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Original Article

Comparison of dual source computed tomography (CT) and diffusion-weighted magnetic resonance imaging (MRI) for pathological classification of esophageal cancer

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Abstract: Objective: The goal of this study was to explore the value of dual-source computed tomography (DSCT) and diffusion weighted imaging (DWI) for pathological classification of esophageal cancer. Methods: CT and magnetic resonance imaging (MRI) were performed on 60 patients with esophageal cancer to detect the normalized iodine concentration (NIC) values, CT enhancement intensities, and apparent diffusion coefficient (ADC) values of the lesions in the arterial and venous phase to compare the differences among esophageal cancer with different grades. The receiver operating characteristic (ROC) curves of NIC values and ADC values of esophageal cancer with different differentiation grades were then analyzed. Results: NIC values and CT enhancement intensities of esophageal carcinoma with different pathological classifications were different. There was statistical significance in the NIC value and CT enhancement intensity between the arterial and venous phases in the same group ($P < 0.05$), but there was no statistical difference in the CT enhancement intensity in the arterial phase ($P > 0.05$). The AUCs of the NIC and ADC values in diagnosing well-differentiated esophageal carcinoma and poorly-differentiated esophageal carcinoma in the arterial and venous phase were 0.801, 0.817, and 0.816, respectively. Conclusions: The ADC value of DSCT and the DWI can reflect the pathological classification of esophageal cancer, and can provide more information for clinical staging, treatment, and prognosis evaluation.

Keywords: Apparent diffusion coefficient, diffusion-weighted imaging, dual source, esophageal neoplasms, normalized iodine concentration

Introduction

Esophageal cancer is a common malignancy of the digestive tract and has a high mortality [1]. Most patients are in advanced stages when clinically diagnosed and can only undergo radiotherapy or chemotherapy instead of surgical treatment. The 5-year survival rate of such patients is very low [2]. The treatment regimen, prognosis, and survival of the patients with esophageal cancer are closely related to their histopathological types, pathological grades, and TNM stages. The pathological features of esophageal cancer are important for the biological behavior and prognosis of the tumor [3]. Dual-source computed tomography (DSCT) is a new type of imaging technology that can provide more data analysis tools and quantitative parameters for diagnosis of diseases. It can provide useful information for substance identification, pathological typing, and pathological classification of tumors [4], and the iodine map of DSCT can indirectly reflect the tumor neovascularization [5], thus further reflecting characteristics of tumor tissue differentiation [6]. Diffusion-weighted imaging (DWI) can diagnose diseases at the cellular and molecular levels [7, 8], and its apparent diffusion coefficient (ADC) value can predict the malignancy degree of esophageal cancer to a certain extent [9, 10]. In this paper, imaging and pathological data of 60 patients with esophageal cancer treated in

