Assessment of risk factors of lymph node metastasis and prognosis of Siewert II/III adenocarcinoma of esophagogastric junction: a retrospective study

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Abstract

Background

Adenocarcinoma of esophagogastric junction (AEG) has a high incidence, while the extent of lymph node dissection (LND) and prognosis are still controversial. The present study aimed to explore the risk factors of lymph node metastasis (LNM) and prognosis in Siewert II/III AEG patients.

Methods

A total of 134 patients who underwent surgical operation between July 2013 and December 2019 at the Beijing Friendship Hospital were retrospectively reviewed. The patients were followed up until January 2020. The data were analyzed using logistic regression. Survival analyses were performed using Cox regression.

Results

Multivariate analysis revealed that the parameters infiltration depth (OR=4.341, 95%CI: 2.498-7.545, P=0.000), gross type (OR=3.626, 95% CI: 1.425-9.228, P=0.007) and intravascular cancer embolus (OR=2.888, 95%CI: 1.106-7.544, P=0.030) correlated with LNM. For all patients, the lymph nodes No. 1, 2, 3, 4, 7, 11 indicated higher lymph node metastatic rate in the abdominal cavity. However, No.5 and No. 6 indicated different tendency, which was higher in Siewert III AEG and lower in Siewert II AEG patients. Mediastinal LNM of Siewert II AEG mainly occurred in No. 110 and No. 111 cases corresponding to 7.1 and 3%, respectively, compared with those noted in Siewert III AEG patients. The 3-year overall survival analysis revealed that LNM (P= 0.046) and chemotherapy (P= 0.007) exhibited significant differences.

Conclusion

The infiltration depth, gross type and intravascular cancer embolus were independent risk factors of LNM. For Siewert II AEG patients, it is reasonable to remove both celiac and mediastinal lymph nodes. This was noted notably for No.1, 2, 3, 4, 7, 11, 110 and No.111. For No.5 and No.6 lymph nodes dissection was not required. For Siewert III AEG patients, mediastinal LND was not required. However, it was necessary to perform pyloric lymphadenectomy, which was performed for No.5 and No.6 lymph nodes. In addition, patients with LNM exhibited worse long-term prognosis. The data indicated that perioperative chemotherapy could improve the prognosis of AEG patients.

Background

Adenocarcinoma of esophagogastric junction (AEG) is a type of adenocarcinoma lesion that originates from the glandular epithelium of the gastrointestinal tract and invades esophagogastric junction [1]. In recent years, the incidence and mortality of AEG have increased [2–4]. This region is a special anatomical location, involving complex operation and multiple lymphatic drainage approaches[5]. The drainage boundary and dissection extends from the lymph nodes around the stomach and it is localized around

the cardia for multiple groups of lymph nodes [6]. As a result, AEG can be treated with diverse surgical methods and exhibits worse prognosis compared with common gastric cancer [7, 8]. Previous studies have shown that mediastinal LNM accounts for 10–20% of all lymphatic metastasis in AEG [9–11]. However, other studies reported that the mediastinal LNM rate was low [12, 13]. Therefore, it is urgent to confirm whether the mediastinal LND of the lymph node drainage areas is required in Siewert II/III AEG in order to improve the curative effect of radical operation and prognosis. The present study attempted to analyze the risk factors of LNM and the follow-up survival data in patients with Siewert II/III AEG in order to provide more accurate treatments for AEG patients with different clinicopathological features.

1. Methods

General information

The clinical data from 134 Siewert II/III AEG patients undergoing surgical treatment (open or laparoscopic surgery) were selected between July 2013 and Dec 2019 from the General Surgery Department, Beijing Friendship Hospital. The 134 cases were retrospectively studied. Prior to surgery, the Siewert II/III AEG patients were diagnosed by routine endoscopy, ultrasound gastroscopy, enhanced CT of abdominal and pelvic cavity as well as pathological biopsy. The pathological biopsy is the gold standard for diagnosing cancer. In addition, preoperative evaluation of the tumor infiltration depth and lymphatic and distant metastasis was performed by endoscopy, ultrasound gastroscopy and enhanced CT for the abdominal cavity and the chest. The early stage AEG patients ($cT_1N_0-3M_0$) received radical gastrectomy initially and no less than 15 lymph nodes were dissected [14, 15]. Subsequently, certain patients ($pT_1N_1-3M_0$) would receive first-line chemotherapy regimen (XELOX or S-1). In addition, the patients with advanced stage AEG ($cT_{2-4}N_0-3M_0$) were confirmed with postoperative pathological examination ($pT_{2-4}N_0-3M_0$) and received first-line chemotherapy regimen (XELOX) following surgery. For advanced stage patients ($cT_{3-4}N_+M_0$) who could not achieve R0 resection, three-cycle preoperative neoadjuvant chemotherapy (ECF) was initially administered. Subsequently, the patients would receive surgery if complete tumor resection was scheduled. Following operation, they would also receive postoperative chemotherapy (XELOX). The present study gained approval from the Ethics committee of the Beijing Friendship Hospital. The requirement for individual consent was waived due to the retrospective nature of the study.

