

RESULTS OF D2 GASTRECTOMY FOR GASTRIC CANCER: LYMPH NODE CHAIN DISSECTION OR MULTIPLE NODE RESECTION?

Resultados da gastrectomia D2 para o câncer gástrico: dissecação da cadeia linfática ou ressecção linfonodal múltipla?

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ABSTRACT – Background - Eastern literature is remarkable for presenting survival rates for surgical treatment of gastric adenocarcinoma superior to those presented in western countries. **Aim** - To analyze the long-term result after D2 gastrectomy for gastric cancer. **Methods** - Two hundred seventy four underwent gastrectomy with D2 lymph node dissection as exclusive treatment. The inclusion criteria were: 1) lymph node removal according to Japanese standardized lymphatic chain dissection; 2) potentially curative surgery described in medical records as D2 or more lymph node dissection; 3) tumoral invasiveness of gastric wall restricted to the organ (T1 –T3); 4) absence of distant metastasis (N0-N2/M0); 5) a minimum of five years follow-up. Clinical pathological data included sex, age, tumor location, Borrmann's macroscopic tumor classification, type of gastrectomy, mortality rates, histological type, TNM classification and staging according to UICC TNM 1997. **Results** - Total gastrectomy was performed in 77 cases (28.1%) and subtotal gastrectomy in 197 (71.9%). The tumor was located in the upper third in 28 cases (10.2%), in the middle third in 53 (19.3%), and in the lower third in 182 (66.5%). Among patients that had their Borrmann's classification assigned, five cases (1.8%) were BI, 34 (12.4%) BII, 230 (84.0%) BIII and 16 (5.9%) BIV. Tumors were histologically classified as Laurén intestinal type in 119 cases (43.4%) and as diffuse type in 155 (56.6%). According to UICC TNM 1997 classification, early gastric cancer (T1) was diagnosed in 68 cases (24.8 %); 51 (18.6%) were T2, and 155 (56.6%) were T3. No lymph node involvement (N0) was observed in 129 cases (47.1%), whereas 100 (36.5%) were N1 (1-6 lymph nodes), and 45 (16.4%) were N2 (7-15 lymph nodes). The median number of lymph nodes dissected was 35. The overall long-term (five-year) survival rate, for stages I to IIIb was 70.4%. **Conclusion** - Digestive surgeons must be stimulated in performing D2 gastrectomies to avoid wasting the only treatment to gastric adenocarcinoma that has proven to be efficient up to this days. It must be emphasized that standardized lymph nodes dissection according to tumor location is more important that only the number of removed nodes.

HEADINGS - Gastric neoplasm. Surgery. Gastrectomy.

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RESUMO – Racional – A literatura oriental é notável por apresentar taxas de sobrevivência para o tratamento cirúrgico do adenocarcinoma gástrico superiores às aquelas apresentadas nos países ocidentais. **Objetivo** - Analisar o resultado a longo prazo após a gastrectomia D2 por câncer gástrico. **Métodos** - Duzentos e setenta e quatro pacientes foram submetidos à gastrectomia com dissecação linfonodal D2 como tratamento exclusivo. Os critérios de inclusão foram: 1) remoção dos linfonodos de acordo com dissecação linfática padronizada Japonesa, 2) operação potencialmente curativa descrita no prontuário como dissecação D2 ou mais linfonodos; 3) invasão tumoral da parede gástrica restrita ao órgão (T1-T3); 4) ausência de metástases à distância (N0-N2/M0); 5) mínimo de cinco anos de acompanhamento. Dados clinicopatológicos incluíam sexo, idade, localização do tumor, classificação de Borrmann do tumor macroscópico, o tipo de gastrectomia, as taxas de mortalidade, tipo histológico, classificação e estadiamento TNM de acordo com a UICC TNM 1997. **Resultados** - Gastrectomia total foi realizada em 77 casos (28,1%) e subtotal em 197 (71,9%). O tumor foi localizado no terço superior em 28 casos (10,2%), no terço médio em 53 (19,3%), e no terço inferior em 182 (66,5%). Borrmann foi atribuído cinco casos (1,8%) como BI, 34 (12,4%) BII, 230 (84,0%) BIII e 16 (5,9%) BIV. Os tumores foram histologicamente classificados como Laurén tipo intestinal em 119 casos (43,4%) e

