

Results of Surgical Treatment of Uncomplicated Colon Cancer. Case Series with Follow-Up

Resultados del Tratamiento Quirúrgico del Cáncer de Colon no Complicado. Serie de Casos con Seguimiento

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SUMMARY: The standard treatment of colonic cancer (CC) continues to be the radical resection of the intestinal segment compromised with free margins, associated or not with adjuvant therapies. The aim of this study was to determine postoperative morbidity (POM) and 5-year overall survival (OS) in patients with uncomplicated colon cancer surgically treated. Retrospective case series of patients with uncomplicated CC undergoing colectomy and lymphadenectomy, consecutively, at Clínica Red Salud Mayor Temuco, between 2007 and 2019. The outcomes variable were POM and 5-years OS. Other variables of interest were surgical time, number of resected lymph nodes, hospital stay and recurrence. Descriptive statistics was used (measures of central tendency and dispersion), and OS analysis was applying Kaplan Meier curves. In this study, 52 patients (53.8 % men) were intervened, with a median age of 68 years. The most frequent localization and stages were right colon (42.3 %); IIIA and IIIB respectively (78.9 %). Median surgical time, number of resected lymph nodes and hospital stay were 98 min, 34 and 4.5 days respectively. POM was 17.3 % (9 cases). With a median follow-up of 58 months, a recurrence of 19.2 % was verified, and the 5-year OS for stages IIA, IIIA, IIIB and IVA was 83.3 %, 73.6 %, 68.2 % and 40.0 % respectively. The results, in terms of POM, mortality and 5-year OS, were similar to national and international series.

KEY WORDS: Colonic Neoplasms; Colonic Neoplasms/surgery; Lymph Node Excision; Sigmoid Neoplasms & Sigmoid Neoplasms/surgery.

INTRODUCTION

About 1.8 million new cases of colorectal cancer and 881,000 deaths were estimated to occur worldwide in 2018 (Bray *et al.*, 2018), and about 12 million deaths per year, from this cause, will occur in 2030 (Itriago *et al.*, 2013). The highest incidence rates are found in Australia, New Zealand, Europe and the United States; and the smallest in Western Africa and South-Central Asia (Ryerson *et al.*, 2016). For example, in the USA, colorectal cancer represents the 4th most common cancer and the 2nd leading cause of cancer-related deaths (Siegel *et al.*, 2019).

In Chile, the adjusted mortality rate for colon and rectal cancer in 2010, for women and men was 7.6 and 9.1 x 100,000 inhabitants respectively; with an increase of 2 and 4 percentage points with respect to a similar measurement in 1990 (Itriago *et al.*).

Colon cancer (CC) standard treatment continues to be the resection of compromised colon segment with free margins (at least 5 cm above and below the tumor) and regional lymphadenectomy (by open or laparoscopic approach). These strategies could be associated or not, to complementary therapies (Athanasίου *et al.*, 2017; Mungo *et al.*, 2017).

Overall survival (OS) at 10 years in uncomplicated CC, in stages I-III, operated with curative intention, ranges from 70 % to 80 % (Bannura *et al.*, 2010; Qin *et al.*, 2017); results that are better for most cancers of the digestive system. Therefore, postoperative morbidity (POM) and mortality of this type of patients must be rigorously controlled.

The aim of this study was to determine postoperative morbidity (POM) and 5-year overall survival (OS) in patients with uncomplicated colon cancer surgically treated.

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MATERIAL AND METHOD

The report of this study was written based on the MInCir Declaration for the reporting of descriptive observational studies (Manterola & Otzen, 2017).

Study design: Case series with follow-up.

Setting: The study was conducted at Clínica Red Salud Mayor Temuco. The recruitment period was between January 2007 and December 2019 (13 years). The minimum follow-up was 12 months.

Participants: Patients operated for uncomplicated CC stages IIIa and IIIb, undergoing colectomy with lymph nodal dissection with oncological criteria; consecutively; in the period and institution indicated above, by the first author (CM). Palliative surgery cases and those who received neoadjuvant treatment were excluded.

