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PULMONARY VASCULAR DISEASE

"Pulmonary Vein Sign" for Pulmonary Embolism Diagnosis in Computed Tomography Angiography

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Abstract

Purposes Considering that pulmonary arterial obstruction decreases venous flow, we hypothesized that filling defects in pulmonary veins can be identified in areas adjacent to pulmonary embolism (PE). This sign was named the "pulmonary vein sign" (PVS), and we evaluated its prevalence and performance for PE diagnosis in computed tomography pulmonary angiography (CTPA).

Methods This retrospective study enrolled consecutive patients with clinical suspicion of PE who underwent CTPA scan. The PVS was defined by the following criteria: (a) presence of a homogeneous filling defect of at least 2 cm in a pulmonary vein; (b) attenuation of the left atrium > 160 Hounsfield units. Using the cases that presented PE on CTPA as reference, sensitivity, specificity, and positive and negative predictive values were calculated for PVS.

Results In total, 119 patients (73 female; mean age, 62 years) were included in this study. PE was diagnosed in 44 (35.8%) patients. The PVS was present in 16 out of 44 patients with PE. Sensitivity was 36.36% (95% confidence interval (CI) 22.83–52.26%); specificity, 98.67% (95% CI 91.79–99.93%); positive predictive value, 94.12% (95% CI 69.24–99.69%); negative predictive value, 72.55% (95% CI 62.67–80.70%). The Kappa index for the PVS was good (0.801; 95% CI 0.645–0.957). PVS was correlated with lobar and segmental pulmonary embolism ($p < 0.01$).

Conclusion Despite a low sensitivity, presence of the pulmonary vein sign was highly specific for PE, with a good agreement between readers. This sign could contribute for PE diagnosis on CTPA studies.

Keywords Pulmonary embolism · Computed tomography pulmonary angiography · Pulmonary vein sign

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Introduction

Pulmonary embolism (PE) is a relatively common medical emergency. Characterized by partial or total obstruction of pulmonary arteries usually due to a thrombus, PE results in a sudden reduction or cessation of perfusion in the corresponding zone [1]. The most common clinical presentations are shortness of breath and chest pain, but cough, fever, hemoptysis, and syncope can occur [2]. As these symptoms are non-specific, imaging plays a fundamental role in the diagnosis of PE [3].

Computed tomographic pulmonary angiography (CTPA) is one of the most accurate imaging modalities for PE diagnosis [4, 5]. The diagnostic criteria for acute PE include an arterial occlusion with failure to enhance the entire lumen due to a filling defect, and the artery could be enlarged compared to adjacent patent vessels. Some ancillary signs have been used for indirect diagnosis of PE [6, 7]. These include regional oligemia (Westermark sign); peripheral, pleural-based, wedge-shaped area of increased opacity (Hampton hump); and prominence of the central pulmonary artery (Fleischner sign) [8]. Determination of the diagnostic value of these ancillary signs may permit more reliable diagnoses when emboli are suboptimally visualized, or they can suggest the diagnosis when PE is not suspected.

The main hemodynamic consequence of PE is an acute mechanical reduction of the pulmonary vascular cross-sectional area, which results in sudden increase in pulmonary vascular resistance and pulmonary arterial pressure, intensifying right ventricular work [9, 10]. In addition, all PE cases show an ipsilateral reduction in venous drainage [9, 10]. Based on the theory that the pulmonary arterial obstruction decreases venous flow, our hypothesis is that we can identify filling defects in the pulmonary veins in areas adjacent to the PE. This sign was named the "pulmonary vein sign" (PVS). The aim of this study was to evaluate the prevalence and performance of this sign to diagnose PE in CTPA.

Materials and Methods

Patient Selection

This study was performed with the approval of our Institutional Review Board (ISCMPA Committee, IRB00002509), and informed consent was waived. We retrospectively analyzed CTPA scans performed between March 2012 and February 2013 of patients who presented in our emergency department with clinical suspicion of PE. All examinations were completed within 48 h of clinical presentation. Subjects were excluded if there were any contraindications for CTPA, such as chronic renal failure or allergy to iodine medium.

