ORIGINAL RESEARCH

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Energy spectrum computed tomography improves the differentiation between benign and malignant solitary pulmonary nodules

Abstract

Purpose: To evaluate the diagnostic efficiency of computed tomography (CT) values at the 40~140 keV monochromatic level for the differential diagnosis of solitary pulmonary nodules (SPNs).

Methods: Energy spectrum CT data of 44 patients with SPNs were analyzed retrospectively; 24 patients with malignant SPNs served as the malignant group and 20 patients with benign SPNs served as the benign group. The basic material concentration and the enhancement degree differences in double-phase enhanced scans were compared between the two groups. The sensitivity and specificity were calculated to determine diagnosis, and were compared with the pathology results.

Results: The CT values at the 40~90 keV monochromatic level and the iodine concentrations of malignant group were higher than those of benign group in the arterial phase (all $P < 0.05$). The enhancement degree of the malignant group was higher than that for the benign group in the arterial phase (36.36 ± 33.18 HU vs 16.93 ± 24.17 HU $t = 2.243$, $P = 0.030$); however, the enhancement degrees of the two groups were similar in the venous phase (21.99 ± 15.87 HU vs 17.62 ± 24.15 HU $t = 0.694$, $P = 0.493$). The area under the curve of the enhancement degree in the arterial phase was 0.792.

Conclusions: Monochromatic imaging and base material concentration of energy spectrum CT can help differentiate between benign and malignant SPNs.

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Correctly differentiating malignant and benign solitary pulmonary nodules (SPNs) is critical for effective treatment [1-3]. Prior radiographs and chest computed tomography (CT) images are useful for determination of nodule growth. Initial diagnosis requires the differentiation between benign and malignant SPNs. Computed tomography (CT) is used to confirm margins and contours, which are closely related to final diagnosis. Energy spectrum CT is widely used to evaluate the internal characteristics of nodules, such as homogeneous attenuation, cavitation, intramodular fat and calcification, in order to differentiate between benign and malignant SPNs. Recently, energy spectrum CT has been used to evaluate the diagnostic efficiency of CT values, the levels of iodine and water and the enhancement degree (based on material-suppressed iodine images) for the differential diagnosis of SPNs. Thus, SPNs are now detected with increasing frequency because of the widespread use of CT. Furthermore, imaging evaluation, including CT, magnetic resonance imaging and positron emission tomography-CT, can be used to detect malignant SPNs [1-3]. Although each noninvasive technique offers valuable data for the detection of both malignant and benign SPNs, CT examination is less expensive in comparison with either magnetic resonance imaging or positron emission tomography-CT.

Although more SPNs have been detected with the improvement of CT technology and the widespread use of low-dose chest CT, characterization of these SPNs has been difficult for clinicians and radiologists [1-3]. Research on imaging of SPNs is in progress. For patients with SPNs, several CT imaging technologies may be used for diagnosis, such as conventional CT [4], enhancement CT [5] and perfusion CT [6-8]. Gemstone CT is a type of dual-energy CT imaging equipment, whose spectrum scanning pattern can be used to obtain a variety of spectral images and parameters, such as material-suppressed iodine images, monochromatic images and base material images [9-11]. The purpose of this paper is to evaluate the value of energy spectrum CT for the differential diagnosis of benign and malignant SPNs, comparing our results with those of previously published studies, to evaluate whether spectral images improve diagnostic efficacy for SPNs.

Materials and methods

Patients and setting

The ethics committee at our institution (Lanzhou University Second Hospital) approved this retrospective study, and all

patients provided written informed consent. From May 2013 to June 2014, 24 patients with malignant SPNs (eight men, 16 women; from 31 to 71 years of age, mean age 53.5 ± 11.1 years) and 20 patients with benign SPNs (nine men, 11 women; from 36 to 70 years of age, mean age 54.9 ± 9.7 years) were studied retrospectively. The presence of SPNs was confirmed in all patients by pathology and immunohistochemistry after surgical resection.