Sample size: Since this is an observational and descriptive study, no sample size was estimated.

Variables: The outcome variables were overall survival (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-Dindo 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; Liu *et al.*, 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). OS was calculated applying the Kaplan-Meier method and the comparison of curves was studied applying the log-rank test.

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 (Helsinki Statement, 2013), were observed. All patients gave their informed consent in writing.

RESULTS

During the study period, 52 patients were operated for uncomplicated CC, with a median age of 68 (44-92) years, 53.8 % were male. 88.5 % of the series had some type of comorbidity (Table I).

Table I. Distribution of clinical variables in patients under study (N = 52)

Variable	N° cases	%
Sex		
Male	28	53.8
Female	24	46.2
Comorbidity		
None	6	11.5
AHT	26	50.0
II-DM	12	23.1
AHT + II-DM	8	15.4
StageAMS		
IIA	6	11.5
IIIA	19	36.6
IIIB	22	42.3
IVA	5	9.6
Tumoral location		
Right colon	22	42.3
Transverse colon	4	7.7
Left colon	12	23.1
Sigmoid colon	14	26.9
Type of colectomy		
Right colectomy	22	42.3
Rightextended colectomy	4	7.7
Left colectomy	12	23.1
Sigmoidectomy	14	26.9

AHT:Arterial hypertension. II-DM:Type II diabetes mellitus. AMS: American Cancer Society.

The most frequent location of the lesions was: right colon (22 cases, 42.3 %) and sigmoid (14 cases, 26.9 %). The most frequent stage was IIIA and IIIB (78.9 %). With 100 % resectability of the series, it was the right colectomy, the most frequently used technique (Figs. 1 and 2, Table I).

The medians of the surgical time, number of resected lymph nodes, and hospital stay were 98 min, 34 resected lymph nodes and 4.5 days respectively (Table II).

POM was 17.3 % (9 cases), most of which were Clavien & Dindo Type I and II (5 cases, 55.6 %); 3 cases of

anastomotic dehiscence stand out (5.8 %), all of which required reoperation (Table III). There was no operative mortality.

With a median follow-up of 58 months, a recurrence of 19.2 % was verified (Table III). On the other hand, the 5-year OS for stages IIA, IIIA, IIIB and IVA was 83.3 %, 73.6 %, 68.2 % and 40 % respectively ($p=0,001$ at months 30, 48, 54 and 60, between stage IVa and the rest of stages) (Fig. 3).

Table II. Distribution of clinical variables in patients under study (N = 52)

Variable	Median	Minimum - Maximum
Age (years)	68	44 - 92
BMI (kg/m ²)	25,2	21 - 41
Symptom time (months)	9	2 - 14
Surgical time (min)	98	60 - 130
Preoperative CEA (ng/ml)	112	3 - 540
Resected lymph nodes (N°)	34	25 - 45
Hospital stay (days)	4.5	3 - 7
Follow-up (months)	58	7 - 144

BMI: Body mass index. CEA: Carcinoembryonic antigen.

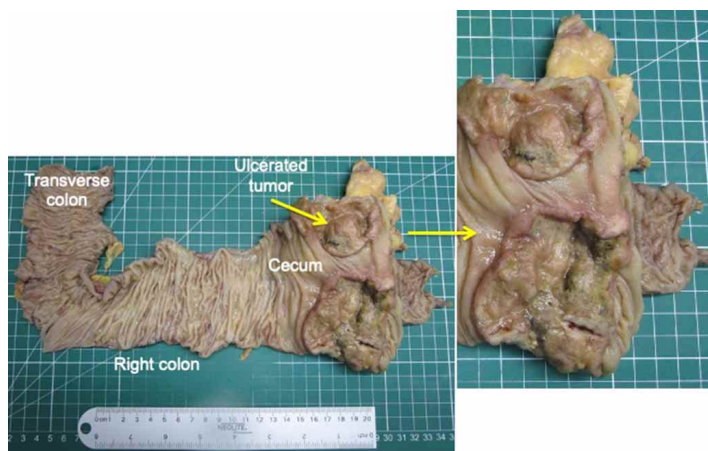


Fig. 1. Surgical specimen fixed and extended, corresponding to a patient with cancer of the cecum, 11 cm in diameter greater; discoidal, ulcerated; Infiltrating to subserous pericolonic fibroadipose tissue, with negative proximal, distal and mesocolonic edges (distance to the tumor: 6; 26.5 and 9 cm respectively). Positive lymph nodes 1 out of 43 examined.

