

# Texture analysis of CT imaging for assessment of esophageal squamous cancer aggressiveness

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**Background:** To explore the role of texture analysis of computed tomography (CT) images in preoperative assessment of esophageal squamous cell carcinoma (ESCC) aggressiveness.

**Methods:** Seventy-three patients with pathologically confirmed ESCC underwent unenhanced and contrast enhanced CT imaging preoperatively. Texture analysis was performed on unenhanced and contrast enhanced CT images, respectively. Six CT texture parameters were obtained. One-way analysis of variance or independent-samples t-test (normality), independent-samples Kruskal-Wallis test or Mann-Whitney U test (non-normality), binary Logistic regression analysis (multivariable), Spearman correlation test, receiver operating characteristic (ROC) curve analysis and intraclass correlation coefficient (ICC) were used for statistical analyses.

**Results:** Kurtosis was an independent predictor for T stages (T1–2 *vs.* T3–4) as well as overall stages (I–II *vs.* III–IV) based on unenhanced CT images, while entropy was an independent predictor for T stages (T1–2 *vs.* T3–4), lymph node metastasis (N– *vs.* N+) and overall stages (I/II *vs.* III/IV). Skew and kurtosis based on unenhanced CT images showed significant differences among N stages (N0, N1, N2 and N3) as well as 90th percentile based on contrast enhanced CT images. In correlation with T stage of ESCC, kurtosis and entropy significantly correlated with T stage both on unenhanced and contrast enhanced CT images. Reversely, entropy and 90th percentile based on contrast enhanced CT images showed significant correlations with N stage ( $r: 0.526, 0.265$ ; both  $P < 0.05$ ), as well as overall stage ( $r: 0.562, 0.315$ ; both  $P < 0.05$ ). For identifying ESCC with different T stages (T1–2 *vs.* T3–4), lymph node metastasis (N– *vs.* N+) and overall stages (I/II *vs.* III/IV), entropy based on contrast enhanced CT images, showed good performance with area under ROC curve area under curve (AUC) of 0.637, 0.815 and 0.778, respectively.

**Conclusions:** Texture analysis of CT images held great potential in differentiating different T, N and overall stages of ESCC preoperatively, while failed to assess the differentiation degrees.

**Keywords:** Computed tomography (CT); texture analysis; esophageal cancer; staging

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## Introduction

Esophageal cancer has very high incidence and mortality rate in both more as well as less developed countries (1). The important indexes reflecting the aggressiveness of esophageal cancer include TNM stage and its differentiation degree (2,3), which might be evaluated by endoscopic ultrasonography (EUS), computed tomography (CT) or endoscopic biopsy preoperatively. EUS performed well in T staging but poorly in N staging with a low sensitivity and specificity (4). In some patients with esophageal obstruction, the endoscopy even fails to go through the narrow lumen. Specimens from endoscopic biopsy are limited to achieve reliable histopathological assessment. Traditional CT could identify T4 stage disease confidently when the tumor invades into adjacent structures, but faces the challenge to differentiate early esophageal cancers due to its lower soft tissue resolution (5). CT evaluation of nodal status is mainly based on size measurement of lymph nodes, which yielded a highly discrepant sensitivity from 11% to 50% and a relatively high specificity from 83% to 95% (6-8).

Quantitative CT imaging brings new perspective into lesion's assessment (9-11). Texture analysis of CT images is one of ways, which could reflect certain components within the tumor, intratumoral heterogeneity of various tumors (12-16). For instance, Ganeshan *et al.* reported that CT texture analysis were associated with tumor metabolism, stage and survival of the primary esophageal lesion (16). And Ha *et al.* found that texture analysis of <sup>18</sup>F-FDG position emission tomography (PET)/CT images had significant different values between adenocarcinoma and squamous cell carcinoma for non-small cell lung carcinoma (13).

Tumor with deeper invasion and lower differentiation degree is more prone to lymph node metastasis (3). Different components within the tumor, such as hypercellular areas, necrosis, hemorrhage, and myxoid changes, can be quantified by CT texture parameters, including lower and higher percentiles (12). Furthermore, skew and kurtosis can represent the deviation from normal distribution of CT value histogram within the tumor, while entropy is able to reflect intratumoral heterogeneity quantitatively which is regarded as the degree of disorder. For instance, Ng *et al.* reported that entropy, kurtosis and skew were related to 5-year overall survival rate in colorectal cancer patients (17). Moreover, Giganti *et al.* found that entropy and skew correlated with the prognosis of gastric cancer patients (18). In general, it is considered that the changes of composition, the deviation from normal

distribution and the degree of disorder within tumor are closely associated with tumor aggressiveness. Thus, the above parameters have been widely investigated in the evaluation of various tumor aggressiveness (12,17,18).

