

# Results of Surgical Treatment of Advanced Gastric Cancer. Case Series with Follow-Up

Resultados del Tratamiento Quirúrgico del Cáncer Gástrico Avanzado.  
Serie de Casos con Seguimiento

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**SUMMARY:** Gastric cancer (CG) is the second leading cause of cancer deaths. The best treatment option for patients with advanced GC (AGC) is still surgery, which involves performing a gastrectomy and D2 lymphadenectomy (D2L). The aim of this study was to determine postoperative morbidity (POM) and 5-year OS in patients resected by AGC without neoadjuvant. Case series with follow-up of patients with AGC undergoing total or subtotal gastrectomies and D2L, consecutively at RedSalud Mayor Temuco Clinic, between 2008 and 2019. The outcome variables were POM and 5-year OS. Other variables of interest were surgical time, number of resected lymph nodes, hospital stay, and recurrence. Descriptive statistics was used, and Kaplan-Meier curves were calculated. In this analysis 38 patients (71.1 % men), with a median age of 65 years, were operated. The most frequent location was subcardial (50.0 %). The most frequent type of resection was total gastrectomy (60.5 %). The median of surgical time, number of resected lymph nodes and hospital stay; was 190 min, 32 and 6 days respectively. MPO was 18.4 %. With a median follow-up of 28 months, a recurrence of 44.7 % was verified; and 5-year OS for stages IIIA, IIIB and IV were 53.3 %, 46.1 % and 20.0 % respectively ( $p=0,007$ ). The results achieved, in terms of POM and OS series were similar to national and international series in which neoadjuvant therapies have not been applied.

**KEY WORDS:** "Stomach Neoplasms"[Mesh] AND "Stomach Neoplasms/surgery"[Mesh]; "Lymph Node Excision"[Mesh]; Gastric Cancers; Surgery, Lymphadenectomy.

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## INTRODUCTION

Gastric cancer (GC) causes 8.2 % of oncological deaths (787,200) and 5.7 % of new cases (969,000) worldwide; being more frequent in men than women (Ferlay *et al.*, 2019). After lung cancer, it is the second leading cause of cancer death, over 780,000 deaths per year (Bray *et al.*, 2018). The areas with the highest incidence rates (> 40 / 100,000) are East Asia and the Andean regions of South America (Global Burden of Disease Cancer Collaboration *et al.*, 2017).

Despite special protocols for its treatment (Macdonald *et al.*, 2001); GC remains one of the leading causes of cancer death in Chile; with a mortality prediction rate of 17.5 x 100,000 inhabitants and 22.5 x 100,000 in men (Carioli *et al.*, 2019); constituting one of the most frequent malignant tumors in men. In La Araucanía region, the overall mortality rate reaches 24.8 x 105 inhabitants and in men 33.7 x 105 (Tapia *et al.*, 2010). The adjusted

rate was estimated at 38.9 and 27.4 x 100,000 inhabitants for men and women respectively for the 1990-2010 period; with a marked decline in the last two decades (Itriago *et al.*, 2013). Despite some stabilization in the general mortality rate from GC, the probability of dying from GC in Chile is approximately 3 %, which makes this disease a public health problem (Ministerio de Salud, 2016).

In Chile, more than 80 % of cases are advanced GC (AGC). These are lesions that infiltrate beyond the submucosa layer. Therefore, a series of strategies have been developed to optimize diagnostic and therapeutic processes (Calderón *et al.*, 2007; Tapia *et al.*, 2011; Ministerio de Salud, 2016).

Surgery remains the mainstay in the treatment of AGC, because, as well as allowing tumor excision, allow to determine a better staging of the disease; In addition, it

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may be applied as cleaning surgery, for eventual application of adjuvant therapies (Cornejo & Portanova, 2006; Díaz de Liaño *et al.*, 2008; Ruiz *et al.*, 2009; Degiuli *et al.*, 2016).