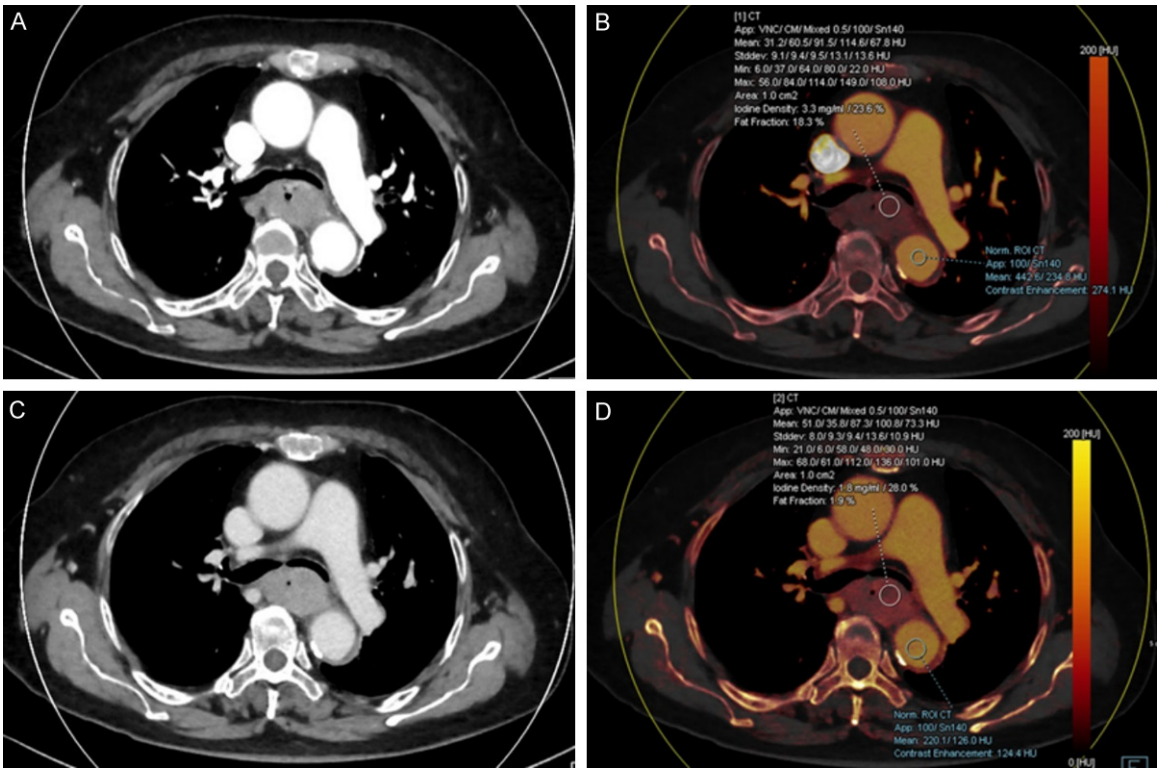

Figure 1. Patients with poorly differentiated squamous cell carcinoma in the middle esophagus. (A and C) are the images of arteriovenous mixed energy (120 kV), showing that the wall of the esophagus is obviously thickened, and the soft tissue masses form. The lumen is narrow and obstructed. The enhanced scanning shows that the lesions are significantly strengthened; (B and D) show I images of the arteriovenous phase (the ratio of soft tissue to iodine is 0.5), indicating that there is a significant deposition of I in the esophageal cancer lesions.

our hospital from December 2014 to December 2017 were compared and analyzed, with the aim to explore and compare the value of DSCT and DWI in the pathological classification of esophageal cancer. This analysis provides more information for preoperative evaluation, development of clinical treatment plans, and prognosis evaluation of patients with esophageal cancer.

Materials and methods

Clinical data

A total of 60 patients confirmed as esophageal squamous cell carcinoma by endoscopic biopsy or postoperative pathology in our hospital from December 2014 to December 2016 were selected, including 43 males and 17 females, aging 48-84 years old, with the average as 65.8 years. Among them, 45 patients were confirmed by pathology, and 15 patients were confirmed by endoscopic biopsy, including 8 cases of upper esophageal cancer, 33 cases of middle esophageal cancer, and 19 cases of lower esophageal cancer. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Nanjing Medical University. Written informed consent was obtained from all participants.

Inclusion criteria: confirmed as mass-type esophageal cancer by endoscopic biopsy or pathology; without previous history of surgery for esophageal neoplasms, radiotherapy, or chemotherapy; all the patients were performed DSCT dual-energy plain scan, dual-phase enhanced scan, and magnetic resonance imaging (MRI); without a history of iodine allergy. Exclusion criteria: allergic to iodine, without severe cardiocerebral insufficiency or thyrotoxicosis, body mass index (BMI) > 30 kg/m^2, with contraindications for MRI.

