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Designed for practictioners involved in oncology, obesity, metabolic, and other abdominal diseases

IN THIS ISSUE

- Post-operative complications in gastric cancer surgery are analyzed in a large series of patients to investigate risk factors related to clinical and oncological features.
- ERAS protocols are spreading worlwide to improve perioperative outcomes. A PSM analysis from the IMIGASTRIC database compares the ERAS and the standard management in patients underwent gastrectomy.
- A rare case of gastric carcinosarcoma is reported with a literature review.
- Dr. Gambardella describes a case of LAGB followed by complications that arose after about thirty years.
- Dr. Aljarboo shows a case of gastric cancer after sleeve gastrectomy.
- A novel surgical approach for GISTs of the gastric antrum is proposed in the technical note section.
- A Correspondence with Prof. V. M. dos Santos is added to discuss gastric signet ring cell carcinoma.

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JGS

CONTENTS

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JGS

RETROSPECTIVE STUDY OPEN ACCESS

Determinants of surgical morbidity in gastric cancer: experience of a single center and literature review

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ABSTRACT

Background:
This study aimed to evaluate the severity of intraoperative and post-operative complications of gastric cancer surgery and to investigate the predictive factors correlated to surgical morbidity.

Methods:
We included 145 patients operated for gastric cancer. We investigated the risk factors associated with complications, length of hospital stay, operative time, and intraoperative blood transfusion (BT). Significant risk factors were analyzed by multiple logistic regression analysis.

Results:
Postoperative complications occurred in 32 patients (22.1 %) and the rate of major complications was 7.6%. The rate of anastomotic fistula was 6.9% and was correlated to diabetes, tumor size, operative time, surgical margin, and extended lymphadenectomy. The mean risk factors for postoperative morbidity were the presence of comorbidities and ASA score ($p = 0.021$), intraoperative BT ($p = 0.045$) and prolonged operative time ($p = 0.055$).

Conclusion:
Surgical morbidity of gastric cancer is correlated to the extent of resection as well as the clinical and histological characteristics.

Key Words:
gastric cancer, surgery, Morbidity, postoperative complications, Prognosis.

Background

Management of gastric cancer has undergone in the last decade remarkable progress both in the neo-adjuvant and adjuvant treatments and in the surgical procedure as regards the extent of resection and the lymph node dissection. These advances are certainly associated with an improvement in the overall prognosis of the neoplastic disease. But this gain has been associated with over- morbidity and mortality that we need to know to prevent it. The rate of postoperative morbidity reported by the largest randomized controlled series varies from 11 to 46%.[1] This significant variability in the literature is explained not only by the differences in the characteristics of the studied populations, the therapeutic procedures but also by the definition of the morbidity used in each study. Thus, to limit the subjectivity in the analysis of the complications, many authors used the Clavien and Dindo classification of postoperative complications published in 2004. This classification seems more straightforward, objective, but above all reproducible, since it evaluates the severity of the complications according to their therapeutic management.[2] This study aimed to assess the severity of intraoperative and postoperative complications of gastric surgery and to investigate the predictive factors correlated to surgical morbidity.

Methods

Approval to conduct this study was obtained from the Institutional Review Board of the Salah Azaiz Institute. We conducted a retrospective study including 145 patients with histologically proven gastric adenocarcinoma who underwent curative or palliative gastrectomy from January 2005 to December 2015. Non-inclusion criteria were as follows:(1) metastatic disease, (2) other synchronous tumoral location, (3) unknown surgery status, (4) unknown vital status; (5) incomplete pathological data.

After institutional review board approval, we collected patient and tumor-related factors through medical records: age, sex, BMI, proteinemia (hypoproteinemia was defined as less than 60g/dl), the hemoglobin level, comorbidities, and American Society of Anesthesiologist (ASA) score, tumor size, depth of invasion and the stage of gastric cancer according to the eighth edition of the American Joint Committee on Cancer TNM classification system.

The surgical variables included the type of procedure (total versus partial gastrectomy), the extent of lymph node dissection (D0, D1.5, and D2) based on the Japanese Gastric Cancer Treatment Guidelines 2010 (version 3)[3] and the number of retrieved lymph nodes (NRLN), multivisceral organ resection (MVR), operative time measured from the first skin incision to the closure of all skin incisions and confirmed by the attending anesthesiologist in the operating room, intraoperative allogeneic blood transfusion and the length of hospital stay.

The extent of the lymphadenectomy was based on the individual surgeon's judgment. Splenectomy was performed in cases of metastatic lymph nodes at the hilum of the spleen or because of iatrogenic injury. The extent of stomach resection was related to the primary tumor site: total gastrectomy was performed in all proximal tumor locations and total gastric tumors, and subtotal gastrectomy was performed for distal tumor locations, provided that a 5 to 6-cm safety margin was present. A multi-visceral resection was performed in all cases of T4 or suspected T4 tumors. After total gastrectomy, reconstruction was made by Roux-en-Y esophagojejunostomy. Esophago-jejunal anastomoses were performed by hand-suture or mechanically with a circular stapler according to the surgeon's choice. The stapled esophageal and jejunal doughnuts were examined for completeness of anastomosis. A hand-sutured or stapler Billroth II followed subtotal gastrectomy. A prophylactic antibiotic of a second- or third-generation cephalosporin was administered to all patients and usually lasted for 5 days following the operation.

The integrity of the anastomosis was routinely evaluated on the seventh postoperative day by a water-soluble contrast swallow and/or by ingestion of methylene blue before reintroducing an oral intake. The anastomotic fistula was diagnosed with extravasation of contrast product during radiological examination and/or with discharge or gastrointestinal content through a drain. Clinical leakage was defined as the presence of either clinical symptoms suggesting potential leakages such as abdominal pain abnormal with drain discharge, fever, and leukocytosis.

Postoperative morbidity and mortality included all adverse events reported within the first 30 days after surgery or during the same hospitalization, and late complications were not included in this study. Surgical complications included anastomotic fistula and leakage, early anastomotic stenosis, septic collection, and wound infection, pleural effusion, ileus, and bleeding. Non-surgical complications were heart failure, pneumonia or respiratory failure, urinary tract infection, decompensation of diabetes, and thromboembolic events. All complication data were graded retrospectively according to the Clavien-Dindo classification from Grade 1 to Grade 5 according to the treatment for each complication. Major complications included all complications classified as grade III A or more according to the Clavien Dindo system.

Statistical analysis

The categorical variables were presented as numbers and percentages. Continuous variables were expressed as the mean ± standard Deviation (SD) with ranges, and groups were compared using the Test t of Student. Moreover, some continuous variables were converted to dichotomous variables for convenience, including the age (≤65 years versus > 65 years), the body mass index BMI (<20 kg/m2 versus ≥ 20kg/m2), hemoglobin rate (≤10 g/dl versus >10 g/dl), the tumor size (<50mm versus≥50 mm) and the NRLN (≤15, 16-25 and≥25). Clinical and pathological data were compared between patients to analyze the major risk factors associated with complications, length of hospital stay, operative time and intraoperative blood transfusion. The groups were compared using the chi-square test or Fisher's exact test. All variables with a p-value <0.2 in the univariate analysis were entered into a multivariate analysis using

a logistic regression model to identify independent factors of perioperative blood transfusion and operative time. We used the Statistical Package for Social Science (SPSS), version 20.0 for Windows, and ap-value less than 0.05 was considered significant.

Results

The clinicopathological characteristics of the patients are summarized in *Table 1*. There were 93 males (64%) and 52 females (36 %), with a mean age of 61.48 years±12.86 (range, 26 to 85 years) and 44 patients (49.5%) were more than 70 years old.

The operative data are summarized in *Table 2*. Total gastrectomy was performed in 77 patients (53.1%) and subtotal gastrectomy in 68 patients (46.9%). Combined organ resection was performed in 34 (23.4 %) patients. D1 lymph node dissection was carried out in 15 cases, and extended lymphadenectomy in 130 patients (89.7%) from which 36 patients (24.8%) had D1.5 lymphadenectomy and 94 patients had D2 lymphadenectomy.

The Mean operative time was 194 minutes ± 53.22 with extremes ranging from 110 to 350mn. Univariate analysis of the factors influencing the operating time is shown in *Table 3*. The mean operative time was significantly increased in patients with proximal and middle third tumors compared with distal tumors (208.81mm vs 181.42mn respectively, p=0.002). Tumor staged T3-T4 required a longer operative time compared to pT1-T2 tumors (199.81mnvs 178.85mn respectively, p=0.032). We also found that the mean operative time was significantly longer with total gastrectomy compared to partial gastrectomy (204.16mnvs 182.56mn respectively, p=0.015), multi-organ resection (215mn vs 187.60mn, p=0.021), D2 dissection compared to D1 / D1.5 dissection (204.02mm vs 188.61mn respectively, p= 0.004) and in case of splenectomy or spleno-pancreatectomy (p = 0.037). On multivariate analysis extended lymphadenectomy and combined organ resection were the only independent factors associated with a longer operative time.

Intraoperative blood transfusion was performed in 77 patients (53.1%), with a mean amount of 2.14 units and extremes ranging from 1 to 4 units. Of the transfused patients, 19 patients (24.7%) required more than three units. Univariate analysis of factors associated with intraoperative blood transfusion is shown in table4. Transfused patients had a longer mean operative time compared to non-transfused patients (23.04mn vs 183.83mn, p=0.054). Significant factors on the univariate analysis were included in the multivariate analysis (*Table4*). Tumor location and combined organ resection were found to be the independent risk factors of intraoperative blood transfusion.

A total of 113 out of 145 (77.9%) patients had no complications, and 32 (22.1%) had at least one medical or surgical complications. Details of postoperative complications are listed in *Table 2*. Eighteen patients (12.4%) had one or more medical complications of which seven patients had significant medical complications. They were dominated by postoperative pneumonia occurring in 13 cases (9%) and pulmonary embolism in 2 cases (1.4%).

Surgical complications occurred in 18 patients within a delay of 10 days (range, 4 to 20 days). The anastomotic fistula was the most common surgical complication occurring in 10 cases (6.9%), and postoperative peritonitis secondary to complete anastomotic leakage was diagnosed in only one patient. From the 145 patients, four (2.8%) required re-laparotomies for serious complications: one case of stenosis of the esophago-jejunal anastomosis, one case of anastomotic leakage, one case of the esophago-jejunal fistula with major ionic disorders and severe dehydration, and one case of a deep abdominal abscess that was not accessible to percutaneous radiologic drainage.

Using the Clavien-Dindo classification, the 32 complicated patients had the following grades: 21 patients (14.5%) had grade II, 3 patients (2.1%) had grade IIIa, 2 patients (1.4%) had grade IIIB and one (1.6%) had grade IVa. Postoperative death (grade V of Clavien-Dindo classification) occurred in five patients (3.4%) within a mean delay of 30 days after surgery (range 18 to 74 days). Three patients died because of anastomotic fistula, one patient died after reoperation for anastomotic stenosis and the last patient died from respiratory failure secondary to pneumonia.

Univariate analysis of clinical and therapeutic predictive factors of postoperative complications is shown in *Table 5*. We found that the mean risk factors for postoperative morbidity were the presence of comorbidities (p = 0.021), intraoperative blood transfusions (p = 0.045) and prolonged operative time (p = 0.055). Hypoproteinemia at diagnosis seems to increase morbidity (28.8% vs 18.3%, p = 0.066). Patients with BMI greater than or equal to 20 had a higher rate of complications than those with a BMI of less than 20 (23.3% vs. 20.8%, p = 0.842). However, we found that age, gender, locally advanced tumors, extended lymphadenectomy, splenectomy or SPC, total gastrectomy, and combined organ resection were not significantly associated with higher postoperative morbidity.

The mean length of postoperative hospital stay was 15.08 days ± 7.48 (range 7-74 days). Univariate analysis of factors associated with the length of hospital stay is represented in *Table 6*. No significant difference was found in the period of hospital stay according to the extent of gastrectomy and lymphadenectomy. However, the duration of hospitalization was significantly increased in patients with comorbidities regardless of age and gender (p= 0.017). Patients who presented postoperative complications had a more extended hospital stay (p <0.001). According to Clavien-Dindo classification, the length of hospital stays progressively increased from non-complicated patients to grade V patients (P<0.0001). The duration of hospitalization is extended by 13.99 days (p = 0.03) in case of anastomotic fistula and by 6.17 days (p = 0.004) in cases of respiratory infections.

The results of the univariate analysis of patient-related risk factors of fistula and leakage showed that these complications were more frequent in diabetic patients (23.5% vs 4.7%; p=0.004). According to laboratory variables, preoperative hypoproteinemia (11.5% in case of hypoproteinemia vs 4.3% with normal proteinemia, p=0.168) and anemia with hemoglobin rate less than 10 g/dl (12.5 % vs 4.8%, p=0.139) were likely to be associated

with a higher rate of fistula even if the difference was not statistically significant. In the analysis of tumor-related factors, anastomotic fistula was significantly associated with tumor size exceeding 50mm (10.3% vs 1.7%, p=0.045), gastric walls rigidity (33.8% vs 5.1%; p=0.016), and the length of the proximal margin of resection (the mean length of the proximal margin in patients with fistula was 41± 24.358 mm vs 57.55± 26.008, p=0.042). When analyzing surgical related factors, we found that the type of gastrectomy, the extent of lymphadenectomy, and combined organ resection were not significantly associated with a more frequent fistula. Nevertheless, the number of retrieved lymph nodes (23.24 ± 11.036 vs 27.5 ± 12.059 in case of anastomotic fistula, p=0.073), as well as the duration of the operation (190.77 ± 12.59 min vs 238±16.96 min in case of fistula, p=0.006), were identified as predictive factors of fistula.

