

Thrombolysis for DVT: Has the Time Arrived?

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Purpose

In *AFP Journal Club*, three presenters review an interesting journal article in a conversational manner. These articles involve hot topics that affect family physicians or “bust” commonly held medical myths. The presenters give their opinions about the clinical value of the individual study discussed. The opinions reflect the views of the presenters, not those of *AFP* or the AAFP.

Article

Bashir R, Zack CJ, Zhao H, Comerota AJ, Bove AA. Comparative outcomes of catheter-directed thrombolysis plus anticoagulation vs anticoagulation alone to treat lower-extremity proximal deep vein thrombosis. *JAMA Intern Med.* 2014;174(9):1494-1501.

For more information on evidence-based medicine (EBM) terms, see the EBM Toolkit at <http://www.aafp.org/afp/ebmtoolkit>.

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Is catheter-directed thrombolysis safe and effective in proximal deep venous thrombosis (DVT)?

Mark: It would be nice to be able to prevent postphlebotic syndrome in patients after a DVT. Postphlebotic syndrome can cause confusion: Is it a new DVT? Is it cellulitis? Is it just postphlebotic syndrome? We know that thrombolysis works to prevent postphlebotic syndrome (number needed to treat = 7¹), but is the risk worth the benefit? It depends.

What does this article tell us?

Mark: This is a retrospective study of the safety of catheter-directed thrombolysis for proximal DVTs in 90,618 patients who were hospitalized between 2002 and 2010 (estimated to be about one-fourth of the cohort hospitalized during those years). Of these patients, 3,649 underwent catheter-directed thrombolysis. Those who received thrombolysis were compared with those who received standard anticoagulation after propensity matching.

In terms of outcomes, all of the risk numbers favored *not* using catheter-directed thrombolysis. The rate of blood transfusion

was 11.1% in the thrombolysis group vs. 6.5% in the anticoagulation group (odds ratio [OR] = 1.85; 95% confidence interval [CI], 1.57 to 2.20; *P* < .001), the rate of pulmonary embolism was 17.9% vs. 11.4% (OR = 1.69; 95% CI, 1.49 to 1.94; *P* < .001), and the rate of vena cava filter placement was 34.8% vs. 15.6% (OR = 2.89; 95% CI, 2.58 to 3.23; *P* < .001). Intracranial bleeding, length of hospital stay, and cost were also more favorable with standard treatment.

Should we believe this study?

Jill: Yes. Although there are some weaknesses that we will discuss later, the study design is generally sound. Two questions we need to ask are: What is propensity matching? Does this do a good job of controlling for possible bias in retrospective studies?

Bob: Propensity matching is used in retrospective studies to adjust for the retrospective design by allowing us to compare like to like; we determine ahead of time how likely it is that an individual will get a particular treatment. The idea is that we sort patients into groups by characteristics. This allows for a balanced comparison, much like in a randomized trial.

Mark: We need to compare two groups that have the same probability of getting a treatment. We may take patients who smoke, are obese, and are hypertensive and figure out how likely they are to get a treatment. We then compare them to other obese, hypertensive smokers so that patients in both groups have the same a priori likelihood of getting a treatment based on underlying factors; it just turned out that the clinicians chose to treat some in this group with the therapy and others without. ▶

The patients can (and should) be stratified even more finely: Smokers who smoke 10 cigarettes per day and have a 5% chance of getting a treatment should be compared to others who have the same characteristics and the same probability of getting the treatment. This allows us to decide whether the outcome is due to the treatment or to the underlying characteristics that lead to the treatment in the first place.

Jill: Propensity matching can also be used in cases in which it would be unethical or unreasonable to do a randomized study. For example, we may want to see how smoking affects the development of lung cancer in people exposed to radon. We can't randomize some participants to smoke (or randomly expose them to radon for that matter), and we can't retrospectively compare smokers directly to nonsmokers. There may be factors associated with smoking that are also important in predicting the outcome (e.g., poverty, education, other chemical exposures). Therefore, we need to compare smokers with a lower educational and income level who were exposed to radon to smokers with the same educational and income level who were not exposed to radon. This is propensity matching.

Bob: So let's talk about what this really means for patients. I think it's time to move away from the term risk-benefit because these are unequal measures. What we are really asking is what is the chance of harm vs. the chance of benefit? As Mark noted, a previous study demonstrated that catheter-directed thrombolysis produced a number needed to treat of 7 (i.e., there is a one in seven chance of decreasing the development of a postphlebotic syndrome compared with traditional therapy).¹ But what is the potential harm, also known as the number needed to harm? Although there is no increase in death rates associated with catheter-directed thrombolysis, one in 22 patients will require blood transfusions, one in 11 will develop a pulmonary embolism, and one in five will require a vena cava filter. On average, catheter-directed thrombolysis leads to 2.2 more days in the hospital per patient and

Main points

- Catheter-directed thrombolysis for proximal DVT is not ready for prime time. Physicians might consider it for patients with phlegmasia and resulting compartment syndrome. It should be avoided in patients who are at high risk of bleeding or who have other risk factors.
- Postphlebotic syndrome can be avoided with catheter-directed thrombolysis, but the number needed to treat is 7.

EBM Points

- Propensity matching is used to remove confounders in retrospective studies. The idea is to balance the groups being compared in their likelihood of needing a therapy.
- Look at the dates the data were generated and not the date of publication. If the data are old, updates in technology and treatments may affect the outcomes.

\$57,000 more in medical costs per hospitalization when compared with traditional therapy.¹

Mark: One problem with this study is that the data are from 2002 to 2010. A lot has changed in anticoagulation and catheter technology since then. How this study applies to catheter-directed thrombolysis in 2014 to 2015, we don't know. A randomized trial using current technology would be ideal.

What should the family physician do?

Mark: This therapy is still experimental. Physicians might want to consider it in a patient with phlegmasia and resulting compartment syndrome, but probably not for those with milder disease.

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