

D1 versus D2 Gastrectomy for Gastric Adenocarcinoma

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ABSTRACT: **Background:** Despite the ongoing decrease in the incidence of gastric cancer, this disease is still a major cause of death. It is still debatable whether D2 lymphadenectomy improves survival and whether this procedure should be performed routinely or selectively.

Objectives: To compare the pathological and short-term results following radical D2-type gastric resection and lymphadenectomy versus the more limited D1 type resection and lymphadenectomy.

Methods: We conducted a retrospective study on 4 years experience treating 164 patients suffering from gastric cancer. We compared the results between the group of patients who underwent a radical D2 type gastric resection and lymphadenectomy (n=100) and those of a relatively small group of patients who intentionally underwent the more limited D1 type (n=34).

Results: The overall number of harvested lymph nodes was 9 ± 4 in the D1 group compared to 30 ± 12 (range 16–69) in the D2 group ($P = 0.001$). Of the 100 patients undergoing a D2 lymphadenectomy, 57% had positive nodes compared to 38% of the 34 patients in the D1 group ($P = 0.045$).

Conclusions: We showed statistically significant differences between D1 and D2 procedures in the overall number of harvested lymph nodes and the proportion of positive nodes to the overall number. Our results support the fact that D2 resection should be recommended as the standard approach of treatment for gastric cancer patients, ensuring a larger number of retrieved lymph nodes and a comparable rate of complications and mortality.

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Although a constant decrease in the incidence of gastric cancer (GC) has been observed around the world, this cancer remains the foremost common malignant neoplasm and the second leading cause of cancer deaths [1,2]. The highest incidence of GC is reported in Japan, Korea, China, Latin America and Eastern Europe [3]. Worldwide, it is estimated that 930,000

new cases are diagnosed yearly and 700,000 deaths occur. In countries such as the United States, the incidence of gastric carcinoma is lower, with 22,000 new cases per year and 13,000 related deaths [4].

Surgical resection is the only potentially curative therapeutic modality for patients with GC and is regarded as the cornerstone of treatment [5,6]. While there are still remarkable disparities in the treatment of GC geographically, in Western countries the diagnosis is usually late and a limited D1 type lymph node dissection is preferred [7].

Although treatment outcomes for this disease have improved in Asia due to early detection and surgical resection with systematic D2 lymph node dissections [8], the majority of Western surgeons continue to practice D1 lymphadenectomy, achieving a 5 year survival rate (5YS) that is much less impressive when compared to the rates of 60% or more that are commonly seen in Asian surgical centers [8]. Although the addition of oncologic treatments has had some impact, they have not significantly changed this grim outlook for GC patients [9]. Today, the state-of-the-art approach to patients with advanced GC is neoadjuvant treatment, with surgery planned as a second stage [10].

The aim of our current study was to compare the pathological and short-term results between a group of patients who underwent radical D2-type gastric resection and lymphadenectomy and those of a relatively small group of patients who intentionally underwent the more limited D1 type resection and lymphadenectomy.

PATIENTS AND METHODS

This study was performed with the authorization of our institutional review board (No. 211/13). We retrospectively studied 164 gastric cancer patients who were treated in our surgical division between the years 2009 and 2013. Data were retrieved from patient charts and a computerized database was created. All patients had undergone preoperative staging using gastroscopy and biopsy, total body computed tomography (CT) (with selective use of positron emission tomography-CT), and tumor markers (CEA, CA 19-9).

Surgery was begun by diagnostic laparoscopy insufflating the peritoneal cavity to 15 mmHg using two 5 mm trocars. Any suspicious lesion was biopsied and sent for frozen sec-

tion. In patients with ascites, fluid was collected and sent for cytology. In all patients other than those with ascites, lavage of the peritoneal cavity was performed with 50 ml of saline, and the collected fluid was sent for cytology.

Our policy was to perform a D2 lymphadenectomy whenever possible, reserving the D1 for palliation or for severely ill or old patients. D2 lymphadenectomy included complete dissection of lymph node stations 7–9; more radical dissection (stations 10–15) was added in cases with clinical suspicion of involvement. Tumor location did not change the radicality of node dissection.

STATISTICAL ANALYSIS

Statistical analysis was performed at Tel Aviv University. In order to compare quantitative (continuous) variables between two independent groups, the two-sample *t*-test was applied as well as the non-parametric Mann-Whitney test. The association between two categorical variables was assessed using either the chi-square test or Fisher's exact test. All statistical tests applied were two-tailed, and a *P* value of ≥ 0.05 was considered statistically significant.

RESULTS

During the period 2009 and 2013 a total of 164 patients with gastric cancer were treated in our center. In 30 patients, surgery was denied due to metastatic disease at the diagnostic laparoscopy stage [Figure 1]. Both surgical groups were similar in age, type of histologic tumor, and stage of the disease (the D1 group had more stage 1 patients with no statistically significant difference). Fifty-three percent of patients who underwent the D1 lymphadenectomy were in stage ≤ 2 compared to 50% in the D2 group. Four patients in the D2 group underwent three cycles of neoadjuvant treatment prior to surgery. None of the D1 group patients received such treatment.