Table 1: Clinical and histological patients' characteristics

Variables		N	%
Age (mean, ±DS, min, max, ans)		61.48 ±12.86 (26-85)	
	≥70 years	44	30.3
	<70 years	101	69.7
Gender	Male	93	64
	Female	52	36
BMI (mean± SD,kg/m2)		19.906 ±2.719 [12.48-28.02]	
	<20kg/m2	72	49.7
	≥20 kg/m2	73	50.3
Hypoproteinemia	No	93	64.1
	Yes	52	35.9
Hb (g/dl)	≤10g/dl	40	27.6
	>10g/dl	105	72.5
Comorbidities	No	101	69.7
	Yes	44	30.3
ASA score	< ASA 3	119	82.
	≥ ASA 3	26	17.9
Tumor location	Upper third	21	14.5
	Middle third	45	31
	Distal third	77	53.1
	Pangastric tumor	2	1.4
Tumor size		64.86 ±34.49 [12-220mm]	
(mean ±DS, min, max, mm)	<50mm	58	40
	≥ 50mm	87	60
Lauren Classification	Intestinal	109	75.2
	Mixed	4	2.8
	Diffuse	32	22.1
Differenciation	Well	63	43.4
	Meanly	47	32.4
	Poorly/undifferenciated	35	24.2
LVI	No	73	50.3
	Yes	72	49.7
PNI	No	76	52.4
	Yes	69	47.6
pT stage	pT1	8	5.5
	pT2	32	22.1
	pT3	61	42.1
	pT4	44	30.3
LN status	N-	26	17.9
	N+	119	82.1
pN stage	pN0	26	17.9
	pN1	31	21.4
	pN2	41	28.3
	pN3a	28	19.3
	pN3b	19	13.1
NRLN (mean ±DS, min, max)		23.63 ± 10.856 [5-57 ganglions]	
	<15	27	18.6
	15-24	61	42.1
	≥25	57	39.3
NMLN (mean ±DS, min, max)		8.16 ±7.854 [1-38 ganglions]	
LNR	LNR0	26	17.9
	LNR1	25	17.2
	LNR2	30	20.7
	LNR3	64	44.2
UICC stage	I	16	11
	II	45	31
	III	77	53
	IV	7	5
Resection	R0	136	93.8
	R1	8	5.5
	R2	1	0.7
Treatment sequency	Surgery alone	47	32.4
	CT-Sur -CT/RTCT	13	9
	Sur+CT ADJ	27	18.6
	SUR+ RTCT/RT ADJ	58	40

CT: chemotherapy, ADJ: adjuvant, RTCT/RT: radio-chemotherapy or adjuvant radiation therapy, SUR: surgery, LVI: lympho-vascular invasion, PNI: perineural invasion, NRLN: number of retrieved lymph nodes, NMLN: number of metastatic lymph nodes
LNR : lymph nodes ratio, SD : standard deviation

Table 2: Surgical and postoperative features of patients

Variables	N	Rate
Gastrectomy		
Total gastrectomy	77	53.1%
Partial gastrectomy	68	46.9%
Combined organ resection	34	23.4%
Transverse mesocolon resection	12	8.3%
Transverse colectomy	5	3.4%
Small bowel resection	4	2.8%
Liver	1	0.7%
Cholecystectomy	1	0.7%
Cephalic duodenopancreatectomy	1	0.7%
SPC	3	2.1%
Splenectomy	11	7.6%
Lymphadenectomy		
D1	15	10.3%
D1.5	36	24.8%
D2	94	64.8%
Number of retrieved lymph nodes		
≤15	34	23.4%
16-25	59	40.7%
≥25	52	35.9%
Intraoperative blood transfusion		
No	68	46.8%
Yes	77	53.1%
Operative time (mean ±SD, mn , range)	194mm ± 53.22 [110-350mn]	
Length of hospital stay (mean ±SD, days , range)	15.08 ±7.485 [7-74 days]	
Postoperative mortality	5	3.4%
Total postoperative complications	32	22.1%
Surgical complications		
Anastomotic fistula	10	6.9%
Isolated duodenal fistula	1	0.7%
Postoperative peritonitis: Anastomotic leakage	1	0.7%
Deep abdominal collection	3	2.1%
Parietal abscess	3	2.1%
Anastomotic stenosis	2	1.4%
Pleural effusion	2	1.4%
Non surgical complications		
Respiratory infection	13	9%
Pulmonary embolism	2	1.4%
Cardiac failure	1	0.7%
Urinary infection	1	0.7%
Diabetic decompensation	1	0.7%
Clavien-Dindo classification		
No complications	113	77.9%
Grade II	21	14.5%
Grade IIIa	3	2.1%
Grade IIIb	2	1.4%
Grade Iva	1	0.7%
Grade V	5	3.4%

Table 3: Univariate and multivariate analysis of factors influencing the operative time

Factors	N	Univariate analysis		Multivariate analysis	
		Operative time (Mean ± SD, mn)	P*	Exp B 95% CI	P
Tumor location			**0.002**	**-**	**-**
Distal	77	181.42±52.897			
Others	68	208.31±50.480			
Tumor size (mm)			0.256	-	-
≥50	87	197.15±53.625			
<50	58	187.84±52.733			
Depth of invasion			**0.034**	**-0.196 [-5.413-32.511]**	**0.160**
T1-T2	40	178.85±49.207			
T3-T4	105	199.81±53.918			
Gastrectomy			**0.015**	**-**	**-**
PG	68	182,56 ± 56,130			
TG	77	204,16 ± 48,878			
MVR			**0.021**	**-**	**-**
No	111	187,60 ± 49,186			
Yes	34	215 ± 61,62			
Splenectomy/ Splenopancreatectomy			**0.037**	**0.287 [22.158 – 80.997]**	**0.001**
No	132	189.57 ± 75.622			
Yes	14	235.71 ± 75.622			
Lymphadenectomy			**0.004**	**-0.196 [-39.918, -3.756]**	**0.018**
D1/D1.5	51	188,61 ± 56,130			
≥ D2	94	204,02 ± 39,586			

TG: total gastrectomy, PG : partial gastrectomy, MVR: multivisceral resection
* test T of Student, SD : standard deviation
CI: confidence interval

Table 4: Univariate and multivariate analysis of clinical, therapeutic and histological factors associated with intraoperative blood transfusion

Variables	N	Univariate analysis			Multivariate analysis	
		No BT	BT	p	OR 95% IC	P
Age (mean±SD, years)		60.64±12.88	62.23±12.89	**0.692**†	**-**	**-**
Gender				**0.864***	**-**	**-**
Male	93	43 (46.2%)	50 (53.8%)			
Female	52	25 (48.1%)	27 (51.9%)			
BMI (mean± SD,kg/m2)	145	20.039±2.79	19.78±2.66	**0.164**†	**-**	**-**
Tumor location				**0.008***	0.174 [0,017-0.330]	**0.03**
Distal	77	44 (57.1%)	33 (42.9%)			
Others	68	24 (35.3%)	44 (67.7%)			
Gastrectomy				**0.007***	**-**	**NS**
TG	77	28 (36.4%)	49 (63.6%)			
PG	68	40 (58.8%)	28 (41.2%)			
MVR				**0.001***	0.267 [0,131-0.497]	**0.001**
No	111	61(55%)	50 (45%)			
Yes	34	7 (20.6%)	27(79.4%)			
Splenectomy/ Splenopancreatectomy				**0.002***	**-**	**NS**
No	131	67 (51.1%)	64 (48.9%)			
Yes	14	1 (7.1%)	13 (92.9%)			
Lymphadenectomy				**0.728***	**-**	**-**
D1	15	9 (60%)	6 (40%)			
D1.5	36	13 (31.6%)	23 (63.9%)			
D2	94	46 (48.9%)	48 (51.1%)			
Operative time (mean± SD, mn)	145	183.82	203.04	**0.054**†	**-**	**NS**
NRLN				**0.042***	0,132 [-0,016-0.189]	**0,097**
≤15	34	21(61.8%)	13(38.2%)			
16-25	59	27(48.8%)	32 (54.2%)			
≥25	52	20 (38.5%)	32(61.5%)			
Depth of invasion				**0.116***	**-**	**-**
T1/T2	40	23 (57.6%)	17 (42.5%)			
T3/T4	105	45 (42.9%)	60 (57.1%)			
Tumor size (mean±SD, mm)	145	51.16±27.62	71.66±38.48	**0.027**†	**-**	**NS**

BMI: Body mass index, TG: total gastrectomy, PG : partial gastrectomy, MVR: multivisceral resection, NRLN: number of retrieved lymph nodes. BT: blood transfusion
† test T of Student.
* test chi2 Pearson
SD: standard deviation

Table 5: Univariate analysis of predictive factors of postoperative complications

Variables		N	Postoperative complications		P Value
			Yes	No	
Age (mean, years)		145	61,16 ± 12,67	62,66 ±13,70	0.563†
BMI (kg/m2)	<20	72	57 (79.2%)	15(20.8%)	0.842*
	≥20	73	56(76.3%)	17 (23.3%)	
Proteinemia (mean, g/l)		145	61,72 ± 7,83	58,88 ±7,093	0.066*
Hypoproteinemia	No	93	76 (81.7%)	17 (18.3%)	
	Yes	52	37 (71.2%)	15 (28.8%)	
Hemoglobin level (g/dl)		145	10,74 ± 1,75	10,62 ± 2,09	0.750†
ASA score	<ASA3	119	96 (80,7%)	23 (19,3%)	0.089*
	≥ASA3	26	17 (65,4%)	9 (34,6%)	
Comorbidities	No	101	84 (83,2%)	17 (16,8%)	0.021*
	Yes	44	29 (65,9%)	15 (34,1%)	
Blood transfusion	No	68	58 (85,3%)	10 (14,7%)	0.045*
	Yes	77	55 (71,4%)	22 (28,6%)	
Splenectomy/ Splenopancreatectomy	No	131	103 (78,6%)	28 (21,2%)	0.537*
	Yes	14	10 (71.4%)	4 (28.6%)	
LND	D1	15	12 (80%)	3 (20%)	0.838*
	D1.5/D2	130	101 (77.7%)	29 (22.3%)	
MVR	No	111	87 (78,4%)	24 (21,6%)	0.814*
	Yes	34	26 (76,5%)	8 (23,5%)	
Gastrectomy	TG	77	56 (72,7%)	21 (27,3%)	0.108*
	PG	68	57 (83,8%)	11 (16,2%)	
Operative time (mn)		145	189,50 ± 51,50	210 ±57,36	0.055†
Tumor size (mean, mm)	≥50mm	58	46(79.3%)	12 (20.7%)	0.744*
	<50mm	87	67(77%)	20(23%)	
Depth of invasion	T4	44	34(77.3%)	10 (22.7%)	0.9*
	T1-T2-T3	101	79 (78.2%)	22 (21.8%)	
Tumor location	Distal	77	62 (80.5%)	15 (19.5%)	0.424*
	Others	68	51 (75%)	17 (25%)	

BMI: Body mass index, TG: total gastrectomy, PG : partial gastrectomy, MVR: multivisceral resection, LND: lymph node dissection
† test T of Student.
* test chi2 Pearson

Table 6: Univariate analysis of factors associated with the length of hospital stay

Factors		N	Length of hospital stay (mean, days) *	P
Age (years)	**≤65**	90	14.41 ± 5.538	0.172
	>65	55	16.16 ± 9.845	
Gender	**Men**	93	14.49 ± 7.933	0.369
	Women	52	14.33 ± 6.618	
Comorbidities	**No**	101	13.81± 5.096	**0.017**
	Yes	44	17.98 ±10.717	
Gastrectomy	**PG**	68	15.61 ± 4.719	0.381
	TG	77	14.47 ± 9.719	
MVR	**No**	111	14.95 ± 8.157	0.707
	Yes	34	15.5 ± 4.737	
Splenectomy/ Splenopancreatectomy	**No**	131	15.02 ± 7.781	0.145
	Yes	14	15.57 ± 3.857	
Lymphadenectomy	**D1/D1.5**	51	14.52 ± 8.32	0.227
	D2	94	16.1 ± 5.54	
Postoperative complications	**No**	113	12.58 ± 2.856	**<0.001**
	Yes	32	23.91 ± 11.292	
Grade Clavien Dindo	**No**	113	12.58 ± 2.856	**<0.001**
	II	21	20.43 ± 4.664	
	IIIa	3	26 ± 8.544	
	IIIb	2	30 ± 14.142	
	Iva	1	20	
	V	5	35 ± 23.082	
Fistula	**No**	135	14.11 ± 5.186	**0.03**
	Yes	10	28.10 ±17.136	
Respiratory infection	**No**	132	14.52 ± 7.457	**0.004**
	Yes	13	20.69 ±5.266	

TG: total gastrectomy, PG : partial gastrectomy, MVR: multivisceral resection
* test T of Student.

