

Lymph node retrieval in radical gastrectomy: the pathologist alone or the surgeon-pathologist team?

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Abstract

Introduction: Lymph node (LN) dissection is an important prognostic factor in gastric cancer. There is little information comparing the LN count depending on whether they are dissected in the operating room or in the pathology laboratory.

Aim: To establish if the LN count is greater in either of them.

Material and methods: From 2015 to 2017 all consecutive gastrectomies with D2 dissection were prospectively evaluated based in either of 2 protocols: One started in the operating room where the surgeon separated the LN levels and then submitted the entire adipose tissue with LNs (undissected) to pathology in separate containers; the pathologist dissected the LNs from the specimens. The second protocol consisted of sending the tissue/LNs to pathology as usual (adipose tissue and LN attached to the stomach).

Results: A total of 83 patients were analysed. The mean age was 58.4 years. The median number of LNs dissected in the protocol starting in the operating room was 56 (IQR: 37–74), whereas the pathology laboratory dissected a median of 39 LNs (IQR 26–53) ($p = 0.005$). The survival of cases dissected by both protocols were comparable (median survival of 48 and 43 months, $p = 0.316$).

Conclusions: The LN final count is significantly higher when LN levels are separated beforehand in the operating room compared to dissection only in pathology; however, this does not impact survival, perhaps because the number of dissected nodes in both groups is high and the quality of the surgery is good.

Introduction

Gastric cancer is the third leading cause of death worldwide, after lung and colorectal cancers. According to the 2018 Globocan report, it is the seventh most prevalent cancer, and each year one million new cases are diagnosed around the world, thus representing a public health problem [1, 2].

The pathological evaluation of gastric cancer allows us to identify prognostic factors such as histological subtype, depth of invasion, lymphovascular invasion, margins, and lymph node involvement [3, 4]. There are several groups of lymph nodes (LN) to which the gastric circulation drains; the proper dissection of these ensures adequate nodal staging of the patient. It is sug-

gested that at least 16 LNs are required to perform this staging; however, it is desirable to have > 30 nodes [4].

There are different techniques for removing the nodes. The D0 technique is the resection of the incomplete N1 nodes, the D1 technique involves the complete N1 nodes, and the D2 technique consists in the removal of N1 and N2 nodes. The type of lymphadenectomy is a controversial topic around the world; however, Asian groups with long experience and European schools have accepted that the standard of care of patients with gastric cancer is the D2 resection.

In patients with non-advanced gastric cancer, LN dissection is one of the most important prognostic factors, and several studies showed that a greater number of LNs is associated with better survival

[5, 6]. The German Gastric Cancer Study (in a 10-year lapse) found that patients with stage II or III with < 25 harvested LNs had the worst survival [7]; hence, the ability of the surgeon to dissect the LN levels and of the pathologist to both identify and sample them for pathological examination become particularly important. One Asian study comparing the number of LNs dissected in the surgery room to the number dissected in the pathology laboratory showed that dissection in the operating room allowed a greater LN count and better survival [8].

Aim

There is no more reported evidence on the difference in the final LN count depending on whether they are dissected in the operating room or in the pathology department, so our objective was to establish if the LN count is significantly greater in either of them. As a secondary objective, we evaluated if either of the 2 protocols has an impact on survival.

Material and methods

Patients and protocols

From 2015 to 2017, a cohort of all consecutive gastrectomy products (total or subtotal gastrectomies) with D2 dissection were prospectively evaluated at the National Cancer Institute of Mexico (INCan), which were resected by the same team of surgeons specialized in gastrointestinal cancer and who had carried out these procedures for at least 5 years. Similarly, the specimens were dissected and evaluated by 2 gastrointestinal pathologists or the resident in oncological pathology under the supervision of the staff pathologist. Lymph node dissection was performed by either of the 2 protocols based on the surgeon's preference. One protocol started in the operating room, where the surgeon identified and separated the LN levels by level using the Japanese gastric cancer classification and then submitted each level to the pathology laboratory in separate containers (without dissecting any nodes). The second protocol consisted of sending the gastrectomy to the pathology laboratory with the LN levels attached to the specimen. For both protocols, in the pathology laboratory, the tissue was fixed for 24 h, and then dissection of LNs was performed routinely, i.e., no special techniques, stains, or solutions were used. The following variables were recorded from the patients and the pathological files: age, sex, number of dissected LNs, number of LNs with metastasis, tumour site, tumour size, tumour deposits, lymphatic vascular invasion, venous vascular invasion, perineural invasion, surgical margin, clinical stage, date of surgery, date of last consultation or death, recur-

rence, adjuvant therapy, and outcome. Patients who had a history of preoperative treatment with chemo and/or radiotherapy were excluded from the study due to the well-known difficulty in identifying and dissecting nodes in this setting.

