Original article

Complications of gastrectomy with lymphadenectomy in gastric cancer

BRUNO ZILBERSTEIN, BRUNO DA COSTA MARTINS, CARLOS EDUARDO JACOB, CLÁUDIO BRESCIANI, FÁBIO PINATEL LOPASSO, ROBERTO DE CLEVA, PAULO ENGLER PINTO JUNIOR, ULYSSES RIBEIRO JUNIOR, RODRIGO OLIVA PEREZ, and JOAQUIM GAMA-RODRIGUES

Department of Gastroenterology, University of São Paulo School of Medicine, Av 9 de Julho 4440, São Paulo, SP 01406-100, Brazil

Abstract

Background. Currently, gastrectomy and extended lymphadenectomy (LN) is the treatment of choice for gastric cancer. Although a survival rate benefit of D2 LN compared to D1 LN has been shown, the D2 LN procedure is not fully employed, due to possible higher morbidity and mortality rates. These higher rates are being questioned in more recent series, in which D1 and D2 LN complication rates have been similar. The aim of this study was to analyze the immediate postoperative complications of patients submitted to total or subtotal gastrectomy with D1 or D2 LN (according to the Japanese guidelines for gastric cancer) at the Gastrointestinal Surgery Division of the Medical School of São Paulo University, between January 2001 and April 2003.

Methods. One hundred consecutive patients were studied; 61 were men and 39, women. Total gastrectomy was performed in 52 patients (13 with D1 LN and 39 with D2 LN), and subtotal gastrectomy was performed in 48 (11 with D1 LN and 37 with D2 LN). Total or subtotal gastrectomy with D1 or D2 LN was performed according to the tumor extent and histological classification (Lauren's diffuse or intestinal type), considering the patient's general condition and the gastric cancer stage. Roux-en-Y reconstruction was performed in almost all patients.

Results. No difference was observed regarding complications and mortality related to the extent of the gastrectomy. Although morbidity was higher in the D1 group, no significant difference was observed. Mortality was higher in the D1 group, and this was probably related to their poor surgical condition and more advanced tumors.

Conclusion. According to these results, it appears that total or subtotal gastrectomy with D2 LN in gastric cancer treatment, performed according to the Japanese guidelines, can be considered a safe procedure, with acceptable morbidity and mortality, when performed by a trained surgical team.

Key words Gastric cancer · Lymphadenectomy · Gastrectomy · Complications

Introduction

Gastric cancer remains one of the most common tumors worldwide, with significant mortality rates [1].

Radical resection with free-margin gastrectomy and extended lymphadenectomy (LN) is the preferred surgical strategy in Asian centers. The extension of the lymph node resection is associated with better survival rates, and D2 LN seems to be superior to D1 [2–5]. However, D2 resection can be associated with higher morbidity and/or mortality rates [6,7]. These results, attributed to the extended lymph node resection, could be related to the surgical team's experience, as well as their learning curve and knowledge in regard to complications of treatment. It is possible, therefore, that D1 and D2 may have similar morbidity and mortality rates, and this would enhance the beneficial effects of D2 [8–10].

The aim of this study was to analyze the impact on morbidity and mortality of D2 LN when compared with D1 LN in patients with GC submitted to total or subtotal gastrectomy at our Institution during the past 3 years.

Patients and methods

Between 2001 and 2003, 100 consecutive patients submitted to gastrectomy for gastric adenocarcinoma were studied. There were 61 men and 39 women. The median age was 61.5 ± 13.1 years, ranging from 33 to 87 years. Twenty-nine patients (29%) had an early gastric cancer, confirmed by postoperative histological examination, and 71 patients (71%) had an advanced cancer.

