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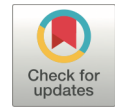
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ORIGINAL ARTICLE

Morbidity and mortality in patients undergoing gastrectomy for gastric cancer

Morbilidad y mortalidad en pacientes llevados a gastrectomía por cáncer gástrico

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Abstract

Introduction. Gastric cancer is the fourth leading cause of cancer death worldwide with more than one million cases diagnosed each year. Surgery with curative intent remains the mainstay of management for resectable patients. Identify patients at increased risk of morbidity and mortality is important for the decision making process, with no ideal tool available yet. Review and analysis of the experience of a referral cancer center may generate useful information.

Methods. Historical cohort observational study. Patients undergoing gastrectomy for gastric adenocarcinoma at the National Cancer Institute in Bogotá, Colombia, between January 1, 2010 and December 31, 2017 were included.

Results. We included 332 patients of which 57.2% were men with mean age of 61 years. Mortality in this series was 4.5% and morbidity was 34.9%. The factor associated with higher risk of death was age with a HR of 1.05 statistically significant value ($p=0.021$). A higher risk was found in the group of patients with ASA greater than II ($p=0.009$). The 17.4% presented complications greater than IIIA of the Clavien Dindo classification.

Conclusions. In this study the morbidity and mortality seems similar to those reported in the literature. Only age and ASA score showed an association with significant statistical value for postoperative complications.

Keywords: stomach neoplasms; gastrectomy; postoperative complications; morbidity; mortality; prognosis.

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Resumen

Introducción. El cáncer gástrico es la cuarta causa de muerte por cáncer a nivel mundial, con más de un millón de casos diagnosticados cada año. La cirugía con intención curativa sigue siendo el pilar del manejo para los pacientes resecables. La identificación de pacientes con mayor riesgo de morbilidad y mortalidad es importante para el proceso de toma de decisiones, sin existir hasta el momento una herramienta ideal. La revisión y el análisis de la experiencia de un centro oncológico de referencia pueden generar información útil.

Métodos. Estudio observacional de cohorte histórica, en el que se incluyeron los pacientes llevados a gastrectomía por adenocarcinoma gástrico en el Instituto Nacional de Cancerología, Bogotá, D.C., Colombia, entre el 1° de enero del 2010 y el 31 de diciembre del 2017.

Resultados. Se evaluaron 332 pacientes, de los cuales el 57,2 % eran hombres con edad promedio de 61 años. La mortalidad en esta serie fue del 4,5 % y la morbilidad de 34,9 %. El factor asociado con mayor riesgo de muerte fue la edad, con un HR de 1,05 ($p=0,021$). Se encontró un mayor riesgo en el grupo de pacientes con ASA mayor a II ($p=0,009$). El 17,4 % presentaron complicaciones mayores a IIIA de la clasificación de Clavien-Dindo.

Conclusiones. En el presente trabajo las cifras de morbilidad y mortalidad son similares a las reportadas en la literatura. Solo la edad y la clasificación de ASA mostraron asociación con valor estadístico significativo para complicaciones postoperatorias.

Palabras clave: neoplasias gástricas; gastrectomía; complicaciones postoperatorias; morbilidad; mortalidad; pronóstico.

Introduction

Gastric cancer (GC) is the fourth leading cause of cancer death worldwide, with more than one million cases diagnosed each year. In Colombia the incidence is high, being the third most frequent cancer and the first cause of death from cancer¹. Gastric resection with associated lymphadenectomy is the mainstay of management for patients with resectable tumors². The decision to carry out surgery with curative intent in a patient with gastric cancer is defined by clinical criteria that include age, functional and nutritional status, comorbidities, and a correct tumor staging based on digestive endoscopy, imaging diagnostic procedures and, frequently, laparoscopy³.

Despite the advances in perioperative care and the refinement of surgical techniques, gastrectomy carries a significant risk of morbidity, which generates a longer hospital stay, care costs, and probable functional sequelae^{4,5}. The percentage of complications after a gastrectomy for cancer has been described between 15% and 25%^{4,6}, with a mortality of 3% to 5%^{6,7}. Possible complications range from minor effects, such as surgical

site infection, to clinical situations that can harm the patient's life, such as bleeding, anastomotic leakage, and pancreatitis⁵.

