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ORIGINAL ARTICLE

Comparison of short-term outcomes of minimally invasive laparoscopic gastrectomy in older adults with locally advanced gastric cancer

Comparación de desenlaces a corto plazo de gastrectomía laparoscópica mínimamente invasiva en adultos mayores con cáncer gástrico localmente avanzado

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Abstract

Introduction. The objective of this study was to compare the short-term outcomes of laparoscopic gastrectomy in adults vs. older patients with locally advanced gastric cancer from a Western country cohort.

Methods. Prospective cohort study in patients undergoing laparoscopic gastrectomy for locally advanced gastric cancer at the Hospital Universitario Erasmo Meoz, de Cúcuta, Colombia, between November 2014 and December 2018. Descriptive, group comparison and bivariate analysis was performed.

Results. Of a total of 116 patients, 51 patients (44%) were 65 years or older and 63 patients (54%) were men. No statistically significant difference was found when comparing patients under 65 years of age with those 65 years of age or older. The median operating time was 240 minutes in both groups (p>0.05), the median macroscopic resection margins were 6 cm vs. 5 cm (p>0.05), the median number of lymph nodes dissected was 25 vs. 19 (p>0.05), the

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median number of positive lymph nodes was 4 vs. 3 (p>0.05), the median stay was 7 days in both groups (p>0.05). The overall rate of postoperative complications did not differ significantly between adults (7%) and older adults (11%) (p>0.05) and no significant differences were observed in the rates of minor complications (Clavien-Dindo grade II; 3-5% vs. 6-12%; p>0.05) and severe (Clavien-Dindo ≥ IIIa; 3-5% vs. 4-8%; p>0.05).

Conclusions. No statistically differences were found in short-term outcomes between adult and older patients with locally advanced gastric cancer treated with laparoscopic gastrectomy. This technique is safe in the elderly.

Keywords: stomach neoplasms; gastrectomy; laparoscopy; minimally invasive surgical procedures; postoperative complications; elderly.

Resumen

Introducción. El objetivo de este estudio fue comparar los desenlaces a corto plazo de la gastrectomía laparoscópica en adultos vs. adultos mayores con cáncer gástrico localmente avanzado en una cohorte de un país occidental.

Métodos. Estudio de cohorte prospectivo en pacientes sometidos a gastrectomía laparoscópica por cáncer gástrico localmente avanzado, en el Hospital Universitario Erasmo Meoz, de Cúcuta, Colombia, entre noviembre de 2014 y diciembre de 2018. Se realizó análisis descriptivo, de comparación de grupos y bivariado.

Resultados. De un total de 116 pacientes, 51 pacientes (44 %) tenían 65 años o más y 63 pacientes (54 %) eran hombres. No se encontró diferencia estadísticamente significativa al comparar los pacientes menores de 65 años con los de 65 años o más. La mediana del tiempo operatorio fue de 240 minutos en ambos grupos (p>0,05), la mediana de los márgenes de resección macroscópica fue 6 cm vs. 5 cm (p>0,05), la mediana de los ganglios linfáticos disecados fue 25 vs. 19 (p>0,05), la mediana de ganglios linfáticos positivos fue 4 vs. 3 (p>0,05), la mediana de estancia fue de 7 días en ambos grupos (p>0,05). La tasa general de complicaciones posoperatorias no difirió significativamente entre adultos (7%) y adultos mayores (11 %) (p>0,05) y no se observaron diferencias significativas en las tasas de complicaciones menores (Clavien-Dindo grado II; 3-5 % vs. 6-12 %; p>0,05) y graves (Clavien-Dindo ≥ IIIa; 3-5 % vs. 4-8 %; p>0,05).

Conclusiones. No se encontraron diferencias estadísticamente significativas en los resultados a corto plazo entre los pacientes adultos y adultos mayores con cáncer gástrico localmente avanzado tratados con gastrectomía laparoscópica. Esta técnica es segura en ancianos.

