



Persistent pulmonary hypertension and right ventricular function after percutaneous mechanical thrombectomy in severe acute pulmonary embolism

To the Editor:

Acute pulmonary embolism is one of the main causes of death, morbidity and hospitalisation [1, 2]. The most common cause of early death in these patients is right ventricular failure [1–3]. Complete resolution of the pulmonary thrombus at 6 months of evolution is not achieved in 57% of patients, with persistent right ventricular dysfunction (RVD) in 6–8% of patients and persistent pulmonary arterial hypertension (PAH) in 7–13.5% of patients who received treatment with heparin or fibrinolytic agents [4–8]. Percutaneous mechanical thrombectomy (PMT) is accepted as a treatment in patients with high-risk acute pulmonary embolism with contraindications to systemic thrombolysis or when the treatment has failed [1, 2, 9].

The main objective of this study was to analyse right ventricular function and the frequency of persistent PAH for up to 24 months or more in patients with acute pulmonary embolism and RVD treated with PMT.

We included patients (from July 2004 to June 2014) with diagnoses of severe acute pulmonary embolism with one or more criteria of RVD by echocardiography (hypokinesia of the free right ventricular wall, right ventricular diastolic diameter (RVDD)/left ventricular diastolic diameter ratio >1, RVDD >30 mm, tricuspid annular plane systolic excursion (TAPSE) <17 mm or increased tricuspid regurgitation jet velocity); shock index >1; simplified pulmonary embolism severity index >1; positive cardiac biomarker; and evidence of thrombus in the central arteries and/or lobar branches from angiotomography or magnetic resonance imaging. Exclusion criteria were prior PAH, right ventricular hypertrophy and less than 6 months of follow-up. The PMT was indicated in patients with failed thrombolysis (persistent clinical instability and residual RVD on echocardiography), a high risk of increased bleeding or a contraindication to thrombolytics [9]. Patients undergoing thrombus fragmentation, mechanical thrombus aspiration with or without “*in situ*” thrombolysis or a combination of both methods were included. The patients were evaluated clinically and by echocardiography at 6 months and then once per year. Right ventricular function was evaluated by echocardiography. PAH was defined as levels of pulmonary systolic arterial pressure (PSAP) ≥ 40 mmHg or ≥ 25 mmHg of the mean pulmonary artery pressure. The PSAP was estimated by peak tricuspid regurgitation jet velocity using the simplified Bernoulli equation and combining this value with the right atrial pressure that was estimated from inferior vena cava diameter and respiratory changes [3].

Continuous variables are presented as mean \pm SD, and categorical variables as frequencies and percentages. Comparisons were made using Fisher’s exact test and t-tests. Survival analysis was performed using the Kaplan–Meier method. p-values <0.05 were considered statistically significant. Analyses were carried out using the statistical package IBM SPSS Statistics for Macintosh Version 20.0 (IBM Corp., Armonk, NY, USA).

Of the 412 patients evaluated for acute pulmonary embolism during the study period, 78 patients underwent PMT and 52 of these were included in the study. We excluded eight patients for prior PAH, six for right ventricular hypertrophy and five for follow-up of less than 6 months. Patients who died in the hospitalisation phase were not included in the analysis (n=7). The mean \pm SD patient age was 51.8 \pm 15.9 years. The most common contraindication to thrombolysis was recent major surgery (38.5%), and the most common risk factor was deep vein thrombosis (50%).

PMT was performed 4.3 \pm 3.1 days (range 1–15 days) after symptom onset. Thrombus fragmentation was the most frequently used procedure (95.2%), followed by aspiration (53.8%) and the combination of both methods in 44.2% of patients. A permanent filter was implanted in the inferior vena cava in 46 (88.5%) out of 52 patients.

After the procedure, the shock index (pre-procedure 1.1 \pm 0.23 *versus* post-procedure 0.7 \pm 0.1; p=0.019), heart rate (pre-procedure 113 \pm 14 *versus* post-procedure 86 \pm 13 beats per min; p=0.005) and systolic systemic arterial pressure (pre-procedure 100 \pm 14 *versus* post-procedure 124 \pm 13 mmHg; p=0.005) improved. No recurrence of pulmonary embolism was documented during in-hospital outcomes.

