

Does the number of lymph nodes harvested reflect the width of lymphadenectomy in gastric carcinoma? Results of a prospective comparative study

Gastrik kanserde çıkarılan lenf nodu sayısı lenfadenektomi genişliğini yansıtıyor mu? prospektive karşılaştırmalı çalışmanın sonuçları

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SUMMARY

Objective: The aim of this study was to evaluate the sufficiency of the surgical technique according to the extended lymph node dissection in gastric cancer patients (GCPs). We supported our findings with the determination of a number of lymph nodes (LNs) in lymph node stations with an autopsy performed on cadavers without any type of cancer.


Method: 55 GCPs were enrolled. Extended lymphadenectomy was performed on 23 autopsy cases as a comparative group. Total gastrectomy and D2 dissection were performed as the standard surgical approach.


Results: According to TNM classification, nine cases (18%) were stratified to stage I, three (6%) to stage II, 22 (36%) to stage III, and 21 (40%) to stage IV. The median number of excised LNs from the 55 cases was 47 (24-95), metastatic LNs were 15 (1-71) in patients. In the autopsy group, the median number was 72 (50-91). If D1 dissection had been performed instead of D2 dissection in the 55 cases, the median number of excised LNs would have been 24 (10-57), and metastatic LNs would have been 5 (1-45). If D1 dissection had been performed in the autopsy group, the median number of excised LNs would have been 36 (20-49).

Conclusions: The number of LNs harvested does not reflect the width of lymphadenectomy. D2 dissection must be performed stationary to achieve adequate extension of the lymphadenectomy. Possible skip metastasis and stage migration will also be reduced so that more efficient oncological results will be achieved.

Keywords: Gastric cancer, lymph node dissection, metastasis, lymph nodes

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ÖZET

Amaç: Bu çalışmanın amacı mide kanseri hastalarında genişletilmiş lenf nodu disseksiyonuna göre cerrahi tekniğin yeterliliğini değerlendirmektir. Bulgularımızı, lenf nodu (LN) istasyonlarında saptanan lenf nodu (LN) sayılarını, herhangi bir kanser türü olmayan kadavralar üzerinde yapılan otopsiler ile destekledik.

Yöntem: 55 mide kanseri hastası çalışmaya alındı. Genişletilmiş lenfadenektomi, 23 otopsi olgusunda karşılaştırmalı grup olarak yapıldı. Hastalara standart cerrahi yaklaşım olarak Total gastrektomi ve D2 disseksiyon uygulandı.

Bulgular: TNM sınıflamasına göre dokuz olgu (% 18) evre I, üç (% 6) evre II, 22 (% 36) evre III ve 21 (% 40) evre IV idi. 55 olguda çıkarılan LN'larının medyan sayısı 47 (24-95), metastatic LN'ları ise 15 (1-71) idi. Otopsi grubundamedyan sayı 72 (50-91) idi. 55 olguda D2 disseksiyonu yerine D1 disseksiyonu yapılsaydı, eksize edilen LN'larının medyan sayısı 24 (10-57) ve metastatik LN sayısı 5 (1-45) olacaktı. Otopsi grubunda D1 disseksiyonu yapılsaydı, eksize edilen LN'larının ortanca sayısı 36 (20-49) olacaktı.

Sonuç: Çıkarılan lenf nodlarının sayısı lenfadenektominin genişliğini yansıtmamaktadır. Yeterli genişlikte lenfadenektomi yapılabilmesi için D2 disseksiyon istasyonel olarak yapılmalıdır. Olası skip metastaz ve evre kayması da böylelikle azaltılmış olacaktır. Böylece daha yeterli onkolojik sonuçlar elde edilecektir.

Anahtar sözcükler: Gastrik kanser, lenf nodu disseksiyonu, metastaz, lenf nodları

INTRODUCTION

The value of extended surgical dissection to remove the draining lymph nodes (LNs) has been controversial for over the years. Japanese surgeons routinely perform the more extended (D2) as opposed to the more limited (D1) lymph node dissection, reasoning that the tumor disseminates outwards in an orderly fashion through lymphatic channels from the stomach (Figure 1, 2). Therefore, extended lymph node dissection should improve both staging and long-term survival¹⁻³. Several non-randomized studies from Western surgeons have also reported excellent survival results with D2 surgery when compared to contemporary reports on conventional surgery⁴⁻⁶. In contrast, randomized controlled trials have shown no evidence of survival benefit for D2 surgery, and it showed evidence of increased postoperative morbidity and mortality⁷⁻¹². Two randomized controlled European trials that compared D1 dissection to D2 dissection failed to show any survival benefit for extended lymphadenectomy⁷⁻¹¹. Lack of experience in terms of the surgical procedure and postoperative care were deemed the most obvious reasons for the poor outcome of extended lymphadenectomy¹³⁻¹⁵. The number of LNs harvested during surgery differs greatly between clinics and surgeons. Whether surgeon experience affects the number of LNs extracted, and whether the quality of the dissection varies between single-center and multicenter studies remain unclear. The removable lymph node number in the upper gastrointestinal tract and the factors influencing this number are currently unknown. The removable lymph node number in gastric cancer surgery signifies wide variability between surgeons and surgery departments.

