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Supraclavicular lymph node metastasis should not be defined as regional lymph node metastasis in cervical and upper thoracic esophageal squamous cell carcinoma

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Abstract. The importance of supraclavicular lymph node (SCLN) metastasis in cervical and upper thoracic esophageal squamous cell carcinoma (ESCC) has not been determined. The aim of the present study was to provide a detailed definition of the range of SCLN regions and to explore whether SCLNs should be considered as a regional lymph nodes for patients with cervical and upper thoracic ESCC. A retrospective analysis was performed on 230 patients with locally advanced cervical or upper thoracic ESCC who underwent radical radiotherapy and chemotherapy. The range of SCLN regions was defined in detail on contrast enhanced computed tomography images of the neck. According to whether the patient had lymph node metastasis in the supraclavicular region, the included patients were divided into two groups, and the survival differences and reasons for treatment failure between the two groups were analyzed. Of the 230 patients with ESCC, 71 (30.87%) exhibited lymph node metastases in the supraclavicular region. The median overall survival time of ESCC patients with and without SCLN metastasis was 17 and 30 months, respectively (P<0.001). After propensity score matching (PSM), the median overall survival time of ESCC patients with and without SCLN metastasis was 17 and 28 months, respectively (P<0.001). During the follow-up period, there were a total of 101 cases of failure of treatment in the irradiation field, 6 cases had esophageal metastasis in the non-irradiated field and 27 cases had regional lymph node metastasis in the non-irradiated field. In addition, there were 33 cases of metastasis to the distant lymph nodes or organs. There was no significant difference in the local treatment failure rate between the groups with or without SCLN metastasis in both the irradiation field and the non-irradiation field, but the probability of distant metastasis in the SCLN metastasis group was significantly higher than that in the group without SCLN metastasis (P=0.025). In conclusion, patients with cervical and upper thoracic ESCC with SCLN metastasis have a poor prognosis and the median overall survival time is closer to that of metastatic ESCC than ESCC with regional lymph node metastasis; therefore, SCLNs should not be defined as regional lymph nodes in patients with cervical and upper thoracic ESCC.

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Key words: supraclavicular lymph node, esophageal squamous cell carcinoma, overall survival, failure

Introduction

In 2020, there were an estimated 604,000 individuals diagnosed with esophageal cancer, with >544,000 esophageal cancer-associated deaths worldwide (1). In China, the esophageal cancer incidence rate ranks it as the 7th most common type of cancer and the 5th most common cause of cancer-associated death, with ~188,000 associated deaths in 2022 (2). Squamous cell carcinoma is the most prevalent histological subtype of esophageal cancer in Asia and Eastern Europe, especially for cervical and upper thoracic esophageal cancer (3). Surgical resection is the primary method of treatment for esophageal squamous cell carcinoma (ESCC) without metastasis (4). However, the optimal treatment plan for ESCC with supraclavicular lymph node (SCLN) metastasis remains uncertain. Western countries typically define SCLN metastasis as distant metastasis regardless of the location of the ESCC (5), while in Asian countries, only for middle and lower thoracic ESCC, SCLN metastasis is indicative of a poor prognosis and should be defined as a distant metastasis, whereas for upper thoracic and cervical ESCC, it should be defined as regional lymph node metastasis (6,7). However, in 2024, in the 12th Edition of Staging of Esophageal Cancer released by the Japan Esophageal Society (JES), SCLN metastasis was defined as a distant metastasis for upper thoracic ESCC (8). Even for cervical ESCC, SCLN metastasis is commonly indicative of a significant deterioration in prognosis and should not be defined as regional lymph node metastasis (9).

Previous studies regarding the prognosis of SCLN metastasis in ESCC are based on cases undergoing surgical resection (9-11). Although an esophagectomy can be used to diagnose lymph node metastasis through pathological examination, for cervical and upper thoracic ESCC, the value of esophagectomy for prolonging overall survival rates is contested (12), Therefore, it is not accurate to predict the prognosis of patients with SCLN metastasis based on the survival rate of ESCC after esophagectomy. In addition, inconsistent definitions of the supraclavicular region may also affect the prognostic value of SCLN, as the conclusions of the studies may not be comparable (8,13).

Chemoradiation therapy for cervical thoracic ESCC with SCLN metastasis is widely adopted in Asian countries due to its generally tolerable toxicity and clinical benefits (14). The aim of the present study was to define the supraclavicular region on contrast-enhanced computed tomography (CT) in order to investigate the prognostic value of SCLN metastasis on cervical and upper ESCC receiving curative chemoradiotherapy.

