim KM's study<sup>[13]</sup>. Caruso *et al*<sup>[16]</sup> reported a significant difference between robotic and open surgery, but the robotic sample is too small to draw conclusions. Among studies comparing the two minimally invasive techniques, only one study<sup>[19]</sup> was able to show a statistically significant benefit in favor of robotic surgery. However, in the latter study<sup>[19]</sup>, the researcher did not report in the published paper the number of D2 procedures in the two groups. In the present study, the oncological success of the procedures shows a balance between the three approaches regarding the residual tumor assessment ( $P = 0.59$ ). The rates of infiltrated margins were low in all performed procedures, demonstrating the success of surgeries performed in referral centers. If one considers the outcomes above alongside the number of retrieved lymph nodes robotic surgery seems to net comparable outcomes to those of open surgery.

In the analysis of the post-operative course, the number of overall complications was lower in the LG than OG group, in Viñuela's study<sup>[17]</sup> ( $P < 0.001$ ). Particularly, significant advantages were found in medical and minor surgical complications. However, no differences were seen for major surgical complications in this study, while the current largest RCT (KLASS Trial)<sup>[23]</sup> didn't show any differences between LG and OG ( $P = 0.13$ ) in the assessment of overall postoperative

complications.

Researchers have obtained inconsistent findings in studies on robotic surgery in terms of demonstrating differences compared to laparoscopy in the analysis of complications<sup>[22]</sup>. Hyun *et al*<sup>[24]</sup>, in his comparison between RG and LG, reported similar results regarding overall complications ( $P = 0.36$ ), but with a higher rate of patients experiencing grade IIIa and IIIb (Clavien-Dindo) complications in the laparoscopic group. Son *et al*<sup>[21]</sup> showed no significant differences in the number ( $P = 0.37$ ) and severity ( $P = 0.88$ ) of complications between the two minimally invasive groups. Park *et al*<sup>[25]</sup> found a rate in favor of the LG approach, but without reaching a significant difference ( $P = 0.12$ ) and with a similar number of severe complications rate ( $P = 0.25$ ) in both groups. In our study, we found no differences in the type ( $P = 0.053$ ) and severity of complications ( $P = 0.11$ ) among the three groups.

Minimally invasive surgery has demonstrated relevant advantages over open surgery with regard to postoperative hospital stay, despite the extreme heterogeneity among studies. A shorter hospital stay was reported in LG in Viñuela's study<sup>[17]</sup> (WMD = 3.6 d, 95%CI: 2.6-4.5,  $P < 0.001$ ).

Previous studies on RG<sup>[14,26]</sup> have shown that the length of hospital stay can be shorter than that of OG or LG. Particularly, Woo *et al*<sup>[26]</sup> found a significant difference ( $P = 0.04$ ) in the rate of patients discharged within the fifth postoperative day in favor of the robotic approach (61%).

Several factors were hypothesized regarding the inflammatory response after surgery, as for example a lesser tissues manipulation in robotic surgery<sup>[27]</sup>. Thus, postoperative bowel recovery in the RG may be shorter than other approaches. Moreover, Song *et al*<sup>[28]</sup> and Park *et al*<sup>[25]</sup> showed some advantages in the RG group regarding ambulation, pain control and postoperative hospital stay. However, differences can be seen among the published studies in the literature. Junfeng *et al*<sup>[19]</sup> didn't show differences between the two groups regarding first flatus, time to start a liquid diet, and postoperative length of stay. Son *et al*<sup>[21]</sup> found advantages in favor of LG in terms of postoperative restoration of bowel function, resumption of oral intake, and hospital stay. Kang *et al*<sup>[18]</sup> reported a significant longer hospitalization in the RG than the LG group, with a mean difference of 1.7 d ( $P = 0.042$ ).

Our analysis showed a statistically significant advantage in hospitalization ( $P < 0.0001$ ) with the minimally invasive approaches without differences between the LG and RG, as well as benefits in all patients' functional recovery steps.

Technological developments have made now possible the use of minimally invasive surgery for gastric cancer.

Several points remain object of debate as the role of the Enhanced Recovery After Surgery protocols, the spread of the robotic system and its cost that, to date, is not comparable to that of traditional laparoscopy.

