Impact of the Number of Harvested Lymph Nodes on the Survival of Egyptian Patients with Gastric Cancer: Middle Eastern Tertiary Center Experience

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Abstract

Background: In the present research, we aimed to estimate the effect of the number of resected lymph nodes (LN) on the survival outcomes of patients with resectable gastric cancer; we investigated whether 16 LNs remained the optimal threshold and whether a specific subset of patients could benefit from further LN dissected.

Method: This cohort study included consecutive patients who underwent surgical resection for gastric cancers from the start of 2012 to the end of 2014. Demographic, clinic-pathologic, laboratory data (including complete blood picture, renal function tests, liver function tests, C-reactive protein, Prothrombin profile, and electrolytes), type of surgery, systemic chemotherapy, treatment, and survival data were retrospectively collected from the patients' files.

Results: The mean overall survival ± standard error (SE) was 23.051 ± 2.249 months with 95% confidence interval (CI) = 18.644-27.459, while the mean disease-free survival ± SE was 20.675 ± 2.414 months with 95% CI = 15.944-25.906. D2 dissection was associated with significantly better OS and disease-free survival (P = 0.001 and P = 0.001, respectively). The mean OS for the patients with <16 lymph node dissected was 13.480 ± 1.468 with 95% CI = 10.603-16.357; whereas for those patients with <16 lymph nodes dissected, it was 20.738 ± 2.065 with 95% CI = 16.690-24.786 months, log-rank = 8.030 (P = 0.005).

Conclusion: The benefit of D2 lymphadenectomy, and subsequently dissecting more LNs, still remains under question; however, if morbidity and mortality are kept at a minimum level, D2 dissection could be advantageous. Our study concluded that harvesting further LNs was associated with more survival benefit.

Keywords: Stomach neoplasms, Lymphadenectomy, Disease-free survival

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Introduction

Gastric cancer (GC) is one of the leading causes of cancer-related deaths worldwide[1, 2] over decades; national screening programs have succeeded to achieve earlier and widespread diagnosis in eastern countries. Nonetheless, in western countries, it is still diagnosed at late stages due to lack of these programs.[3]

Radical gastrectomy with regional lymphadenectomy is the standard care for all resectable GCs.[4] GC has a great tendency for lymph node (LN) spread; once invading the mucosa, nodal spreading takes place from the primary site.[5]

LN status is the strongest prognosticator for survival in early GC; the five-year and 10-year cancer-related survival rates have been reported to be respectively 98% and 95% in pT1N0 stage treated with adequate lymphadenectomy. These survival rates however declined to 70%-80% in pT1N1/N2 stages, and further decreased to below 30% in N3 stage.[6] Furthermore, the risk of recurrence could exceed 50% in T1N3a cases and reach 80% in T1N3b. [7] Over years, LN dissection has been highly controversial among different oncologic surgeons; Japanese specialists considered D2 lymphadenectomy as the standard procedure[8] whereas other Asian surgeons believed that extended lymphadenectomy achieved higher survival and lower recurrence rates.[9]

On the contrary to previous Japanese and Asian surgeons, western oncologic surgeons did not consider D2 lymphadenectomy as a standard treatment in the clinical practice,[8] possibly due to lower incidence of GC and lesser confidence of western oncologic surgeons in this procedure as a result of higher rates of surgical complications and perioperative mortality.

Recently, D2 lymphadenectomy has been considered as a standard treatment in western countries following spleen and pancreas preservation.

In 2014, Jiang et al.[8] analyzed eight RCTs published between 1988 and 2010, drawing a comparison between D1 and D2 procedures; D2 gastrectomy was associated with a significantly greater morbidity, such as anastomotic leakage, pancreatic leakage, reoperation rates, wound infection, and pulmonary complications. Furthermore, the overall five-year survival rate did not show any significant difference between the two procedures. Overall, postoperative mortality was significantly lower in the D1 gastrectomy (RR = 0.58, 95% confidence interval (CI): 0.47-0.71, $P < 0.001$), but upon subgroup analysis, the patients were not found to be significantly different with pancreas and spleen
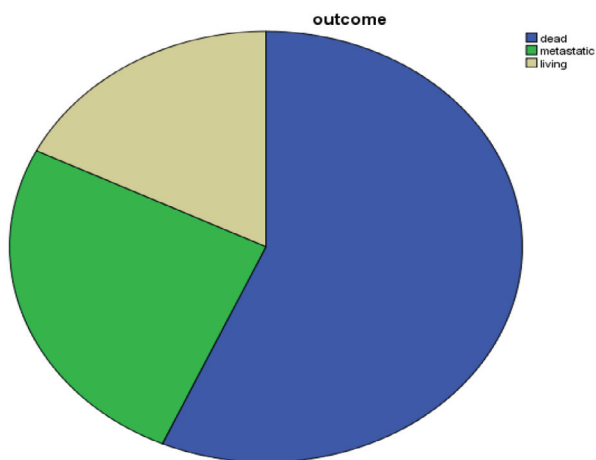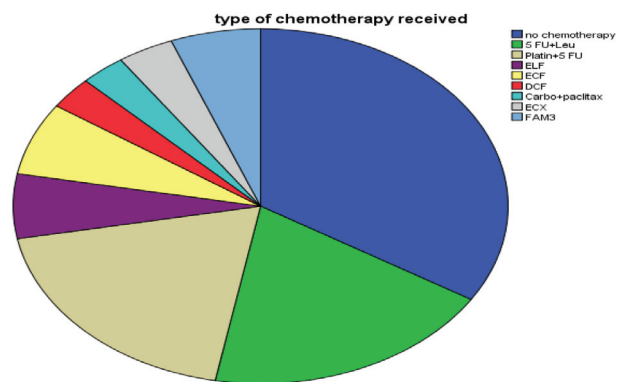

