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RESEARCH

Patterns of Lymph Node Recurrence after Esophagectomy of pT2-3 N0M0 Esophageal Squamous Cell Carcinoma

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Abstract

Purpose This study aims to elucidate the distribution patterns of lymph node recurrence (LNR) in patients with pT2-3N0M0 esophageal squamous cell carcinoma (ESCC) following esophagectomy.

Methods A comprehensive retrospective analysis was conducted on 96 pT2-3N0M0 ESCC patients who experienced postoperative LNR at our institution between January 2010 and August 2019. LNR sites were systematically categorized into cervical, mediastinal, and abdominal regions. Computed tomography imaging was digitally reconstructed to precisely map recurrence locations, followed by rigorous statistical analysis of distribution patterns.

Results The final cohort comprised 96 patients with confirmed LNR, with males constituting 79.2% of the sample and a median age of 61 years. Mediastinal LNR was determined to be the most prevalent (69.8%), followed by cervical (43.8%) and abdominal (33.3%) regions. Cervical recurrences were predominantly identified in lymph node station 104R/L (7.8%), while mediastinal recurrences were predominantly localized to station 106recR (14.5%) and station 105 (10.4%), and abdominal recurrences were concentrated in stations 16a2 (3.6%) and 9 (3.6%). Computerized tomography reconstruction demonstrated a distinctive "T"-shaped distribution of LNR in the cervical and upper mediastinal regions in proximity to major vascular structures. The primary tumor location was not found to significantly influence LNR distribution patterns ($P > 0.05$).

Conclusions LNR in pT2-3N0M0 ESCC predominantly manifests in cervical and upper mediastinal lymph nodes. Administering targeted adjuvant radiotherapy to high-risk patients may be an effective strategy for enhancing therapeutic outcomes. Prospective multicenter studies are warranted to validate these preliminary findings.

Keywords Clinical target volume · Esophageal squamous cell carcinoma · Lymph node recurrence · Postoperative recurrence · Adjuvant radiotherapy

Introduction

Esophageal carcinoma (EC) is a disease characterized by significant mortality rates. Esophagectomy constitutes one of the primary therapeutic interventions [1]. However, due to the distinctive anatomical configuration of the esophagus, coupled with its intricate lymphatic network, vascular structures, and the proximity of vital adjacent organs, complete resection of esophageal lesions and comprehensive lymph node dissection in the drainage area are frequently challenging during surgical procedures [2, 3]. Even among patients with pathologically confirmed negative lymph nodes following esophagectomy, the recurrence rate remains substantially elevated. Research has demonstrated that for esophageal squamous cell carcinoma (ESCC) patients with negative lymph nodes, the estimated local recurrence rate can be as high as 26.4–45.1% [4]. Historically, greater research emphasis has been placed on EC patients with positive lymph nodes, while data regarding ESCC patients with negative lymph nodes remain insufficient. Nevertheless, the risk of postoperative recurrence in lymph node-negative EC patients continues to be considerable. Studies indicate that approximately 30% of patients without lymph node metastasis experience tumor recurrence or metastasis subsequent to surgical intervention [5]. The prognosis of these patients cannot be determined solely by the quantification of positive lymph nodes. Consequently, it is essential to conduct additional investigations into other clinicopathological

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parameters that might influence the postoperative recurrence and prognosis of these lymph node-negative EC patients, particularly those with pT2-3 N0M0 ESCC. Currently, there exists a paucity of studies concerning the postoperative recurrence of EC patients within this specific subgroup, rendering this research domain highly exploratory.

In previous research, the overall recurrence rate of pT2-3 N0M0 ESCC following surgical intervention was documented at 36.3%, comprising lymph node metastasis of 26.0%, hematogenous metastasis rate of 15.1%, and anastomotic recurrence rate of 4.3%. Lymph node recurrence (LNR) has been identified as the predominant form of recurrence, typically manifesting within a 3-year postoperative period [6]. A more comprehensive examination of LNR patterns within this patient cohort, combined with obtaining detailed information regarding the anatomical distribution of LNRs, could potentially illuminate novel approaches for region-specific targeted radiotherapy.

To precisely characterize the anatomical distribution of LNR, data were retrospectively analyzed from patients who experienced postoperative LNR at the First Affiliated Hospital of Anhui Medical University. The specific locations of LNR following esophagectomy were systematically documented. Based on the observed distribution characteristics, reconstruction maps were generated utilizing computerized tomography (CT) scan images. Subsequently, founded on the identified recurrence patterns, the feasibility of selective prophylactic radiotherapy administration to specific anatomical regions will be extensively investigated.

Patients and Methods

Patient Selection

A retrospective review of patient records from January 2010 to August 2019 was conducted to identify individuals who underwent radical esophageal cancer surgery at the institution. Following comprehensive screening, a cohort of 96 patients diagnosed with postoperative LNR in pT2-3 N0M0 ESCC was ultimately selected for inclusion in the analysis. Furthermore, detailed documentation of the precise anatomical locations of LNR was meticulously maintained for subsequent evaluation.

Inclusion criteria were as follows: (1) patients who had undergone radical surgery with complete tumor resection (R0 resection); (2) patients whose postoperative pathological examination confirmed ESCC; (3) patients with postoperative pathological staging classified as pT2-3 N0M0 (in accordance with the 8 th edition of the American Joint Committee on Cancer TNM staging system); (4) patients who had not received any form of neoadjuvant or adjuvant anti-tumor therapy; (5) patients who subsequently developed LNR following surgical intervention; (6) patients for whom radiological evidence documenting the initial site of LNR post-surgery was available.

