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Research paper

# Patent foramen ovale in patients with pulmonary embolism: A prognostic factor on CT pulmonary angiography?

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ABSTRACT

*Background:* Patent foramen ovale (PFO) in patients with acute pulmonary embolism (PE) represents a risk factor for mortality, but this has not been evaluated for CT pulmonary angiography (CTPA). The purpose of the present study was to assess the relationship between PFO and mortality in patients with acute PE diagnosed on CTPA.

*Materials and methods:* This retrospective study included 268 adults [173 women, mean age 61 (range 22–98) years] diagnosed with acute PE on non-ECG-gated 64-slice CTPA in 2012 at our medical center. The images were reviewed for PFO by a panel of cardiothoracic radiologists with an average of 11 years of experience (range 1–25 years). CT signs of right heart strain and PE level were noted. Transthoracic echocardiograms (TTE), when available (n = 207), were reviewed for PFO by a cardiologist with subspecialty training in advanced imaging and with 3 years of experience. The main outcome was 30-day mortality. Fischer's exact test was utilized to compare mortality.

*Results:* PFO prevalence on CTPA was 22% (58/268) and 4% (9/207) on TTE. Overall 30-day mortality was 6% (16/268), 9% (5/58) for patients with PFO and 5% (11/210) for those without (p = 0.35). CT signs of right heart strain trended with higher mortality, but statistically significant only for hepatic vein contrast reflux [14% (6/44) vs 4% (10/224), p = 0.03]; right ventricular (RV) to left ventricular (LV) diameter ratio > 1 [8% (13/156) vs RV:LV ≤ 1 3% (3/112), p = 0.07], septal bowing [10% (4/42) vs without 5% (12/226), p = 0.30].

*Conclusion:* PFO was demonstrated on CTPA in a proportion similar to the known population prevalence, while routine TTE was less sensitive. Mortality was non-significantly higher in patients with acute PE and PFO in this moderate-sized study. A larger study to answer this clinically important question is worthwhile.

Pulmonary embolism (PE) is the third most common acute cardiovascular disease in the United States with an estimated incidence of 60–70 per 100,000[1]. Computed tomography pulmonary angiography (CTPA) is the most commonly performed imaging study for PE allowing visualization of both the clot and its associated complications such as right heart dysfunction, a predictor of adverse outcomes.[2] Interestingly, patent foramen ovale (PFO), a normal variant with a prevalence of 24–27% in the general population,[3,4] has been implicated as a prognostic factor in PE. Limited but often cited literature has described the presence of PFO detected on contrast echocardiography in patients with PE to be significantly associated with ischemic stroke, peripheral arterial embolism and in-hospital death.[5,6] Another study showed that PFO can be well demonstrated on non-ECG-gated CT, with a sensitivity of 55% and specificity of 98%.[7] Because CTPA is the most common imaging modality for PE, we designed the present study to investigate the relationship between PFO detected on CTPA and 30-day mortality in patients with PE.

## 1. Methods

This retrospective cohort study was approved by Montefiore Medical Center's institutional review board and was HIPAA compliant. Informed consent was waived. We retrospectively identified all adults diagnosed PE on CTPA between January 1, 2012 and December 31,

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2012 who were imaged in the emergency department or as inpatients. 345 patients were initially identified. 73 imaged on a 16-detector row CT were excluded as was a patient whose medical record number was incorrect. The remaining patients underwent CTPA on a 64-detector row CT, 3 of whom were excluded due to artifacts from an implant cardioverter defibrillator (n = 1) and disagreement with the initial PE diagnosis (n = 2). The remaining 268 patients formed the study cohort.

Age, sex, ethnicity, body mass index, vital signs at presentation and medical history were recorded.

Routine PE protocol was performed on a 64-slice CT scanner (GE LightSpeed VCT 64). The tube voltage was chosen based on patient size (100, 120 or 140 kVp). The tube current varied as dose modulation was performed. Computed tomography dose index (CTDIvol) and dose-length product (DLP) were noted for each study. Effective radiation exposure in mSv was estimated using a conversion factor of 14 μSv/mGy*cm[8]. For the timing run, 20 cc of Isovue 370 (iopamidol, Bristol-Myer Squibb) was injected, followed by another 60–70 cc of contrast at a rate of 3–4 cc/s in suspended respiration. CT axial images with 1.25 mm-thick axial contiguous reconstructions, and sagittal and coronal CT images at 3 mm × 3 mm in thickness were archived on PACS.

Images were reviewed for each patient by two members of a panel of six cardiothoracic radiologists with an average of 11 years of experience (range 1–25 years). A consensus regarding the presence or absence of a PFO was sought and when consensus was not achieved a third member of the panel served as a tie breaker. PFO was diagnosed based on the presence of a channel or contrast flow between the left and right atrium in either direction (Fig. 1). Considering the evolution of the septum primum and secundum, the orientation of the patent foramen ovale is expected to be higher on the left atrial side. This specific orientation allowed distinction between potential PFO and artifacts.[9]

All studies were reviewed to identify the most proximal level of PE and categorized as either subsegmental or more proximal.

Signs of right heart dysfunction including leftward bowing of the interventricular septum, hepatic vein contrast reflux and right ventricular (RV) to left ventricular (LV) diameter ratio > 1 derived from measurements on the axial images were recorded (see Fig. 2).

