# Correspondence on 'Low-dose thrombolysis for submassive pulmonary embolism' by Yilmaz and Uzun

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To the Editor,

We recently read with great interest the article by Yilmaz and Uzun,[1] describing the efficacy and safety of low dose thrombolytic therapy (TT) in patients with acute submassive pulmonary embolism (PE). We would like to emphasize a few points in light of current evidence.

PE is one of the most frequently reported thrombotic complications,[2] and is more prevalent in critically ill patients with coronavirus disease 2019 (COVID-19). Thirty-day results have shown that patients with COVID-19 and PE received no significant benefit from empirically administered prophylactic anticoagulants at moderate doses against venous thrombosis or mortality.[3] In submassive PE, the specific role of TT remains under scrutiny.[4–9] The PEITHO trial (Fibrinolysis for patients with intermediate-risk pulmonary embolism) aimed to test the benefit of single bolus weight-based tenecteplase in a stratum of patients with submassive PE.[6] The authors have reported a correlation between TT and significantly decreased hemodynamic decompensation and collapse risk, although with higher risk of severe extracranial and intracranial bleeding.[6] Additionally, this trial included the efficacy and safety results of standard-dose TT.[6]

In a prospective study, Yilmaz *et al* demonstrated significant elimination of major bleeding complications, along with optimal clinical outcomes using a half-dose thrombolysis strategy (50 mg/2 hours).[1] Moreover, Rothschild *et al* reported risks of major bleeding (11%) and 30-day mortality (4.4%) involved with the application of half-dose systemic TT against acute submassive PE, similar to a previous study on systemic TT.[7] Interestingly, Sharifi *et al* showed good clinical outcomes and no bleeding in patients with submassive PE using a different half-dose TT strategy, which involved the administration of a 10 mg intravenous (IV) bolus within 1 min followed by 40 mg IV bolus infusion within 2 hours.[8] Considering the evidence regarding systemic TT, use of this therapeutically effective systemic drug (tissue plasminogen activator) seems to be correlated with significant bleeding risks, regardless of the administration route or dose.

Hence, for managing deteriorating PE cases with moderate-high bleeding risk, we suggest administering low-dose TT (50 mg/6 hours) over a prolonged period. Unlike the previous indications of preventing intermediate-major bleeding, our recent findings support overall favorable clinical outcomes with the aforementioned low-dose strategy.[9] In the present study, the bleeding rate was 12.5% (minor bleeding in two cases) using the TT regimen. We still acknowledge the evidence regarding the efficacy of this strategy for treating acute submassive PE. We simply suggest that low-dose slow infusion of TT could help achieve a lower incidence of bleeding. There is no randomized trial to confirm that this strategy decreases clinical deterioration, increases exercise tolerance, and improves quality of life. Further research in this direction could help physicians reliably select the best reperfusion therapy.

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