Palabras claves: neoplasias gástricas; gastrectomía; laparoscopia; procedimientos quirúrgicos mínimamente invasivos; complicaciones posoperatorias; anciano.

Introduction

It has been 28 years since Kitano et al. published the first report of laparoscopic total gastrectomy in a patient with early gastric cancer (GC) [1], and from that moment on, the use of this technique has gradually increased. Multiple clinical trials have compared laparoscopic gastrectomy (LG) with open gastrectomy (OG) in the treatment of gastric cancer, finding similar outcomes in mortality and no significant differences in serious adverse events [2,3].

LG possibly benefits patients with GC, reducing hospital stay time and post-surgical morbidity [4,5], while being similar to OG in lymph node count [6-8]. Despite the technical challenge, LG with D2 lymphadenectomy is considered a feasible and safe procedure for the treatment of locally advanced gastric cancer [9-15] in patients with high body mass index (BMI) and advanced age [16].

Gastric cancer is the third cause of death from cancer in the world [17] and in Colombia it is the first, mainly affecting people with limited resources, the elderly or those from urban areas [18,19]. In general, gastric cancer is diagnosed by endoscopy of the upper digestive tract in Latin America in advanced stages due to the lack of application of

screening tests [20]. The objective of our study was to compare the short-term perioperative outcomes of LG in adult and older patients with locally advanced gastric cancer. The secondary objective was to determine the variables that correlate with hospital stay.

Methods

The Hospital Universitario Erasmo Meoz is a reference center in the northeastern region of Colombia and has offered minimally invasive surgery for the management of gastric cancer since October 2014. A prospective analytical study was designed, in which the patients treated were selected in a consecutive fashion from November 2014 to December 2018.

Participants and eligibility

The patients selected for the study had advanced stage gastric cancer, with no evidence of invasion into adjacent structures in presurgical studies. The participants underwent a pre-surgical evaluation using upper digestive tract endoscopy, blood count, kidney function tests, liver profile, electrocardiogram, and nutritional evaluation. Preoperative imaging studies included chest x-ray, echocardiogram, and thoraco-abdominal tomography. All patients underwent physiatry evaluation in the perioperative period. Patients with tumors located proximal to the cardio-esophageal junction received preoperative neoadjuvant treatment.

Inclusion and exclusion criteria

All patients with locally advanced gastric cancer who underwent consecutive laparoscopic gastrectomy with D2 lymphanectomy were included. Patients under 18 years of age, with stromal tumors (GIST) and those who had metastatic tumors to adjacent structures were excluded. Likewise, patients in whom gastric cancer was not detected in histopathological studies were excluded.

Surgical technique

The team of surgeons who participated in the study have performed more than 60 laparoscopic gastrectomies in compliance with quality standards. The procedure starts with the placement of five trocars, one 12 mm, another 11 mm, and three 5 mm. The main surgeon is located between the patient's lower limbs, using the French technique. Nodal dissection and omentectomy are performed using scalpel-based ultrasound energy. In both total and subtotal gastrectomy, the resection is extended to a D2 dissection involving stations 1, 3, 4sb, 4d, 5, 6, 7, 8ª, 9, 11p, and 12ª.

A white linear endostapler was used for the section of the left gastric artery, and a linear endostapler with a gold load was used for the duodenal and esophageal sections. To extract the surgical piece, a 6 cm mini-laparotomy incision is made at the level of the hypogastrium, with protection of the wound by placing a manual assistance mechanism. The wound is subsequently washed with chlorhexidine. The section of the jejunum is performed at 40 cm from the angle of Treitz with a white loading linear endostapler.

In total gastrectomy, the distal part of the sectioned intestine is ascended in an antemesocolic manner and the end-to-lateral esophago-jejunal anastomosis is performed using mechanical suture with a circular stapler 21. In cases of laparoscopic subtotal gastrectomy, a lateral gastro-jejunostomy is performed. lateral on the posterior gastric aspect with a 60 mm blue loading endostapler. To reduce the risk of bleeding, hemostatic sealants are used. The extraction of the pneumoperitoneum is done by protecting the surgical wounds with trocars, avoiding contact with CO_2.

