Original Article

Association between 2D echocardiographic right atrial volume to left atrial volume (RAV/LAV) ratio and in-hospital prognosis in thrombolysed acute pulmonary thromboembolism patients

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A B S T R A C T

Right atrial volume/Left atrial volume (RAV/LAV) ratio is a good hemodynamic parameter in acute pulmonary thromboembolism (PTE), whose prognostic ability by 2D echocardiography is not studied to date. We conducted a 27 month, prospective observational study on 55 eligible acute PTE thrombolysed (29: Tenecteplase; 26: Streptokinase) patients. The primary endpoint was a composite of in-hospital death and poor right ventricular reverse remodelling at the time of discharge. The incidence of primary end-point and death were 40% and 7.2% respectively. On regression analysis, RAV/LAV ratio was the only predictor of the primary endpoint, with an optimal cut-off of 3.8 (accuracy 75%).

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1. Introduction

Current guidelines advocate trans-thoracic echocardiography (TTE) for early risk stratification following acute pulmonary thromboembolism (PTE) based on, right ventricular strain (RV-S) findings namely RV dilatation, RV free wall hypokinesia (McConnell sign), systolic flattening of the inter-ventricular septum, and RV dysfunction. However, their overall prognostic power is low, particularly in low-risk PTE patients, and might be attributed at least in part, for using qualitative criteria that are subject to inter-observer variability. Thus there is an increased interest in objective quantitative criteria.

Right atrial size has been shown to correlate positively with the severity of the pulmonary arterial obstruction and greater the clot burden in the pulmonary arteries, the smaller the left atrial size thus assessing the ratio of the atrial volumes may provide accurate prognostic information; in addition, it can be represented as a quantitative data, thus improving the robustness of risk stratification.

2. Methods

This was a single centre, prospective observational study conducted on high and intermediate-high risk PTE patients after IEC approval. PTE was diagnosed by CT pulmonary angiogram (CTPA) or clinically based on acute presentation (<2 weeks), D-Dimer elevation, and echocardiographic RV-S findings. Patients with known cardiac or pulmonary diseases that affect RV function like organic valvular heart disease, congenital heart disease, cardiomyopathies, obstructive or restrictive or vascular pulmonary disorders, and recurrent PTE were excluded. Routine haematological investigations, 12 lead ECG, and 2D-TTE were done in all patients.

2.1. Imaging

Right atrial volume (RAV) and left atrial volume (LAV) were measured at end-systole, in apical four-chamber view by single plane Simpson method. The ratio is then calculated by dividing both the volumes (Fig. 1). CTPA before thrombolysis (CTPA-O) was performed depending on logistic circumstances, and CT pulmonary artery obstruction (Qanadli) index was calculated.

2.2. In-hospital management

2.2.1. Thrombolytic therapy (TT)

Patients were thrombolysed with either weight-adjusted (0.5 mg/kg) Tenecteplase (TNK) bolus or standard streptokinase
(STK) infusion of 1,00,000 U/h (after initial bolus of 2,50,000 U) for a minimum of 24 h. If hemodynamic stability was not achieved then the same agents were used as extended thrombolysis (TNK: 0.5 mg/kg/24 per hour or STK: 1,00,000 U per hour infusions).

2.2.2. Anticoagulation
After completion of TT, Heparin was infused at a rate of 1000U/h (adjusted to maintain aPTT at 2.0 to 2.5 times the normal) and later enoxaparin was administered at a dose of 1 mg/kg/SC twice daily. Overlapping acenocoumarol was started on day 2, and the dosage was adjusted until INR fell in the therapeutic range of 2.0–3.0.

During TT patients were objectively evaluated every 6 h, and any complications were managed according to the standard treatment protocol.