Exclusion criteria were as follows: (1) patients whose age was below 18 years or exceeded 85 years; (2) cases with incomplete postoperative clinical and pathological documentation; (3) patients diagnosed with a secondary primary malignancy or multiple-site neoplasms; (4) cases where precise information regarding postoperative LNR was unavailable; (5) patients presenting with cervical esophageal cancer or gastroesophageal junction tumors.

Follow-up

Following esophagectomy, a standardized surveillance protocol is implemented as follows: during the initial 2-year period, patients are monitored at 2–4-month intervals; subsequently, from years two through five post-operatively, assessments are conducted biannually; beyond the 5-year mark, annual evaluations are performed. The primary diagnostic modalities employed during these surveillance visits encompass CT scans of the cervical, thoracic, and abdominal regions. Supplementary ultrasonographic examinations of the cervical or abdominal areas may be executed when deemed appropriate. Upon detection of pathological abnormalities, contrast-enhanced CT or magnetic resonance (MR) imaging is indicated for comprehensive evaluation. When clinically warranted, additional diagnostic procedures, including positron emission tomography (PET), fine-needle aspiration cytology, and histopathological examination of biopsy specimens, are utilized to establish definitive diagnoses. The surveillance terminus for all study participants was established in December 2021.

Diagnostic Criteria for LNR

The diagnosis of regional LNR is predominantly dependent upon imaging modalities, such as contrast-enhanced CT, MR, and PET. For superficial lymph nodes, a definitive diagnosis can be directly established through cytological biopsy procedures.

The diagnostic criteria for LNR have been established as follows: (1) when contrast-enhanced CT or MR imaging demonstrates a lymph node with a short-axis diameter ≥ 10 mm, or when ≥ 3 lymph nodes are identified within the same anatomical region, or when evidence of lymph node necrosis or extracapsular invasion is observed; (2) when lymph nodes are visualized within the tracheoesophageal groove, irrespective of their dimensional parameters, accompanied by clinical manifestations of hoarseness or vocal cord paralysis; (3) when sequential imaging studies reveal temporal alterations in lymphatic structures, characterized by

substantial volumetric enlargement, numerical increases, or the emergence of previously undetected lymph nodes; (4) when definitive evidence of malignant metastasis is procured through fine-needle aspiration cytology or histopathological biopsy specimens; (5) when PET examination demonstrates a standardized uptake value ≥ 2.4.

Regional Lymph Node

The LNR localization was determined in accordance with the standard lymph node anatomical classification delineated by the Japan Esophagus Society and the anatomical distribution of abdominal lymphatic drainage in gastric cancer. Recurrent sites were subsequently categorized into three distinct regions: the cervical lymph node drainage area, the mediastinal lymph node drainage area, and the abdominal lymph node drainage area [7, 8].

The specific lymph node zones were classified as follows: (1) cervical lymph nodes: comprising No.100, No.101, No.102, No.103, and No.104 lymph nodes; (2) mediastinal lymph nodes: subdivided into thoracic upper mediastinum nodes (No. 105, No. 106 tb, No.106recR/L, 106pre), thoracic middle mediastinum nodes (No.107, No.108, and No.109), and thoracic lower mediastinum nodes (lower No.110, No.111, No.112, No.113, and No.114); (3) abdominal lymph node region: encompassing group 1–16 lymph node regions within the abdominal cavity as designated in gastric cancer classification.

CT Images Reconstruction of LNR

Owing to the notable morphological alterations in anatomical structures, including the anastomotic site and the mediastinal stomach subsequent to radical esophagectomy, a 65-year-old male subject was designated as the reference patient for CT examination. The subject was positioned in a supine orientation on a stabilized framework, with upper extremities crossed anteriorly to the frontal region and bilateral cubital articulations naturally situated lateral to the cranium. The imaging parameters encompassed a scanning trajectory extending from the cricoid cartilage level to approximately 2 cm inferior to the bifurcation of the abdominal aorta, with subsequent image reconstruction performed at a slice thickness of 1.25 mm.

The patient's CT scan images were imported into the radiotherapy contour delineation software system (version V1.0.0.19001) and the Pinnacle radiotherapy planning system (version 9.8.0.6007, Philips Medical Systems, Fitchburg, WI, USA) for subsequent volumetric image delineation and three-dimensional reconstruction.

With reference to anatomical landmarks, including adjacent organs, vascular structures, and osseous formations, the locations of recurrent lymph nodes were delineated on corresponding anatomical positions in the standardized patient's CT images by two radiation oncologists in collaboration with a radiologist. The site of the initial LNR was exclusively documented. When multiple recurrent sites were identified simultaneously or within a 1-month interval, individual markings were applied, provided that the central points could be differentiated. Positive lymph nodes were designated by circular markers of a 6-mm diameter positioned at the nodal central points. In certain instances, lymph nodes demonstrated confluent patterns. Where differentiation was possible, markers were distributed with maximal uniformity; otherwise, a single marker was placed at the central point of the confluent mass.

Statistical Analysis and Image Processing

Statistical analyses of categorical and continuous variables were conducted utilizing IBM SPSS Statistics software (version 27.0; IBM Corp., Armonk, NY, USA). The Mann–Whitney U test was specifically employed for the comparative assessment of non-parametric continuous variable distributions. Statistical significance was established at $P < 0.05$.

