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Surgical Management of Malignant Intestinal Obstruction: Outcome and Prognostic Factors

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Rezumat

Managementul chirurgical al ocluziilor intestinale de cauză malignă: rezultate și factori de prognostic

Context: Ocluzia intestinală de cauză malignă este o complicație frecventă la pacienții cu cancer în stadii avansate. Prognosticul este slab, cu o rată medie de supraviețuire mai mică de 3 luni. Tratamentul clinic, procedurile endoscopice sau chirurgicale sunt opțiuni pentru managementul obstrucției intestinale maligne. Nu există o strategie de management general acceptată.
Obiective: Evaluarea factorilor de prognostic ai pacienților cu obstrucție intestinală malignă care au fost supuşi unui tratament chirurgical.
Metode: A fost efectuată o analiză retrospectivă incluzând pacienții unei singure instituții medicale, cu diagnostic de obstrucție intestinală malignă. Au fost evaluate datele demografice, perioada de internare, complicațiile postoperatorii şi supraviețuirea globală. Regresia logistică a fost utilizată pentru evaluarea factorilor prognostici asociați.
Rezultate: Două sute treizeci şi trei de intervenții chirurgicale au fost efectuate datorită suspiciunii de obstrucție intestinală malignă pe o perioadă de şapte ani. Acest diagnostic a fost confirmat în cazul a 210 intervenții chirurgicale (90,1%). Principalele cauze ale obstrucției maligne au fost cancerul colorectal (49,5%) şi cancerul ginecologic (21,9%). Rata complicațiilor severe a fost de 11,42%. Rata mortalității intraspitaliceşti a fost de 40,95% (interval de încredere 95%: 34,16-47,74%). Deficiența funcțională, ureea serică crescută şi nivelurile scăzute de albumină au fost asociate cu o rată mai mare a mortalității.

Concluzie: Obstrucția intestinală malignă implică prognostic slab, cu o rată ridicată a mortalității intraspitaliceşti şi complicații postoperatorii severe. Decizia privind gestionarea obstrucției intestinale maligne trebuie să fie multimodală şi individualizată, în funcție de factorii de prognostic individuali.

Cuvinte cheie: obstrucție intestinală, ascită, neoplasme peritoneale, îngrijiri paliative

Abstract

Background: Malignant intestinal obstruction is a frequent complication in advanced stages cancer patients. The prognosis is poor, with mean survival rate beneath 3 months. Clinical treatment, endoscopic or surgical procedures are options for malignant intestinal obstruction management. There is no generally accepted management strategy.

Objectives: To evaluate prognostic factors of patients with malignant intestinal obstruction who underwent surgical treatment.

Methods: A retrospective analysis was performed including patients of a single institution with diagnosis of malignant intestinal obstruction. Demographic data, in-hospital stay, postoperative complications, and overall survival were assessed. Logistic regression was used to evaluate associated prognostic factors.

Results: Two hundred thirty-three surgeries were performed due to suspicion for malignant intestinal obstruction over a seven-year period. This diagnosis was confirmed in 210 operations (90.1%). The main causes of malignant obstruction were colorectal (49.5%) and gynecological cancer (21.9%). The rate of severe complications was 11.42%. In-hospital mortality rate was 40.95% (CI 95%: 34.16-47.74%). Functional status impairment,high serum urea, and low albumin levels were associated to higher mortality rate.

Conclusion: Malignant intestinal obstruction implies poor prognosis, with high in-hospital mortality rate and severe postoperative complications. The decision regarding management of malignant intestinal obstruction must be multimodal and individualized, according to individual prognostic factors.

Key words: intestinal obstruction, ascitic fluid, peritoneal neoplasms, palliative care

Introduction

Malignant intestinal obstruction (MIO) is a common complication in advanced stages cancer patients. Currently, MIO is defined as clinical evidence of intestinal obstruction distal to Treitz ligament, with the presence of primary intra-abdominal neoplasm or extra-abdominal cancer with peritonealdissemination (1). The most frequent intra-abdominal neoplasms associated to MIO are colorectal and ovarian cancers (2). Thereported prevalence is 24% in advanced colorectal cancer and 42% in advanced ovarian cancers (3, 4). Breast cancer and melanoma are the most frequent extra-abdominal cancers associated with MIO (5).