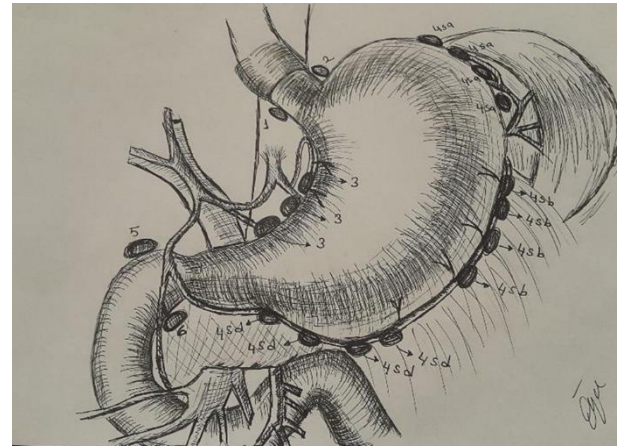


Figure 1: D1 lymph node stations in gastric cancer surgery

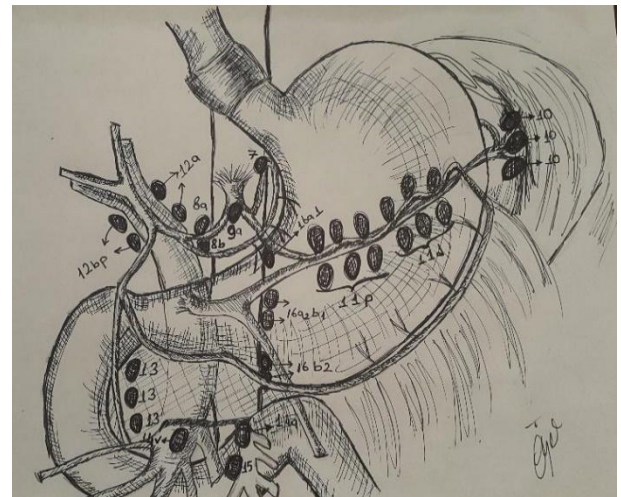


Figure 2: D2 lymph node stations in gastric cancer surgery

The purpose of the present study was to evaluate the sufficiency of the surgical technique according to the extended lymph node dissection (ELND) in gastric cancer patients (GCPs). Extended

lymphadenectomy was performed according to the Japanese Research Society for Gastric Cancer (JRSGC) guidelines¹⁴. We supported our findings with the determination of the number of lymph nodes in lymph node stations with an autopsy performed on cadavers without any type of cancer.

MATERIAL AND METHODS

The prospective study design involved collecting data from 126 GCPs referred to the General Surgery Department of Istanbul University Medical Faculty between January 2006 and July 2009; 55 of these patients were enrolled in the study. Extended lymphadenectomy was performed on 23 fresh autopsy cases (comparative group). Ethical approval was obtained from the Istanbul University Medical Faculty Local Ethics Committee-2009/1822 and the Ethics Committee of the Forensic Medicine Institute of the Turkish Republic Justice Department-2009/547.

Preoperative Evaluation

Preoperative patient evaluation and staging included physical examination, complete blood count and biochemical parameters, chest X-ray, abdominal computed tomography (CT), and upper gastrointestinal endoscopy. Tumors were classified into three groups according to the predominant anatomical site: antrum, corpus, or cardia. GCPs were informed of the study and signed a consent form preoperatively.

Inclusion and Exclusion Criteria

Patients with a histologically confirmed diagnosis of gastric carcinoma were included if clinical data predicted that surgical resection would be curative. Patients were evaluated according to the American Society of Anesthesiologists classification. Those included were under 80 years of age with no serious respiratory, urinary, and/or cardiovascular insufficiency. Patients with remnant stomach cancer and/or concomitant tumor, and those who had previously undergone neoadjuvant chemotherapy or chemoradiotherapy were excluded.