Figure 2. The type of chemotherapy given to 136 patients; 46 (33.8%) patients did not receive chemotherapy, while 26 (19.1%) received 5FU + leucovorin. The same number of patients received platinol + 5FU. ECF (epirubicin + cisplatin + 5FU) was given to nine (6.6%) patients, while ELF regimen (etopoisde + leucovorin + 5FU) was given to eight (5.9%). The same number of patients received FAM regimen (5FU+ Adriamycin + mitomycin C). DCF (docetaxel + cisplatin + 5FU) and carboplatin + paclitaxel regimens were given to an equal number of patients (four (2.9%) in each regimen).

Figure 1. This figure illustrates the treatment outcomes developed in 136 patients with gastric cancer.

Table 1. Clinicopathological characteristics of 136 patients with gastric cancer

Characteristics	N = 136	%
Age (mean ±SD)	52.198 ± 13.012	
Min.-Max.	22-85 years	
Median	52 years	
Gender		
Male	52	38.2%
Female	84	61.8%
M/F ratio	1:1.615	
Site		
Pylorus	55	40.4%
Body	28	20.6%
Cardia	19	14.7%
Linitis plastic	14	10.3%
GE junction	7	5.1%
Antrum	7	5.1%
fundus	6	4.4%
T stage		
T1	4	2.9%
T2	23	16.9%
T3	48	35.3%
T4	61	44.9%
LN dissection		
Done	92	67.6%
Not done	44	32.4%
Pathologic subtype		
Adenocarcinoma	90	66.2%
Mucinous carcinoma	9	6.6%
Signet ring carcinoma	35	25.7%
Squamous cell carcinoma	2	1.5%
Pathologic grade		
G1	29	21.3%
G2	37	27.2%
G3	32	23.5%
G4	38	27.9%
Lauren classification of adenocarcinoma		
Intestinal (well-differentiated)	64	47.1%
Diffuse (undifferentiated)	26	19.1%

Data are expressed as mean ±SD, number, and percentage; G: Grade; LN: Lymph node; SD: Standard deviation

preservation in D1 and D2 groups, proving that the higher D2-associated mortality in older trials was mainly due to spleen and/or pancreas resection.

Nowadays, D2 procedure is recommended as the standard procedure by many countries and international guidelines.

However, the matter was changed for advanced GC, and whether D2 lymphadenectomy is adequate or extended D2 lymphadenectomy with or without para-aortic LN (PAN) dissection is needed remains controversial. Japanese guidelines recommended extended D2 plus PAN dissection after neo-adjuvant chemotherapy as a promising treatment for patients with clinically detected PAN involvement or with extensive N2 nodal metastases.[10]

It is generally agreed that a more extensive LN dissection will harvest further LNs to be examined pathologically, subsequent to which the stage assignment would improve. Meanwhile, this is not true for GC because treatment outcomes have not consistently improved in several studies with the increase in the number of LN dissected.

Table 2. Types of surgery done on 136 patients

surgery	N	%
Primary surgery		
Radical surgery	90	66.2%
Total gastrectomy	30	22.1%
Distal gastrectomy	35	25.7%
Proximal gastrectomy	16	11.8%
Subtotal gastrectomy	6	4.4%
Partial gastrectomy	1	0.7%
Gastroesophagectomy	1	0.7%
Whipple's operation	1	0.7%
Palliative surgery	46	33.8%
Feeding jejenostomy	8	5.9%
Gastrojejenostomy	16	11.8%
Biopsy	22	6.2%
LN dissection	92	67.6%
Mean ±SD	15.293 ± 12.079	
D1 dissection		
Mean ± SD	5.68 ± 6.546	
D2 dissection		
Mean ±SD	9.55 ± 6.652	
Additional surgeries		
DP+ splenectomy	11	8.1%
Splenectomy	8	5.9%
Distal esophagectomy	7	5.1%
Colectomy	4	3%
DP	1	0.7%
Omentectomy	1	0.7%
Hepatic metastatectomy	1	0.7
Enteroeterostomy	1	0.7%
First part duodenectomy	1	0.7%

Data are expressed as number, percentages, mean ±SD; SD: Standard deviation; DP: Distal pancreatectomy; LN: Lymph node

The 2009 revised AJCC recommended a minimum number of 16 LNs to be dissected for accurate staging.

The Dutch trial[11] has reported a significant decrease in the recurrence after D2 procedure following a 15-year follow-up from the conclusion of its accrual.

Recently, long-term survival analysis of the Italian trial[12] has demonstrated a survival benefit for patients with locally advanced GC and positive nodes treated with extended D2 gastrectomy without spleno-pancreatectomy which involved more than 16 LN dissected.

Hence, we aimed to evaluate the effect of the number of resected LNs on survival outcomes in patients with resectable GC. We also investigated whether 16 LNs remained the optimal threshold and whether specific subsets of patients could benefit from more LN dissected.

Patients and Methods

This cohort study included consecutive patients who underwent surgical intervention for GCs from the start of 2012 to the end of 2014, at surgical oncology department of South Egypt Cancer Institute (SECI). They were treated with chemotherapy with or without radiotherapy at clinical oncology department of Assiut University Hospital, Assiut University. The subjects who were found to have inadequate surgery at time of operation were included, but those with M1 disease and neoadjuvant chemotherapy were excluded.