The GraphPad Prism 9 software was employed for the quantitative analysis of lymph node distribution, whereas radiotherapy contour delineation software and the Pinnacle radiotherapy planning system (version 9.8.0.6007; Philips Medical Systems, Fitchburg, WI, USA) were implemented for CT image reconstruction.

Results

Baseline Characteristics of Included Patients

A total of 96 patients with pT2-3 N0M0 ESCC who had undergone surgical intervention and subsequently developed LNR were incorporated into this investigation. The comprehensive demographic characteristics and clinicopathological data were systematically collated and analyzed. Within this cohort, 76 patients (79.2%) were identified as male and 20 patients (20.8%) as female. The patients' ages ranged from 41 to 82 years, with a calculated median age of 61 years. With respect to tumor classification, 54 patients (56.3%) were diagnosed with T2-stage disease, while 42 patients (43.7%) presented with T3-stage pathology. Regarding anatomical distribution, upper thoracic ESCC was observed in nine patients (9.4%), middle thoracic ESCC was identified in 68 patients (70.8%), and lower thoracic ESCC was diagnosed in 19 patients (19.8%). At the conclusion of the follow-up period, patients were stratified into three distinct categories based on recurrence localization: cervical LNR, mediastinal LNR, and abdominal LNR. Mediastinal LNR

was determined to be the predominant site of recurrence, being documented in 67 patients (69.8%), followed by cervical LNR manifesting in 42 patients (43.8%), and abdominal LNR occurring in 32 patients (33.3%).

LNR in different regions is predominantly manifested in male patients aged between 55 and 66 years. A higher incidence of LNR has been documented in patients with pT3-stage disease compared to those with pT2-stage pathology. The middle thoracic region has been identified as the most prevalent site of recurrence, with tumors being predominantly moderately differentiated. Statistical analyses have demonstrated that tumor dimensions predominantly exceed 3 cm, whereas a minority of cases present with tumors measuring less than 3 cm. Open esophagectomy (OE) remains the predominant surgical intervention utilized. Intraoperative pathological examinations have revealed markedly low frequencies of carcinoma nodules, vascular invasion, and perineural involvement. Postoperative lymph node dissection typically yielded fewer than 15 nodes per specimen. It was observed that a subset of patients exhibited concurrent recurrence across multiple anatomical regions. The quantitative distribution and relative frequency of LNR across all groups have been comprehensively presented in Table 1.

LNR Pattern

AAs demonstrated in Table 2, a cohort comprising 96 patients was enrolled in this investigation. Specifically, nine patients were diagnosed with upper thoracic ESCC, 68 patients with middle thoracic ESCC, and 19 patients with low thoracic ESCC. The distribution of postoperative LNR was subjected to comprehensive statistical analysis. The findings suggest that the primary anatomical location of ESCC does not appear to significantly influence the distribution pattern of postoperative LNR. Statistical evaluations reveal that, irrespective of the primary tumor site, postoperative LNR in thoracic ESCC was predominantly concentrated in the mediastinal lymph node region, with the cervical lymph node region representing the second most common site of recurrence. Furthermore, no statistically significant difference was observed in the distribution of postoperative lymph node metastasis of ESCC across the different primary sites ($P > 0.05$).

Distribution of LNR

To further delineate the anatomical distribution of recurrent lymph nodes, a systematic mapping of all LNR locations was conducted in 96 patients with postoperative pT2-3 N0M0 ESCC exhibiting lymphatic metastasis, resulting in the identification of 193 affected lymph nodes. Within this distribution, the mediastinal lymphatic region was observed to contain the predominant proportion of recurrences, with 95 nodes (49.3%), followed by the cervical lymphatic region, with 57 nodes (29.5%), and the abdominal lymphatic region comprising 41 nodes (21.2%). The site-specific distribution of LNR has been illustrated in Fig. 1.

The predominant LNR in the cervical region was identified at stations 104R and 104L (15/193, 7.8%), subsequently followed by station 102R (5.2%), station 102L (4.1%), station 101R (2.6%), and station 101L (2.1%). Mediastinal LNR was primarily concentrated in station 106, with 106recR exhibiting the highest recurrence frequency (14.5%), followed by 106recL (5.7%), 106 tb (4.1%), and 106pre (3.6%). In other mediastinal regions, the most frequently observed recurrence sites were station 105 (10.4%), station 107 (4.1%), and station 108 (3.1%), respectively, whereas stations 109, 112, and 113 demonstrated comparatively lower recurrence rates. Within abdominal lymph nodes, recurrence was most commonly detected at station 16a2 (8/193, 4.1%) and station 9 (3.6%), followed by stations 16a1, 8, and 12, each with recurrence rates of 2.6%. A recurrence rate of 2.1% was observed in stations 3 and 13, while LNR was infrequently detected in stations 7, 10, and 11. The numerical distribution and corresponding percentages of patients with regional recurrence are presented in Table 3.

Thirty-six patients (37.5%) were observed with LNR in a single region, whereas 35 patients (17.7%) manifested LNR in two regions simultaneously. These two presentations exhibited the highest frequency of occurrence. 17 patients were identified with LNR in three regions simultaneously. The manifestation of LNR in four or more regions concurrently was observed to be uncommon.

CT Image Reconstruction of LNR

With respect to the anatomical structures depicted on CT images, CT scans of 193 patients with LNRs were extracted. The center of each lymph node was utilized as a reference point, and an 8 mm radius circle centered on this point was delineated, with positions subsequently marked individually on a template CT image. Subsequently, contour drawing software for radiotherapy treatment was employed to delineate the surrounding vasculature and adjacent organs. Ultimately, the CT images were fused to generate a three-dimensional reconstructed image, which facilitates an intuitive visualization of the lymph node locations and their spatial relationships with adjacent vasculature and organs.