Data collection

Data were collected prospectively by interns and general surgery residents. The variables evaluated included age, sex, BMI, comorbidities, pharmacological history, perioperative studies, type of procedure, and operative time. For the anatomopathological findings, tumor location and size, degree of tumor differentiation, lymphatic and vascular invasion, number of resected nodes, affected nodes, and tumor resection margins were taken into account. The stage was classified following the recommendations of the American Joint

Committee. Two investigators independently reviewed the validity of the retrospectively collected data and controversies were resolved by consensus.

Outcomes

The primary outcome of the study was the presence of medical or surgical complications in the immediate perioperative period, using the Clavien-Dindo classification. Using multivariate linear regression analysis, variables correlated with hospital stay were sought.

Statistical analysis

The latest version of R was used for statistical analysis. In the description of the categorical variables, absolute and relative frequencies were used. Continuous variables were represented using measures of central tendency. For the bivariate analysis, Fisher's exact test was used for categorical variables, ANOVA analysis of variance for ordinal variables, and Student's T test for the analysis of continuous and dichotomous variables. The differences were considered statistically significant with values of $p<0.05$. Simple and multiple regression models were created considering hospital stay as the dependent variable. To evaluate the assumptions, the Q-Q curve was used to determine the symmetric distribution of the dependent variable and homoscedasticity was assessed using the residual versus adjusted curve. The model that best fitted was chosen following the forward/backward methodology.

Results

Demographic characteristics

During the study period, 116 participants were included. The median age was 64 years; 51 (44%) patients were 65 years or older (Table 1). The tumor was visible on preoperative CT in 105 (91%) patients, 41% located in the fundus, and 41% in the gastric antrum.

Surgical variables

Of the surgical procedures performed, 90 (78%) were total laparoscopic gastrectomy and 26 (22%) were subtotal. The average operating time was 256 minutes and the hospital stay was 10 days. There were no intraoperative deaths. All patients had Roux-en-Y reconstruction. The average number of nodes resected was 25, with 8 nodes classified as affected (Table 2).

Table 1. Demographic characteristics of the patients included in the study.

Variable	n=116
Age (years), median (IQR)	64 (55-70)
≥ 65 years, n (%)	51 (44%)
Gender, n (%)	
Female	53 (46%)
Male	63 (54%)
Body mass index (kg/m2), median, (IQR)	22 (20-25)
ASA classification, n (%)	
I	2 (2%)
II	24 (21%)
III	90 (78%)
Comorbidities, n (%)	46 (40%)
Diabetes mellitus	15 (13%)
Cardiovascular	11 (10%)
Peripheral vascular	10 (9%)
Respiratory	7 (6%)
Neurologic	6 (5%)
Gastrointestinal	4 (3%)
Kidney	3 (3%)
Hepatic	1 (1%)
Non-metastatic secretory solid tumor	4 (3%)
Metastatic secretory solid tumor	1 (1%)
Anticoagulants, n (%)	4 (3%)
Antiplatelet agents, n (%)	1 (1%)
Previous abdominal surgeries, n (%)	18 (16%)
Supra-mesocolic	5 (4%)
Infra-mesocolic	11 (9%)
Supra e infra-mesocolic	2 (2%)
Tumor visible on preoperative tomography, n (%)	105 (91%)
Gastroesophageal junction	14 (12%)
Gastric fundus	47 (41%)
Gastric antrum	48 (41%)
Location unclear	3 (3%)
Neoadjuvant treatment, n (%)	14 (12%)

IQR: interquartile range; ASA: American Society of Anesthesiologists.
Source: Authors' own elaboration.

Table 2. Description of the interventions and anatomopathological findings.

