

## Isolated Clot, Real Error

March 1, 2018

Parks A, Fang MC. Isolated Clot, Real Error. PSNet [internet]. 2018.

<https://psnet.ahrq.gov/web-mm/isolated-clot-real-error>

---

### Case Objectives

- Appreciate that errors are common in the management of venous thromboembolism disease.
- Describe patients with venous thromboembolism in whom anticoagulation may not be necessary.
- State key principles in the treatment of venous thromboembolism.
- Describe the appropriate evaluation for thrombophilia and cancer in patients with venous thromboembolism.
- Recognize CT pulmonary angiography may lead to overtreatment of subsegmental pulmonary emboli.

### The Case

A 65-year-old woman underwent an elective hysterectomy and had a complicated postoperative course, including excessive bleeding during the procedure. She was given multiple blood products and developed acute respiratory distress syndrome (ARDS) and respiratory failure requiring mechanical ventilation. She spiked a fever, and her temperature remained elevated through her sixth day in the intensive care unit (ICU). An extensive evaluation for infection failed to reveal a source.

On rounds, the team decided to order whole-leg Doppler ultrasounds of both lower extremities looking for a deep venous thrombosis (DVT) as a cause of the fevers. That afternoon, the intern checked the results and noted the first line of the final result stated "Positive. Thrombosis of right lower extremity." Because she was trying to sign out at the end of the day, she did not read the entire report. No other provider reviewed the official results.

The next day on rounds, the intern reported to the rest of the ICU team that the ultrasound was positive for a DVT. Because of the patient's life-threatening postoperative bleeding, the team agreed the patient was not a candidate for anticoagulation (the usual treatment for DVT). Instead, they ordered an inferior vena cava (IVC) filter in the hopes that it would prevent a pulmonary embolism (PE). She tolerated the placement of the filter without complication.

The next week, a new team started in the ICU. They were reviewing the plan of care and discussed the reason for the IVC filter (an unusual intervention given recent studies questioning its overall benefit). The senior resident reviewed all of the radiology records and read the original ultrasound report, which did state there was a thrombosis in the right lower extremity, but went on to describe it as being localized to the great saphenous vein. This particular vein is considered a superficial vein, meaning that a clot in it carries very low risk for PE and should not have been treated with placement of an IVC filter. The team determined that the next step in management should have been active surveillance with repeat ultrasound.

The team recognized the error and disclosed it to the patient and family. The family was upset but understood the confusion. A repeat ultrasound of the right leg showed resolution of the thrombosis. The IVC filter was removed the following day without complication. The patient experienced no direct consequences from the placement of the IVC filter and slowly recovered over the next few weeks.

## The Commentary

by Anna Parks, MD, and Margaret C. Fang, MD, MPH

Venous thromboembolism (VTE) is a common cardiovascular condition that affects more than 500,000 people each year.<sup>(1)</sup> Although substantial evidence and numerous guidelines exist, many common errors are made in the management of VTE. In this commentary, we will discuss specific management aspects of this case and offer recommendations ([Table](#)) to help clinicians avoid common areas of mismanagement when treating VTE.

### Specific Errors in This Case

*Routine evaluation of suspected deep vein thrombosis does not require whole-leg ultrasound.* This patient underwent whole-leg ultrasound in the workup of fever, which then revealed a superficial vein thrombosis. However, guidelines recommend against obtaining routine whole-leg ultrasound when deep vein thrombosis (DVT) is suspected.<sup>(2,3)</sup> Whole-leg ultrasounds that examine the proximal and distal veins are time-consuming, require specialized operators, and may identify thromboses, such as calf vein DVTs, that are unlikely to progress to pulmonary embolism (PE).<sup>(4)</sup> In addition, false positive findings are common and may lead to potentially harmful treatment with anticoagulants. In this patient, it would have been reasonable to ultrasound just the proximal veins if DVT was a concern.

*Anticoagulation is not always necessary for superficial vein thrombosis or isolated calf vein thrombosis.* This patient actually had a thrombosis of a superficial vein (great saphenous vein), not a deep vein, and placing an inferior vena cava (IVC) filter probably had more risks than benefits. In this patient, obtaining serial ultrasounds to look for clot propagation of the superficial vein thrombosis would have been preferable. Even if the thrombosis had been in the deep venous system, filter placement or anticoagulation is not always required. For example, isolated calf vein DVTs (in the deep veins, e.g., anterior tibial) have a low risk of progressing to PE. Updated guidelines now recommend surveillance without anticoagulants for calf vein thromboses in patients with high bleeding risk or who do not have risk factors for extension. Factors that increase risk of extension to proximal DVT and swing the balance in favor of anticoagulation include an elevated D-dimer, unprovoked clots, active cancer, or severe symptoms, as well as patients with

extensive thrombus or clot close to the proximal system.(2) Some clinicians maintain that thrombosis confined to the calf muscle veins (soleus and gastrocnemius) have lower risk of proximal extension and thus would favor surveillance for these clots, while others do not make this distinction.(4)

