

Reply to the Letter to the Editor: "Interpreting Reduced-Dose Slow-Infusion Thrombolysis in Intermediate-High-Risk Pulmonary Embolism"

We read the Letter to Editor (AJC-2026-290-6598) entitled "Interpreting reduced-dose slow-infusion thrombolysis in intermediate-high risk pulmonary embolism" on our published paper with great interest.^{1,2} We fully agree with the author of this letter regarding the lack of the currently available, evidence-based guideline recommendations favouring the full-, or low-dose systemic alteplase (t-PA) in IHR PE, in the absence of hemodynamic deterioration.³ However, the comparisons of efficacy and safety outcomes between our low-dose, slow infusion t-PA regimens and a weight-based bolus of tenecteplase given over a period of 5-10 seconds in the Pulmonary Embolism Thrombolysis (PEITHO) trial should also be considered methodologically unacceptable and misleading.⁴

As mentioned in our manuscript, a reduced-dose, slow-infusion intravenous t-PA strategy aims to achieve gradual pulmonary reperfusion and right-ventricular unloading while limiting peak systemic fibrinolytic exposure and bleeding risk.² The concept is promising, but superiority over anticoagulation, conventional half-dose alteplase, or catheter-based treatment has not been established. However, published multiple real-world results suggest the potential benefits of low-dose, slow-infusion t-PA protocols in this setting.⁵⁻⁷ The ongoing PEITHO-3 and STRATIFY randomized trials are expected to provide more definitive and clinically reliable answers regarding the efficacy and safety concerns of low-dose t-PA regimens in patients with IHR risk PE.^{8,9} Until clarification of the convincing results derived from randomized clinical trials, low-dose, slow-infusion t-PA therapy may be considered an individualized treatment strategy in the decision-making for specific circumstances.

Declaration of Interests: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study has received no financial support.

REFERENCES

1. Anatol J. *Cardiol*; 2026.
2. Kültürsay B, Tanyeri S, Keskin B, et al. Effectiveness and safety of reduced-dose and slow-infusion intravenous tissue-type plasminogen activator regimen in patients with acute pulmonary embolism at intermediate-high risk. *Anatol J Cardiol*. 2025;29(12):715-722. [CrossRef]
3. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). *Eur Heart J*. 2020;41(4):543-603. doi:10.1093/eurheartj/ehz405 [CrossRef].
4. Meyer G, Vicaut E, Danays T, et al. Fibrinolysis for patients with intermediate-risk pulmonary embolism. *N Engl J Med*. 2014;370(15):1402-1411. [CrossRef] <https://www.ncbi.nlm.nih.gov/pubmed/24716681>
5. Zientek E, Talkington K, Gardner J, et al. Low-Dose alteplase versus Conventional Anticoagulation to treat Submassive Pulmonary Embolism in Hispanic Patients. *Int J Angiol*. 2022;32(2):131-135. [CrossRef]



Copyright©Author(s) - Available online at anatoljcardiol.com.
Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

LETTER TO THE EDITOR REPLY

Barkın Kültürsay¹
Seda Tanyeri²
Berhan Keskin³
Hacer Ceren Tokgöz²
Dicle Sırma²
Çağdaş Buluş²
Şeyma Zeynep Atıcı²
Şeyma Nur Çiçek²
Furkan Baturalp Erdoğan²
Ahmet Sekban²
Mustafa Bulut⁴
Zübeyde Bayram³
Selahattin Akyol²
Aykun Hakkör³
Şeyhmus Külahaçioğlu²
Ali Karagöz²
Nihal Özdemir²
Cihangir Kaymaz⁵

¹Department of Cardiology, Tunceli State Hospital, Tunceli, Türkiye

²Department of Cardiology, University of Health Sciences, Koşuyolu Heart Training and Research Hospital, İstanbul, Türkiye

³Department of Cardiology, Medipol University Faculty of Medicine, İstanbul, Türkiye

⁴Department of Cardiology, Ahi Evren Thoracic and Cardiovascular Surgery Training and Research Hospital, Trabzon, Türkiye

⁵Department of Cardiology, Başkent University İstanbul Hospital, İstanbul, Türkiye

Corresponding author:

Cihangir Kaymaz
✉ cihangirkaymaz2002@yahoo.com

Available Online Date:

September 21, 2026

Cite this article as: Kültürsay B, Tanyeri S, Keskin B, et al. Reply to the letter to the editor: "interpreting reduced-dose slow-infusion thrombolysis in intermediate-high risk pulmonary embolism". *Anatol J Cardiol*. 2026;XX(X):1-2.

DOI: 10.14744/AnatolJCardiol.2026.6764

6. Güner A, Kalçık M, Aykan AÇ, et al. Clinical safety and efficacy of thrombolytic therapy with low-dose prolonged infusion of tissue type plasminogen activator in patients with intermediate-high risk pulmonary embolism. *Blood Coagul Fibrinolysis*. 2020;31(8):536-542. [\[CrossRef\]](#)
7. Qi W, Gong M, Huang H, Zhou Y, Su H. Efficacy and safety of low-dose prolonged infusion thrombolysis with rt-PA for acute intermediate-high risk pulmonary embolism. *Pulm Circ*. 2026;16(1):e70274. [\[CrossRef\]](#)
8. Sanchez O, Charles-Nelson A, Ageno W, et al. Reduced-Dose Intravenous Thrombolysis for Acute Intermediate-High-risk Pulmonary Embolism: Rationale and Design of the Pulmonary Embolism International THrOmbolysis (PEITHO)-3 trial. *Thromb Haemost*. 2022;122(5):857-866. [\[CrossRef\]](#)
9. Kjaergaard J, Bang LE, Sonne-Holm E, et al. Randomized trial of low-dose, ultrasound-assisted thrombolysis or heparin for pulmonary embolism. *Cardiovasc Res*. 2026;122(4):539-549. [\[CrossRef\]](#)