Variable	n=116
Type of intervention, n (%)	
Total laparoscopic gastrectomy	90 (78%)
Subtotal laparoscopic gastrectomy	26 (22%)
Conversion, n (%)	4 (3%)
Local infiltration	3 (3%)
Adhesions	1 (1%)
Intraoperative death	0
Histological type, n (%)	
Intestinal adenocarcinoma	78 (67%)
Diffuse adenocarcinoma	16 (14%)
Adenocarcinoma with signet ring cells	3 (3%)
Mucinous carcinoma	6 (5%)
Gastrointestinal stromal tumor	1 (1%)
Other unclassified neoplasms	10 (9%)
Degree of differentiation, n (%)	
Low	62 (53%)
Moderate	38 (33%)
High	9 (8%)
Mucinous	5 (4%)
Unknown	2 (2%)
Lymphatic invasion, n (%)	101 (87%)
Vascular invasion, n (%)	100 (86%)
Diameter, margins and lymph nodes (media ± SD)	
Largest tumor diameter (mm)	64 ± 36
Macroscopic proximal margin (cm)	6 ± 4
Macroscopic distal margin (cm)	5 ± 4
Total lymph nodes	25 ± 13
Affected lymph nodes	8 ± 11
Operating time, minutes (media ± SD)	256 ± 42
Roux-en-Y reconstruction, n (%)	116 (100%)
Hospital stay, days (media ± SD)	10 ± 8

SD: standard deviation
Source: Authors' own elaboration.

Oncological variables

More than half of the patients had tumors classified as intestinal adenocarcinoma. Only 3% of the tumors corresponded to adenocarcinoma with signet ring cells. Ten tumors could not be classified histologically. Low tumor differentiation grade was the most frequent. When comparing tumor stages in patients younger than 65 years with those aged 65 years or older, no statistically significant differences were found (Table 3).

Table 3. Description of the tumor stage in each age group.

	< 65 years (n=65) n (%)	≥ 65 years (n=51) n (%)	p-value
Stage			
p0	2 (3)	--	>0.05
pIA	2 (3)	1 (2)	>0.05
pIB	4 (6)	6 (12)	>0.05
pIIA	8 (12)	7 (14)	>0.05
pIIB	13 (20)	12 (24)	>0.05
pIIIA	16 (25)	12 (24)	>0.05
pIIIB	12 (18)	9 (18)	>0.05
pIIIC	6 (9)	3 (6)	>0.05
pIV	--	--	--
Unknown	1 (2)	1 (2)	>0.05

Source: Authors' own elaboration.

Complications

Four procedures required conversion, three due to local infiltration and one due to the presence of adhesions secondary to a previous abdominal procedure. 11% of patients had some medical complication, with atelectasis and pneumonia being the most common. Surgical complications that required reintervention occurred in 5% of the patients, with hemorrhagic complications being the most frequent (Table 4).

Comparison between adults and older adults

When adults and older adults were compared, no statistically significant differences were found in operative time, macroscopic resection margins, dissected lymph nodes, or positive lymph nodes. Likewise, the overall rate of postoperative complications did not differ significantly. The frequency of minor complications (Clavien-Dindo grade II) was 3-5% vs. 6-12% (p>0.05) and severe cases (Clavien-Dindo ≥IIIa) 3-5% vs. 4-8% (p>0.05).

Hospital stay

The median hospital stay was 7 days in both groups, without a statistically significant difference (p>0.05). When analyzing in multiple linear regression with adjusted R-squared value of 0.4783, residual error of 5.693 and 108 degrees of freedom, we found that medical complications

Table 4. Description of complications and their classification according to Clavien-Dindo.

		Clavien-Dindo n (%)					
	n (%)	I	II	IIIa	IIIb	IV	V
Medical complications	13 (11)	4 (3)	9 (8)				
Atelectasis	4 (3)	4 (3)					
Pneumonia	4 (3)		4 (3)				
Central venous catheter infection	1 (1)		1 (1)				
Urinary tract infection	1 (1)		1 (1)				
Acute myocardial infarction	1 (1)		1 (1)				
Heart failure	2 (2)		2 (2)				
Surgical complications	6 (5)				6 (5)		
Bleeding	4 (3)				4 (3)		
Anastomosis leak	1 (1)				1 (1)		
Esophagojejunal fistula	1 (1)				1 (1)		

Source: Authors' own elaboration.