Demographic, clinicopathologic, laboratory data (including complete blood picture, renal function tests, liver function tests, C-reactive protein, Prothrombin profile, and electrolytes), type of surgery, systemic chemotherapy (CTR), treatment, and survival data were retrospectively

Table 3. Correlations between LN dissection and survival outcomes

LN dissection	OS		DFS	
	r	*P*-value	r	*P*-value
Total LN dissected	0.309	0.003*	0.285	0.006*
D1 dissection	0.227	0.029*	0.170	0.104
D2 dissection	0.352	0.001*	0.343	0.001*

Data were analyzed using Spearman correlation; r: Correlation coefficient; LN: Lymph node; *significant, *P* < 0.05; OS: Overall survival; DFS: Disease-free survival

collected from the patients' files after institutional review board approval at SECI (approval ID = 99).

Surgical consideration

Surgical resection is the principal therapy for GC; the most common procedures are total, subtotal, or distal gastrectomy. The choice of procedure and extent of nodal dissection were determined with the ability to obtain clear microscopic margins, traditionally, to maintain a 5-cm safety margin proximally and distally to the primary as much as possible. Esophagogastrectomy for tumors at cardia and gastroesophageal junction was also done (proximal gastrectomy with lower third esophagectomy).

Traditionally, distal gastrectomy or subtotal distal gastrectomy was done in our center for antral tumors involving removal of distal two thirds of stomach. While subtotal gastrectomy was also done for advanced antral tumors to entail removal of nearly four fifths of the stomach, total gastrectomy was performed mainly for stomach body and fundus tumors. Nevertheless, recently, surgery of GC involves mainly total and subtotal or partial gastrectomy in our center.

D1 lymphadenectomy involved removal of all the perigastric LNs, while D2 lymphadenectomy, in addition to D1, involved removal of LNs along hepatic, left gastric, celiac, and splenic arteries, as well as these LNs in the splenic hilum, which necessitated splenectomy with or without distal pancreatectomy in certain cases. In the patients with regionally advanced disease, removal of adjacent organs (multi-organ resection) was required, like the first part of duodenum, liver, spleen, and pancreas.

Adjuvant radiotherapy

Based on different studies and guidelines that recommended postoperative radiotherapy (RT)

for those with advanced GC, 3DCRT with 40-45 Gy over 20-25 fractions given concurrently with capecitabine (xeloda) as a radiosensitizer was practiced.

Adjuvant chemotherapy

Even though numerous studies have not demonstrated a consistent survival benefit from adjuvant chemotherapy, patients with advanced N stage, in D2 dissection, were treated with postoperative chemotherapy, including regimens like 5 fluorouracil (5FU) + leucovorin, cisplatin + 5FU, carboplatin + paclitaxel, etoposide+ leucovorin+5FU (ELF), epirubicin + cisplatin + 5FU (ECF), docetaxel+cisplatin + 5FU (DCF), epirubicine + cisplatin + xeloda (ECX), and 5FU + Adriamycin+mitomycin C (FAM) regimens. Preoperative chemoradiation for T3-T4 lesions and/or N+ lesions concurrently with Mayo-clinic regimen was received.

We anticipated a bias in our analysis related to the effect of stage migration as a mechanism leading to seemingly superior survival after dissecting more LNs; this meant that patients with fewer LNs could be down-staged and subsequently imprecisely compared with those with a more favorable group; thus, we divided the subjects into two groups, namely those with LN dissection of <16 LNs and those with ≥16 LNs dissected. Afterwards, we compared the survival outcomes of the groups.

Statistics

The null hypothesis in this study showed no rise in disease-free survival (DFS) and overall survival (OS) with an increase in the number of LN harvested. We estimated that a total number of 136 patients achieved a power of 81% using the main test of Mann-Whitney test, effect size of 0.5, and α error probability of 0.05. For descriptive statistics, mean, median, SD, SE, and

Table 4. Univariate analysis of prognostic factors of OS and DFS

Prognostic factors	DFS		OS	
	Mean ± SD	*P*-value	Mean ± SD	*P*-value
T-stage				
T1	18.5 ± 15.968	<0.0001	22 ± 14.605	<0.0001
T2	15.391 ± 11.563		18.562 ± 12.485	
T3	13.792 ± 13.219		16.021 ± 13.253	
T4	4.426 ± 7.221		7.043 ± 7.044	
Grade				
G1	18.103 ± 13.351	0.001	20.414 ± 12.965	<0.0001
G2	8.513 ± 12.388		11.459 ± 12.837	
G3	9.687 ± 10.227		12.812 ± 10.979	
G4	5.526 ± 7.504		8.868 ± 6.830	
Type of CTR				
No CTR	3.587 ± 7.413	0.001	6.369 ± 7.202	<0.0001
5FU+leucovorin	12.5 ± 9.655		14.038 ± 9.610	
Cisplatin +5FU	16.076 ± 13.314		20 ± 13.266	
ELF	15.5 ± 18.015		16.875 ± 17.041	
ECF	6.222 ± 4.763		9.333 ± 4.769	
DCF	9.5 ± 3.785		11.750 ± 2.872	
Carbo.+paclitax	23.250 ± 7.50		32.250 ± 7.410	
ECX	9.6 ± 16.318		13.4 ± 14.432	
FAM	11.625 ± 14.715		15.375 ± 12.270	
Lymphadenectomy				
Done	14.076 ± 12.169	<0.0001	16.794 ± 12.326	0.001
Not done	1.477 ± 3.015		4.954 ± 3.184	