*Use of IVC filter was not indicated.* Because the clinicians treating this patient did not initially realize the clot was superficial, an IVC filter was placed. Since the 1990s, the use of IVC filters has increased markedly despite limited evidence on their efficacy. To date, the only universal recommendation for IVC filters is for acute treatment of proximal DVT and/or PE in patients with absolute contraindications to anticoagulation.(5,6) Randomized trials in the modern era assessing outcomes of IVC filter placement (which only included patients who were also treated with anticoagulants) did not find a clear benefit to filter placement.(7) Inferior vena cava filters are not entirely benign interventions. They can lead to occlusion, embolization, fracture, and filter-associated lower extremity DVT. In contrast to what is sometimes observed in clinical practice, filters should not be used as a way to prevent VTE after trauma surgery, nor should they be placed when patients are able to receive anticoagulation.(2,7)

## **Other Common Pitfalls in the General Management of VTE**

*Double-check the dosing of direct oral anticoagulants.* Direct oral anticoagulants (DOACs), such as dabigatran, rivaroxaban, apixaban, and edoxaban, are now widely used in the treatment and prevention of VTE. Unlike warfarin, DOACs do not require routine dose adjustment or monitoring. However, clinicians should be aware of several important aspects of DOAC dosing. First, both underdosing and overdosing are associated with adverse clinical outcomes. A recent study found that 43% of patients whose renal function merited dose reduction were prescribed standard doses, which increased bleeding risk. In addition, 13% of patients without an indication for dose reduction received lower-than-standard doses; this was more common in elderly patients.(8) DOAC dosing should follow recommended guidelines and take into account renal function. Clinicians should also remember that for acute VTE treatment, rivaroxaban and apixaban require an initial period of higher dosing (3 weeks and 1 week, respectively), followed by a lower dose to complete the treatment course.

*Don't treat provoked VTE for longer than 3 months.* The initial period of anticoagulation after acute VTE is to suppress acute thrombus propagation. Following this initial period, continued anticoagulation is designed to prevent new thrombus formation. Provoked VTE—such as in the setting of surgery—does not require anticoagulation beyond 3 months.(3) In this setting, longer courses of treatment do not provide benefits and expose patients to increased bleeding risk.(9)

*Make sure thrombophilia testing is indicated and correctly performed.* Testing for thrombophilia, such as for Factor V Leiden mutation, antiphospholipid antibodies, or protein C or S deficiency, is overused and often incorrectly ordered. Thrombophilia testing during the acute VTE period or during anticoagulation can produce inaccurate results. A retrospective study of 1300 patients with acute VTE found that 24% were tested for thrombophilia, even though only 25% of tested patients met the eligibility criteria for testing.(10) Thrombophilia testing is rarely indicated for provoked VTE or in patients who require indefinite anticoagulation and where testing will not change management.(11) Clinicians should consider testing in (i) young (<50 years) patients with unprovoked VTE or VTE provoked by weak factors (minor surgery or prolonged air travel); (ii) those with first-degree family members with VTE at a young age; (iii) recurrent

VTE events, especially at a young age; and (iv) VTE at unusual sites, such as splanchnic or cerebral veins.(12) When testing for the antiphospholipid antibody syndrome, remember that repeat confirmatory testing should be obtained at least 12 weeks apart because single positive results often represent false positives.

*Venous thromboembolism should not always prompt additional cancer screening.* Patients with cancer have a significantly higher VTE risk, leading some clinicians to search aggressively for undiagnosed cancer in patients with acute VTE. The Screening for Occult Malignancy in Patients with Idiopathic Venous Thromboembolism (SOME) trial randomized 854 patients with acute unprovoked VTE to routine cancer screening versus routine cancer screening plus a computed tomography (CT) scan of the abdomen and pelvis.(13) Adding a CT scan did not reduce the number of missed cancers during follow-up, shorten the time to cancer diagnosis, increase the detection of occult or early-stage cancers, or reduce cancer-related mortality. So, when faced with an acute unprovoked VTE, clinicians should stick to routine and limited age- and sex-appropriate cancer screening.(14)

*Bridging is not always needed when interrupting anticoagulation.* Bridging anticoagulation refers to the use of a short-acting anticoagulant during periods when a longer acting anticoagulant needs to be temporarily interrupted, such as to accommodate an invasive procedure. Although widely used in clinical practice, there is growing evidence that bridging may offer little benefit in terms of reducing thrombotic risk, while significantly increasing bleeding risk. Randomized trial evidence does not support bridging for the majority of patients with atrial fibrillation.(15) Observational data now suggests that bridging is overused for VTE as well.(16) Bridging should be reserved for patients at high risk for VTE recurrence, such as patients in the active treatment phase (i.e., first 3 months) of VTE management.