The identification of patients with the highest risk of morbidity and mortality is necessary for the decision-making process⁵, without an ideal tool to date. The review and analysis of the experience of a reference cancer center can generate useful information. The objective of this study was to describe the early morbidity and mortality in a series of patients who underwent gastrectomy for cancer at the National Institute of Cancerology in Bogotá, Colombia, over a 7-year period.

Methods

Historical cohort observational study, which included patients undergoing gastrectomy for gastric adenocarcinoma, between January 1, 2010 and December 31, 2017, at the National Institute of Cancerology in Bogotá, Colombia. The surgeries were performed by expert gastrointestinal surgeons or by general surgeons graduated from their second specialty training, always under the supervision of a senior surgeon. Roux-en-Y re-

construction was performed in all patients and in all total gastrectomies, esophagojejunal reconstruction was performed with circular mechanical suture, regardless of the surgical approach (open or minimally invasive).

The data was recorded in a database in the REDCAP system. In addition to demographic variables, physical status classification according to The American Society of Anesthesiologists (ASA), comorbidities, lesion characteristics, type of surgical procedure, operative time and bleeding, and TNM classification (AJCC 7th Edition)⁸, need for transfusion, hospitalization time, postoperative complications according to the Clavien-Dindo classification⁹, and 30-day mortality were recorded. When more than one event occurred in a single patient, the most severe complication was recorded.

In the descriptive component of the statistical analysis, frequency and percentage were used in the case of categorical variables, and mean with its standard deviation in the case of quantitative variables. The statistical analysis related to the exploration of risk factors for mortality was carried out using Cox proportional hazards models; in these models, crude estimators were calculated, significance levels of 5%, and cases of loss to follow-up with unknown outcome were taken as right censors. The analyzes were carried out with the Stata[®] program (StataCorp LLC, College Station, USA) version 16.

Results

Characteristics of the patients and the procedures performed

Three-hundred-thirty-two patients were evaluated, of which 57.2% (n=190) were men, with a mean age of 61 years (Table 1). The average body mass index (BMI) was 23.9 kg/m²; 25 patients (7.8%) were found to be underweight (BMI < 18.5 kg/m²) and 119 (37.4%) were overweight (BMI > 25 kg/m²); 95% of the patients (n=318) were classified as ASA II and III; 66.6% of the cases (n=221) had some comorbidity, the most frequent being arterial hypertension (27.2%), followed by lung disease (9.2%) and diabetes (8.3%). In 61 patients (18.6%) there were other diseases such as hypothyroidism, senile dementia, obesity, anxiety

disorder, rheumatoid arthritis, neurological disorders and another type of cancer.

The average tumor size was 5 cm, the average hemoglobin level was 12.8 g/dl, and the albumin level was 3.6 g/dl. Regarding pathological staging, pT1 tumor status was found in 58 patients (17.5%); pT2 and pT3 in 113 (34%) each, pT4 in 154 (46.3%), 23 of them T4b, and seven patients without data. Regarding lymph node involvement, pN0 was described in 97 patients, N1 and N2 in 50 each, N3a in 83, N3b in 46, and no data in six patients. No metastasis (M0) was observed in 310 patients, M1 in 13, and no data in nine patients (Figure 1).

Table 1. Clinical characteristics of patients undergoing gastrectomy for gastric cancer (n=332).

Variable	Frequency	Percentage
Age, mean	61.06 years	
Sex		
Male	190	57.2
Female	142	42.8
ASA classification		
I	10	3.0
II	188	56.6
III	130	39.2
IV	4	1.2
Comorbidity		
No	111	33.4
Yes	221	66.6
Arterial hypertension	91	27.4
Chronic obstructive pulmonary disease	31	9.3
Diabetes	28	8.4
Coronary heart disease	10	3.0
Others	61	18.3
Tumor location		
Fundocorporal (upper)	19	5.7
Corporoantral (middle)	153	46.1
Antral (lower)	151	45.5
Pangastric	9	2.7
Histological type		
Intestinal	194	58.5
Diffuse	100	30.1
Mixed	21	6.3
Others	17	5.1

Source: Own authors.

