

Clinicopathological factors affecting lymph node metastasis in patients with esophageal and gastroesophageal carcinomas

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Background

Lymph node (LN) metastasis is a valid marker of prognosis in esophageal cancer. It is important to estimate the factor that affects LN metastasis to determine the prognosis and type of treatment.

Aim

The objective of this study was to investigate clinicopathologic predictors for LN metastasis in resectable esophageal cancer.

Patients and methods

A total of 41 patients with resectable esophageal cancer receiving primary curative resection without neoadjuvant therapy for esophageal cancer between 2010 and 2015 (12 adenocarcinoma, 29 squamous cell cancer) who had surgical resection with systematic lymphadenectomy were included. Specimens were assessed for the prevalence and pattern of lymphatic spread.

Result

The rate of LN metastasis per depth of invasion increased with T3 stage (46.15%). The percentage of LN metastasis increases with adenocarcinoma and with grade 3, which accounted for 58.3 and 75%, respectively.

Tumors located at the lower esophagus tend to metastasize to LN, with prevalence of 55.5% for lower esophagus and 43.7% for gastroesophageal junction.

Conclusion

The depth of invasion, tumor differentiation, sex, pathological type, and tumor location help in predicting higher rates of LN metastasis.

Keywords:

clinicopathological factor, esophageal cancer, lymph node metastasis in esophageal cancer

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Introduction

Esophageal cancer is the eighth most common cancer and sixth most common cause of death owing to cancer worldwide [1].

Lymph node (LN) metastasis is the single most important prognostic factor in esophageal cancer, and this leads to poor survival [2], whereby an increasing number of metastatic LNs are related to a progressively bad prognosis. On average, patients with a single LN metastasis survive significantly longer than those with two or more LN metastases [3,4].

However, the number of retrieved LNs depends on multiple factors. From the surgeon's standpoint, the number of dissected LNs will depend on the surgical approach and the number of dissected fields [5].

It is very difficult to identify patients with esophageal cancer at high risk for LN metastasis because the esophageal lymphatic drainage system is so complicated that it is made up of abundant lymph capillaries [6,7].

To find risk factors related to LN metastasis, we conducted a retrospective study to identify clinicopathologic predictors for LN metastasis in resectable esophageal cancer.

Patients and methods

Study design and patients

This retrospective study was conducted at the Surgical Oncology Department of the National Cancer Institute, Cairo University, during the period from January 2010 till January 2015. The study is retrospective no names and no trials no need for ethical approval or consent has been approved by the department of surgery in NCI and Cairo University. The study included 41 patients with esophageal cancer and gastroesophageal junction (GEJ) treated with esophagectomy and LN dissection. Patients with metastatic disease and early esophageal cancer (stage

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1 and CIS (carcinoma in situ)) were excluded. Clinicopathologic characteristics of the patients were retrieved from the patient's files, including age, family history, history of smoking, clinical presentation, preoperative computed tomography, upper gastrointestinal endoscopy, type of surgery, pathology data (tumor site, size, histological type, grade), and LN state. Tumor site was determined by endoscopic examination and radiologic imaging and pathologically confirmed after surgery.

Pathological examination

Esophageal resection specimens were evaluated pathologically using a standardized protocol in which the resection margins, the esophageal body, and regional LNs were extensively sampled in the Department of Pathology at the National Cancer Institute, Cairo University. Tumor stage was classified according to AJCC TNM staging system [8].

Statistical analysis

Data were coded and entered using the statistical package for the social sciences, version 23 (IBM, Chicago, Illinois, USA). Data were summarized using mean, SD, median, minimum, and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the nonparametric Kruskal–Wallis and Mann–Whitney tests. For comparing categorical data, χ^2 test was performed. Exact test was used instead when the expected frequency is less than 5. *P* values less than 0.05 were considered as statistically significant.

Results

This study collected 41 patients who underwent esophagectomy and LN dissection in the National Cancer Institute, Cairo University. There were 18 (43.9%) patients who had positive LNs: 50% of the patients had pN1, 44.44% had pN2, and 5.5% had pN3.

A total of 424 LNs were resected in all groups. The mean number of dissected LNs was 10.3 per person, with a range of 0–26.

The mean age of the patients was 52.9 ± 9.76 years and ranged between 29 and 67 years. Approximately 78% of the patients were under 60 years old at the date of diagnosis.

Males represented 51.2% of the patients, whereas females were 48.7%.

There were 36.58% (15 patients) in T2 stage and 63.41% (26 patients) in T3 stage.