In recent years, CT texture analysis has also been applied in the assessment of esophageal cancer preliminary, whereas most of those studies just focused on the evaluation or prediction of treatment response in esophageal cancer (19-21). Few papers mentioned the correlation between the texture parameters based on contrast enhancement CT images and stage of esophageal cancer (16,22), yet those parameters were based on PET which leads to overspending and radiation overusing. Since CT texture analysis could reflect intratumoral heterogeneity quantitatively from the perspective of non-invasive imaging, we hypothesized that with the development of esophageal cancer's aggressiveness, its biological components, microstructures as well as microenvironments would take some changes, which might be reflected by texture analysis of CT images.

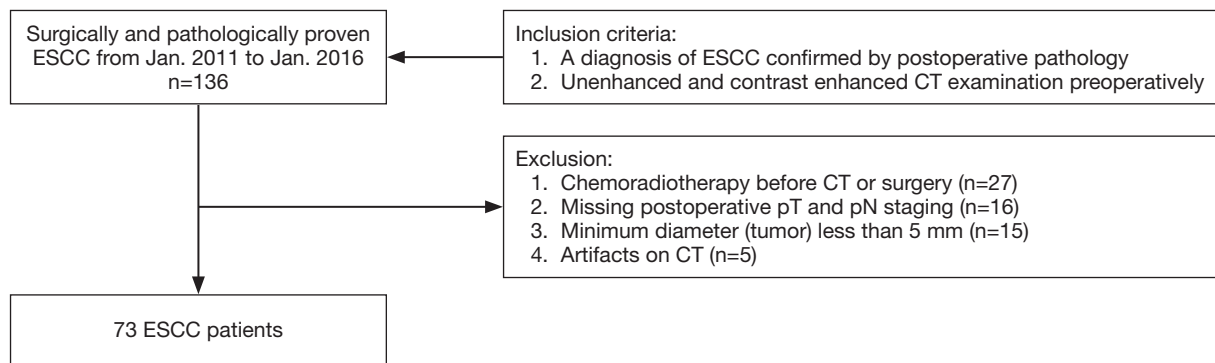
Therefore, the purpose of this study was to explore the correlation between texture analysis of CT images and the aggressiveness of esophageal squamous cell carcinoma (ESCC), and to explore the role of CT texture parameters in preoperative assessment of ESCC's aggressiveness.

## Methods

### Patients

This retrospective study was approved by the local ethics committee and informed consent from the patients was waived. From January 2011 to January 2016, a total of 136 patients with a clinical diagnosis of ESCC were collected and reviewed. The inclusion criteria were: (I) with a diagnosis of ESCC confirmed by postoperative pathology; (II) with unenhanced and contrast enhanced CT examination preoperatively. The exclusion criteria were: (I) with any local or systematic treatment before CT examination or surgery (27/63, 42.9%); (II) without definite information of postoperative pathologic T and N staging (16/63, 25.4%); (III) with a minimum diameter of tumor less than 5 mm insufficient to contain a region of interest (ROI) (15/63, 23.8%); (IV) poor CT image quality for post processing due to artifacts (5/63, 7.9%), respectively.

The study workflow diagram with respect to patient selection is shown in *Figure 1*. A total of 73 patients served as our study cohort, whose clinicopathological characteristics are shown in *Table 1*.



**Figure 1** The study workflow diagram with respect to patient selection. ESCC, esophageal squamous cell carcinoma; pT, pathological tumor; pN, pathological node status.