Inclusion criteria

(1) Patients who were diagnosed as Siewert type II/III AEG (epicenter of the tumor located between 1 cm above to 5 cm below the esophagogastric junction) by pathological biopsy and endoscopy were included in the study. (2) The patients were evaluated based on the clinical stage and the epicenter of the tumor prior to the surgery, including abdominal enhanced CT and/or ultrasound gastroscopy. (3) The clinical stage was $T_1-4N_0-3M_0$. Tumor staging was assessed as follows: Invasion of the tumor into the esophagogastric junction and location of its center at least 2 cm below the esophagogastric junction or invasion of the tumor into the esophagogastric junction and location of its center within 2 cm below the esophagogastric junction. For any of the aforementioned cases, the 8th version AJCC/UICC TNM staging

system for gastric cancer was adopted. If the tumor invaded the esophagogastric junction and its center was located within 2 cm below the esophagogastric junction, then the 8th version of the AJCC/UICC TNM staging system for esophageal cancer was adopted [16]. (4) The patients who had a physical fitness score, ECOG ≤ 2 points and were tolerant to radical gastrectomy were also included in the selection process. (5) Patients who did not have previous history of gastrointestinal operation, chemotherapy or radiotherapy were included in the study.

Exclusion criteria

The exclusion criteria used in the present study were the following: (1) Patients who suffered from gastric remnant carcinoma, recurrent cancer of gastric remnant or multiple primary malignant neoplasm of pelvis or had malignancy history within 5 years. (2) Patients who were unwilling to receive operations. (3) Patients who were confirmed with metastatic gastric cancer or gastric cancer of other parts intraoperatively. (4) Patients who suffered from uncontrollable internal diseases (including unstable angina, myocardial infarction and cerebrovascular accident that occurred within 6 months). (5) Patients who were unable to receive general anesthesia or surgical treatment due to conditions of other organs.

Mediastinal lymphadenectomy

The patients were placed in the supine position and the operation was performed through the ventral esophageal hiatus. Initially, an opening of the esophageal hiatus and an incision of both sides on the diaphragmatic feet at 1–2 cm were made. Subsequently, the surrounding tissue was dissociated, which was anterior to the pericardium, posterior to the aorta, lateral to the left and right pleura and upward to the inferior pulmonary vein. Thirdly, at the low margin of the inferior pulmonary vein, the tissue was stripped down along to the esophageal wall to the pre-cut line and the lymphatic connective tissue around the esophageal area was removed completely. Finally, the inferior mediastinal lymph node dissection was completed.

Observatory indicators

The clinical characteristics and the histopathological data of the enrolled Siewert II/III AEG patients were recorded, including gender, age, tumor site, tumor size, gross type, histological classification, infiltration depth, surgical approach, intravascular cancer embolus and cancerous node nodules. According to the age group proposed by the WHO, the patients were divided into the age < 60 years group and the age ≥ 60 years group. Tumor size was referred to the maximum diameter of the tumors. The gross type was divided into protruded type, flat type and depressed type according to the Japanese Gastric Cancer Guidelines (2014). Histological classification was divided into differentiated type (well-and-moderate differentiated adenocarcinoma, tubular adenocarcinoma) and undifferentiated type (poor differentiated adenocarcinoma, mucinous adenocarcinoma and signet-ring cell carcinoma).

Follow-up

The patients were followed up every 6 months after surgery. After discharge, the patients were followed up by means of outpatient visit, telephone or mail. During the follow-up period, the patients received

physical examination, laboratory tests, chest and abdominal CT scan assessment and annual endoscopic examination. Every patient had a minimum follow-up period of three years. The survival time was estimated from the operation date to the death date or until January 2020. The survival rate was determined by dividing the number of patients who survived for three years by the total number of enrolled patients.