Patients and methods

Patients. Information on patients with ESCC diagnosed and treated at the First Affiliated Hospital of Yangtze University (Jingzhou, China) between December 2019 and December 2021 was collected. The inclusion criteria were as follows: i) A histopathological diagnosis of ESCC; ii) cases of cervical and upper thoracic ESCC; that is, the primary tumor of the esophagus was located between the esophageal inlet and the lower edge of the azygos vein based on CT images; iii) patients were aged between 18 and 70 years old; iv) an Eastern Cooperative Oncology Group performance status score of 0-1 (15); v) cases of locally advanced ESCC that received curative radiotherapy and chemotherapy; and iv) except for SCLN metastasis, patients showed no evidence of distant metastasis prior to treatment. The exclusion criteria were as follows: i) A histopathological diagnosis of adenocarcinoma or other non-squamous cell carcinoma; ii) a hypopharyngoscopy revealed the presence of hypopharyngeal cancer; iii) individuals receiving palliative chemotherapy or palliative radiotherapy; and iv) patients with a survival time of <3 months after curative chemoradiotherapy.

The diagnostic criteria for metastatic lymph nodes included at least one of the following: i) Lymph node with the shortest diameter ≥0.6 cm on contrast-enhanced CT; ii) fluorodeoxyglucose-positron emission tomography (FDG-PET)/CT image displayed a maximum standard uptake value >3.0; and iii) lymph nodes confirmed as metastatic through ultrasound-guided biopsy. The diagnosis and location of the metastatic lymph nodes were determined by a radiologist and a radiation oncologist.

The Ethics Committee of the First Affiliated Hospital of Yangtze University approved the present study (approval no. 2021005), and as it was a retrospective analysis, the requirement for informed patient consent was waived.

Radiotherapy procedure. Intensity-modulated radiation therapy or volumetric modulation arc radiotherapy was used for all radiation treatments. All patients included in the analysis underwent a contrast-enhanced CT scan to obtain images of the entire cervical region, chest and upper abdomen, with a slice thickness of 2.5 mm on a Siemens Somatom 48 CT simulator (Siemens Healthineers). The obtained images were transferred to the Eclipse 11 Treatment Planning System (Varian Medical Systems, Inc.).

Gross target volume (GTV) includes gross target volume of the primary tumor (GTV_{-p}) and gross target volume of the metastatic lymph nodes (GTV_{-n}). GTV_{-p} includes esophageal tumors detected by CT scans, esophageal barium examination, endoscopy, endoscopic ultrasound or FDG-PET/CT. GTV_{-n} is defined as the presence of metastatic lymph nodes in the mediastinal and supraclavicular regions. The clinical target volume of the primary tumor (CTV_{-p}) was positioned as a 3-cm extension along the GTV_{-p} and 0.5 cm on the lateral edge of the esophagus. CTV of the lymph nodes (CTV_{-n}) encompassed a 0.6-cm margin around the GTV_{-n}. The planning target volume around the CTV (PTV_{-c}) was established by adding a uniform 0.5-cm margin around the CTV (CTV_{-p} + CTV_{-n}). The planning target volume around the GTV (PTV_{-g}) was defined as a 0.3-cm margin around the GTV (GTV_{-p} + GTV_{-n}).

The prescribed dosage was 50.4 Gy/28 fractions to the PTV_{-c} and 59.92 Gy/28 fractions to the PTV_{-g}. Organs at risk included the spinal cord, lungs and heart. The treatment plan was evaluated based on the dose-volume histogram. The treatment plan generally required that the percentage of total lung volume treated with ≥5 Gy (V5 of the whole lung) was ≤60%, the V20 of the whole lung was ≤28%, the V30 of the whole lung was ≤18% and the V30 of the heart was ≤30%. The maximum spinal cord dose was <45 Gy. Cone beam CT online validation radiotherapy was performed for 5 consecutive days in the first week, and then once a week thereafter.

Chemotherapy and immunotherapy. The sequential, induction and consolidation chemotherapy treatment used 5-fluorouracil + cisplatin (FP) or docetaxel + cisplatin (TP) with the following regimen: For FP, cisplatin (25 mg/m^2/day) for 3 days and 5-fluorouracil (750-1,000 mg/m^2/day) for 5 days, repeated every 3 weeks; and for TP, docetaxel (75 mg/m^2) for 1 day and cisplatin (25 mg/m^2/day) for 3 days, repeated every 3 weeks.