(p=0.001), surgical complications (p<0.0002), comorbidities (p=0.02), and previous use of anticoagulants (p=0.02), were 48% correlated with changes in the variability of hospital stay (p<0.0002). When evaluating the model with a significance level of 0.05, this model did not satisfy the assumption of homoscedasticity and Kurtosis (Figure 1).

Discussion

In recent years, the use of minimally invasive surgery has increased due to the benefits it provides to the patient. The reduction in pain, early postoperative recovery, better aesthetic results and lower costs have made oncological surgery become minimally invasive. Large-scale retrospective studies revealed that, compared with open surgery, laparoscopic surgery for locally advanced GC can lead to better short-term outcomes and comparable long-term oncological outcomes. Inokuchi et al., in 2017, pointed out that LG was associated with a significantly earlier onset of food intake and a significantly shorter period of hospitalization in patients with advanced gastric cancer. Similarly, in 2019, Norero et al. showed a better recovery rate, fewer wound and abdominal wall complications in patients who underwent laparoscopic surgery, data comparable to our results, which demonstrates that laparoscopic gastrectomy is associated with low complication rates [11,21-23].

In the study carried out in 2019 by Dias et al., a positive correlation was found between age and hospitalization, a theory that is explained by the comorbidities of the patients, and it was also evidenced that patients over 65 years of age and with ASA III/IV had a higher probability of serious complications [24]. Chan et al. compared the open versus laparoscopic technique in patients with advanced gastric adenocarcinoma in a group of patients with D2 lymph node dissection and found that there was a shorter hospital stay, less bleeding, and fewer complications in laparoscopic surgery [25].

Although our study did not compare the two surgical techniques, a median hospital stay of 7 days was found, which was less than that reported in the aforementioned study, which was 9 days. The above confirms that using the laparoscopic technique may be associated with a shorter hospital stay [26]. In 48% of cases, changes in the variability of hospital stay associated with factors such as medical complications, surgical complications, comorbidities, and previous use of anticoagulants were observed.

Kim et al., in 2018, studied patients over 80 years of age, finding that advanced age is one of