Obstruction can be caused by several reasons including: extrinsic compression, with peritoneal implants compressing bowel loops; mural invasion with muscular intestinal wall spread can lead to impairment of motility; mesenteric or nervous plexus invasion can also lead to functional motility disorders (6).

The most common symptoms are nausea (100% of the cases), vomiting (87-100% of the cases), abdominal pain (72-80%), abdominal distension (56-90%) and no flatus or stool elimination in the last 72 hours (85-93%) (7).

MIO prognosis is usually poor, regardless of

the chosen therapeutic strategy. The mean survival rate is around 3 months (8), and the mortality is 80% higher compared to benign intestinal obstruction (9).

MIO management is multimodal. Clinical initial management is based on fasting, parental hydration, nasogastric decompression, symptomatic drugs, corticoids, and antisecretory drugs (7). Management can also be performed with palliative chemotherapy; or patients can be treated by endoscopic stents and surgical procedures. Choosing the best management strategy is a great challenge, since patients with MIO usually have poor oncologic prognosis and are frail and functionally impaired (8).

Surgical intervention is generally indicated only after clinical management failure, or worsening clinical condition, and aims to reestablish intestinal transit. Nonetheless, surgical treatment is the modality with the best results for intestinal deobstruction (10).

Thus, this study aimed to perform a descriptive analysis of patients with MIO who underwent surgical intervention, and to analyze prognostic factors associated with MIO.

Methods

Patients

A retrospective analysis of patients submitted to surgical intervention due to MIO suspicion was performed in a single Brazilian institution, between 2009 and 2016.

Clinical and demographic data were extracted and assessed. Karnofsky Performance Status (KPS), laboratory studies, in-hospital stay, overall survival, postoperative complications, graded by Clavien-Dindo scale (11), were also analyzed.

Statistical Analysis

Quantitative variables were assessed by means and standard deviation (SD). Qualitative variables were assessed by frequency and percentage. Survival analysis was performed by Kaplan-Meier curves and log-rank test. Odds Ratio and logistic regression evaluated outcomes. The significance level adopted was 0.05. Software SPSS 22.0 (Chicago, IL) was used for statistical analysis.

Results

In the period 2009-2016, 1,953 exploratory laparotomies were performed, of which 233 were performed due to suspected MIO (11.9%). In 210 surgeries, suspected MIO was confirmed after surgery (90.1%), and the remaining cases presented with obstruction of benign intra-abdominal origin.

The main primary neoplasm associated with MIO was colorectal (49.5%),followed by gynecological (21.9%), as shown in *Fig. 1.*

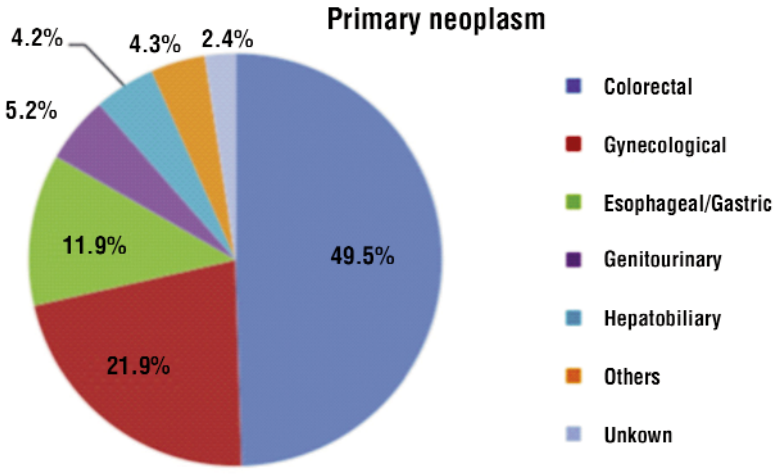

Figure 1. Chart of the primary neoplasm of patients with malignant intestinal obstruction. Colorectal and gynecological cancers are the most common causes of malignant obstruction

The postoperative in-hospital mortality rate was 40.95% (CI 95%:34.16-47.74%). Of those patients that were discharged, the 30-day mortality rate was 21.3% (CI 95%: 5.7-17%). Patients with benign obstruction had a postoperative in-hospital mortality of 13.1% (CI 95%:3.8-22.4%). Of those that were discharged, the 30-day mortality rate was null.

