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## Pharmacomechanical therapy for deep-vein thrombosis

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## Pharmacomechanical Therapy for Deep-Vein Thrombosis

**TO THE EDITOR:** Regarding the recently published trial by Vedantham et al. (Dec. 7 issue),<sup>1</sup> we wish to comment on the results that show an apparent lack of effectiveness of pharmacomechanical catheter-directed thrombolysis in preventing the post-thrombotic syndrome in patients with acute proximal deep-vein thrombosis. Only 58% of the patients had deep-vein thrombosis involving the iliac or common femoral veins, whereas 42% had femoral deep-vein thrombosis, which is associated with a lower risk of the post-thrombotic syndrome.<sup>2</sup> In addition, a high percentage of patients (28%) received a venous stent (vs. 5.7% of the patients in the CAVENT [Catheter-Directed Venous Thrombolysis in Acute Iliofemoral Vein Thrombosis] trial<sup>3</sup>). We wonder whether stent occlusion may have contributed to a higher incidence of the post-thrombotic syndrome in the pharmacomechanical-thrombolysis group than in the control group. Finally, various nonstandardized methods of pharmacomechanical catheter-directed thrombolysis were used, which makes interpretation difficult. Despite all these factors, the incidence of moderate-to-severe post-thrombotic syndrome was substantially lower in the pharmacomechanical-thrombolysis group than in the control group, and there were similar rates of major bleeding events at 24 months in the two groups. Given these issues, we believe that the outcomes of this trial are not generalizable. However, this trial does highlight the need for further studies with careful selection of patients and a more standardized approach.

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No potential conflict of interest relevant to this letter was reported.

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**THE AUTHORS REPLY:** Patients with femoral deep-vein thrombosis were included in our trial because they also are at high risk for the post-thrombotic syndrome (which occurred in our trial in 44% of the patients with femoral deep-vein thrombosis vs. 50% of those with iliofemoral deep-vein thrombosis).<sup>1</sup> Even in patients with iliofemoral deep-vein thrombosis, pharmacomechanical thrombolysis did not prevent the post-thrombotic syndrome (which occurred in 49% of the patients with iliofemoral deep-vein thrombosis in the pharmacomechanical-thrombolysis group and in 51% of those in the control group). However, pharmacomechanical thrombolysis resulted in a lower rate of moderate-to-severe post-thrombotic syndrome and in less severity of the symptoms and signs of the post-thrombotic syndrome than was observed in the control group. These benefits appeared to be confined to patients with iliofemoral deep-vein thrombosis.

The thrombolytic methods used in this trial were standardized and reflected contemporary practice in the United States.<sup>2</sup> All the operators were credentialed, and there were rigorous requirements for thrombolytic-drug administration and device use. Per accepted practice, stenting of residual iliac-vein lesions causing a reduction

of more than 50% in the vein diameter, a pressure gradient of more than 2 mm Hg, or robust collateral filling was encouraged.<sup>3,4</sup> In the absence of a convincingly higher rate of recurrent deep-vein thrombosis in the pharmacomechanical-thrombolysis group than in the control group, it is unlikely that stent thrombosis was an important contributor to the post-thrombotic syndrome. The broad inclusion criteria, contemporary thrombolytic methods, and accommodation of physician expertise that were used in our trial support the generalizability of its results.

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Since publication of their article, the authors report no further potential conflict of interest.

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## Pleural Disease

**TO THE EDITOR:** With regard to the article by Feller-Kopman and Light (Feb. 22 issue),<sup>1</sup> the distinction between spontaneous pneumothorax that occurs in apparently healthy persons and pneumothorax caused by preexisting pulmonary disease may seem arbitrary in terms of treatment, but an important aspect of the management of this condition is an evaluation for genetic disorders.

A total of 10% of patients with spontaneous pneumothorax have a family history of pneumothorax.<sup>2</sup> Heterozygous mutations in the tumor-suppressor gene *FLCN* predispose to the Birt-Hogg-Dubé syndrome, which is the most common genetic disorder in persons with familial pneumothorax. This syndrome, which is identified in 10 to 15% of persons with familial pneumothorax, is associated with renal cancer.<sup>3</sup> Spontaneous pneumothorax is also a complication of certain genetic disorders that affect the integrity of connective tissue, transforming growth factor  $\beta$  signaling, or both. These disorders include Marfan's syndrome, the Loeys-Dietz syndrome, vascular Ehlers-Danlos syndrome, and homocystinuria. Moreover, inhibition of mechanistic target of rapamycin (mTOR) is a therapeutic target for pulmonary disease in tuberous sclerosis and lymphangioleiomyomatosis.<sup>4</sup>

The identification of a genetic disorder that

predisposes to pneumothorax is valuable in guiding surveillance for life-threatening extrathoracic manifestations and in counseling at-risk family members. Identification of molecular mechanisms presents possible therapeutic targets.

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No potential conflict of interest relevant to this letter was reported.

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**TO THE EDITOR:** Feller-Kopman and Light did not mention two possible therapeutic options for refractory hepatic hydrothorax. These options are placement of a transjugular intrahepatic portosystemic shunt (TIPS) and liver transplantation.

The use of a TIPS has been investigated in a number of uncontrolled studies and several case