The concurrent chemotherapy regimen included FP, or TP, or monotherapy with S1, with the following regimen: For FP, cisplatin (25 mg/m^2/day) for 3 days and 5-fluorouracil (450-500 mg/m^2/day) for 5 days, repeated every 4 weeks; and for TP, docetaxel (75 mg/m^2) for 1 day and cisplatin (25 mg/m^2/day) for 3 days, repeated every 4 weeks. Alternatively, S1 was used as monotherapy, taken continuously for 2 weeks and then discontinued for 1 week, or taken only on the day of radiotherapy (Monday-Friday), with weekend rest (40 mg twice per day if the body surface area was <1.25 m^2; 50 mg twice per day if the body surface area was ≥1.25-1.5 m^2; or 60 mg twice per day if the body surface area was ≥1.5 m^2).

Consolidation immunotherapy using either 200 mg carolizumab or teralizumab was administered on day one, and repeated every 3 weeks.

Definition of regional lymph nodes. The range of lymph node regions was defined using contrast-enhanced CT images based on the JES criteria, 12th edition (8), with JES lymph node numbering. Briefly, for Group I (no. 101), the cervical para-esophageal lymph nodes, the boundaries defined on CT images were as follows: Upper boundary, lower edge of cricoid the cartilage; lower boundary, apex of the lung; anterior boundary, posterior edge of the thyroid; posterior boundary, longus colli muscle; lateral boundary, medial edge of the internal carotid artery; and inner boundary, esophageal wall. As the probability of no. 104 lymph node metastasis is different, lymph node region no. 104 was distinguished into Group II and Group III. Group II was defined as the vascular sheath area with the following boundaries: Upper boundary, lower edge of the cricoid cartilage; lower boundary, lung apex level; anterior boundary, anterior edge of the internal carotid artery; and posterior boundary, posterior edge of the internal jugular vein. Group III was defined as the vascular lateral space with the following boundaries: Upper boundary, lower edge of the cricoid cartilage; lower boundary, at the apex level; front boundary, posterior margin of the internal jugular vein; and posterior boundary, trapezius muscle. Group IV was defined as the regional lymph nodes of the thoracic region (nos. 105-112) (8).

Follow-up and statistical analysis. Follow-up was conducted using the hospital's electronic case system and by telephone. The last follow-up was on December 31, 2023, with a median follow-up time of 33 months (range, 24-48 months). The Kaplan-Meier method was used to estimate overall survival (OS), and a log-rank test was used to compare survival between the Kaplan-Meier curves. Age and body mass index (BMI) were compared using a Kruskal-Wallis test. PSM analysis [including age, sex, BMI, tumor location, T-stage, lymph node status, clinical stage based on the American Joint Committee on Cancer (AJCC) staging system 8th edition (5) and treatment method] was performed using a 1:1 nearest neighbor matching method with a caliper width of 0.2. After balancing the clinical characteristics of the two groups of ESCC patients, namely those with or without SCLN metastasis, via PSM, the OS curve was plotted. The categorical variables were evaluated using a χ^2 test; when one of the expected frequencies was ≤5, Fisher's test was used instead. P<0.05 was considered to indicate a statistically significant difference. All statistical analysis was performed using GraphPad Prism version 10 (Dotmatics).

Results

Baseline characteristics of the patients. During the research period, data on 230 eligible patients with ESCC was collected from the First Affiliated Hospital of Yangtze University. A total of 208 ESCC (90.4%) were diagnosed with lymph node metastasis by contrast-enhanced CT scans, 18 cases (7.8%) were pathologically diagnosed with lymph node metastasis according to ultrasound-guided biopsy and 4 cases (1.7%) were diagnosed with lymph node metastasis by FDG-PET/CT. The number of sequential, induction and consolidation chemotherapy cycles ranged from 1-6, with a median of 3 cycles. The duration of consolidation immunotherapy was 1-24 months, with a median time of 10 months. The recruited patients were divided into two arms based on the presence or lack of SCLN metastasis: Arm A consisted of Group I or Group IV lymph node metastasis accompanied with no. 104 (Group II and Group III) lymph node metastasis; and Arm B consisted of Group I (no. 101) or Group IV lymph node metastasis without no. 104 (Group II and Group III) lymph node metastasis. As the probability of lymph node metastasis in the supraclavicular region alone without mediastinal lymph node metastasis was extremely low, these cases were not calculated.