The 360-day overall survival in patients with malignant obstruction was 16.4%. In patients with benign obstruction, this rate was 62% and differences between the survival curves were statistically significant (p<0.001). The overall survival curvescan be seen in *Fig. 2*.

The patients' characteristics with malignant obstruction can be seen in *Table 1*. The mean follow-up was 17.5 months (SD 16,05).

At the time of MIO diagnosis, 21.9% had pulmonary metastasis and 29% had liver metastasis.At this point, most patients had previous history of any other treatment for cancer: 86.7% had previous history of surgery, 83.8% was previously submitted to systemic chemotherapy and 22.8% was previously submitted to radiotherapy.

The anatomical obstruction position was in small bowel in 77.6%, and the remaining colon was affected. Therefore, the most used tactical surgery approach was intestinal bypass (20.48%), enterectomy (18.57%), and loop ileostomy (17.62%). No anastomosis was performed in most of the cases (55.70%). Non-therapeutic laparotomy occurred in 14.3% of the cases, generally due to high level of intra-abdominal adhesions, with the aspect of "frozen abdomen". See *Table 2*.

The mean length of clinical management

Table 1. Characteristics of patients with malignant intestinal obstruction submitted to surgery

Number of patients (N)	210
Gender (F/M)	1.61
Age (years)	56.57 (SD 13,96)
BMI (k/m2)	22.46 (SD 4,55)
KPS	80.73 (SD 15,02)
Metastasis	
Lung	46 (21.9%)
Liver	61 (29%)
Previous treatment	
Surgery	182 (86.7%)
Chemotherapy	176 (83.8%)
Radiotherapy	48 (22.8%)

BMI: Body mass index; KPS: Karnofsky Performance Status; SD: Standard Deviation

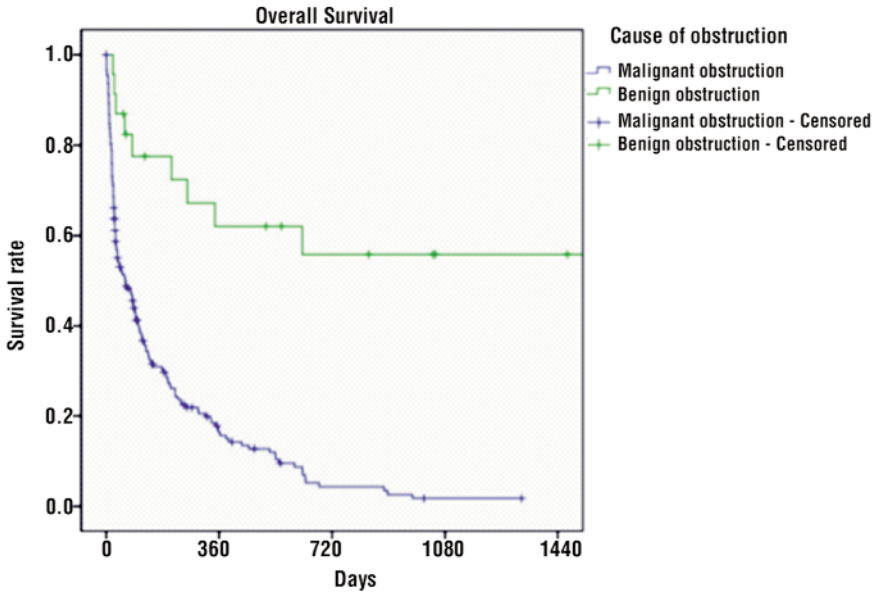

Figure 2. Overall survival of patients submitted to surgery for suspected malignant intestinal obstruction. The confirmed malignant cases showed a survival rate lower than cases with benign conditions

Table 2. Surgical techniques utilized for the management of malignant intestinal obstruction