Age, sex, body mass index (BMI), and cause of death were recorded for the comparative autopsy cases. Exclusion criteria included: intra-abdominal or visceral malignancy, hematologic or lymphatic pathology, penetrating firearm or sharp object injury to the abdomen, previous abdominal surgery, and age under 16 or over 70 years.

The standard approach to patients with gastric carcinoma

All patients with a diagnosis of gastric carcinoma received consent forms preoperatively. Clinical staging was determined according to the tumor size, node status, metastasis (TNM) staging system (6th Edition)¹⁷. (We designed this trial before publishing the 7th edition). Surgical success and need for adjuvant therapy were evaluated by the Oncology Council, members of which were lecturers from the General Surgery, Pathology, and Oncology departments. Patients were followed-up every 3 months postoperatively.

Surgical Technique

For patients eligible for curative resection, total gastrectomy and extended lymphadenectomy were performed as we described in our previous study (18). The lymph nodes were excised and placed in numbered boxes by the same surgeon in the operating room. All samples were submitted for pathological examination.

Autopsy dissection

Lymph node dissection was performed on 23 cadavers to remove lymph nodes situated at stations 1–16 according to the Japanese Research Society for Gastric Cancer (JRSGC) guidelines¹⁴. All stations were dissected, boxed, and numbered by the same surgeon. All samples were stored and submitted for pathological examination.

Pathological Examination

The fatty-fibrous tissues and the gastric specimens excised from the study group and the fatty-fibrous tissues excised from the autopsy cases were submitted to the Pathology Department of Istanbul University Medical Faculty. After fixation in formalin for 24 h, tissue samples were taken from the specimens and coded lymph nodes for conventional histopathological assessment. The following data were collected: prognostic parameters including localization, diameter, invasion depth, histological type and degree of tumor differentiation, presence of vascular and perineural invasion including distance to proximal and distal surgical margins, number of lymph nodes removed from each station and number of metastatic lymph nodes. For the autopsy cases, the total number of lymph nodes at each station was recorded.

Surgical Method

The number of station LNs excised, and the numbers of metastatic LNs were recorded for the study group, and the number of station LNs excised was recorded for the autopsy cases. Furthermore, the number of LNs excised and the number of metastatic LNs was evaluated in both

groups, assuming that D1 dissection (dissection of lymph node stations 1 to 6), modifying dissection A (dissection of station 7 in addition to stations 1 to 6) and modifying dissection B (dissection of stations 7 to 9 in addition to stations 1 to 6) were performed for both groups. Additionally, the rate of metastatic LNs was evaluated according to tumor localization and T-stage in both study groups.

Skip Metastasis

The presence of lymph node metastasis in N2-group (next level) stations and the absence of metastasis in perigastric stations (first level) (skip metastasis) were investigated according to histopathological findings. Similarly, skip metastasis rates were assessed in the study group, assuming that D1 dissection, modifying dissection A, and modifying dissection B were performed.

Stage migration (Will Rogers Phenomenon)

The total number of LNs excised, and the number of metastatic LNs was re-evaluated assuming that D1 dissection, modifying dissection A and modifying dissection B were performed, and the cases were re-staged according to both the TNM and the pN (pathological lymph node) staging systems. Stage migration rates were evaluated to compare the findings with the present disease stages and pN stages.

Surgical Mortality and Morbidity

Any death occurring during the postoperative 30-day follow-up was considered surgical mortality and any surgical complication that developed within that period was considered surgical morbidity. Surgical mortality and morbidity rates were evaluated. Potential parameters affecting mortality and morbidity were investigated.

Statistics

Statistical analysis was performed using SPSS version 16.0 for Windows (Statistical Package for Social Sciences, Inc. Chicago, IL; ABD for Windows 16.0). Student's t-test, Mann-Whitney U test, analysis of variance (ANOVA) and Chi-squared tests were used to compare qualitative data and for demographic statistical analysis (mean standard deviation, frequency). The 95% confidence interval (CI) was determined. A p value of <0.05 was considered statistically significant.

RESULTS

Demographic Findings

Fifty-five GCPs were included in the study group. The median age was 58 years (range 31–80 years). Fourteen patients were female (25 %), and 41 were male (75 %). Comorbidity was observed in 54 % ($n = 33$) of cases. Heart disease was present in 19 cases, respiratory disease in 4 cases, and both respiratory and heart disease in 7 cases.

Harvested Lymph nodes

The median number of lymph nodes excised from the 55 GCPs was 47 (24–95), the median number of metastatic LNs found was 15 (1–71). In the autopsy group, the median number was 72 (50–91). The number of LNs harvested according to the JRS GC guidelines is presented in Table 1.

