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Chronic thromboembolic pulmonary hypertension: Comparison of dual-energy computed tomography and single photon emission computed tomography in canines

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ABSTRACT

Purpose: To compare diagnostic accuracy between dual-energy CT lung perfused blood volume (Lung PBV) imaging and single photon emission computed tomography (SPECT) in detecting chronic thromboembolic pulmonary hypertension (CTEPH) with histopathological results as reference standard in a canine model.
Materials and methods: Eighteen CTEPH canines were included into this experimental study. All procedures including paracentesis, embolization, scanning, pressure measurement and feeding medicine were repeated each two weeks, until systolic/diastolic pressure in canines was ≥30/15 mmHg or mean pulmonary artery pressure ≥20 mmHg, and then sacrificed for histopathology examination. Two radiologists (readers 1 and 2) and two nuclear radiologists (readers 3 and 4) analyzed images of conventional CT pulmonary angiography in dual-energy CT mode, Lung PBV imaging and SPECT, respectively. The presence, numbers, and locations of pulmonary emboli (PE) were recorded on a per-lobe basis. Pathological examination was served as reference standard. Sensitivity, specificity and accuracy of Lung PBV and SPECT were calculated. Kappa statistics were used to quantify inter-reader agreement.
Results: With histopathological results as reference standard, the sensitivities of 72.2%, 78.8%, 81.2%, specificities of 75.9%, 87.5%, 84.8%, accuracies of 73.8%, 83.1%, 83.1%, for readers 1, 2 and both with Lung PBV, respectively. Readers 3, 4 and both had sensitivities of 14.3%, 25.7%, 33.3%, specificities of 90.0%, 86.7%, 93.3%, accuracies of 49.2%, 53.8%, 60.0% with SPECT for detecting CTEPH. Inter-reader agreements were good for dual-energy CT (kappa = 0.662) and SPECT (k = 0.706) for detecting CTEPH.
Conclusion: Dual-energy CT had a higher accuracy to detect CTEPH than SPECT in this canine model study.

1. Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is defined as the persistence of pulmonary hypertension (mean pulmonary artery pressure greater than 25 mmHg) after a single or recurrent pulmonary embolism (PE) event. CTEPH is characterized by the obstruction of pulmonary arteries by organizing thrombi, small vessel arteriopathy, and the development of a high pulmonary vascular resistance [1]. CTEPH is not a rare condition, but it is underdiagnosed, with estimated incidence ranging from 0.5% to 3.8% of patients after acute PE, and in up to 10% of those with a history of recurrent PE [2–4]. For patients with mean pulmonary artery pressure greater than 30 mmHg, the 5-year survival is 30% [5]. CTEPH is the only form of pulmonary hypertension that can be surgically treated [6–8]. Therefore, an accurate and early imaging diagnosis of CTEPH is of paramount importance.

Computed tomography pulmonary angiography and single photon emission computed tomography (SPECT) are important techniques in the diagnosis of CTEPH [9–12]. However, no con-

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sensus has been reached on which modality is the gold standard for detecting CTEPH. For example, Tunariu et al. [13] reported that V/Q scintigraphy showed a significantly higher sensitivity than conventional single-source, single-energy multi-detector computed tomography pulmonary angiography for detecting CTEPH. However, Lu et al. [14] concluded that both V/Q scanning and computed tomography pulmonary angiography are accurate methods for the detection of CTEPH with excellent diagnostic efficacy. Dual-energy CT can simultaneously provide both morphological and functional information, opening new horizons in the imaging of acute and chronic PE [15–18]. Some clinical reports [10,12] demonstrated that lung perfusion imaging based on dual-energy CT is feasible for the evaluation of pulmonary perfusion in acute PE and CTEPH and is comparable to pulmonary scintigraphy. However, the aforementioned clinical studies have not used histopathological results as an independent outside reference standard. Thus, the purpose of this study was to evaluate the diagnostic accuracy of dual-energy CT and SPECT in the diagnosis of CTEPH in a canine model.