como o tipo difuso em 155 (56,6%). De acordo com a UICC TNM foram câncer gástrico precoce (T1) foi diagnosticada em 68 casos (24,8%); 51 (18,6%) T2 e 155 (56,6%) T3. Nenhum envolvimento linfonodal (N0) foi observado em 129 casos (47,1%), enquanto 100 (36,5%) eram N1 (1-6 linfonodos) e 45 (16,4%) N2 (7-15 gânglios linfáticos). O número médio de linfonodos dissecados foi de 35. A sobrevida em cinco anos para os estádios de I a III B foi de 70,4%. **Conclusão** - Cirurgias digestivas devem ser estimuladas a realizarem gastrectomias D2 para não deixar de lado o único tratamento para adenocarcinoma gástrico que provou ser eficiente os dias atuais. Deve ser enfatizado que a padronização da dissecação linfática de acordo com a localização do tumor é mais importante do que apenas o número de gânglios removidos.

DESCRITORES - Câncer gástrico. Cirurgia. Gastrectomia.

INTRODUCTION

Eastern literature is remarkable for presenting survival rates for surgical treatment of gastric adenocarcinoma superior to those presented in western countries. Numerous causes are related to that, such as epidemiological factors, early diagnosis, and the controversial systematic D2 lymph node dissection according to Japanese rules¹⁴.

In the last three decades, regarding radical lymph node dissection as the main reason for the aforementioned better survival rates, in our Division it has been adopted the Japanese concept and standardization of lymphadenectomy for gastric cancer.

As the best quality control pattern for surgical treatment is for sure long term follow-up, the aim of this study was to analyze the long-term result after D2 gastrectomy for gastric cancer.

METHODS

Medical records from 540 consecutive patients with gastric adenocarcinoma treated at the Digestive Surgery Division of the University of São Paulo (HCFMUSP) from January 1994 to December 2000 were studied. Two hundred seventy four underwent gastrectomy with D2 lymph node dissection as exclusive treatment, as defined by the Japanese Gastric Cancer Association.

The inclusion criteria were: 1) lymph node removal according to Japanese standardized lymphatic chain dissection (1); 2) potentially curative surgery described in medical records as D2 or more lymph node dissection; 3) tumoral invasiveness of gastric wall restricted to the organ (T1 –T3); 4) absence of distant metastasis (N0-N2/M0); 5) a minimum of five years follow-up.

Clinical pathological data included sex, age, tumor location, Borrmann's macroscopic tumor classification, type of gastrectomy, mortality rates, histological type, TNM classification and staging according to UICC TNM 1997.

During statistical analysis the probability of survival was calculated according to the Kaplan-Meier method and different survival curves were compared

through log-rank test. Univariate analysis was applied in order to compare the above parameters and survival.

RESULTS

One hundred sixty three (59.5%) were male, with a 1.5:1 male/female ratio. Mean age was 62.3 + 14 years (15 to 93). Total gastrectomy was performed in 77 cases (28.1%) and subtotal gastrectomy in 197 (71.9%). The tumor was located in the upper third in 28 cases (10.2%), in the middle third in 53 (19.3%), and in the lower third in 182 (66.5%).

Among patients that had their Borrmann's classification assigned, five cases (1.8%) were BI, 34 (12.4%) BII, 230 (84.0%) BIII and 16 (5.9%) BIV. Tumors were histologically classified as Laurén intestinal type in 119 cases (43.4%) and as diffuse type in 155 (56.6%). According to UICC TNM 1997 classification, early gastric cancer (T1) was diagnosed in 68 cases (24.8 %); 51 (18.6%) were T2, and 155 (56.6%) were T3. No lymph node involvement (N0) was observed in 129 cases (47.1%), whereas 100 (36.5%) were N1 (1-6 lymph nodes), and 45 (16.4%) were N2 (7-15 lymph nodes).