Frequency of lymph node metastasis by tumor localization

Gastric tumors located proximally metastasized mostly to stations 1, 7, 9, 3 and 2 (59, 55, 50, 44 and 39%, respectively), tumors located medially metastasized mostly to stations 3, 8, 9, 4 and 6 (81, 54, 54, 46 and 46%, respectively), tumors located distally metastasized mostly to stations 6, 8, 9, 4 and 3 (57, 48, 38, 38 and 33%, respectively) and disseminated tumors metastasized mostly to stations 3, 4, 7 and 9 (100, 80, 80, 100%, respectively).

Table 1: Median number of lymph nodes removed and the median number of tumor-positive lymph nodes in each station

Station Number	The median number of lymph nodes removed			P < 0.05
	Total number of lymph nodes harvested in the study group	Total number of tumor-Metastatic lymph nodes	Total number of lymph nodes harvested in the autopsy group	
Station 1	3 (0 - 24)	0 (0 - 7)	3 (1 - 10)	0.411
Station 2	4 (0 - 13)	0 (0 - 6)	3 (1 - 7)	0.438
Station 3	4 (0 - 18)	1 (0 - 15)	6 (1 - 11)	0.83
Station 4	3 (0 - 12)	0 (0 - 9)	11 (4 - 17)	0.001
Station 5	0 (0 - 7)	0 (0 - 4)	2 (1 - 4)	0.006
Station 6	7 (1 - 17)	0 (0 - 16)	9 (4 - 18)	0.812
Station 7	6 (0 - 13)	0 (0 - 5)	6 (2 - 12)	0.42
Station 8	7 (0 - 17)	0 (0 - 15)	3 (2 - 9)	0.484
Station 9	4 (1 - 25)	1 (0 - 8)	4 (1 - 7)	0.145
Station 10	1 (0 - 8)	0 (0 - 5)	5 (1 - 10)	0.001
Station 11	1 (0 - 10)	0 (0 - 4)	5 (2 - 11)	0.001
Station 12	1 (0 - 17)	0 (0 - 2)	4 (2 - 9)	0.003
Station 16	2 (0 - 20)	0 (0 - 4)	6 (1 - 12)	0.001

How must many lymph nodes be excised for radical surgery?

If D1 dissection had been performed instead of D2 dissection in the 55 study cases, the median number of excised LNs would have been 24 (10–57), and the median number of metastatic LNs would have been 5 (1–45). If D1 dissection had been performed in the autopsy group, the median number of excised LNs would have been 36 (20–49). If D1 dissection had been performed instead of D2 dissection, at least 25 LNs would have been obtained, and the percentage of patients with less than 15 excised LNs would have been 7%. In the autopsy group, the corresponding percentages were 96 and 0%, respectively. If modifying

dissection A had been performed for both groups, the percentage of cases with more than 25 excised LNs would have been 57% in the study group, and 96% in the autopsy group. If modifying dissection B had been performed, these percentages would have been 93 and 100%, respectively. When the dissection techniques and the percentage of cases with more than 25 excised LNs were analyzed with regards to tumor localization, this percentage would have been 50% for tumors located in the upper 1/3 after D1 dissection, 72% after modifying dissection A, and 98% after modifying dissection B. The percentage of LNs removable by each dissection technique is shown in Table 2.

Table 2: Ratio of lymph nodes removed by dissection type

	Dissection type			
	D1dissection	Modified	Modified	D2 dissection
	(%)	Dissection A (%)	Dissection B (%)	(%)
Patient group				
< 25 lymph node	%49	%43	%7	2
< 15 lymph node	%7	%0	%0	0
≥ 25 lymph node	% 51	%57	%93	98
Autopsy group				
< 25 lymph node	% 4	%4	%0	0
< 15 lymph node	%0	%0	%0	0
≥ 25 lymph node	%96	%96	%100	100

Skip metastasis

Skip metastasis was found in four patients (7%). Skip metastasis was only affected by the number of lymph nodes retrieved: the probability of skip metastasis increased as the number of LNs retrieved decreased ($p < 0.0001$). The effect of

patient demographics and tumor characteristics on skip metastasis is presented in Table 3. The results from the study group showed that the probability of skip metastasis decreased as the dissection was expanded (Table 3).