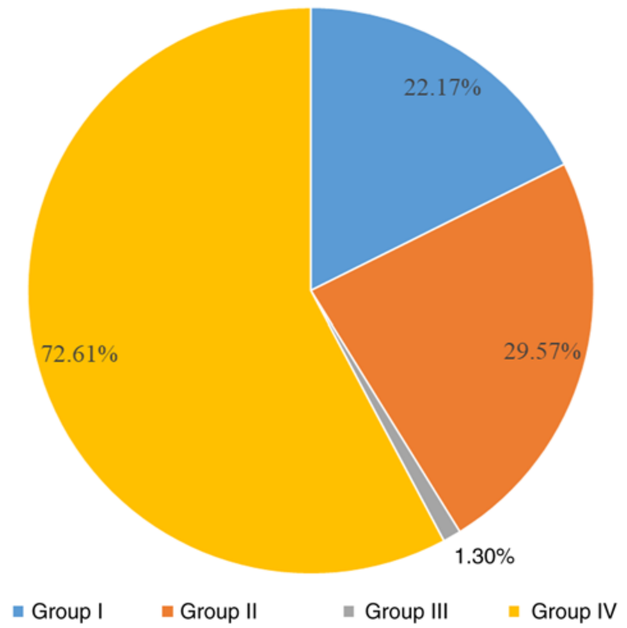

Figure 1. Distribution of metastatic lymph nodes in 230 cervical and upper thoracic esophageal squamous cell carcinoma.

Table I shows the detailed information of the patients with ESCC and a comparison between the two arms. There were no significant differences in baseline clinical characteristics between the two groups.

Distribution of metastatic lymph nodes. All enrolled patients had lymph node metastases, among which 51 (22.17%) cases were in Group I, 68 (29.57%) cases were in Group II, 3 (1.30%) were in Group III and 167 (72.61%) were in Group IV. The probability of lymph node metastasis in the different groups is shown in Fig. 1. Due to the importance and inconsistency in the definition of SCLNs, the range of para-esophageal and supraclavicular lymph nodes was delineated on the CT map as shown in Fig. 2.

OS times. The median OS times of patients in Arm A and Arm B were 17 and 30 months, respectively (P<0.001). The OS rates in Arm A after 1, 2 and 3 years were 65, 16, and 9.7%, respectively. The OS rates in Arm B after 1, 2 and 3 years were 80, 55, and 40%, respectively. After PSM (54 patients in each group), the median OS times in Arm A and Arm B were 17 and 28 months, respectively (P<0.001). The OS rates in Arm A after 1, 2 and 3 years were 72, 18 and 11%, respectively. The OS rates in Arm B after 1, 2 and 3 years were 81, 54 and 39%, respectively (Fig. 3).

Failure patterns. During the follow-up period, there were a total of 101 ESCC cases with treatment failure in the irradiation field, 6 cases had esophageal metastasis in the non-irradiated

Table I. Baseline clinical characteristics of the 230 eligible patients with esophageal squamous cell carcinoma.

		Before PSM			After PSM		
Characteristics	Value	Arm A[b] (n=71)	Arm B[c] (n=159)	P-value	Arm A[b] (n=54)	Arm B[c] (n=54)	P-value
Median age (range), years	64 (45-80)	64	64	0.861	64	64	0.952
Sex, n (%)				0.189			0.391
Male	202 (87.83)	59	143		45	49	
Female	28 (12.17)	12	16		9	5	
Median BMI (range), kg/m^2	19.8 (15.57-28.37)	21.2	18.7	0.062	20.8	19.3	
Main tumor location, n (%)				0.081			0.202
Cervical	63 (27.39)	25	38		19	12	
Upper thoracic	167 (72.61)	46	121		35	42	
Clinical depth of tumor invasion				0.758			0.999
cT1-2	5 (2.17)	2	3		1	1	
cT3	223 (96.96)	68	155		52	52	
cT4	2 (0.87)	1	1		1	1	
Clinical lymph node metastasis[d], n (%)				0.236			0.319
cN1	149 (64.78)	42	107		31	37	
cN2	81 (35.22)	29	52		23	17	
Clinical stage[d], n (%)				<0.0001[a]			-
II, cT2N1M0	5 (2.17)	0	5		0	0	
III, cT3N1M0, cT1-3N2M0	153 (66.52)	0	153		0	0	
IVA, cT4N1-2M0	1 (0.43)	0	1		0	0	
IVB, cT1-4N1-2M1[e]	71 (30.87)	71	0		0	0	
Treatment status, n (%)				0.851			0.344
Sequential chemoradiotherapy	11 (4.78)	3	8		3	3	
Concurrent chemoradiotherapy alone	197 (85.65)	63	134		47	46	
Induction chemotherapy + concurrent chemoradiotherapy	7 (3.04)	1	6		1	2	
Concurrent chemoradiotherapy + consolidation chemotherapy	10 (4.35)	3	7		2	2	
Concurrent chemoradiotherapy + consolidation immunotherapy	5 (2.17)	1	4		1	1	