Discussion

In our study, the rate of postoperative complications was 22.1% which seems consistent with the data in the literature.[1] However, we found a lower rate of major complications according to Clavien and Dindo classification (7.6%), and this can be explained not only by the small number of the patients but also by a retrospective classification of complications based on data collected from medical records. The most common complications reported in the literature are respiratory complications occurring in 1.1% to 12.32% of cases[4], decompensation of chronic disease, and gastroparesis.

Anastomotic leakage occurring in 1 to 11.5%, intra-abdominal abscesses, pancreatic fistulas, intraperitoneal hemorrhages, postoperative occlusions, postoperative pancreatitis, and eviscerations were the most common surgical complications.[5, 6] However, Marrelli reported a higher rate of intra-abdominal infection of 14.2% with more extensive lymph node surgery.[7] In this study, we reported a rate of 9% of pneumonia, 6.9% of anastomotic fistula, and 4.2% of suppurative complications. According to Baiocchi, the postoperative mortality rate was also very variable. Western centers reported a mortality rate of 5%, while Eastern centers reported a lower rate of 2%.[1] In our series, postoperative deaths occurred in 3.4% of cases within an average of 30 days after the intervention, which seemed consistent with the literature data.

The extent of surgical resection, particularly the type of gastrectomy and lymphadenectomy, represent the most crucial factor of postoperative morbidity in gastric cancer.

Many studies evaluated the impact of extended lymphadenectomy on perioperative morbidity and mortality and the results were variable between the Asian series, particularly Japanese, and the Western series (*Table 7*). Two large randomized Western multicenter trials compared D1 and D2 lymphadenectomy: The British MRC ST01 study, conducted by Cuschieri[8, 9] and the Dutch trial conducted by Bonenkamp[10, 11] reported that D2 lymphadenectomy was associated with an increased rate of morbidity and included and a longer hospital stay. These two trials were included in a Cochrane meta-analysis[12] showing that D2 lymph node dissection had tripled the rate of mortality with a relative risk of 2.93 (95% CI= 1,45-3.45) and concluded that the "excess mortality" of the D2 lymphadenectomy was related not only to spleno-pancreatectomy but also to the learning curve of the surgeons. However, several other randomized studies such as the German multicenter prospective study conducted by Siewert who had shown that D2 lymphadenectomy retrieving more than 25 lymph nodes was not significantly correlated with additional morbidity and mortality. [13] Although many studies reported a significant gain in survival with a D2-D3 lymphadenectomy, this extended lymph node dissection was associated to a higher rate of postoperative complications with a longer hospital stay, longer operative time and higher rate of blood transfusion.[14-16] However, the Japanese prospective study of Takeshi Sano et al. found that the incidence of serious complications was not different in the two groups.[17] Several reports have reported that splenectomy did not provide survival benefits and described a higher postoperative morbidity rate with and without splenectomy[18, 19], especially infectious complications[18] such as intra-abdominal abscess and pulmonary infections[20] and concluded that the use of prophylactic splenectomy to remove macroscopically negative lymph nodes near the splenic hilum in patients undergoing total gastrectomy for proximal gastric cancer should be avoided. However, in other randomized studies, D2 lymphadenectomy with splenectomy was not correlated to postoperative morbidity and mortality as well as the length of hospital stay and operative time.[17, 21, 22] In our series, no significant difference in duration of hospitalization or overall postoperative complication was found according to the extent of lymphadenectomy. Although splenectomy and left pancreatectomy exposed to a higher risk of complications (28.6% vs 21.4%), the difference was not statistically significant (p = 0.537) with a comparable length of hospital stay. Our results can be explained by the low proportion of splenectomy and left pancreatectomy (7.6% and 2.1% respectively) and by the selection of patients for extensive lymphadenectomy who were younger and with an ASA sore <3. However, in our study, extended lymphadenectomy led to an increased intraoperative morbidity with more blood transfusion and longer operative time.

Several studies investigated the impact of the type of gastrectomy on postoperative morbidity and mortality with variable results. In fact, since the extent of the gastrectomy depended on the site of the tumor and its size, most of the studies had essentially compared total gastrectomy to partial gastrectomy in distal tumors. These studies were included in a recent meta-analysis published in 2016 by Qi et al.[23], combining data from 5447 patients included in 10 retrospective studies and one prospective randomized study. In this meta-analysis, TG was associated with a higher risk of postoperative complications (RR = 1.76, 95% CI = 1.31-2 .36, p = 0.0002) and especially more frequent intra-abdominal abscesses (RR = 3.41, 95 % CI = 1.21-9.63, p <0.05) compared to partial gastrectomy with a similar rate of postoperative mortality (RR = 1.48, 95% CI = 0.90-2.44, p = 0.12). Moreover, the impact of the type gastrectomy on morbidity and mortality, regardless of the tumor location, has been reported in several other studies suggesting that TG is associated with higher rates of postoperative complications and morbidity, such as the Dutch trial (OR = 2.04, 95% CI = 1.01-3.79, p = 0.02). In the analysis of surgical morbidity and mortality of the Randomized "Critics" trial where 636 patients were included, total gastrectomy and oesophago-gastrectomy were independent risk factors for both surgical and medical postoperative complications (OR = 1.88, 95% CI = 1.30-2.72, p = 0.001) with higher rates of surgical revision and longer hospital stay.[24] Nakagawa et al. performed a retrospective analysis of the risk factors of postoperative complications in 539 patients who were previously prospectively collected.[25]

In this study, total gastrectomy was the only independent factor of high-grade complications according to the Clavien and Dindo classification (OR = 2.075, 95% CI = 0.26-0.896, p = 0.021). However, several other studies had reported comparable morbidity rates between the

Table 7: Randomized trials comparing the impact of the extent of lymphadenectomy on surgical morbidity and mortality

Study	LND	Morbidity	Mortality	Hospital stay (days)	Blood Transfusion
British MRC STO1	**D1:** N=200	28%	6,5%	18 (6 à 101 days)	NE
Cuschieri et al[8, 9]	**D2:** N=200	46%	13%	23 (10 à 147 days)	
		p<0,001	**p=0,015**	**P=0,01**	
Dutch study	**D1:** N=539	25%	4%	18 (7 à 143 days)	NE
Bonenkamp et al[10, 11]	**D2:** N=539	43%	10%	25 (7 à 277 days)	
		p<0,001	**p<0,001**	**p<0,001**	
Scandinavian study	**D1:** N=114	16,8%	1,8%	11 (3 à 66 days)	400ml
Danielson et al[14]	**D2:** N=109	33%	3,7%	12 (6 à 69 days)	550ml
		p=0,008	**p=0,438**	**p=0,012**	**p=0,047**
Taiwanese study	**D1:** N=110	4,5%	NE	NE	NE
Wu et al[15]	**D3:** N=113	17,1%			
		p<0,05			
Chilean study	**D1:** N=74	4%	2%	NE	NE
Butte JM[16]	**D3:** N=103	26%	5%		
		p<0,05	**p<0,05**		
Japanese study	**D1:** N=263	20,9%	0,8%	21 days	14,1%
Takeshi Sano et al[17]	**D2:** N=260	28,1%	0,8%	24 days	30%
		P=0,067	**p=0,99**	**p<0,01**	**p<0,001**
German study	**D1:** N=558	7,3%	5%	NE	NE
Siewert[13]	**D2:** N=1096	7,8%	5,2%		
		NS	**NS**		
Corean study	**TG:** N=103	8,7%	1%	11 (8 à 60 days)	NE
Yu et al[21]	**TGS:**N=104	15,4%%	1,9%	11 (1 à 71 days)	
		p=0,142	**p=1**	**p=0,272**	
Chilean study	**TG:** N=97	39%	3,1%	18,4 (8 à 81 days)	NE
Csendes et al[20]	**TGS:** N=90	50%	4,4%	21,6 (9 à 81 days)	
		P=0,04	**p=0,7**	**p=0,06**	
Italian study	**D1:** N=133	12%	2,2%	12,8 (8 à 78 days)	NE
Degiuli et al[22]	**D2:** N=134	17,9%	3%	13,1 (7 à 79 days)	
		P=0,178	**P=0,772**	**p=0,732**	

NE: Non evaluated, TG: total gastrectomy without splenectomy, GTS: total gastrectomy with splenectomy. LND: lymph node dissection

two surgical procedures. Indeed, the retrospective study of Park et al.[26] involving 719 patients did not report a significant difference between GT and GP regarding postoperative morbidity (19.3% versus 13.6% respectively, p = 0.103). However, Persiani found that the length of hospital stay exceeding ten days was particularly observed with total gastrectomy.[27] These results support the data from our series, where postoperative morbidity was not significantly correlated with the type of gastrectomy with a comparable rate of fistula and length of hospital stay even though the incidence of complications appeared to be higher in case of GT (27.3%) compared to GP (16.2%). However, TG was associated with higher perioperative morbidity with and increased rate of blood transfusion (63.6% vs 41.2%, p= 0.007) which is consistent with the results of the meta-analysis of Sun et al.[28] and also a longer operative time (210mn vs 189.5mn, p= 0.015) which is consistent with the results of Gockel et al. and Papenfuss et al.[29, 30]

The benefit of multivisceral resection (MVR) for locally advanced gastric ADK is controversial because of the increased mortality and morbidity. In the systematic review carried out by Brar[31] including 17 studies with 1343 patients, the morbidity rate varied between 11.8% and 90% and perioperative mortality ranged from 0 to 15%. In contrast, in our study, MVR did not significantly increase the rate of postoperative complications (23.5% vs 21.6%, p = 0.814) and fistula (11.8% vs. 5.4%, p = 0.245) but was correlated to higher intraoperative morbidity with a significant lengthening of the operative time and an increase of blood transfusion requirement. Our findings were similar to that of the large multicenter and observational study published by Pacelli in 2013, who found that MVR was not associated with an increase in mortality (p = 0.55) or morbidity (33.9% vs 31.6%, p = 0.38).[32]

The impact of intraoperative blood transfusions on

short-term and long-term outcomes has been widely debated. In our study, blood transfusion had led to a significant increase in the rate of complication and fistula. Indeed, many authors had identified blood transfusions as an independent risk factor of major complications[30, 33] and supported the hypothesis that allogeneic blood transfusions induced immunosuppression that might increase the risk of infectious complications and leading to an extension of hospital stay.[34] Otherwise, in this study, transfused patients had a longer mean operation time than non-transfused patients (203.4 minutes vs183.82mn respectively, p=0.054), and the same results were also reported by Xiao et al.[34] and Ojima et al.[35] We also found that postoperative complication was correlated to the duration of surgical procedure and we stated that patients who developed an anastomotic fistula had a significantly longer operative time (238 min vs 190.77 min, p = 0.006) which is consistent with the results of the study of Migita et al.[5] who reported a significant correlation between anastomotic leakage and the duration of the surgical procedure (330 min vs 290 min, p = 0.0416) and the finding of Nakagawa et al. who reported that operating time exceeding 240mn was a risk factor for high-grade complications.[25]

Several intrinsic factors of postoperative morbidity of gastric cancer have been reported in the literature such as age, sex, nutritional status, and co-morbidities as well as tumor characteristics. The impact of gender and hormonal status on postoperative morbidity and mortality remains controversial. Although our results as well as those of Persiani et al.[27], Nakagawa et al.[25] and Lee et al.[36] did not support the correlation between gender and postoperative morbidity and mortality, the results of Critics trial[24] as well the 15-year results of the Dutch trial[37] have shown that men were exposed to a higher risk of post-operative complications and death. On the other hand, Sah et al. stated that women aged between 46 to 56 years were significantly predisposed to a higher risk of postoperative complications suggesting that hormonal instability related to menopausal status could result in a change of the host's response to stress and surgical trauma.[38]

Malnutrition can lead to the abnormal function of macrophages, neutrophils, and lymphocytes, which can inhibit the immune response and increase the surgical morbidity[39] and the incidence of major postoperative complications according to Clavien Dindo classification.[36] In the recent study by Zheng et al. including 1976 patients, the group of malnourished patients with hypoproteinemia (412 patients) had a significantly higher complication rate (21.4% vs 15.5%, p = 0.005).[40] Although we only recorded the level of proteinemia, we found that patients with hypoproteinemia had a higher rate of complications (28.8% vs 18.3%, p=0.066) and fistula (11.5% vs 4.3%, p = 0.168). Obesity (BMI> 25) is frequently associated with other co-morbidities such as diabetes, cardiovascular and respiratory diseases and according to The Japanese study by Ojima T, overweight patients had a longer duration of intervention and a higher rate of postoperative complications (anastomotic release, pancreatic fistula).[41] However, in our series, postoperative complications were not significantly increased in patients with a BMI greater than 20 kg/m2. These findings are comparable to those of several other studies which had not objectified a correlation between the weight of the patients and the specific surgical complications, and which had identified hypoalbuminemia as the only independent factor of morbidity.[25, 42]