**Table 1** Clinicopathologic characteristics of patients with esophageal squamous carcinomas

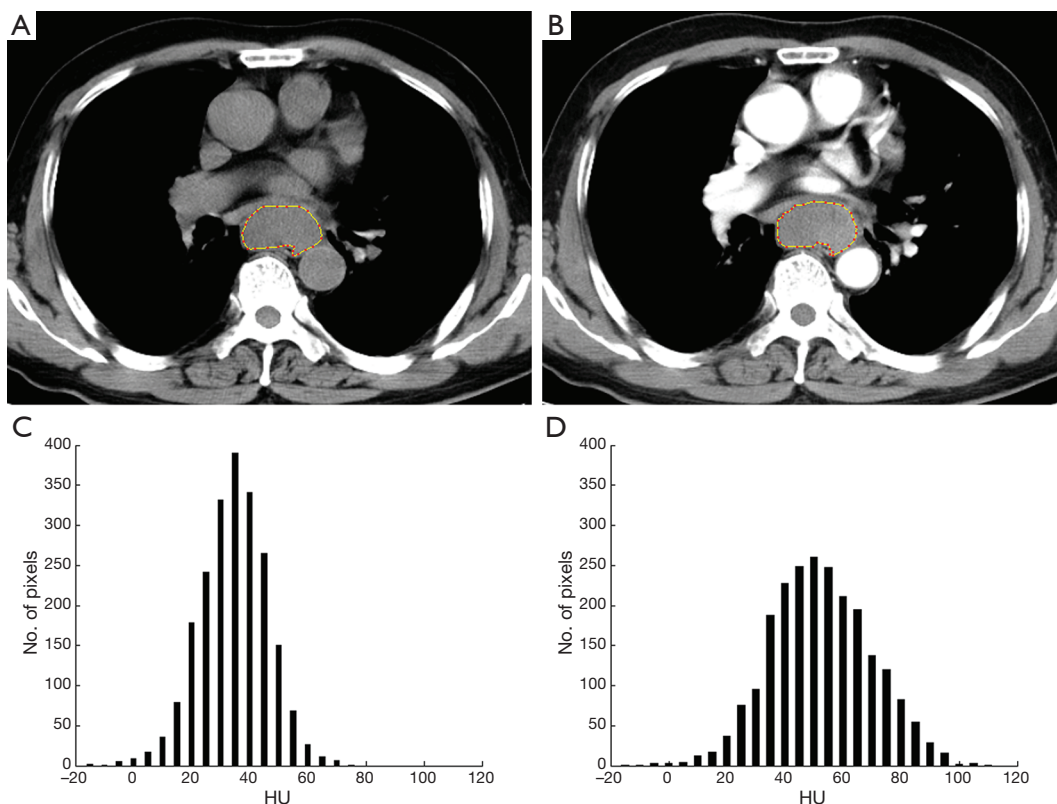
Characteristics	n	Percentage (%)
<b>Gender</b>		
Male	55	75.3
Female	18	24.7
<b>Differentiation degree</b>		
Poor	10	13.7
Moderate	45	61.6
Well	18	24.7
<b>T stage</b>		
T1	14	19.2
T2	23	31.5
T3	34	46.6
T4	2	2.7
<b>N stage</b>		
N0	37	50.7
N1	16	21.9
N2	13	17.8
N3	7	9.6
<b>Overall stage</b>		
I	13	17.8
II	31	42.5
III	28	38.4
IV	1	1.4

### CT examination

Patients fasted for at least six hours before CT examination. The patients were trained to hold breath before CT examinations. Patients were in supine position with feet first in 16- or 64-slice multidetector CT scanners (Light Speed Pro 16, VCT, or HD Discovery 750, GE Healthcare, US). The scan ranged from the oropharynx to cardia of stomach. After unenhanced CT scan, a total of 100–120 mL iohexol (Omnipaque 350 mg I/mL, GE Healthcare, Shanghai, China) was administered intravenously at a flow rate of 3.0 mL/s by using a high pressure syringe (Medrad Stellant CT Injector System; One Medrad Drive Indianola, PA, US). Contrast-enhanced CT images were obtained at one phase after 25–30 seconds following contrast agent administration. CT scan parameters were as follows: tube voltage, 120 kVp; tube current, 250–350 mA; slice thickness, 5 mm; slice interval, 5 mm; field of view, 35–50 cm; matrix, 512 × 512; rotation time, 0.7 s; pitch, 1.375; reconstruction algorithm, standard.

### Image interpretation and post-process

Two radiologists with 7- and 10-year experience in gastrointestinal imaging, who were blinded to pathologic information, performed CT image interpretation and post-process independently. The unenhanced and contrast-enhanced CT images were loaded into our in-house software (Image analyzer 1.0, China) for texture analysis. ESCC presented as thickening of esophageal wall or a mass lesion, with varying degree enhancement on contrast enhanced images. Axial unenhanced and contrast enhanced



**Figure 2** A 71-year-old man with pathologically diagnosed moderately differentiated squamous carcinoma at stage IIIB (T3/N2/M0). (A) Axial unenhanced CT image shows a mass in middle of the oesophagus, and the outline indicates the ROI; (B) corresponding contrast enhanced CT image shows mild enhancement of this lesion; (C) Histogram obtained from unenhanced CT image shows pixel distribution with a bin size of 5 HU; mean =37 HU, 10th and 90th percentile =23 and 50 HU, skew =-1.57, kurtosis =51.14, and entropy =3.81, respectively; (D) Histogram obtained from contrast enhanced CT image shows; mean =55 HU, 10th and 90th percentile =35 and 77 HU, skew =1.89, kurtosis =44.65, and entropy =4.17, respectively. ROI, region of interest; HU, hounsfield units.

