A novel quantitative model based on gross tumor volume corresponding to anatomical distribution measured with multidetector computed tomography to determine the resectability of non-distant metastatic esophageal squamous cell carcinoma

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Abstract. It is important to accurately determine the resectability of thoracic esophageal squamous cell carcinoma (ESCC) for treatment decision-making. Previous studies have revealed that the CT-derived gross tumor volume (GTV) is associated with the staging of ESCC. The present study aimed to explore whether the anatomical distribution-based GTV of non-distant metastatic thoracic ESCC measured using multidetector computed tomography (MDCT) could quantitatively determine the resectability. For this purpose, 473 consecutive patients with biopsy-confirmed non-distant metastatic thoracic ESCC who underwent contrast-enhanced CT were randomly divided into a training cohort (TC; 376 patients) and validation cohort (VC; 97 patients). GTV was retrospectively measured using MDCT. Univariate and multivariate analyses were performed to identify the determinants of the resectability of ESCC in the TC. Receiver operating characteristic (ROC) analysis was performed to clarify whether anatomical distribution-based GTV could help quantitatively determinate resectability. Unweighted Cohen's Kappa tests in VC were used to assess the performance of the previous models. Univariate analysis demonstrated that sex, anatomic distribution, cT stage, cN stage and GTV were related to the resectability of ESCC in the TC (all $P<0.05$). Multivariate analysis revealed that GTV [$P<0.001$; odds ratio (OR) 1.158] and anatomic distribution ($P=0.027$; OR, 1.924) were independent determinants of resectability. ROC analysis revealed that the GTV cut-offs for the determination of the resectability of the upper, middle and lower thoracic portions were 23.57, 22.89 and 22.58 cm^3, respectively, with areas under the ROC curves of >0.9. Unweighted Cohen's Kappa tests revealed an excellent performance of the ROC models in the upper, middle and lower thoracic portions with Cohen k-values of 0.913, 0.879 and 0.871, respectively. On the whole, the present study demonstrated that GTV and the anatomic distribution of non-distant metastatic thoracic ESCC may be independent determinants of resectability, and anatomical distribution-based GTV can effectively be used to quantitatively determine resectability.

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Abbreviations: ESCC, esophageal squamous cell carcinoma; MDCT, multidetector computed tomography; GTV, gross tumor volume; TC, training cohort; VC, validation cohort; ROC, receiver operating characteristic; NCCN, National Comprehensive Cancer Network; ICC, intraclass correlation coefficient; AUC, area under the receiver operating characteristic curve

Key words: esophagus, squamous cell carcinoma, tomography, X-ray computed, volume, anatomy

Introduction

Esophageal cancer ranks seventh worldwide in terms of morbidity and is the sixth leading cause of cancer-associated mortality (1). Esophageal squamous cell carcinoma (ESCC) accounts for 90% of esophageal cancer cases globally (2). Endoscopic treatment is now well constituted as a favorable technique for early-stage cancer, while esophagectomy remains the mainstay for locally advanced ESCC (3). When the tumor reaches a more advanced stage, neoadjuvant

chemoradiotherapy, chemotherapy, immunotherapy or immunotherapy plus chemotherapy are also used (3-5). Furthermore, patients with distant metastases (non-regional lymph node involvement or T_{4b}-stage cancer) are considered unresectable, and these patients cannot be treated with surgery but only with chemoradiotherapy or chemotherapy (3,6). As regards to patients with non-distant metastatic ESCC, it is essential to determine the resectability in order to select the optimal treatment strategy to improve prognosis.

The most common diagnostic technique for ESCC is mainly based on endoscopic biopsy followed by multidetector computed tomography (MDCT) (7). Computed tomography (CT) is mainly applied for disease diagnosis and treatment guidance (8,9). A previous study suggested that CT is a reliable method with which to measure tumor volume (10). CT-derived tumor volume associates well with treatment failure rate, nodal metastases and the disease survival rate. Previous researchers have confirmed that gross tumor volume (GTV) measured using CT may be an indicator for predicting the T category and/or N stage of ESCC (11,12). Ou *et al* (8) reported that the longer length and greater sphericalness indicates more tumor invasions based on CT radiomic features, which increases the possibility of unresectable ESCC. However, their study (8) did not provide an easy-to-understand method, but only a CT radiomics model to determine resectability. To the best of our knowledge, a simple and practicable procedure without the requirement of additional computational resources is not yet available to determine the resectability of non-distant metastatic ESCC when compared with the radiomics model. Thus, the aim of the present study was to explore a simple and practicable quantitative model based on the GTV of non-distant metastatic ESCC. This was measured using multidetector CT corresponding to the anatomical distribution for the pre-operative determination of resectability in order to facilitate the selection of personalized treatment options by clinicians.

