



High prevalence of pulmonary vein thrombi in elderly patients with chest pain, which has relationships with aging associated diseases



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ABSTRACT

Aim: Pulmonary vein thrombi (PVT) are believed to be rare. Some cases of PVT were reported in patients with lung cancer, thoracic surgery or catheter ablation. PVT are a possible cause of systemic embolism, but little is known about its complications. Since 2012, we have reported seven cases of PVT in patients without these predisposing factors.

The aim of the present study was to clarify whether PVT were rare or not in patients without these predisposing factors and how can we treat patients with PVT.

Methods: We performed 64-slice multidetector CT (64-MDCT) scans on 57 consecutive Japanese patients (28 men and 29 women; age = 73.8 ± 8.6 years old) with chest pain, but they didn't have lung cancer, thoracic surgery or catheter ablation, from September 2012 to March 2013.

Results: Coronary artery plaque was detected in 32 patients (56%). PVT were clearly demonstrated in 35 patients (61%), which indicated that PVT are not rare. Furthermore, 32 patients (91%) among 35 patients with PVT had no cerebral infarctions. In older people, PVT are not uncommon and have many clinico-pathologic correlations. Small or fine thrombi in the pulmonary vein should occlude a small artery of every organ and make effects on many diseases, which are not recognized by almost all medical doctors.

Conclusions: PVT are common observation in patients with chest pain and no clear predisposing factor. Further studies are required to assess if PVT can be considered as an etiology of chest pain and to determine its optimal management.

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1. Introduction

Pulmonary vein thrombi (PVT) are believed to be rare, and they are not generally recognized as a cause of systemic thrombosis such as ischemic stroke and acute myocardial infarction. Although PVT was reported to have no association to ischemic stroke [1], we think that PVT are potentially life-threatening condition and cause ischemic stroke like other cardiac thrombi such as left atrial appendage thrombi and left atrial thrombi [2,3]. More than 15% of embolic strokes are reported to be associated with cardiac thrombi, and the left atrial appendage is believed as the most predisposed location [4,5].

PVT have been reported to be associated with lung cancer [6,7], lung surgery [8–10] and radiofrequency catheter ablation [11,12]. Since 2012, we have reported seven cases of PVT in patients without such predisposing factors on cardiac CT scans using a 64-slice multidetector CT (64-MDCT) [13–20]. The quality of these images has been good, and one

of them was linked to thrombi in the left atrium that could be demonstrated by transthoracic echocardiography (TTE) [16]. These data showed that 64-MDCT and TTE can illustrate thrombi clearly and noninvasively.

The useful therapy for PVT management is treatment with anticoagulants, such as warfarin and dabigatran. Recently, dabigatran has been reported to be effective for stroke prevention and to have a lower bleeding risk compared to warfarin [21]. Although antibiotics were used in earlier cases, they lack a proven role when the PVT are not associated with infection [22,23]. If lung infarction is suspected because of a severe clinical status, then embolectomy or lobe resection may be indicated [22,24].

The aim of the present study was to clarify whether PVT were rare or not in patients with chest pain, but they didn't have these predisposing factors and whether dabigatran dissolved PVT or not.

2. Methods

2.1. Study population

We retrospectively reviewed the 64-MDCT scans of 57 consecutive Japanese patients (28 men and 29 women; age = 73.8 ± 8.6 years

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old; range: 43 to 89 years old) with chest pain at Kyowa Hospital in Japan, from September 2012 to March 2013. We assessed the data retrospectively. These patients had no evidence of lung cancer, lung surgery or radiofrequency catheter ablation. Biochemical screening tests, such as total bilirubin, were examined using traditional methods within two weeks before the 64-MDCT scans. This study was retrospective study, so ethical committee approval was not obtained. Patient consent was not obtained but the presented data are anonymized and risk of identification is low.