The aim of this study was to determine postoperative morbidity (POM) and 5-year overall survival (OS) in patients resected by AGC without neoadjuvant.

## MATERIAL AND METHOD

The report of this study was written based on the MIInCir Declaration for the reporting of descriptive observational studies (Manterola & Astudillo, 2013).

**Study design:** Case series with follow-up.

**Setting:** The study was conducted at Clínica RedSalud Mayor Temuco. The recruitment period was between January 2008 and December 2019 (12 years). The minimum follow-up was 7 months.

**Participants:** All patients with AGC consecutively undergoing gastrectomy with extended lymph node dissection (D2), by the first author (CM), were included. Cases of exploratory laparotomy due to disseminated disease, palliative surgeries and those who received additional treatments in addition to surgery were excluded.

**Sample size:** Since this is an observational and descriptive study, no sample size was estimated. All patients with AGC undergoing D2-gastrectomy in the period and institution indicated were considered.

**Variables:** The outcome variables were OS and POM. The latter measured up to 30 days after surgery; it was considered dichotomous (present or absent); severity was estimated applying the Clavien proposal (Clavien *et al.*, 2009). Other variables of interest were age, sex, tumor location, stage of the disease (American Joint Committee on Cancer & American College of Surgeons, 2018), type of surgery, operative mortality and recurrence.

**Follow-up protocol:** After hospital discharge, all patients were followed up with strict controls at least at months 1, 2, 3 and 6; and after that once a year. During the controls, a clinical evaluation, general laboratory tests and computed tomography of the abdomen and pelvis were realized. In addition, information on death certificates obtained from the Civil Registry and Identification was used, when necessary.

**Statistical methods:** Data collection was carried out and analyzed with the Stata 11.0 / SE® program. Descriptive statistics was used, applying measures of central tendency and dispersion (averages, standard deviations and extreme values). The SV was calculated applying the Kaplan-Meier method.

**Biases:** These were reduced with a masked data collection and a complete follow-up of the patients that make up this series for at least 6 months (the last patient recruited).

**Ethics:** Ethical guidelines for research defined by the Declaration of Helsinki (World Medical Association, 2013), were observed. All patients gave their informed consent in writing.

## RESULTS

During the study period, 38 patients were operated for AGC, with a median age of 65 (34-87) years, 71.1 % of which were male. 78.9 % of the series had some type of comorbidity (Tables I and II).

Table I. Distribution of clinical variables in patients under study. (N = 38)

Variable	N° cases	%
Sex		
Male	27	71.1
Female	11	28.9
Comorbidity *		
None	8	21.1
AHT	14	36.8
II-DM	9	23.7
AHT + II-DM	6	15.8
Cholelithiasis	7	18.4
Abdominal hernia	3	7.9
TNM stage		
IIIA	15	39.5
IIIB	13	34.2
IV	10	26.3
Lauren type		
Diffuse	21	55.3
Intestinal	17	44.7
Tumor location		
Subcardial	19	50.0
Body	9	23.7
Antrum	10	26.3
Type of surgery		
D2-Total gastrectomy	23	60.5
D2-Subtotal gastrectomy	15	39.5

\* : Some patients had more than one comorbidity. AHT: Arterial hypertension. II-DM: Type II diabetes mellitus.

Table II. Distribution of clinical variables in patients under study. (N = 38)

Variable	Median	Minimum - Maximum
Age (years)	65	34 - 87
BMI (kg/m <sup>2</sup> )	25,5	17 - 43
Symptom time (months)	9	2 - 12
Surgical time (min)	190	90 - 225
Resected lymph nodes (N°)	32	25 - 45
Hospital stay (days)	6	4 - 9
Follow-up (months)	28	12 - 132

BMI: Body mass index

The most frequent location of the lesions was subcardial (50.0 %). All cases were stage III or IV according to TNM classification (mainly IIIA, 39.5 %); and 55.3 % were Lauren's diffuse type. With 100 % resectability of the

series, the most common type of resection was D2-total gastrectomy (60.5 %) (Table I, Figs. 1 and 2).

