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

LETTER TO THE EDITOR
REPLY

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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.

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