European Journal of Radiology 84 (2015) 1614–1620

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Factors affecting the lung perfused blood volume in patients with intrapulmonary clots after anti-coagulation therapy

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ARTICLE INFO

Article history:
Received 3 March 2015
Received in revised form 21 April 2015
Accepted 8 May 2015

Keywords:
Pulmonary embolism
Intrapulmonary clot burden
Computed tomography (CT)
Dual energy CT
Anti-coagulation therapy

ABSTRACT

Objectives: Factors affecting the improvement in the lung perfused blood volume (LPBV) were evaluated based on the presence of intrapulmonary clots (IPCs) after anti-coagulation therapy using 64-slice dual-energy CT.

Materials and methods: 96 patients exhibiting venous thromboembolism underwent initial and repeated LPBV examinations between December 2008 and July 2014. Fifteen patients were excluded due to pulmonary comorbidities, and a total of 81 patients were included in this study. Acute pulmonary embolism (PE) was diagnosed in 46 of the patients (56.7%). LPBV images were three-dimensionally reconstructed with two threshold ranges: 1–120 HU (V_{120}) and 1–5 HU (V_5), and the relative value of V_5 per V_{120} expressed as $\%V_5$. These values were subsequently compared with indicators of the severity of PE, such as the D-dimer level, heart rate and CT measurements. This study was approved by the local ethics committee.

Results: In patients with IPCs, the D-dimer, V_5 and $\%V_5$values were significantly larger ($p \leq 0.01$) in the initial LPBV, although these differences disappeared in subsequent LPBV after treatment. The right ventricular (RV) diameter, RV/left ventricular (RV/LV) diameter ratio and $\%V_5$ values were also significantly reduced, whereas the V_5 value did not significantly decrease ($p = 0.07$), but V_{120} value significantly increased ($p < 0.001$) after treatment. However, in patients with IPCs the change rate in $\%V_5$ [(subsequent-initial)/initial $\%V_5$] showed a better correlation with that in V_5 ($r = 0.94$, $p < 0.001$) rate than that in V_{120} ($r = 0.19$, $p = 0.19$) after treatment.

Conclusions: Increased whole lung perfusion (V_{120}) and a decreased low perfusion volume (V_5) affect the improvement in the $\%V_5$ values after treatment.

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1. Introduction

Pulmonary embolism (PE) is a potentially fatal disorder and the third most common acute cardiovascular disease, after myocardial infarction and stroke [1]. CT pulmonary angiography (CTPA) has the advantage of allowing for more comprehensive assessments of the IPC burden, associated underlying lung diseases, and other causes of acute chest pain [2–4]. CTPA with CT venography (CTV) has higher diagnostic sensitivity than CTPA alone, with similar specificity. The predictive value of both CTPA and CTPA–CTV is high with concordant clinical assessments [5]. The acquisition of lung perfused blood (LPBV) images using dual-energy CT (DECT) also makes it possible to directly extract the iodine component by applying the material decomposition theory [6]. Furthermore, the LPBV can be visualized on functional images using an iodine perfusion map and morphological images, such as those of CTPA, using the combination of two different energies. The results of quantitative

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http://dx.doi.org/10.1016/j.ejrad.2015.05.018
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evaluations of the LPBV with a low attenuation range demonstrate a correlation with factors suggesting the severity of PE [7,8]. The LPBV values after treatment have also been reported to reflect the degree of pulmonary perfusion before and after treatment, including the compensatory increase in lung perfusion [9] however, there are no detailed analyses of factors affecting increased LPBV values after treatment.

The purpose of this study was to evaluate factors affecting the improvement of quantitative values of LPBV in patients with IPCs after anti-coagulation therapy compared with those observed in subjects without IPCs.

2. Materials and methods

2.1. Patients and parameters

A total of 469 patients (170 males, mean age: 62.7 ± 16.3 years) suspected of having venous thromboembolism (VTE) underwent contrast-enhanced LPBV using the dual-energy technique between December 2008 and July 2014. A total of 96 patients exhibiting VTE underwent repeated LPBV. Fifteen patients were excluded due to pulmonary comorbidities, such as severe pulmonary emphysema, massive pleural effusion or atelectasis, severe bronchopneumonia or insufficient breath-holding on the initial CT scan; therefore, a total of 81 patients (35 males, mean age: 60.1 ± 15.7 years) were included in this study, and their initial LPBV images were divided into two groups based on the presence of intrapulmonary clots (IPCs). The interval between the initial and subsequent LPBV scans ranged from 6 to 160 days, because patients with a previous history of VTE tend to have repeated PE as the surveillance time increases. Acute PE was diagnosed in 46 patients (19 males, mean age: 57.6 ± 17.3 years) based on the presence of IPCs. The diagnosis of acute PE was made when any of following findings were noted on CTPA using weighted-average images approximated to 120-kV images combined with LPBV: a complete filling defect with the lack of enhancement of the entire lumen of the pulmonary arteries, a partial filling defect surrounded by areas of contrast enhancement or a peripheral filling defect that formed an acute angle with the pulmonary arterial wall with a regional perfusion defect. Deep venous thrombosis (DVT) was also diagnosed using delayed CTV of the lower extremities after the LPBV scan, in addition to echocardiography and the detection of D-dimer level (normal value: 0–1 mg/L) within 24 h. The thin-slice LPBV images were retrospectively and three-dimensionally reconstructed with two thresholds ranging from 1 to 120 HU (V_{120}) and 5 HU (V_5). The V_{120} value indicated the whole pulmonary perfusion volume in this study, and the relative value of V_5 per V_{120} was expressed as $\%V_5$. The study protocol was approved by the local ethics committee. Informed consent for CTPA was obtained individually from all patients; however, informed consent for retrospective volumetric LPBV quantification after treatment was waived.

