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Interpreting Reduced-Dose Slow-Infusion Thrombolysis in Intermediate–High-Risk Pulmonary Embolism

LETTER TO THE EDITOR

To the Editor,

We read with interest the article by Kültürsay et al[1] evaluating reduced-dose, slow-infusion systemic thrombolysis in patients with intermediate–high-risk (IHR) pulmonary embolism (PE). The authors share a large single-center experience in a field where evidence remains limited, adding useful data to the literature.

However, some points require careful discussion. Current international guidelines do not recommend routine systemic thrombolysis in IHR PE, instead favoring anticoagulation with close monitoring and reserving thrombolysis for patients who develop hemodynamic deterioration.[2,3] This recommendation is based on randomized studies showing no mortality benefit and a higher risk of major and intracranial bleeding with early thrombolysis. Therefore, any upfront thrombolytic approach in this population represents a departure from guideline-based first-line management

In this context, the clinical outcomes reported in the study should be interpreted cautiously. Despite early administration of low-dose, slow-infusion thrombolysis, hemodynamic decompensation occurred in 3.2% of patients. This rate is comparable to that observed in conservatively managed patients in the PEITHO trial, where hemodynamic decompensation occurred in 5.0% of the anticoagulation-only group and 1.6% of the tenecteplase group.[4] Importantly, although thrombolysis reduced hemodynamic decompensation in PEITHO, it did not improve survival and was associated with significantly more bleeding events.[4]

The fact that hemodynamic deterioration still occurred despite early thrombolytic therapy raises an important clinical question. An initial strategy of anticoagulation with careful monitoring, followed by standard-dose thrombolysis as rescue treatment when deterioration occurs, might have achieved similar outcomes while avoiding early thrombolytic exposure in patients who would otherwise remain stable.

In addition, although slow infusion of thrombolytics is biologically reasonable, clinical evidence supporting this approach is limited. No randomized trials have directly compared different systemic infusion strategies in IHR PE. Ongoing studies, such as Pulmonary Embolism International THrOmbolysis-3 (PEITHO-3), which evaluates reduced-dose thrombolysis versus anticoagulation alone, are expected to provide more definitive answers.[5]

Overall, the study contributes valuable real-world data; however, its findings are better interpreted as exploratory rather than directly practice-changing. At present, the results do not clearly show that early low-dose, slow-infusion thrombolysis improves outcomes beyond those achieved with guideline-recommended management.

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