Data were expressed as mean ±SD, analyzed using Mann Whitney test and Kruskal-Wallis test; CTR: Chemotherapy; 5FU: 5-fluorouracil; ELF: Etopoisde + leucovorin + 5FU; ECF: Epirubicin + cisplatin+5FU; DCF: Docetaxel + cisplatin + 5FU; carbo. + paclitax.: Carboplatin + paclitaxel; ECX: Epirubicin + cisplatin + xeloda; FAM: 5FU+adriamycin+mitomycin C; SD: Standard deviation; OS: Overall survival; DFS: Disease-free survival; *P*-value<0.05

percentages were used. For significant tests between two variables, Mann-Whitney test was utilized while for more than two variables, we employed Kruskal-Wallis test (the dependent
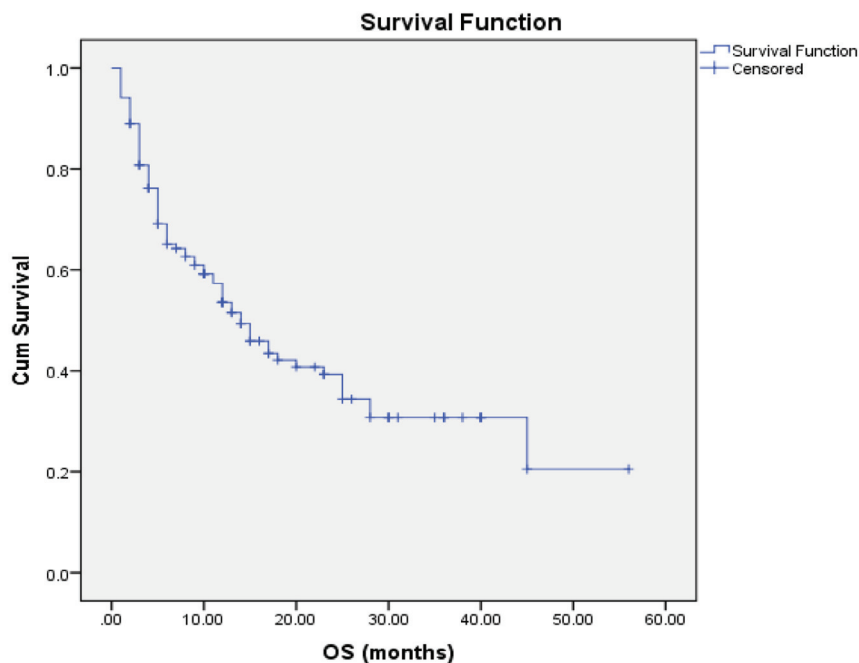

Figure 4. This figure exhibits the mean overall survival developed among 136 patients with gastric cancer.
OS: Overall survival; Cum: Cumulative

Table 5. Multivariate analysis of prognostic factors of OS

	B	SE	*P*-value	HR	95% CI for HR	
					Lower	Upper
Grade	0.295	0.143	0.039	1.343	1.015	1.778
D1	0.044	0.034	0.193	1.045	0.978	1.118
D2	-0.063	0.036	0.084	0.939	0.874	1.008
Chemotherapy	-0.358	0.107	0.001	0.699	0.567	0.862
T	0.410	0.219	0.061	1.507	0.981	2.314

Data were analyzed by Cox regression proportional hazard test; T: Tumor stage; D1: D1 lymphadenectomy; D2: D2 lymphadenectomy; HR: Hazard ratio; SE: Standard error; CI: Confidence interval; OS: Overall survival

variable was a quantitative one and the independent variables were qualitative). Spearman correlation was used to investigate the relationship between LN dissection and survival. We utilized Kaplan-Meier method to obtain the estimates of OS and DFS with a corresponding two-sided 95% confidence intervals. Log-rank test was employed for the comparisons between the survivals with a *P*-value <0.05. Through the use of Cox regression, the survival analysis of predictors of OS and DFS was carried out.

DFS was calculated based on the duration between the time of diagnosis and the time of relapse or death. Meanwhile, OS was calculated through the period between the time of diagnosis and death of any cause or the last follow-up

mentioned in patients' files. All the data were calculated via SPSS version 20.

Results

From the start of 2012 until the end of 2014, 136 patients with gastric carcinoma underwent surgical intervention at surgical oncology department of SECI, who were recruited in our study. We followed through their files for five years in order to calculate DFS and OS.

Our data were non-parametric and mainly right skewed and heavy tailed (positive kurtosis).

The median age of the study patients was 52 years; females were more affected than males with inverted M/F ratio. The pylorus was the most common site affected by cancer, followed
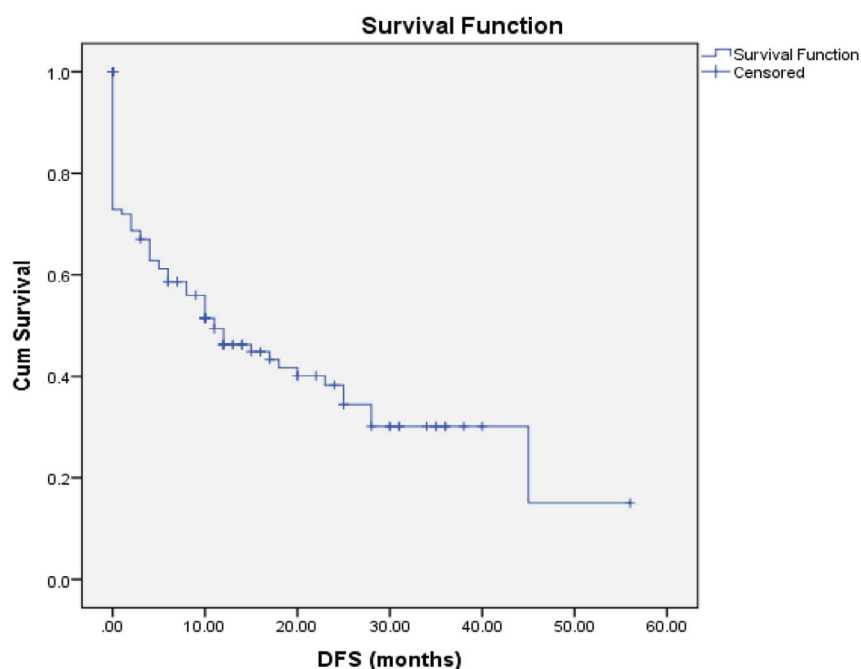