The indication for performing either total or subtotal gastrectomy was based on tumor location and surgical tumor-free margins. Proximal surgical margins were determined according to the Japanese Gastric Cancer

Table 1. Patient distribution according to extent of lymphadenectomy

Parameters	D1 (<i>n</i> = 24)	D2 (<i>n</i> = 76)	<i>P</i> value
Sex			
Male	16	45	0.3 ^a
Female	8	31	
Mean age; years (SD)	61.8 (± 22)	61.5 (± 12.3)	0.9852 ^b
Type of operation			
STG	11	37	0.8074 ^a
TG	13	39	
Type of reconstruction			
Roux-en-Y	23	74	0.23 ^a
B II	1	2	
Resection of other organs	3	13	0.25 ^b
Mean surgical time; min (SD)	381 (± 116)	412 (± 86)	0.26 ^b
Mean anesthetic time; min (SD)	464 (± 127)	493 (± 87)	
Patients with transfusion	18	43	0.10 ^a
Complications	24	76	0.22 ^a
Number of patients with complications	11 (45.8%)	21 (27.6%)	0.09 ^a
Mean number of dissected lymph nodes (SD)	29 (± 15.5)	46 (± 18.7)	0.004 ^{b*}
T			
T1	3	26	0.0183 ^a
T2	3	14	
T3	14	34	
T4	4	2	
N			
N1	8	23	0.25 ^a
N2	4	13	
N3	5	3	
M			
M0	21	74	0.0531 ^a
M1	3	2	
Stage			
Ia	1	24	0.0686 ^a
Ib	2	9	
II	5	13	
IIIa	5	11	
IIIb	5	14	
IV	5	5	

TG, Total gastrectomy; STG, subtotal gastrectomy

* Statistically significant

^a χ^2 test^bStudent's *t*-test

Association (JGCA) recommendations considering the histological type (Nakamura's differentiated or undifferentiated and/or Lauren's intestinal or diffuse type). For differentiated/intestinal-type tumors, a surgical margin of at least 5 cm was observed, and the surgical margin was at least 10 cm for undifferentiated/diffuse-type tumors. Subtotal gastrectomy was performed in 48 patients (D1 LN in 11, and D2 LN in 37). Total gastrectomy was performed in 52 patients (D1 LN in 13, and D2 LN in 39; Table 1).

D2 lymphadenectomy was performed according to the Japanese Research Society for the Study of Gastric Cancer (JRS GC) guidelines. D1 lymphadenectomy was performed only in patients with severe comorbidities or in patients with early gastric cancer with minimal tu-

mors and low probability of lymph node metastasis according to the Japanese criteria. There were 76 D2 LN resections and 24 D1 LN resections. The mean number of dissected lymph nodes was 29 ± 15.5 in D1 LN and 46 ± 18.7 in D2 LN (Table 1).

Roux-en-Y reconstruction was employed in 97 patients, and Billroth II (B II) in 3.

Postoperative complications were studied, considering the extent of the gastric resection and extent of the LN; with analysis of mean surgical and anesthetic times, necessity for transfusion, associated resected organs, mean number of dissected and metastatic lymph nodes, and tumor stage (TNM). The statistical analysis was performed utilizing the χ^2 test and Student's *t*-test, with 95% confidence intervals.

