

Dramatic Normalization of the Echocardiographic Pulmonary-to-Left Atrial Ratio with Thrombolysis in a Case of Life-Threatening Submassive Pulmonary Emboli



Isabel G. Scalia, BSc, Andrea Z. Riha, MBBS, FRACP, Agatha Kwon, BSc,
Katrina Newbigin, MBBS, RANZACR, and
Gregory M. Scalia, MBBS, MMedSci, FRACP, FCSANZ, FACC, FASE, *Brisbane, Australia*

INTRODUCTION

Patients with suspected acute pulmonary embolus are often sent for echocardiography as part of their workup.¹ Patients are referred to determine whether there is evidence of right ventricular (RV) dysfunction² or enlargement and/or significant pulmonary hypertension.³ It is a common clinical experience that patients with confirmed submassive pulmonary emboli often have only minimally elevated RV systolic pressures (RVSPs).⁴ Guideline-driven therapy⁵ recommends the use of thrombolysis in the setting of shock. Normotensive patients may be considered for thrombolysis in the presence of both RV dysfunction and elevated troponin levels (intermediate to high risk).^{6,7}

Physiologically, acute pulmonary embolism represents an abrupt and sudden increase in transpulmonary gradient.⁸ The echocardiographic pulmonary-to-left atrial ratio (ePLAR) has recently been demonstrated to be a noninvasive analog of transpulmonary gradient.⁹ This parameter (Figure 1D), which assesses the difference in RV and left atrial pressure via the formula

$$\text{ePLAR (m/sec)} = \text{TRV}_{\text{max}} \text{ (m/sec)} / \text{mitral E/e'}$$

correlates well with transpulmonary gradient and differentiates precapillary from postcapillary pulmonary hypertension in patients being investigated for consideration of specific vasodilator therapies (TRV_{max} is tricuspid regurgitation maximum velocity, mitral E is transmitral pulse wave maximum E-wave velocity, and e' is septal mitral annular maximal Doppler Tissue Imaging e-wave velocity). Higher ePLAR values suggest higher transpulmonary gradients and precapillary pulmonary hypertension. Lower ePLAR values suggest higher left atrial pressures with minimal increase in transpulmonary gradient and postcapillary pulmonary hypertension (Figure 1B). As such, acute pulmonary embolism should result in a sudden increase in transpulmonary gradient and therefore ePLAR.

CASE PRESENTATION

A 74-year-old man presented with a history of increasing shortness of breath with associated pleuritic chest pain for several days. He had a history of multiple myeloma in remission in the setting of previous colon cancer. He was tachycardic to a rate of 120 beats/min, however, his blood pressure was within the normal range, and the electrocardiogram showed no acute ischemic changes. He was tachypneic to a rate of 40 breaths/min and was unable to complete sentences. Ultrasound at the time identified bilateral deep vein thrombosis, however, no obvious causative agent was identified. Computed tomographic pulmonary angiography revealed bilateral submassive pulmonary emboli in the left and right main pulmonary arteries (Figure 2). Urgent echocardiography showed a mildly dilated right ventricle with moderate systolic dysfunction (Figure 3A and Video 1). There was moderately severe pulmonary hypertension with an RVSP of 63 mm Hg (Table 1). The left ventricle was underfilled and hyperdynamic. Filling pressures were low, as evidenced by a mitral E/e' ratio of 5 (Figure 1C). Transpulmonary gradient was high, as indicated by an ePLAR of 0.78 m/sec (normal range for age, 0.30 ± 0.09 m/sec) (Figure 1A).

Although the patient was hemodynamically stable, thrombolysis with tissue plasminogen activator (10 mg bolus over 10 min and 90 mg over 2 hours) was undertaken on the basis of RV dysfunction. Following thrombolysis, the patient had almost complete symptomatic resolution over 3 hours, with no major complications. Repeat echocardiography following lysis showed normalization of RV function (Video 2) and left ventricular filling (mitral E/e' ratio 8.3) (Figure 3B). There was near complete resolution of the pulmonary hypertension (RVSP 37 mm Hg) and transpulmonary gradient (ePLAR 0.33 m/sec) (Figure 1A). Further echocardiographic improvement was observed at 1 month after lysis (Video 3), with an RVSP of 26 mm Hg and an ePLAR of 0.20 m/sec (Figure 1A and C).