Inspection methods

DSCT: Using the Somatom Definition Flash (SIEMENS AGFWB, Munich, Germany), the 60 patients with esophageal cancer were exam-

Table 1. Comparison of the NIC value and CT enhancement among different groups ($\bar{x} \pm s$)

Pathological grade	n	NIC value (mg/ml)		CT enhancement (HU)	
		Arterial phase	Venous phase	Arterial phase	Venous phase
Well-differentiated	17	1.54 ± 0.34	1.55 ± 0.52	14.40 ± 3.91	25.65 ± 4.43
Moderately-differentiated	24	1.72 ± 0.50	1.80 ± 0.62	14.26 ± 7.35	27.55 ± 6.82
Poorly-differentiated	19	2.10 ± 0.40	2.19 ± 0.35	16.17 ± 6.89	30.77 ± 6.38
F		7.869	6.974	0.547	3.335
P		0.001	0.002	0.582	0.043

Note: NIC: normalized iodine concentration. The results of the pairwise comparison reveal that: the NIC values in the arterial and venous phase: The NIC values between the well-differentiated cases and poorly differentiated cases, as well as between the moderately differentiated cases and poorly differentiated cases, are statistically significant ($P < 0.05$); the difference in the NIC values between well-differentiated cases and moderately differentiated cases shows no statistical significance ($P > 0.05$). The degree of CT enhancement in the venous phase: The difference between the well-differentiated cases and the poorly-differentiated cases is statistically significant ($P < 0.05$), and there is no significant difference between the other two groups (all $P > 0.05$).

ined in a dual-energy mode, and all the patients underwent plain and enhanced scanning. Parameters of conventional scanning: tube voltage 120 kV, effective current 250 mAs, layer thickness 5 mm, layer spacing 5 mm, pitch 0.7, speed 0.28 s/turn, FOV: 300 mm. DS Enhanced Scanning: Intravenous injection of iohexol (Huirui Pharmaceutical, Lianyungang, Jiangsu, China) using a double-cylinder high-pressure syringe, injection rate 3.5 ml/s, dose: 1.5 ml/kg, total 60-80 ml. Then, 20 ml of saline was injected using the same rate, and the bolus tracking software of contrast agent was used (Bolus Tracking), with the aorta on the same layer selected as the monitoring plane, for arterial phase scanning 10 seconds delayed and venous phase scanning 35 seconds delayed after reached the threshold (100 HU). After scanning, layer spacing and layer thickness were automatically reconstructed to l mm. Real-time dynamic exposure dose adjustment (Care Dose 4D; Siemens Medical Solutions) was turned on for the acquisition of all the data.

MRI: using the Siemens AVANTO 1.5T MRI instrument (SIEMENSAGFWB, Munich, Germany); parameters of routine scanning and imaging: T1 weighted image (T1WI) axial position, T2 weighted image (T2WI) axial position, and T2WI coronal position, scanning time 17 to 40, layer thickness 5 mm, field of vision (FOV) 350 mm × 350 mm~400 mm × 400 mm; DWI inspection plane, layer thickness, FOV, and layer spacing were consistent, TR 5700 ms, TE 70 ms, matrix 128 × 128, layer thickness 5 mm; the ADC images were generated when b = 0 and 600 s/mm^2 at the same time.

Post-processing methods and observation indexes of CT

All the images were sent to the DSCT Syngo. VIA workstation for the post-processed using its Liver VNC software. The measurements were performed by two physicians. The CT values, normalized iodine concentrations (NIC) in the plane, arterial and venous phase of esophageal cancer lesions were measured, and NIC = iodine concentration measured in the lesion/iodine concentration measured in the aorta on the same level. In this study, when measuring the iodine concentration in the region of interest, the normalized ROI in the measurement software was placed on the same layer of aorta for normalization, and then DS-ROI was used to plot the region of interest at the lesion. The resulting iodine concentration was the NIC. CTA = CT arterial phase-CT plain scan, which was defined as the enhancement degree of the arterial phase, CTP = CT venous phase-CT plain scan, which was the enhancement degree of the venous phase. The ROI size and location of the same patient was kept as consistent as possible in the scanning of plain, arterial, and venous phase, and the ROI shall be averaged after measuring 3-5 times at the same level to increase the measurement accuracy.