CT images showing the largest area of the lesion was selected. And the ROIs were manually drawn to cover the boundary of the lesion including necrosis within the tumor, carefully excluding adjacent water or air. Examples of unenhanced and contrast enhanced CT images ROIs and signal intensity histograms are shown in *Figure 2*. The mean area of the ROIs was  $349.73 \pm 259.58$  (range, 71.51–1,376.93)  $\text{mm}^2$  and  $369.13 \pm 259.05$  (range, 70.34–1,436.53)  $\text{mm}^2$  in the unenhanced and contrast enhanced CT images, respectively. After drawing the ROIs, CT texture analysis was performed and six parameters based on hounsfield unit (HU) values were generated, including: (I) mean (mean HU value); (II–III) 10th and 90th percentiles (10th and 90th percentile HU value of a cumulative histogram); (IV) skew (asymmetry of the histogram distribution); (V) kurtosis (peakedness of the histogram

distribution); and (VI) entropy (the irregularity of grey-level HU). Unenhanced and contrast enhanced CT images were analyzed independently. And the average value of the two radiologists was calculated for statistical analyses except interobserver agreement analysis.

#### **Pathological analysis**

Patients underwent resectable surgery by two surgeons with 18- and 10-year experience in general thoracic surgery. Histopathological analysis of the resected specimens was performed by one pathologist with 6-year experience in gastrointestinal pathology. The pathological types, differentiation degree, T and N stage of the specimens were reviewed and recorded according to the American Joint Committee on Cancer (7th edition).

### Statistical analyses

Shapiro-Wilk tests were used to check normality assumption for all parameters. The results showed in *Tables S1-S5*. Firstly, Independent samples *t*-test (normality) or Mann-Whitney U test (non-normality) was used to compare texture parameters between different T stages (T1-2 vs. T3-4), lymph node metastasis (N- vs. N+) and overall stages (I/II vs. III/IV). Secondly, the texture parameters which were significant in Independent samples *t*-test (normality) or Mann-Whitney U test (non-normality) were tested by binary Logistic regression analysis (multivariable) to identify the above pathological characteristics. Then, diagnostic performance of CT texture parameters which were significant in logistic regression analysis in differentiating the above pathological characteristics with receiver operating characteristic (ROC) curve analysis. One-way analysis of variance (normality) or independent-samples Kruskal-Wallis test (non-normality) was used to detect the difference of texture parameters among different N (N0, N1, N2 and N3) and differentiation degrees (poor, moderate and well). Correlations between CT texture parameters and T, N, and overall stages as well as differentiation degrees were analyzed with Spearman correlation test (*r*, 0.000-0.300, poor; 0.301-0.500, moderate; 0.501-0.800, good; 0.801-1.000, excellent). Interobserver agreement in measurement of CT texture parameters was evaluated by calculating intraclass correlation coefficient (ICC) (0.000-0.200, poor; 0.201-0.400, fair; 0.401-0.600, moderate; 0.601-0.800, good; 0.801-1.000, excellent). Statistical analyses were performed with SPSS (version 22.0 for Microsoft Windows x64, SPSS, Chicago, US). A two-tailed P value less than 0.05 was considered statistically significant.

## Results

### Differences of CT texture parameters among different pathologic characteristics in ESCCs

According to independent samples *t*-test (normality) or Mann-Whitney U test (non-normality), multiple texture parameters have significant differences between different T stages (T1/2 vs. T3/4) and overall stages (I/II vs. III/IV) based on unenhanced and contrast enhanced CT images (both  $P < 0.05$ ) (*Table S6*). And binary logistic regression analysis (multivariable) showed that entropy based on contrast enhanced CT images was independent predictor for T stage (T1-2 vs. T3-4;  $P = 0.030$ ), lymph node metastasis (N- vs. N+;  $P = 0.001$ ) and overall stage

(I-II vs. III-IV;  $P = 0.001$ ). Entropy and kurtosis based on unenhanced CT images were independent predictors for T stage (T1-2 vs. T3-4;  $P = 0.035, 0.026$ , respectively). And kurtosis based on unenhanced CT images was independent predictor for overall stage (I-II vs. III-IV;  $P = 0.020$ ) (*Table S7*). There were significant differences of skew and kurtosis based on unenhanced CT images among ESCCs at different N stages using one-way analysis of variance (normality) or independent-samples Kruskal-Wallis test (non-normality), as well as 90th percentile and entropy based on contrast enhanced CT images ( $P < 0.05$ ). There were no significant differences of all parameters at different differentiation degrees of ESCCs (all  $P > 0.05$ ) (*Table S8*).

### Correlations between CT texture parameters and tumor stages as well as differentiation degrees

Based on unenhanced CT texture analysis, kurtosis and entropy correlated with T stages of ESCC significantly ( $r$ : 0.418, 0.283; both  $P < 0.05$ ). Mean, 10th-90th percentile, skew and kurtosis, correlated with both N and overall stages significantly ( $r$ : -0.261 to 0.309, -0.273 to 0.530; all  $P < 0.05$ ) (*Table 2*).