As illustrated in Fig. 2, recurrent lymph nodes were predominantly distributed in the cervical and upper mediastinal regions. These nodes were primarily concentrated in the 102R, 104R/L, 105, 106recR/L, 106 tb, 106pre, 107, and 108 regions, thereby constituting a “T” shaped pattern. For enhanced visual clarity, the locations of LNRs were color-coded according to the different sites of the primary tumors. This coding methodology facilitates a

Table 1 Characteristics of patients with LNR

Characteristics	Cervical LNR ($n = 42$)	Mediastinal LNR ($n = 67$)	Abdominal LNR ($n = 32$)
Sex			
Male	32 (76.2%)	51 (76.2%)	26 (81.3%)
Female	10 (23.8%)	16 (23.8%)	6 (18.7%)
Age			
≤ 55 years	7 (16.7%)	6 (4.5%)	2 (6.3%)
56–66 years	18 (42.8%)	37 (55.2%)	20 (62.5%)
> 66 years	17 (40.5%)	27 (40.3%)	10 (31.2%)
T stage			
T2 N0	27 (64.3%)	35 (52.2%)	19 (59.4%)
T3 N0	15 (35.7%)	32 (47.8%)	13 (40.6%)
Surgery			
Minimally invasive esophagectomy (MIE)	19 (45.2%)	29 (43.3%)	16 (50.0%)
Open esophagectomy (OE)	21 (50.0%)	33 (49.3%)	10 (31.3%)
MIE and OE	2 (4.8%)	5 (7.4%)	6 (18.7%)
Location			
Upper thoracic region	6 (14.3%)	7 (10.5%)	3 (9.4%)
Middle thoracic region	26 (61.9%)	48 (71.6%)	21 (65.6%)
Low thoracic region	10 (23.8%)	12 (17.9%)	8 (25.0%)
Differentiation			
Poorly differentiated	9 (21.4%)	16 (23.9%)	7 (21.9%)
Moderately differentiated	28 (66.7%)	47 (70.1%)	23 (71.9%)
Well-differentiated	5 (11.9%)	4 (6.0%)	2 (6.2%)
Tumor diameter (long axis)			
≤ 3 cm	16 (38.1%)	31 (46.3%)	10 (31.2%)
> 3 cm	26 (61.9%)	36 (53.7%)	22 (68.8%)
Tumor diameter (short axis)			
≤ 3 cm	38 (90.5%)	50 (74.6%)	24 (75.0%)
> 3 cm	4 (9.5%)	17 (25.4%)	8 (25.0%)
Vessel invasion			
Yes	4 (9.5%)	3 (4.5%)	2 (6.3%)
No	38 (90.5%)	64 (95.5%)	30 (93.7%)
Perineural invasion			
Yes	39 (92.9%)	4 (6.0%)	1 (3.1%)
No	3 (7.1%)	63 (94.0%)	31 (96.9%)
Carcinoma nodules			
Yes	2 (4.8%)	1 (1.5%)	0 (0.0%)
No	40 (95.2%)	66 (98.5%)	32 (100.0%)
Resected lymph nodes			
< 15	29 (69.1%)	41 (61.2%)	21 (65.6%)
≥ 15	13 (30.9%)	26 (38.8%)	11 (34.4%)

comprehensive visualization of the correlation between the primary tumor location and the LNR location. From multiple anatomical perspectives, it is evident that these recurrent lymph nodes are closely situated around the adjacent vasculature. In the abdominal cavity, recurrent lymph nodes were predominantly identified in regions 16a2, 9, 16a1, 8, and 12. These nodes encircle the abdominal aorta and its branches, with a notable concentration between the celiac trunk and the inferior margin of the left renal vein, predominantly on the left lateral aspect. Furthermore, a subset of lymph nodes was observed within the hepatogastric space or in proximity to the hepatoduodenal ligament.

Table 2 Distribution of postoperative LNR in different primary locations of ESCC patients

Characteristics	Total ($n = 96$)	Upper thoracic esophageal cancer ($n = 9$)	Middle thoracic esophageal cancer ($n = 68$)	Low thoracic esophageal cancer ($n = 19$)	*P* value
Cervical LNR	42 (43.8%)	6 (66.7%)	26 (38.2%)	10 (52.6%)	0.46
Mediastinal LNR	67 (69.8%)	7 (77.8%)	48 (70.6%)	12 (63.2%)	0.23
Thoracic upper mediastinum	45 (46.9%)	5 (55.6%)	28 (41.2%)	12 (63.2%)	0.20
Thoracic middle mediastinum	34 (35.4%)	4 (44.4%)	23 (33.8%)	7 (36.8%)	0.15
Thoracic low mediastinum	19 (19.8%)	1 (11.1%)	16 (23.5%)	2 (22.2%)	0.36
Abdominal LNR	32 (33.3%)	3 (33.3%)	21 (30.9%)	8 (42.1%)	0.34