Figure 5. The mean DFS achieved among 136 patients with gastric cancer.
DFS: Disease-free survival; Cum: Cumulative

Table 6. Multivariate analysis of prognostic factors of DFS

	B	SE	*P*-value	HR	95% CI for HR	
					Lower	Upper
Grade	0.292	0.146	0.045	1.339	1.006	1.782
D2	-0.112	0.062	0.072	0.894	0.792	1.010
Total LD	0.048	0.033	0.145	1.049	0.984	1.120
Chemotherapy	-0.334	0.105	0.001	0.716	0.583	0.880
T	0.363	0.228	0.111	1.438	0.919	2.248

Data were analyzed by Cox regression proportional hazard test; T: Tumor stage; D2: D2 lymphadenectomy; LD: Lymph node dissection; HR: Hazard ratio; SE: Standard error; CI: Confidence interval; DFS: Disease-free survival

by the body. The tumor was rarely found at an early stage, but T3 and T4 lesions together represented over 80% of the cases. 67.6% of our patients underwent lymphadenectomy. The most prevalent pathologic type was adenocarcinoma and the most common grades were G4, G2, G3, and G1 as described in table 1.

Regarding the patients' outcomes after the follow-up, 77 (56.6%) patients died, 35 (25.7%) developed metastasis, and 24 (17.6%) are still alive (Figure 1).

Types of surgery

Out of 136 subjects, distal gastrectomy was performed in 26.47%, total gastrectomy in 22.1%, proximal gastrectomy in 12.5%, and subtotal

gastrectomy in 5.15% of them. Palliative surgeries were done in 33.8% of them and all surgeries were summarized in the following table (table 2). The mean LN dissected was 15.293 ± 12.079 and distributed between D1 and D2 dissections, as shown in table 2. Figure 3 represents the mean number of the dissected LNs in each type of radical surgery with mean $\pm$SE for total gastrectomy, subtotal gastrectomy, proximal gastrectomy, and distal gastrectomy, which were 17.03 ± 2.6, 17.9 ± 4.7, 11.2 ± 2.2, and 15.6 ± 1.9, respectively; there were no significant differences ($P = 0.4$).

OS and DFS

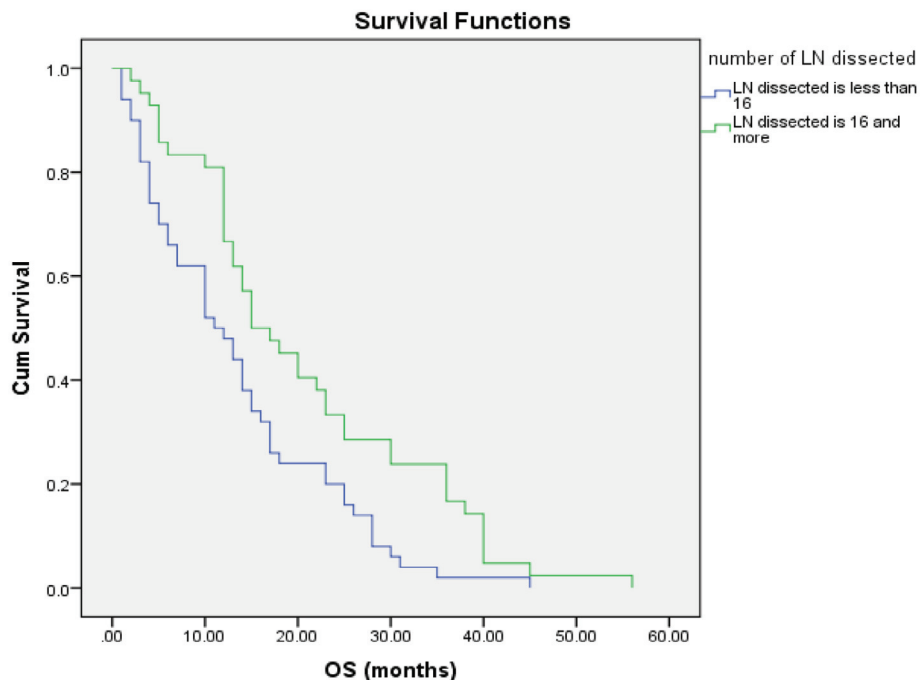The mean OS $\pm$ SE was 23.1 ± 2.3 months

Figure 6. This figure illustrates the comparison between the OS curves for the patients with less than 16 LNs dissected and those with 16 LNs or more dissected.
LN: Lymph node; OS: Overall survival; Log-rank = 8.030, *P* = 0.005

with 95% CI = 18.6-27.5 while the median ± SE was 14 ± 2.0 with 95% CI= 10.1-17.9 (Figure 4).