*Use low-molecular-weight heparin as the initial treatment for cancer-related VTE.* Guidelines recommend using low-molecular-weight heparin (LMWH) as monotherapy, instead of warfarin or a DOAC, for the initial 3 to 6 month treatment of cancer-related VTE.(2) In practice, patients with cancer and VTE are not always prescribed extended-duration LMWH.(17) Randomized trial evidence supports the greater efficacy of LMWH over warfarin for VTE in cancer.(18) An open-label randomized controlled trial in cancer patients with VTE showed that the DOAC edoxaban was as effective as LMWH in preventing VTE recurrence but at the expense of increased major bleeding; additional trials are ongoing to further evaluate DOACs in this setting.(19) Although issues of patient preference and cost should be considered, clinicians should attempt to use LMWH as first-line treatment.

*CT pulmonary angiogram may lead to overtreatment of incidentally identified subsegmental PEs.* The widespread availability and advancement of CT pulmonary angiogram (CTPA) technology has contributed to increased detection of small or subsegmental PEs.(20) However, the clinical consequences of isolated subsegmental PEs are unclear. Moreover, CTPA is not always accurate, and the interpretation of CTPAs may vary by radiologist.(21) When faced with an incidentally identified subsegmental PE, clinicians should carefully consider whether it truly represents a real finding. Next, they should consider whether the PE really requires anticoagulation, assessing for factors that increase the risk of progression to more proximal PE. Guidelines now suggest that asymptomatic subsegmental PE in low-risk patients can be managed with simple clinical surveillance.(3)

In this case, several errors led to the adverse events: ordering a whole-leg ultrasound, misinterpreting a superficial vein thrombosis as a true DVT, and placing an IVC filter when it was not indicated. Ideally, this patient would have received an ultrasound of just the proximal veins. Then, when a superficial vein thrombosis was identified, serial ultrasounds could have been performed and both an IVC filter and anticoagulation could likely have been avoided.

Venous thromboembolism is a condition commonly faced by both inpatient and outpatient clinicians. Acknowledging that individual cases are often nuanced and influenced by many complex factors, including the lack of high-quality evidence in specific situations as well as variation in patient preference, we hope this discussion helps provide general guidance for clinicians to avoid common pitfalls in the management of VTE.

## Take-Home Points

- Errors are common in the management of venous thromboembolism disease.
- Anticoagulation is not necessary for all venous thromboembolism discovered on imaging. For example, anticoagulation is not always necessary for superficial vein thrombosis, isolated calf vein thrombosis, or subsegmental pulmonary embolism.
- Pharmacologic treatment of venous thromboembolism should follow evidence-based guidelines.

**Anna L. Parks, MD** Chief Resident, Department of Medicine University of California, San Francisco

**Margaret C. Fang, MD, MPH** Associate Professor of Medicine, Division of Hospital Medicine University of California, San Francisco Medical Director, UCSF Anticoagulation Clinic

## References

1. Beckman MG, Hooper WC, Critchley SE, Ortel TL. Venous thromboembolism: a public health concern. *Am J Prev Med.* 2010;38:S495-S501. [\[go to PubMed\]](#)
2. Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest.* 2012;141(suppl 2):e419S-e494S. [\[go to PubMed\]](#)
3. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. *Chest.* 2016;149:315-352. [\[go to PubMed\]](#)
4. Palareti G. How I treat isolated distal deep vein thrombosis (IDDVT). *Blood.* 2014;123:1802-1809. [\[go to PubMed\]](#)
5. Duffett L, Carrier M. Inferior vena cava filters. *J Thromb Haemost.* 2017;15:3-12. [\[go to PubMed\]](#)
6. Brunson A, Ho G, White R, Wun T. Inferior vena cava filters in patients with cancer and venous thromboembolism (VTE): patterns of use and outcomes. *Thromb Res.* 2016;140(suppl 1):S132-S141. [\[go to PubMed\]](#)

