Texas Heart Institute Journal

New Horizons in Pulmonary Embolectomy

Novel Pharmacomechanical Thrombolysis for Treating Intermediate-Risk Acute Pulmonary Embolism: The Bashir Endovascular Catheter

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Acute pulmonary embolism (PE) is the third most common cause of cardiovascular death.[1] Although there is little debate about how to manage low- or high-risk acute PE, therapeutic strategies for patients who have intermediate-risk acute PE are continuously evolving. This condition is associated with a substantial risk of death at 90 days and with possible progression to acute hemodynamic decompensation. In the Fibrinolysis for Patients with Intermediate Risk Pulmonary Embolism (PEITHO) trial,[2] normotensive patients were divided into 2 groups: one group was given tenecteplase plus heparin, and the other, placebo plus heparin. In the anticoagulation-only group, 28 of 499 patients (5.6%) died or progressed to hemodynamic decompensation, compared with 13 of 506 (2.6%) in the tenecteplase group; however, the rates of major bleeding and stroke were significantly higher in the tenecteplase group. The investigators recommended great caution in considering fibrinolytic therapy for hemodynamically stable patients with intermediate-risk PE, right ventricular (RV) dysfunction, and elevated cardiac troponin levels.[2] Systemic fibrinolytic therapy reduced the risk of hemodynamic decompensation but significantly increased the risk of stroke and intracranial hemorrhage (ICH).[2]

Patients with acute PE and RV strain have a low cardiac reserve and are subject to sudden decompensation. The therapeutic goal in patients with intermediate-risk PE, particularly in those at high intermediate risk, is to improve symptoms while lowering the risk classification or preventing near-term hemodynamic decompensation. Minimizing the risk of severe hemorrhagic complications while accelerating thrombus resolution is guiding new therapies for intermediate-risk acute PE.

Principles of Catheter-Directed Therapies for Acute Pulmonary Embolism

Two main goals of catheter-directed therapies for acute PE are unloading the RV and reestablishing blood flow across the pulmonary vascular bed to minimize ventilation-perfusion mismatch and thus improve oxygenation. Accordingly, the reduction in thrombus burden must sufficiently reduce the resistance to blood flow, unload the RV, and ensure flow to the distal alveolar vasculature that improves the alveolar gas exchange. Although thrombus can be aspirated from the segmental and even subsegmental pulmonary arteries by means of mechanical thrombectomy alone, adequate pulmonary vascular perfusion often necessitates infusion of an agent to lyse thrombi that occlude the distal small-caliber resistance and alveolar vessels.

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Safety and Effectiveness of Catheter-Directed Thrombolysis

The risk of major bleeding, especially ICH, has dampened enthusiasm for catheter-directed thrombolysis (CDT). Higher doses of tissue plasminogen activator (tPA) may reduce overall thrombus burden more effectively than lower doses do, but higher doses increase the risk of major bleeding. In a large study from the National Inpatient Sample, 50 of 7,119 patients (0.7%) who underwent CDT for deep vein thrombosis experienced ICH.[3] Of note, ICH also developed in 255 of 130,930 patients (0.2%) who underwent anticoagulation therapy without CDT.[3] Although rigorous patient selection and lower doses of tPA can reduce the risk of ICH during CDT, new catheter designs for targeted tPA delivery hold better promise for reducing bleeding risk without compromising the effectiveness of thrombolysis.

The Bashir Endovascular Catheter

The novel Bashir Endovascular Catheter (BEC) (Thrombolex, Inc.) enables both targeted thrombolytic delivery and mechanical thrombectomy to fragment thrombus and promptly restore alveolar blood flow in the presence of acute PE. The BEC (7F) has a spiral-cut infusion basket comprising 6 mini-infusion catheters with a total of 48 laser-drilled holes (Fig. 1). The basket comes in longer (12.5 cm) and shorter (10 cm, Bashir Short-Basket) versions, to accommodate pulmonary arteries of varying length. Each version shortens by approximately 2.5 cm when fully expanded and can reach a maximum diameter of 45 mm. The nitinol-reinforced spiral-cut basket can be collapsed and expanded repeatedly to create fissures in multiple planes within thrombus and thus fragment it.

Thrombus fragmentation increases the total surface area on which endogenous and exogenous fibrinolytic agents can bind to the clot-bound fibrin receptors. At the same time, the enlarged central channel created by the expanded basket promotes blood flow within the thrombus. Targeted infusion minimizes the thrombolytic agents from flowing downstream into the systemic circulation, thus lowering bleeding risks. Pulse-spraying diluted tPA through the expanded basket creates multiple trapped bubbles of the drug that continue to lyse the thrombus from within, even after the device is withdrawn from the patient's body. Figure 2 shows the successful dissolution of a saddle PE after treatment with the BEC.