CT examination

All patients underwent a conventional CT scan and a two-phase enhanced CT scan in the spectral imaging mode. The traditional unenhanced and two-phase enhanced energy spectrum CT scans were performed by a High Definition CT system (Discovery CT 750HD, GE Healthcare, USA). All patients underwent imaging craniocaudally in the supine position.

The scan parameters were as follows: tube voltage 120 kVp; automatic mAs in plain CT scan; 80/140 kVp fast switch within 0.5 ms; two contrast-enhanced frame rotating speed 0.6 s; fixed-tube current 600 mA; pitch of 1.375:1; collimator thickness of 0.625 mm; reconstruction of layer thickness and interval of 1.25 mm; iodine contrast agent of iohexol (300 mgI/ml); velocity of 3 ~ 4 ml/s; dose of 1.0 ml/kg body weight; high-pressure syringe bolus of iohexol injection at the elbow vein; and ascending aorta monitoring trigger threshold 50 HU. Arterial phase (AP) imaging began 8 s after the trigger attenuation threshold (50 HU) was reached, at a delay of 30 s after AP imaging, and venous phase (VP) imaging began. All patients were asked to hold their breath after inspiration to ensure the same inspiration level during every scan.

Image analysis

Images of all patients were transferred to the AW 4.6 Workstation of energy spectrum CT imaging system, and GSI viewer software was adopted for image analysis. The CT value of lesions in the traditional mixed energy plain scan, the monochromatic CT value, and the iodine and water concentration in two-phase enhanced energy spectrum CT scan were recorded with a circular region of interest (ROI). The size of one-third to two-thirds of the lesion avoids necrosis, cystic areas, calcification, and larger vessels as much as possible in the course of measurement. Every patient was imaged three times, and the average of the three times served as the final result.

Statistical analysis

Statistical analysis was performed using SPSS 19.0 software with the appropriate test. Measurement data were expressed as mean $\pm$ standard deviation, independent-samples t-test was used for comparison between the two groups. Count of the threshold of CT values in monochromatic images, iodine (water) concentration in iodine (water)-based material decomposition images and enhancement degree were based on material-suppressed iodine images, and sensitivity and specificity were counted when the Youden's index was at its maximum. Differences between the two groups were considered significant if $P < 0.05$. The pathologic results were used as the gold standard.

Results

In this study, we included forty-four participants who were diagnosed by pathologist following surgical resection. Twenty-four of the patients were diagnosed with malignant SPNs and twenty are diagnosed with benign SPNs. For all patients, a non-contrast CT scan of entire chest was obtained and then a two-phase contrast enhanced CT scan was performed in the spectral imaging mode. All images were read by two independent radiologists with 1–20 years' experience in reading chest CT images, and in case of discrepancy a third expert reader made the final decision.

The CT value at the 40 ~ 90 keV monochromatic level and the iodine concentration of malignant pulmonary nodules group were higher than those in the benign pulmonary nodules group in the arterial phase (all $P < 0.05$); There was no difference between the two groups in terms of the CT value at the 100 ~ 140 keV monochromatic level in the arterial phase (all $P > 0.05$) or between the two groups in terms of the CT value at the 40 ~ 140 keV monochromatic level and the iodine concentration in the venous phase (all $P > 0.05$) (Table 1).

The enhancement degree of malignant group pulmonary nodules was higher than that in benign group pulmonary nodules in the arterial phase (36.36 ± 33.18 HU vs 16.93 ± 24.17 HU, $t = 2.243$, $P = 0.030$); however, the enhancement degree of the two groups was similar in the venous phase (21.99 ± 15.87 HU vs 17.62 ± 24.15 HU, $t = 0.694$, $P = 0.493$) (Table 2).