Statistical analysis

The Kolmogorov-Smirnov test was performed to test normality for numerical variables, and then the median and interquartile range (IQR) were used; for the qualitative variables, the count and percentage were used. For the comparison of variables, the Mann-Whitney *U* test was used for numerical variables and the χ^2 test or Fischer's exact test, according to the observed distribution, for the categorical variables. Survival analysis was performed with the Kaplan-Meier method, comparing survival estimates with the log-rank test. All analyses were performed using SPSS version 22.0 (IBM, Armonk, New York, USA), and a 2-tailed *p*-value < 0.05 was considered statistically significant for all tests.

This study was approved for our Institutional Review Board (Acceptation number: INC/187/19).

Results

A total of 83 patients were analysed, of whom 43 (53.1%) were women. The mean age was 58.4 years (IQR: 23–69). All evaluated variables are summarized in Table I. The gastrectomies with the LN levels separated in the operating room obtained a median of 56 LNs (IQR: 37–74), with a median of 1 LN with metastasis (IQR: 0–2). The gastrectomies with LN dissection in the pathology laboratory had a median of 39 LNs dissected (IQR: 26–53) with a median of 2 positive LNs (IQR: 1–6). This difference was significant (*p* = 0.005, Table II). Apart from the LN count, there were no differences in the basal variables between the 2 study groups (Table III).

The median follow-up of the patients was 48 months (range: 1–52). Univariate analysis of overall survival showed statistical association with factors already known to be associated with worse prognosis (high histological grade, diffuse subtype, advanced nodal and pathological stage, vascular and perineural invasion). However, the survival of cases dissected by the pathologist and cases dissected by the surgeon were comparable (median survival of 48 and 43 months, respectively, *p* = 0.316).

Discussion

In this study of 83 patients with gastrectomy, it was found that there is a greater number of dissected LN if previous management is performed in the operating room, with a median of 56 vs. 39 LNs, respectively. This

Table I. Characteristics of 83 patients undergoing surgery for gastric cancer

Variable	Value	Variable	Value
Tumour site, <i>n</i> (%):		Perineural invasion, <i>n</i> (%):	
Antrum	13 (16)	No	32 (39.5)
Fundus	6 (7.4)	Yes	49 (60.5)
Corpus	40 (49.4)	Subtype, <i>n</i> (%):	
Pylorus	11 (13.6)	Intestinal	38 (46.9)
<i>Linitis plastica</i>	11 (13.6)	Diffuse	36 (44.4)
Tumoural stage, <i>n</i> (%):		Mixed	7 (8.6)
pT1	15 (18.5)	Number of lymph node resected – median (minimum–maximum)	
pT2	7 (8.6)		46 (26–156)
pT3	16 (19.8)	Number of positive lymph nodes – median (minimum–maximum)	
pT4	43 (53.1)		2 (0–64)
Nodal stage, <i>n</i> (%):		Dissector, <i>n</i> (%):	
pN0	31 (38.3)	Surgeon	36 (44.4)
pN1	17 (21)	Pathologist	45 (55.6)
pN2	14 (17.3)	Adjuvant therapy, <i>n</i> (%):	
pN3	19 (23.5)	No	22 (27.2)
Pathological metastatic stage, <i>n</i> (%):		Yes	59 (72.8)
M0	69 (85.2)	Recurrence, <i>n</i> (%):	
M1	12 (14.8)	No	58 (71.6)
Histologic grade, <i>n</i> (%):		Yes	23 (28.4)
Grade 1	19 (23.5)	Outcome, <i>n</i> (%):	
Grade 2	57 (70.4)	Alive	62 (76.5)
Grade 3	5 (6.2)	Dead	19 (23.5)
Lymphovascular invasion, <i>n</i> (%):			
No	32 (39.5)		
Yes	49 (60.5)		

Table II. Number of lymph nodes dissected from 83 gastrectomies according to the dissection site

Dissection site	Median lymph node count (interquartile range)	<i>P</i> -value*
Surgery room	56 (37–74)	0.005
Pathology laboratory	39 (30–53)	

*Mann-Whitney *U* test.

difference was not associated with improved oncological outcomes.