Materials and methods

Patients. The present retrospective study was approved by the constituted Ethics Committee of the Affiliated Hospital of North Sichuan Medical College (Nanchong, China; approval no. 2021ER044-1). The ethics committee waived the need for informed consent before all patients participated in the study.

From January 2017 to December 2020, at total of 489 consecutive patients with biopsy-confirmed thoracic ESCC who underwent MDCT scans were analyzed. In accordance with the National Comprehensive Cancer Network (NCCN) guidelines (6), the diagnostic criteria for unresectable esophageal cancer on CT were as follows: i) cT_{4b} tumors with the involvement of the trachea, heart, great vessels or adjacent organs including the lungs, liver, pancreas and spleen were considered unresectable; ii) ESCC with multi-station, bulky lymphadenopathy was considered unresectable; or iii) ESCC with distant metastases, including non-regional lymph nodes (stage IV) was considered unresectable. In the case that ESCC was not considered unresectable based on the criteria, the tumor was regarded as resectable. Among the 489 patients, 342 and 147 patients had been classified as resectable and unresectable ESCCs, respectively.

The patients with resectable and unresectable ESCC were recruited based on the following inclusion criteria (8): i) The patients were classified as having resectable and unresectable ESCC according to the NCCN guidelines, as depicted using MDCT (6); ii) the patients did not accept any pre-operative tumor-related treatments (e.g., radiotherapy or chemotherapy) prior to undergoing the CT scans; iii) the patients did not have distant metastases from ESCC on the CT findings; and iv) patients with a single primary tumor of non-distant metastatic thoracic ESCC. The exclusion criteria in the present study were as follows: i) The quality of the CT images was poor (n=5); ii) the clinicopathological information was incomplete (n=4); or iii) ESCC was considered resectable on the basis of the NCCN guidelines, but the patients were not able to tolerate general anesthesia and surgery (n=7). As a result, 16 of the 489 patients were excluded, and a total of 473 patients were included in the study.

Among the 473 patients, 331 and 142 were classified as resectable and unresectable ESCCs, respectively. In the resectable group, the resectability of ESCC was confirmed using a histopathological biopsy during surgery, and the margin was confirmed to be negative after the surgery. Of the 331 patients with resectable ESCC, 20 patients accepted neoadjuvant therapy after the CT scans and prior to surgery; the tumor size then markedly decreased after therapy and the cases then became resectable tumors and underwent surgical treatment, and the resectability was also confirmed using a histopathological biopsy during surgery. Ultimately, 331 patients with resectable ESCC and 142 patients with unresectable cancer were randomly divided into the training cohort (TC; n=376) and the validation cohort (VC; n=97). The clinicopathological information of the patients in the TC and VC is presented in Table I. A schematic diagram of the selection process used in the present study is presented in Fig. 1.

Contrast-enhanced CT. All patients underwent thoracic contrast-enhanced scans with a 64-row MDCT scanner (LightSpeed VCT; GE Medical Systems). The interval time between CT and surgery ranged from 2 to 14 days (mean, 8 days). Prior to the acquisition of CT data, the patients were required to drink 100 to 200 ml water as esophageal negative contrast material. Following a conventional unenhanced CT scan with the patients in the supine position, the contrast-enhanced data acquisition commenced 25 to 30 sec after the beginning of contrast material injection [Omnipaque™ (Iohexol); GE Healthcare; Cytiva] at a rate of 3.0 ml/sec for a total of 70 to 100 ml via a 20-gauge needle inserted into an antecubital vein with an automated injector (Vistron CT Injection System; Medrad, Inc.). The dosage of the injected contrast agent was tailored to the body weight of the patient at a ratio of 1.5 ml/kg body weight and was then flushed with 20 ml saline. Examinations were executed during one breath hold at full suspended inspiration for 10-15 sec. The parameters of MDCT scanning were as follows: A tube voltage of 120 kV, tube current of 200 mA, detector collimation of 64x0.6 mm, a rotation time of 0.5 sec, a pitch of 0.9, slice thickness of 5-mm and a matrix of 512x512 mm. The anatomic coverage of the CT scan was from the thoracic