Out of the 167 (49.7%) total gastrectomies performed, most of them were open (94.9%) (Table 2). There were 32 extended resections, with six colectomies, three distal pancreatectomies, two of them with splenectomy, one central pancreatectomy by direct extension only to the body of the pancreas, and 15 splenectomies. Other procedures included nonanatomic liver resection, cholecystectomy, oophorectomy, pancreaticoduodenectomy, and small bowel resection. Mean intraoperative bleeding was 300 ml and 118 patients (35.5%) received perioperative transfusion. The mean hospital stay was 12.6 days.

D1 dissection (38.5%) was performed in patients with non-curative surgery or with very high surgical risk. D2 dissection, which is the one of choice in patients with advanced GC as recommended by international guidelines^{10,11}, was performed in 57.6% of patients.

Complications and mortality

There were 116 complications (Figure 2), for a general morbidity of 34.9%, which when minor complications (grade I of the Clavien-Dindo classification) were excluded dropped to 27.4%, and when only complications were included. older than IIIA in the same classification, was 17.4%. Leakage from the esophagojejunal anastomosis with six cases was the most frequent complication, followed by leakage from the duodenal stump.

Mortality was 4.5%; table 3 shows the causes of mortality of the patients, identifying the leak of the esophagojejunal anastomosis as the most frequent. Of the 15 deceased patients, six (40%) had multivisceral resection (extended gastrectomy).

Regarding the factors associated with a higher risk of death, age showed a HR of 1.05, with a statistically significant value ($p=0.021$), meaning that the older the age, the greater the risk of mortality, with an increased risk of die of 5% for each year. A higher risk was also found in patients with ASA greater than II ($p=0.00$); however, due to the sample size, an HR estimate was not achieved. In the absence of multivisceral resection there was a lower risk of death ($HR=0.22$; $p=0.005$).

The variables gender, BMI, comorbidities, tumor size, location, albumin level, type of lymph node dissection, type of gastrectomy, and surgical time were not related to the risk of mortality (Table 4).

Discussion

The decision to perform a gastrectomy with curative intent in patients with gastric cancer requires knowledge and anticipation of the surgical risk. Recognize how to mitigate the occurrence of complications or even avoid surgery when a morbidity and mortality that exceeds the potential benefit is expected, is estimated taking into account the characteristics of the patient, the particularities of the

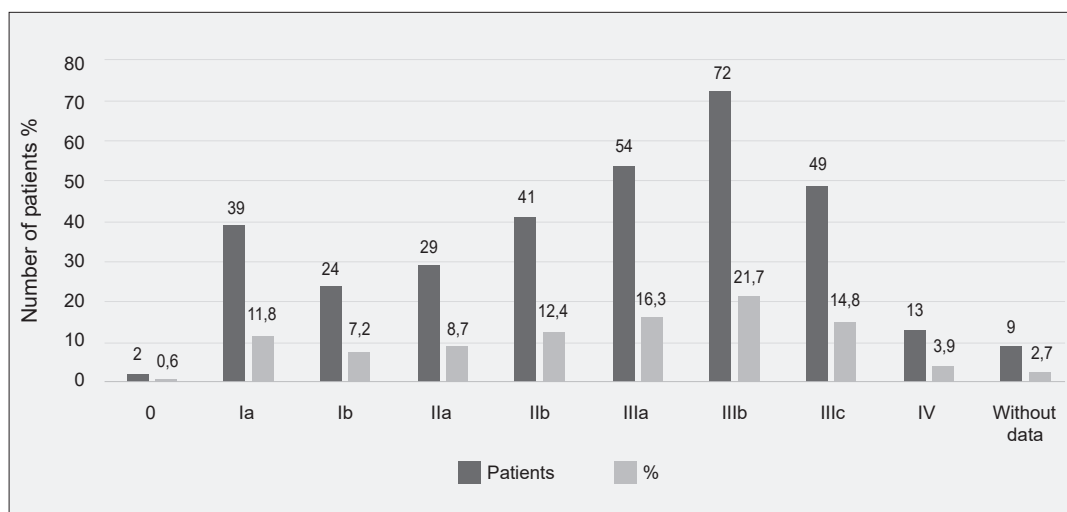


Figure 1. pTNM stage of patients according to AJCC 7th Edition. Source: Own authors.