The medians of the surgical time, number of resected lymph nodes, and hospital stay were 190 min, 32 y 6 days respectively (Table II).

POM was 18.4 % (7 cases), all of which were Clavien & Dindo type I or II (Table III). There was no operative mortality.

With a median follow-up of 28 months, a recurrence of 44.7 % was verified (Table III). On the other hand, the 5-year OS for stages IIIA, IIIB and IV was 53.3 %, 46.1 % and 20.0 % (p=0,007) respectively (Figs. 3 and 4).

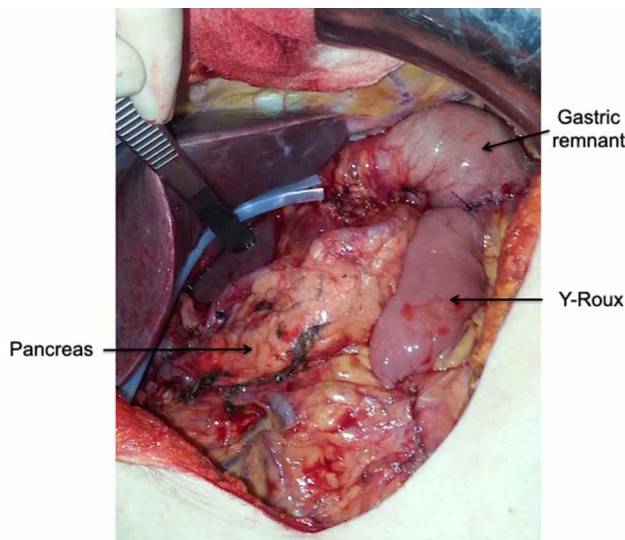


Fig. 1. D2-subtotal gastrectomy. The gastric remnant, the Y-Roux gastrojejunal reconstruction, and pancreas can be observed.

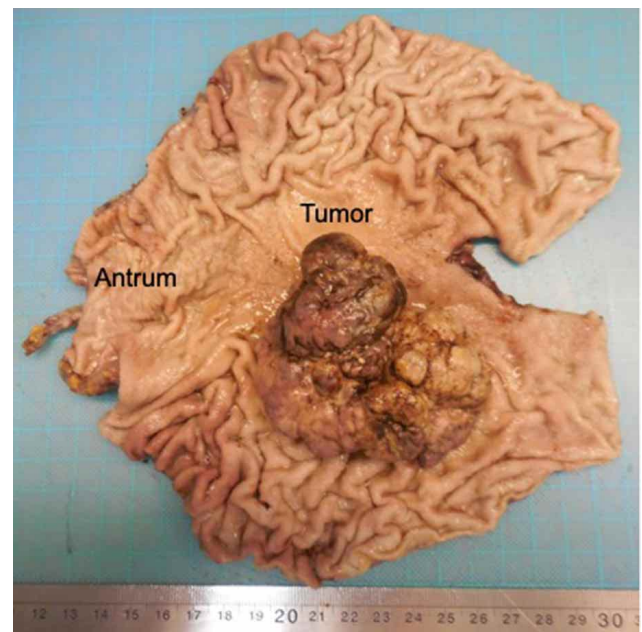


Fig. 2. Surgical specimen of subtotal gastrectomy for AGC. An extensive and proliferative tumor that involves a large part of the gastric body.