Based on contrast enhanced CT texture analysis, kurtosis and entropy significantly correlated with T stage ( $r$ : 0.277, 0.267;  $P = 0.018, 0.022$ , respectively). The 90th percentile and entropy correlated with both N and overall stages of ESCC significantly ( $r$ : 0.265, 0.526;  $r$ : 0.315, 0.562, respectively; both  $P < 0.05$ ) (*Table 2*).

No parameters showed significant correlation with differentiation degrees in ESCC both on unenhanced and contrast enhanced CT ( $P > 0.05$ ) (*Table 2*).

### Diagnostic performance for differentiating pathologic characteristics

For identifying ESCC with different T stages (T1-2 vs. T3-4), lymph node metastasis (N- vs. N+) and overall stages (I-II vs. III-IV), the results of ROC curve analysis were shown in *Figure 3*.

Based on unenhanced CT images, kurtosis and entropy could differentiate different T stages (T1-2 vs. T3-4), with an area under curve (AUC) of 0.652 and 0.653, respectively. Kurtosis identified different overall stages (I-II vs. III-IV) with an AUC of 0.744.

Based on contrast enhanced CT images, entropy differentiated different T stages (T1-2 vs. T3-4), lymph node metastasis (N- vs. N+) and overall stages (I/II vs. III/IV)



**Table 2** Correlations between unenhanced CT texture parameters and tumor stage of esophageal squamous carcinoma

Parameters	T stage		N stage		Overall stage		Differentiation degree	
	r	P	r	P	r	P	r	P
Unenhanced CT								
Mean	-0.099	0.406	-0.309	0.008*	-0.306	0.008*	0.073	0.538
10th percentile	-0.211	0.331	-0.287	0.014*	-0.273	0.019*	0.090	0.447
90th percentile	-0.093	0.434	-0.289	0.013*	-0.304	0.009*	0.060	0.611
Skew	-0.164	0.165	-0.261	0.026*	-0.401	<0.001*	-0.071	0.552
Kurtosis	0.418	<0.001*	0.309	0.008*	0.530	<0.001*	0.090	0.450
Entropy	0.283	0.015*	0.120	0.312	0.169	0.154	-0.019	0.876
Enhanced CT								
Mean	0.035	0.767	0.132	0.267	0.188	0.111	-0.021	0.859
10th percentile	-0.027	0.882	-0.028	0.811	0.024	0.839	-0.027	0.822
90th percentile	0.073	0.538	0.265	0.024*	0.315	0.007*	-0.042	0.724
Skew	0.018	0.888	-0.149	0.209	0.027	0.818	-0.124	0.298
Kurtosis	0.277	0.018*	0.073	0.539	0.192	0.104	0.072	0.545
Entropy	0.267	0.022*	0.526	<0.001*	0.562	<0.001*	-0.034	0.773

\*, P<0.05 with Spearman correlation test. CT, computed tomography.

with an AUC of 0.637, 0.815 and 0.778, respectively.

Mean and 10th percentiles based on unenhanced CT images, and entropy based on contrast enhanced CT images showed excellent interobserver agreement with ICCs over 0.800 (Table S9).

## Discussion

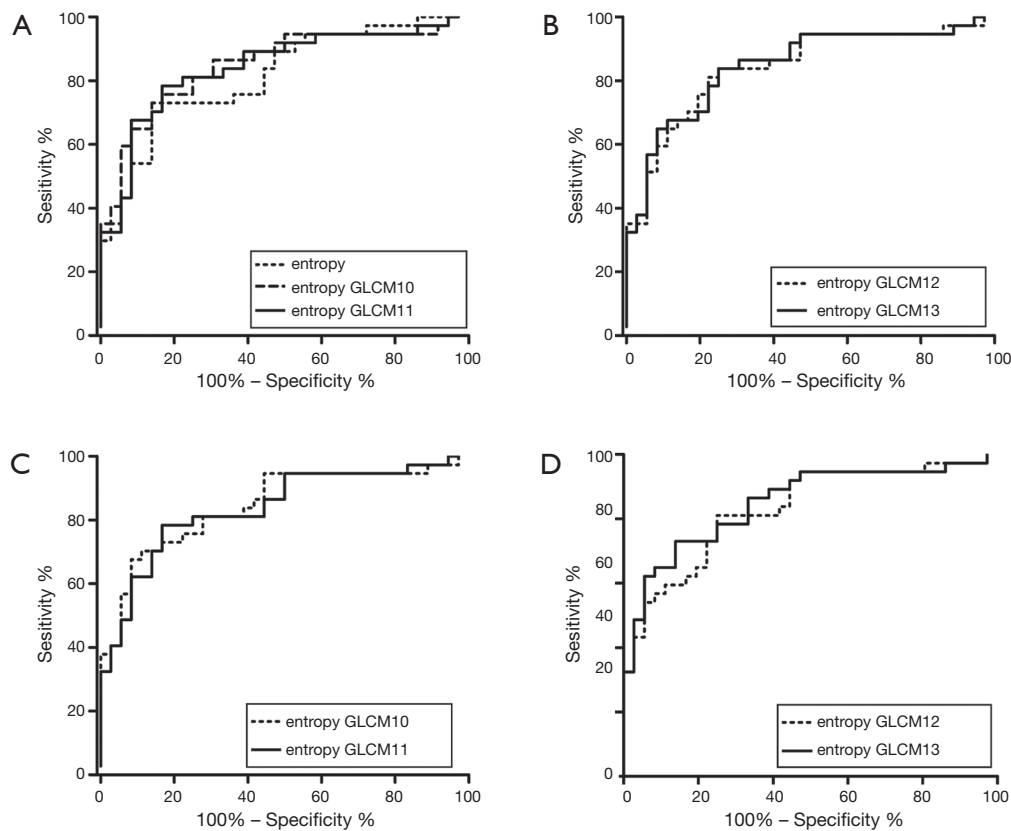
We confirmed the correlations between CT texture parameters and T, N and overall stage of ESCC in this study.