TABLE 1 Echocardiography

Characteristics	Right ventricular function					
	Baseline	6-month control	p-value	Final control	p-value	
Subjects n	52					
RVDD mm	42.6±5.1	42.6±5.1	37.4±5.7	0.0001	35.1±5.9	0.018
RVH	52 (100%)	100%	20.9%	0.001	16.6%	0.067
TAPSE mm	13.4±2.8	13.3±2.7	20.7±2.4	0.0001	22.0±2.9	0.016
PSAP mmHg	60.8±17.7	60.8±17.7	42.8±14.8	0.0001	34.6±12.1	0.001
PSSM	52 (100%)					
LVEF	59.9±6.9%					
RV/LVEDD >1	52 (100%)					

RVDD: right ventricular diastolic diameter; RVH: right ventricular hypokinesia; TAPSE: tricuspid annular plane systolic excursion; PSAP: pulmonary systolic arterial pressure; PSSM: paradoxical septal systolic motion; LVEF: left ventricular ejection fraction; RV/LVEDD: right ventricular/left ventricular end diastolic diameter ratio.

The mean±SD follow-up was 40.2±16.7 months (range 11–84 months). During the first 6 months, follow-up was complete in 52 patients (100%), and 48 (92.3%) patients completed follow-up for ≥24 months. Four patients were re-admitted to hospital, two patients for recurrence of severe pulmonary embolism (4.1%) and two for complicated pneumonia. Reduction of PSAP was progressive, with PSAP ≥50 mmHg documented in 34.6% of patients at 6 months and in only 4.1% of patients after 24 months (two out of 48 patients). Ventilation–perfusion lung scans and tomography studies were performed on all eight (16.7%) patients with PSAP levels ≥40 mmHg during the follow-up period. In two patients, diagnoses of chronic pulmonary embolism were completed. All patients received oral anticoagulation with acenocoumarol during the first 6 months of follow-up.

Improvements of right ventricular function were greater during the first 6 months. TAPSE increased 55.6%, the RVDD was reduced 12.2%, and the PSAP was reduced by 29.6%. However, right ventricular function continued to improve after 6 months (table 1). Complete recovery of hypokinesia of the free right ventricular wall in the first 6 months was documented in 79.1% of patients. Overall survival (extra-hospital phase) at 5 years was 96.2%, 82.1% were in New York Heart Association functional class 1 and 83.6% were free from recurrence of severe pulmonary thromboembolism.

The main results of our study are as follows: 1) in 16.7% of our patients, PSAP ≥40 mmHg was documented at 24 months; 2) 4.1% of patients with long-term follow-up presented PAH from chronic pulmonary embolism; and 3) improvement of right ventricular function occurred mainly during the first 6 months of evolution.

RIBEIRO *et al.* [8] reported that 43% of patients treated with heparin and/or thrombolysis had residual PAH after 12 months of follow-up. In patients with submassive pulmonary embolism, KLINE *et al.* [6] demonstrated systolic right ventricular pressure ≥40 mmHg at 6 months in 7% of patients who received heparin only and in 11% of those that received heparin and alteplase.

In our patients, PSAP >50 mmHg at 42 months was low (4.1%). The reduction in PSAP levels was higher during the first 6 months (29.6%), with a further 21.4% reduction after this time. These results are consistent with the results of NIJKEUTER *et al.* [4], who observed complete resolution of thromboembolism by tomography in 43% of patients at 6 months.

The cumulative incidence rates of PAH from symptomatic chronic pulmonary embolism among patients with an acute episode of pulmonary embolism have been reported to be 3.8% at 2 years [10–12]. In our population with follow-up up of 24 months or more, the PAH incidence from chronic pulmonary thromboembolism was 4.1%.

Several studies have evaluated right ventricular function in patients with acute pulmonary embolism treated with heparin or fibrinolytic therapy. MENEVEAU *et al.* [5] showed that reversal of RVD occurs in 80% of patients within the first 48 h in patients with submassive and massive pulmonary embolism. Most of the contractile right ventricular deficit improves at 6 months [5, 13]. RIBEIRO *et al.* [8] reported that 8.3% of patients persisted with RVD at 12 months of echocardiographic follow-up.

Long-term evaluations of right ventricular function in patients undergoing PMT have not been published. In the PERFECT (pulmonary embolism response to fragmentation, embolectomy, and catheter thrombolysis)

trial, a significant improvement in right ventricular function in the acute phase was documented [14]. In our study, TAPSE increased >50%, and mobility of the free right ventricular wall was completely restored in most patients during the first 6 months. The recovery of the right ventricle persisted after 6 months, with a 9.1% increase in TAPSE values and a 21.4% reduction in PSAP levels. The benefit of the PMT and local thrombolysis in patients with markedly elevated PSAP levels may be limited, suggesting chronic character of the pulmonary embolism. We excluded patients with prior PAH, right ventricular hypertrophy and/or clinical conditions related to PAH (*i.e.* obesity) to reduce this possibility.

The current study provides valuable information on the right ventricular function and incidence of PAH in patients with severe acute pulmonary embolism undergoing PMT with follow-up for longer than 24 months.



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Percutaneous mechanical thrombectomy in acute PE restores right ventricle function in most patients at 40 months <http://ow.ly/lhTh304sqeY>

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