The group of patients who underwent gastric resection comprised 42 females and 92 males, with a mean age of 70 years in the D1 group compared to 68 in the D2 group. As expected, total gastrectomies were performed more often in the D2 group. Table 1 summarizes the clinical and pathological data.

The overall number of harvested lymph nodes (LN) was 9 ± 4 (range 0–15) in the D1 group compared to 30 ± 12 (range 16–69) in the D2 group. These figures were statistically significant ($P = 0.001$). The mean number of positive LNs was 1.5 ± 2 for the D1 group vs. 7 ± 12 in the D2 group ($P = 0.0007$). Of the 100 patients undergoing D2 lymphadenectomy, 57% had positive nodes compared to 38% in the D1 group ($P = 0.045$) [Figure 2].

Both groups had a similar complication rate: 5 patients (14.7%) in the D1 group (1 patient with grade IV, 2 patients with grade III and 2 with grade I complications according to the Clavien-Dindo classification) compared to 19 patients (19%)

Figure 1. Patient classification into groups

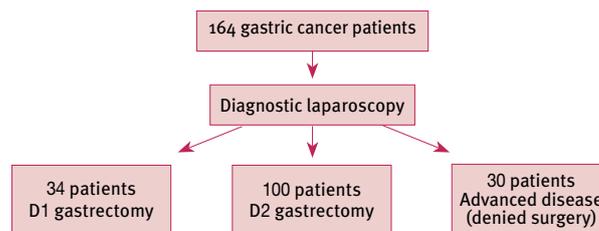
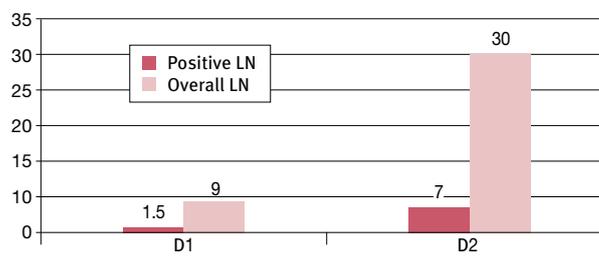


Figure 2. Mean number of harvested and positive lymph nodes



in the D2 group (2 patients with grade IV, 7 with grade III, 2 with grade II and 8 with grade I complications according to the Clavien-Dindo classification) ($P > 0.05$). Readmission rates at 90 days were similar: 14.7% in the D1 group vs. 19% in the D2 group.

DISCUSSION

More than 60% of patients with GC in the Western world are diagnosed at an advanced stage [11,12]. In addition, the fact that the majority of these patients will undergo a D1 lymphadenectomy and not the D2 type lymphadenectomy practiced in the East helps explain the grim results of GC in the West. Reviewing the INT0116 trial showed that only 10% of patients had undergone a D2 resection, while the rest of the patients had D0–D1 types of resection [8].

The extent of lymphadenectomy has been defined by the JGASG (Japanese Gastric Cancer Group) who identified 20 lymph node stations and three categories of lymphadenectomies. Of these, D1 is the most limited and D3 the most extensive [9].

With regard to the extent of lymphadenectomy, there has been an ongoing debate for more than three decades [13,14]. Two large European trials, the Dutch Gastric Cancer Trial [15] and the UK Medical Research Council (MRC) [16], showed that the standard use of D2 resection, which is a technically demanding procedure, did not improve survival and was associated with much higher morbidity compared to the D1 type of resection. Deng et al. [17] showed that dissected lymph node ≥ 15 was an important factor to improve the prognosis of lymph node-positive gastric cancer patients after potential curative

resection. Chang and co-authors [18] found that patients with node-negative gastric cancer who underwent a more radical D2 dissection (more than 15–20 nodes) had better survival rates with no correlation to postoperative complication rate. Only recently the 15 year follow-up results of the randomized nationwide Dutch D1D2 trial showed the long-term benefit of D2 over D1 lymphadenectomy without higher morbidity or mortality in patients who had undergone the spleen-preserving procedure [19].

The German Gastric Carcinoma Study Group provided a possible explanation for the improved survival in a group of patients with pN0 who had undergone D2 resection compared to a limited D1 dissection. These researchers succeeded to show by immunohistochemical techniques that the negative nodes found on routine histological examination had a higher

frequency of micro-involvement by isolated malignant cells [1].

Regarding the situation in Israel, around 650–700 GC cases are diagnosed each year [2], most of them at an advanced stage [20]. The overall 5YS of Israeli GC patients ranges around 26–29%, a fact that can easily be explained by two factors: its advanced stage at presentation and the limited use of lymphadenectomy. A study by Dreznik et al. [21], at a single institute in Israel, describes 461 patients who had a gastrectomy with a mean number of 11 lymph nodes harvested per patient.