2.2. LPBV images acquisition

The initial and subsequent LPBV examinations were performed with 64-slice dual-source CT scanner (Somatom Definition, Siemens Healthcare, Forchheim, Germany) using the dual-energy technique. The system was equipped with two X-ray tubes and two corresponding detectors oriented in the gantry with an angular offset of 90°. The first detector array (corresponding to tube A) provided a field of view (FOV) of 50 cm, whereas the second detector array (corresponding to tube B) was restricted to a FOV of 26 cm. The tube voltages were previously set to 80 and 140 kVP for LPBV, and the tube current was adjusted four times higher for the 80-kVP tube (200 mAs) than for the 140 kVP tube (50 mAs). The detector collimation was set to 32 × 0.6 mm, the gantry rotation time was 0.33 s, and the pitch value was 0.5. The LPBV scan started with a bolus-tracking measurement in the pulmonary artery at a threshold of 100 HU after the intravenous administration of low-osmolar nonionic iodinated contrast material (body weight less than 60 kg: 300 mgI/ml and body weight over 60 kg: 350 mgI/ml, Omnipaque; Daiichi-Sankyo, Tokyo) via a 20-G catheter into the antecubital vein using the dual-phase technique (100 ml of pure contrast medium followed by 30 ml of saline) at a rate of 4 ml/s. The caudocranial scan direction was chosen to minimize the streak artifacts from dense contrast material in the superior vena cava or subclavian vein. Using these imaging parameters, the entire chest could be imaged in 12–17 s.

2.3. Reconstruction of the LPBV images and CT measurements

In all patients, three stacks of DEpCT images were semi-automatically generated: a set of 140 kVp images, a set of 80 kVp images and a set of weighted average images with a 1.0-mm thickness. The weighted average images were approximated to 120 kV images that were automatically generated from the combination of the 140-kV and 80-kV data using a weighting factor of 6:4 (140 kV: 80 kV). The transverse CTPA images were reconstructed using a soft tissue kernel (D30f), and native iodine CT scans were generated using the LPBV application mode of a dedicated dual-energy post-processing software program (Syngo Dual Energy software, Siemens Healthcare). The presence of IPCs was evaluated using CTPA images, and quantitative CT measurements were obtained on axial CT images, including the right ventricular (RV) diameter, RV/left ventricular (LV) diameter ratio, pulmonary artery (PA) diameter and PA/aorta (Ao) diameter ratio.

In the patients with IPCs, the perfusion disturbances caused by IPCs were visualized as low-attenuation areas on CTPA with color-coded LPBV (Fig. 1A). For quantification of the LPBV, the whole LPBV images were automatically reconstructed three-dimensionally based on the attenuation thresholds ranging from 1 to 120 (Fig. 1B) and 5 HU (Fig. 1C) using a workstation (AZE VirtualPlace ™, AZE, Tokyo). The volume rendering technique without surface rendering dilation was applied to each threshold range, and the trachea or main bronchus were extracted from the three-dimensional images. The volumetric values were expressed as the V_{120} with the threshold ranging from 1 to 120 HU and V_5 from 1 to 5 HU. In this study, V_{120} was considered to be a whole perfusion value of LPBV based on our experience. The relative value of V_5 per V_{120} was expressed as $\%V_5$. This relative value (%V5) is reported to have correlations with factors suggesting the severity of PE [7]. The quantitative CT measurements were compared between the initial (Fig. 1B and C) and subsequent LPBV images (Fig. 1E and F) after treatment based on the presence of IPCs.

2.4. Statistical analysis

Fisher's exact test and the Mann–Whitney *U* test were used for the qualitative and quantitative comparisons of the patient characteristics, CT measurements and volumetric LPBV values based on the presence of IPCs. The differences between the volumetric values on the initial and subsequent LPBV images were also evaluated based on the presence of IPCs using paired *t*-tests. The rate of improvement in $\%V_5$ (subsequent/initial $\%V_5$) was compared with the change in the V_{120} [=100 × (initial V_{120} − subsequent V_{120})/initial V_{120}] and V_5 [=100 × (initial V_5 − subsequent V_5)/initial V_5] using the statistical software program used to perform the calculations, SPSS for Windows, release 19.0 (SPSS, Japan).

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