7. Mismetti P, Laporte S, Pellerin O, et al; PREPIC2 Study Group. Effect of a retrievable inferior vena cava filter plus anticoagulation vs anticoagulation alone on risk of recurrent pulmonary embolism: a randomized clinical trial. *JAMA*. 2015;313:1627-1635. [\[go to PubMed\]](#)
8. Yao X, Shah ND, Sangaralingham LR, Gersh BJ, Noseworthy PA. Non-vitamin K antagonist oral anticoagulant dosing in patients with atrial fibrillation and renal dysfunction. *J Am Coll Cardiol*. 2017;69:2779-2790. [\[go to PubMed\]](#)
9. Kearon C, Akl EA. Duration of anticoagulant therapy for deep vein thrombosis and pulmonary embolism. *Blood*. 2014;123:1794-1801. [\[go to PubMed\]](#)
10. Meyer MR, Witt DM, Delate T, et al. Thrombophilia testing patterns amongst patients with acute venous thromboembolism. *Thromb Res*. 2015;136:1160-1164. [\[go to PubMed\]](#)
11. Hicks LK, Bering H, Carson KR, et al. The ASH Choosing Wisely campaign: five hematologic tests and treatments to question. *Hematology Am Soc Hematol Educ Program*. 2013;2013:9-14. [\[go to PubMed\]](#)
12. Connors JM. Thrombophilia testing and venous thrombosis. *N Engl J Med*. 2017;377:2298. [\[go to PubMed\]](#)
13. Carrier M, Lazo-Langner A, Shivakumar S, et al; SOME Investigators. Screening for occult cancer in unprovoked venous thromboembolism. *N Engl J Med*. 2015;373:697-704. [\[go to PubMed\]](#)
14. Delluc A, Antic D, Lecumberri R, Ay C, Meyer G, Carrier M. Occult cancer screening in patients with venous thromboembolism: guidance from the SSC of the ISTH. *J Thromb Haemost*. 2017;15:2076-2079. [\[go to PubMed\]](#)
15. Douketis JD, Spyropoulos AC, Kaatz S, et al; BRIDGE Investigators. Perioperative bridging anticoagulation in patients with atrial fibrillation. *N Engl J Med*. 2015;373:823-833. [\[go to PubMed\]](#)
16. Clark NP, Witt DM, Davies LE, et al. Bleeding, recurrent venous thromboembolism, and mortality risks during warfarin interruption for invasive procedures. *JAMA Intern Med*. 2015;175:1163-1168. [\[go to PubMed\]](#)
17. Khorana AA, McCrae KR, Milentijevic D, et al. Current practice patterns and patient persistence with anticoagulant treatments for cancer-associated thrombosis. *Res Pract Thromb Haemost*. 2017;1:14-22. [\[Available at\]](#)
18. Akl EA, Kahale L, Barba M, et al. Anticoagulation for the long-term treatment of venous thromboembolism in patients with cancer. *Cochrane Database Syst Rev*. 2014;7:CD006650. [\[go to PubMed\]](#)
19. Raskob GE, van Es N, Verhamme P, et al. Edoxaban for the treatment of cancer-associated venous thromboembolism. *N Engl J Med*. 2018;378:615-624. [\[go to PubMed\]](#)
20. Wiener RS, Schwartz LM, Woloshin S. Time trends in pulmonary embolism in the United States: evidence of overdiagnosis. *Arch Intern Med*. 2011;171:831-837. [\[go to PubMed\]](#)

21. Hutchinson BD, Navin P, Marom EM, Truong MT, Bruzzi JF. Overdiagnosis of pulmonary embolism by pulmonary CT angiography. *AJR Am J Roentgenol.* 2015;205:271-277. [\[go to PubMed\]](#)

## Table

**Table. Ten Common Pitfalls in Venous Thromboembolism Treatment.**

1. Don't obtain whole-leg ultrasound in the routine evaluation of suspected DVT
2. Superficial vein thrombosis and isolated calf vein thrombosis do not always require anticoagulation
3. Only use an IVC filter if truly indicated
4. Double-check the dosing of direct oral anticoagulants
5. Don't treat provoked VTE for longer than 3 months
6. Make sure thrombophilia testing is indicated and correctly performed
7. Venous thromboembolism should not always prompt additional cancer screening
8. Bridging is not always needed when interrupting anticoagulation
9. Use low-molecular-weight heparin as the initial treatment for cancer-related VTE
10. CT pulmonary angiogram is not always accurate and may lead to overtreatment of incidentally identified subsegmental PEs

\*DVT=deep vein thrombosis; IVC=inferior vena cava; VTE=venous thromboembolism; PE=pulmonary embolism

*This project was funded under contract number 75Q80119C00004 from the Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Health and Human Services. The authors are solely responsible for this report's contents, findings, and conclusions, which do not necessarily represent the views of AHRQ. Readers should not interpret any statement in this report as an official position of AHRQ or of the U.S. Department of Health and Human Services. None of the authors has any affiliation or financial involvement that conflicts with the material presented in this report. [View AHRQ Disclaimers](#)*