Although in the studies by Persiani et al., Gil-Rendo et al., and Nakagawa et al., morbidity and mortality were correlated neither to age nor to co-morbidities and ASA score, but to the extensive surgery[25, 27, 43], other studies including that of Papenfuss reported that the implication of age as a factor of morbidity and mortality would most probably be related to the increased incidence of comorbidities with higher ASA score after 60 years and the alteration of the immune mechanisms.[30] In our series, the age of patients was not identified as a risk factor for morbidity even though we found that the average age of patients who died postoperatively was 75 years (range, 65-84 years). However, we found that postoperative complications were more frequent in the case of comorbidities with a higher rate of anastomotic fistula in diabetic patients and a longer duration of hospitalization. The predictive morbidity value of the ASA score in our study was similar to that of Lee et al. who reported a linear increase of surgical morbidity with ASA score without significant difference (19.5% for ASA1, 24% for the ASA2, and 31.4% if the ASA score was greater than or equal to 3; p= 0.088).[36]

Some authors had identified clinical and histological features of gastric tumors as intrinsic risk factors for postoperative morbidity. It has been reported that morbidity and mortality were higher in the upper and middle third gastric tumors.[43] On the contrary, in our study, there was no difference regarding postoperative morbidity according to the tumor location (p=0.424). However, intraoperative morbidity was found to be higher in the proximal, middle, and total gastric tumors compared to distal tumors and the tumor site represents an independent risk factor of intraoperative blood transfusion. Also, the operative time was significantly shorter in distal tumors compared to other locations. These findings were like those of Yu et al. and Liu et al. who suggested that the incrimination of the proximal tumor site in postoperative morbidity would be more related to larger resections and more difficult anastomosis with more blood transfusion and longer operative time and not to the tumor location itself.[44, 45]

The correlation between the risk of postoperative complications and the tumor size can be explained by the fact that large tumors are associated with increased surgical technical difficulties, an extension of the type of gastrectomy, and the need for multi-visceral resections.[33, 42] Contrariwise, in our study, we found no significant difference in terms of post complications according to the tumor size. However, when analyzing the specific surgical complications, we found that tumors larger than 50 mm were significantly associated to a higher rate of fistula and an increase of blood transfusion requirement which is supported by the finding of Wang et al. who divided 513 patients into four groups according to the tumor size (≤2, ≤3, ≤5,> 5 cm) and stated that the rate of postoperative complications was comparable between the four groups (p = 0.682) with a significant increase in blood transfusion with larger tumor (30% for sizes ≤2, 33.7%

for sizes ≤3, 46.3% for sizes ≤5 and 63.9% for sizes> 5 cm, p <0.001).[46] The majority of authors as well as our finding had not demonstrated a strong correlation between postoperative morbidity and tumor stage and the depth of parietal invasion even if locally advanced tumors would be particularly associated with larger resections and more frequent surgical difficulties.[23, 24, 26, 27] However, we stated that surgery of T3-T4 tumors was associated with an increase of the intraoperative morbidity which was assessed by a longer operative time and more frequent blood transfusion supporting the results of Ojima et al. and Zhou et al.[35, 47]

Our study has some limitations not only its retrospective nature and the small number of included patients but also a lack of evaluation of the predictive factors of surgical mortality because of the low number of postoperative deaths.

Conclusion

Our study was able to analyze the intraoperative morbidity by determining the factors influencing the operative time and the intraoperative transfusions and suggested that it depends not only on the extent of the surgery and particularly the multi-visceral resections and the extension of the lymphadenectomy but also on the tumoral characteristics. In addition, the use of the Clavien and Dindo classification allowed an objective assessment of postoperative morbidity that depends on the patient's terrain and the association of comorbidities and tumor characteristics. We also identified the predictive factors of an anastomotic fistula which represented the most severe complication. Moreover, the occurrence of complications and their grade was the determinant of the length of postoperative hospital stay. Further studies focusing on late complications, functional results, and quality of life are needed to improve the surgical outcomes.

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Further information is available from the corresponding author on reasonable request.

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JGS

COMPARATIVE STUDY OPEN ACCESS

The effect of ERAS management in gastric cancer: assessment from the IMIGASTRIC study

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ABSTRACT

Background:

Establish protocols to enhance the surgical management (ERAS) can improve outcomes, shortening hospital stay and save resources.

Several studies have carried out for colorectal surgery, while a lack of evidence for gastrectomy remains.

This study aims to evaluate the impact of ERAS strategies in a large series of patients underwent gastric cancer surgery.

Methods:

This is a propensity score-matched case-control study, comparing an ERAS group with a control group. Data were recorded through a tailored and protected web-based system. Primary outcomes: hospital stay, complications rate. Among the secondary outcomes, there are: POD of mobilization, POD of starting liquid diet and soft solid diet.

Results:

Patients in the ERAS and control groups were 1:1 matched by the closest propensity score on the logit scale and with a Caliber = 0.2. The successful matching resulted in a total sample of 440 patients.

The two groups showed no differences in all baseline patients characteristics, type of surgery (P=0.31) and stage of the disease (P=0.61).

A benefit in favor of the ERAS management was found in the length of hospital stay (P=0.0004) and complications rate (P=0.001).

Conclusion:

An ERAS program can safely be established in referral centers for gastric cancer, enabling to significantly improve the main clinical outcomes.

Key Words:

ERAS; Enhanced Recovery After Surgery; gastric cancer; gastric surgery; gastrectomy.

Background

Gastric cancer is the second leading cause of cancer death in the world and surgery plays the most important role in the treatment of this disease.

However, surgery for gastric cancer remains a high-risk procedure with clinically significant postoperative stress, complications, and significant sequelae.

Significant advances in the management of surgical patients have been in last decades for gastric cancer.

This has led to the concept of enhanced recovery after surgery (ERAS) with the objective of reducing the length of hospital stay accelerating postoperative recovery and reducing surgical stress.

The ERAS protocols have many items, including the pre-operative patient education, preoperative carbohydrate loading, early mobilization and feeding starting from the first postoperative days.

Most of studies on this field were published for colorectal surgery, while only few authors described ERAS protocols in gastric cancer surgery.

In the present study, we have evaluated the effects on postoperative functional recovery outcomes after gastrectomy in patients undergoing an ERAS program in comparison with a conventional surgical management.

Methods

Type of Study

This is a multi-institutional propensity score-matched case-control study, comparing patients undergoing a perioperative management based on the ERAS society principles (*Table 1*) and control patients undergoing conventional surgical management.

Data were collected in the context of the IMIGASTRIC study and after sharing a specific study protocol.[1]

The study was registered at clinical trials.gov with a registration number of NCT02325453.

Perioperative
• Education on the ERAS protocol administered;
• No routine use of mechanical bowl preparation;
• Allow oral meal intake until 6 hours before surgery;
• No routine use of nasogastric tube or abdominal drainage
• Maintain normal body temperature during surgery
• Antibiotic prophylaxis before skin incision without a postoperative prolonged use
Postoperative
• Avoid over-hydration and restricted fluid administration (20ml/kg/d) until full resumption of oral intake;
• Encourage early active ambulation from POD 1 (more than 2h/day);
• Remove urinary catheter as early as POD 1;
• Start early oral intake from POD 2;
• Evaluate patient recovery with discharge criteria to determine the discharge plan.

Table 1: ERAS management.

Time Period and Sites

Data entered into the IMIGASTRIC registry regarding procedures performed until data extraction (November 2019) were analyzed. All involved centers are referral institutions with a well-established gastric cancer program. All diagnostic and surgical interventions at these centers were done according to international guidelines and information stored in institutional prospective data collection systems.

Inclusion criteria

- Histologically proven gastric cancer
- Preoperative staging work-up performed by upper endoscopy and/or endoscopic ultrasound, and CT scan and in accordance to international guidelines
- Early Gastric Cancer[2, 3]
- Advanced Gastric Cancer[2, 3]
- Patients treated with curative intent in accordance to international guidelines[4, 5]

Exclusion criteria

- Distant metastases: peritoneal carcinomatosis, liver metastases, distant lymph node metastases, Krukenberg tumors, involvement of other organs
- Patients with high operative risk as defined by the American Society of Anesthesiologists (ASA) score > 4
- History of previous abdominal surgery for gastric cancer
- Synchronous malignancy in other organs
- Palliative surgery

Data Collection and Reported Outcomes

This study reported descriptive findings and outcomes among the two groups. Basic patient characteristics, tumor findings, and surgical procedure details were reported. The outcomes section offers a comparison regarding operative results, postoperative recovery, and complications.

Source of Data Analyzed

Data gathered were obtained from existing records, diagnostic tests, and surgical intervention descriptions. Data were collected and recorded by all institutions through a specific online shared protected system (https://imigastric.logix-software.it/).

The present study was reported in accordance with the STROBE guidelines and statement[6].

Propensity Score Matching

Propensity score matching analysis was carried out using SPSS software version 23 and R software version 3.1, through the Custom Dialog "PS Matching". Each patient's propensity score was calculated by a multivariable logistic regression model using the covariates of institution, age, sex, comorbidities, body mass index (BMI), surgical approach (open, laparoscopic, robotic) type of gastrectomy, stage of disease.

Patients in the ERAS and Control group were 1:1 matched by the closest propensity score on the logit scale and with a Caliper = 0.2

Statistics

IBM SPSS Statistics V.23 was used to carry out the statistical analysis. An intention to treat analysis was performed.

The dichotomous variables were expressed as numbers and percentages, while continuous variables as mean and SD, or median and IQR (minimum and maximum values). Continuous variables were compared using independent T test.

Pearson's $\chi 2$ test or Fisher's exact test, as appropriate, was used for analysis of categorical data. A P value of

<0.05 was considered statistically significant.

Results

At the time of this analysis, 1445 patients entered in the IMIGASTRIC registry had information on the ERAS management.

The matching analysis resulted in a total sample of 440 patients, 220 from the ERAS group and 220 from the Control group. The successful matching permitted to obtain a homogeneous distribution of all patient's characteristics (*Table 2*).

Table 3 shows no significant differences between groups in surgical approach (P=0.14), type of gastrectomy (P=0.31), stage of the disease (P=0.61).

A significantly shorter hospital stay (P=0.0004; *Figure 1*) was found in the ERAS group versus the Control group (*Table 4*).

The most relevant benefit was shown in the resumption of a liquid (P=0.01; *Figure 2*) and a soft solid diet (P=0.007; *Figure 3*).

No significant differences in patient mobilization (P=0.56) and first flatus (P=0.07) were found.

The ERAS group showed some advantages in the intravenous analgesic use (P<0.0001; *Figure 4*) than the control group, but no differences were found in the length of antibiotic use (P=0.31).

In this study the adoption of an ERAS protocol resulted in a significant reduction in post-operative complications (P=0.001) than the Control group.

Variable	ERAS	Control	P value
Total no.	**220**	**220**	
Age mean±SD	67.14±13.03	67.18±12.62	0.97
BMI mean±SD	24.00±4.18	24.14±3.04	0.69
Sex no. (%)			0.77
M	132(60)	128(58.2)	
F	88(40)	92(41.8)	
ASA no. (%)			0.93
I	50 (22.7)	51 (23.2)	
II	109 (49.5)	114 (51.8)	
III	61 (27.8)	55(25)	
Comorbidities no. (%)	145 (65.9)	147 (66.8)	0.46

Table 2: Basic patients' characteristics.

Variable	ERAS	Control	p value
Type of gastrectomy No. (%)			0.31
Distal	134 (60.9)	140 (63.6)	
Total	86 (39.1)	80 (36.4)	
Surgical approach No. (%)			0.14
Open	75 (34.1)	87 (39.5)	
MIS	145 (65.9)	133 (60.5)	
Tumor stage No. (%)			0.61
0	9 (4.1)	9 (4.1)	
IA	39 (17.7)	36 (16.4)	
IB	18 (8.2)	17 (7.7)	
IIA	29 (13.2)	32 (14.5)	
IIB	27 (12.3)	24 (10.9)	
IIIA	25 (11.4)	36 (16.4)	
IIIB	32 (14.5)	38 (17.3)	
IIIC	41 (18.6)	28 (12.7)	

Table 3: Surgical and pathological characteristics.

Outcome	ERAS	Control	p value
Intraoperative complications no. (%)	8 (3.6)	10 (4.5)	0.81
Intraoperative death no. (%)	0 (0)	0 (0)	1
Hospital stay (days) mean±SD	10.35±4.76	13.77±13.61	<0.001
Mobilization (days) mean±SD	2.37±1.91	2.65±6.92	0.56
Liquid diet (days) mean±SD	3.89±2.7	4.76±4.41	0.01
Solid diet (days) mean±SD	6.79±4.91	9.05±10.87	0.007
Peristalsis (days) mean±SD	2.55±1	2.59±1.13	0.67
First flatus (days) mean±SD	3.31±1.18	3.54±1.52	0.07
Antibiotic use (days) mean±SD	4.75±3.86	5.24±5.83	0.31
Analgesic use (days) mean±SD	2.82±1.35	4.34±2.76	<0.001
Complications no. (%)	18 (8.2)	43 (19.5)	0.001
Complications after discharge no. (%)	11 (5)	10 (4.5)	0.5

Table 4: perioperative outcomes.