The wire lumen of the BEC (diameter, 0.025 in) enables continuous, real-time monitoring of pulmonary artery pressures and mixed venous oxygen saturations during tPA infusion. Operators can thus individualize

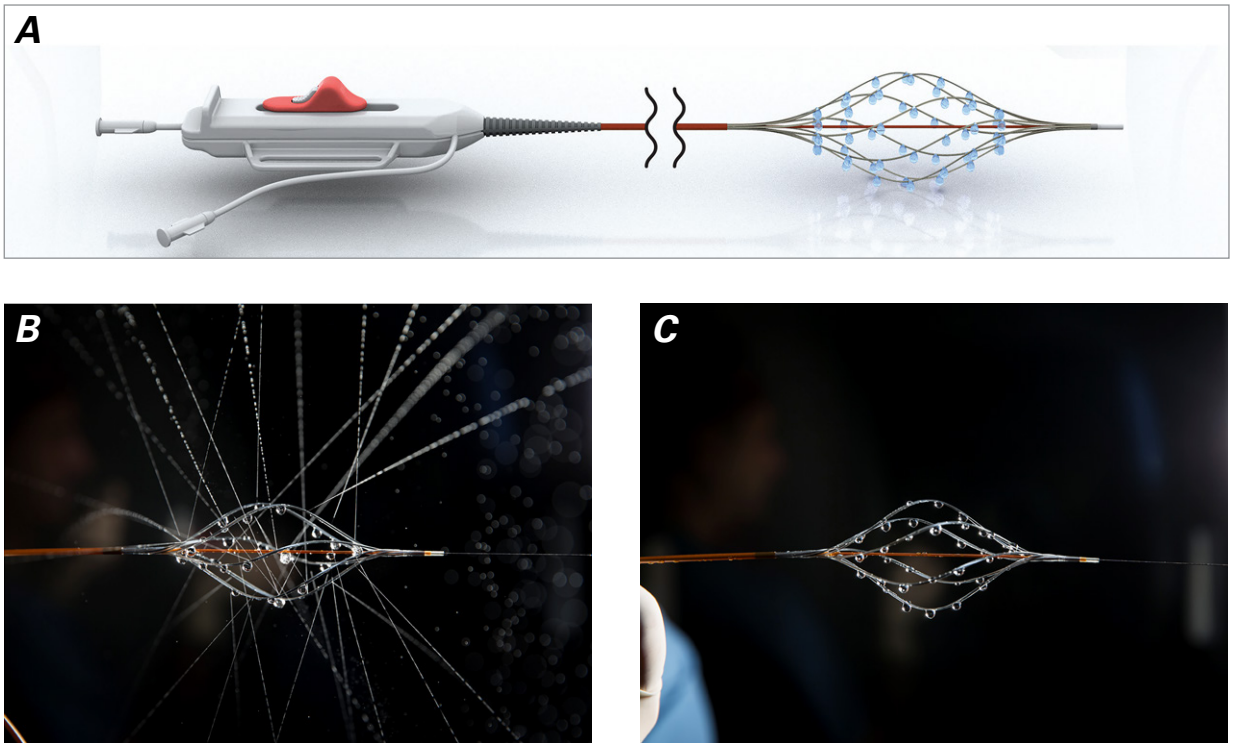

Fig. 1 *Photographs show* ***A****) the Bashir Endovascular Catheter, and tissue plasminogen activator* ***B****) pulse-sprayed and* ***C****) infused through an expanded basket.*

(Images courtesy of Joseph V. Labolito, Temple University)