Statistical analysis

Statistical analysis was performed using the SPSS 21.0 software. The count data were expressed as frequency and percentages and were compared using the χ^2 test, corrective χ^2 test or Fisher's exact test. Ranked data were expressed as frequency and percentages and were compared using the rank sum test. Multivariate analyses were performed using the logistic regression method. Survival analyses were performed using the Cox regression. A P value less than 0.05 ($P < 0.05$) was considered for significant differences.

2. Results

Baseline data and clinicopathological characteristics

A total of 134 Siewert type II/III AEG patients, including 112 men (83.6%) and 22 women (16.4%), with a male to female ratio of 5.1:1 were included in the study. The patient age ranged from 27 to 82 years and the mean age was 62.1 years. A total of 53 cases out of 134 patients were < 60 years old (39.6%), whereas 81 cases were $\geq$ 60 years old (60.4%). A total of 99 patients suffered from Siewert II AEG, whereas 35 patients suffered from Siewert III AEG. Among them, 71 patients were combined with lymphatic metastasis and the remaining 63 patients did not present with lymphatic metastasis. No patients suffered from distant metastasis (Table 1).

Table 1

Correlation between clinicopathological factors and lymphatic metastasis in 134 patients of Siewert II/III
AEG

Clinicopathologic factors	Number	Lymphatic metastasis [n(%)]	No lymphatic metastasis [n(%)]	P value
Age <60 ≥60	53 81	31(58.5%) 40 (49.4%)	22(41.5%) 41(50.6%)	0.302
Gender M F	112 22	59 (52.7%) 12 (54.5%)	53(47.3%) 10(45.5%)	0.873
Tumor site Siewert II Siewert III	99 35	51(51.5%) 20(57.1%)	48(48.5%) 15(42.9%)	0.566
Tumor size <2 cm ≥2 cm	20 114	1(5%) 70 (61.4%)	19 (95%) 44 (38.6%)	0.000
Gross type Protruded Flat Depressed	11 14 109	2(18.2%) 1(7.1%) 68(62.4%)	9(81.8%) 13(92.9%) 41(37.6%)	0.000
Surgical approach Proximal gastrectomy Total gastrectomy	59 75	25(42.4%) 46(61.3%)	34(57.6%) 29(38.7%)	0.037
Infiltration depth T _{is} T ₁ T ₂ T ₃ T ₄	1 30 19 42 42	0(0.0%) 2(6.7%) 6(31.6%) 26(61.9%) 37(88.1%)	1(100%) 28(93.3%) 13(68.4%) 16(38.1%) 5(11.9%)	0.000
Histological classification Differentiated Undifferentiated	68 66	26(38.2%) 45(68.2%)	42(61.8%) 21(31.8%)	0.001
Intravascular cancer embolus Negative Positive	74 60	26(35.1%) 45(75%)	48(64.9%) 15(25%)	0.000
Cancerous nodule Negative Positive	127 7	64 (50.4%) 7(100%)	63(49.6%) 0(0%)	0.014

Pattern of lymphatic metastasis

According to the NCCN guidelines (2nd edition, 2019), No. 1, 2, 7, 3, 11, 4 and 8 indicated higher LNM rate in the abdominal cavity of Siewert II AEG, whereas the metastatic rates for these cases were 29.3%, 25%, 24.5%, 22.9%, 14.8%, 12.4% and 11.1%, respectively (Table 2). Moreover, two patients with Siewert II AEG included mediastinal lymph nodes that were prone to metastasize (No.110 and No. 111, Table 3), with a metastatic rate of 7.1% and 3.0%, respectively. In contrast to these observations, the pyloric lymph node, such as No.5 and No.6, rarely exhibited LNM (Table 2). No.5 (10%) and No.6 (16.7%) lymph nodes exhibited higher LNM rates in Siewert III AEG patients, while mediastinal LNM was not found in 35 patients compared with those of the Siewert II AEG patients. Positive metastatic rate of the No.112 lymph node was not found in the patients examined (Table 3).