We found that kurtosis and entropy based on unenhanced CT images differed significantly among ESCCs at different T stages (T1/2 vs. T3/4) as well as entropy based contrast enhanced CT images. Moreover, kurtosis and entropy significantly correlated with T stage both on unenhanced and contrast enhanced CT images. Kurtosis reflected the peakedness degree of the pixel density histogram and entropy represented the degree of tumor chaos and complexity. With progression of T stage, the CT values within the tumor became more heterogeneous, the distribution of the pixel density form deviated from the normal distribution, so the value of kurtosis and entropy became larger. In our study, some parameters (mean, 10th,

90th percentile and skew) were unreliable for T stage of ESCC both in unenhanced and contrast enhanced CT.

Our study showed that entropy differed significantly among ESCCs at different N stages, based on contrast enhanced CT image (P<0.001), while there were no significant differences on unenhanced CT image (P>0.05). In correlation with N stage of ESCC, entropy based on contrast enhanced CT images (r: 0.526; P<0.001) was also superior to unenhanced CT images (P>0.05). Entropy reflected the heterogeneity of the pixel density in CT images. In contrast enhanced CT images, entropy represented the heterogeneity of the tumor's blood supply. We found that as the heterogeneity of blood supply with the tumor increased, its potential of lymph node metastasis also increased. There was a report that metabolic parameters of non-small cell lung carcinoma correlated with entropy assessed by texture analysis of FDG-PET images (23). The correlation between some parameters (mean, 10th, 90th percentile, skew and kurtosis) based on the unenhanced CT images and N stage of ESCC was weak, as well as 90th percentile based on the contrast enhanced CT images in our study.

It was interesting to found that most texture parameters



**Figure 3** ROC curves of texture parameters derived from CT images in differentiating different pathological characteristics of ESCCs. (A) ROC curves of kurtosis and entropy based on unenhanced CT images in differentiating different T stages (T1–2 vs. T3–4), with an AUC of 0.652 and 0.653, respectively; (B) ROC curve of entropy based on contrast enhanced CT images differentiating different T stages (T1–2 vs. T3–4) with an AUC of 0.637; (C) ROC curve of entropy based on contrast enhanced CT images in differentiating lymph node metastasis (N– vs. N+) with an AUC of 0.815; (D) ROC curves of kurtosis based on unenhanced CT images and entropy based on contrast enhanced CT images in differentiating overall stages (I/II vs. III/IV) with an AUC of 0.744 and 0.778, respectively. ROC, receiver operating characteristic; ESCC, esophageal squamous cell carcinoma; AUC, area under curve.

which correlated with N stage were also correlated with overall stage. Nevertheless, their correlation with overall stage was weaker than N stage but stronger than T stage, which might be due to a higher weight of N stage than T stage in overall stage. In our study, energy based on contrast enhanced CT images significantly correlated with overall stage of ESCC, which was in accordance with the results of some previous studies. For example, Dong *et al.* reported that entropy and energy based on PET images correlated significantly with ESCC stage according to AJCC 7th (22). Ganeshan *et al.* also found that entropy showed significant differences between patients with esophageal cancers at stages I–II and III–IV (16).

However, we failed to detect any significant differences of CT texture parameters among ESCCs with different

differentiation degrees. Dong *et al.* also reported that no significant correlation was found between texture parameter and histological grade (22). Hence, the role of texture analysis on CT or PET images in evaluating differentiation degree of ESCC remains undetermined.