Computed Tomography Protocol

Computed tomography angiography was performed using a multidetector scanner (64-slice LightSpeed VCT XT scanner, GE Healthcare Technologies, Waukesha, Wisconsin, United States of America). Lungs were scanned from the base to the apex in the caudocephalic direction using the following parameters: using the following scan parameters: 225 mAs, 120 kV, 0.5 mm collimation, rotation time of 0.75 s with a 3.5 cm/s table movement per gantry rotation. Administration of contrast material was performed using an automatic power injector (CT Injector, Ulrich Medical, Ulm-Jungingen, Germany) at a flow rate of 4.5 mL/s. All patients received 1 mL of Omnipaque 350 mg/mL per kilogram body weight (Amersham Health, Cork, Ireland). Administration of each bolus was followed immediately by a 60 mL saline flush. The helical acquisition was initiated after the start of the bolus administration of contrast medium, which was determined by a region of interest (ROI) with a threshold of 130 HU in the left atrium. (Smart Prep; GE Medical Systems). We routinely use this protocol to increase the contrast fill in subsegmental vessels.

Imaging Evaluation

Image interpretation was performed by two radiologists specifically trained in thoracic imaging, with 10 and 9 years of experience. After these two radiologists had conducted independent analyses, they reviewed the images together with a third senior chest radiologist with more than 20 years of experience to reach final consensus. Findings were analyzed according to the Fleischner Society's Glossary of Terms [11].

For acute PE diagnosis, the following criteria had to be included: (a) arterial occlusion with failure to enhance the entire lumen due to a large filling defect, and artery could be enlarged compared to adjacent patent vessels; (b) partial filling defect surrounded by contrast material, producing the "polo mint" sign on images acquired perpendicular to the long axis of a vessel and the "railway track" sign on longitudinal images of the vessel; (c) a peripheral intraluminal filling defect that forms acute angles with the arterial wall.

The PVS was defined by the following criteria: (a) presence of a homogeneous filling defect in the least 2 cm of a pulmonary vein; and (b) attenuation of the left atrium $>$ 160 HU. We hypothesized that this filling defect would be a consequence of a decreased venous flow due to

pulmonary arterial obstruction. Likewise, we have settled this threshold for attenuation of the left atrium for a better visualization of pulmonary veins.

Statistical Analysis

All results were analyzed using commercial software (SPSS ver. 20, SPSS Inc., Chicago, IL, USA; Excel 2010, Microsoft Corporation, Redmond, WA, USA). Two-tailed p values < 0.05 were considered to indicate statistical significance. Based on the CT images, prevalences were obtained for all radiological findings. Using the cases that presented PE on CTPA as reference, sensitivity, specificity, and positive and negative predictive values were calculated for the PVS. Values for likelihood ratios for a positive test were calculated as the sensitivity, divided by 1 minus the specificity; and likelihood ratios for a negative test were calculated as 1 minus the sensitivity, divided by the specificity [12, 13]. Agreement between radiologists was assessed using kappa statistics. Interpretation was conducted based on the following parameters: kappa < 0.20, poor agreement; kappa $= 0.21$–0.40, fair agreement; kappa $= 0.41$–0.60, moderate agreement; kappa $= 0.61$–0.80, good agreement; kappa $= 0.81$–1.00, very good agreement [14]. Fisher´s exact test was used to assess any associations between the PVS and other parenchymal findings. 95% confidence intervals (CI) were calculated for the proportions, according to Wilson score interval with continuity correction [15].

Results

The study protocol included 119 patients (female, $n = 73$ (61.34%); mean age, 62 years; age range, 11–88 years). Median total CTPA scanning time was about 7.40 min (SD $\pm$ 1.45 min) for the entire chest, varying according to the covered volume. The time interval for repositioning the patient from bed to the magnet and back has not been assessed. All findings were of sufficient quality for conclusive interpretation.

Pulmonary embolism was diagnosed in 44 (35.8%) patients. Among these patients, considering the possibility of emboli in different levels in the same subject, 10.92% ($n = 13$) had emboli in the pulmonary trunk, 11.76% ($n = 14$) in lobar arteries, 20.17% ($n = 24$) in the segmental level, and 6.72% ($n = 8$) were subsegmental PE (Table 1).

The PVS was present in 16 out of 44 patients with PE. Figure 1 depicts an example of the PVS associated with PE in the right lower lobe. Sensitivity was 36.36% (95% confidence interval (CI) 22.83–52.26%); specificity, 98.67% (95% CI 91.79–99.93%); positive predictive value, 94.12% (95% CI 69.24–99.69%); negative predictive value, 72.55% (95% CI 62.67–80.70%). Positive likelihood ratio was 27.27 (95% CI 3.74–198.66), and negative likelihood ratio was 0.64 (95% CI: 0.52–0.81). The Kappa index for the pulmonary vein sign between the two radiologists was good (0.801; 95% CI 0.645–0.957).