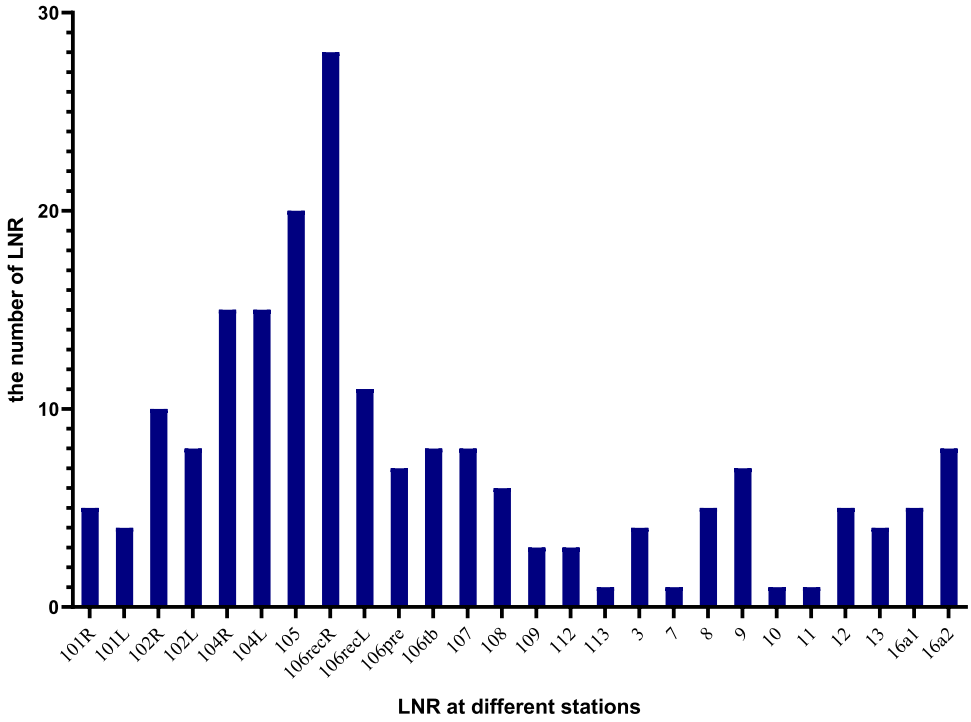

Fig. 1 Distribution at different stations of LNR

Discussion

Currently, a significant deficiency exists in the research literature regarding ESCC patients with postoperative pathological lymph node negative status. Considerable controversy continues to surround the necessity of adjuvant therapeutic interventions for this patient population. In clinical settings, individualized treatment approaches are predominantly implemented. Despite the fact that certain medical centers have conducted studies on pN0 stage ESCC, the resultant findings remain inconsistent across investigations. A comprehensive retrospective analysis was conducted on 222 patients with pT3 N0M0 stage who underwent esophagectomy. The results revealed that 58 patients (25.6%) experienced LNR within a five-year period. Mediastinal lymph nodes were identified as the most prevalent recurrence site. The data demonstrated that the recurrence rate specifically affecting mediastinal lymph nodes was remarkably elevated at 50.0% (29/58), whereas recurrence rates in alternative anatomical locations were observed to be less than 10% [9]. Correspondingly, a previous investigation had established that the predominant recurrence pattern in pN0 stage ESCC following surgical intervention was local recurrence (38/45, 84.4%), with LNR constituting the most frequent manifestation (37/38, 97.4%). Notably, recurrence was frequently observed at the cervicothoracic junction, which represents a critical anatomical location for the prevention of postoperative recurrence in pN0 ESCC [5]. In the present investigation, the most frequently affected regional lymph node sites in pT2-3 N0M0 EC were identified as station106recR/L, station 105, station 104R/L, and station 102R, findings that align with results documented in additional studies. These observations suggest that LNR was predominantly concentrated within the neck and upper mediastinal region.

Table 3 Number and proportion of patients with recurrence region

Stations	Number ($n = 193$)	Proportion
Cervical LNR	57	29.5%
101R	5	2.6%
101L	4	2.1%
102R	10	5.2%
102L	8	4.1%
104R	15	7.8%
104L	15	7.8%
Mediastinal LNR	95	49.2%
105	20	10.4%
106recR	28	14.5%
106recL	11	5.7%
106pre	7	3.6%
106 tb	8	4.1%
107	8	4.1%
108	6	3.1%
109	3	1.6%
112	3	1.6%
113	1	0.5%
Abdominal LNR	41	21.2%
3	4	2.1%
7	1	0.5%
8	5	2.6%
9	7	3.6%
10	1	0.5%
11	1	0.5%
12	5	2.6%
13	4	2.1%
16a1	5	2.6%
16a2	8	4.1%

Theoretically, the implementation of appropriate postoperative adjuvant radiotherapy (PORT) may facilitate the reduction in recurrence rates of cervical and mediastinal lymph nodes, thereby potentially enhancing overall survival (OS). However, contemporary evidence suggests that in lymph node-negative EC patients, neither radiotherapy administered in isolation nor PORT has been demonstrated to significantly ameliorate survival outcomes. Previous investigations have established that lymph node-negative EC patients do not derive therapeutic benefits from PORT [10, 11]. This discrepancy can potentially be attributed to two principal factors: (1) suboptimal stratification of patient populations in certain studies, which subsequently impeded the detection of survival benefits; (2) insufficient sample sizes that were characterized by inadequate statistical power to identify clinically meaningful OS improvements. Furthermore, radiation-related toxicities, including radiation pneumonitis, non-neoplastic pericardial effusions, pleural effusions, and gastrointestinal bleeding, have been correlated with elevated mortality rates in PORT cohorts.