[a]P<0.0001; [b]with SCLN metastasis; [c]without SCLN metastasis; [d]based on the American Joint Committee on Cancer staging system; [e]M1, SCLN without distant metastasis. SCLN, supraclavicular lymph node; BMI, body mass index.

field and 27 cases had regional lymph node metastasis in the non-irradiated field. In addition, there were 33 cases of metastasis to the distant lymph nodes or organ.

There was no significant difference in the local failure rate between the groups with and without SCLN metastasis in the irradiation field and the non-irradiation field, but the probability of distant metastasis in the patients with SCLN metastasis was significantly higher than that in the patients without SCLN metastasis (P=0.025). Details of the failure patterns are shown in Table II.

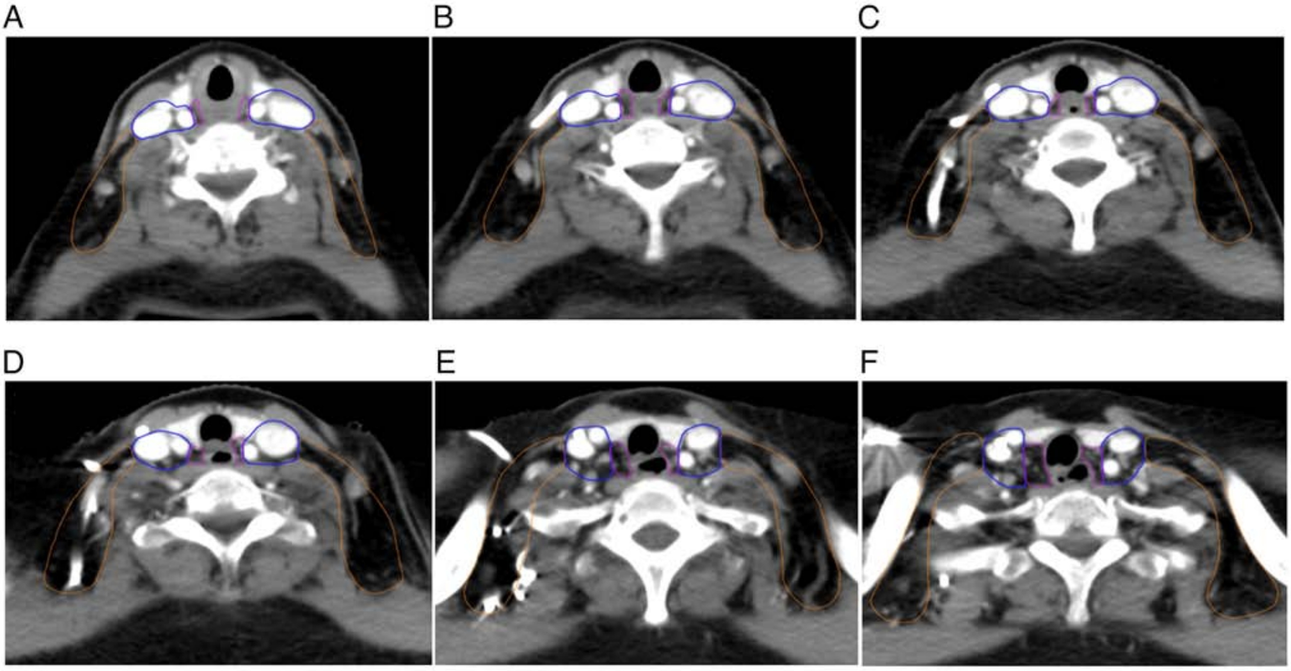

Figure 2. Range of para-esophageal and supraclavicular lymph nodes on the CT map. (A to F) CT images of the cevical region at different levels. (A) Level of the lower margin of the cricoid cartilage. (B-E) Starting from image (A), images are captured at intervals of 5 mm in sequence. (F) Level of the upper margin of the lung apex. Purple lines indicate the lymph node area in Group I, blue lines indicate the lymph node area in Group II and yellow lines indicate the lymph node area in Group III. CT, computed tomography.