The mean DFS ± SE was 20.7 ± 2.4 months with 95% CI = 15.9-25.9 whereas the median ± SE was 11 ± 2.9 with 95% CI = 5.4-16.6 (Figure 5).

Relationships between the type and number of LN dissected and survival outcomes in the patients with resected GC

The rise in the number of LN dissected correlated positively with survival. This correlation was mild, but significant with exception of D1 dissection and DFS. In accordance with recent recommendations of different guidelines, D2 dissection was associated with significantly better OS and DFS ($P = 0.001$ and $P = 0.001$, respectively) (Table 3).

Our patients were sub-grouped into two groups, namely those with less than 16 LNs dissected and those with 16 LNs or more dissected; the OS curves of both groups were compared using log-rank test, showing a significantly higher OS for those with 16 LNs or more dissected log-rank = 8.030, $P = 0.005$. The mean OS for the former was 13.5 ± 1.5 with 95% CI = 10.6-16.4, while for the latter, it was 20.7 ± 2.1 with 95% CI = 16.69-24.79 months (Figure 6).

Furthermore, DFS for those with lower LNs dissected was significantly different from that of higher LNs dissected with log-rank = 5.465 and $P = 0.019$. The mean DFS for the former was 11.2 ± 1.5 with 95% CI = 8.3-14.2 whereas for the latter, it was 17.5 ± 2.01 with 95% CI = 13.5-21.4 (Figure 7).

Other possible prognostic factors of OS and DFS

There were no significant impacts of pathologic subtype, Lauren classification of adenocarcinoma, sex, age, or the site on DFS and OS. However, following the analysis using Post Hoc test via LSD, Linitis plastica had a significantly lower DFS than cardia ($P < 0.01$), pylorus ($P < 0.025$), and body ($P < 0.05$); in addition, it had a significantly lower OS than cardia ($P < 0.35$) only.

Once we tried to find which T stage gained further survival benefit from more LNs dissected, we found that the patients with T1 only had more LNs dissected, which was translated into better survival, an effect which was not seen in T2. The patients with T3 had more LNs dissected than
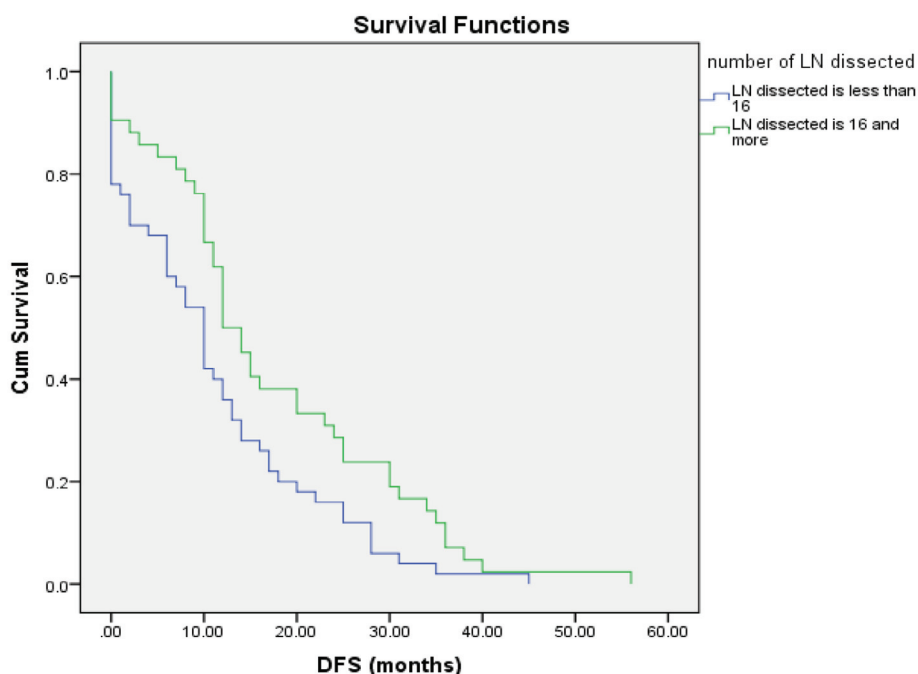

Figure 7. This figure demonstrates the comparison between DFS curves for the patients with less than 16 LNs dissected and those with 16 LNs or more dissected.
DFS: Disease-free survival; LN: Lymph node; Cum: Cumulative; Log-rank = 5.465, $P = 0.019$

T2 or T4 ones, but it did not improve the survival outcomes ($P < 0.041$) (Figure 8).

T-stage, lymphadenectomy, the type of chemotherapy, and pathologic grade had a significant impact on DFS and OS. Regarding the type of chemotherapy, the subjects receiving carboplatin plus paclitaxel had a significantly better DFS and OS than those receiving most chemotherapy regimens (no CTR, ECF, DCF, ELF, FAM, and ECX). Nonetheless, there were insignificant differences between carboplatin + paclitaxel and the other two regimens of Platinol +5FU and 5FU+leucovorin (Table 4) (Figures 9 and 10).

We performed multivariate Cox regression to predictors of OS and DFS; there was an increase in the mortality rate by 34.3% for each grade increase for OS ($P = 0.039$) and by 33.9% for DFS ($P = 0.045$). Furthermore, for each increase in the lines of chemotherapy received, there was a decrease in the hazard of death by 69.9% for OS ($P = 0.001$) and 71.6% for DFS ($P = 0.001$). According to the tables below, the mortality rate increased by 4.5% for each increase in the number of the cases undergoing D1 ($P = 0.193$) in OS;

this finding is contradictory to the results of many papers. The increase in the number of dissected LNs was associated with the rise in the mortality rate by 4.9% ($P = 0.145$) (Tables 5 and 6).