Table 2
Abdominal lymph node metastasis rate in Siewert II and Siewert III AEG patients

Lymph node group	Siewert II (% n/N)	Siewert III (% n/N)	Total lymph node metastasis rate (% n/N)
No.1	29.3% (27/92)	47.4%(9/19)	32.4% (36/111)
No.2	25% (20/80)	27.3% (3/11)	25.3% (23/91)
No.3	22.9% (22/96)	47.4%(9/19)	26.9% (31/115)
No.4	12.4% (12/97)	11.8% (2/17)	12.3% (14/114)
No.5	0% (0/73)	10% (1/10)	1.2% (1/83)
No.6	3.4% (2/58)	16.7% (2/12)	5.7% (4/70)
No.7	24.5% (24/98)	27.8% (5/18)	25% (29/116)
No.8	11.1% (10/90)	11.8% (2/17)	11.2% (12/107)
No.9	7.4% (5/68)	20% (3/15)	9.6% (8/83)
No.10	5.9% (1/17)	0% (0/5)	4.5% (1/22)
No.11	14.8% (8/54)	21.4% (3/14)	16.2% (11/68)
No.12	0% (0/44)	0% (0/11)	0% (0/55)
No.19	0% (0/4)	0% (0/3)	0% (0/7)
No.20	0% (0/8)	0% (0/3)	0% (0/11)

Table 3
Mediastinal lymph node metastatic rate in patients with Siewert II/III
AEG

Lymph node grouping	Siewert II (% , n/N)	Siewert III (% , n/N)
No.110	7.1% (7/99)	0% (0/35)
No.111	3.0% (3/99)	0% (0/35)
No.112	0% (0/99)	0% (0/35)

Univariate analysis

Among the 134 Siewert II/III AEG patients included in the present study, 71 cases suffered from LNM with a metastatic rate of 53%. Of these, the metastatic rates were 5% and 61.4% in patients with a tumor size of < 2 cm and $\geq$ 2 cm, respectively. This suggested that patients with a tumor size of $\geq$ 2 cm were more prone to LNM ($P = 0.000$). In addition, the LNM rate in patients with differentiated tumors was 38.2%, which was lower than that of 68.2% in patients with undifferentiated tumors ($P = 0.001$), whereas the LNM rate was elevated following an increase in the tumor infiltration depth ($P = 0.000$). The LNM rates in patients with intravascular cancer embolus and without intravascular cancer embolus were 75% and 35.1%, respectively ($P = 0.000$). Moreover, the parameters gross type ($P = 0.000$), surgical approaches ($P = 0.037$) and cancerous nodule ($P = 0.014$) were all significantly different between these two groups (Table 1). However, the parameters age, gender, tumor site were not associated with LNM (Table 1).

Multivariate analysis

As shown in Table 4, the parameters infiltration depth, gross type and intravascular cancer embolus were independent risk factors of LNM in Siewert II/III AEG patients. The LNM rate of advanced tumors was 4.341 times higher than that of the early tumor (95%CI: 2.498–7.545). The risk of depressed gross type was associated with lymph node metastasis and was 3.626 times higher than that of the other two types (95% CI: 1.425–9.228). The risk of lymph node metastasis in patients with intravascular cancer embolus was 2.888 times higher than that of patients without intravascular cancer embolus (95%CI: 1.106–7.544) (Table 4).

Table 4
Multivariate analysis results for risk factors of lymph node metastasis in type II/III AEG patients

Index	B	S.E	Walds	P	OR	95%CI
Infiltration depth	1.468	0.282	27.107	0.000	4.341	2.498–
Gross type	1.288	0.477	7.306	0.007	3.626	7.545
Intravascular cancer embolus	1.061	0.490	4.687	0.030	2.888	1.425– 9.228 1.106– 7.544
Constant	-10.504	1.958	28.772	0.000	0.000	-

Follow-up and survival analysis

The follow-up time of the 134 AEG patients was 1–75 months, whereas the median interval follow-up time was 27.9 months. During the follow-up period, 10 patients were lost to follow-up. The loss to follow-up rate was 7.5%. Among the 134 patients, 32 cases did not survive due to postoperative complications (7 patients), recurrence or distant metastasis (25 patients). Of these patients, 71 cases were followed up for more than 3 years. The median interval follow-up time period was 41.6 months, of which, the 3-year overall survival (OS) rate of the AEG patients without LNM (5 cases) and with LNM (23 cases) were 82.1% and 46.5%, respectively ($P = 0.046$, Fig. 1). In addition, the 3-year OS rate of AEG patients who accepted chemotherapy was higher than that of those who did not accept chemotherapy ($P = 0.007$, Fig. 2). The differences were significant ($P < 0.05$).