Table I. Table I. Clinical information of the patients in the training (resectable vs. unresectable, 263 vs. 113) and validation cohorts (resectable vs. unresectable, 68 vs. 29).

Variable	Training cohort (n=376)	Validation cohort (n=97)
Median age, years (range)	66 (42-86)	65 (49-86)
Sex (male:female)	287:89	65:32
Anatomic distribution, n (%)		
Upper thoracic portion	43 (11.5)	23 (23.7)
Middle thoracic portion	272 (72.3)	44 (45.4)
Lower thoracic portion	61 (16.2)	30 (30.9)
T stage, n (%)		
cT_1	56 (14.9)	16 (16.5)
cT_2	59 (15.7)	16 (16.5)
cT_3	151 (40.2)	46 (47.4)
cT_{4a}	25 (6.6)	4 (4.1)
cT_{4b}	85 (22.6)	15 (15.5)
N stage, n (%)		
N_0	168 (44.7)	41 (42.3)
N_1	102 (27.1)	24 (24.7)
N_2	67 (17.8)	17 (17.5)
N_3	39 (10.4)	15 (15.5)
GTV, cm^3 (mean ± SD)	22.88±20.95	22.40±19.26

GTV, gross tumor volume; SD, standard deviation.

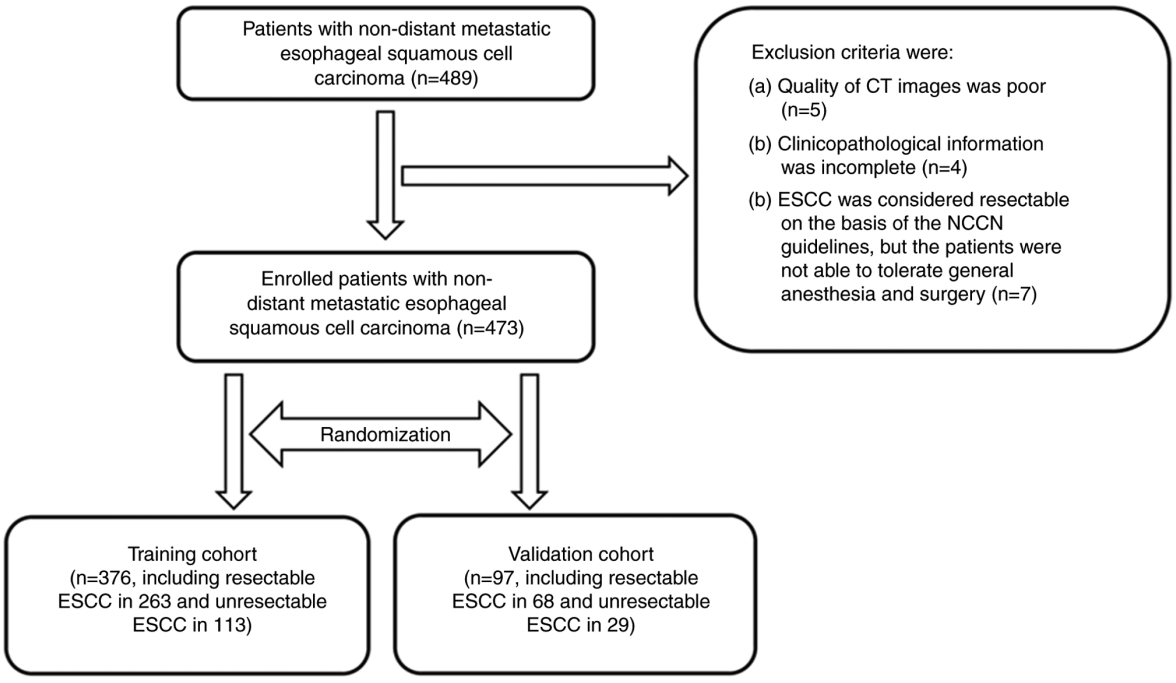

Figure 1. Flow chart of the present study. ESCC, esophageal squamous cell carcinoma; NCCN, National Comprehensive Cancer Network.