Table 2. Characteristics of the surgical technique.

Variable	Frequency	Percentage
Type of surgery		
Distal gastrectomy	167	50.3
Total gastrectomy	165	49.7
Type of approach		
Open approach	315	94.9
Laparoscopic	17	5.1
Lymph node dissection type		
D0	5	1.5
D1	128	38.5
D2	191	57.6
D3	1	0.3
No data	7	2.1
Extended resection		
No	300	90.3
Yes	32	9.7
Splenectomy	15	4.5
Colectomy	6	1.8
Distal pancreatectomy	4	1.2
Others	7	2.1

Source: Own authors.

tumor and the magnitude of the best treatment for oncological control of the disease².

Postoperative morbidity and mortality in radical gastrectomy are not negligible and constitute an indicator of adequate management, approach, and selection of patients when defining surgery^{2,12}. The frequency and magnitude of postoperative complications are essential aspects in the analysis of oncological results². The figures for complications after gastrectomy vary greatly, between 11% and 46%, because they come mostly from retrospective studies, among which there is no unanimity in the classification of the severity of the events^{2,4,12-20}. In this study, when only complications greater than IIIA were included in the Clavien-Dindo classification, morbidity was 17.4%, a figure very similar to that of other series^{2,4,12,16,15}.

We recognize the need to establish a common language in relation to the classification of surgical complications that allows the different series to be compared^{13,14}. Some authors refer to minor vs. major, early vs. late, or local vs. systemic complications^{17,20}; however, the categorization of these complications should be simple, reproducible, flexible and applicable, regardless of

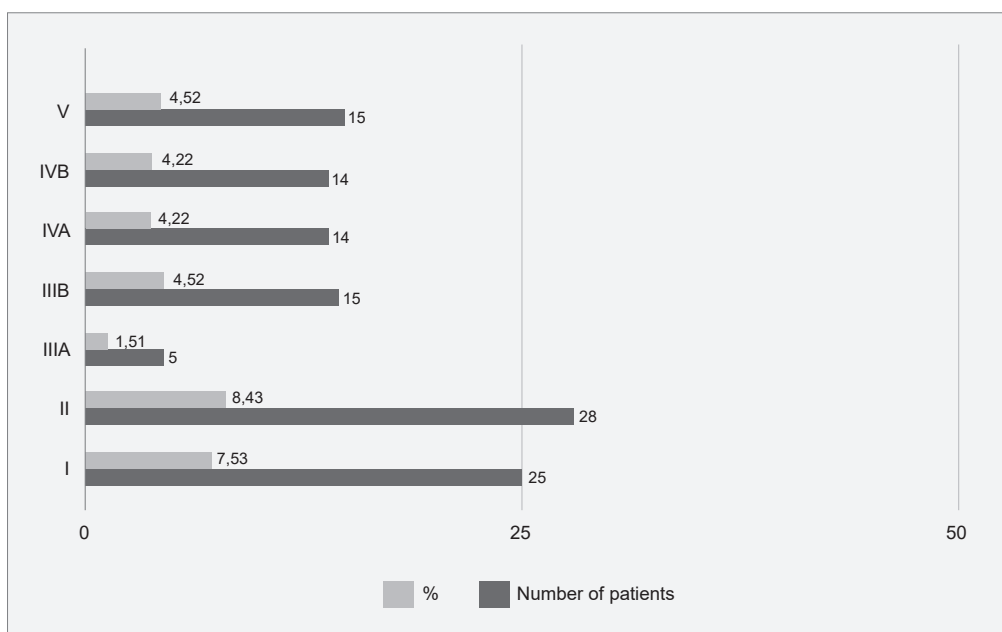
**Figure 2.** Complications according to Clavien-Dindo. Source: Own authors.

Table 3. Cause of mortality in patients undergoing gastrectomy and D2.