The median number of lymph nodes dissected was 35 and the mean number of lymph nodes dissected per patient was 35.0 + s.d.16.1 (ranging from 15 to 92). The mean number of lymph nodes involved was 2.7 + s.d.3.8 (0 to 14). The clinical staging of patients according to TNM-UICC criteria was Ia in 56 cases (20.4%), Ib in 37 (13.5%), II in 67 (24.5%), IIIa in 72 (26.3%) and IIIb in 42 (15.3%).

Post-operative overall mortality rate, considering 30 days mortality, was 4.4% (12 patients). In total gastrectomy was 5.2% (four patients) and 4.1% in subtotal gastrectomy (eight patients) (Table 1).

The median follow-up was 60.6 months. In the present study it was achieved 87.6% of long term follow-up. The overall long-term (five-year) survival rate, for stages I to IIIb according to our inclusion criteria, was 70.4% (Figure 1 and 2).

In 36.2% (54) of patients the number of lymph nodes dissected ranged from 15 to 25, and in 63.8% (98) had more than 25 nodes dissected. Excluding T1 tumors where lymph node dissection could be a bias, and comparing their survival five-year curves, there

TABLE 1 - Clinicopathological data

Sex (M:F)		1.5 : 1
Mean age		62.3 ± 14
Gastrectomy	total	77
	subtotal	197
Tu location	upper 1/3	43
	middle 1/3	52
	lower 1/3	179
Borrmann	BI	5
	BII	34
	BIII	230
	BIV	16
Histology	intestinal	119
	diffuse	155
	T1	68
	T2	51
	T3	155
	N0	129
	N1	100
Stage	N2	45
	Ia	56
	Ib	37
	II	67
	IIIa	72
IIIb	42	

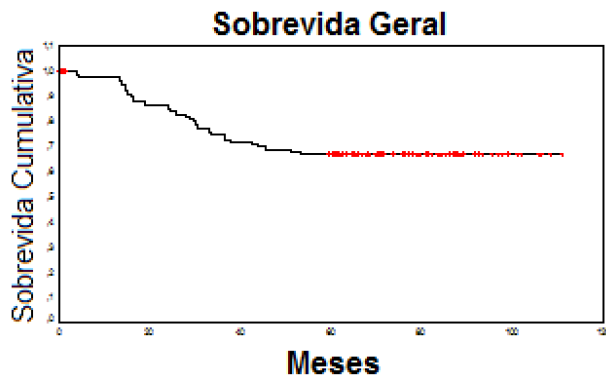


FIGURE 1 – Overall Survival

was no statistical difference among them ($p > 0.5$).

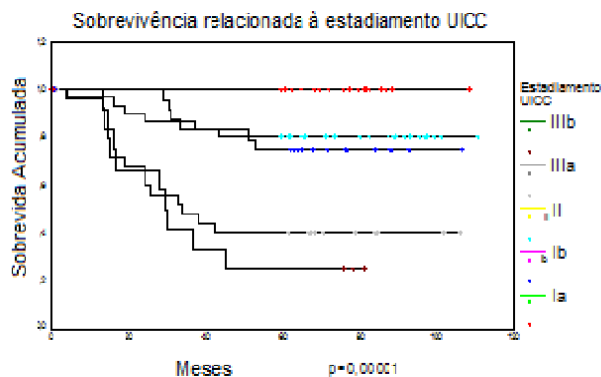


FIGURE 2 – UICC stage related survival

Univariate analysis demonstrated that staging (UICC TNM 1997), pN and pT were statistically related to survival rates, respectively $p < 0.0001$, $p < 0.0001$, $p < 0.002$.