To our knowledge, there is only one previously published study in which, when comparing the final LN count, it was evident that the specimens managed with prior separation in the operating room allowed a greater number of dissected nodes and better survival [8]. In the aforementioned study the LNs were dissected by the surgeon. Our results confirm this finding; however, the surgeon did not dissect the LNs, but simply separated the LN levels and submitted them to pathology in

different containers, with no adipose tissue attached to the stomach. Also, we did not find survival differences between the groups, perhaps due to the difference in the mean number of retrieved LNs (29.64 ±11.50 in the surgeon group vs. 20.71 ±8.56 in the pathology group) [8].

Theoretically, dissecting a greater number of LNs in the operating room could improve survival, because the importance of dissecting an adequate number of nodes in gastrectomy products is well known, and there is evidence that the greater the number of LNs, the better the patient outcome. For example, one study demon-

Table III. Basal characteristics of 83 gastrectomies according to lymph node dissection protocol

Variable	Surgery room (n = 35)	Pathology laboratory (n = 45)	P-value*
Pathologic T, n (%):			0.184
pT1	4 (11.4)	4 (8.9)	
pT2	5 (14.3)	5 (11.1)	
pT3	7 (20)	9 (20)	
pT4	19 (54.3)	27 (60)	
Pathologic N, n (%):			0.129
N0	10 (28.6)	12 (26.7)	
N1	9 (25.7)	12 (26.7)	
N2	7 (20)	9 (20)	
N3	9 (25.7)	12 (26.7)	
Pathologic M, n (%):			0.875
M0	30 (85.7)	38 (84.4)	
M1	5 (14.3)	7 (14.6)	
Lymphovascular invasion, n (%):			0.506
No	15 (42.9)	16 (35.6)	
Yes	20 (57.1)	29 (64.4)	
Venous invasion, n (%):			0.752
No	26 (74.3)	32 (71.1)	
Yes	9 (25.7)	13 (28.9)	
Perineural invasion, n (%):			0.506
No	15 (42.9)	16 (35.6)	
Yes	20 (57.1)	29 (64.4)	
Subtype:			0.577
Intestinal	14 (40)	23 (51.1)	
Diffuse	18 (51.4)	18 (40)	
Mixed	3 (8.6)	4 (8.9)	

*According to χ^2 test or Fisher exact test.

strated how the number of dissected LNs is an independent factor associated with overall survival in resectable carcinomas; the authors found in 12,507 patients divided into groups according to the LN count (16–29, 30–44 and > 45 nodes) that hazard ratios for survival were 0.87, 0.79, and 0.68, respectively [5]. Another study established that a greater LN count correlated with better survival in patients with clinical stages II and III, (5-year survival of 59.5% vs. 53.6% for patients with D3 dissection compared to D1, respectively). However, this difference could depend on surgical experience [6]. Another recent study compared 2 large databases, one from the USA and another from Korea, with a total of 25,290 patients; after comparing the number of LN removed and survival, the cut-off point was found to be 29 LNs removed, and stage-by-stage survival was improved with more than 29 LNs dissected ($p < 0.001$) [9].

Despite these data, we found no statistically significant differences in overall survival in the studied groups. The explanation for this is that although the group of the previous dissection in the operating room obtained more LNs, the group that was dissected only in the pathology laboratory has a high number of nodes, which is sufficient to make an adequate staging of the patient and suggests good quality of surgery, and we agree that a high LN count is important in the resectability of gastric cancer.

The limitations of our study are the low number of cases and short duration of surveillance; however, the study has several strengths because the surgery was performed by the same surgeons in a short period, without substantial differences in the surgical technique and in technology. In addition to the final analysis, the total dissection was performed by the patholo-

gist, who in all cases did his best to dissect the largest number of nodes, and having the levels separately forced the maximum identification of LNs by levels.

Conclusions

The final LN count is significantly higher when lymph node levels are separated beforehand in the operating room and are sent to the pathology laboratory in separate containers for further dissection by the pathologist, compared to dissection only in the pathology laboratory; however, this does not have an impact on survival, perhaps because the number of dissected nodes in both groups was high and the quality of the surgery was good. In some cases, separating the LN levels from the gastrectomy allows the pathologist to find more LNs.

Conflict of interest

The authors declare no conflict of interest.

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