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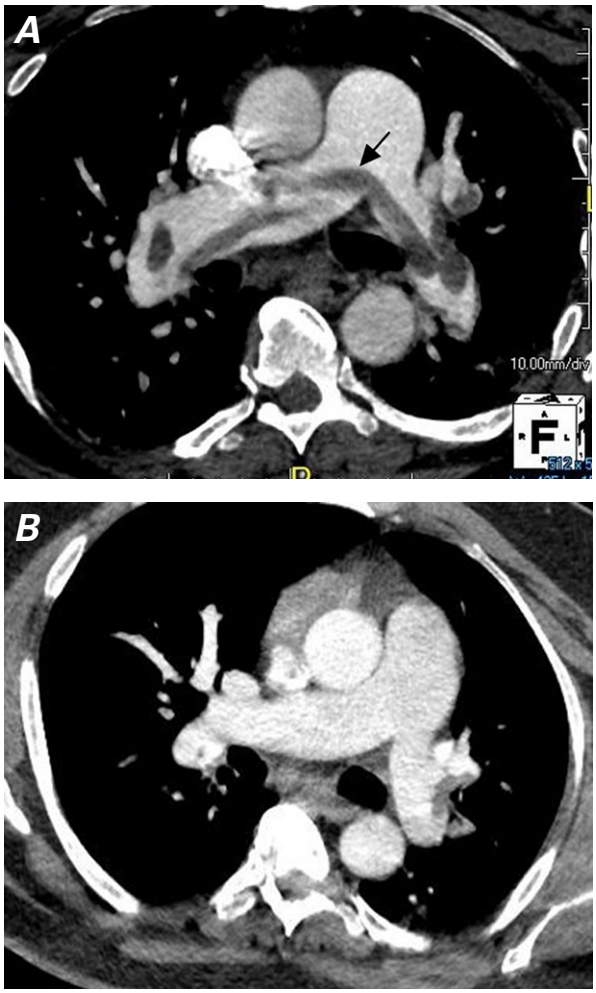

Fig. 2 *Computed tomograms (cross-sectional views) show* ***A****) a saddle pulmonary embolus (arrow) and* ***B****) resolution after thrombolysis with use of the Bashir Endovascular Catheter.*

therapy by shortening the infusion duration and reducing the tPA dose as the patient's hemodynamic status improves.

The first-in-human study of the BEC was conducted at 4 sites in the United States, in 9 patients who had intermediate-risk acute PE and symptom duration of <14 days.[4] Device use was successful in all cases, with no associated adverse events or major bleeding. At 48 hours, the mean RV-to-left ventricular diameter ratio was reduced by 37%, from 1.52 ± 0.27 at baseline to 0.97 ± 0.06 (P=0.0009). Thrombus burden was reduced by 37.1% (evaluated with use of the Modified Miller Index) from 25.4 ± 5.3 at baseline to 16 ± 4 at 48 hours (P=0.0005). The total 8-hour dose of tPA for bilateral PE in 8 of 9 patients was 14 mg (7 mg/lung), and it was 12 mg for unilateral PE. The average dose administered was close to that administered in arm 3 of the Optimum Duration of Acoustic Pulse Thrombolysis Procedure in Acute Intermediate-Risk Pulmonary Embolism (OPTALYSE PE) trial,[5] in which different dosing regimens were evaluated during ultrasound-assisted thrombolysis in patients with intermediate-risk PE. Of note, the mean reduction in thrombus burden was 14% ± 11.7% with use of the EkoSonic Endovascular System (Boston Scientific Corporation). Although our trial did not compare the EkoSonic system with the BEC, our results suggest more effective thrombus resolution.

The BEC's safety and effectiveness are being evaluated in the RESCUE trial,[6] sponsored by the National Heart, Lung, and Blood Institute. This prospective multicenter trial is currently enrolling patients.

Conclusion

Catheter-directed therapies for intermediate-risk acute PE have evolved. Optimal device designs are needed to improve patient outcomes and minimize bleeding events. The BEC enables targeted tPA delivery across a wider cross-sectional thrombotic area than that currently afforded by other CDT devices. This capability maximizes the number of plasminogen binding sites as thrombus is fragmented, enabling adequate reperfusion of the pulmonary alveolar vasculature with substantially lower doses of tPA than are typical. An early feasibility study has suggested promising results, and outcomes are being evaluated further in a larger multicenter study.

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Conflict of interest disclosures: Dr. Bashir has equity interest in Thrombolex, Inc., and receives research support from the National Institutes of Health. Dr. Singh has received a research grant and funding support from the Donald Guthrie Research Foundation.

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Erratum

Editorial Error

In the article titled "Novel Pharmacomechanical Thrombolysis for Treating Intermediate-Risk Acute Pulmonary Embolism: The Bashir Endovascular Catheter,"[1] published online 15 December 2021, the *Texas Heart Institute Journal* editorial staff inadvertently changed *thrombotomy* to *thrombectomy*. The following sentence on page 2 of the PDF should read as follows: "The novel Bashir Endovascular Catheter (BEC) (Thrombolex, Inc.) enables both targeted thrombolytic delivery and mechanical *thrombotomy* to fragment thrombus and promptly restore alveolar blood flow in the presence of acute PE."

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