The mean tumor size was $5.15 \text{ cm} \times 3.76 \text{ cm}$ (21.05 cm^2). It ranged from 1.5 to 88 cm^2 .

The relationships between sex, age, pathology, tumor location, tumor size, tumor differentiation, T stage, and LN metastasis are shown in Table 1.

Univariate analysis showed that LN metastasis was significantly associated with male's sex, depth of invasion T3, grade 3 pathological differentiation, adenocarcinoma, and lower esophagus location.

Female patients had the lowest (30%) rate of LN metastasis, whereas males had the highest rate (57.14%).

The rate of LN metastasis per depth of invasion increased with T3 stage (46.15%) than T2.

The percentage of LN metastasis increase with adenocarcinoma and with grade 3, which accounted for 58.3 and 75%, respectively.

Tumors located at the lower esophagus tend to metastasize to LNs: 55.5% for lower esophagus, and 43.7% for GEJ.

There was no significant relation between LN metastasis and both age and tumor size (Table 2).

Discussion

LN metastasis is an important prognostic factor of esophageal carcinoma, which can affect the type of treatment of esophageal cancer.

The main goal of this study was to examine the clinicopathological factor affecting the rate of LN metastasis in patients with tumors of the esophagus. GEJ as the preoperative evaluation of LN status remains a difficult problem in clinical practice.

Our study showed that the rate of LN metastasis of the esophageal cancer increased with the increase of T stage, poor tumor differentiation, male sex, and adenocarcinoma.

Male sex shows a high rate of LN metastasis than female, which accounted for 57.14% of all male patients.

In our study, adenocarcinoma has the highest tendency to metastasize to regional LNs in comparison with

Table 1 Relationship between clinicopathological factors and lymph node metastasis

Correlational analyses	Cases	Cases with lymph node metastasis	Rate of lymph node metastasis	P value
Sex				
Male	21	12	57.14285714	0.0001
Female	20	6	30	
Age				
≤40.00	5	3	60	0.1833
41.00–50.00	7	4	57.14285714	
51.00–60.00	20	6	30	
61.00–70.00	9	5	55.55555556	
Pathological type				
Squamous cell carcinoma	29	11	37.93103448	0.0001
Adenocarcinoma	12	7	58.33333333	
Tumor size				
≤10.00	9	5	55.55555556	0.041
Surface area (cm²)				
>10.00–20.00	18	8	44.44444444	
>20.00–30.00	10	3	30	
≥30.00	4	2	50	
Grade				
2	33	12	36.36363636	0.0001
3	8	6	75	
pT				
2	15	6	40	0.281
3	26	12	46.15384615	
Location				
Upper esophagus	4	1	25	0.0001
Mid esophagus	12	5	41.66666667	
Lower esophagus	9	5	55.55555556	
GEJ	16	7	43.75	

GEJ, gastroesophageal junction.

Table 2 Relationship between T stage and N stage

T	N0	N1	N2	N3
2				
15	9	4	2	0
3				
26	14	5	6	1

SCC (squamous cell carcinoma) (58.3 and 37.9%, respectively).

There was a significant correlation between the degree of differentiation and LN metastasis. The lower the degree of differentiation, the higher the rate of LN metastasis. The rates of LN metastasis in grade 2 and grade 3 groups were 36.3 and 75%, respectively.

Bollschweiler *et al.* [9] reported that grade 1/grade 2 were correlated with a lesser rate of LN metastasis compared with grade 3.

With the increase in the depth of tumor, there is an increase in the number of positive LNs, as T3 shows more positive LNs than T2.

Siewert *et al.* [10] revealed that the prevalence of LN metastasis in cases where the lesion was at least pT2 was more than 50%, regardless of histology, and almost all patients with T4 tumors had LN metastasis.

Thomas *et al.* [11] also proved that the depth of tumor invasion was predictive of regional LN status.

Moving downward of tumor location in the esophagus increases the tendency to LN metastasis.

The age and tumor size were not significantly associated with increases in the mean LN metastasis, as the distribution of patients with respect to these factors was not uniform.

This study has some drawbacks: first, it is a retrospective study, and second, the sample size is small, so further prospective studies with larger sample sizes are needed to verify the results.

Conclusion

The depth of invasion, tumor differentiation, sex, pathological type, and tumor location are risk factors that increase LN metastasis, and the tumor size and age were independent risk factors of LN metastasis in esophageal carcinoma.

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Conflicts of interest

There are no conflicts of interest.

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