DISCUSSION

Following an acute, submassive pulmonary embolism, passage of blood from the right ventricle to the left atrium is impaired. Consequently, there is pressure work overload of the right ventricle¹⁰ and, more importantly, underfilling of the left heart, particularly the left atrium. The latter is the physiologic underpinning of the shock presentation of patients with massive embolic load.¹¹ The acute increase in RV afterload causes significant myocardial dysfunction, as evidenced by reduced tricuspid annular plane systolic excursion,¹² McConnell's sign, and, more recently, reduced longitudinal strain.^{2,13,14} Importantly, however, the absence of pulmonary hypertension on initial echocardiography does not exclude significant embolic burden.^{15,16}

From the Heart Care Partners (I.G.S., A.K., G.M.S.); Department of Cardiology, Wesley Hospital (A.Z.R., G.M.S.); Wesley Medical Imaging (K.N.); and School of Medicine, the University of Queensland (G.M.S.) Brisbane, Australia.

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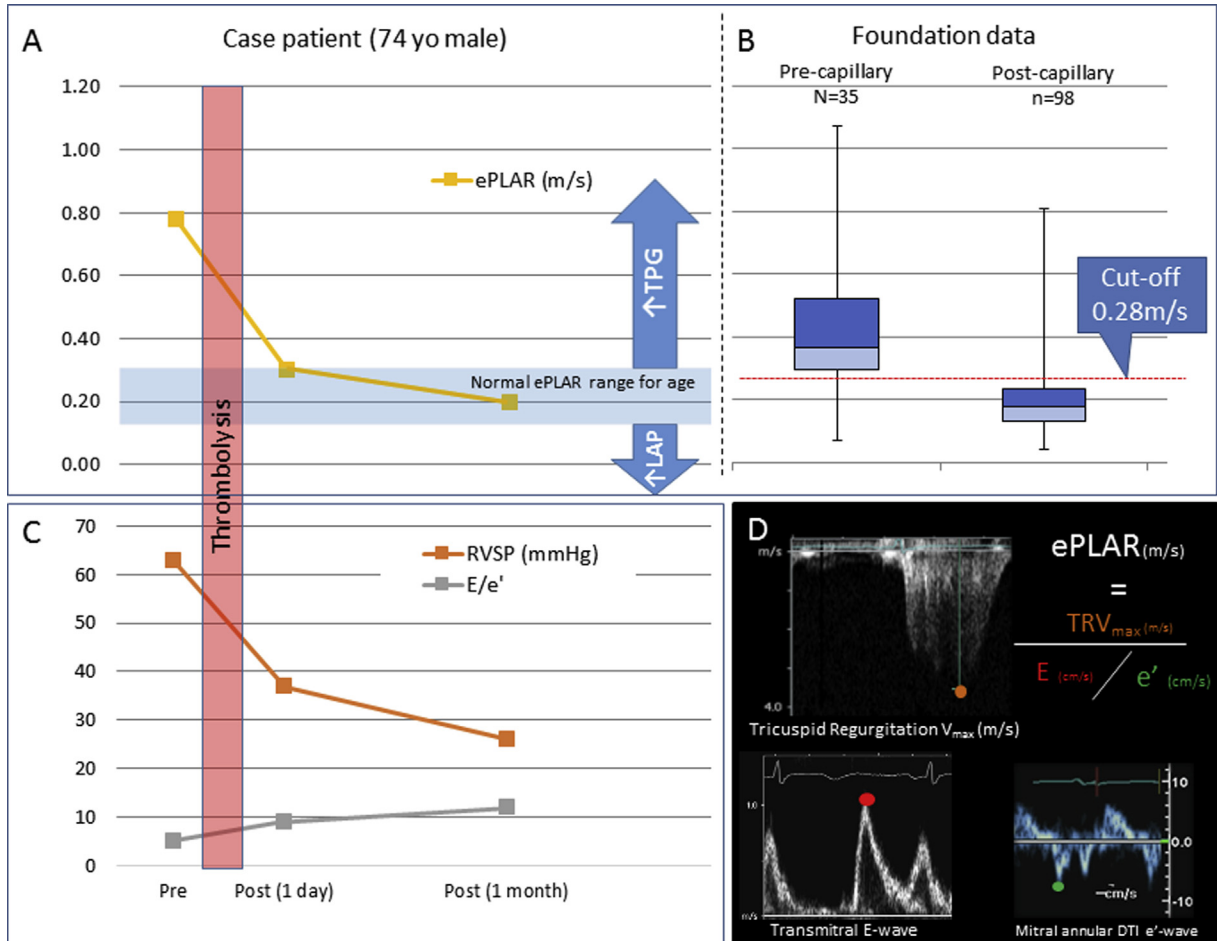