With the significant advancement of three-dimensional conformal radiotherapy (3D-CRT) and intensity-modulated radiotherapy techniques, these innovative therapeutic modalities have been demonstrated to exhibit superior efficacy in organ preservation and enhanced precision of radiation delivery. At present, a consensus has yet to be established regarding the therapeutic value of adjuvant radiotherapy for pT2-3 N0M0 ESCC, with surveillance predominantly advocated as the standard approach. Despite numerous investigations conducted across various research institutions, the outcomes remain inconsistent. Evidence from previous research [12] indicates that 3D-CRT constitutes a safe and efficacious treatment option for postoperative patients with pT2-3 N0M0 EC. The documented 5-year overall survival and disease-free survival rates are 74% and 71%, respectively, which exceed previously documented figures. Prior investigations conducted by this research group have elucidated that postoperative T-stage, surgical methodology, tumor anatomical position, and histological differentiation grade represent independent prognostic factors for recurrence in pT2-3 N0M0 ESCC patients, with LNR identified as the predominant pattern of disease relapse [6]. Consequently, it is postulated that for patients exhibiting high-risk characteristics for postoperative recurrence, adjuvant localized radiotherapy may be warranted in lymphatic regions, demonstrating increased susceptibility to recurrent disease.

A retrospective study has elucidated that for ESCC with negative lymph nodes, the recommended delineation for the clinical target volume (CTV) encompasses the supraclavicular lymph nodes, the upper mediastinal lymphatic region, and the primary tumor site [13]. Based on an analysis of local recurrence patterns observed in 338 patients who underwent radical surgical intervention for ESCC, among whom 146 individuals (43.2%) were diagnosed with negative lymph nodes, it was determined that the supraclavicular and superior mediastinum regions should be incorporated as standard targets in postoperative radiotherapy protocols. The recurrence rate at the original tumor location was ascertained to be 3.6%. Consequently, it was not deemed necessary to incorporate this anatomical region within the CTV parameters [14]. Concordant findings were documented in an independent investigation, which advocated for a CTV extension from the seventh cervical vertebra (C7) to the inferior margin of the pulmonary venous structure [15].

In this study, it was observed that LNR in pT2-3 N0M0 ESCC was predominantly concentrated in the neck and upper mediastinum regions. Consequently, it is recommended that the postoperative CTV should primarily focus on the areas where the recurrent laryngeal nerve and supraclavicular region are situated. LNR was identified in station 101R/L. Therefore, it is proposed that the neck lymph

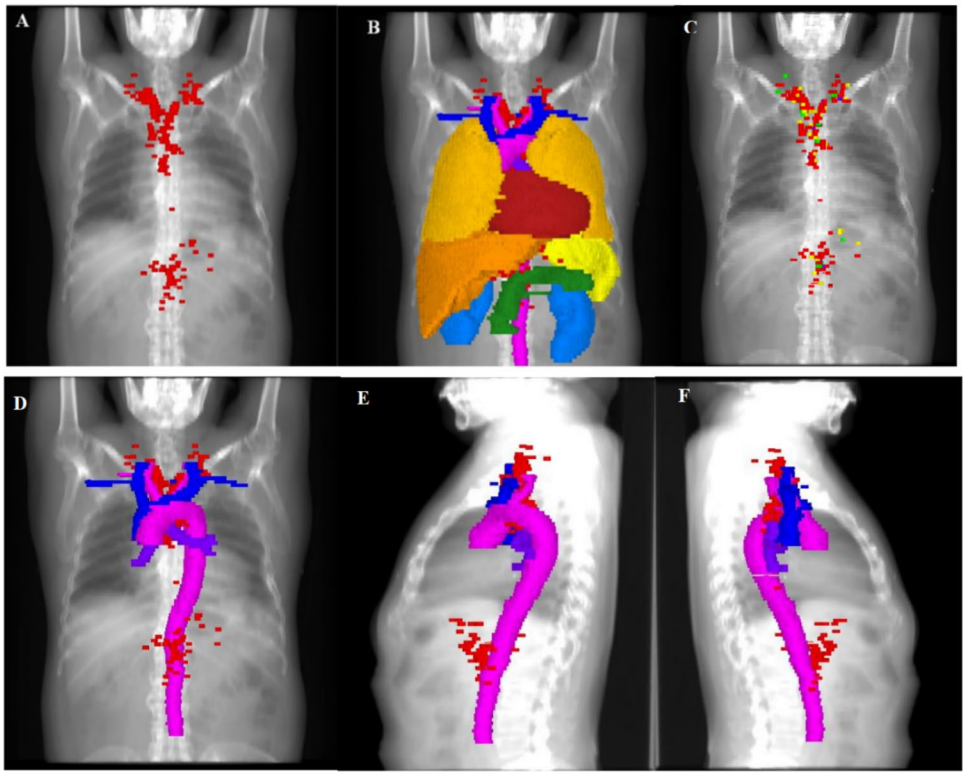

Fig. 2 Recurrent lymph nodes marked on template CT images. **A** Distribution of all LNRs. **B** Distribution of LNRs across different primary sites: green represents upper ESCC, red denotes middle ESCC, and yellow indicates lower ESCC. **C** Anatomical relationship between the recurrent lymph nodes and adjacent blood vessels and organs. **D** Front view of the distribution of recurrent lymph nodes and surrounding blood vessels. **E** Left-to-right view. **F** Right-to-left view