Table 3: Effect of patient demographics and tumor characteristics on skip metastasis

Patient and tumor-related factors	Skip metastasis-negative	Skip metastasis-positive	P < 0.05
Age	13	1	0.983
	38	3	
BMI (kg/ m ²)	23.7	24.4	0.85
Tumor diameter (cm)	1.5	1	0.06
Tumor stage			
T1	4	0	
T2	17	1	0.878
T3	30	3	
T4	0	0	
Nodal status			
N0	9	0	
N1	15	1	0.806
N2	9	0	
N3	18	3	
Number of lymph nodes retrieved	51	38	0.001

BMI: Body mass index

Stage migration

Stage migration was observed in 18 study group cases (33%). When analyzed in terms of the pN stage, stage migration was observed in 16 cases (30%). When examined according to dissection technique, stage migration was observed in 24% of the cases with modifying dissection A and 2% with modifying dissection B.

No tumor-related variables affected stage migration in a statistically significant manner; however, the number of metastatic LNs excised from stations 7, 8 and 9 affected stage migration significantly ($p < 0.05$), (Table 4).

Postoperative Mortality and Morbidity

Postoperative mortality occurred in two cases (3.6 %): one patient died of sudden respiratory failure while in intensive care 7 days postoperatively, and one patient died of pneumonia, pleural effusion, and acute respiratory

distress syndrome 20 days after surgery. Morbidity occurred in 13 cases (24 %). Pneumonia (14 %) was a common cause of morbidity. Two cases underwent surgery for intraabdominal bleeding: in one of the patients, despite the lack of any active bleeding focus, long-term antibiotic use led to coagulopathy, while in the other patient bleeding from the splenic capsule led to splenectomy. Anastomotic leakage was observed in one case which required total parenteral nutrition and percutaneous drainage. The intraabdominal collection was observed in three cases. In two of them, percutaneous drainage was performed under CT guidance. The other patient who was ineligible for drainage was followed up with antibiotic therapy. No patient- or tumor-related factors were found to affect morbidity.

Table 4: The effect of station metastatic lymph nodes to the stage migration

Stations	Stage Migration		P<0.05
	Number of patients without stage migration (n)	Number of patients with stage migration (n)	
1 no Metastasis (-)	23	10	0.905
Metastasis (+)	15	7	
2 no Metastasis (-)	32	11	0.106
Metastasis (+)	6	6	
3 no Metastasis (-)	19	7	0.545
Metastasis (+)	19	10	
4 no Metastasis (-)	23	9	0.598
Metastasis (+)	15	8	
5 no Metastasis (-)	27	14	0.374
Metastasis (+)	11	3	
6 no Metastasis (-)	22	8	0.456
Metastasis (+)	16	9	
7 no Metastasis (-)	25	7	0.05
Metastasis (+)	13	10	
8 no Metastasis (-)	24	6	0.042
Metastasis (+)	14	11	
9 no Metastasis (-)	23	4	0.011
Metastasis (+)	15	13	
10 no Metastasis (-)	32	13	0.492
Metastasis (+)	6	4	
11 no Metastasis (-)	30	14	0.77
Metastasis (+)	8	3	
12 no Metastasis (-)	36	13	0.245
Metastasis (+)	2	4	
16 no Metastasis (-)	35	14	0.284
Metastasis (+)	3	3	

DISCUSSION

Regardless of tumor location, the general tendency is to extract as many LNs as possible through complete resection and extended lymph

node dissection. The invasion depth of the tumor, the existence of lymph node metastasis, the number of LNs extracted, and the existence of

distant metastasis are the most important factors in determining prognosis¹⁹⁻²¹.

Noguchi *et al.*²² and Maruyama *et al.*²³ showed that the metastatic lymph node count increases when the lymph node dissection width is expanded. Therefore, the number of LNs harvested is the best parameter known at present to evaluate the radicality of the surgical procedure. Studies addressing this issue and median lymph node counts are shown in Table 5^{7,24-28}. The median number of LNs extracted varies between 55 and 74 in Eastern studies and between 17 and 45 in Western studies.

Although increased lymph node dissection width affects the metastatic lymph node counts, a key issue that needs to be studied further is the physiological number of LNs thought to be located in the human gastrointestinal tract^{18,29-31}.

In contemporary gastric cancer staging, the location and number of LNs and the number of metastatic LNs detected are important parameters in the pathological evaluation of specimens. The

minimal number of LNs required for adequate TNM staging is 15. Siewert *et al.*⁵ categorized dissection procedures according to the number of LNs extracted: D2 dissection (> 25) and D1 dissection (< 25). Siewert *et al.*⁵ showed that the number of lymph nodes extracted correlated with the extent of dissection, which is now accepted worldwide.

In the present study, 25 or more LNs were extracted from 51% of the living cases; whereas the percentage was 96% in the autopsy group, even when D1 dissection (stations 1–6) was performed instead of D2 dissection. If D1 dissection only had been performed in our study group, the percentage of patients from whom less than 15 LNs was extracted would have been 7% (2% for the autopsy group). Although the number of excised LNs is more useful for the TNM classification (29, 30), we concluded that stationary lymph node dissections might be more reliable than the extracted number of LNs in gastric cancer surgical treatment.