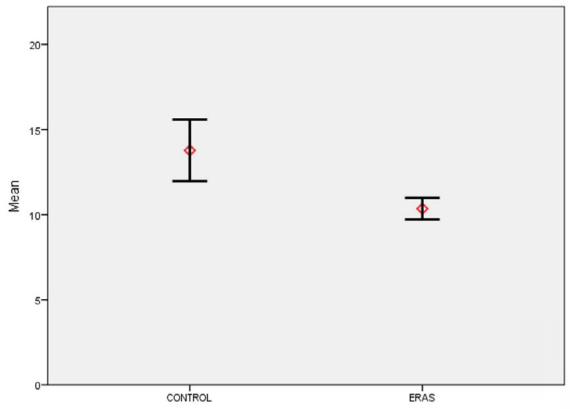

Figure 1: mean difference between groups in the length of hospital stay.

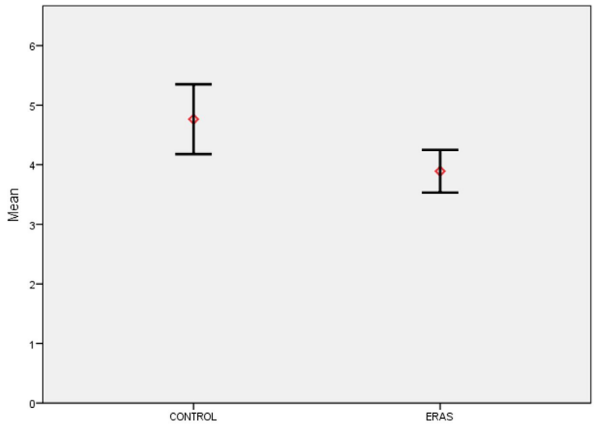

Figure 2: mean difference between groups in starting a liquid intake.

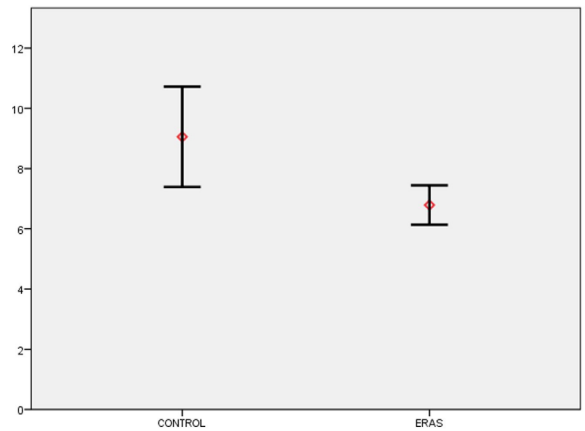

Figure 3: mean difference between groups in starting a soft solid diet.

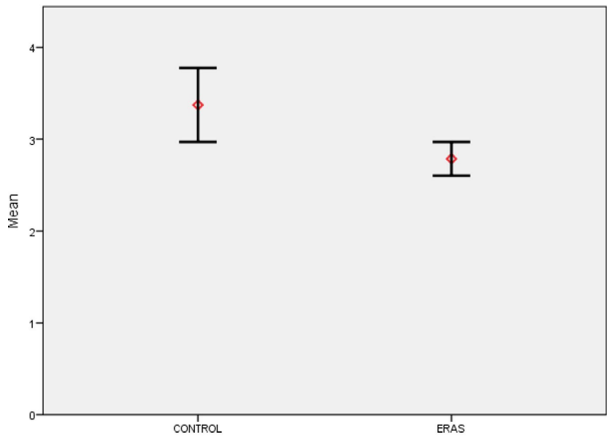

Figure 4: mean difference between groups in the length of intravenous analgesic use.

Discussion

The present study evaluated the role of the ERAS program in the management of gastric cancer patients using a propensity score case matched analysis to perform a comparison with a conventional care treatment.

A significant decrease in the length of hospital stay and in-hospital postoperative complications were the most relevant findings.

Important items in the ERAS protocol are early mobilization and feeding[7], which is especially facilitated by the absence of the NG tube and drainage, as well as an early removal of the urinary catheter. Smart[8] showed that failure of early patient mobilization is associated with prolonged hospital stay.

Yamada[9] in his study showed that the recovery of bowel function was significantly earlier in the ERAS group than in the conventional group.

In addition, Wang[10] reported that the first day of flatulence after gastric surgery was a mean of one day earlier in patients who received fast-track surgery compared to those who received conventional care.

Some factors such as prolonged fasting and placement of the nasogastric tube appear to cause nausea and contribute to a delay of intestinal recovery[11].

In our study, there was not a significant difference regarding the first flatus. However, we believe that this outcome is subject to a high risk of bias. Instead, variables regarding the oral recovery of food intake can be considered more reliable.

We found a significant advantage in favor of the ERAS group in all steps of food intake, from starting a liquid diet (3.89±2.7 vs 4.76±4.41; P<0.01) to the resumption of a solid diet (6.79±4.91 vs 9.05±10.87; P=0.007).

The ERAS protocols require the patient be not subjected to long periods of fasting.

Early postoperative nutrition reduces postoperative catabolism, accelerates the return of bowel function, and decreases the risk of complications. This was especially studied in colorectal surgery[12, 13].

Moreover, Lewis et al.[14] confirmed in their meta-analysis that keeping patients in a fasting state is not beneficial.

Several studies have shown that early oral feeding is feasible and brings benefits in gastric surgery[10, 15]; however, this point remains controversial.

Even if an early postoperative oral feeding has been shown to speed up the recovery after various types of surgery, this approach after gastrectomy has always been seen with suspicion because of some concerns, not actually well demonstrated in the literature, that early food intake may cause anastomotic leakage or intestinal obstruction.

In recent years, several studies have confirmed that early oral food intake after gastric surgery is safe and might be associated with enhanced recovery and shorter hospital stay[9, 16].

Particularly, a randomized controlled study has reported data on the safety of early oral feeding starting in the second postoperative day (POD 2) after gastrectomy[17].

The Makuuchi[18] and Pedziwiatr[19] studies, comparing ERAS and conventional management after gastrectomy, have confirmed that oral feeding in POD 2 is safe and allows the reduction of post-operative administration of intravenous fluids and an early discharge[20].

Sugisawa[21] focused on the rate of anastomotic leakage and aspiration pneumonia to evaluate the real risks of early nutrition.

In his study, the incidence of anastomotic leakage was 0.8%, a figure he highlighted as not only lower than that of the subjects in his historical cohort (1.7%), but also a result not different or lower (0.8-1.9%) when compared to previous data in studies in which conventional perioperative care was reported. Therefore, the author concluded that early oral nutrition is not able to adversely affect the anastomotic site. The same results were obtained by Yamada[9, 22], showing a similar incidence in anastomotic leaks (1.1%).

In our study, the adoption of an ERAS program resulted in a significant reduction in hospital stay with a mean difference of 3.42 days compared to conventional management.

Similar results were obtained by Sugisawa[21] and Wang[10].

In our study, a significant reduction in patients with postoperative complications (8.2% versus 19.5%; P=0.001) was shown in the ERAS group. Moreover, no differences in readmissions for complications after discharge were shown (P=0.5).

In conclusion, the adoption of a management based on the ERAS principles for gastric cancer can safely improve the patient's functional recovery, allowing an early discharge and a reduction of overall complications.

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Contributors

FG, FF, CC, MC, MP conceptualized and designed the study, acquired, and analyzed data, interpreted the study results, drafted the manuscript, and critically revised the final version of the manuscript.

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Competing interests
No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

Availability of data and materials
Further information is available from the corresponding author on reasonable request.

Ethics approval
This study is conducted in compliance with ethical principles originating from the Helsinki Declaration, within the guidelines of Good Clinical Practice and relevant laws/regulations. Trial registration number: NCT02325453.

Provenance and peer review
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JGS

CASE REPORT OPEN ACCESS

Laparoscopic adjustable gastric banding's multiple complications: when complications arise even after 30 years, a case report.

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ABSTRACT
Laparoscopic adjustable gastric banding (LAGB) is a popular bariatric surgical procedure. The introduction of laparoscopy has increased the use of this procedure, making it the most commonly performed bariatric surgery. Patients undergoing LAGB have achieved satisfactory results in terms of weight loss, a reduction in co-morbidities, and improved quality of life. Nonetheless, complications with LAGB are well documented and include migration, erosion, prolapse, infection, pouch dilation, gastric perforation, and most commonly, lack of weight loss following the failure of the procedure. This case report presents a patient with slippage and pouch dilation, erosion of the stomach, and port site problems, including infection, occurring 28 years after LAGB.

Keywords:
Laparoscopic adjustable gastric banding, LAGB, long-term complication, reoperation.

Background

Currently, obese patients are being offered an increasing number of treatment options, including bariatric surgery, a popular and viable therapeutic choice. Among the most frequently performed bariatric procedures, laparoscopic adjustable gastric banding (LAGB) has the lowest morbidity and mortality rates, despite being burdened with complications such as band slippage and erosion that often require revisionary surgery.[1] In this report, we describe the complex case of a 73-year-old female patient with a body mass index (BMI) of 41.6 kg/m2 who underwent LAGB in September 1992 and came to our attention 28 years later, presenting with fever, epigastric pain, and multiple LAGB-related complications, which necessitated laparoscopic removal.

Case Report

A 73-year-old Caucasian female presented to the emergency department feeling generally unwell and reporting fever and abdominal pain over the past 14 days. She had a history of pain, nausea, and vomiting. Her medical history was significant for severe obesity, with a BMI of 41.6 kg/m2, diabetes, hypertension, and LAGB 28 years prior. Upon examination, the patient had abdominal pain, especially in the epigastric region, and pain and redness from the LAGB port. Her laboratory results showed leukocytosis (16,000/mm3) and a C reactive protein level of 157 mg/L. A direct abdominal X-ray and routine gastrografin upper gastrointestinal series showed a slippage of the band. To rule out suspicion of erosion of the gastric wall, we carried out an abdominal CT scan, which came back positive for leakage, free air, and inflammation around the port. A laparoscopy was performed, and multiple adhesions, with evidence of inflammation, were seen in the upper abdomen, around the band, and between the stomach and the liver.

Initially, there was no visualization of the band; however, with blunt and gentle maneuvers, using the harmonic ace, we isolated the band and cut it off with scissors (*Figure 1*).

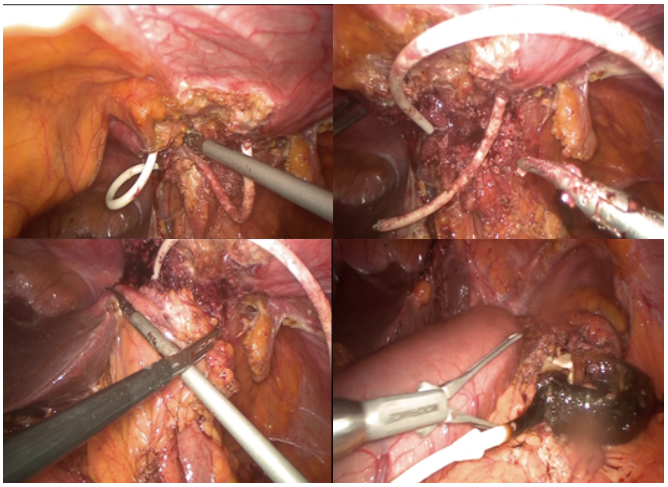

Figure 1: surgical steps for bandage removal: lysis of the adhesions between the stomach, liver, and abdominal wall.

During the maneuvers to remove the bandage, the presence of stomach erosion on the anterior wall was highlighted, and the breach was approached with forceps and sutured with a 45 mm endostapler using a load for thick tissues (*Figure 2*).

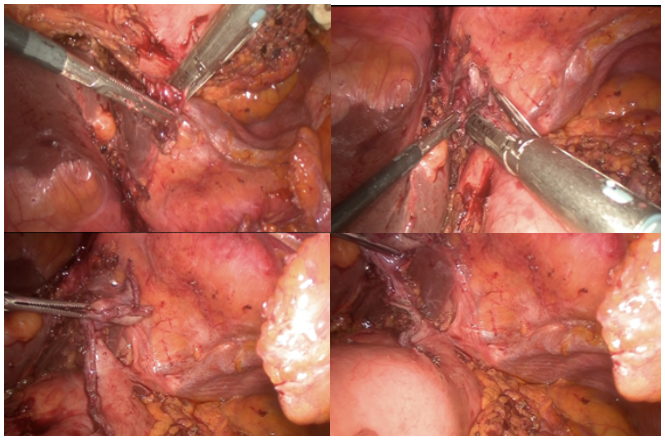

Figure 2: dissection around the gastric lesion and removal of the eroded tissue using a mechanical stapler.

A peri-gastric drain was placed and a nasogastric tube was left in place postoperatively. The operation lasted 50 minutes. There was no blood loss and no intra- or postoperative complications.

The nasogastric tube and drain were removed on postoperative day 2, and on postoperative day 3, the patient resumed oral intake, beginning with liquids. The patient was discharged from the hospital on postoperative day 5. At the postoperative control, no complications were seen after 1 month and 3 months.

Discussion

LAGB is a restrictive operation frequently performed on obese patients, together with laparoscopic sleeve gastrectomy.[1,2] For prolonged weight loss, bariatric surgery is currently the only effective treatment for obesity beyond lifestyle change and various drug treatments.[3] The first adjustable gastric band was implanted by Kuzmak in the 1980s using laparotomy. With the advent of laparoscopic surgery, providing a minimally invasive approach, LABG became an effective option to treat obesity.[4,5] The introduction of laparoscopy has increased the international popularity of LAGB, making it the most common bariatric surgery in the world.[6] Several studies have indicated how quickly patients lose weight over the years.[7-11] Most international studies have shown that weight loss occurs within two years of the procedure, with a peak in weight loss at 3–4 years.[7,12,13].