Table 2. Patient distribution according to occurrence of complications

Parameters	Complications (<i>n</i> = 33)	No complications (<i>n</i> = 67)	<i>P</i> value
Mean age; years (SD)	65.3 ($\pm$ 12.4)	59.7 ($\pm$ 13.2)	0.03 ^b
Type of operation			
STG	12	35	0.1347 ^a
TG	21	32	
Type of lymphadenectomy			
D1	10	14	0.22 ^a
D2	23	53	
Type of reconstruction			
Roux-en-Y	32	65	0.8604 ^a
B II	1	2	
Resection of other organs	9	7	0.0309 ^{a*}
Mean surgical time; min (SD)	409 ($\pm$ 86)	402 ($\pm$ 95)	0.9396 ^b
Mean anesthetic time; min (SD)	486 ($\pm$ 87)	486 ($\pm$ 95)	1.0000 ^b
Patients with transfusion	22	39	0.26 ^a
Mean number of dissected lymph nodes (SD)	45.2 ($\pm$ 27)	41.1 ($\pm$ 16)	0.28 ^a
Mean number of metastatic lymph nodes (SD)	5.6 ($\pm$ 13.2)	5.7 ($\pm$ 11)	0.9932 ^b
T			
T1	9	20	0.8153 ^a
T2	6	11	
T3	15	33	
T4	3	3	
Early	9	20	0.7893 ^a
Advanced	24	47	
N			
N1	10	21	0.9731 ^a
N2	6	11	
N3	2	6	
N+	18	38	0.8371 ^a
N0	15	29	
M			
M0	32	63	0.5259 ^a
M1	1	4	
Stage			
Ia	7	19	0.7912 ^a
Ib	5	6	
II	7	11	
IIIa	5	11	
IIIb	7	12	
IV	2	8	

TG, Total gastrectomy; STG, subtotal gastrectomy

*Statistically significant

^a χ^2 test^bStudent's *t*-test

Results

The results are presented in Table 1 (patient distribution according to the extent of LN), Table 2 (patient distribution according to occurrence of complications), and Table 3 (postoperative complications and mortality rates according to extent of the LN).

Of the 24 patients with D1 LN, 5 developed respiratory complications (20.8%), which were treated with antibiotics and ventilatory support, with full recovery in

3 of them and two deaths. Three patients developed anastomotic leakage. One of these patients had a duodenal stump fistula, which was treated by conservative management. One of the other two patients developed an esophagojejunal fistula, and the other patient had a gastrojejunal fistula; both died of abdominal sepsis. The overall morbidity rate was 45.8%. Fatal outcomes were observed in 5 patients (20.8%) (Table 3).

Of the 76 patients with D2 LN, 5 developed respiratory complications (6.5%), which were treated by anti-

Table 3. Postoperative complications and mortality rates according to extent of lymphadenectomy

	D1 (<i>n</i> = 24)	D2 (<i>n</i> = 76)	χ^2 value	Total (<i>n</i> = 100)
Leakage	3 (12.5%)	5 (6.5%)	0.3513	8 (8%)
Cavitary abscess	0	7 (9.2%)	0.1231	7 (7%)
Respiratory complications	5 (20.8%)	5 (6.5%)	0.0424*	10 (10%)
Acute renal failure	0	4 (5.2%)	0.2513	4 (4%)
Total no. of patients	11 (45.8%)	21 (27.6%)	0.0956	32 (32%)
Mortality	5 (20.8%)	3 (3.9%)	0.0078*	8 (8%)

*Statistically significant

biotics and ventilatory support, with full recovery in 4, and one death, which was associated with abdominal sepsis due to jejunostomy leakage. Five patients (6.5%) developed anastomotic leakage (4 due to duodenal stump fistula and 1 due to esophagojejunal fistula), which was managed conservatively in 4 patients and surgically in 1 patient (duodenal stump fistula). Seven patients (9.2%) developed cavitary abscesses, mostly in the left subphrenic space. Four were treated conservatively with drainage and antibiotics, and 3 were operated, with one death. The overall morbidity rate was 27.6%. Fatal outcomes were observed in 3 patients (3.9%) (Table 3).

The incidence of complications was higher in the D1 LN group, but this difference was not statistically significant ($P = 0.09$). When complications were considered individually, respiratory complications were the only ones that reached a statistically significant difference between the D1 LN and D2 LN groups ($P = 0.04$). Although seven patients in the D2 LN group had cavitary abscesses and in the D1 LN group none, had this complication, the difference was not statistically significant ($P = 0.12$).

Also, associated resection of other organs showed an important correlation with morbidity, independently of the extent of the LN or the gastrectomy (Table 2).

Mortality rates were significantly higher in patients treated by D1 LN (20.8%) when compared to D2 LN (3.9%).