2. Materials and methods

2.1. Animal model

The study protocol was approved by our local Animal Experiment Committee and performed according to local animal care guidelines. Eighteen canines with a body weight of 12.0–16.0 kg were included in this study. Anesthesia was induced with ketamine (Fujian Kutian Pharmaceutical Company Limited), diazepam (Tianjin Jin-Yao Amino Acid Company Limited) and atropine (Tianjin Jin-Yao Amino Acid Company Limited) via intramuscular injection and maintained with a mixture of propofol (10 mg/ml; AstraZeneca, Caponago, Italy), diazepam (Tianjin Jin-Yao Amino Acid Company Limited), and atropine (Tianjin Jin-Yao Amino Acid Company Limited) intravenously infused via the right or left great saphenous vein [19]. Blind placement of a 24-gauge Angiocath (Deseret Medical Inc., Sandy, UT, USA) into the right femoral vein was performed using the Seldinger technique and a 5F custom-made catheter was inserted [20]. Then, PE was induced by injection of autologous thrombi with a size of 0.3 × 1 cm, generated from 15 ml of fresh blood [21]. Before and after embolization, digital subtraction arteriography (DSA) was obtained on an Axiom Artis dTA unit (Siemens Medical Solutions, Forchheim, Germany) after injection of 20.0 ml of Ultravist (300 mg I/ml, 2.0 ml/kg; Bayer HealthCare, Leverkusen, Germany) with a flow rate of 4.0 ml/s and a pressure of 400 psi. For pulmonary artery pressure measurement, a 5F custom-made catheter was positioned in the main pulmonary artery with fluoroscopic guidance (BV 300; Philips HealthCare, Hamburg, Germany). The distal end of the vena cervicalis catheter was attached to the PX260 pressure sensor (Edwards Lifesciences, LLC Irvine, CA, USA), and the pulmonary artery mode was chosen. Then, pulmonary arterial systolic pressure, pulmonary arterial diastolic pressure and mean pulmonary arterial pressure were measured in real time. Postoperatively, for antifibrinolytic effect, 5.0 g tranexamic acid (110.0 mg/kg) was administered for three consecutive days after each meal. All procedures including blood gas measurements, embolization, pressure measurements, and imaging examinations were repeated every two weeks, until the systolic/diastolic pressure was above 30/15 mmHg or the mean pulmonary artery pressure was greater than 20 mmHg [22]. Every animal was sacrificed by excessive intravenous propofol administration (AstraZeneca S.P.A., 10 mg/ml) mixed with 2 ml diazepam (Tianjin Jin-Yao Amino Acid Company Limited), and 1 ml atropine (Tianjin Jin-Yao Amino Acid Company Limited) to proceed with histopathological examination after the experiment. All interventional procedures were performed by one interventional radiologist (Z.H.H, with 3 years of experience in small animal intervention) who was not involved in subsequent image analysis. Fig. 1 shows the flowchart of this experimental study.

2.2. Scanning protocols

2.2.1. Dual-energy CT

All CT examinations were performed using a dual-energy CT scanner (Somatom Definition Flash; Siemens Medical Solutions). Contrast-enhanced CT was performed one hour before and after pulmonary embolization for baseline and postembolic images. The animals were centered in the scanner so that the entire thorax was within the field of view (FOV) of both the larger (“A”) and the smaller (“B”) tube detector. Then, a contrast-enhanced CT scan in dual-energy (DE) mode was performed using 2.0 ml/kg bodyweight of contrast medium (Ultravist 300 mg/ml, Bayer HealthCare) administered at a flow rate of 3.0 ml/s, followed by 15.0 ml of saline solution into the femoral vein via a 24-gauge catheter by using a power injection system (Ulrich Medical, Ulm, Germany). The CT scan was triggered by using a bolus tracking technique (CARE Bolus, Siemens Medical Solutions) with the region of interest (ROI) placed in the pulmonary trunk. Image acquisition started 6 s after the CT attenuation reached the pre-defined threshold of 100 Hounsfield units (HU). Further CT scan parameters were as follows: gantry rotation time of 0.33 s, detector collimation of 32 × 2 × 0.6 mm, pitch of 0.5; X-ray tube A was operated at 80 kVp and 213 mAs, and tube B was operated at 140 kVp and 51 mAs.

2.2.2. SPECT

After CT scanning, perfusion scintigraphy by SPECT of the lungs was performed in supine position immediately after intravenous administration of 50 Mbq of technetium-99m (^{99}mTc)-labeled macro-aggregated albumin (CIS-US, INC, Bedford, Maryland, USA). Images were acquired in eight standard projections (anterior, posterior, right anterior oblique, left anterior oblique, right posterior oblique, left posterior oblique, left lateral, and right lateral) by rotating the head of the camera (E-CAM; Siemens Medical Solutions) around the thorax of the canine. The camera was equipped with a low energy, high resolution collimator. A window of 20% centered on the energy peak of ^{99}mTc (140 keV) and a matrix of 512 × 512 pixels was selected for the accumulation of at least 1000 counts per view.

2.3. Image reconstruction and analysis

2.3.1. Dual-energy CT

From the spiral projection raw data of both tubes, 3 image datasets were automatically reconstructed (80 kVp, 140 kVp, and fused average weighted 120 kVp images with 30% density information from 80 kVp images and 70% from 140 kVp images) with slice thickness of 0.75 mm and increment of 0.50. All images were transferred to a commercially available workstation (Syngo MMWP VE40A, Siemens Medical Solutions). Fused average weighted 120 kVp images were used to obtain maximum intensity projection images and multi-planar reformations in the axial, coronal, and sagittal planes. Dedicated DE analysis software was used to obtain lung perfusion blood volume images (Lung PBV) in axial, coronal, and sagittal planes. Color-coded red and yellow represent high blood flow perfusion, while blue represents low blood flow, and black represents a flow defect. The CT number range was from −960 HU to −200 HU for lung perfusion images. A 16 bit grey-scale and PET Rainbow 16 bit were used to show lung perfusion images (100% of functional blood flow images).

All CT images were evaluated by two radiologists (C.X.T. [reader 1] and Y.E.Z. [reader 2] with 4 and 9 years of experience in computed tomography pulmonary angiography interpretation, respectively)