node regions for CTV should encompass station 101R/L, station 104R/L, and station 102R/L. The anatomical upper boundary is defined as the lower margin of the cricoid cartilage, with the outer margin extending to the inner margin of the carotid sheath down to the level of the clavicle. In the mediastinal region, LNR predominantly manifests in station 105, station 106recR/L, station 106 tb, station 106pre, station 107, and station 108, accounting for 91% of mediastinal recurrent lymph nodes, which corroborates findings from previous research [16]. Due to the complex anatomical structure, the upper boundary of the mediastinal lymph node region is recommended to be established at the upper edge of the subclavian artery, which functions as the upper boundary of the 106recR/L and connects with the cervical lymph node drainage area. Significant controversy exists regarding the lower boundary of the mediastinal region, with divergent perspectives on whether to include the entire mediastinum [17, 18]. The current investigation revealed that the recurrence rate of lymph nodes in the lower thoracic region was relatively minimal, with an incidence rate exceeding 90% in the upper and middle mediastinal regions. Consequently, it is suggested that the CTV should incorporate the middle and upper mediastinum, with the lower boundary extending to the root of the lower pulmonary vein (the lower boundary of station 108). Based on the aforementioned results, the recommended irradiation range of the cervical and mediastinal lymph node drainage areas following pT2-3 N0M0 stage ESCC surgery is depicted in Fig. 3.

In this study, postoperative lymph node metastasis rates were analyzed in patients with varying primary tumor sites. The results demonstrated no statistically significant variations in lymph node metastasis rates across different anatomical sites among patients with distinct primary locations. This observation indicates that primary tumor location might not constitute the sole determinative factor in evaluating lymph node metastasis risk. Among patients experiencing LNR, the recurrence frequency in abdominal lymph nodes was observed to be comparatively lower than that documented in cervical and upper mediastinal lymph nodes. Taking into consideration the adverse effects associated with radiation therapy, elective irradiation of the abdominal lymph node region may potentially expose patients to unnecessary toxicity, predominantly manifested as gastrointestinal reactions. These adverse manifestations can significantly diminish patients' quality of life and potentially compromise their tolerance to subsequent therapeutic interventions. Following a comprehensive assessment of the therapeutic benefits and potential risks of radiotherapy, it has been concluded that for patients with pT2-3 N0M0 ESCC, vigilant surveillance of the abdominal lymph node region is currently recommended. For patients exhibiting favorable physical status, prophylactic interventions targeting the abdominal lymph node area may also be considered as a viable option.

This study also has the following limitations: (1) This investigation was conducted retrospectively. The detailed surgical documentation regarding lymphadenectomy techniques

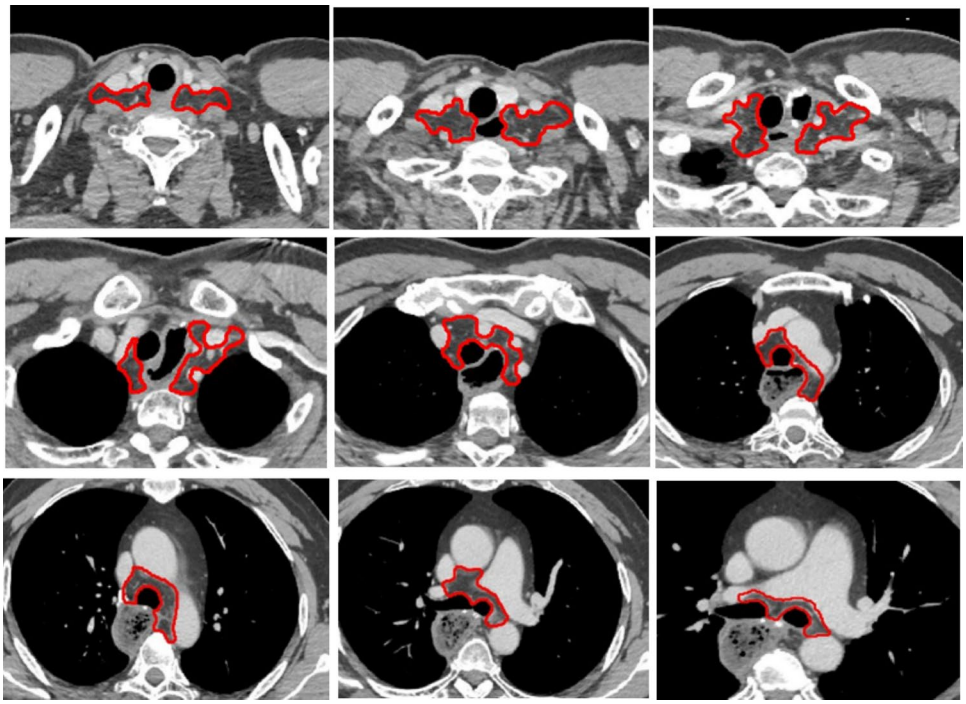

Fig. 3 Suggestion for delineating the CTV of the neck and mediastinal lymph node areas

employed during operations was not sufficiently comprehensive, and variability exists in the standardization of lymph node dissection quantities across different patients; (2) the precise localization of LNR was predominantly determined by imaging findings during the follow-up period. Only 11.4% (11/96) of patients underwent lymph node puncture for pathological diagnosis, and 9.4% (9/96) received PET/CT examination. Pathological confirmation could not be obtained for the majority of lymph nodes, potentially resulting in false positives; (3) due to anatomical variations among patients, the positions of certain lymph nodes on template CT images may have been inaccurately delineated; (4) the recommendations for the CTV were formulated based solely on initial LNR regions, without consideration of the complete survival period. This data insufficiency might underestimate recurrence probabilities; (5) the data were collected exclusively from a single institution, potentially introducing institutional bias. The analytical approach remained relatively elementary, without subjection to detailed stratification analysis.