Entropy based on contrast enhanced CT images performed better than unenhanced CT images in identifying ESCCs with lymph node metastasis and overall stages (I–II vs. III–IV), especially for lymph node metastasis (AUC = 0.815). Many studies have highlighted the value of entropy in differentiating positive-human papillomavirus from negative-human papillomavirus primary oropharyngeal squamous cell (24), identifying colorectal cancer patients with metastatic liver disease (25), and predicting lung cancer recurrence after stereotactic ablative radiotherapy (26).

Most parameters showed good or excellent interobserver agreement, with ICCs ranging from 0.699 to 0.921, indicating their stability. While a few parameters showed poor or fair interobserver agreement with ICCs ranging from 0.336 to 0.509. For example, skew showed the worst interobserver agreement (ICC =0.336) which was not suitable for evaluating CT texture images of ESCC.

Our study had some limitations. Firstly, patients of ESCC at stage M1 were not included due to lack of postoperative pathologic information, which might cause some selection bias to our study. Secondly, the ROIs were manually drawn on CT without reference to pathologic specimens, and only one slice showing the largest area of the lesion was selected rather than whole lesion analysis. Thirdly, CT texture analysis was only performed on primary tumors rather than lymph nodes, which might compromise the prediction efficiency. Finally, CT images were obtained from two CT scanners which might affect the texture analysis, while a previous study showed the effect of variations in acquisition parameters of CT may be limited when performing texture analyses (27). All the above issues required further investigation.

In conclusion, our study demonstrated that texture analysis on CT images could help to evaluate preoperative staging of ESCC, especially kurtosis and entropy based on unenhanced images for T staging and entropy based on contrast enhanced images for N and overall staging. And CT texture parameters proved useful in assessing ESCC's aggressiveness, which might facilitate personalized treatment and improve the prognosis of patients with ESCC.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Ethical Statement:* This retrospective study was approved by the local ethics committee (No. 2016-183-1) and informed consent from the patients was waived.

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## Supplementary

**Table S1** The P values of CT texture parameters among esophageal squamous carcinomas at different T stages for Shapiro-Wilk tests of normality assumption

Parameters	Unenhanced CT		Contrast enhanced CT	
	T1-2	T3-4	T1-2	T3-4
Mean	0.533	0.003	0.151	0.250
10th percentile	0.609	0.405	0.180	0.320
90th percentile	0.524	<0.001	0.502	0.873
Skew	0.751	0.437	0.098	0.276
Kurtosis	0.001	0.007	0.008	0.001
Entropy	0.273	0.877	0.286	0.476

The parameters verify normality assumption if the P value is larger than 0.05. T1-2, T1 and T2 stages were categorized as T1-2 group; T3-4, T3 and T4 stages were categorized as T3-4 group. CT, computed tomography.

**Table S2** P values of CT texture parameters among esophageal squamous carcinomas with lymph node metastasis for Shapiro-Wilk tests of normality assumption

Parameters	Unenhanced CT		Contrast enhanced CT	
	N-	N+	N-	N+
Mean	0.351	0.036	0.590	0.733
10th percentile	0.294	0.388	0.226	0.341
90th percentile	0.528	<0.001	0.472	0.896
Skew	0.649	0.415	0.027	0.950
Kurtosis	<0.001	0.003	0.001	<0.001
Entropy	0.178	0.538	0.272	0.085

The parameters verify normality assumption if the P value is larger than 0.05. N-, without lymph node metastasis; N+, with lymph node metastasis; CT, computed tomography.

**Table S3** P values of CT texture parameters among esophageal squamous carcinomas at different overall stages for Shapiro-Wilk tests of normality assumption

Parameters	Unenhanced CT		Contrast enhanced CT	
	I-II	III-IV	I-II	III-IV
Mean	0.535	0.138	0.575	0.805
10th percentile	0.643	0.561	0.478	0.661
90th percentile	0.489	0.003	0.657	0.914
Skew	0.926	0.323	0.001	<0.001
Kurtosis	0.001	0.001	0.001	<0.001
Entropy	0.181	0.807	0.305	0.195

The parameters verify normality assumption if the P value is larger than 0.05. I-II: I and II stages were categorized as I-II group; III-IV: III and IV stages were categorized as III-IV group; CT, computed tomography.

**Table S4** P values of CT texture parameters among esophageal squamous carcinomas at different differentiation degrees for Shapiro-Wilk tests of normality assumption

Parameters	Unenhanced CT			Contrast enhanced CT		
	Poor	Moderate	Well	Poor	Moderate	Well
Mean	0.906	0.075	0.221	0.157	0.471	0.240
10th percentile	0.580	0.305	0.237	0.023	0.357	0.449
90th percentile	0.896	0.009	0.154	0.656	0.733	0.222
Skew	0.892	0.768	0.268	0.621	0.210	0.741
Kurtosis	0.944	<0.001	0.586	0.636	<0.001	0.004
Entropy	0.982	0.727	0.931	0.253	0.037	0.150

The parameters verify normality assumption if the P value is larger than 0.05. CT, computed tomography.