The spectrum curves of the CT values of SPNs on different monochromatic energy levels between the two groups in the arterial and venous phase are presented in Figure 1. The ROC curve of the CT value at different monochromatic energy levels, the base material concentration and the enhancement degree are presented in Figure 2 and Table 3.

FIGURE 1. Computed tomography values of solitary pulmonary nodules on different monochromatic energy levels between two groups: in arterial (a) and venous (b) phase

TABLE 1: Comparison of the computed tomography values and concentration between two groups in arterial and the venous phase

Monochromatic level/base material	Phase	Computed tomography value (HU)		<i>t</i>	<i>P</i>
		Malignant (n=24)	Benign (n=20)		
40 keV	AP	181.17±105.66	120.55±83.24	2.082	0.043
	VP	135.35±40.60	122.02±82.82	0.696	0.490
50 keV	AP	125.46±67.06	85.35±56.92	2.114	0.041
	VP	94.65±25.65	86.51±56.83	0.629	0.532
60 keV	AP	89.10±42.83	61.92±42.00	2.114	0.040
	VP	67.77±16.64	62.94±42.25	0.514	0.610
70 keV	AP	67.94±28.16	49.12±32.09	2.071	0.045
	VP	52.24±11.83	49.87±32.46	0.333	0.741
80 keV	AP	55.90±19.76	41.92±25.42	2.052	0.046
	VP	43.68±9.54	42.54±25.83	0.200	0.842
90 keV	AP	47.31±14.99	35.97±22.02	2.024	0.049
	VP	37.55±8.68	36.70±22.47	0.170	0.866
100 keV	AP	41.05±11.80	32.01±19.66	1.833	0.067
	VP	32.97±8.33	32.71±20.16	0.058	0.954
110 keV	AP	36.62±10.09	29.22±18.10	1.711	0.095
	VP	29.73±8.29	29.89±18.62	-0.037	0.970
120 keV	AP	33.50±9.32	27.24±17.08	1.542	0.131
	VP	27.46±8.38	27.90±17.63	-0.109	0.914
130 keV	AP	31.11±9.05	25.74±16.35	1.378	0.175
	VP	25.71±8.51	26.38±16.90	-0.171	0.865
140 keV	AP	29.24±9.04	24.55±15.81	1.233	0.224
	VP	24.34±8.64	25.19±16.38	-0.219	0.828
IC (100 µg/cm ³)	AP	18.29±8.29	12.51±9.46	2.161	0.036
	VP	14.43±5.51	12.61±9.34	0.804	0.426
WC (mg/cm ³)	AP	1018.65±12.05	1017.82±13.57	0.215	0.831
	VP	1016.59±9.90	1018.41±14.12	-0.501	0.619

Abbreviations: AP, arterial phase; CT, computed tomography; IC, iodine concentration; VP, venous phase; WC, water concentration

TABLE 2: Comparison of enhancement degree between malignant and benign solitary pulmonary nodules in the arterial and venous phases

Enhancement degree	Malignant (n=24)	Benign (n=20)	<i>t</i>	<i>P</i>
Arterial phase	36.36±33.18	16.93±24.17	2.243	0.030
Venous phase	21.99±15.87	17.62±24.15	0.694	0.493

Table 3: Threshold of computed tomography value, enhancement degree and iodine concentration

Monochromatic level	40 keV	50 keV	60 keV	70 keV	80 keV	90 keV	IC	Enhancement degree
AUC	0.798	0.796	0.775	0.752	0.738	0.719	0.781	0.792
Threshold	112.66	77.38	60.17	52.52	50.77	31.34	11.50	14.74
Sensitivity (%)	91.67	91.67	83.33	70.83	62.50	87.50	91.67	91.67
Specificity (%)	70	65	65	70	85	40	65	65

Abbreviations: AUC, area under the curve; CT, computed tomography; IC, iodine concentration

Discussion

Energy spectrum CT is used to evaluate SPN perfusion function based on the Hounsfield threshold. The perfusion map provided by energy spectrum CT could be used for assessment of SPN perfusion status; therefore, measurements of iodine wash-in and wash-out patterns of SPNs can be used to determine between benign and malignant SPN using an energy spectrum CT. In particular, differentiate between benign and malignant SPN can be made specifically in the arterial phase.