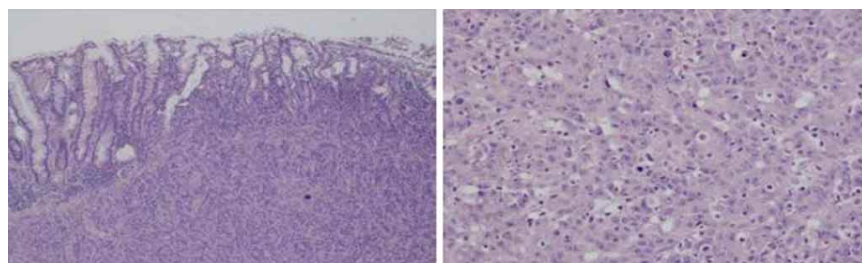


Fig. 2. Histological sections of a patient with right colon cancer. Histological type: poorly differentiated tubular adenocarcinoma; high-grade, with positive lymphovascular invasion.

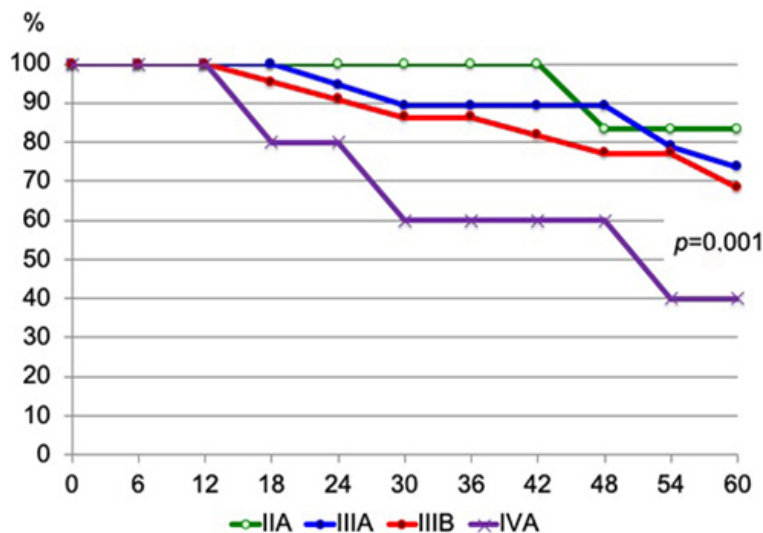


Fig. 3. Actuarial survival curve of the series (total and by stages).

Table III. Postoperative morbidity in patients under study (N = 52).

Variable	N° cases	%
POM		
Present	9	17.3
Absent	43	82.7
POM etiology		
Anastomotic leakage	3	5.8
Surgical site infection	3	5.8
Respiratory infection	2	3.8
Left ureteral injury *	1	1.9
POM according Clavien		
I	3	5.8
II	2	3.8
IIIb	4	7.7
Recurrence		
Yes	10	19.2
No	42	80.8

POM: Postoperative morbidity* : The ureteral injury was repaired in the course of the same intervention.

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 (Bannura *et al.*; Renouf *et al.*, 2013; Qin *et al.*). Generating evidence regarding results of CC surgery in a regional and private health center is relevant, since most of the series in our country correspond to public hospitals of the metropolitan area.

Comment on observed results: Surgery is essential in the treatment of CC 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 (Liu *et al.*).