Surgical approach	
Intestinal bypass	43 (20.48%)
Enterectomy	39 (18.57%)
Loop ileostomy	37 (17.62%)
Loop colostomy	29 (13.81%)
Colectomy	12 (5.71%)
End ileostomy	11 (5.24%)
Others	9 (4.28%)
Nontherapeutic laparotomy	30 (14.29%)
Number of anastomosis	
0	117 (55.7%)
1	75 (35.7%)
2	17 (8.1%)
3	1 (0.5%)

Table 3. Severe postoperative complications. The in-hospital mortality was 75% among patients with severe complications (Clavien-Dindo > IIIa)

Severe surgical complications (Clavien-Dindo > IIIa)	24 (11.42%)
Anastomotic leak	9 (37.5%)
Evisceration/Eventration	9 (37.5%)
Intestinal perforation	7 (29.16%)
Mucocutaneous separation	5 (20.83%)
In-hospital mortality	18 (75%)

Table 4. Causes of mortality in 86 patients with malignant intestinal obstruction submitted to surgery

Obstruction (nontherapeutic surgery)	25 (29.07%)
Obstruction (unsuccessful surgery)	6 (6.98%)
Postoperative complications	14 (16.28%)
Sepsis of unknown origin	22 (25.28%)
Urinary or pulmonary infection	3 (3.49%)
Unknown	5 (5.81%)
Others	5 (5.81%)
Acute renal failure	3 (3.49%)
Bleeding	3 (3.49%)

before surgery was 5.36 days(CI 95%: 4.6-6.12). In patients that demanded postoperative intensive care (55.2%), the mean ICU stay was 6.13 days (SD 5,57).

Twenty-four (11.42%) patients evidenced severe surgical complications (Clavien-Dindo ≥ IIIa), as seen in *Table 3*. The most frequent severe surgical complication was anastomosis leakage, followed by evisceration or eventration. The in-hospital mortality of patients that presented severe complications was 75%.

Among 86 patients who died during hospitalization, the most frequent cause of death was due to the intestinal obstruction itself, either due to impossibility to perform surgery (nontherapeutic laparotomy) or due to the inefficient surgical procedure. Other common complications were sepsis and surgical complications. See *Table 4*.

To discriminate survival predictors factors, Odds Ratio (OR) were calculated for in-hospital stay mortality, and the 30-, 90- and 180-day mortality. The primary neoplasm was individually assessed and two groups were analyzed (colorectal and gynecological cancer vs. other neoplasm). The colorectal and gynecological cancer group showed a statistically significant lowerprobability for mortality than other neoplasms in the 90-day (OR: 2.95) and 180-day (OR: 3.06), as seen in *Table 5*.

The type of surgical procedure did not show any association with mortality, otherwise,

Table 5. Univariate analysis for in-hospital survival and survival up to 30, 90 and 180 days, comparing primary neoplasms

	In-hospital		30 days		90 days		180 days	
	OR	CI for OR	OR	CI for OR	OR	CI for OR	OR	CI for OR
Colorectal	1.00	1.00	1.00	1.00				
Gynecological	0.95	(0.46 – 1.97)	1.08	(0.53 – 2.22)	0.97	(0.48 – 1.98)	1.29	(0.59 – 2.80)
Upper GI	1.76	(0.71 – 4.31)	1.21	(0.49 – 2.97)	2.82	(1.02 – 7.79)	3.72	(1.01 – 13.64)
Urologic	1.95	(0.54 – 6.98)	2.69	(0.72 – 10.03)	4.01	(0.80 – 20.10)	2.28	(0.45 – 11.51)
Hepatobiliary	2.43	(0.63 – 9.42)	2.30	(0.60 – 8.91)	3.56	(0.70 – 18.17)		
Others	1.30	(0.32 – 5.27)	1.23	(0.30 – 4.99)	3.12	(0.60 – 16.25)	1.78	(0.34 – 9.30)
Colorectal/Gynecological	1.00		1.00		1.00		1.00	
Others	1.53	(0.82 – 2.83)	1.31	(0.71 – 2.43)	2.95	(1.48 – 5.90)	3.06	(1.33 – 7.06)

nontherapeutic surgery led to a higher risk for mortality. See *Table 6*.