entrance to the middle level of the left kidney. All the image data were then directly transferred to the General Electric Advantage Workstation 4.4 at the mediastinal window settings (conventional window level, 40 HU; window width, 400 HU).

GTV measurement. According to the NCCN guidelines (6), the thoracic esophagus was divided into the upper, middle and lower portions through the lower edge of the azygos vein and the lower edge of the lower pulmonary vein. GTV values of resectable and unresectable ESCC based on the involved

thoracic portions in TC and VC were measured using the General Electric Advantage Workstation 4.4 at the mediastinal window. In order to obtain GTV, the esophageal wall was considered as abnormal when the thickness exceeded 5 mm on the axial image (13). GTV was calculated by multiplying the sum of all the tumor areas by the layer thickness based on a previously published method (11,12). The circumference of the ESCC was manually depicted along the visible margin of the thickened esophageal wall on each axial contrast-enhanced CT scan in order to automatically obtain the cross-sectional area of the tumor (Fig. 2). The aforementioned procedure and analysis were repeated on each contiguous axial slice where the tumor was visible. To accurately measure the tumor areas of ESCC, care was taken to avoid the liquid and air in the lumen of the esophagus.

Subsequently, two radiologists (reader 1, DG with 4 years of experience in radiology and Reader 2, TWC with 25 years of experience in radiology) measured the GTV of all patients with non-distant metastatic ESCC independently in the TC and VC, without any knowledge of the histopathological results in order to determine the interobserver reproducibility of the measurement. Prior to the aforementioned CT measurements, Reader 1 was trained in measurements randomly in 20 patients of the TC by Reader 2. To verify the intraobserver reproducibility of GTV, measurements in the TC and VC were repeated 1 month later by Reader 1.

Statistical analysis. All statistical analyses were performed using SPSS (version 26.0 for windows; IBM Corp.). The intraclass correlation coefficient (ICC) was used to evaluate the interobserver and intraobserver reliability of the repeated measurements of GTV. ICC values <0.5, between 0.5 and 0.75, between 0.75 and 0.9, and >0.90 represented poor, moderate, good and excellent reliability, respectively (14).

Univariate and multivariate analyses were performed using the TC dataset. P<0.05 was considered to indicate a statistically significant difference. The univariate analysis of possible determinants of non-distant metastatic ESCC resectability was performed using the χ^2 or Fisher's exact tests in the TC. The variables with significant differences were then enrolled into the binary logistic regression analysis to clarify the independent determinants. Subsequently, the Mann-Whitney U test was applied to compare the GTV between patients with resectable and unresectable ESCC corresponding to different anatomic distributions. In the case that a significant difference was demonstrated, receiver operating characteristic (ROC) analysis was performed to ascertain whether the cut-off values of GTV based on anatomic distributions could determinate the resectability. Finally, the performance of the models derived from the TC was validated using unweighted Cohen's Kappa tests in the VC (15). Cohen k-values between 0.61 and 0.8, and >0.81 were indicative of good and excellent agreements, respectively; otherwise, the agreement is considered unsatisfactory (16).

Results

Inter- and intraobserver agreements of GTV measurements. The inter- and intra-observer ICC values of the repeated measurements of GTV were 0.988 and 0.994, respectively (Table II); this indicated the excellent reliability of the GTV measurements by Reader 1. Consequently, the values of the initial measurement by Reader 1 were regarded as the final results for further analyses.