Minimally invasive surgery is safe in ensuring

a proper gastric oncological procedure with some advantages in the postoperative period, but undoubtedly, the best possible strategy should be tailored on the characteristics of the patient and the stage of disease.

## COMMENTS

### Background

Technological advancements have allowed the spread of minimally invasive surgery in gastric cancer, but a number of issues are currently being debated, including the possibility in performing an effective extended lymph node dissection or the real advantages of the robotic systems.

### Research frontiers

Trials in this particular field aim to assess the effects on perioperative outcomes and the patient's quality of life while still respecting oncological principles. One of the main objective of surgical research is to verify the possibility to perform complex minimally invasive surgical procedures and their reproducibility worldwide.

### Innovations and breakthroughs

The present article is the first, in its field, that has analyzed data from a multi-institutional registry, thus allowing to verify the effect of minimally invasive surgery for gastric cancer on a large scale. Advantages in favor of these approaches were found in all postoperative steps of patient's recovery, while no differences were found regarding lymph nodes retrieval and complications, in the comparison with the open approach.

### Applications

Robotic and laparoscopic surgery can be considered for the treatment of gastric cancer and not limited to early stages. The availability of advanced technologies and the team experience can safely offer this approach in eligible patients.

### Terminology

Laparoscopic gastrectomy is a procedure performed through a laparoscope, a fiber optic cable system which allows viewing of the intra-abdominal field. The surgery is carried out after creating a pneumoperitoneal space. Robotic gastrectomy is performed with a surgical system which allows the surgeon to move articulated instruments through a remote console. This technique uses the pneumoperitoneum, too.

### Peer-review

The article deals with a comparison between the surgical treatment options for gastric cancer. The whole set up of this retrospective study is very good. The variables chosen for evaluation provide useful information. The study included a large number of patients.

## REFERENCES

- 1 NCCN. Clinical Practice Guidelines in Oncology: Gastric Cancer. Available from: URL: [http://www.nccn.org/professionals/physician\\_gls/pdf/gastricpdf](http://www.nccn.org/professionals/physician_gls/pdf/gastricpdf)
- 2 Parisi A, Nguyen NT, Reim D, Zhang S, Jiang ZW, Brower ST, Azagra JS, Facy O, Alimoglu O, Jackson PG, Tsujimoto H, Kurokawa Y, Zang L, Coburn NG, Yu PW, Zhang B, Qi F, Coratti A, Anecchiarico M, Novotny A, Goergen M, Lequeu JB, Eren T, Leblebici M, Al-Refai W, Takiguchi S, Ma J, Zhao YL, Liu T, Desiderio J. Current status of minimally invasive surgery for gastric cancer: A literature review to highlight studies limits. *Int J Surg* 2015; **17**: 34-40 [PMID: 25758348 DOI: 10.1016/j.ijso.2015.02.021]
- 3 Parisi A, Desiderio J. Establishing a multi-institutional registry to compare the outcomes of robotic, laparoscopic, and open surgery for gastric cancer. *Surgery* 2015; **157**: 830-831 [PMID: 25633739 DOI: 10.1016/j.surg.2014.12.007]