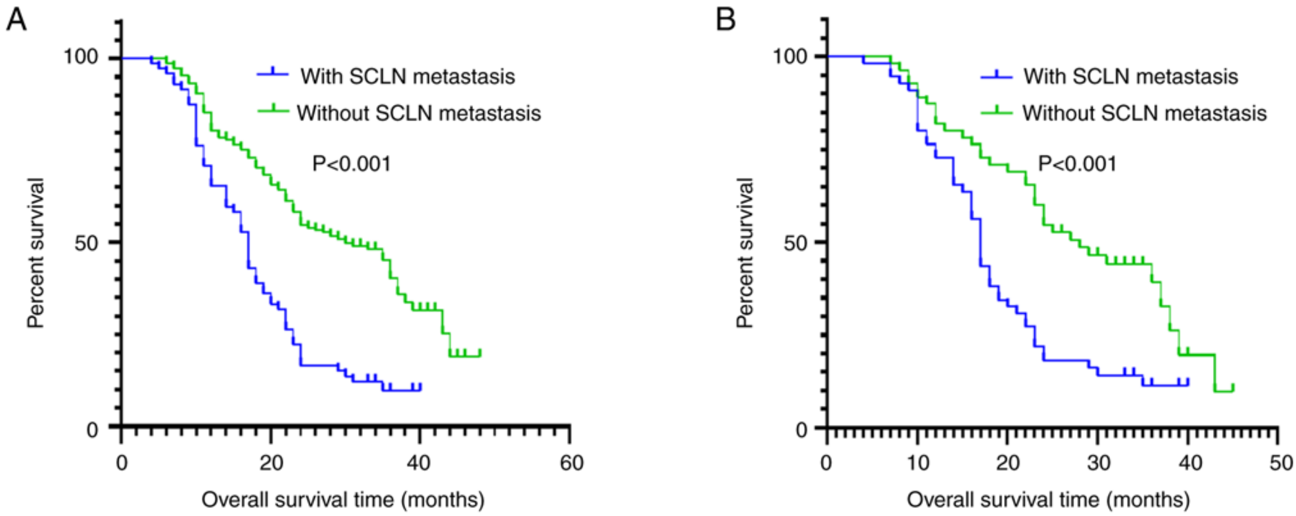

Figure 3. Survival curves of patients with a regional lymph node metastasis with and without SCLN metastases (A) before and (B) after propensity score matching. SCLN, supraclavicular lymph node.

Discussion

Due to significant differences in the pathological types and primary tumor sites of esophageal cancer between the Asian and Western populations, there is controversy regarding the prognostic guiding value of SCLN metastasis. Western countries tend to define metastases of the supraclavicular lymph nodes as distant metastases (5), whereas Asian countries suggest that the staging of SCLN should be determined based on the location of the esophageal cancer (8). Additionally, the definition of the supraclavicular region varies among different tumor types (8,13).

The description of the SCLN region in esophageal cancer by the AJCC 8th edition (5) and the JES 12th edition (16) guidelines is not sufficiently detailed. For example, there is no accurate description of the upper and lower boundaries of the region. For surgeons, the boundary definition of the supraclavicular region does not need to be very detailed, but this can lead to misjudgment of SCLN metastasis, thus raising the question of the predictive value of SCLN for prognosis. Zhong *et al* (17) divided the supraclavicular region into 6 subregions, and showed that nasopharyngeal cancer mainly spread to the subregions of the carotid sheath space, and vascular lateral space (VLS) I and II, whereas ESCC tended

Table II. Failure patterns in the entire esophageal squamous cell carcinoma cohort.

Type of failure	Arm A[a] (n=71)	Arm B[b] (n=159)	P-value
Irradiation field failure, n (%)			
Esophageal recurrence	15 (21.13)	30 (18.87)	0.690
Regional lymph nodes recurrence	17 (23.94)	39 (24.53)	0.924
Non-irradiation field failure, n (%)			
Esophagus failure	1 (1.41)	5 (3.14)	0.669
Regional lymph nodes failure	8 (11.27)	19 (11.95)	0.999
Metastasis to distant lymph nodes or organs, n (%)	16 (22.54)	17 (10.69)	0.025[c]

[a]With SCLN metastasis; [b]without SCLN metastasis; [c]P<0.05. SCLN, supraclavicular lymph node.

to spread to the subregions of the para-esophageal space, the sub-thyroid pre-trachea space, the carotid sheath space and VLS I. Therefore, subdividing the supraclavicular region can assist in the delineation of the CTV during radiotherapy.