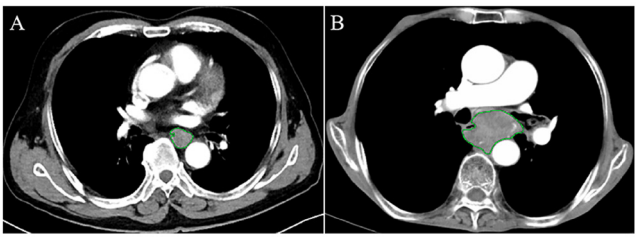

Figure 2. Manual delineation along the edge of thickened esophageal wall on a contrast-enhanced CT scan. (A) Region of interest of resectable esophageal squamous cell carcinoma in the middle thoracic portion in a male aged 64 year. (B) Region of interest of unresectable esophageal carcinoma with the invasion of the left main bronchus in the middle thoracic portion in a male aged 74 years.

Univariate analysis of GTV and clinicopathological factors: Resectable vs. unresectable ESCC in the TC. The GTV and possible clinicopathological factors associated with the resectability of non-distant metastatic thoracic ESCC in TC are presented in Table III. According to univariate analysis, sex, anatomical distribution, cT stage, cN stage and the GTV of non-distant metastatic thoracic ESCC in TC were more likely to be related to the resectability (all P<0.05). However, no significant difference in age was demonstrated between the resectable and unresectable groups.

Multivariate analysis of the resectability of non-distant metastatic thoracic ESCC in TC. According to the aforementioned univariate analysis, binary logistic regression analysis was performed for sex, anatomical distribution, cT stages, cN stages and GTV to identify the independent determinants that could be used to evaluate the resectability of non-distant metastatic thoracic ESCC. The logistic regression analysis demonstrated that the GTV [P<0.001; odds ratio (OR), 1.158; 95% CI, 1.039-1.290] and anatomic distribution (P=0.027; OR, 1.924; 95% CI, 0.344-10.773) were independent determinants of the resectability in the TC, as in Table IV.

Association of GTV of non-distant metastatic thoracic ESCC based on anatomic distributions with the resectability in TC. Mann-Whitney U test was used to investigate the association of GTV with the resectability of non-distant metastatic ESCC individually in the upper, middle and lower thoracic portions of esophagus. The results demonstrated that the GTV of non-distant metastatic ESCC based on anatomic distributions could help determine the resectability (all P<0.001; Table V).

ROC analysis of GTV of non-distant metastatic thoracic ESCC based on anatomic distributions to quantitatively determine resectability in the TC. ROC analysis was performed in the TC to identify the accuracy of GTV of non-distant metastatic thoracic ESCC corresponding to anatomic distributions for determining the resectability. The GTV cut-off values of 23.57, 22.89 and 22.58 cm^3 were

Table II. Inter- and intra-observer agreements of GTV measurements.

Agreement analysis	ICC value	95% CI	P-value
Inter-observer agreement	0.988	0.982-0.992	<0.001
Intra-observer agreement	0.994	0.991-0.996	<0.001

GTV, gross tumor volume; ICC, intraclass correlation coefficient; 95% CI, 95% confidence interval.

Table III. Univariate analysis of GTV and clinicopathological determinants of non-distant metastatic ESCC in the training cohort.

Parameter	Resectable ESCC (n=263)	Unresectable ESCC (n=113)	P-value
Age (mean, years)	65.02±7.60	66.61±8.11	0.327
Sex (%)			0.002
Male	189 (71.9)	98 (86.7)	
Female	74 (28.1)	15 (13.3)	
Anatomical distribution, n (%)			<0.001
Upper thoracic portion	19 (7.2)	24 (21.2)	
Middle thoracic portion	193 (73.4)	79 (69.9)	
Lower thoracic portion	51 (19.4)	10 (8.9)	
T stage, n (%)			<0.001
cT_1	56 (21.3)	0 (0)	
cT_2	55 (20.9)	4 (3.6)	
cT_3	140 (53.2)	11 (9.7)	
cT_{4a}	12 (4.6)	13 (11.5)	
cT_{4b}	0 (0)	85 (75.2)	
N stage, n (%)			<0.001
cN_0	161 (61.2)	7 (6.2)	
cN_1	75 (28.5)	27 (23.9)	
cN_2	27 (10.3)	40 (35.4)	
cN_3	0 (0)	39 (34.5)	
GTV, mean ± SD (cm^3)	13.84±7.96	43.91±26.12	<0.001

GTV, gross tumor volume; ESCC, esophageal squamous cell carcinoma; SD, standard deviation.