Post-processing methods of MRI and ADC measurement

Two high-grade MRI diagnosticians performed the measurement independently targeting the largest lesion level, referring to the lesions with high signal intensities of T2WI and DWI, and

Table 2. Comparison of the ADC value (10^{-3} mm^2/s) among different groups ($\bar{x} \pm s$)

Degree of differentiation	n	ADC	F	*P*
Well-differentiated	17	1.16 ± 0.11	21.594	< 0.001
Moderately-differentiated	24	1.03 ± 0.09		
Poorly-differentiated	19	0.95 ± 0.12		

Table 3. Results of ROC analysis of NIC value and ADC value against esophageal carcinoma with different differentiation degrees

Index	AUC	*P*	Threshold	Sensitivity (%)	Specificity (%)
NIC_A (mg/ml)	0.801	< 0.001	1.88	82.9	73.7
NIC_P (mg/ml)	0.817	< 0.001	1.92	80.5	89.5
ADC	0.816	< 0.001	1.04	65.9	89.5

Note: NIC: normalized iodine concentration, NICA: NIC value in the arterial phase, NICP: NIC value in the venous phase, ADC value: apparent diffusion coefficient value.

avoiding the necrotic area. ROI was then mapped on the ADC map. Each lesion was measured three times for the average.

Statistical analysis

SPSS16.0 software was used for the statistical analysis; the measurement data are expressed as mean ± standard deviation ($\bar{x} \pm s$) and the comparison of the NIC values, CT enhancement, and curve slopes of esophageal cancer with different pathological classifications were used for one-way analysis of variance. When the variance was equal, the LSD method was used for the pairwise compare among the three groups. When the variance was not equal, the Dunnett T3 method was used for pairwise comparison among the three groups. The ROC curve was used to evaluate the diagnostic efficacy of the NIC and ADC values against moderately/well-differentiated esophageal cancer and poorly differentiated esophageal cancer. The test level was $\alpha = 0.05$, with $P < 0.05$ considered as statistical significance.

Results

Imaging of DSCT

Esophageal cancer appears irregular thickening of the esophagus wall, which can form a soft-tissue density mass centered on the wall of the tube. The esophageal cavity appears narrow and slim to varying degrees. The enhanced scanning shows moderate to significant enhancement. I imaging shows accumulation of I in the cancer lesions, and larger lesions being associated with necrosis, whereas the distribution of I could be uneven (**Figure 1**).

Comparison of the NIC values and CT enhancement

The pathological types of the selected patients were all esophageal squamous cell carcinomas, including well-differentiated esophageal carcinomas in 17 cases, moderately differentiated esophageal carcinomas in 24 cases, and poorly differentiated esophageal carcinomas in 19 cases. **Table 1** shows that the NIC values of esophageal cancer with different pathological grades are different. As the pathological grades gradually increased, the NIC values of the lesions gradually increased. The univariate analysis of variance targeting the NIC values of the three groups revealed statistical significance in the NIC value between well-differentiated and poorly differentiated cases, as well as between the moderately differentiated and poorly differentiated cases, in the arterial and venous phase ($P < 0.05$), but there was no statistical significance in the NIC value between well-differentiated and moderately differentiated cases ($P > 0.05$). Comparison of the degree of CT enhancement of esophageal cancer with different pathological grades also revealed statistical significance between well-differentiated and poorly differentiated cases in the arterial and venous phase ($P < 0.05$). There was no statistical significance between the other two groups ($P > 0.05$).

Comparison of the ADC values

Table 2 shows that the ADC values of the lesions increase with the degree of tumor differentiation, and the pairwise comparison among the three groups showed differences between any two groups were statistically significant ($P < 0.05$).

Differential diagnosis of well, moderately, or poorly differentiated esophageal cancer

Patients with different differentiation degrees of esophageal cancers were divided into two groups: the poorly differentiated case group (P)

and the moderately/well-differentiated case group (MW). Taking the esophageal cancer lesions as the objective, the ROC curve was used to analyze the differential diagnosis efficacy of the NIC value and ADC value against moderately/well differentiated esophageal cancer and poorly differentiated esophageal cancer. According to the results of the ROC analysis, **Table 3** shows the AUC of the NICp curve was the largest, namely its diagnostic efficiency was the greatest. Selecting 1.92 mg/ml as the diagnostic threshold, the sensitivity and specificity were both high, reaching 80.5% and 89.5%, respectively.