Case #	Cause of death	POP day	Sex	Age	ASA	Gastrectomy type	Extended surgery/ organ
1	Acute myocardial infarction	1	M	69	II	Total	Transverse colectomy
2	Esophageal-jejunal anastomosis leak	3	M	66	III	Total	No
3	Esophageal-jejunal anastomosis leak	6	M	54	II	Total	Distal pancreatectomy
4	Bronchial aspiration	6	M	61	II	Total	Nefrectomy
5	Duodenal stump leak	7	F	78	III	Distal	No
6	Acute myocardial infarction	8	F	69	III	Distal	No
7	Peritonitis ileum lesion	10	F	83	II	Total	No
8	Esophageal-jejunal anastomosis leak	12	M	46	III	Total	No
9	Esophageal-jejunal anastomosis leak	12	M	69	II	Total	No
10	Peritonitis	14	M	74	III	Distal	No
11	Postoperative bleeding	16	M	76	II	Distal	No
12	Esophageal-jejunal anastomosis leak	16	F	77	II	Total	Splenectomy
13	Duodenal stump leak	18	M	73	III	Total	No
14	Esophageal-jejunal anastomosis leak	29	M	82	III	Total	Liver resection
15	Hemoperitoneum	30	M	57	II	Total	Adrenalectomy

* POP: post-operative; ASA: American Society of Anesthesiologists; M: male; F: female. Source: Own authors.

Table 4. Risk with statistical p-value according to variables.

Variable	HR	p	CI 95%
Age	1.05	0.02	1 - 1,1
ASA			
I	1		
II	1.95	0	7,55 - 5,03
III-V	1.77	.	.
Sex			
Male	1		
Female	1.40	0.48	0,55 - 3,54
BMI			
< 18,5	1		
18.5-24.9	0.55	0.45	0,12 - 2,59
> 25	0.45	0,35	0,09 - 2,37
Comorbidities			
Yes	1		
No	0.86	0.75	0,34 - 2,19
Tumor size	1.12	0.20	0,94 - 1,33
Location			
Distal	1		
Proximal	1.37	0.52	0,53 - 3,53
Albumin	0.59	0.23	0,26 - 1,38
Type of dissection			
D1	1.00		
D2	0.91	0.86	0,35 - 2,41
Procedure			
Subtotal gastrectomy	1.00		
Total gastrectomía	2.24	0.11	0,83 - 6,05
Multivisceral resection			
Yes	1.00		
No	0.22	0.01	0,08 - 0,64
Surgical time	1.01	0.07	1,00 - 1,01

Source: Own authors.

cultural origin. The Clavien-Dindo classification proposed in 2004²¹ meets these requirements, which is why it has been applied to various types of surgery and more and more articles report it in cases of gastrectomy^{2,4,16,17}.

Measuring the risk of postoperative complications is very important in decision-making in cancer patients. Several authors^{2,6,12} have shown that factors such as age (over 60 years), high BMI, open surgery, total gastrectomy, extended gastrectomy, and higher tumor stage are significantly associated with a higher risk of complications. In the present study, only age greater than 60 years and ASA greater than II were risk factors associated in a statistically significant manner with postoperative complications, probably in relation to the sample size.

Lee et al.⁴ analyzed 881 cases of gastrectomy, with only 1.9% of complications greater than grade IIIA, and identified age over 60 years, open surgery, total and extended gastrectomy, and higher tumor stage as risk factors. In the work of Galata et al.¹², where 1007 patients were included without using the Clavien-Dindo classification, the total percentage of complications was 25.3% and for those classified as major (10.6%), with no statistically significant difference between total and subtotal gastrectomy, negatively impacting overall survival.

The Italian PNE (Piano Nazionale Esiti) project of the National Agency for Regional Health Services reported a 30-day mortality for GC gastrectomy of 6.3%. In centers with low surgical volume, mortality can vary between 10% and 20%, while in those with high volume (more than 100 cases treated per year) it is 3% to 5%¹⁴, correlated with the high surgical volume. with lower mortality²⁰.