2.2. 64-MDCT scan procedures

The patients were examined using 64-MDCT within one month after onset of chest discomforts such as chest pain in many cases. The patients were connected to electrocardiogram (ECG) leads and placed in the supine position to enable CT and ECG synchronization. The subjects underwent 64-MDCT angiography as a traditional method. All of the 64-MDCT scans were performed with a 64-detector row CT (Aquilion64, Toshiba, Tokyo, Japan). Individuals presenting with baseline heart rates (65 bpm) within 1 h prior to a 64-MDCT scan were administered oral beta-blocker (metoprolol 20 mg) therapy to slow the heart rate. High baseline heart rates make the quality of images worse. Nitroglycerin 0.3 mg sublingual was administered immediately prior to contrast injection. The images were obtained during single breath-holds. Non-ionic contrast (Omnipaque300 syringe 80 mL, Iohexol, Daiichi-Sankyo) was administered into an antecubital vein via a dual-head injector at a dose of 0.07 mL/kg \times body weight (kg) per second (mL/s) to 5.0 mL/s over 14 s in all of the cases. The scan volume included the area under the bifurcating tracheae region to the heart base and the upper abdomen. For scanning in the craniocaudal direction, collimation of 32.0 mm was used at a rotation time of 0.35 s. The detector scan area was 32.0 mm². The thickness was 0.5 mm, the tube voltage was 135 kV and the effective current was 440 mA. The slice thickness of the reconstruction was 0.5 mm. Automatic triggering with a region of interest at the descending aorta (a threshold of 150 HU) was used. After scan completion, the 64-MDCT scans were reconstructed using retrospective ECG triggering. Axial slices were reconstructed using an ECG-gated half-scan reconstruction algorithm. Numerous phases were reconstructed within the cardiac cycle to optimize structural visualization without motion artifacts. PVT images were obtained at the same time when 64-MDCT scans were examined to assess coronary artery stenosis. If we had changed the conditions of scans for getting PVT images, then PVT might have been identified in more cases. We defined a pulmonary vein thrombus as a clear defect of contrast enhancements in the pulmonary vein. If an unclear defect in the pulmonary vein was identified, we defined it as no thrombus in the pulmonary vein; consequently, the rate of thrombus might be underestimated in this paper, and there is a possibility that more patients had PVT than we report here. Because PVT could not be clearly defined here, it is difficult to compare the two groups (patients with PVT versus patients without PVT) because some of the patients in the group defined as without PVT might have actually had PVT.

3. Statistical analysis

The distribution of the continuous variables was determined using the Kolmogorov–Smirnov test. Continuous variables with normal distributions were summarized as the means \pm standard deviations (SD) or numbers (percentages). The difference between the means of the two independent groups was calculated using Student's *t* test, which was also used to compare the values of patients with PVT to the values of patients without PVT. For all statistics, a two-sided *p* value <0.05 was considered statistically significant. The data were analyzed using commercially available XLSTAT statistical software (Version 2013.4, Addinsoft).

4. Results

4.1. Patients with PVT vs. patients without PVT

Coronary artery plaque was observed in 32 patients (56%). PVT were clearly identified in 35 patients (61%). The mean age of the 35 patients with PVT was 75.3 \pm 7.2 years (19 men and 16 women; range: 60 to 88 years), and the mean age of the 22 patients without PVT was 71.4 \pm 10.2 years (9 men and 13 women; range: 43 to 89 years). The difference in mean age between the two groups was not significant (*p* = 0.097). The 33 patients with PVT were treated with dabigatran, and the 2 patients with PVT were treated with warfarin because they experienced dyspepsia after taking dabigatran.

4.2. Laboratory data

The laboratory investigation revealed that the mean total bilirubin value (normal range: 0.3–1.1 mg/dL) of the 35 patients with PVT was 0.72 \pm 0.52 mg/dL (range: 0.3 to 2.8 mg/dL), and 9 of these patients had values >0.08 mg/dL. Furthermore, the mean total bilirubin values of the 22 patients without PVT was 0.51 \pm 0.18 mg/dL (range: 0.3–0.8 mg/dL), with no values >0.08 mg/dL. The difference in mean total bilirubin between the two groups was not significant (*p* = 0.074), and the mean values for glutamic-oxaloacetic transaminase (normal range; 10–40 IU/L) and glutamic-pyruvic transaminase (normal range 5–40 IU/L) in the 35 patients with PVT were 28.7 IU/L and 22.0 IU/L, respectively; none of the 22 patients without PVT exhibited any significant differences between these factors (28.2 IU/L and 25.0 IU/L, respectively). In addition, among the 35 patients with PVT, the D-dimer serum levels were examined in 23 patients. The mean D-dimer value was 0.72 \pm 0.72 μ g/mL. Among these patients, six (26%) had values greater than 1.0 μ g/mL (normal range: <1.0 μ g/mL); the mean D-dimer value was 1.59 \pm 0.69 μ g/mL, and the highest level was 2.9 μ g/mL.

4.3. Dabigatran therapy

At the same day of 64-MDCT scan examination, patients were started to be treated with anticoagulants if PVT were identified. After 3 months of dabigatran (33) or warfarin (2) treatment, only one of the 35 patients with PVT presented PVT that had dissolved almost entirely [19], and some of PVT dissolved partially [20], but others of PVT did not dissolve significantly. Among the PVT patients, 3 had cerebral infarctions, and 1 patient with atrial fibrillation (AF) and 1 patient with paroxysmal atrial fibrillation (pAF) did not experience cerebral infarction. During and after the treatment, chest pain and cerebral infarction occurs in no patients and the patients felt better.

5. Discussion

5.1. Findings

In this manuscript, we show that some elderly patients with chest pain have PVT, as assessed using a 64-MDCT scan, and that these PVT were difficult to dissolve with 3 months of warfarin or dabigatran treatment.

The novel findings of this study were that PVT are not rare in elderly patients with chest pain and that PVT may be common in older individuals. In this study, the timing of getting PVT images is adjusted to get the best images coronary artery plaque and our definition of a thrombus in the pulmonary vein tended to underestimate the number of patients with PVT, and the proportion of patients with PVT may therefore be greater than 61%.

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