3. Discussion

Lymph node metastasis is one of the most important prognostic factors for AEG [17]. In addition, AEG can cause LNM and hematogenous metastasis at an early stage. Hence, the long-term prognosis of AEG patients has been demonstrated to be poor [18]. Radical surgery has been proposed as the effective treatment for AEG, including complete resection of lesions and lymph node dissection [19, 20]. However, Siewert II/III AEG is characterized by specific anatomical location and complex lymphatic drainage direction. Therefore, the correct evaluation of the lymph node metastasis can determine the extent of optimal lymph node dissection. The development of a reasonable treatment protocol is of great significance for improving the long-term prognosis in lymphatic metastasis patients with II/III AEG.

Certain studies have reported that the rates of mediastinal LNM are estimated from 5–25% [11, 13, 21, 22], whereas the recurrence rates of mediastinal LNM following surgery ranged from 0 to 11% [12, 21, 23, 24]. In the present study, Siewert II AEG was associated with celiac and thoracic lymph node metastasis. Metastasis to the celiac lymph nodes was noted, such as in the cases of No.1, 2, 7, 3, 11, 4, 8. In addition, the rate of mediastinal lymph nodes, such as that for No. 110 and No. 111, ranged from 3 to 7.1%. Particular attention has to be paid in order to perform both celiac and thoracic lymphadenectomy. However, in view of the low LNM rate of pyloric lymph nodes (No.5 and No.6) [25], tumor resection may be considered for this type of patients. Yamashita et al further showed similar results in a previous retrospective study [26]. Siewert III AEG patients did not present with mediastinal LNM and presented with tumor recurrence in the thoracic cavity. It should be noted that the mediastinal LND can increase surgical trauma and cardiopulmonary complication, notably in the elderly population [27]. Therefore, mediastinal LND is not necessary for Siewert III AEG patients. However, No.5 and No.6 LNM rates were estimated to 10% and 16.7%, respectively. A previous study reported that the dissection of pyloric lymph nodes could improve long-term prognosis for Siewert III AEG [25, 28]. Therefore, this type of patients should be treated with dissection of the pyloric lymph nodes. Moreover, we should emphasize on the en-bloc resection and avoid fragmented resection [29].

The assessment of the risk of LNM can aid the selection of the appropriate extent of lymph node dissection and individualized treatment strategy. At present, there is no effective method to evaluate LNM prior to surgery. However, the clinicopathological data exert a favorable prediction effect. In the present study, the infiltration depth, gross type and intravascular cancer embolus were independent risk factors for lymph node metastasis in patients with Siewert II/III AEG. Previous studies have reported that the LNM rate was significantly increased following an increase in the tumor infiltration [30]. The present study indicated similar outcomes demonstrating that the LNM rate was increased from 0 to 88.1% when the tumor infiltrated deeper gradually. This outcome may be attributed to the abundance of lymphatic capillaries in the submucosa, resulting in lymph node metastasis [31, 32]. In addition, whether the gross type is a risk factor for LNM remains a controversial issue. Several studies have demonstrated that the gross type was associated with LNM, while other reports have produced opposite results [31, 33, 34]. Moon et al reported that the gross type was not an independent risk factor for LNM [35]. However, in the present study, the LNM rates of the depressed type (62.4%) and protruded type (18.2%) metastases were higher than those of the flat type (7.1%). The gross type was a risk factor for LNM, which was in accordance with the results of Choi et al [36]. The present study indicated that although the gross type was not associated with LNM in the multivariate analysis, the opposite findings were noted in the univariate analysis [36]. A similar Chinese study reported that the gross type was associated with metastasis and recurrence in the upper gastric cancer [37, 38]. Hence, the gross type may become a useful indicator for the prediction of LNM. However, we need to further verify these findings using large-sample data. In addition, among the 60 patients who were combined with intravascular cancer embolus, 45 patients exhibited LNM. The incidence was higher than those patients who did not present with intravascular cancer embolus. A previous study demonstrated that 54 gastric cancer patients with intravascular cancer embolus exhibited 51 cases with lymph node metastasis (94.4%) [32]. This may be due to the capillary wall that does not contain a basal membrane and is composed of endothelial cells. The majority of these cells are irregularly arranged. Therefore, the capillary wall has greater permeability than the capillary and is more susceptible to cancer cell invasion [32]. Nevertheless, since it is difficult to determine whether patients present with intravascular cancer embolus preoperatively, tumor infiltration depth and gross type remain valuable indicators for the prognosis of the disease.