In our study, we demonstrated that energy spectrum CT improved the ability to differentiate between benign and malignant SPNs. There was a significant difference in iodine concentration in malignant SPNs compared with benign SPNs at the CT value of the 40~90 keV monochromatic level, while there was no significant difference between the two groups at the CT value of the 100~140 keV monochromatic level in the AP. The significant difference seen at the low-energy level but not the high-energy level can be attributed to X-ray attenuation characteristics. The sensitivity and specificity at the 40~90 keV monochromatic level were 87.5%–91.7% and 40%–70%, respectively, and 91.7% and 65% for the iodine concentration in the AP.

Early diagnosis of lung cancer is crucial for early treatment and management. With the widespread use of spiral CT and multiline spiral CT in clinical applications, chest CT scanning has become one of the most widely-used measures in the diagnosis of SPNs. It is difficult for the traditional single parameter in the mixed-energy image analysis of CT values to fully reveal the inherent characteristics of lesions, and CT value measured on a conventional CT image is unstable to beam-hardening artifacts [2]; several studies have shown that the use of monochromatic energy imaging can reduce image noise and beam-hardening artifacts [12]. In this study, we investigated the potential of using quantitative parameters, provided by monochromatic images, material decomposition images and material-suppressed iodine images, in dual-energy spectral CT imaging for the differentiation of benign and malignant SPNs.

To a certain extent, the enhancement degree can reflect the SPNs blood supply, and there is a close positive correlation between the blood supply and the number of blood vessels, which depends on angiogenesis factors. Thus, the enhancement degree reflects the expression of these factors. Malignant SPNs usually have a high expression of these angiogenesis factors, and the enhancement degree can help us differentiate benign from malignant SPNs [14-16].

FIGURE 2. (a) Receiver operating characteristic (ROC) curve of computed tomography value on different monochromatic energy level, (b) ROC curve of base material concentration and (c) ROC curve of the enhancement degree.

Previous studies have shown high sensitivity and moderate specificity for the enhancement degree when the threshold is 15 HU or 20 HU [1,17-19], and our current study shows similar outcomes. The diagnostic sensitivity and specificity of the enhancement degree were 91.67% and 65% when the threshold was set at 14.74 HU in the AP, despite different measurement methods between the previous study and our own, but the similar diagnosis efficacy suggests that the enhancement degree of the SPNs based on material-suppressed iodine has a certain value for differential diagnosis. The enhancement degree in our study was defined as a CT value of the 70 keV monochromatic level image minus that of the material-suppressed iodine image. A single enhanced spectral CT scan allows for the measurement of the degree of enhancement and reduces radiation exposure by avoiding baseline non-enhanced scans [17,19]. A previous study showed that virtual non-enhanced CT had the potential to replace true non-enhanced CT [17,20]. We observed that the material-suppressed iodine image, as a virtual non-enhanced CT, which has a perfect image match, can reduce the measurement error from the position change of SPNs in different phases.

We also found that the area under the curve of the enhancement degree [21,22], iodine concentration and 40 keV and 50 keV monochromatic the arterial phase were similar, which may be due to the linear correlation between CT attenuation value and iodine concentration for both monochromatic and polychromatic images [23]; thus, we did not do a series of parallel tests.

Our study had several limitations. First, it is a retrospective study carried out in a single center. Second, other variable factors could have affected the outcome of patients; for example, different medical conditions of the patients. Third, it was a challenge to compare our results to those from other studies. Finally, the study only reviewed patients with a single lung nodule; hence, comprehensive studies with larger sample size are warranted.

In summary, monochromatic imaging and base material concentration of energy spectrum CT can help us differentiate benign SPNs from malignant ones.

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