Discussion

Esophageal cancer is a highly malignant gastrointestinal cancer, and its incidence has increased year by year in recent years [11]. The pathological type of esophageal cancer is more common in squamous cell carcinoma, accounting for more than 90%, but adenocarcinoma is rare. Pathologically, esophageal cancer is divided into well-differentiated, moderately differentiated, or poorly differentiated according to its differentiation degree.

Previous studies [12] have found that tumors are mainly supplied by host vessels in the early stages. The further development of tumors will promote the massive neovascularization. The worse the tumor differentiation, the richer the tumor neovascularization, but such vessels are immature, distorted, disordered, and with high vascular permeability. The pathological basis of CT-enhanced scanning is the filling of iodine contrast media in tissue microvessels, which reveals a positive correlation of the degree of tumor enhancement with intratumoral microvessel density and structure and in turn can reflect the angiogenesis inside tumors [13]. DSCT-NIC can reflect the degree of tumor differentiation, and the main reason may be that the intensity of angiogenesis is different in tumors with different degrees of differentiation. The blood supply of poorly differentiated tumors is relatively richer, so the iodine deposited in the lesion can be higher during enhanced scanning, which can be used to reflect the differentiation degree of the tumor by measuring the concentration of iodine in the lesion. Therefore, theoretically esophageal cancer lesions with different differentiation degrees have different iodine filling status, and the lower the differentiation degree, the higher the density of tumor microvessels, and the higher the NIC measured [14-17].

DWI can detect the pathophysiological changes of tissues and organs in early stages on the molecular level [18] and the ADC value can be used to quantitatively assess the microstructure changes in tumors [19-21]. Studies have shown that the ability of free diffusion of water molecules in tumor tissue is the main factor affecting the ADC value [22]. In pathology, the lower the differentiation degree of esophageal cancer, the larger the tumor cells, namely the tumor cells may increase and arrange more closely, which reduces the extracellular space of tumor tissue and limits the free diffusion of water molecules, so the ADC value will be reduced. Therefore, esophageal cancer with the different differentiation degrees theoretically has different ADC values.

The results of this study show that esophageal cancer with different differentiation levels has different NIC values, that lower the differentiation degree and a higher NIC value. Therefore, this may be due to the differences in the blood supply and microvessel density among esophageal cancer with different pathological grades. The pairwise comparison showed statistical significance between well-differentiated and poorly-differentiated esophageal carcinomas, and between moderately differentiated and poorly-differentiated esophageal carcinomas ($P < 0.05$), but the NIC values between well-differentiated and moderately-differentiated esophageal carcinomas were not statistically significant ($P > 0.05$), which may be explained as that well-differentiated and moderately differentiated esophageal cancer both have higher differentiation degrees, so the status of tumor angiogenesis in such cases is almost the same and the iodine deposition in such lesions can't show much difference. At the same time, the ADC values of esophageal cancer with different pathological grades were measured in this study, and the results showed that the ADC values were also different. Pairwise comparison resulted in statistical significance between well-differentiated and poorly-differentiated esophageal cancer, well-differentiated and moderately differentiated esophageal cancer, and moderately-differentiated and poorly-dif-

ferentiated esophageal cancer ($P < 0.05$). Therefore, it can be considered that the ADC value can be used as a quantitative index to identify the malignancy degree of esophageal cancer.

In addition, this study also analyzed the differential diagnostic value of the NIC value and ADC value against well/moderately differentiated esophageal cancer and poorly differentiated esophageal cancer through analyzing the ROC, and the results show that these two indexes both have diagnostic values, in which the AUC of NIC was the largest in diagnosing well/moderately differentiated from poorly differentiated esophageal cancer in the venous phase. Therefore, its diagnostic efficiency was the highest, with the corresponding diagnostic threshold as 1.92 mg/ml and high sensitivity and specificity (80.5% and 89.5%, respectively). The differential diagnosis threshold of ADC value in diagnosing well/moderately differentiated from poorly differentiated esophageal cancer was 1.04×10^{-3} mm^2/s, and the sensitivity and specificity were 65.9% and 85.9%, respectively. It has been shown through comparison that both of these indexes can be helpful to identify tumor angiogenesis, and the value of iodine quantitative analysis is higher.

Disclosure of conflict of interest

None.

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