In the present study, survival analysis revealed that LNM exhibited significant differences in the 3-year overall survival rate. The data indicated that patients with LNM exhibited worse long-term prognosis. It was reported that proximal gastric cancer could develop LNM and exhibit early recurrence [39]. Kim et al revealed that the survival rate was decreased following an increase in the LNM rate [40]. The data indicated that LNM was an independent prognostic risk factor for 86 patients [41]. A study conducted in China revealed that the 3-year and 5-year survival rates of 231 gastric cancer patients without LNM were 69.7% and 63%, respectively, while the survival rates of 481 gastric cancer patients with LNM were 38.4% and 28.7%, respectively ($P = 0.001$) [38]. In addition, a multi-center study demonstrated that Siewert II AEG patients with mediastinal LNM exhibited a higher recurrence rate and a poor prognosis [12]. As a result, LNM should be considered a prognostic evaluation index for gastric cancer patients who have received radical operation.

However, perioperative chemotherapy can improve the long-term prognosis of AEG patients to some extent. The current result was consistent with previous studies [42]. The EORTC40954 clinical trial indicated that the preoperative chemotherapy combined with surgery could increase R0 resection but failed to show survival benefit in stage III and IV (cM0) of AEG or gastric cancer patients [43]. In addition, the FNCLCC and FFCD9703 clinical trials revealed that perioperative chemotherapy could improve the curative surgical rate, the overall survival (OS) and the disease-free survival (DFS) [44]. In 2011, the ACTS-GC trial reported that postoperative treatment with S-1 chemotherapy could prolong the 5-year OS and DFS [45]. The CLASSIC study for stage II to stage IIB gastric cancer revealed that patients who received chemotherapy following surgery exhibited optimal prognosis than those treated with surgery alone [46]. Recently, the POET trial compared chemotherapy and surgery with induction chemotherapy, chemoradiotherapy and surgery [47]. The data demonstrated that induction chemotherapy and chemoradiotherapy could prolong progression-free survival (PFS) [47]. Therefore, chemotherapy has become a necessary treatment modality in advanced AEG.

The present study exhibits certain limitations. It is a retrospective, single-center study, involving a small number of samples. Therefore, the results are unlikely to fully reflect the regulation of LNM and long-term prognosis. There may be certain bias in the analysis of the clinical data. Hence, we need to further confirm the current findings by large-sample, randomized controlled studies.

Conclusions

In summary, LNM in patients with Siewert II/III AEG was mainly associated with the parameters infiltration depth, gross type and intravascular cancer embolus. For Siewert II AEG patients, it is reasonable to excise both celiac and mediastinal lymph nodes, notably for No.1, 2, 3, 4, 7, 11, 110 and No.111 lymph nodes. However, pyloric lymph nodes did not require dissection. For Siewert III AEG patients, the mediastinal LND was not required. However, it is necessary to perform celiac lymphadenectomy, including pyloric lymph nodes. Moreover, patients with LNM exhibited worse long-term prognosis. Perioperative chemotherapy can improve the prognosis of AEG patients. All the results remain to be further verified using large-sample, multi-center, randomized controlled studies.

List Of Abbreviations

Adenocarcinoma of esophagogastric junction (AEG); lymph node metastasis (LNM); lymph node dissection (LND); overall survival (OS); disease-free survival (DFS); progression-free survival (PFS); National Comprehensive Cancer Network (NCCN); American Joint Committee on Cancer (AJCC); Union for International Cancer Control (UICC).

Declarations

Ethics approval and consent to participate

This study gained approval from the Ethics committee of Beijing Friendship Hospital. The need for individual consent was waived due to the retrospective nature of the study.

Consent for publication

Not applicable

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Zhi Zheng, Hai-qiao Zhang, Rui Xu carried out the studies, participated in the collection of the data and drafted the manuscript. Jie Yin and Jun Cai performed the statistical analysis and participated in its design. Jun Zhang, Guang-yong Chen and Zhong-tao Zhang aided the preparation of the manuscript. All authors read and approved the final manuscript.

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Figures

Figure 1

The 3-year OS rate of AEG patients without LNM and with LNM was 82.1% and 46.5%, respectively (P=0.046).

Figure 2

The 3-year OS rate of AEG patients who accepted chemotherapy was higher than those who did not accept chemotherapy ($P=0.007$).