Discussion

Our study elucidated a significantly positive correlation between the survival outcomes and total number of LNs dissected. Moreover, there was a significant survival benefit for those undergoing D2 dissection and those with ≥16 LNs dissected.

GC ranks the fifth most common cancer after lung, breast, colorectal area, and prostate cancers; about half of the world's incidence of GC lies in East Asia.[13]

Generally, the removal of more LNs may improve locoregional control through dissecting further LNs containing micro-metastases, thereby ameliorating the survival. Wu et al.[14] proved that nodal micro-metastases were associated with worse survival. Our results were in agreement with the findings reported by Wu et al. Meanwhile, they were not in a line with those by Coburn et al.,[15] who demonstrated that harvesting more LNs
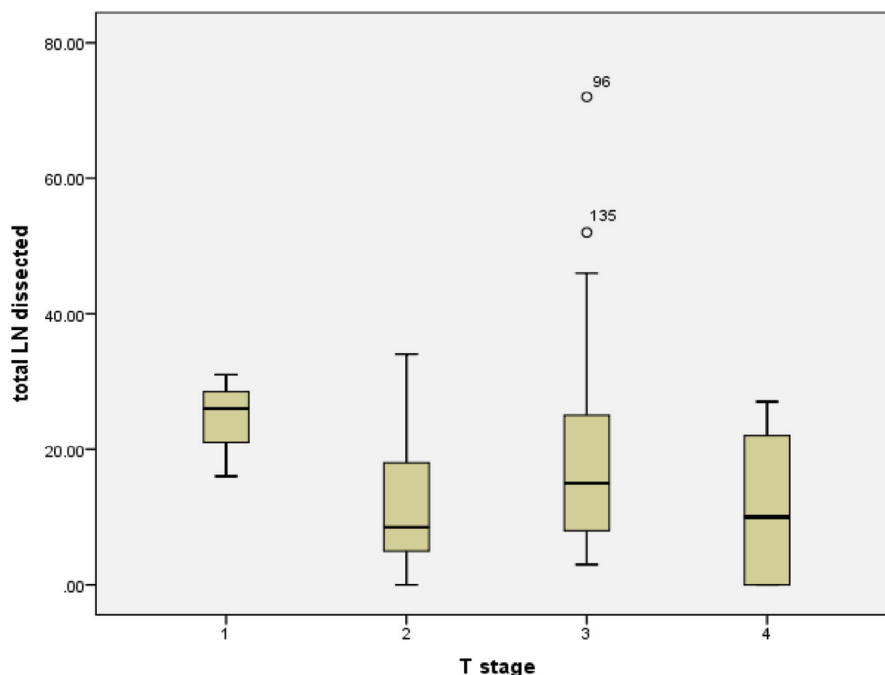

Figure 8. The figure illustrates different numbers of lymph nodes dissected according to different T stages.
LN: Lymph node; *P*<0.041

in early stages did not improve the survival in these patients as the risk of LN metastasis is considered low.

Eastern trials have proven survival benefits from D2 lymphadenectomy, while western experiments have not validated this survival benefit except after splenic preservation (± pancreatic preservation), which has in turn led to the recommendation of D2 lymphadenectomy as a standard practice for GC.[16-19]

In line with previous studies and recommendations, our results demonstrated a positively significant correlation between DFS ($P = 0.001$) and OS ($P = 0.001$) with D2 lymphadenectomy. However, table 6 depicts that the increase in the number of the cases undergoing D2 dissection resulted in a decrease the hazard of death by 6.1%, but it was non-significant ($P = 0.084$).

A prospective multi-center German GC study on 1,654 patients showed that dissection of > 25 LNs had a significant impact on survival in patients with stage II tumors.[20] Moreover, the Memorial-Sloan Kettering nomogram, which was done based on 1,039 patients with R0 resection for gastric adenocarcinoma, found that the number of both positive LNs and negative LNs provided prognostic information for disease specific survival (DSS).[21] Overall, these studies supported indirectly our results where patients with ≥16 LNs dissected achieved better DFS and OS.

The hypothesis that dissecting further LNs is associated with improved survival has been previously discussed in other cancers, including colon and esophageal cancers. A secondary analysis of the intergroup trial INT-0089, involving 3,322 patients with stage II and III colon cancer, determined the effect of the number of LNs examined on survival rate. It demonstrated that the survival significantly increased as more LNs were analyzed irrespective of the number of positive LNs.[22]

Sepideh et al.[23] reported no incremental increase in the adjusted HR for DSS beyond 16 LNs removed for GC. The obtained results herein are not in agreement with those of Sepideh et al., where significant increase in OS and DFS was achieved with the rise in LNs harvested.