Over the past years, more than 400 gastrectomies with D2 lymphadenectomy have been performed in our medical center, but because of a lack of complete data (due to two computer system changeovers and implementation of a new method of lymph node harvesting), we decided to report on our last 5 years of experience performing D2 gastrectomies.

Table 1 presents the overall characteristics of patients with GC treated in our surgical division. At the level of diagnostic laparoscopy, which is performed routinely in our center [22], 30 of the 164 patients (22.5%) were denied curative surgery due to advanced/metastatic disease which was not detected in the preoperative staging. A total of 100 patients underwent a D2 lymph node dissection as compared to 34 who underwent a D1 dissection (very sick, elderly or patients who required palliation for bleeding or obstruction). In this group of patients who underwent D1 type of lymph node resection we intentionally decided to perform a less aggressive and radical dissection. Table 2 presents the data of our operated patients.

The only statistically significant variations in D1 versus D2 procedures were noticed in the overall number of harvested lymph nodes ($P = 0.001$) and the mean number of positive nodes per patient ($P = 0.007$) [Table 2, Figure 2]. The overall number of patients with positive nodes was 38% in the D1 group compared to 57% in the D2 group ($P = 0.045$). These data may explain the role of radicality of lymphadenectomy

Table 1. Demographic, clinical and pathological data

		D1 vs D2				P value
		D1 34		D2 100		
Gender	Female	10	29.4%	32	32.0%	1
	Male	24	70.6%	68	68.0%	
Age (range) in years		70 ± 12 (40–87)		68 ± 11 (36–89)		0.45
Tumor location	EGJ	0	0.0%	4	4.0%	0.3
	Upper third	5	14.7%	16	16.0%	
	Middle third	6	17.6%	30	30.0%	
	Lower third	21	61.8%	46	46.0%	
	Linitis plastica	2	5.9%	4	4.0%	
Type of gastrectomy	Proximal	4	11.8%	16	16.0%	0.1
	Total	4	11.8%	26	26.0%	
	Subtotal	26	76.5%	58	58.0%	
Pathology	Adenocarcinoma	25	73.5%	69	69.0%	0.8
	Signet ring	9	26.5%	31	31.0%	
Differentiation	Unknown	2	5.9%	8	8.0%	0.8
	Poorly	19	55.9%	62	62.0%	
	Moderately	11	32.4%	24	24.0%	
	Well	2	5.9%	6	6.0%	
Vascular invasion	8	23%	37	37%	0.12	
Mean no. of harvested LN		9 ± 4		30 ± 12		0.001
Mean no. of positive LN		1.5 ± 2		7 ± 12		0.007
No. of positive patients		13 (38%)		57 (57%)		0.045
Stage	Carcinoma in situ	0	0.0%	2	2.0%	0.07
	1	16	47.1%	29	29.0%	
	2	2	5.9%	19	19.0%	
	3	10	29.4%	22	22.0%	
	4	6	17.6%	28	28.0%	

EGJ = esophagogastric junction, LN = lymph nodes

Table 2. Length of stay, complications, and readmission

	D1 (34)	D2 (100)	P value
LOS (days)	13.4 ± 14.9	11.6 ± 7.2	> 0.05
Complication	5 (14.7%)	19 (19.0%)	> 0.05
Wound infection/collection	1	5	
Sepsis	2	1	
Cardiac	2	2	
Pulmonary		5	
Leak		2	
Other		4	
Readmission 90 days	5 (14.7%)	19 (19%)	> 0.05
Surgical	4	12	
Internal	1	7	
Death	2 (5.9%)	5 (5.0%)	> 0.05

in reducing the rate of stage migration.

Part of the debate regarding the extent of lymphadenectomy relates to complication and mortality rates. Past clinical data have reported high morbidity and mortality rates for patients undergoing D2 versus D1 lymphadenectomy [23]. However, recent data have shown there were no differences in these rates between groups, provided splenectomy and distal pancreatectomy were avoided as part of the D2 dissection. We did not perform either of these procedures in any of the 100 patients undergoing a D2 lymphadenectomy, and overall morbidity and mortality was low and similar in both our groups.

At our academic center, most gastrectomies are performed by residents (at an advanced stage of their training) supervised by a senior surgeon. Moreover, there are only three surgical oncology attendants who are allowed to perform D2 lymphadenectomies, a fact that might explain our better results.

CONCLUSIONS

Our results support the fact that D2 resection should be recommended as the standard approach of treatment for gastric cancer patients, offering better oncological results, with comparable rates of complications and mortality.

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**“Imagine there’s no countries
It isn’t hard to do
Nothing to kill or die for
And no religion, too
Imagine all the people
Living life in peace”**

John Lennon (1940-1980), British singer-songwriter who co-founded the Beatles, a band that impacted the popular music scene like no other before, or since. His rebellious nature and acerbic wit is expressed in his music, writing, drawings, on film and in interviews. His criticism of the Vietnam War resulted in a lengthy attempt by Richard Nixon’s administration to deport him, while some of his songs were adopted as anthems by the anti-war movement and the larger counterculture