

Clot-busting drugs not recommended for most patients with blood clots

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Not all patients with blood clots in their legs - a condition known as deep vein thrombosis - need to receive powerful but risky clot-busting drugs, according to results of a large-scale, multicenter clinical trial.

The study showed that clearing the clot with drugs and specialized devices did not reduce the likelihood that patients would develop post-thrombotic syndrome, a complication that can leave patients with chronic limb pain and swelling, and can lead to difficulty walking or carrying out their daily activities. Use of the potent drugs did, however, raise the chance that a patient would experience a dangerous bleed.

"What we know now is that we can spare most patients the need to undergo a risky and costly treatment," said principal investigator Suresh Vedantham, MD, a professor of radiology and of surgery at Washington University School of Medicine in St. Louis.

The findings are published Dec. 7 in *The New England Journal of Medicine*.

Between 300,000 and 600,000 people a year in the United States are diagnosed with a first episode of deep vein thrombosis and, despite standard treatment with [blood thinners](#), roughly half will develop post-thrombotic syndrome. There is no treatment to prevent the potentially debilitating complication. However, small studies had suggested that a procedure that delivers [clot-busting drugs](#) directly into the clot may reduce the chance the syndrome will develop. The procedure is currently used as a second-line treatment to alleviate pain and swelling in people who do not improve on blood thinners.

The Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis (ATTRACT) study - a randomized controlled trial primarily funded by the National

Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH) - was designed to determine whether performing the procedure as part of initial treatment for patients when they are first diagnosed with deep vein thrombosis would reduce the number of people who later develop the syndrome. In 2008, then-Acting Surgeon General Steven K. Galson, MD, issued a national call to action on deep vein thrombosis and specifically called for research into the benefits and risks of removing clots.

"The clinical research in deep vein thrombosis and post-thrombotic syndrome is very important to the clinical community and of interest to the National Heart, Lung, and Blood Institute," said Andrei Kindzelski, MD, PhD, the NHLBI program officer for the ATTRACT trial. "This landmark study, conducted at 56 clinical sites, demonstrated in an unbiased manner no benefits of catheter-directed thrombolysis as a first-line deep vein thrombosis treatment, enabling patients to avoid an unnecessary medical procedure. At the same time, ATTRACT identified a potential future research need in more targeted use of catheter-directed thrombolysis in specific patient groups."

The study involved 692 patients, randomly assigned to receive blood thinners alone or blood thinners and the procedure. Each patient was followed for two years.

In the procedure, doctors insert a thin, flexible plastic tube through a tiny incision in the leg and navigate it through the veins using X-ray and ultrasound guidance, until it rests within the clot. They instill a drug known as tissue plasminogen activator through the tube, give it time to digest the clot and then suck out or grind up any remaining fragments using specialized catheter-mounted devices. The procedure is expensive, costing thousands of dollars, and often requires a hospital stay.

The clinical trial showed that routine use of the procedure did not reduce the chance of developing post-thrombotic syndrome. The complication developed in 157 of 336 (47 percent) of people who underwent the procedure and 171 of 355 (48 percent) of people who did not, a difference that is not statistically significant.

The procedure did reduce the severity of post-thrombotic syndrome, easing patients' long-term symptoms. About 24 percent of people on blood thinners alone experienced moderate to severe pain and swelling, but only 18 percent of people who were treated with blood thinners and clot busters did so.

The procedure also alleviated pain and swelling in the early stages of the disease, when patients are often very uncomfortable.

However, the researchers noted a worrisome increase in the number of people who developed major bleeding after undergoing the procedure. While the numbers were small - one patient (0.3 percent) on standard treatment experienced a bleed, compared with six (1.7 percent) of those who received clot-busting drugs - and none of the bleeds was fatal, any increase in bleeding is a red flag. The potential for catastrophic bleeding is why powerful clot-busting drugs usually are reserved for life-threatening emergencies such as heart attacks and strokes.

"We are dealing with a very sharp double-edged sword here," said Vedantham, who also is an interventional radiologist at the university's Mallinckrodt Institute of Radiology. "None of us was surprised to find that this treatment is riskier than blood-thinning drugs alone. To justify that extra risk, we would have had to show a dramatic improvement in long-term outcomes, and the study didn't show that. We saw some improvement in disease severity but not enough to justify the risks for most patients."

While the study showed that most patients should not undergo the procedure, the data hint that the benefits may outweigh the risks in some patients, such as those with exceptionally large clots.

"This is the first large, rigorous study to examine the ability of imaging-guided treatment to address post-thrombotic syndrome," Vedantham said. "This study will advance patient care by helping many people avoid an unnecessary procedure. The findings are also interesting because there is the suggestion that at least some patients may have benefited. Sorting that out is going to be very important. The ATTRACT trial will provide crucial guidance in designing further targeted studies to determine who is most likely to benefit from this procedure as a first-line treatment."

For now, the [procedure](#) should be reserved for use as a second-line [treatment](#) for some carefully selected [patients](#), who are experiencing particularly severe limitations of leg function from [deep vein thrombosis](#) and who are not responding to blood-thinners, Vedantham added.

Provided by Washington University School of Medicine

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