Table 5: Median numbers of lymph nodes removed

Study	year	Operation	Patient number (n)	Lymph node number (median)	Annual patient number (n)
Single-center study					
MSKCC (I) ²¹	2000	D2	154	30(15-45)	73
Present study (patient group)	2009	D2+PAN	55	47(24-95)	22
YCU(II) ²¹	2000	D2	194	55(28-82)	29
Present study (autopsy group)	2009	D2+PAN	23	72(50-91)	–
Multicenter study					
MRC (III) ⁵	1996	D2	200	17	1.5
Netherland gastric cancer group (Bonenkamp, 1995)	1995	D2	331	26(0-105)	1
PGCSG (IV) ²²	2007	D2	134	28(25-31)	5.5
IGCSG (V) ²³	1997	D2	118	39(22-89)	6
GGCS (VI) ²⁴	1998	D2	1096	45(24-58)	19.2
JCOG (VII) ²⁵ (Group A)	2004	D2	263	54(14-161)	7
JCOG 9501 (Group B)	2004	D2+PAN	260	74(30-235)	7

I: MSKCC: Memorial Sloan–Kettering Cancer Center; II: YCU: Yokohama City University; III: MRC: Medical Research Council; IV: PGCSG: Polish Gastric Cancer Study Group; V: IGCSG: Italian Gastric Cancer Study Group; VI: GGCS: German Gastric Cancer Study Group; VII: Japanese Clinic Oncology Group.

In early-stage tumors and in high-risk cases, in which lymphadenectomy is precluded by poor general status, the percentage of patients in whom more than 25 lymph nodes were detected was 57% with modified dissection A, whereas with modified dissection B that percentage was 93%. When subgroup analysis was performed according to tumor location, the percentages observed were 50% for D1 dissections, 72% for modified dissection A, and 98% for modified dissection B in the upper 1/3 of placed tumors. In median placed tumors, the same percentages were 95%, 62%, and 100% respectively, lower one third-placed tumors, and those were 46%, 72% and 95% for each technique applied. Modified dissection B can be performed when extended lymphadenectomy is considered risky due to poor general health status. Therefore, station dissection must depend on tumor location and on the T stage determined preoperatively. Lymph node counts determined through pathological examination reflect the radicality of operation.

Another important issue in gastric cancer staging is skip metastasis. Skip metastasis is defined as the invasion of the second-tier LNs by the tumor while the first-tier LNs remain clear. Published gastric cancer studies report skip metastasis ratios between 2.5% and 16.7% (34-37). Park *et al.*³⁴ examined 589 cases retrospectively and reported skip metastasis in 2.4% of cases. Saito *et al.*³⁷ examined 313 cases retrospectively and reported skip metastasis in 6.7% of cases. In both studies, skip metastasis was detected more frequently at stations 7, 8 and 9 than at stations 10 and 11. Park *et al.*³⁴ concluded that the number of LNs extracted affected the occurrence of skip metastasis considerably. In our study, the results from the study group showed that the probability of skip metastasis decreased as the dissection was expanded (Table 3). Skip metastasis was observed in 7% of cases, and the most frequent occurrence of skip metastasis was at the 8th station. The number of LNs extracted was the only variable: the lower that number, the higher the occurrence of skip metastasis ($p < 0.001$). In addition, skip metastasis was eliminated completely by D2 dissection and was reduced by up to 75% by modified dissection.

Extended lymph node dissection also influences stage migration. Stage migration is defined as the displacement of a fixed value used in a study due to a different surgical intervention or classification included in the study and, thus, results in significant alterations in survival outcome and disease staging. Bunt *et al.*³⁸ reported a stage migration rate of approximately 30% when D1

dissection was performed instead of D2 dissection. In our study, the stage migration rate was 33%. Stage migration was detected in 4% of stage 1 cases, 15% of stage 2 cases, and 14% of stage 3 cases, and was shifted further when D2 dissection was performed. Stage migration ratios were assessed by dissection type with pN staging and were as follows: 30% with D1 dissection, 24% with modified dissection A, and 9% with modified dissection B; with TNM staging, the corresponding percentages were 33%, 24%, and 2%, respectively. In our study group, significant stage migration was observed at stations 7, 8, and 9, where metastatic LNs were detected. Hence, reduced stage migration, which can be accomplished by extended lymph node dissection, would help improve postoperative treatment options and survival rates. Moreover, for critical patients lacking the physical endurance required for extended lymph node dissection, skip metastasis and stage migration can be reduced remarkably by performing D1+B dissection (dissection of stations 8, 7 and 9). Therefore, if D2 dissection cannot be performed, modified dissection B may be a suitable alternative.