- 4 **Desiderio J**, Jiang ZW, Nguyen NT, Zhang S, Reim D, Alimoglu O, Azagra JS, Yu PW, Coburn NG, Qi F, Jackson PG, Zang L, Brower ST, Kurokawa Y, Facy O, Tsujimoto H, Coratti A, Annecchiarico M, Bazzocchi F, Avanzolini A, Gagniere J, Pezet D, Cianchi F, Badii B, Novotny A, Eren T, Leblebici M, Goergen M, Zhang B, Zhao YL, Liu T, Al-Refaie W, Ma J, Takiguchi S, Lequeu JB, Trastulli S, Parisi A. Robotic, laparoscopic and open surgery for gastric cancer compared on surgical, clinical and oncological outcomes: a multi-institutional chart review. A study protocol of the International study group on Minimally Invasive surgery for GASTRIC Cancer-IMIGASTRIC. *BMJ Open* 2015; **5**: e008198 [PMID: 26482769 DOI: 10.1136/bmjopen-2015-008198]
- 5 Japanese classification of gastric carcinoma: 3rd English edition. *Gastric Cancer* 2011; **14**: 101-112 [PMID: 21573743 DOI: 10.1007/s10120-011-0041-5]
- 6 **Murakami T**. Pathomorphological diagnosis. Definition and gross classification of early gastric cancer. *Gann Monogr Cancer Res* 1971; (**11**): 53-55
- 7 Japanese gastric cancer treatment guidelines 2010 (ver. 3). *Gastric Cancer* 2011; **14**: 113-123 [PMID: 21573742 DOI: 10.1007/s10120-011-0042-4]
- 8 **Waddell T**, Verheij M, Allum W, Cunningham D, Cervantes A, Arnold D. Gastric cancer: ESMO-ESSO-ESTRO clinical practice guidelines for diagnosis, treatment and follow-up. *Eur J Surg Oncol* 2014; **40**: 584-591 [PMID: 24685156 DOI: 10.1016/j.ejso.2013.09.020]
- 9 **Washington K**. 7th edition of the AJCC cancer staging manual: stomach. *Ann Surg Oncol* 2010; **17**: 3077-3079 [PMID: 20882416 DOI: 10.1245/s10434-010-1362-z]
- 10 **Clavien PA**, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R, Vonlanthen R, Padbury R, Cameron JL, Makuuchi M. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg* 2009; **250**: 187-196 [PMID: 19638912 DOI: 10.1097/SLA.0b013e3181b13ca2]
- 11 **von Elm E**, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg* 2014; **12**: 1495-1499 [PMID: 25046131 DOI: 10.1016/j.ijsu.2014.07.013]
- 12 **Huang KH**, Lan YT, Fang WL, Chen JH, Lo SS, Hsieh MC, Li AF, Chiou SH, Wu CW. Initial experience of robotic gastrectomy and comparison with open and laparoscopic gastrectomy for gastric cancer. *J Gastrointest Surg* 2012; **16**: 1303-1310 [PMID: 22450954 DOI: 10.1007/s11605-012-1874-x]
- 13 **Kim KM**, An JY, Kim HI, Cheong JH, Hyung WJ, Noh SH. Major early complications following open, laparoscopic and robotic gastrectomy. *Br J Surg* 2012; **99**: 1681-1687 [PMID: 23034831 DOI: 10.1002/bjs.8924]
- 14 **Kim MC**, Heo GU, Jung GJ. Robotic gastrectomy for gastric cancer: surgical techniques and clinical merits. *Surg Endosc* 2010; **24**: 610-615 [PMID: 19688399 DOI: 10.1007/s00464-009-0618-9]
- 15 **Kim HI**, Han SU, Yang HK, Kim YW, Lee HJ, Ryu KW, Park JM, An JY, Kim MC, Park S, Song KY, Oh SJ, Kong SH, Suh BJ, Yang DH, Ha TK, Kim YN, Hyung WJ. Multicenter Prospective Comparative Study of Robotic Versus Laparoscopic Gastrectomy for Gastric Adenocarcinoma. *Ann Surg* 2016; **263**: 103-109 [PMID: 26020107 DOI: 10.1097/SLA.0000000000001249]
- 16 **Caruso S**, Patriti A, Marrelli D, Ceccarelli G, Ceribelli C, Roviello F, Casciola L. Open vs robot-assisted laparoscopic gastric resection with D2 lymph node dissection for adenocarcinoma: a case-control study. *Int J Med Robot* 2011; **7**: 452-458 [PMID: 21984205 DOI: 10.1002/rcs.416]
- 17 **Viñuela EF**, Gonen M, Brennan MF, Coit DG, Strong VE. Laparoscopic versus open distal gastrectomy for gastric cancer: a meta-analysis of randomized controlled trials and high-quality nonrandomized studies. *Ann Surg* 2012; **255**: 446-456 [PMID: 22330034 DOI: 10.1097/SLA.0b013e31824682f4]
