In patients with an acute proximal deep vein thrombosis, pharmacomechanical catheter-directed thrombolysis does not reduce the rate of post-thrombotic syndrome

Question

In patients who have symptomatic proximal deep vein thrombosis (DVT), does pharmacomechanical catheter-directed thrombolysis (PCDT) plus anticoagulant therapy prevent post-thrombotic syndrome compared with anticoagulant therapy alone?

The study

Who? 692 adults who had proximal DVT (involving the femoral, common femoral, or iliac vein), with symptoms occuring within 14 days of randomization.

What? PCDT plus anticoagulant therapy was compared with anticoagulant therapy alone. Patients in both groups received compression stockings.

PCDT plus anticoagulant therapy	vs	Anticoagulant therapy
Delivery of a fibrinolytic drug (alteplase) into the thrombus with mechanical thrombus maceration and aspiration within 14 days of DVT symptom onset. Anticoagulation during the procedure consisted of an infusion of therapeutic dose low-molecular-weight heparin or unfractionated heparin. Routine anticoagulation and compression stockings (knee high, providing 30-40 mmHg of pressure).		Routine anticoagulation and compression stockings (knee high, providing 30-40 mmHg of pressure).

What the researchers found

The rate of post-thrombotic syndrome did not differ for patients who received PCDT plus anticoagulant therapy compared with those who received anticoagulant therapy alone. However, patients who received PCDT had higher rates of major bleeding during the first 10 days of treatment.

The bottom line

In patients who have an acute proximal DVT, adding PCDT to anticoagulant therapy does not decrease the rate of post-thrombotic syndrome compared with anticoagulant therapy alone.

Summary of findings

PCDT plus anticoagulant therapy therapy vs anticoagulant therapy alone in people who have an acute proximal DVT

Outcomes	Rate of events with PCDT plus anticoagulant therapy	Rate of events with anticoagulant therapy	Absolute effect of PCDT
Post-thrombotic syndrome at 24 months	47%	48%	PCDT did not decrease the rate of post-thrombotic syndrome.*
Major bleeding within 10 days	1.7%	0.3%	About 1 more person out of 100 had a major bleed after receiving PCDT.

*Although the rates for the 2 groups look different, the differences were not statistically significant—this means that the difference could simply be due to chance rather than due to the different treatments.

This Evidence Summary is based on the following article:

Vedantham S, Goldhaber SZ, Julian JA, et al. ***Pharmacomechanical Catheter-Directed Thrombolysis for Deep-Vein Thrombosis.*** *N Engl J Med. 2017;377:2240-2252. doi: 10.1056/NEJMoa1615066. PubMed (https://www.ncbi.nlm.nih.gov/pubmed/29211671?dopt=Abstract)*

Does pharmacomechanical catheter-directed thrombolysis (PCDT) reduce the development of post-thrombotic syndrome after proximal deep vein thrombosis (DVT)?

Why is post-thrombotic syndrome after DVT important?

Post-thrombotic syndrome is a common complication that occurs in 25-50% of patients with a proximal lower-extremity DVT. Symptoms of PTS include lower-extremity pruritus, edema, pain, heaviness, venous stasis dermatitis, and skin ulceration. Most patients who develop post-thrombotic syndrome do so within 2 years of being diagnosed with DVT. The development of post-thrombotic syndrome can impair quality of life, interfere with ability to work, and is costly to the health care system. Therefore, reducing the rate of post-thrombotic syndrome PTS is a clinically important outcome.

What is pharmacomechanical catheter-directed thrombolysis?

Previous studies have looked at post-thrombotic syndrome rates after infusing fibrinolytic agents directly into the thrombus (a procedure called "catheter-directed thrombolysis"). PCDT uses infusion of thrombolytics *in combination* with a device that mechanically "chews up" the thrombus. The hypothesis is that actively removing the thrombus opens the vein more rapidly and restores blood flow, thereby reducing post-thrombotic syndrome.

What were the results of the ATTRACT Trial, and how can I apply them to my patient?

Most current guidelines state that PCDT can be considered in patients with an iliofemoral DVT, as long as the procedure occurs within 14 days of the start of symptoms.[1,2] However, these recommendations were made before the results of the ATTRACT Trial were published. The ATTRACT Trial found that adding PCDT to anticoagulation did *not* significantly decrease the overall rate of post-thrombotic syndrome after 2 years, and patients who received PCDT had a higher incidence of early major bleeding. Although the trial found that the rate of *moderate or severe* post-thrombotic syndrome was decreased with PCDT, patient-reported quality of life did not improve after 24 months. A prespecified subgroup analysis showed that adding PCDT to anticoagulation did not reduce the rate of post-thrombotic syndrome even in patients with iliofemoral (more proximal) DVT compared with femoropopliteal (more distal) DVT. Overall, the ATTRACT Trial showed that adding PCDT to standard anticoagulation did *not* change long-term outcomes.

This trial showed that the benefit of PCDT may be to reduce patient-reported leg pain and edema in the short term (within 30 days of symptom onset). However, the reduction in patient-reported pain with PCDT was small (a reduction of about 0.3 points on a 7-point Likert pain scale) and came at a cost of higher major early bleeding rates (with about 1 out of 100 patients having a major bleed within 10 days after PCDT).

Did this trial have any limitations?

- The type of device and duration of fibrinolytic infusion used for PCDT therapy varied. Some devices and treatment protocols may be better than others at reducing post-thrombotic syndrome rates.
- More patients in the anticoagulant therapy alone group missed at least 1 of the assessments for post-thrombotic syndrome. Therefore, the rate of post-thrombotic syndrome in this group may be higher than what was reported. However, it is reassuring that the overall rate of post-thrombotic syndrome in this trial is similar to what other studies have reported.[3]

Doctor, I have just been told I have a DVT, and my leg is very large and painful. Can you do something to remove the clot?

There is an invasive procedure called pharmacomechanical catheter-directed thrombolysis (PCDT), which uses a combination of "clot busting" medications and a mechanical device to break up the clot. However, a recent study showed that while PCDT reduced pain and swelling by a small amount in the short term, it did not reduce the risk of long-term complications such as post-thrombotic syndrome (chronic painful swelling of the leg), and more important, it caused more serious bleeding than treatment with anticoagulants (blood-thinners) alone. Most people will see improvement in their leg symptoms as their body works on slowly breaking down the clot over time. Anticoagulant therapy is taken to prevent further clotting while healing is taking place.

1. Thrombosis Canada. (2017). Deep Vein Thrombosis (DVT): Treatment. [online] Available at: http://thrombosiscanada.ca/clinicalguides.

2. Kearon, C., Akl, E., Ornelas, J., et al. Antithrombotic Therapy for VTE Disease. Chest, 2016;149:315-352.

3. Roumen-Klappe, E., den Heijer, M., Janssen, M., et al. The post-thrombotic syndrome: incidence and prognostic value of non-invasive venous examinations in a six year follow-up study. Thromb Haemost. 2005;94:825-30.

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