CONCLUSION

The number of LNs harvested does not reflect the width of lymphadenectomy. D2 dissection must be performed stationarily to achieve adequate extension of the lymphadenectomy. Possible skip metastasis and stage migration will also be reduced so that more literal oncological results will be achieved.

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Ethics Committee Approval: Ethical approval was obtained from the Istanbul University Medical Faculty Local Ethics Committee-2009/1822 and the Ethics Committee of the Forensic Medicine Institute of the Turkish Republic Justice Department-2009/547.

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REFERENCES

1. Mc Culloch P, Nita ME, Kazi H, Gama-Rodrigues J. Extended versus limited, lymph nodes dissection technique for adenocarcinoma of the stomach. *Cochrane Database of Systematic Reviews*. 2003; (4) CD 001964 *Cochrane Database Syst Rev*.
2. Quadri HS, Smaglo BG, Morales SJ, *et al*. Gastric adenocarcinoma: Multimodal Approach. *Front Surg* 2017; 3: 4: 42.
3. Wang H, Xing XM, Ma LN, *et al*. Metastatic lymph node ratio and Lauren classification are independent prognostic markers for survival rates of patients with gastric cancer. *Oncol Lett* 2018;15:6:8853-62.
4. Pacelli F, Doglietto GB, Bellantone R, *et al*. Extensive versus limited lymph node dissection for gastric cancer: a comparative study of 320 patients. *Br J Surg* 1993; 80: 1153-56.
5. Siewert JR, Böttcher K, Roder J, Busch R, Hermanek P, Meyer HJ. Prognostic relevance of systemic lymph node dissection in gastric carcinoma. German Gastric carcinoma Study Group. *Br J Surg* 1993; 80: 1015-18.
6. Sue-Ling HM, Johnston D, Martin IG, *et al*. Gastric cancer: a curable disease in Britain *BMJ* 1993; 307: 591-96.
7. Cuschieri A, Fayers P, Fielding J, *et al*. Postoperative morbidity and mortality after D1 and D2 resections for gastric cancer: preliminary results of the MRC randomised controlled surgical trial. *Lancet* 1996; 347: 995-99.
8. Cuschieri A, Weeden S, Fielding J, *et al*. Patients survival after D1 and D2 resections for gastric cancer: long-term results of the MRC surgical trial. *Brit J Cancer* 1999; 79: 1522-30.
9. Robertson CS, Chung SC, Woods SD, *et al*. A prospective randomised trial comparing R1, subtotal gastrectomy with R3 total gastrectomy for antral cancer. *Ann Surg* 1994; 220: 176-182.
10. Bonenkamp JJ, Songun I, Hermans J, *et al*. Randomised comparison of morbidity after D1 and D2 dissection for gastric cancer in 996 Dutch patients. *Lancet* 1995; 345: 745-48.
11. Bonenkamp JJ, Hermans J, Sasako M, Van de Velde CJ. Extended lymph node dissection for gastric cancer. *NEJM* 1999; 340: 908-58.
12. Dent DM, Madden MV, Price SK. Randomised comparison of R1 and R2 gastrectomy for gastric carcinoma. *Br J Surg*. 1988; 75: 110-12.
13. Wu CW, Hsiung CA, Lo SS, Hsieh MC, Shia LT, Whang-Peng J. Randomised clinical trial of morbidity after D1 and D3 surgery for gastric cancer. *Br J Surg* 2004; 91: 281-87.
14. Dequili M, Sasako M, Calgaro M, *et al*. Italian gastric cancer study group. Morbidity and mortality after D1 and D2 gastrectomy for cancer: interim analysis of the Italian gastric cancer study group (IGCSG) randomised surgical trial. *Eur J Surg Oncol* 2004; 30: 303-08.
15. Sasako M, Sano T, Yamamoto S, *et al*. D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer. *N Eng J Med* 2008; 359: 453-62.
16. Japanese Gastric Cancer Association (JGCA). Japanese classification of gastric carcinoma-2nd English Edition. *Gastric cancer* 1998; 1:10-24.
17. Sobin LH, Wittekind C. International Union Against Cancer (UICC) TNM classification of malignant tumours [M]. 6th edition. New York: Wiley, 2002: 70-72.
18. Asoglu O, Matlim T, Kurt A, *et al*. Guidelines for Extended lymphadenectomy in gastric cancer: A prospective comparative study. *Ann Surg Oncol* 2013; 20: 218-25.
19. Maruyama K. The most important prognostic factors for gastric cancer patients: A study Using Univariate and Multivariate analyses *Scand J Gastroenterol* 1988; 22: 63-68.
20. Asoglu O, Karanlik H, Parlak M, *et al*. Metastatic lymph node ratio is an independent prognostic factor in gastric cancer. *Hepatogastroenterology* 2009; 56: 908-13.
21. Degiuli M, De Manzoni G, Di Leo A, *et al*. Gastric cancer: Current status of lymph node dissection. *World J Gastroenterol* 2016; 22: 10: 2875-93.
22. Noguchi Y, Imada T, Matsumoto A, Coit DG, Brennan MF. Radical surgery for gastric cancer. *Cancer* 1989; 64: 2053-62.
23. Maruyama K, Gunven P, Okabayashi K, Sasako M, Kinoshita T. Lymph node metastasis of gastric cancer. *Ann Surg*. 1989; 210: 596-602.
24. Noguchi Y, Yoshikawa T, Tsuburuya A, Motohashi H, Karpeh MS, Brennan MF. Is gastric carcinoma different between Japan and the United States. *Cancer* 2000; 89: 2237-46

