Catheter-Directed Interventions for Acute Pulmonary Embolism

The Jury Is Still Out

To the Editor:

The paucity of prospective data regarding catheter-directed interventions for the treatment of acute massive or submassive pulmonary embolism (PE) is well recognized, and and Kuo and colleagues are to be commended for presenting the first prospective registry of such patients, to our knowledge, in this issue of CHEST (see page 667). Their use of a composite clinical success outcome is important as the combination of hemodynamic stabilization, echocardiographic improvement, and survival increases the face validity of this more patient-centric outcome compared with radiographic improvement alone.

The authors’ conclusion that standard catheter-directed thrombolysis may be equivalent to ultrasound-accelerated thrombolysis is also an astute one, considering that many retrospective studies examine the latter one alone. The comparative effectiveness of these two methods is a consideration that we also have questioned, with similar results, and will be of importance as catheter-directed PE interventions continue to mature.

However, the pragmatic interpretation of this study within the broader scope of practice remains unclear, as the lack of a comparison arm limits analysis against anticoagulation or systemic thrombolysis for either the composite end point or outcomes such as mortality. Many retrospective series have demonstrated the relative safety and efficacy of these procedures for immediate improvement of hemodynamics; this study, though prospective, may not be unique.

The inclusion of subjects in the study is unclear; though consecutive patients were enrolled, there is no mention of exclusions, withdrawals, or deviations from standard protocol. No subjects were included who failed first-line anticoagulation therapy, which is unusual in our experience. Cause of death, especially in those with submassive PE, was also not reported. In addition, the absence of quantitative echocardiogram measures such as the right ventricular to left ventricular diameter ratio, and reliance on institution-specific, nonblinded, single-reader echocardiogram interpretation may introduce bias for the primary outcome.

Although 101 patients were enrolled, the low average number of yearly cases per participating institution (six) may increase sampling error. The absence of major complications aside from minor bleeding, especially in those with absolute contraindications to thrombolytics, is a surprising finding, suggesting that these excellent early results are unlikely to be sustained.

Finally, as the authors themselves noted, no postdischarge follow-up was included, limiting generalizability outside the immediate periprocedural period and preventing long-term evaluation including development of chronic thromboembolic pulmonary hypertension. Despite the prospectively collected nature of the data, these considerations suggest that for PE intervention, the jury is still out: Cautious interpretation of these results may be prudent until a larger sample and comparative data are available for analysis.

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References

Response

To the Editor:

We appreciate the compliments by Dr Liang and colleagues regarding our article in this issue of CHEST. They are quick to note that the PERFECT (Pulmonary Embolism Response to Fragmentation, Embolectomy, and Catheter Thrombolysis) registry lacks a comparison arm, but this was obviously not the aim of our study. We previously acknowledged that registry data need confirmation by randomized trials, but we also emphasized that randomized controlled trials (RCTs) need validation by observational data, since RCTs are limited by abundant exclusion criteria. Therefore, the strength of the PERFECT registry is data collection on real-world patients with very few exclusion criteria, minimizing sampling error.

Several doubts, some self-contradictory, were expressed that need clarification. The claim that our study is not unique compared with a review is mistaken. The cited review was limited by mostly single-center retrospective studies and included only patients receiving ultrasound-assisted thrombolysis (USAT). By contrast, our prospective multicenter registry enrolled patients receiving either catheter-directed therapy (CDT) or USAT and revealed no advantage with USAT. Our inclusion criteria for massive and submassive pulmonary embolism (PE) were clearly defined along with three exclusion criteria. The claim that no subjects were included who failed anticoagulation treatment is untrue. We used CDT as first-line treatment escalation in 97% of patients (98 of 101) who failed anticoagulation treatment and as rescue therapy in three who failed treatment with anticoagulation and systemic tissue plasminogen activator. We also reported four deaths due to massive PE and two deaths from submassive PE. The observation that echocardiographic interpretations were not quantitative is a valid point. Nevertheless, alleviation of heart strain was validated in the majority by quantitative pulmonary artery pressure reduction—a reasonable proxy for improvement in right ventricular function. Dr Liang and colleagues appear surprised by the absence of major complications and they express uncertainty by stating the “jury is still out” on CDT, but these opinions contradict their own review: “There is increasing evidence that percutaneous CDIs [CDTs] are an essential, effective, and safe alternative to systemic thrombolysis or anticoagulation.”

The lack of long-term follow-up data was previously addressed, and longitudinal outcomes were not the primary aim of our registry. Currently, long-term data following systemic thrombolysis are also lacking, and more studies are needed to determine if escalation therapies can reduce the risk of chronic thromboembolic pulmonary hypertension. However, we believe it is essential to first understand whether CDT can be safely performed with immediate and short-term benefits—a primary aim of PERFECT.

Dr Liang and colleagues rightfully emphasize the need for more comparative data; however, they fail to mention the limitations of RCTs while ignoring the plethora of existing randomized data. The hypothesis that treatment escalation is beneficial has already been proved in multiple trials, and a meta-analysis of RCTs involving 2,115 patients with massive or submassive PE revealed lower all-cause mortality in those receiving systemic thrombolysis vs anticoagulation alone. However, systemic thrombolysis was also associated with a higher risk of major bleeding and hemorrhagic stroke. Consequently, Chatterjee and colleagues acknowledged future research should focus on the ideal method of thrombolytic administration to maximize clinical benefit and minimize bleeding risk. The PERFECT registry helps answer this call by studying the effects of targeted drug delivery using low-dose CDT as an alternative to systemic thrombolysis.

The PERFECT registry is also the first, to our knowledge, to include and safely treat patients who are not candidates for systemic thrombolysis. This is significant because 50% of patients with PE have contraindications to systemic thrombolysis, so a comparative study (CDT vs systemic thrombolysis) would exclude too many patients and introduce high sampling error. Therefore, RCTs demonstrating treatment efficacy in trial populations will need further validation by effectiveness data from real-world populations. From this standpoint, the pragmatic interpretation of the PERFECT registry is clearer within the broader scope of practice, since we now have stronger real-world evidence to support early trial data. Indeed, to our knowledge, PERFECT is the first multicenter registry revealing the clinical safety and effectiveness of CDT for acute PE in a real-world population.

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References