Table 1 Pulmonary embolism prevalence and the "pulmonary vein sign" performance in 119 patients

Parameters	*n* (%)	95% CI
Prevalence	44 (36.97)	–
Location		
Main	13 (10.92)	–
Lobar	14 (11.76)	–
Segmental	24 (20.17)	–
Subsegmental	8 (6.72)	–
"Vein sign" performance		
Sensitivity	36.36%	22.83–52.26
Specificity	98.67%	91.79–99.93
PPV	94.12%	69.24–99.69
NPV	72.55%	62.67–80.70
LR+	27.27	3.74–198.66
LR−	0.64	0.52–0.81
Kappa index	0.80	0.64–0.96

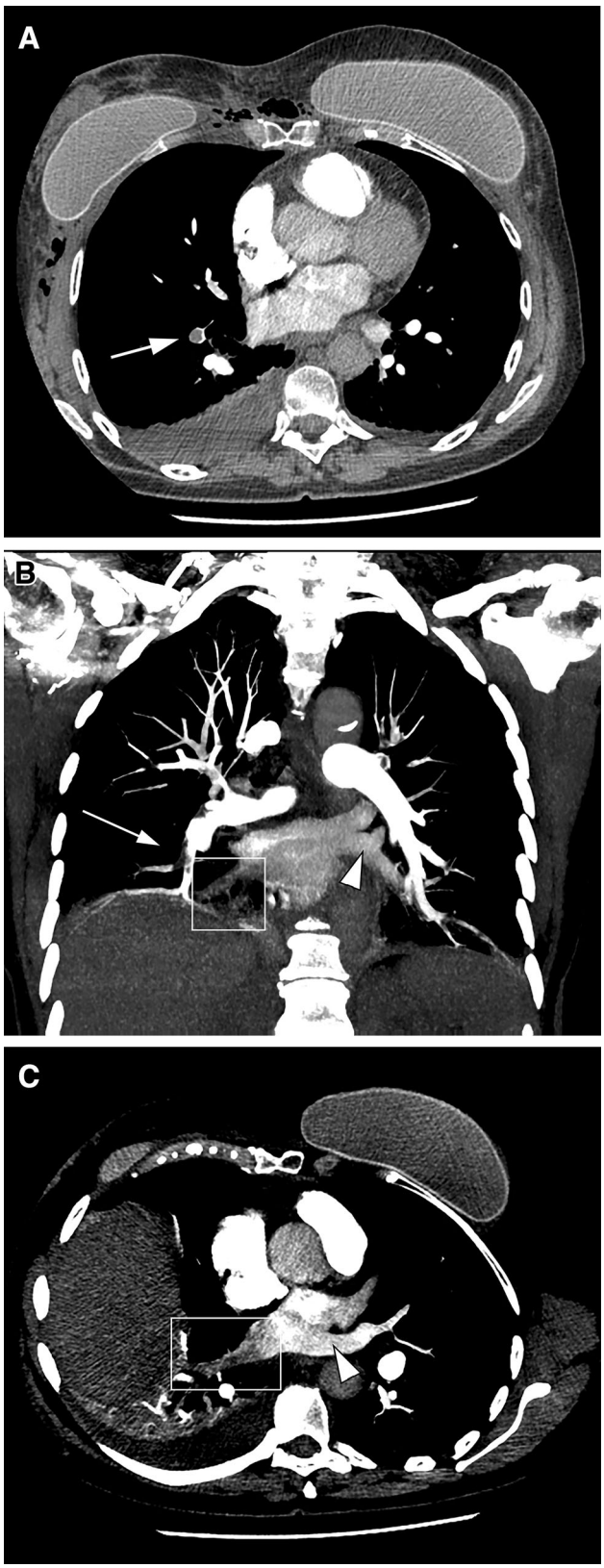
CI confidence interval, *LR+* positive likelihood ratio, *LR−* negative likelihood ratio, *NPV* negative predictive value, *PPV* positive predictive value

There was a statically significant association between the PVS and PE location at lobar and segmental levels ($p < 0.01$). Among the 44 patients with PE, six had localized (unilobar) embolisms and this location was not correlated with the PVS ($p = 0.21$). There was a statistically significant association between unilateral PE and the PVS ($p < 0.05$).

Prevalences of other pulmonary findings are presented in Table 2. Pulmonary nodule, bronchial thickening, and linear brands were the most common additional pulmonary findings (prevalences, 37.5, 22, and 20%, respectively). None of the correlations between these features and PE was statistically significant.