Discussion

Extended LN was introduced in Japan in late 1960, for the treatment of gastric cancer, and has been shown to be associated with better overall survival [11,12]. Since that time, this procedure has been well accepted in Japan and is currently the procedure of choice for the treatment of gastric cancer in Japan.

In the Western world, an early review of 1983 patients with gastric cancer treated by extended lymphadenectomy, reported by Gilbertsen [13], showed no beneficial

effect on overall survival rates. These results led several centers in the West to abandon this procedure as the preferred treatment strategy.

Advances in intensive care, anesthesiology, and perioperative procedures have significantly reduced the morbidity and mortality rates associated with major gastric operations [5,14,15]. Furthermore, the excellent results obtained in Japan with extended LN for the treatment of gastric cancer [16] have led to several studies that have compared survival, and morbidity and mortality rates associated with different LN procedures.

In the Netherlands, a randomized multicenter study was performed between 1990 and 1993, including 33 hospitals and 70 surgeons [6]. Higher morbidity and mortality rates were observed in the group of patients treated by D2 LN. However, in this study, there was significant heterogeneity in surgical techniques leading to inadequate lymph node dissection, i.e., the resection of lymph nodes that were not supposed to be removed, or the missing of those that were supposed to be removed [11]. Similar results were observed in the United Kingdom in prospective and randomized trials [7].

In both the above studies [6,7], the higher mortality and morbidity rates in patients treated by D2 LN were closely related to postoperative complications associated with splenectomy and distal pancreatectomy [7,10,17].

In Germany, 1654 patients treated for gastric cancer were studied between 1986 and 1989. Patients treated by D2 LN had at least 25 lymph nodes removed, and those in stages II and IIIa showed better overall survival than patients treated by D1 LN. Morbidity and mortality rates were similar in both groups, independent of the LN extent [4]. In the United States, similar results were observed. Furthermore, mortality rates associated with D2 LN were as low as 1.6% [10].

Several studies have shown that other factors can be related to an unpleasant outcome after gastrectomy for gastric cancer, and that they be even more important than the LN extent; for example, splenectomy or associated organ resection [10,18–20], as shown in this study.

Table 4. Differences in morbidity and mortality rates in patients submitted to gastric resection for gastric cancer at several centers worldwide

	Morbidity		Mortality	
	D1	D2	D1	D2
Bonenkamp et al. [6] 1995	25%	43%	4%	10%
Cuschieri et al. [7] 1996	28%	46%	6.5%	13%
Siewert et al. [4] 1993	28.9%	30.5%	5.1%	5%
Smith et al. [5] 1991	35%	44%	0	1.6%
Jentschura et al. [8] 1997	—	25.7%	—	7.5%
Roviello et al. [9] 2002	—	17%	—	2%
NCC — Tokyo [2] 1993	—	—	0.5%	1%
This study	45.8%	27.6%	20.8%	3.9%

The higher morbidity and mortality rates observed in our patients treated by D1 LN could be explained by their poor medical condition, which determined the choice of a limited surgical procedure. It must also be considered that, in this group, there were only three patients with early gastric cancer; therefore, most patients in this group had advanced disease, thus enhancing the poor results.

D2 LN was performed in most of the patients, reflecting our standard procedure following the Japanese guidelines. The good postoperative outcome was probably related to a good selection of patients, and also to a standardized pattern of lymph node dissection. For differences in the morbidity and mortality rates of patients submitted to gastric resection for gastric cancer in several centers worldwide, see Table 4.

Conclusion

In conclusion, the extended LN dissection (D2) in this study was not associated with higher morbidity and mortality rates than the D1 procedure. Therefore, the D2 procedure can be strongly considered in the surgical strategy for curative gastric cancer management.

It is noteworthy that the mortality and morbidity rates after D2 LN were lower than those reported in the Western literature [6,7]. This could be explained by our extensive experience with the Japanese lymph node dissection method, achieved at our institution in the past 30 years.

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