**Table S5** P values of CT texture parameters among esophageal squamous carcinomas at different N stages for Shapiro-Wilk tests of normality assumption

Parameters	Unenhanced CT				Contrast enhanced CT			
	N0	N1	N2	N3	N0	N1	N2	N3
Mean	0.351	0.924	0.016	0.365	0.590	0.959	0.981	0.337
10th percentile	0.294	0.734	0.019	0.351	0.226	0.535	0.862	0.411
90th percentile	0.528	0.855	0.002	0.176	0.472	0.245	0.686	0.290
Skew	0.649	0.805	0.373	0.427	0.027	0.977	0.995	0.949
Kurtosis	<0.001	0.136	0.050	0.490	0.001	0.001	0.065	0.034
Entropy	0.178	0.854	0.800	0.072	0.272	0.159	0.964	0.407

The parameters verify normality assumption if the P value is larger than 0.05. CT, computed tomography.

**Table S6** CT texture parameters for variance comparison in different T, lymph node metastasis and overall stages of esophageal squamous carcinomas

Parameters	Unenhanced CT (I-S test or M-W test)			Contrast enhanced CT (I-S test or M-W test)		
	T1-2/T3-4	N-/N+	I-II/III-IV	T1-2/T3-4	N-/N+	I-II/III-IV
Mean	0.343	0.005*	0.003*	0.557	0.061	0.238
10th percentile	0.169	0.003*	0.001*	0.273	0.614	0.993
90th percentile	0.440	0.006*	0.003*	0.961	0.004*	0.025*
Skew	0.315	0.006*	<0.001*	0.939	0.196	0.001*
Kurtosis	0.025*	0.023*	<0.001*	0.083	0.336	<0.001*
Entropy	0.027*	0.216	0.306	0.030*	<0.001*	<0.001*

I-S test, independent samples t-test; M-W test, Mann-Whitney U test. \*, P<0.05. T1-2, T1 and T2 stages were categorized as T1-2 group; N-/N+: N-, without lymph node metastasis and N+, with lymph node metastasis; T3-4, T3 and T4 stages were categorized as T3-4 group; CT, computed tomography.

**Table S7** P values of Binary Logistic regression analysis for CT texture parameters which were significant in Independent samples t-test or Mann-Whitney U test

Parameters	Unenhanced CT			Contrast enhanced CT		
	T1-2/T3-4	N-/N+	I-II/ III-IV	T1-2/T3-4	N-/N+	I-II/III-IV
Kurtosis	0.035	-	0.020	-	-	-
Entropy	0.026	-	-	0.030	0.001	0.001

T1-2, T1 and T2 stages were categorized as T1-2 group; N-/N+, N- without lymph node metastasis and N+ with lymph node metastasis; T3-4, T3 and T4 stages were categorized as T3-4 group. CT, computed tomography.

**Table S8** CT texture parameters for variance comparison in different N stages and differentiation degrees of esophageal squamous carcinomas

Parameters	Unenhanced CT		Contrast enhanced CT	
	(One-way analysis of variance/I-S Kruskal-Wallis test)		(One-way analysis of variance/I-S Kruskal-Wallis test)	
	N stage	Differentiation degree	N stage	Differentiation degree
Mean	0.058	0.565	0.064	0.458
10th percentile	0.091	0.370	0.202	0.141
90th percentile	0.078	0.780	0.015*	0.529
Skew	0.012*	0.703	0.258	0.637
Kurtosis	0.035*	0.740	0.516	0.662
Entropy	0.625	0.225	<0.001*	0.874

One-way analysis of variance (normality); I-S Kruskal-Wallis test, independent-samples Kruskal-Wallis test (non-normality); \*, P<0.05. They were used to detect the difference of texture parameters among different N stages (N0, N1, N2 and N3) and differentiation degrees (poor, moderate and well).

**Table S9** Interobserver agreement of texture parameters of esophageal squamous carcinomas based on unenhanced and contrast enhanced CT images

Parameters	Unenhanced CT		Contrast enhanced CT	
	ICC	95% CI	ICC	95% CI
Mean	0.876*	0.766-0.934	0.726	0.483-0.855
10th percentile	0.921*	0.851-0.958	0.763	0.553-0.875
90th percentile	0.772	0.569-0.880	0.743	0.514-0.864
Skew	0.336	0.255-0.649	0.469	0.004-0.719
Kurtosis	0.509	0.072-0.740	0.708	0.448-0.846
Entropy	0.699	0.431-0.841	0.882*	0.776-0.937

\*, ICC >0.800, indicating an excellent interobserver agreement. ICC, intraclass correlation coefficient.