Particularly interesting is the work of Papenfuss et al.⁶, with 2580 patients, using the ACS NSQIP protocol (American College of Surgeons National Surgical Quality Improvement Program), where they reported a morbidity of 23.6% and a mortality of 4.1%, and the variables related to more complications were the performance of total gastrectomy and multivisceral resections, this last factor also identified in our series with a higher risk of complications.

Table 5 shows the values of morbidity and mortality in different studies, in comparison with those of the present study. Postoperative complications occur, not only as a consequence of surgical factors, but also due to the condition of the patient and the tumor to be treated, which

is why surgeons need to know the patient prior to surgery. After a gastrectomy with curative intent, the presence or absence of complications is a factor that can influence the patient's prognosis; therefore, the classification of the severity of complications is essential in the analysis of outcomes and surgical results^{20,22}.

This work has limitations because it is retrospective, the simple size, and it collects information from a single hospital center.

Conclusions

From these data and their analysis, we found that several factors derived from the patient (age, gender, nutritional status, comorbidities), the tumor (early, advanced) and the type of treatment (total gastrectomy, subtotal gastrectomy, lymphadenectomy, extended gastrectomy), may be associated with increased risk of complications. In the present study, the morbidity and mortality figures are similar to those reported in the literature; however, only age and ASA classification were associated risk factors with significant statistical value for postoperative complications.

Table 5. Comparison of morbidity and mortality with respect to other representative series.

Author	Year	Number of patients	Morbidity	Mortality	Clavien-Dindo
Cuschieri ⁸	1999		46%	13%	No
Hartgrink ⁹	2004		43%	10%	No
Papenfuss ⁵	2014	2580	23.6%	4.1%	No
Lee ³	2014	881	22.4% ASA > IIIA 1.9%	0.5%	Yes
Rosa ¹⁰	2014	936	25.3%	3.7%	No
Galata ⁷	2019	1107	25.3%	4.7%	No
Baiocchi ¹²	2020	1349	29.8% ASA > IIIA 19%	3.6%	Yes
Martínez ²⁰	2013	69 TG	20.2%	4.3%	No
Selby ¹⁵	2015	238 TG		2.5%	No
Nevo ²	2014	112	ASA > IIIA 14%	1.8%	Yes
Kubota ¹¹	2014	1395 TG, STG, PG	ASA > II 14.8%		Yes
Martin ¹⁹	2016	3678 GC 2316	21.7%	5.2%	No
INC serie actual		332	27.4% 17.4% > IIIA	4.5%	Yes

* TG: total gastrectomy, STG: subtotal gastrectomy, PG: proximal gastrectomy, GC: gastric cancer. Source: Own authors.

Compliance with ethical standards

Informed consent: This study is a retrospective chart review, and as such, there is no need for informed consent. The study was approved by the institution's Research Ethics Committee.

Conflict of interest: none declared by the authors.

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Author's contributions

- Conception and design of the study: Ricardo Oliveros-Wilches, Raúl Eduardo Pinilla-Morales, Diego Andrés Buitrago-Gutiérrez.
- Acquisition of data: Ricardo Oliveros-Wilches, Raúl Eduardo Pinilla-Morales, Elio Fabio Sánchez-Cortés, Diego Andrés Buitrago-Gutiérrez.
- Data analysis and interpretation: Ricardo Oliveros-Wilches, Raúl Eduardo Pinilla-Morales, Helena Facundo-Navia, Ricardo Sánchez-Pedraza, Elio Fabio Sánchez-Cortés, Diego Andrés Buitrago-Gutiérrez.
- Drafting the manuscript: Ricardo Oliveros-Wilches, Raúl Eduardo Pinilla-Morales, Helena Facundo-Navia, Ricardo Sánchez-Pedraza, Diego Buitrago, Elio Fabio Sánchez-Cortés, Diego Andrés Buitrago-Gutiérrez.
- Critical review and final approval: Ricardo Oliveros-Wilches, Raúl Eduardo Pinilla-Morales, Helena Facundo-Navia, Ricardo Sánchez-Pedraza, Elio Fabio Sánchez-Cortés, Diego Andrés Buitrago-Gutiérrez.

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