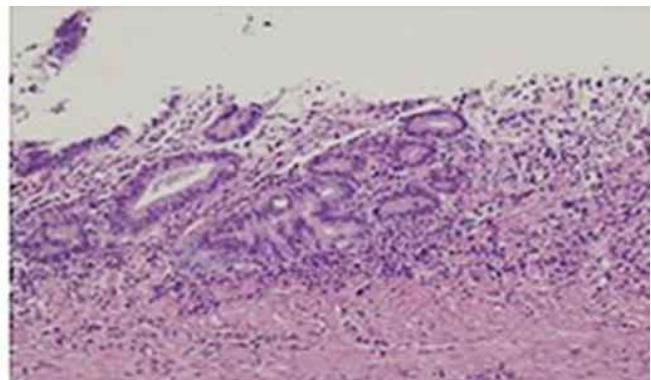
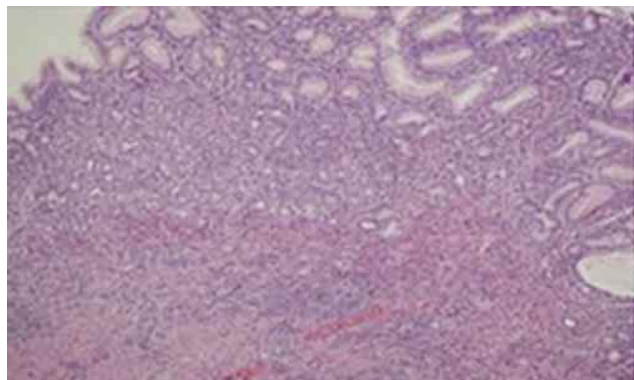


Fig. 3. Microphotographs of a subcardial GC, adenocarcinoma type, well-differentiated tubular.

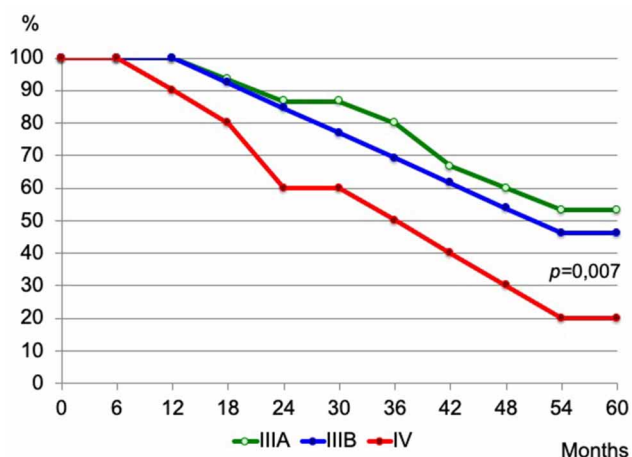


Fig. 4. Actuarial survival curves of the series by stages (IIIA, IIIB and IV).

Table III. Postoperative morbidity in patients under study. (N = 38)

Variable	N° cases	%
POM		
Present	7	18.4
Absent	31	81.6
POM etiology		
Seroma	4	10.5
Surgical site infection	2	5.3
Intra-abdominal collection	1	2.6
POM according Clavien		
I	5	13.1
II	2	5.3
Recurrence		
Yes	17	44.7
No	21	55.3

POM: Postoperative morbidity

## DISCUSSION

**Novelty of the proposal:** The novelty of the proposal is that it is a single-center and regional casuistry of patients of a private health institution; with comparable results with different series from national and international referral centers (Cornejo & Portanova; Díaz de Liaño *et al.*, 2008, 2009; Ruiz *et al.*; Tapia *et al.*, 2010, 2011; Valenti *et al.*, 2011; de Steur *et al.*, 2013; Chen *et al.*, 2016; Degiuli *et al.*; Randle *et al.*, 2016; Tóth *et al.*, 2016; Yang *et al.*, 2016; Bhandare *et al.*, 2017; Uslu *et al.*, 2018; Wang *et al.*, 2018).

Comment on observed results: Surgery is essential in the treatment of GC and is considered curative when all macroscopic disease is removed, followed by the histological demonstration of the absence of neoplasia on the margins of the surgical specimen. Thus, R0 resection will be considered when in-block excision of the tumor with disease-free histological margins was performed (Bhandare *et al.*; Uslu *et al.*; Wang *et al.*).