DISCUSSION

There are several western prospective and retrospective studies concerning D2 lymphadenectomy results in the treatment of gastric adenocarcinoma. Most of them do not show any advantage in long-term survival outcome when compared to D1 dissection^{2,4,21}. Other studies as the German one observed better results in a subgroup of D2 dissected patients. A few other studies had better long-term results, but failed in achieving the good Japanese results^{13,19}.

In the last 30 years, due to an intense and rich exchange of specialists between Japanese institutions and our Department, the proposed and nationally adopted method of lymph node dissection in Japan was gradually introduced among our surgeons⁶.

The incidence of gastric adenocarcinoma is considered intermediate in Brazil when compared to other countries such as Japan or Chile, although nearly 2000 patients have been admitted to our Department for gastric cancer treatment in the last three decades.

The survival outcome of this study is very similar to that coming from Japan¹⁰ (Table 2).

TABLE 2 - Five-year survival rates by new TNM staging system

Stage	NCC ^a	Eighteen Jap-Inst ^b	HC-FMUSP(n) ^c
Ia	93.3	90	98.2 (21)
Ib	88.7	85	77.2 (26)
II	73.2	75	78.9 (42)
IIIa	55.6	50	43.5 (44)
IIIb	31.8	30	25.7 (18)

^aNational Cancer Center – Japan (11)

^bEighteen Japanese Institutions and Hospitals (8)

^cNumber of patients

Probably stage IV patients will hardly have a surgical curative procedure, and that is the reason why they were excluded from this analysis.

The 30-day mortality in this study was slightly higher than of Japanese publications^{7,8,12}, probably due to more advanced staging in the time of treatment and also to clinical and nutritional conditions of the majority of our patients. On the other hand, it seems that the patients had a better outcome than other Western studies^{1,2,3,5,15}.

There is a great controversy in medical literature about the required number of lymph nodes dissected to perform a good lymphadenectomy of compartments 1 and 2. UICC rules prescribe that only 15 nodes should be enough to provide a good staging of patients¹⁷. Japanese as some authors¹⁵ recommend a higher number, apparently due to dissection of more than 25 nodes in cadavers²⁰. Even though the range of nodes dissected was 17- 44 nodes¹⁷. Most of medical reports do not usually refer to this issue, thus preventing the reader from inferring which was their dissected number. On the other hand, palliate

resections with deliberate D1 lymphadenectomy can remove much more than 25 nodes.

Adopting this very strict criteria, the mean number of lymph nodes dissected in this study was 35 nodes per patient.

In order to determine what influence has the total number of lymph nodes dissected, an analysis of this study was made excluding T1 tumors, usually supposed to be N0. The comparison of the survival curves of patients with more than 25 nodes removed and less than 25, but more than 15 nodes, there was no statistical difference. It must be stressed that all dissections followed the rules proposed by Japanese standardization, that is removal of lymph nodes according to tumor location and not taking account only the number of nodes removed. It was considered that 15 nodes were enough to stage correctly the patients.

The observation of the five-years survival rates showed that, if systematic dissection of lymph node chains is performed according to the Japanese rules, dissection of at least 15 lymph nodes was enough to reach comparable rates to those obtained when more than 25 nodes were dissected. This was also well demonstrated by recent Italian and Dutch studies^{11,16,18}. It can be speculated if surgeon's intention was to perform a D2 lymph node dissection was a decisive factor to get such a result. D2 lymphadenectomy was likewise performed in cases that featured less than 26 nodes dissected, but more than 15^{11,18}. Previous publication from NCC⁹, a service where D2 or plus dissection is routinely performed, reports that 13% of cases (568 out of 4362) had less than 25 nodes dissected.

CONCLUSION

Digestive surgeons must be stimulated in performing D2 gastrectomies to avoid wasting the only treatment to gastric adenocarcinoma that has proven to be efficient up to this days. It must be emphasized that standardized lymph nodes dissection according to tumor location is more important that only the number of removed nodes.

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