In clinical practice, it is necessary to determine whether lymph node metastasis is located on a regional lymph node based on contrast-enhanced CT images before treatment. The present study provided a detailed description of the boundary lines between the cervical para-esophageal lymph node region (no. 101) and the SCLN region (no. 104). Based on the difference in probabilities of lymph node metastasis in the supraclavicular region, no. 104 was divided into two regions: Group II and Group III. Group II and Group III are equally important for radiotherapy of head and neck cancer (17), and breast cancer (18), and thus both should be included in the irradiation field. However, the present study showed that the probability of Group III metastasis in the cervical and upper thoracic segments of ESCC was only 1.3%. Luo *et al* (19) reported that the probability of lymph node metastasis in Group III was lower than that observed in the present study at only 0.6%. However, the study included esophageal cancer in the upper, middle and lower thoracic segments, but did not include cases of cervical esophageal cancer. Yu *et al* (20) analyzed the pattern of lymph node treatment failure after surgery for thoracic ESCC and found that lower cervical recurrence primarily occurred in the 4.3-cm area extending from both sides of the midline of the body, which matched the Group I and Group II areas described in the present study. Similarly, it was confirmed that prophylactic irradiation of lymph nodes in esophageal cancer was unnecessary for Group III (20).

Group IV and Group I are lymph node regions adjacent to the upper thoracic and cervical esophagus, respectively. The present results showed that the probability of metastasis in these two regions reaches 72.61 and 22.17%, which is consistent with the longitudinal distribution of the para-esophageal lymphatic vessels. Group II is located in the carotid artery and venous sheath area, and the probability of lymph node metastasis in this area reaches 29.57%. This is also a site that should be considered when elective nodal irradiation is chosen for cervical and upper thoracic esophageal cancer (21). However, the gap between the posterior edge of the internal jugular vein and the posterior edge of the sternocleidomastoid muscle has not been separately listed, as reported by Zhong *et al* (17), as the probability of lymph node metastasis at the posterior edge of the internal jugular vein was extremely low and thus could be incorporated into Group III.

In the present study, it was found that the probability of metastasis to supraclavicular lymph nodes (Group II + Group III) was 30.87%. Numata *et al* (9) found that the probability of SCLN metastasis was 25.4%, but the study only included cases of cervical ESCC that underwent radical surgery. Yu *et al* (20) analyzed the lymph node drainage patterns in esophageal cancer based on postoperative lymph node recurrence patterns. Surgery may cause blockage of some lymphatic ducts and changes in lymph node metastasis pathways (22). In the present study, a judgment was made based on the CT imaging at the initial diagnosis, reducing the interference of treatment.

The results of the present study showed that the median OS time of ESCC patients with SCLN metastasis was 17 months, which was lower than that of patients without SCLN metastasis, but still higher than the median OS time of 12.6 months reported in the Keynote 590 study for locally advanced unresectable or metastatic ESCC (23). Local treatment was still necessary for patients with SCLN metastasis. Liu *et al* (24) reported that ESCC patients with supraclavicular lymph node metastasis could benefit from surgery after neoadjuvant treatment (24). Moreover, a retrospective study (6) showed that SCLN metastasis had no significant impact on the median survival time of patients with upper thoracic ESCC, with the median survival time of the SCLN metastasis group and the other regional lymph node metastases group recorded as 25.0±3.0 and 30.0±4.6 months, respectively (P=0.067). However, Numata *et al* (9) retrospectively analyzed 67 cases of cervical esophageal squamous cell carcinoma treated with radical surgery. Compared with patients with only para-esophageal lymph node metastasis, the 3-year survival rate in the group with combined para-esophageal lymph node metastasis and SCLN metastasis significantly decreased (60.1 vs. 7.8%, respectively). ESCC with SCLN metastasis was associated with the location of the primary lesion. Okamura *et al* (25) reported a 5-year survival rate of 18.6-28.4% for thoracic esophageal cancer with SCLN metastasis after curative esophagectomy. The prognosis of ESCC with SCLN metastasis varied depending on the different segments of the thoracic region. Wen *et al* (26) reported that upper thoracic esophageal cancer with SCLC metastasis has a median survival time of only 12 months and that surgery cannot improve the prognosis of this group of patients. A retrospective study by Park *et al* (7) analyzed 611 ESCC cases that underwent radical esophagectomy and 3-field lymph node dissection. The results showed that for upper ESCC, the 5-year survival rates of patients with and without pathologically confirmed SCLN were 27.1 and 39.6%, while for middle and lower ESCC, the 5-year survival rates of patients with and without pathologically confirmed SCLN were 21.5 and 43.6%. The treatment method also affected the prognosis of patients with ESCC with SCLN metastasis. The 1-, 2- and 3-year OS rates for upper ESCC with SCLN metastasis receiving curative radiotherapy and chemotherapy were 50, 31, and 12%, respectively, while the OS rates for the group receiving curative surgery after 1, 2 and 3 years were 50, 0 and 0%, respectively (26). A meta-analysis showed that prophylactic SCLN dissection for ESCC did not prolong the 3- and 5-year survival rates (27). Therefore, regardless of the location of the primary lesion or the differences in treatment methods, the occurrence of SCLN metastasis was often indicative of a very poor prognosis. Therefore, supraclavicular lymph node metastases should be defined as distant metastases rather than regional lymph node metastases.