Patients undergoing LAGB have achieved excellent results in terms of quality of life, weight loss, and reduction in comorbid conditions.[14] Nonetheless, complications of LAGB are well documented in the literature.[10,12,15-17] Complications following gastric banding can be divided into band-related and port-related issues. If present, these complications can lead to the general failure of the procedure and make the patient susceptible to major infectious complications. Considering the long-term complication rate of 40% [18,19], in case of doubt regarding the onset of these complications, diagnostic investigations must be carried out. In the case examined, the patient had a

double problem: a band-related complication that had also caused a gastric lesion, and a port-related one for the pocket infection. The most common LAGB-related complications include pouch dilation (or enlargement) and band slippage, reported in 1–21% of LAGB patients. [20] In comparison, gastric prolapse, gastric obstruction, esophageal dilation, band erosion, gastric necrosis, and port problems represent less common complications. [14,20]

Other complications described include cholelithiasis/ cholecystitis, ventral hernia, dehydration, hemorrhage, pancreatitis, leak, and injury during the operation (liver hematoma/spleen injury).[10] Gastric necrosis is an extremely rare but potentially fatal complication of LAGB, typically developing because of prolapse, pouch dilation, or obstruction.[18] Overall, a complication incidence of 1.2% and a late reoperation rate of 12.5% have been reported.[11]

Conclusion

We presented a difficult case involving multiple complications related to LAGB, which necessitated laparoscopic removal. The complications were band-related and port-related: band slippage, gastric lesion, pocket infection, and trocar site hernia as well as the failure of the procedure in terms of a lack of weight loss. She was investigated for possible sources of sepsis. In conclusion, we advocate the need for careful follow-up for all patients with a history of LAGB who present with abdominal complaints, even though the band is correctly positioned. Whenever LAGB-related complications are suspected, patients should be monitored closely. If the symptoms persist or the pouch remains dilated, a prompt diagnostic operation should be performed to avoid more severe complications, such as gastric necrosis. To avoid complications related to LAGB, at the first abdominal symptoms, we suggest direct abdominal X-ray and a routine gastrografin upper gastrointestinal series for earlier identification and intervention in order to minimize morbidity and mortality in patients who develop a leak.[21] In case of suspicion of erosion of the gastric wall or suffering, perform an abdominal CT scan, searching for alteration of wall enhancement and intramural air density along the gastric wall or gastric pneumatosis. A plain radiograph can reveal if the band is oriented correctly or a gastric distention is evident. The success of the intervention and the avoidance of potentially serious complications also depend on the follow-up that this type of patient must undergo, which must be pursued even after many years, as in this case, the patient immediately stopped undergoing the band monitoring, leading to potentially fatal complications almost 30 years later.

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JGS

CASE REPORT OPEN ACCESS

A Case of Gastroesophageal Cancer after Laparoscopic Sleeve Gastrectomy

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ABSTRACT
Gastric cancer has been reported in relatively few cases after sleeve gastrectomy, which has become a common bariatric procedure. In this paper, we present a 58-year-old woman diagnosed with gastric cancer by esophagogastroduodenoscopy (EGD) 4 years after sleeve gastrectomy. For that, she underwent distal esophagectomy and total gastrectomy with Roux-en-Y esophagojejunostomy. Preoperative endoscopy is recommended before planning surgery in patients with gastroesophageal reflux symptoms. In addition, annual EGD should be considered after sleeve gastrectomy in patients with risk factors for gastric cancer.

Keywords:
Bariatric surgery, gastric cancer, sleeve gastrectomy.

Background

Obesity is a major cause of morbidity and mortality worldwide, including its reported risk for causing esophageal and gastric cancer.[1, 2] Bariatric surgery, in general, offers an efficient solution to reducing weight, with non-surgical therapy being ineffective in a large number of cases. Sleeve gastrectomy is a widely used procedure, with possible reported complications such as leakage, strictures, bleeding, nutrient deficiency, and gastroesophageal reflux disease (GERD).[3] However, relatively few cases of gastric adenocarcinoma post-sleeve gastrectomy were reported (to the best of our knowledge, 7 cases have been reported in English literature).

Case Report

The patient is a 58-year-old woman known to have hypertension, hypothyroidism, bronchial asthma, rheumatoid arthritis, and a history of GERD. She denied having a family history of gastrointestinal (GI) malignancy, and she has no history of smoking. She underwent laparoscopic sleeve gastrectomy in April 2016 in another institution; at that time, she had a body mass index (BMI) of 52 kg/m2. In October 2017, the patient presented with failure to reduce her weight beyond a BMI of 42 kg/m2. An esophagogastroduodenoscopy (EGD) was performed due to symptoms of GERD and iron deficiency anemia and showed a moderate hiatal hernia with mild reflux esophagitis (grade A, Los Angeles classification). In addition, a biopsy was taken from the patient's stomach, which showed chronic gastritis with the presence of Helicobacter pylori (H. Pylori) and no dysplasia or malignancy. The patient received treatment of H. Pylori and revisional surgery and hiatal hernia repair was planned to control her symptoms and her weight, but the procedure was not completed due to a long waiting list.

In January 2020, the patient underwent EGD due to progressive mild dysphagia to solid and liquid food over 4 months, which showed an ulcerated polypoid mass at the gastroesophageal junction 35cm from the incisors, with the rest of stomach and duodenum showing normal mucosa (*Figure 1*).

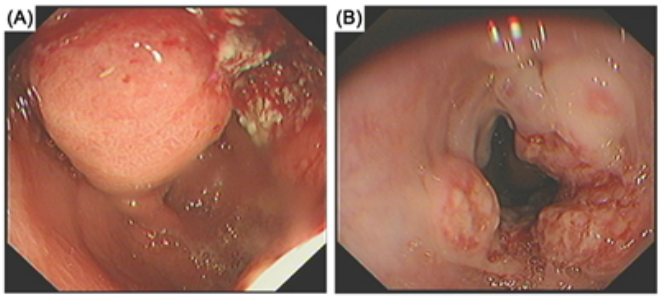

Figure 1: EGD showing polypoid mass on the gastroesophageal junction (A) with ulceration shown along the gastroesophageal junction (B).

A biopsy from the mass showed invasive moderately differentiated adenocarcinoma. The tumor markers were alpha-fetoprotein (AFP) <0.75 ng/mL, carcinoembryonic antigen (CEA) 3.5 ng/mL, carbohydrate antigen (CA-125) 13 U/mL, and carcinoid antigen (CA19-9) 57 U/mL. Staging computed tomography for the chest, abdomen, and pelvis (CT CAP) and positron emission tomography (PET-CT) showed hypermetabolic polypoid circumferential thickening involving the known herniated stomach with extension into the gastroesophageal junction associated with multiple gastrohepatic and left para-aortic lymphadenopathy (*Figure 2*).

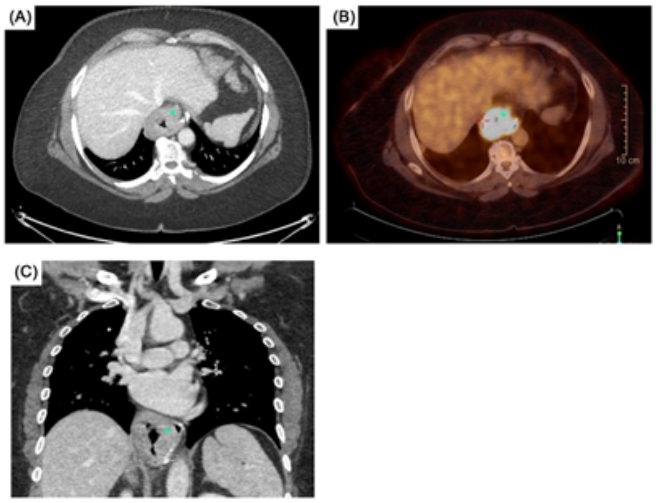

Figure 2: (A) Axial view of CT chest with asterisk showing the cancer, (B) PET-CT with asterisk showing the cancer with hypermetabolic activity, (C) Coronal view of CT chest with asterisk showing the cancer with hiatal hernia noted.).

The patient was taken for diagnostic laparoscopy with peritoneal lavage for staging, where the tumor was seen at the cardia of the stomach up to the gastroesophageal junction, with great omentum seeding visualized. A biopsy was taken, and the solid organs were intact with no ascites. The biopsy from the omental seeding showed no evidence of metastatic carcinoma. The cytology report from the peritoneal fluid showed scattered atypical cells and mucin, with degenerated mesothelial cells in a background of lymphocytes and red blood cells, which are signs of malignancy. The case was discussed during the multidisciplinary tumor board meeting, which planned for neoadjuvant chemotherapy. The patient started in 4 cycles (5-Fluorouracil, Leucovorin, Oxaliplatin, and Docetaxel) for approximately 8 weeks. The follow up after chemotherapy with PET-CT showed almost complete resolution of the mass with only mild gastroesophageal thickening showing minimal metabolic activity (*Figure 3*).

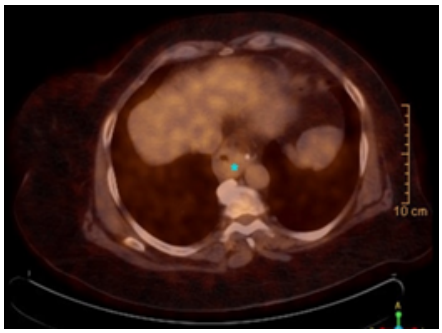

Figure 3: PET-CT, with asterisk showing almost complete resolution of the previously seen hypermetabolic gastroesophageal junction mass.

In June 2020, the patient underwent surgery, distal esophagectomy, and total gastrectomy with Roux-en-Y esophagojejunostomy and saw an uneventful recovery.

Final pathological staging (pT2 N1M0) showed no lymphovascular or perineural invasion, and all surgical margins were free.[4] The patient was discharged on day 11 post operation, after ensuring no leaks via an upper GI study.

Discussion

Gastric cancer is uncommon in Saudi Arabia.[5] Its incidence is decreasing worldwide due to the early detection and eradication of H.pylori infection, which is one of the most common independent risk factors.[6] In addition, there are multiple environmental and genetic factors. Hiatal hernia and GERD are considered significant risk factors for esophageal and gastric cardia adenocarcinoma, with an increase in fold when combined.[7] Nowadays, preoperative EGD is performed routinely before planning any bariatric surgery in our institution, although it is still debated and selective in many studies.[8] It is important to check for signs of gastritis, H.pylori, and dysplasia or masses before surgery, especially before gastric bypass since the patient's anatomy will be disturbed. Interestingly, there are reported cases of gastric cancer diagnosed after sleeve gastrectomy. Two cases have been reported to have GERD, which was the only underlying risk factor.[9, 10] Another two patients were known to have hiatal hernia, which was repaired during the sleeve gastrectomy.[11, 12] However, there was no H.pylori detected in those cases. The resected stomach during planned bariatric surgery is sent for histopathology in some cases and is typically unremarkable.[13] In this case, there were multiple risk factors ,including H.pylori infection, which was treated, hiatal hernia, persistent GERD, and obesity. There was an interval between the two EGDs done after the surgery, which could give rise to further degeneration. Another interesting aspect is to consider sending the resected stomach during sleeve gastrectomy for histopathology in such patients, as they are considered high risk.[14] It is worth pointing out that post-operative EGD might be necessary in high-risk patients, and it should be done annually after to detect any dysplasia or masses.[15]

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AAA, FA, AA, BA conceptualized and designed the study, acquired, and analyzed data, interpreted the study results, drafted the manuscript, and critically revised the final version of the manuscript.

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CASE REPORT OPEN ACCESS

Gastric carcinosarcoma with rhabdomyosarcomatous differentiation: a case report and literature review

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ABSTRACT
Gastric carcinosarcoma with rhabdomyosarcomatous differentiation is a rare tumor. Herein, we report the case of a 34-year-old man with a history of dysphagia, upper abdominal fullness, and poor appetite. Endoscopic findings showed a large friable mass that originated from the gastric cardia and lesser curvature of the high body. Consequently, radical total gastrectomy with Roux-en-Y esophagojejunostomy was performed. Histopathological analysis of the resected specimen revealed that the mass had invaded the serosa without regional lymph node metastasis; moreover, the tumor was positive for desmin and myogenin. Finally, we conclude this report with literature review and discussion.

Key Words:
Gastric tumor, gastric carcinosarcoma, rhabdomyosarcomatous.

Background

Carcinosarcoma is an uncommon biphasic malignant tumor composed of carcinoma and sarcoma components. In the upper gastrointestinal tract, carcinosarcoma is more frequently found in the esophagus; however, its gastric localization has been reported rarely.[1-3] The presentation of gastric carcinosarcoma with rhabdomyosarcomatous differentiation is even rarer, with only 12 cases reported thus far.[4-15]

Herein, we report the case of a male patient who developed gastric carcinosarcoma with rhabdomyosarcomatous differentiation and provide the clinical and histopathological features of this tumor. Moreover, we also review and discuss relevant literature.