Table IV. Multivariate analysis of the resectability of non-distant metastatic thoracic ESCC in the training cohort.

Parameter	P-value	OR	95% CI
Sex	0.795	1.418	0.782-5.179
Anatomical distribution	0.027	1.924	0.344-10.773
T stage	0.551	1.502	0.490-12.951
N stage	0.605	1.831	0.647-7.845
GTV	<0.001	1.158	1.039-1.290

GTV, gross tumor volume; ESCC, esophageal squamous cell carcinoma; OR, odds ratio; 95% CI, 95% confidence interval.

enabled to identify the resectability in patients at the upper, middle and lower thoracic portions, respectively. It was discovered that the GTV of non-distant metastatic ESCC could help determine the resectability with areas under the ROC curve (AUCs) of 0.932, 0.947 and 0.906 in the upper, middle and lower thoracic portions (Fig. 3), respectively. The GTV of non-distant metastatic thoracic ESCC based on an anatomic distribution less than the cut-off value indicated that the tumor would be more likely to be resectable. The cut-off value, AUC, sensitivity, specificity, positive predictive

Table V. The Mann-Whitney U tests for investigating the association of GTV with the resectability of non-distant metastatic ESCC based on anatomic distributions in TC.

	GTV, cm^3 (mean ± SD)		
Anatomic distribution	Resectable ESCC (n=263)	Unresectable ESCC (n=113)	P-value
Upper thoracic portion	10.61±4.71	31.97±13.14	<0.001
Middle thoracic portion	13.79±8.17	47.81±28.26	<0.001
Lower thoracic portion	15.25±7.86	41.81±24.72	<0.001

GTV, gross tumor volume; ESCC, esophageal squamous cell carcinoma; TC, training cohort; SD, standard deviation.

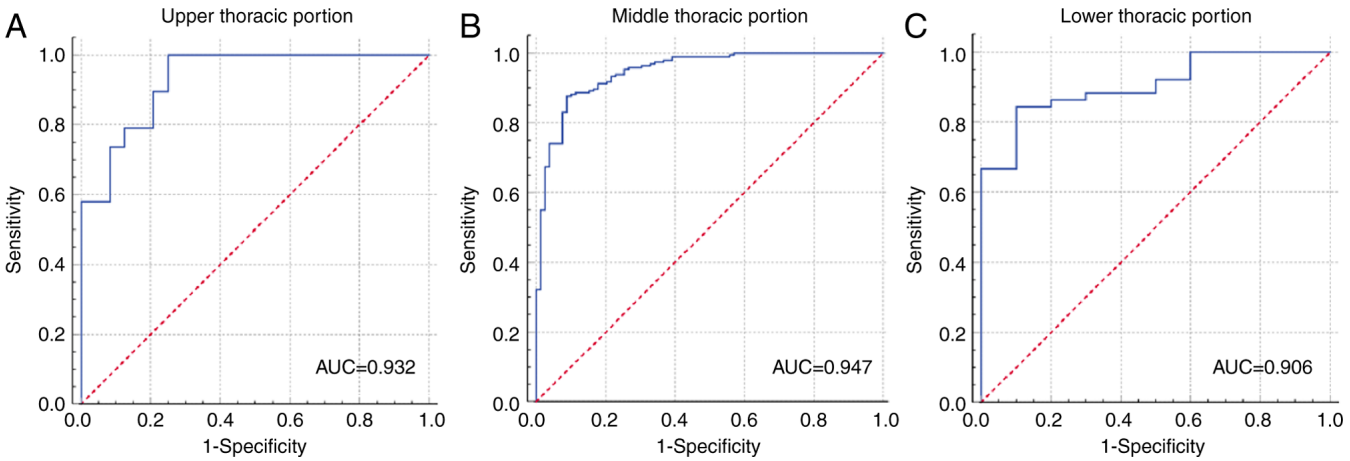

Figure 3. ROC curve analysis for the determination of resectability. (A) ROC curve of non-distant metastatic ESCC in the upper thoracic portion; (B) ROC curve of non-distant metastatic ESCC in the middle thoracic portion; (C) ROC curve of non-distant metastatic ESCC in the lower thoracic portion. ROC, receiver operating characteristic; ESCC, esophageal squamous cell carcinoma; AUC, area under the ROC curve.

value, negative predictive value and accuracy of GTV of non-distant metastatic ESCC for determining resectability are summarized in Table VI.