In the future, with the participation of multicenter studies and the accumulation of more cases, certain predictors are anticipated to be identified to enhance clinical value and derive individualized clinical recommendations. Additionally, further validation regarding whether postoperative adjuvant radiotherapy confers actual survival benefits to patients with pT2-3 N0M0 ESCC will be conducted through prospective studies to further evaluate and validate the research findings.

Conclusion

This study has demonstrated that LNR after pT2-3 N0M0 ESCC was predominantly localized in the cervical and superior mediastinal regions, specifically at lymphatic stations 106recR/L, 105, 104R/L, and 102R. The administration of targeted adjuvant radiotherapy for high-risk patients could be regarded as a potentially efficacious strategy for optimizing therapeutic outcomes. Future investigative efforts should be directed toward multicenter prospective trials to substantiate these findings and further elucidate the optimal radiotherapy protocol, as well as its potential contribution to survival enhancement in this specific patient population.

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Author contributions M.K. collected the clinical data and conducted patient follow-up, and wrote the manuscript. Y.C.W. analyzed the data. L.N. reviewed the manuscript. All authors read and approved the final manuscript. All participants gave their consent to have their data recorded and analyzed anonymously.

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Ethics Approval and Consent to Participate This study was approved by the Ethics Committee of the First Affiliated Hospital of Anhui Medical University (Reference number: Quick-PJ 2022–11-26) and agreed to be published.

Competing interests The authors declare no competing interests.

References

1. Ajani JA, D'Amico TA, Almhanna K, et al. Esophageal and esophagogastric junction cancers, version 1.2015. J Natl Compr Canc Netw. 2015;13:194–227.
2. Sun ZG, Wang Z. Clinical study on lymph node metastatic recurrence in patients with N0 esophageal squamous cell cancer. Dis Esophagus. 2011;24:182–8.
3. Wang Y, Zhu L, Xia W, et al. Anatomy of lymphatic drainage of the esophagus and lymph node metastasis of thoracic esophageal cancer. Cancer Manag Res. 2018;26(10):6295–303.
4. Nishimori H, Hayashi S, Naito M, et al. Mucosal lymphatic vessels of the esophagus distant from the cancer margin: morphometrical analysis using 27 surgically removed specimens of squamous cell carcinoma located in the upper or middle thoracic esophagus. Okajimas Folia Anat Jpn. 2011;88(2):43–7.
5. Guo XF, Mao T, Gu ZT, et al. Clinical study on postoperative recurrence in patients with pN0 esophageal squamous cell carcinoma(J). J Cardiothorac Surg. 2014;9:150.
6. Niu L, Hu B, Zhang L, et al. Risk factors for postoperative recurrence of pT2-3N0M0 esophageal squamous cell carcinoma and patterns of its recurrence. Biosci Trends. 2024;17(6):475–83.
7. Japan Esophageal Society. Japanese classification of esophageal cancer, 11th Edition: part II and III(J). Esophagus. 2017;14(1):37–65.
8. Xu S, Feng L, Chen Y, et al. Consistency mapping of 16 lymph node stations in gastric cancer by CT-based vessel-guided delineation of 255 patients. Oncotarget. 2017;8(25):41465–73.
9. Shen WB, Gao HM, Zhu SC, et al. Analysis of the causes of failure after radical surgery in patients with PT3N0M0 thoracic esophageal squamous cell carcinoma and consideration of postoperative radiotherapy. World J Surg Oncol. 2017;15(1):192.
10. Xiao ZF, Yang ZY, Liang J, et al. Value of radiotherapy after radical surgery for esophageal carcinoma: a report of 495 patients. Ann Thorac Surg. 2003F;75(2):331–6.
11. Chen J, Zhu J, Pan J, et al. Postoperative radiotherapy improved survival of poor prognostic squamous cell carcinoma esophagus. Ann Thorac Surg. 2010;90(2):435–42.
12. Zhang WC, Wang QF, Xiao ZF, et al. The guiding effect of failure mode of thoracic esophageal squamous cell carcinoma after radical operation on the field of radiotherapy. Chin J Radiat Oncol. 2012;21(1):38–41.
13. Wang Y, Zhang L, Ye D, et al. A retrospective study of pattern of recurrence after radical surgery for thoracic esophageal carcinoma with or without postoperative radiotherapy. Oncol Lett. 2018;15(3):4033–9.
14. Wang X, Luo Y, Li M, et al. Recurrence pattern of squamous cell carcinoma in the midthoracic esophagus: implications for the clinical target volume design of postoperative radiotherapy. Onco Targets Ther. 2016;3(9):6021–7.
15. Yu J, Ouyang W, Li C, et al. Mapping patterns of metastatic lymph nodes for postoperative radiotherapy in thoracic esophageal squamous cell carcinoma: a recommendation for clinical target volume definition. BMC Cancer. 2019;19(1):927.
16. Xiao ZF, Yang ZY, Miao YJ, et al. Influence of number of metastatic lymph nodes on survival of curative resected thoracic esophageal cancer patients and value of radiotherapy: report of 549 cases. Int J Radiat Oncol Biol Phys. 2005;62(1):82–90.
17. Liu Q, Cai XW, Wu B, et al. Patterns of failure after radical surgery among patients with thoracic esophageal squamous cell carcinoma: implications for the clinical target volume design of postoperative radiotherapy. PLoS One. 2014;9(5):e97225.
18. Qiao XY, Wang W, Zhou ZG, et al. Comparison of efficacy of regional and extensive clinical target volumes in postoperative radiotherapy for esophageal squamous cell carcinoma. Int J Radiat Oncol Biol Phys. 2008;70(2):396–402.