77% (207/268) of patients had a transthoracic echocardiogram (TTE), which was reviewed by a cardiologist with subspecialty fellowship training in advanced imaging (3 years of experience0 for the presence of PFO. Patients were imaged in an echocardiography laboratory that is accredited by the Inter societal Commission for the Accreditation of Echocardiography Laboratories (ICAEL). Philips I.E. 133 ultrasonography machine was used for the majority of imaging. Presence or absence of PFO was determined by the visual examination of color Doppler flow across the intra atrial septum in the apical four chamber view (patient in the left lateral position) and in the subcostal view (patient supine). PFO was determined to be present if color Doppler signal was seen across the intra atrial septum on either of those images. Because this was a retrospective analysis of images, and the original echo study was not performed for evaluation of PFO, agitated saline (bubble study) was not administered to confirm absence or presence of PFO. Valsalva maneuver was also not routinely used in this analysis.

The main outcome was 30-day mortality. Overall mortality until the end of the collection data period on December 3rd, 2015 were also obtained. Bivariate analyses were performed. A p-value < 0.05 was considered significant.

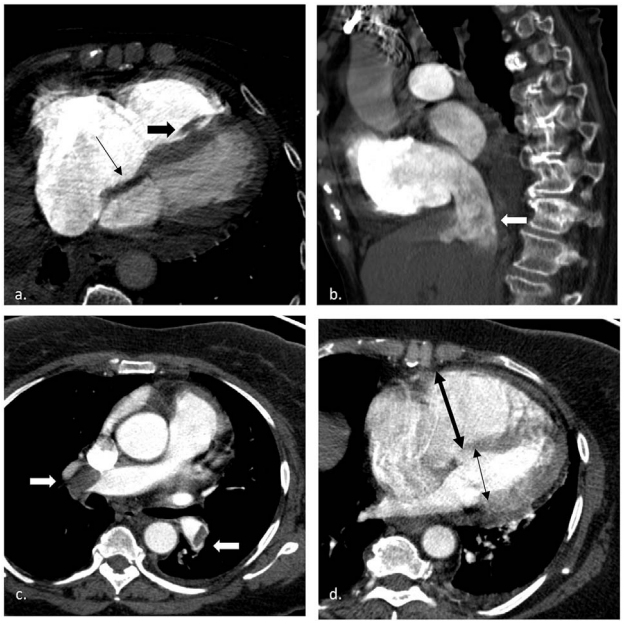


**Fig. 2.** Signs of right heart strain on CTPA in patients with pulmonary embolism. **(a)** Axial image shows leftward bowing of the atrial (thin arrow) and ventricular (thick arrow) septum. **(b)** Sagittal image demonstrate reflux of contrast in the inferior vena cava to the hepatic veins (white arrow). **(c, d)** Same patient with bilateral proximal pulmonary emboli (c, white arrow) with the right ventricle (d, thick double sided arrow) being larger than the left ventricle (d, thin double sided arrow).

## 2. Results

The median $CTDI_{vol}$ was 37 mGy and the median DLP was 561 mGy cm with an effective mean dose of 7.9 mSv for all included studies. Of note, since the time of the study, our department has instituted aggressive dose reduction strategies.[10]

PFO was identified in 22% (58/268) of patients on CTPA. Demographics and other patient characteristics were similar between the PFO and non-PFO patients (Table 1).

87% (234/268), had at least one sign of right heart dysfunction including 86% (181/210) of those without and 91% (53/58) of patients with PFO, p = 0.38.

43 (16%) patients had subsegmental PE and 225 (84%) patients had more proximal PE.

Overall 30-day mortality was 6% (16/268). Mortality was 9% (5/58) for patients with PFO versus 5% (11/210) for those without PFO (11/210; 5%), p = 0.34 (see Table 2). Contrast reflux into the hepatic veins was significantly related to mortality [14% (6/44) vs 4% (10/224) without contrast reflux (OR 3.38)], p = 0.03. Mortality was non-significantly higher for right ventricular (RV) to left ventricular (LV)

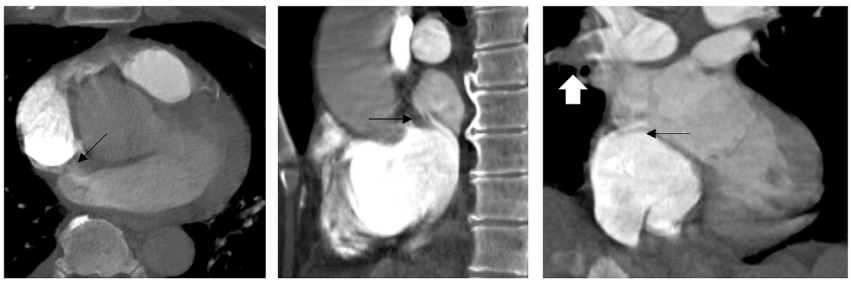

**Fig. 1.** PFO on non-gated CTPA. A gradient of contrast (black arrows) suggests a right to left shunt subtly seen in a single axial image (A), but more conspicuous on sagittal (B) and coronal (C) planes. Lobar right pulmonary embolism is seen (white arrow).