Discussion

In this study, we have tried to demonstrate an association between the PVS in CTPA scans and pulmonary embolism. Although this sign had not been reported previously in literature, other authors have studied the diagnostic performance of other ancillary CT signs of PE [8, 16]. Worsley et al. described classic signs for PE, such as Westermark, Fleischner, and Hampton hump signs, presenting sensitivities ranging from 8 to 22%, and



◀**Fig. 1** Images from a 46-year-old woman on the seventh post-operative day after bilateral breast augmentation surgery, with history of mastectomy due to breast cancer. Patient presented at the emergency department with sudden chest pain and dyspnea. Axial (**a**) and coronal (**b**) computed tomography images demonstrating a filling defect on a segmental pulmonary artery of the right lower lobe (white arrow). A filling defect greater than 2 cm is also noted in the adjacent pulmonary vein on the coronal (**b**) and oblique (**c**) CT reconstructions (white square), characterizing the "pulmonary vein sign." Comparatively, the other pulmonary veins are normally filled with contrast media (white arrowhead)

specificities ranging from 80 to 96% [8]. However, this study evaluated these signs at chest radiographies for patients that PE was angiographically confirmed. Despite methodological differences, our study demonstrated comparable low sensitivity (36.4%) and high specificity (98.7%) for the PVS. Additionally, we demonstrated a PE prevalence (36.97%) similar to several previous CTPA series [16–21].

There was a statistically significant correlation for the PVS and lobar and segmental pulmonary emboli but not for clots in the pulmonary trunk neither for subsegmental PE. This could be due to the small sample size and low prevalence of subsegmental PE (6.72%). However, some physiopathology mechanisms might be also accountable for this association. Usually initial pulmonary hemodynamic changes due to PE occurs from a reflex mechanism that causes vasoconstriction of small pulmonary arteries, increasing pulmonary arteriolar resistance [22]. When PE is massive or repetitive, mechanical blockage of the pulmonary vascular bed might result in sustained pulmonary hypertension [22]. This mechanism could also affect the PVS, which could be transient with small PEs. In a recent study by Koike et al. [23] that used dual-energy CT to assess lung perfusion in PE, the authors have found that difference in perfusion blood volume of the lung between patients with and those without PE tend to be larger in the early phase than in the late phase (respectively, 14 vs. 40 s from the start of injection of contrast media). This result might have reflected the reduction of pulmonary perfusion from the pulmonary artery and an enhanced role of systemic collaterals in patients with PE. This could also interfere in the PVS, as an increase in perfusion blood volume of the lung due to systemic collateral flow during late acquisition images could also increase venous flow, modifying PVS presentation.

Despite frequent additional pulmonary findings, no statistically significant correlation was found with pulmonary embolism. In a study by Coche et al. that tried to determine the value of lung parenchymal and pleural findings in patients with clinical suspicion of PE, a statistically significant difference was found only for wedge-shaped consolidations and linear bands [16]. Although we have not analyzed consolidations

Table 2 Prevalence of other pulmonary findings

Imaging findings	Prevalence *n* (%)	Unilateral *n* (%)	Bilateral *n* (%)
Consolidation	12 (10.0)	8 (66.7)	4 (33.3)
Pleural effusion	15 (12.6)	3 (20.0)	12 (80.0)
Pulmonary fibrosis	8 (6.7)	0	8 (100)
Atelectasis	12 (10.0)	2 (16.7)	10 (83.3)
Linear bands	24 (20.0)	9 (37.5)	15 (62.5)
Lung mass	6 (5.0)	0	6 (100)
Bronchial thickening	26 (22.0)	0	26 (100)
Bronchiectasis	2 (1.6)	2 (100)	0
Pulmonary nodule	45 (37.8)	5 (11.1)	40 (88.9)

None of the correlations between these features and PE was statistically significant

according to their morphology likewise, these findings were not associated with PE in our series.

Some limitations of this study include a small sample size. Further prospective studies should also try to evaluate any correlation between the PVS and clinical indicators of pulmonary embolism, such as the Wells score and/or mortality risk. In addition, estimating a mean time between the PE event and the sign presentation could be helpful to further characterize this finding. We have analyzed the PVS in patients with acute PE. Further studies could investigate this finding in chronic PE and/or non-thrombotic embolism. Some patients included in our sample presented structural abnormalities in the lungs, such as pulmonary fibrosis and lung masses, what could affect pulmonary circulation, influencing on the accuracy of the PVS. The PVS should also be investigated in situations of decreased venous flow, such as left heart dysfunction and pulmonary veno-occlusive disease, which probably affect this sign prevalence and accuracy.

In summary, despite a low sensitivity, presence of the "pulmonary vein sign" was highly specific for PE, with a good agreement between readers. This sign could contribute for PE diagnosis on CTPA studies.

Compliance With Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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