Unweighted Cohen's Kappa tests to validate the performance of the ROC models in VC. Unweighted Cohen's Kappa tests in the VC were executed to validate the agreement in the diagnostic efficiency of the ROC models of GTV corresponding to anatomic distributions to determine the resectability of non-distant metastatic thoracic ESCC. The results revealed that the models obtained excellent agreements in VC with all Cohen k-values >0.87, as presented in Table VII.

Discussion

The present study demonstrated that GTV and anatomic distribution could be potential independent factors for determining the resectability of non-distant metastatic thoracic ESCC. Thus, the present study subsequently investigated whether GTV corresponding to the anatomic distributions of thoracic ESCC can be used to determine the resectability and to determine how this can be achieved.

As demonstrates in the present study, the resectability of ESCC decreased as the GTV increased. Previous studies (11,12,15) have reported that GTV measurement on a CT scan may be associated with tumor TNM staging. The GTV can be a comprehensive index that can reflect the depth of tumor invasion, tumor diameter and tumor length (15). According to American Joint Committee on Cancer criteria (17), the T stage of ESCC is mainly defined based on the depth of tumor infiltration. With the increase in the depth of tumor invasion, it is easier to detect the local tumor invasion of adjacent structures (18). Another previous study demonstrated that the longer length and greater sphericalness indicates an increased number of tumor invasions, which leads to the increased possibility of unresectable ESCC (8). It can be hypothesized that the greater GTV based on the longer length and deeper infiltration of ESCC indicates an increased possibility of unresectability. Therefore, GTV was selected as an alternative factor for analysis in the present study. To the best of our knowledge, the present study is the first to demonstrate that the GTV may be strongly related to the resectability of non-distant metastatic ESCC in the TC.

The present study also indicated that the anatomic distribution of non-distant metastatic thoracic ESCC may be another independent determinant of resectability in the TC. The esophagus is divided into the cervical region, and the upper, middle and lower thoracic regions by the thoracic entrance, the inferior edge of the azygos vein arch and the inferior edge of inferior pulmonary vein, respectively (19). ESCC is most commonly observed in the middle

Table VI. ROC analysis of the ability of anatomy-based GTV to quantitatively determine the resectability of non-distant metastatic ESCC in TC.

Anatomic Distribution	GTV cut-off value (cm^3)	AUC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Upper thoracic portion	23.57	0.932	100.0	75.0	76.0	100.0	86.1
Middle thoracic portion	22.89	0.947	87.6	91.1	96.0	75.0	88.6
Lower thoracic portion	22.58	0.906	84.3	90.0	97.7	52.9	85.2

ROC, receiver operating characteristic; GTV, gross tumor volume; ESCC, esophageal squamous cell carcinoma; TC, training cohort; AUC, area under the receiver operating characteristic curve; PPV, positive predictive value; NPV, negative predictive value.

Table VII. Results of unweighted Cohen's Kappa tests in the validation cohort for the validation of the performance of the receiver operating characteristic models.

Anatomic distribution	Cohen k-value	95% CI	P-value
Upper thoracic portion	0.913	0.746-1.080	<0.001
Middle thoracic portion	0.879	0.716-1.042	<0.001
Lower thoracic portion	0.871	0.699-1.043	<0.001

95% CI, 95% confidence interval.

thoracic portion, followed by the lower and upper thoracic portions (20). According to a previous study (21), upper thoracic ESCC may be diagnosed as advanced-stage cancer with a high possibility of invading adjacent organs; patients with this type cannot undergo esophagectomy, which indicates that the treatment strategies of ESCC may vary based on different anatomical distributions. Clinically, the upper edge of the resected esophagus should be 5 cm away from the upper edge of the tumor. Patients with upper thoracic esophageal cancer within 5 cm from the cricopharyngeal muscle should receive radical chemoradiotherapy, with no consideration of surgical treatment according to NCCN guidelines (6). If the proximal end of the upper thoracic esophageal cancers is <5 cm from the cricopharyngeal muscle, the resection margin may be insufficient (22). The surgical resection of the middle and lower thoracic ESCC cannot be limited by the tumor anatomic location, as the upper edge of the tumor anatomic location is >5 cm away from the cricopharyngeal muscle (6). Thus, the anatomical distribution of non-distant metastatic thoracic ESCC can be an independent determinant for esophagectomy.