Non-Communicable Disease is a denominator used by WHO for oncological diseases (Porta, 2014). It represents a public health problem and will have a sustained increase over time. So, it is projected that by 2030, they will account for almost 70 % of the total deaths in the world (WHO, 2004).

Thus, GC is responsible for the loss of 15 million years of healthy life (DALYs); either due to premature death or disability (Salomon, 2010).

In relation to the burden of cancer disease, oncological diseases ranked 7th in importance of DALYs in 2004; which translated into an immense 221,529 years of

life loss, affecting 6 % of the total DALYs of the population, ranking first in men (followed by prostate and lung cancer), and fourth in women (after cancers of the breast, gallbladder, and uterine cervix) (Ministerio de Salud, 2008).

The 5-year OS observed in this study, in the 3 stages measured, is similar to that reported in other series in which only patients with AGC treated with protocols that did not consider neoadjuvant were included (Al-Moundhri *et al.*, 2006; Alici *et al.*, 2006; Garrido *et al.*, 2007; Bhandare *et al.*; Uslu *et al.*; Wang *et al.*). Applying the surgery and adjuvant therapy modality is due to the strong evidence regarding the inappropriate internal and external validity of the Macdonald protocol (Manterola *et al.*, 2006), used as a national protocol for treating GC in our country (Macdonald *et al.*); that it has only undergone cosmetic modifications by Ministerio de Salud in its application in the last 15 years.

**Limitations of the study:** Among the limitations, it should be noted that this is a small series, in which all patients underwent surgery by the same surgeon. On the other hand, in the last cases, the follow-up is brief.

## CONCLUSIONS

By way of conclusion, it can be stated that the results verified in this series, in terms of POM, mortality and 5-year OS in patients with AGC, are comparable to national and international series in which neoadjuvant therapies have not been applied.

**MANTEROLA, C. & CLAROS, N.** Resultados del tratamiento quirúrgico del cáncer gástrico avanzado. Serie de casos con seguimiento. *Int. J. Morphol.*, 38(5):1479-1484, 2020.

**RESUMEN:** El cáncer gástrico (CG) es la segunda causa de muerte por cáncer. La mejor opción terapéutica para pacientes con CG avanzado (CGA), sigue siendo la cirugía, que supone la realización de gastrectomía asociada a linfadenectomía D2 (LD2). El objetivo de este estudio fue determinar morbilidad postoperatoria (MPO) y supervivencia (SV) en pacientes resecaados por CGA sin neoadyuvancia. Serie de casos con seguimiento, de pacientes con CGA sometidos a gastrectomía total o subtotal con LD2, de forma consecutiva, en Clínica RedSalud Mayor Temuco, entre 2008 y 2019. Las variables resultado fueron MPO y SV actuarial global (SVAG) a 5 años. Otras variables de interés fueron: tiempo quirúrgico, número de linfonodos resecaados, estancia hospitalaria y recurrencia. Se utilizó estadística descriptiva, con medidas de tendencia central y dispersión; y análisis de SV con curvas de Kaplan Meier. Se intervinieron 38 pacientes (71,1 % hombres), con una mediana de edad de 65 años. La localización más frecuente fue subcardial (50,0 %); el tipo de resección más frecuente fue gastrectomía total (60,5 %). Las medianas del tiempo quirúrgico, del número de linfonodos resecaados y de estancia hospitalaria; fue 190 min, 32 y 6 días respectivamente. La MPO fue 18,4 %. Con una mediana de seguimiento de 28 meses, se verificó recurrencia de 44,7 %; y SVAG a 5 años para estadios IIIA, IIIB y IV de 53,3 %, 46,1 % y 20,0 % respectivamente ( $p=0,007$ ). Los resultados obtenidos, en términos de MPO, mortalidad y SVAG, fueron similares a series de centros de derivación nacionales e internacionales en los que no se ha aplicado terapias neoadyuvantes.

**PALABRAS CLAVE:** Cáncer gástrico; Cirugía; Linfadenectomía.

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