Whether accompanied by SCLN metastasis or not, recurrence within the irradiation field was the primary cause of treatment failure. The results of the present study showed that the recurrence rate in the irradiation field with SCLN metastasis group was 45.07%, while the recurrence rate in the irradiation field without SCLN metastasis group was 43.4%. Xu *et al* (28) reported that the local treatment failure rate and distant metastasis rates of locally advanced ESCC after concurrent chemoradiotherapy were 26.6 and 16.3%, but they did not describe the location of local failure, and there was no indication of whether there was a difference in the probability of distant metastasis with or without SCLN metastasis. The present study showed that the probability of distant organ metastasis in the group with SCLN metastasis was significantly higher than that in the group without SCLN metastasis, at 22.54 and 10.69%, respectively.

Autopsy anatomical data of esophageal tumor cases indicated that the lymphatic vessel count in the longitudinal muscle layer of the supraclavicular region was significantly lower than that in the upper and lower mediastinum. This anatomical feature determines that the supraclavicular region is prone to lymph node skip metastasis, which is often indicative of a poor prognosis (29).

The present study has several limitations. Firstly, 90.4% of the cases included in the study were defined as lymph node metastasis based on the short diameter of lymph nodes (≥0.6 cm) on contrast-enhanced CT, rather than being based on a pathological diagnosis or PET-CT. This is since, in the real world, not every patient agreed to continue with a mediastinal lymph node biopsy. PET-CT has a higher specificity and sensitivity than CT in diagnosing lymph node metastasis (30); however, PET-CT is expensive, and medical insurance cannot reimburse the cost of this examination. Most patients cannot afford the economic burden of PET-CT. Therefore, in the real world, contrast-enhanced CT is more often used to diagnose lymph node metastasis. Secondly, certain cases in the present study received sequential radiotherapy and chemotherapy, while others received chemotherapy consolidation and immune consolidation treatment. However, the majority of patients only received curative synchronous radiotherapy and chemotherapy, which may have led to a certain degree of bias in the results. Thirdly, there are slight differences between cervical and upper thoracic ESCC. Compared with upper thoracic ESCC, cervical ESCC is closer to the larynx, and surgeons needs to consider whether to preserve the larynx while operating (31). However, the present study mainly included cases of ESCC treated with radical chemoradiotherapy, so it was not affected by surgery. In addition, the etiology, histopathological types and lymph node metastasis patterns of cervical ESCC are similar to those of upper thoracic ESCC. A number of studies classified the two conditions into the same category of upper esophageal cancer for analysis (12,28). Therefore, when exploring the pattern of supraclavicular lymph node metastasis and survival after curative chemoradiotherapy, the present study included cervical and upper thoracic esophageal cancer together, which did not affect the results.

Despite these limitations, the results of the present study showed that for cervical and upper thoracic esophageal cancer, SCLN metastasis was a poor prognostic factor and should not be defined as regional lymph node metastasis.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

HZ and WZ conceived and designed the study, and wrote and revised the manuscript. MZ and YS collected medical record information, and collected and assessed the clinical and pathological characteristic data of enrolled cases. SL and YX followed up on the cases and analyzed the patterns of failure. WF and LD conducted statistical analysis and drew the figures. MZ, YS, SL and YX confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The Ethics Committee of the First Affiliated Hospital of Yangtze University approved the present study (Jingzhou, China; approval no. 2021005).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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