According to SEER 21 (2012-2016), the median age of gastric cancer was 68 years, with males twice more commonly affected than
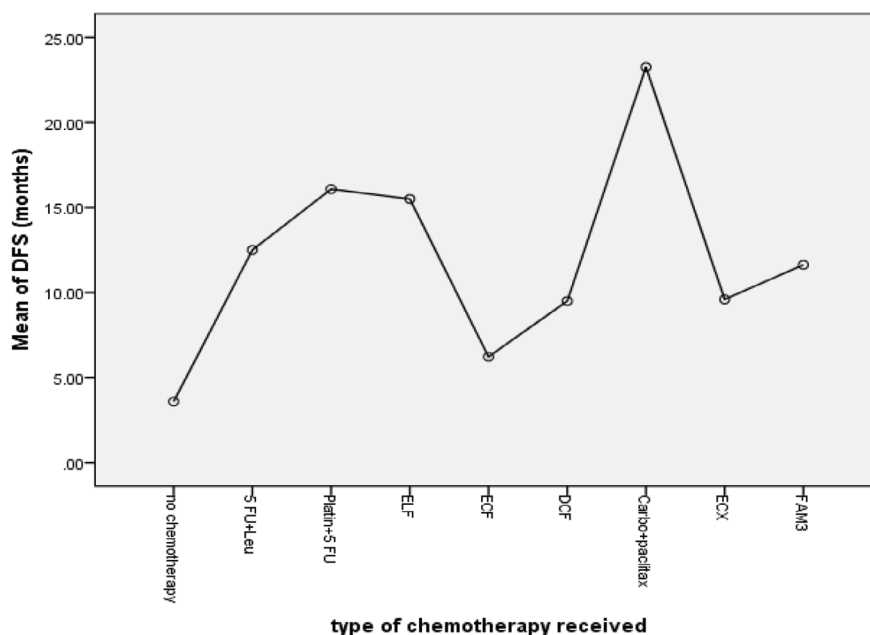

Figure 9. This figure illustrates the mean plot of the relation between the type of chemotherapy and DFS.
5FU + leu: 5FU + leucovorin; 5FU: 5-fluorouracil; ECF: Epirubicin + cisplatin + 5FU; ELF: Etopoisde + leucovorin + 5FU; FAM: 5FU + Adriamycin + mitomycin C; DCF: Docetaxel + cisplatin + 5FU; carbo.+paclitax.: carboplatin + paclitaxel; ECX: epirubicin + cisplatin + xeloda; DFS: Disease-free survival

females. On the other hand, in Egypt, the incidence rates are commonly lacking, until the availability of National Cancer Registry Program of Egypt with an estimated incidence of gastric cancer during the period of 2008-2011 to represent about 1.26% of all cancer incidences with a tendency to increase with age, with the highest age in the age range of 70-74; however, GC represented 5% of all the cancers registered in the age range of 50-54.[24]

There were certain limitations in our study; primarily, the patients were heterogeneous groups as those with R2 resections (incisional or excisional biopsy), who were included without lymphadenectomy. In addition, this work recruited 136 patients, but LN dissection was carried out only in 92 patients. Furthermore, stage migration occurred due to inadequate number of LN dissected as 50 patients underwent less than 16 LN harvested. Finally, it was a single-center experience with a small sample size.

Conclusion

The benefit of D2 lymphadenectomy and dissection of more LNs still remains under question. Meanwhile, provided that morbidity and mortality are kept at a minimum level, D2 dissection is advantageous. The current research concluded that harvesting further LNs was associated with more survival benefit.

Conflict of Interest

None declared.

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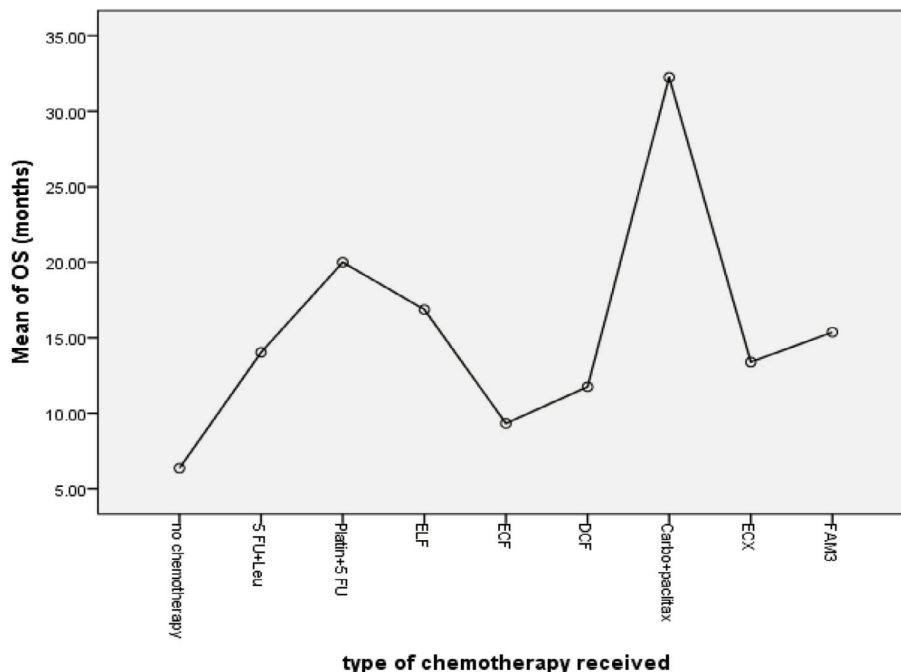

Figure 10. This figure shows the mean plot of the relation between the type of chemotherapy and OS.
5FU + leu: 5FU + leucovorin; 5FU: 5-fluorouracil; ECF: Epirubicin + cisplatin + 5FU; ELF: Etopoisde + leucovorin + 5FU; FAM: 5FU + Adriamycin + mitomycin C; DCF: docetaxel+cisplatin+5FU; carbo.+paclitax.: carboplatin + paclitaxel; ECX: Epirubicin + cisplatin + xeloda; OS: Overall survival

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