- 18 **Kang BH**, Xuan Y, Hur H, Ahn CW, Cho YK, Han SU. Comparison of Surgical Outcomes between Robotic and Laparoscopic Gastrectomy for Gastric Cancer: The Learning Curve of Robotic Surgery. *J Gastric Cancer* 2012; **12**: 156-163 [PMID: 23094227 DOI: 10.5230/jgc.2012.12.3.156]
- 19 **Junfeng Z**, Yan S, Bo T, Yingxue H, Dongzhu Z, Yongliang Z, Feng Q, Peiwu Y. Robotic gastrectomy versus laparoscopic gastrectomy for gastric cancer: comparison of surgical performance and short-term outcomes. *Surg Endosc* 2014; **28**: 1779-1787 [PMID: 24385251 DOI: 10.1007/s00464-013-3385-6]
- 20 **Eom BW**, Yoon HM, Ryu KW, Lee JH, Cho SJ, Lee JY, Kim CG, Choi IJ, Lee JS, Kook MC, Rhee JY, Park SR, Kim YW. Comparison of surgical performance and short-term clinical outcomes between laparoscopic and robotic surgery in distal gastric cancer. *Eur J Surg Oncol* 2012; **38**: 57-63 [PMID: 21945625 DOI: 10.1016/j.ejso.2011.09.006]
- 21 **Son T**, Lee JH, Kim YM, Kim HI, Noh SH, Hyung WJ. Robotic spleen-preserving total gastrectomy for gastric cancer: comparison with conventional laparoscopic procedure. *Surg Endosc* 2014; **28**: 2606-2615 [PMID: 24695982 DOI: 10.1007/s00464-014-3511-0]
- 22 **Marano A**, Choi YY, Hyung WJ, Kim YM, Kim J, Noh SH. Robotic versus Laparoscopic versus Open Gastrectomy: A Meta-Analysis. *J Gastric Cancer* 2013; **13**: 136-148 [PMID: 24156033 DOI: 10.5230/jgc.2013.13.3.136]
- 23 **Kim HH**, Hyung WJ, Cho GS, Kim MC, Han SU, Kim W, Ryu SW, Lee HJ, Song KY. Morbidity and mortality of laparoscopic gastrectomy versus open gastrectomy for gastric cancer: an interim report--a phase III multicenter, prospective, randomized Trial (KLASS Trial). *Ann Surg* 2010; **251**: 417-420 [PMID: 20160637 DOI: 10.1097/SLA.0b013e3181cc8f6b]
- 24 **Hyun MH**, Lee CH, Kwon YJ, Cho SI, Jang YJ, Kim DH, Kim JH, Park SH, Mok YJ, Park SS. Robot versus laparoscopic gastrectomy for cancer by an experienced surgeon: comparisons of surgery, complications, and surgical stress. *Ann Surg Oncol* 2013; **20**: 1258-1265 [PMID: 23080320 DOI: 10.1245/s10434-012-2679-6]
- 25 **Park JY**, Jo MJ, Nam BH, Kim Y, Eom BW, Yoon HM, Ryu KW, Kim YW, Lee JH. Surgical stress after robot-assisted distal gastrectomy and its economic implications. *Br J Surg* 2012; **99**: 1554-1561 [PMID: 23027072 DOI: 10.1002/bjs.8887]
- 26 **Woo Y**, Hyung WJ, Pak KH, Inaba K, Obama K, Choi SH, Noh SH. Robotic gastrectomy as an oncologically sound alternative to laparoscopic resections for the treatment of early-stage gastric cancers. *Arch Surg* 2011; **146**: 1086-1092 [PMID: 21576595 DOI: 10.1001/archsurg.2011.114]
- 27 **Hiki N**, Shimizu N, Yamaguchi H, Imamura K, Kami K, Kubota K, Kaminishi M. Manipulation of the small intestine as a cause of the increased inflammatory response after open compared with laparoscopic surgery. *Br J Surg* 2006; **93**: 195-204 [PMID: 16392101 DOI: 10.1002/bjs.5224]
- 28 **Song J**, Kang WH, Oh SJ, Hyung WJ, Choi SH, Noh SH. Role of robotic gastrectomy using da Vinci system compared with laparoscopic gastrectomy: initial experience of 20 consecutive cases. *Surg Endosc* 2009; **23**: 1204-1211 [PMID: 19263147 DOI: 10.1007/s00464-009-0351-4]

**P- Reviewer:** Christodoulidis G, Inokuchi M, Mann O, Yu SP  
**S- Editor:** Ma YJ **L- Editor:** A **E- Editor:** Zhang FF





Published by **Baishideng Publishing Group Inc**  
8226 Regency Drive, Pleasanton, CA 94588, USA  
Telephone: +1-925-223-8242  
Fax: +1-925-223-8243  
E-mail: [bpgooffice@wjgnet.com](mailto:bpgooffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>



ISSN 1007-9327