Figure 1 (A) ePLAR values (m/sec) from echocardiography of a 74-year-old man with bilateral submassive pulmonary emboli at the time of presentation (before thrombolysis) and after thrombolysis (1 day and 1 month). (B) Box-and-whisker plot of ePLAR values (m/sec) in foundation data of patients with precapillary ($n = 35$) and postcapillary ($n = 98$) pulmonary hypertension.⁹ The established optimal statistical cutoff for differentiating precapillary and postcapillary physiology is 0.28 m/sec.⁹ (C) RVSP (mm Hg) and mitral E/e' ratio of case patient before and after thrombolysis. (D) Echocardiographic representation of components of ePLAR. LAP, Left atrial pressure; TPG, transpulmonary gradient; TRV_{max} , tricuspid regurgitation continuous-wave peak velocity.

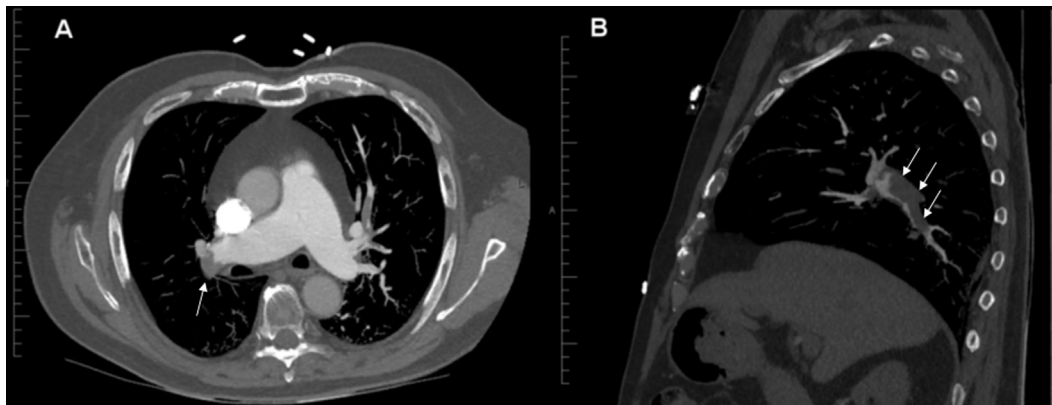


Figure 2 Computed tomographic pulmonary angiogram of a 74-year-old man with bilateral submassive pulmonary emboli (white arrows): (A) coronal and (B) sagittal.

Transpulmonary gradient has been shown to correlate well with the novel parameter ePLAR in patients with chronic pulmonary arterial hypertension.⁹ In patients with chronic thromboembolic pulmonary hypertension, ePLAR has been shown to be

significantly elevated, supporting the diagnosis of a chronic precapillary etiology for increased right-heart pressures.¹⁷ Real-time changes in ePLAR have been demonstrated in a case of an adverse drug reaction to bleomycin, which supports the immediate