The cT and cN stages of non-distant metastatic ESCC did not exhibit any independent effects on resectability in the present study. The approximate representation of one-dimensional data and the interaction could interpret the loss of the impact of the cT and cN stages of ESCC in the multivariate analysis (23,24), which has been proven to be related to the GTV of ESCC in previous studies (11,12).

Based on the independent determinants in TC, the present study subsequently took both GTV and tumor location into consideration to perform the ROC analysis, in order to explore a novel quantitative model for determining the resectability of non-distant metastatic thoracic ESCC for the first time. The results of ROC analysis demonstrated that GTV corresponding to anatomic distributions measured using MDCT could well determine the resectability of non-distant metastatic ESCC with AUC values of >0.9. Higher AUCs were obtained to determine the resectability of thoracic ESCC using the current ROC models when compared with the previous CT radiomics model (maximum AUC, 0.947 vs. 0.924) (8). The likely reason for this may be that the present study specifically involved GTV corresponding to esophageal anatomical distribution and excluded the patients with distant metastasis. In addition, the results of unweighted Cohen's Kappa tests revealed that the results obtained had excellent reliability with Cohen k-values >0.87. The clinical significance of the aforementioned quantitative ROC models corresponding to the combination of GTV and anatomic distribution may thus help to determine the resectability of non-distant metastatic ESCC and may aid in the selection of optimal treatment strategies.

The present study had several limitations which should be mentioned. Firstly, the present study was a retrospective single-center research and included the data of patients obtained from January 2017 to December 2020. However, the present study demonstrated a good performance for the resectability of ESCC due to the large sample size; in addition, the authors aim to collect data from the previous 1 to 2 years to carry out related research in the future to confirm the current findings. Secondly, all samples were from patients with ESCC. In the future, the authors also aim to further investigate whether the findings obtained in the present study are also applicable to patients with esophageal adenocarcinoma. Thirdly, the GTV of ESCC was obtained by manually depicting the abnormally thickened esophageal wall as opposed to using a machine learning algorithm. However,

the present study exhibits repeatability in measuring the GTV of ESCC. Fourthly, the methods used in the present study may be not applicable to patients with a decreased renal function or allergies, as these patients cannot undergo contrast-enhanced CT to identify smaller ESCC lesions or distinguish between the tumor itself and surrounding tissues. The authors thus aim to conduct relevant research using magnetic resonance imaging in the future. Lastly, the present study did not compare the prognosis of patients with non-distant metastatic thoracic ESCC shown to be eligible for surgery as per the NCCN guidelines and that of cases for which eligibility for surgery was calculated using the GTV, in order to determine which method is associated with an improved prognosis. Thus, further studies are required to determine prognosis in future.

In conclusion, the present study demonstrated that the GTV and anatomic distribution may be potential independent determinants of the resectability of non-distant metastatic thoracic ESCC. GTV based on anatomic distributions can effectively quantitatively determine resectability with AUCs >0.9. It is hoped that the findings presented in the present study may provide a novel quantitative procedure that can be used to help clinicians formulate the optimal treatment strategy for patients.

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Availability of data and materials

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

Authors' contributions

TWC, RL and XMZ participated in the design of the study. DG, BGT, JO, HYZ, ZYY and KYL contributed to data analysis. TWC, DG, BGT and JO drafted and revised the manuscript. TWC, DG, BGT and JO proofread the manuscript. TWC submitted the manuscript. TWC and DG confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Review Committee of the Affiliated Hospital of North Sichuan Medical College (approval no. 2021ER044-1). The ethics committee waived the need for informed consent due to the retrospective nature of the study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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