25. Kulig J, Popiela T, Kolodziejczyk P, Sierzega M, Szczepanik A; Polish Gastric Cancer Study Group. Standard D2 versus extended D2 lymphadenectomy for gastric cancer: an interim safety analysis of a multicenter, randomised clinical trial. *Am J Surg* 2007; 193: 10-15.
26. Dequili M, Sasako M, Ponzetto A, *et al.* Extended lymph node dissection for gastric cancer: results of a prospective multi-center analysis of morbidity and mortality in 118 consecutive patients. *Eur J of SurgOncol* 1997; 23: 310-14.
27. Siewert JR, Böttcher K, Stein HJ, Roder JD. Relevant prognostic factors in gastric cancer: ten-year results of the German Gastric Cancer Study. *Ann Surg* 1998; 228: 449-61.
28. Sano T, Sasako M, Yamamoto S, *et al.* Gastric cancer surgery: morbidity and mortality results from a prospective randomised controlled trial comparing D2 and extended para-aortic lymphadenectomy. Japan clinical oncology group study 9501. *J ClinOncol* 2004; 22: 2767-73.
29. Bonenkamp JJ, Hermans J, Sasako M, van de Velde CJ. Quality control of lymph node dissection in the Dutch randomized trial of D1 and D2 lymph node dissection for gastric cancer. *Gastric Cancer* 1998; 1: 152-59.
30. Bunt AM, Hermans J, van de Velde CJ, *et al.* Lymph node retrieval in a randomized trial on Western-type versus Japanese type surgery in gastric cancer. *J ClinOncol* 1996; 14: 2289-99.
31. Wagner PK, Ramaswamy A, Rüschoff J, Schmitz-Moormann P, Rothmund M. Lymph node counts in the upper abdomen: anatomical basis for lymphadenectomy in gastric cancer. *Br J Surg* 1991; 78: 825-27.
32. Aurello P, D'Angelo F, Rossi S, *et al.* Classification of lymph node metastases from gastric cancer: comparison between N-site and N-number systems. Our experience and review of the literature. *Am J Surg* 2007; 73: 359-66.
33. Kodera Y, Yamamura Y, Shimizu Y, *et al.* The number of metastatic lymph nodes: a promising prognostic determinant for gastric carcinoma in the latest edition of the TNM classification. *J Am CollSurg* 1998; 187: 597-603.
34. Park SS, Ryu JS, Min BW, *et al.* Impact of skip metastasis in gastric cancer. *Anz J Surg* 2005; 75: 645-49.
35. Kikuchi S, Kurita A, Natsuya K, *et al.* First drainage lymph node(s) in gastric cancer: analysis of the topographical pattern of lymph node metastasis in patient with pN1 tumors. *Anticancer Res* 2003; 23: 601-04.
36. Arai K, Iwaski Y, Takahashi T. Clinicopathological analysis of early gastric cancer with solitary lymph node metastasis. *Br J Surg* 2002; 89: 1435-37.
37. Saito H, Tsujinai S, Ikeguchi M. Clinical significance of skip metastasis in patients with gastric cancer. *Gastric Cancer* 2007; 10: 87-91.
38. Bunt AM, Hermans J, Smit VT, *et al.* Surgical pathologic stage migration confounds comparisons of gastric cancer survival rates between Japan and western countries. *J of Clin Oncol* 1995; 13: 19-25.