A logistic regression was performed to assess clinical and laboratorial patients' characteristics associated to in-hospital mortality, and 30-, 90- and 180-day mortality. KPS was associated with the outcome in all assessed periods. Serum urea, C-reactive protein, and albumin were associated to higher mortality during in-hospital stay and in 30 days, and serum albumin was associated to higher mortality in 90 days as well. Hemoglobin were associated to higher mortality in 90 and 180 days. See *Table 7* and *8*.

Discussion

Patients with MIO show poor prognosis, with low survival rates. In this study, the 360-day survival rate was 16.4%. Postoperative in-hospital mortality rate was 40.95%. Previous reports also presented high mortality rate, with 30-day postoperative mortality ranging 6–32% (12-25).

The main cause of death in operated patients was intestinal obstruction itself, in cases where nothing could be done in the surgery or in which surgery was unsuccessful. Thus, usually palliative care is the mainstay

Table 6. Univariate analysis for in-hospital survival and survival up to 30, 90 and 180 days, comparing surgical techniques

	In-hospital		30 days		90 days		180 days	
	OR	CI for OR	OR	CI for OR	OR	CI for OR	OR	CI for OR
Intestinal bypass	1		1		1		1	
Enterectomy	2.36	(0.87 – 6.40)	1.41	(0.54 – 3.69)	1.06	(0.43 – 2.61)	0.64	(0.25 – 1.6)
Loop ileostomy	2.25	(0.89 – 5.65)	1.84	(0.71 – 4.78)	1.12	(0.45 – 2.78)	1.68	(0.59 – 4.78)
Loop colostomy	1.04	(0.35 – 3.12)	0.66	(0.21 – 2.08)	1.10	(0.41 – 2.93)	1.39	(0.46 – 4.19)
Colectomy	1.89	(0.54 – 6.59)	2.42	(0.63 – 9.26)	0.95	(0.26 – 3.54)	0.65	(0.17 – 2.51)
End ileostomy	2.06	(0.58 – 7.28)	2.90	(0.72 – 11.67)	1.67	(0.41 – 6.76)	4.64	(0.51 – 42)
Nontherapeutic surgery	12.4	(3.96 – 38.95)	7.94	(2.64 – 23.93)	13.33	(2.71 – 65.49)	13.46	(1.58 - 114.68)

Table 7. Logistic regressionwith enter method for in-hospital survival and survival up to 30, 90 and 180 days, comparing clinical and laboratory findings of patients

	In-hospital		30 days		90 days		180 days	
	Exp(B)	p	Exp(B)	p	Exp(B)	p	Exp(B)	p
Female		0.867		0.541		0.472		0.893
Age		0.789		0.614		0.975		0.912
BMI		0.200		0.564		0.101		0.094
KPS	1,023	0.022	1,031	0.004	1,033	0.005	1,045	0.002
Comorbidities		0.858		0.813		0.881		0.715
Lung metastasis		0.337		0.794		0.532		0.362
Liver metastasis		0.753		0.904		0.604		0.573
Ascites		0.808		0.358		0.938		0.486
Point of obstruction		0.800		0.606		0.312		0.186
Laboratory								
Hemoglobin		0.403		0.237	1,186	0.026	1,221	0.021
Leucocytes		0.294		0.219		0.081		0.258
C-reactive protein	0,995	0.003	0,996	0.018		0.054		0.340
Creatinine		0.133		0.067		0.146		0.330
Urea	0,985	0.003	0,984	0.002		0.109		0.234
Sodium		0.716		0.591		0,955		0.376
Potassium		0.279		0.215		0.500		0.361
Albumin	2,003	<0.001	1,718	0.004	1,804	0.002		0.174
INR		0.463		0.194		0.999		0.811

(B): Coefficient; BMI: Body mass index

Table 8. Regressions coefficients for predictors with a p-value less than 0,05 for in-hospital survival and survival up to 30, 90 and 180 days