Case report

A 34-year-old man had been experiencing dysphagia along with upper abdomen fullness and poor appetite for 2 months; he had lost 12 kg of body weight over the previous 6 weeks. Initially, he went visited a local clinic, where panendoscopy was performed; the results revealed a large (size, 4 cm) friable tumor, stretching from the cardia to the lesser curvature side of the high body (*Figure 1*). The tumor arose from the submucosal layer with infiltration to the mucosal layer. A biopsy sample was obtained and sent for pathological examination. The histopathological analysis confirmed the presence of malignancy with rhabdomyosarcomatous differentiation.

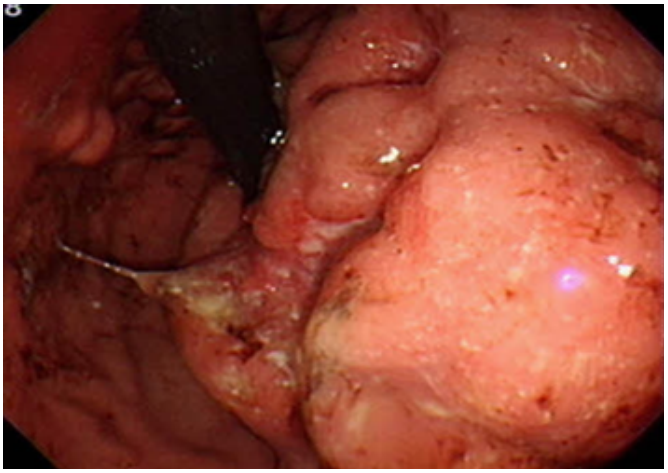

Figure 1: Panendoscopy revealed a tumor stretching from the cardia to the lesser curvature side of the high body.

The patient was referred to Cathay General Hospital for further evaluation. The levels of tumor markers CEA, CA19-9, and SCC were all within the normal range. Abdominal computed tomography (CT) revealed an irregular lobular mass, measuring approximately 7.5 × 6.5 × 8.5 cm3, stretching from the esophagogastric junction (EGJ) to the lesser curvature of the gastric high body, with at least three enlarged regional lymph nodes around the EGJ and lesser curvature of the stomach (*Figure 2A, 2B*). Nevertheless, chest CT revealed absence of pulmonary metastasis.

The patient subsequently received total gastrectomy with Roux-en-Y esophagojejunostomy (*Figure 3*).

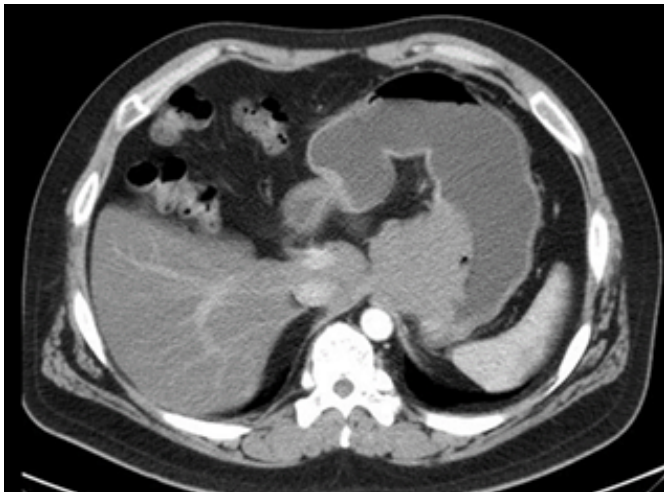

Figure 2A: Irregular lobular mass lesion stretching from the EGJ to the lesser curvature of the gastric high body.

Figure 2B: A 3 cm submucosal mass at distal esophagus, suspect regional lymphadenopathy.

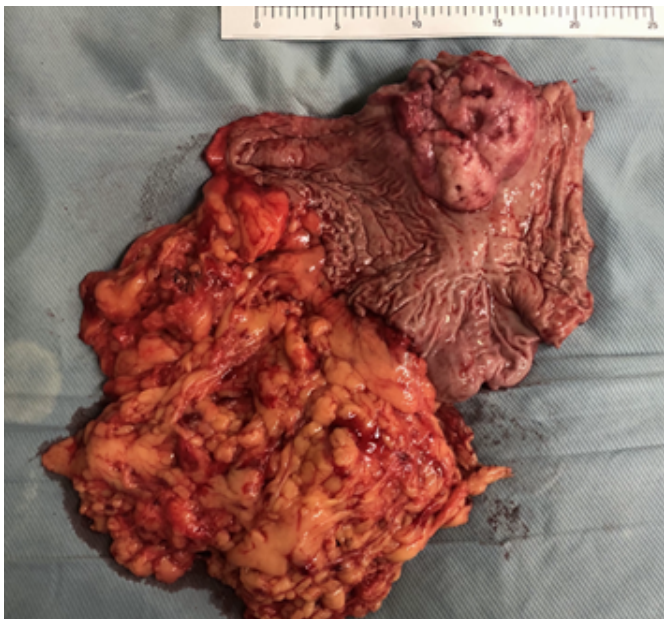

Figure 3: Polypoid tumor with central ulceration at the cardiac region

Macroscopic examination of the excised tissue revealed an 11.2 × 8.9 cm2 tumor mass, invading up until the serosa (*Figure 4*), but no lymph node metastasis was found. Histopathological examination revealed complex glandular formation with marked nuclear atypia and small, loose clusters of atypical cells, with indistinct to little eosinophilic cytoplasm and marked pleomorphic and hyperchromatic nuclei (*Figure 5*). Moreover, immunohistochemical analysis showed that the loose, atypical cells were positive for CK(AE1/3), myogenin, and desmin but negative for S-100, CD117, CD34, and CD45RB. Taken together, these results confirmed the diagnosis of gastric carcinosarcoma with rhabdomyosarcomatous differentiation, at a pathological stage of T4aN0M0 (Stage IIB).

Based on this diagnosis, the patient was administered six cycles of dacarbazine and doxorubicin for chemotherapy. Moreover, because the paraesophageal lymphadenopathy was inaccessible during surgery, the patient was also administered local radiotherapy, as suggested by our radiation oncologist.

Finally, owing to favorable recovery, the patient was discharged on the 14th postoperative day. At the 16-month follow-up, the patient did not show any evidence of recurrence.

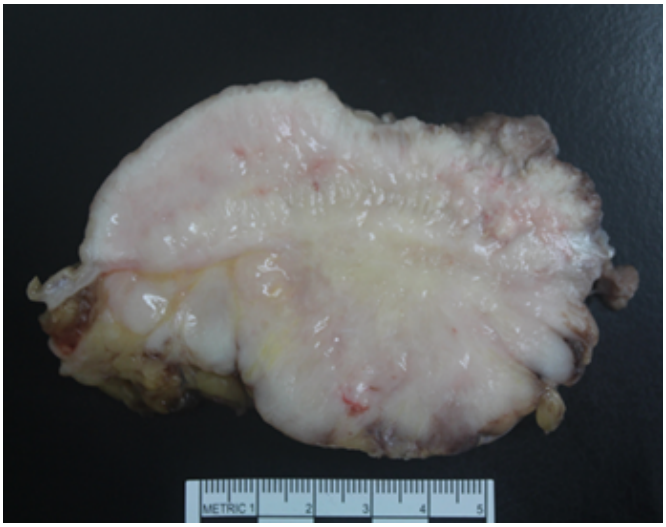

Figure 4: Tan-white and firm tumor invading from the mucosa to the serosa

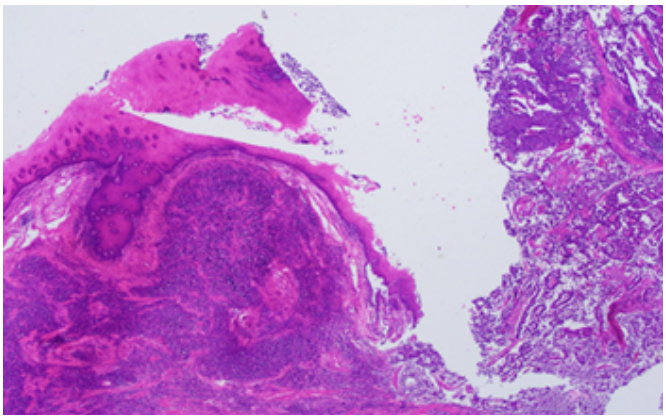

Figure 5A: Glandular structure and solid pattern.

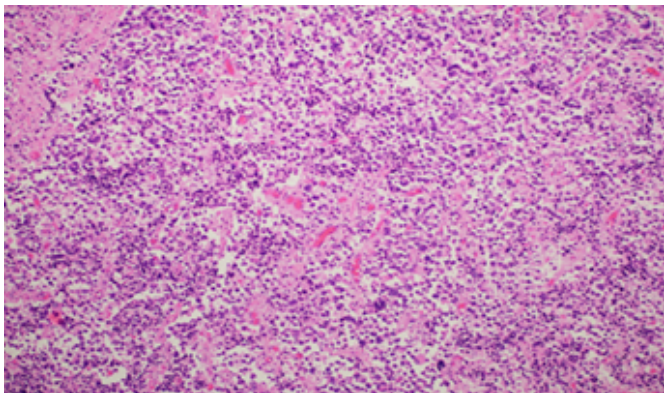

Figure 5B: Single neoplastic cells with marked pleomorphism.

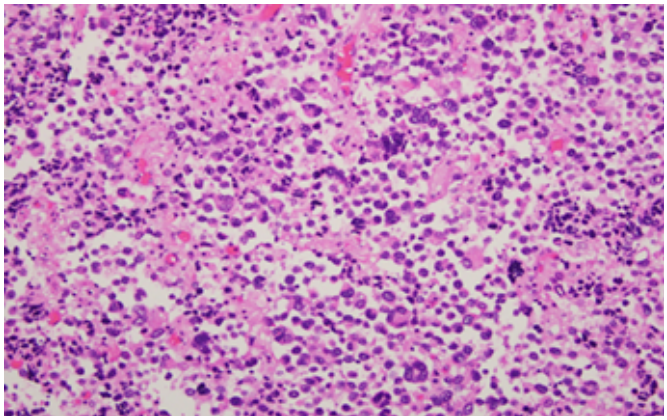

Figure 5C: Single neoplastic cells with marked pleomorphism, eosinophilic cytoplasm, and apoptosis.

Discussion

Based on the conventional histological findings, the World Health Organization defines carcinosarcoma as a malignant tumor composed of intimately mixed epithelial and mesenchymal elements of a type ordinarily found in malignancies of adults.[16] Carcinosarcoma can have a wide variety of localization sites, with the uterus being the most common site. However, as mentioned, localization in the stomach is rare. *Table 1* presents various features of gastric carcinosarcoma with rhabdomyosarcomatous differentiation included in all 12 relevant cases reported thus far.[5-15]

In all 12 cases, no clinical feature was associated with age, sex, or location. However, polypoid lesions were the most commonly reported.[17] The tendency of gastric rhabdomyosarcoma to metastasize to the lymph node and lungs is consistent with the observations of rhabdomyosarcoma originating from other sites.

The current gold standard technique for definitive diagnosis is based on immunohistochemical staining of endoscopic biopsy or on surgical findings. Radical gastrectomy is the treatment of choice when feasible, even when the tumor shows rapid growth and malignant potential. The therapeutic effects of chemotherapy or radiotherapy have not been reported thus far. Moreover, given that this condition is rare and is diagnosed at advanced stage in most cases, no applicable standard chemotherapy regimen is available yet.

Author	Age/sex	Location	Size (cm)	Gross Feature	Depth of invasion	Outcome
Stout (1953) [8]					Submucosa	
Kyogoku (1960) [4]	49/M					Dead, 36 mon
Matsukuma (1977) [9]	74/M	Remnant Stomach	15x11	Polypoid	Serosa	Dead, 5 mon
Machida (1981) [7]	39/F	Cardiac	7x6	Polypoid	Submucosa	Dead, 5 mon
Fox (1990) [10]	68/F	Body	15x10	Polypoid	Mucosa	Dead, 26 mon
Sugai (1991) [11]	78/M	Pylorus	9x7	Polypoid	Serosa	Dead, 5 mon
Melato (1993) [5]	73/M	Remnant Stomach	7x5.5	Polypoid	Serosa	
Nakayama (1997) [6]	69/M	Remnant Stomach	20x18	Polypoid		
Tsuneyama (1999) [12]	63/M	Pylorus	7x6.5	Polypoid	Subserosa	Alive,10 mon
Sato Y(2001) [13]	67/F	Fundus	8x7	Polypoid		Alive, 11 mon
Fujiie (2016) [14]	71/F	Body	2x1.5	Polypoid	Subserosa	Alive, 36 mon
Tokuda (2019) [15]	82/M	Body	8x8	Polypoid	Subserosa	Dead, 3 mon
Our case	34/M	Cardia	11x9	Polypoid	Serosa	Alive, 16 mon

Table 1: Reported cases of gastric carcinosarcoma with rhabdomyosarcomatous differentiation.