We observed that location of the primary lesions was mainly in the right colon (42.3 %). This is similar to previous reports (Bannura *et al.*; Tapia *et al.*, 2010; Huang *et al.*, 2016).

Regarding surgical techniques for CC, there is no controversy. For example, in tumors of the transverse colon or hepatic angle the tendency is to perform extended right hemicolectomies. Special attention must be fixed on the surgical margins, since there is evidence in terms that the existence of a tumor in these margins is associated with up to 85 % of recurrences (Merkel *et al.*, 2016).

Iatrogenic perforation of the tumor during surgery is a significant factor because it conditions an increase in local recurrence (Maurer *et al.*, 2017). This fact is independent of the stage and the degree of tumor fixation (Tokodai *et al.*, 2016). We do not see this complication in our patients.

Although reports of surgical mortality for uncomplicated CC fluctuate between 1.5 % and 9 % (Kwaan *et al.*, 2013; Healy *et al.*, 2016; Mungo *et al.*), postoperative mortality was not recorded in this series.

POM of our series (17.3 %), is similar to other (Bannura *et al.*; Marinello *et al.*, 2016). On the other hand, the reports regarding anastomotic filtration in elective colectomies, fluctuate between 6 % and 9 % (Ruggiero *et al.*, 2011; Marinello *et al.*; García-Granero *et al.*, 2017). This complication was verified in 3 cases (5.8 %).

The local recurrence was verified in 19.2 % of cases, lower than reported after curative resection, which can reach

31 % (Alnimer *et al.*, 2017). There is evidence that this is associated with vascular or lymphatic permeation to a number of resected lymph nodes less than 12, as well as the type of resection (R1 and R2) (Kojo *et al.*, 2017).

In relation to 5-year OS, our data (83.3 %, 73.6 %, 68.2 % and 40 % for stages IIA, IIIA, IIIB and IVA respectively), can be considered very suitable compared to what has already been published regarding uncomplicated CC without neoadjuvant treatments (Bannura *et al.*; Perdawid *et al.*, 2012; Kwaan *et al.*; Renouf *et al.*). This may be due to the number of lymph nodes resected, because, there is evidence supporting that the resection of more than 12 lymph nodes, are associated with better survival, especially in stages IIA and IIIA; and in in right-sided CC (Huang *et al.*; Yang *et al.*, 2018). Both characteristics were present in a many of our patients.

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 uncomplicated CC, are comparable to national and international series in which neoadjuvant therapies have not been applied.

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RESUMEN: El tratamiento estándar del cáncer de colon (CC), continua siendo la resección radical del segmento intestinal comprometido con márgenes libres (al menos 5 cm por encima y debajo del tumor), pudiendo asociarse o no a terapias complementarias. El objetivo de este estudio fue determinar morbilidad postoperatoria (MPO) y supervivencia actuarial global (SVAG) a 5 años en pacientes resecados por CC no complicado. Serie de casos con seguimiento, de pacientes con CC no complicado, sometidos a colectomía subtotal y linfadenectomía, de forma consecutiva, en Clínica Red Salud Mayor Temuco, entre 2007 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 resecados, 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 52 pacientes (53,8 % hombres), con una mediana de edad de 68 años. La localización y estadios más frecuentes fueron colon derecho (42,3 %); IIIA y IIIB respectivamente (78,9 %). La resecabilidad de la serie fue 100 %. La medianas del tiempo quirúrgico, del número

de linfonodos resecaados y de estancia hospitalaria; fueron de 98 min, 34 y 4.5 días respectivamente. La MPO fue 17,3 % (9 casos). Con una mediana de seguimiento de 58 meses, se verificó una recurrencia de 19,2 %; y una SVAG a 5 años para los estadios IIA, IIIA, IIIB y IVA; de 83,3 %; 73,6 %; 68,2 % y 40,0 % respectivamente. Los resultados obtenidos, en términos de MPO, mortalidad y SVAG a 5 años, fueron similares a series de nacionales e internacionales.

PALABRAS CLAVE: Cáncer de colon; Cáncer de sigmoides; Linfadenectomía.

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