2.3. Study endpoints

2.3.1. Primary endpoint
A composite incidence of:

1. all-cause in-hospital death,
2. Incidence of poor reverse RV remodelling\(^{10,11}\) at the time of discharge, which was defined as, RV dysfunction (TDI-S\(^{-}\) of lateral tricuspid annulus <10 cm/s) and/or RV dilatation (end-diastolic RV/LV diameter ratio of >0.66) and/or elevated RV systolic pressure (RVSP > 50 mmHg).

2.3.2. Secondary endpoint
A composite incidence of prolonged (>12 h) hemodynamic support and/or extended thrombolysis (need for TNK infusion or STK infusion for >24 h).

2.4. Statistical analysis
Continuous and categorical variables were reported as mean and number of observations (n), respectively. Bland–Altman plot was used to assess the inter-observer agreeability of RAV/LAV ratio. Multivariate logistic regression analysis was performed to determine the predictors of in-hospital outcomes, and correlation was tested with Kendall’s tau rank test. EZR® (3.5.2, R foundation) was used for statistical analysis. A \( p < 0.05 \) was considered significant statistically.

3. Results

3.1. Clinical and investigatory data
55 eligible patients with a mean age of 40.2 (±9.5) years (58.2%, females) were included. 43 (78.2%) patients presented with high-risk PTE and 29 (52.7%) patients were thrombolysed with TNK. The mean PTE severity index (PESI) score was 126.05. ECG was abnormal in 96.3% of the population, and S1Q3T3 was present in 22 patients. The mean Daniel score was 7.05 (±4.54). Classic TTE signs of PTE, namely McConnell’s sign and 60:60 sign, were present in 52.7% and 41.8% of patients, respectively. Only 24 patients underwent CTPA-O due to internal logistic reasons and had a mean Qanadli index of 49.8 (±5.7) (Supplement).

3.2. RAV/LAV ratio
The mean RAV and LAV were 68.5 ml and 18.8 ml, respectively, yielding a mean RAV/LAV ratio of 3.67 (±0.26). The intra-class correlation coefficient for RAV/LAV ratio was 0.82 (\( P < 0.01 \)) and it had a significant positive correlation with Qanadli index (\( \tau = +0.57; p < 0.01 \)) (Supplement).

3.3. Endpoints
In-hospital MACE rate was 40% and the secondary end-point incidence was 36.5% (19/52). In-hospital mortality rate was 7.2% (4/55).

In multivariate regression analysis, only the RAV/LAV ratio independently predicts the primary but not the secondary outcome. High PESI and TNK use were associated with a higher and lower need for prolonged (or intense) therapy, respectively (Table 1).

RAV/LAV ratio (AUROC: 0.77; \( p < 0.01 \)) of >3.8 was found to be an optimal cut-off (Fig. 1) (sensitivity = 77.3% and specificity = 69.7%) for predicting primary end-point (accuracy of 74.1%). A PESI score of >125 predicts the need for intense therapy (AUROC: 0.7; \( p < 0.01 \)) with an accuracy of 67.3% (Supplement).
4. Discussion

In acute PTE, the RAV/LAV ratio reflects the integration of multiple haemodynamic parameters, including the diastolic and systolic function of the RV, and filling volumes and pressures of the left heart. In fact, in PTE patients CT derived RAV/LAV ratio was associated with in-hospital mortality, and increased TTE derived RA/LA area ratio was associated with higher embolic burden and poor long-term survival. However, to date, no studies have assessed the prognostic ability of 2D-TTE derived RAV/LAV ratio in this population.

Interestingly TNK was found to be associated with a lower incidence of intense therapy, i.e., causes rapid improvement in hemodynamic status compared to STK; a similar finding was also documented in other studies.

5. Conclusion

RAV/LAV ratio is a simple, reproducible, independent prognostic marker of in-hospital adverse events in thrombolysed PTE patients with 3.8 as an optimal cut-off (75% accuracy). It also showed a good positive correlation with the extent of pulmonary vascular obstruction (Qanadli index).

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**Conflicts of interest**

All authors have none to declare.

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**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ihj.2020.09.008.
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