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TECHNICAL NOTE OPEN ACCESS

"Dovetail" gastric resection: a novel model in the treatment of gastrointestinal stromal tumors

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ABSTRACT
Gastrointestinal stromal tumors (GISTs) are the most common malignant subepithelial lesions of the gastrointestinal tract. The prognosis of this disease is associated with the tumor size and mitotic index. The standard treatment of a GIST without metastasis is surgical resection. The stomach is the most frequent site of the disease and many technical solutions have recently been proposed as shown also by the dramatic increase in publications on this field. There are many studies that suggest laparoscopy may be an acceptable surgical treatment option compared to open surgery for gastric GIST. However, open surgery assumes great importance in large tumors located in difficult-to-access locations. Here, we present a case involving a 60-year-old man who was diagnosed with gastric antrum GIST, according to a preoperative examination and postoperative pathology. Then, the patient successfully underwent an atypical gastric resection. We proposed a novel surgical technique to be considered in case of gastric benign disease or GIST localized at the gastric antrum.

Keywords:
Gastrointestinal stromal tumors, GIST, gastric resection.

Background

Gastrointestinal stromal tumors (GISTs) are the most frequent malignant subepithelial lesions of the digestive tract. Their origin is from the interstitial cells of Cajal located within the muscle layer and their main characteristic is an overexpression of the receptor tyrosine kinase KIT. The prognosis is associated with tumor size and mitotic index while standard treatment is surgical resection for non-advanced stages of disease. The surgeon's objective is to achieve the R0 resection with the largest possible free margin.[1] Laparoscopic surgery is a valid surgical treatment option compared to open surgery for gastric GIST.[2] It is possible to choose between an open surgery or a laparoscopic resection for gastric GIST in selected patients, especially for tumors less than 5 cm, or located on the anterior wall, greater curvature, less curvature. In these cases, laparoscopic surgery demonstrated better short-term outcomes than open resection.[3]

Large lesions located at the level of the anthro-pyloric region often need major resections. In this technical note, we propose a new gastric resection for giant GISTs of the gastric antrum as an alternative to Billroth I (B-I) and Billroth II (B-II) and Roux-en-Y (R-Y) reconstructions burdened by perioperative and postoperative effects.

Case Report

A 60-year-old male patient with a history of hypertension was admitted with the chief complaint of upper abdominal pain for 3 month; The pain abdominal distension, and discomfort that was accompanied by a sour regurgitation and weight loss. He had no family history of malignant tumors. Routine blood, routine urine, blood biochemical tests were normal, and the tumor marker test results were all within normal ranges. Gastroscopy revealed a giant smooth bulge covered with normal mucosa with a maximum diameter of 7 cm in the gastric antrum that indicated a probable stromal tumor (*Figure 1*).

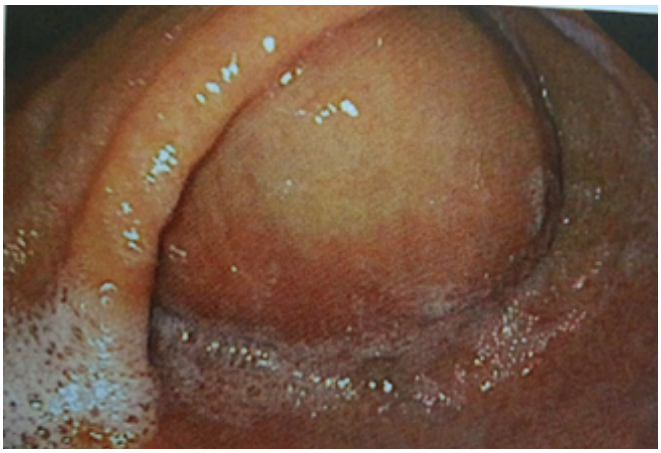

Figure 1: Gastroscopy revealed a giant smooth bulge covered with normal mucosa with a maximum diameter of 7 cm in the gastric antrum that indicated a probable stromal tumor.

Computed tomography confirmed the presence of this lesion in the gastric antrum, without adenopathy or liver metastasis. After multidisciplinary meeting, we suspected the diagnosis of stromal tumour and we decided to perform open surgery. The patient underwent laparotomy and we performed an atypical gastric resection (*Figure 2-3*).

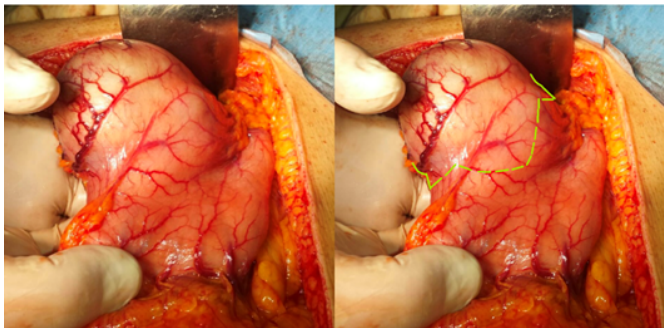

Figure 2: Neoplastic region and surgical resection.

Figure 3: Surgical specimen.

The post-operative course was uneventful. The patient recovered well and was discharged six days after his operation. The histopathology of the gastric fundus indicated GIST; features included spindleshaped cells, no significant atypia, signs of extensive necrosis, mitotic 5/50HPF . Immunohistochemistry demonstrated the following: CD117 (+), CD34 (+), SMA (+), S-100 (-), and vimentin (+) (*Figure 4*).

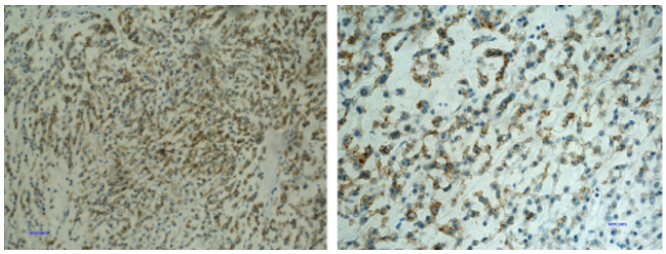

Figure 4: Cytoplasmic and membrane expression of CD117.

All margins were negative. The fragment of oment and the lymph nodes were unlawful. Combining these immunohistochemical results with the preoperative examination, intraoperative findings, and postoperative pathology, a diagnosis of gastric antrum GIST was made. The patient's prognosis, according with the tumor size and mitotic index, was an intermediate risk. Considering the prognosis, oral imatinib was administrated. The patient regularly underwent reexaminations with

gastroscopy and abdominal CT scan. There were no recurrences or distal metastases detected after 24 months of follow up.

Technical Note

A small incision was made between the xiphoid and umbilicus. First, an exploratory laparotomy was performed.

The greater omentum of the stomach was dissected from the middle portion of the transverse colon, exposing the posterior wall of the stomach and opening the lesser sac. The gastroepiloic artery and vein at the greater curve are ligated and transected, preserving the arcade vessels of the proximal part of the stomach. The access to the epiploon retrocavity allowed to control the integrity of the gastric wall. The omentum minus was opened along the lesser gastric curvature. The right gastric artery was exposed and its branches tied. Gastrotomy was performed on the antral side. The eversion of the anterior gastric wall revealed a giant smooth bulge covered with normal mucosa with a maximum diameter of 7 cm in the gastric antrum that indicated a possible stromal tumor. "Dovetail" gastric wall resection including the tumor was performed while maintaining a safety margin of at least 2 cm. This semi-circular resection of the anterior and posterior gastric wall, posteriorly partial, allowed the removal of the lesion. Lymphnodes stations #5 and #6 were also included. A termino-terminal anastomosis was performed between the wall of the gastric body and the proximal portion of the pylorus with manual suturing. A nasogastric tube was placed and then removed on the fourth post-operative day.

Discussion

The most effective treatment for gatric GIST is radical resection. This is still the only treatment option that provides the highest chance of medium to long-term overall and disease-free survival. Gastrointestinal reconstruction procedure options after distal or subtotal gastrectomy for patients with gastric disease are still controversial.[4]

The three possible reconstructions for patients with gastric cancer or benign gastric disease are reconstructions B-I and B-II, R-Y. However, patients undergoing B-I and B-II reconstruction often show reflux symptoms as a complication. On the contrary, the R-Y reconstruction is superior to the traditional B-I and B-II reconstructions in the prevention of reflux symptoms and in preventing gastritis that seems to increase the risk of gastric carcinogenesis. However, the R-Y is a more complex reconstruction and some patients show the delayed gastric emptying syndrome, known as Roux stasis syndrome. To avoid complications, some technical shrewdnesses are necessary as an adequate length of the alimentary limb.[5]

We proposed a novel atypical gastric resection technique for gastric antral GIST as an alternative to B-I, B-II and R-Y reconstructions that, as previously reported, are burdened by negative postoperative effects. The ideal reconstruction method should fit the patient's physical condition, reduce the risk of postoperative complications, and improve the patient's quality of life. The reconstruction method is often a matter of the surgeon's preference. We choose the reconstruction method on the basis of the tumor location. For this Gastric antrum GIST we prefer to do a semi-cicular "Dovetail" resection including the tumor, maintaining a safety margin of 2 cm. This resection strategy led to good functional results, such as increased food intake, post-operative body weight retention and no complaints of postprandial symptoms. The "Dovetail" method has the physiological advantage of allowing the food to pass through the duodenum, with a better effect on digestion and absorption of nutrients. The natural transition improves long-term nutritional status and quality of life. We suggest to perform this type of atypical resection for GISTs or benign gastric tumors involving the antrum that seems to be effective and safe with optimal clinical and oncological outcomes.

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DG, AAS, AB, VB, EC, LB, MT conceptualized and designed the study, acquired, and analyzed data, interpreted the study results, drafted the manuscript, and critically revised the final version of the manuscript.

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CORRESPONDENCE OPEN ACCESS

Gastric signet ring cell carcinoma

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ABSTRACT
Zemni I et al. reviewed clinic and pathological characteristics and outcomes of gastric signet ring cell carcinomas (J Gastric Surg 2020; 2(3):71-78) focusing on the major prognostic factors of progression-free survival and overall survival including hypoproteinemia, tumor size, stenosis, advanced stage, and recurrence. Most patients were males under 60 years of age. The data were compared with those of non-signet ring cell gastric carcinomas. There was no significant difference in the 5 years overall survival between the compared groups. The increasing incidence of aggressive tumors in an advanced stage with poor outcome is emphasized and additional comments are about gastric signet ring cell tumors that affected a female and an elderly male.

Key Words:
Gastric cancer, signet ring cell carcinoma, pathology, prognosis.

Dear Editor,

We read the article by Zemni et al. reviewing the clinic and pathological characteristics and outcomes of 36 cases of gastric signet ring cell carcinoma (SRCC) in Tunisia. [1] This group was compared to 109 patients with non-signet ring cell gastric carcinomas. The main prognostic factors of progression-free survival and overall survival in SRCC were hypoproteinemia, large tumor size with stenosis, advanced stage, and recurrence. The tumor sites were cardia (8.3%), fundus (33.3%), antrum (52.8%), and total organ (30.4%). The patients had 54.25 ± 11.49 years and 75% were under 60 years; 58.3% were males. More frequent manifestations were epigastric pain (94.9%), weight loss (86.1%), anorexia (80.6%), asthenia (77.8%), vomiting (41.7%), and bleeding (11.1%). The median postoperative follow up was 35.3 (2-139) months, without significant difference in the 5 years overall survival between the SRCC and the non-SRCC. The authors emphasized the current increasing incidence of this aggressive subtype characterized by advanced stage and worse survival outcome than the non-SRCC.[1]

In this setting, two additional comments seem adequate to enhance awareness of non-specialists working in primary health attention about the gastric malignant tumors. A 40-year-old woman presented headache, dizziness, vomiting, mental confusion, ecchymosis, epistaxis, metrorrhagia, melena, anisocoria, as well as nuchal stiffness.[2] Tomography images of the brain revealed a chronic right parietal subdural hematoma managed by surgical drainage, but the clinical condition evolved to irreversible shock. Autopsy studies detected unsuspected cancer measuring 3.0 cm at the gastric antrum. There was marantic endocarditis, metastases (lungs, liver, bone marrow, lymph nodes, kidney, pancreas, thyroid, uterus, ovaries, adrenals, and meninges). Worthy of note were disseminated ring signet cells of gastric tumor that caused meningeal vessels leak.[2] The authors highlighted the origin of Trousseau's syndrome in mucin-producing cancer. A 71-year-old man presented fever, dyspnea, hemoptysis enterorrhagia and melena, and had diagnoses of a malignant sigmoid polyp, Saint's triad, and Heyde syndrome.[3] Besides, the endoscopic biopsy of an antral lesion revealed a gastric signet-cell tumor. In the preoperative period, he suddenly died, and the autopsy study was not authorized. The role played by Trousseau's syndrome in the causa mortis was strongly considered; however, the hypothesis of a paraneoplastic thromboembolic event was not confirmed. The authors commented on the concomitance of two cancers with the Saint's triad, which disagrees with the hypothesis of an inverse relationship between these conditions.

The three manuscripts herein briefly mentioned may propitiate more awareness about gastric cancers in special, with an increased interest in the possibility of paraneoplastic phenomena associated with other mucin-producing malignancies. Another concern is related to the decreasing rate of autopsies in the last years, with a consequently increased number of diagnostic pitfalls, under-diagnosis, or misdiagnosis.

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