	B	S.E	Wald	df	EXP(B)	Cox & Snell R Square	p
In-hospital							
KPS	0,023	0,010	5,250	1	1,023	0,028	0,220
C-reactive protein	-0,005	0,002	8,571	1	0,995	0,046	0,003
Urea	-0,015	0,005	9,080	1	0,099	0,050	0,003
Albumin	0,695	0,020	12,487	1	2,003	0,080	<0,001
30 days							
KPS	0,300	0,011	8,183	1	1,031	0,045	0,004
C-reactive protein	-0,004	0,002	5,586	1	0,100	0,030	0,018
Urea	-0,016	0,005	9,192	1	0,984	0,053	0,002
Albumin	0,541	0,190	8,126	1	1,718	0,052	0,004
90 days							
KPS	0,032	0,011	8,046	1	1,033	0,046	0,005
Hemoglobin	0,170	0,076	4,951	1	1,186	0,025	0,026
Albumin	0,590	0,194	9,205	1	1,804	0,058	0,002
180 days							
KPS	0,044	0,014	9,831	1	1,045	0,061	0,002
Hemoglobin	0,200	0,087	5,307	1	1,221	0,026	0,021

in the management of patients with MIO. In this case, the relief of symptoms such as nausea, cramps, distension and abdominal discomfort are the priorities.

The surgical decision should always be considered, since it is the most effective approach in clearing intestinal obstruction or even in symptoms palliation. Also, surgery may improve survival in these cases (14,20, 26). However, caution should be taken, once there is high probability for nontherapeutic laparotomy, due to the so-called "frozen abdomen", in which surgery is technically impossible. In addition, due to the high risk for severe complications, this decision should be carefully considered on a case-by-case and individualized basis. In this study, the incidence of severe postoperative complications was 11.42%. In other casuistries the incidence of severe complications ranged from 7 to 44% (12-15,17,18-25,26).

Before deciding for surgery, prognostic factors of each patient should be evaluated. Variables such as age, nutrition and functional performance status should be taken into account, even in cases where surgery is technically feasible (3,27).

Postoperative mortality in patients with nutritional deficiency and hypoalbuminemia is known to be higher (5,6). In our study, hypoalbuminemia was associated with higher in-hospital mortality and higher 90-day mortality. The use of parenteral nutrition during the perioperative period, while questionable in palliative patients (28), should be considered in selected cases.

Although the presence of ascites did not show a significant difference for mortality in this study, some studies have shown that refractory ascites may be associated with worse postoperative results and should be taken into consideration as prognostic factor, mainly when their volume exceeds 3000 cc3 (15, 29).

In the univariate analysis, chemotherapy prior to surgery was associated with higher postoperative mortality. Other studies have shown similar findings (30, 31). Such findings may be justified becausein patients with advanced cancer undergoing chemotherapy, progression to MIO frequently is progression of the disease, which no longer responds to the first lines of palliative chemotherapy (32).

As a limitation of this retrospective study, the high number of uncontrolled variables, the absence of well-establishedpre-specified protocol for operative intervention, and the heterogeneous casuistry (regarding clinical

status and characteristics of each neoplasm) increase the risk of bias. However, in the lack of controlled clinical trials, this study can be supportive to MIO patient evaluation to provide the best therapeutic option.

Treatment should be multidisciplinary in patients with malignant bowel obstruction, with the participation of oncology, surgery, nutrology, psychology, palliative care team, among others. Also crucial is the participation of patients and their families when deciding on therapeutic strategies. Patients and family members should be aware of the prognostic factors, risks of complications and probability of non-resolution of the condition, even with interventional measures such as surgical procedures.

Conclusions

MIO implies poor prognosis, with high in-hospital mortality rate and severe postoperative complications. Under nourishment, anemia, renal failure and low performance status are associated to high mortality.The decision regarding management of MIO must be multimodal and individualized, according to individual prognostic factors.

Author's Contributions

Jorge Henrique Bento de Sousa: analysis and interpretation of data, Edno Tales Bianchi: acquisition of data and drafting the article, Francisco Tustumi: paper drafting, Paulo César Leonardi: revising the paper critically for relevant intellectual content, Ulysses Ribeiro Junior: revising the paper critically for relevant intellectual content, • Ivan Ceconello: conception and design of the study.

Conflict of Interest

Authors have no conflict of interest.

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