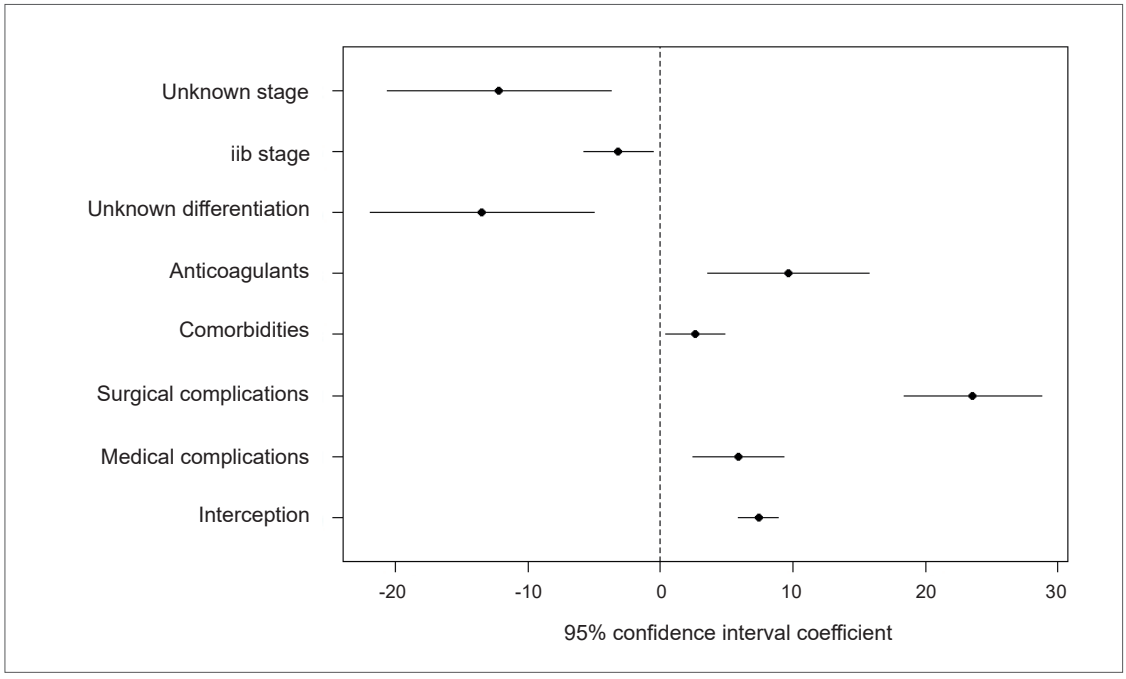

Figure 1. Variability of "hospital stay" in a multiple linear regression model.

the highest risk factors for postoperative complications, since they are the patients with the most comorbidities, being cardiovascular diseases (hypertension, coronary heart disease or stroke) and diabetes, which occur most frequently [27]. In contrast, our findings are more encouraging, since there was no statistically significant difference in the appearance of short-term complications when comparing the group of patients under and over 65 years of age, which tells us about the safety of the laparoscopic technique. for the treatment of locally advanced gastric cancer. No differences were found in terms of the operative results of the procedure between the two age groups, so it is concluded that age is not a variable that affects the development of laparoscopic gastrectomy.

A faster postoperative intestinal recovery and a similar risk of developing postoperative complications were observed, comparing the laparoscopic approach with open surgery. Considering in this way that GL is a more feasible option than open surgery to improve the quality of life in elderly patients.

In 2018, a study by Fujiya et al. found that postoperative pneumonia was the most observed complication [28]. In our study, similarly, it was recorded that the medical complications with the highest incidence were pneumonia and atelectasis.

Acceptable short-term results have been reported only in studies incorporating experienced surgeons [29]. Significant accumulation of surgical experience is required, which according to Xu et al., in 2018, is completed after 30 to 50 laparoscopic operations [30]. Thus, the safety and oncologic efficacy of GL are largely influenced by regional incidence, case volume at individual centers, and surgeon experience. Therefore, GL is considered a safe and effective therapeutic option, which complies with international recommendations. It is superior in terms of operative morbidity and potentially superior in terms of oncological outcomes for patients with surgically resectable advanced gastric cancer [31].

Despite the advantages of our study, it is important to recognize its limitations. It is an observational study, in which randomization was

not performed, so it is possible that there were biases in the results. The number of patients is limited, however, it is the local registry with the highest number of cases. The outcomes evaluated are short-term, so we do not know the long-term safety of the intervention in the evaluated population.

Conclusion

Given the absence of local research on GL as a treatment for advanced gastric cancer, our study has marked importance, allowing us to evaluate the feasibility and safety of this procedure carried out in adults and older adults with this pathology, and can be used to future investigations.

Compliance with ethical standards

Informed consent: The study was approved by the medical ethics committee of the institution where the data were collected. Likewise, it adheres to the regulations dictated by Resolution 008430 of 1993 of the Colombian Ministry of Health, according to which it is considered to represent a very low risk. All patients gave informed consent for participation in the study.

Conflict of interest: The authors declare no conflicts of interest.

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Author's contributions

- Conception and design of the study: Hender Alirio Hernández-Martínez, Deivys Jesús López-Melo, Alexander Bahamon-Flórez, Luis Fernando Conde-Buitrago, Guillermo Labrador.
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- Drafting the manuscript: Daniela Charris-Suarez, Rafael Alberto Olarte-Ardila, Juan Sebastián Castillo, Wilmer Galvis-Ballesteros, Freddy Quintero-Álvarez.
- Critical review Daniela Charris-Suarez, Rafael Alberto Olarte-Ardila, Juan Sebastián Castillo, Wilmer Galvis-Ballesteros, Freddy Quintero-Álvarez.

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