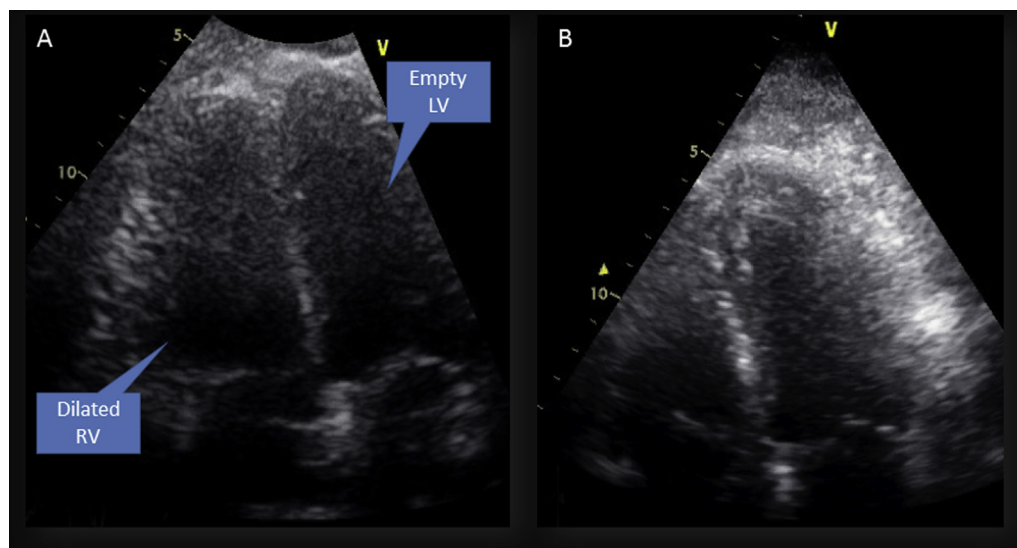


Figure 3 Echocardiography of a 74-year-old man with bilateral submassive pulmonary emboli. **(A)** Prethrombolysis four-chamber view showing dilated right ventricle (RV) and underfilled (empty) left ventricle (LV). **(B)** One day after thrombolysis, four-chamber view showing complete normalization of left and right ventricular size and function.

Table 1 Hemodynamic data acquired by transthoracic echocardiographic before, 1 day after, and 1 month after thrombolysis for submassive pulmonary emboli

Thrombolysis	TRV _{max} (m/sec)	RVSP (mm Hg)	Mitral E (m/sec)	Mitral e' (m/sec)	E/e' ratio	ePLAR (m/sec)
Before	3.9	63	0.4	0.08	5.0	0.78
1 day after	2.7	37	0.5	0.06	8.3	0.33
1 month after	2.4	36	0.5	0.04	12.5	0.20

reactivity of this parameter to acute changes in transpulmonary gradient.¹⁸

It is hypothesized that ePLAR will have a considerably higher yield than RVSP in detecting hemodynamic perturbations in patients with acute submassive pulmonary embolism. This will be composed of increases (if any) in TRV_{max} associated with reduced mitral E/e'. Certainly, in this case, the initial data supported severe precapillary pulmonary hypertension with a very high ePLAR. Resolution of the obstruction to transpulmonary flow transit with thrombolysis was matched with an immediate improvement in ePLAR. Further improvement over the next month was associated with a further decrease in ePLAR, into the normal range for age, suggesting normal transpulmonary gradient. It has also been shown that with age, as left-heart filling pressures naturally rise, ePLAR declines.⁹ Thus, assessment of normal versus abnormal values in each patient must take age into consideration (Figure 4).

CONCLUSION

Patients with submassive pulmonary emboli are often observed to have minimal increases in RVSP with associated significant decreases in left atrial filling pressure. This phenomenon was numerically reflected in this patient by the echocardiographic parameter ePLAR, which was significantly elevated at the time of bilateral submassive pulmonary emboli. Subsequent thrombolysis was shown to relieve the embolic burden, both symptomatically and echocardiographi-

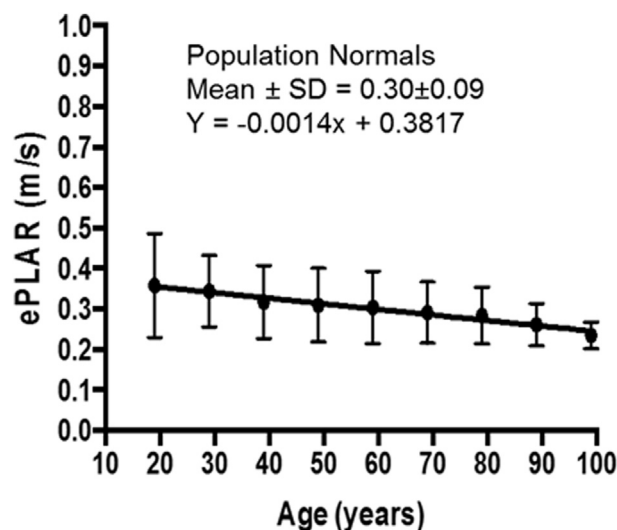


Figure 4 Population ePLAR values (m/sec) for 1,000 normal subjects showing linear decrease with age. Reproduced with permission.⁹

cally, with acute decreases in both RVSP and ePLAR. One-month follow-up confirmed this result, with preserved RV systolic function and normalization of RVSP and ePLAR.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.case.2017.03.002>.

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