

Is It Time to End the Therapeutic Nihilism Toward Treating VTE in Cancer Patients?

Cases highlighting the potential for early benefit and improved quality of life and function associated with the use of FlowTrierer and ClotTrierer Systems in patients with cancer and VTE.

WITH SIRISH A. KISHORE, MD, AND WILLIAM C. DILLON, MD, FACC



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The annual incidence rate of cancer in the United States is approximately 191 to 434 patients per 100,000 patients and is associated with a mortality rate of approximately 27.5% to 52%.¹ Venous thromboembolism (VTE) is a common complication of malignancy and a significant contributor to morbidity and mortality. For a patient with cancer, the risk of developing either deep vein thrombosis (DVT) or pulmonary embolism (PE) is up to 15% per year—four- to sevenfold higher than in the general population.² Not surprisingly, cancer patients account for an estimated 18% of total VTE cases.³

Although cancer itself is a well-known and established risk factor for thromboembolic events, multiple other cancer-, treatment-, and patient-specific VTE risk factors have been identified.^{4,5} These include advanced stage, primary tumor site, histopathologic type and grade, certain treatment regimens (antiangiogenic, hormonal, or erythropoiesis-stimulating drugs; radiation; indwelling venous access devices; transfusions; surgery), comorbidities (infections, renal disease, arterial thromboembolism, pulmonary disease), obesity, prothrombotic genotype, VTE history, diminished performance status, and certain biomarkers (inflammatory markers, platelet/leukocyte counts, hemoglobin levels).^{4,6} Also, the risk of developing VTE is highest in the first 3 to 6 months after cancer diagnosis.⁶ VTE diagnosis portends a worse prognosis in cancer patients than in noncancer patients, with a

threefold greater risk of recurrence and a twofold greater risk for major bleeding.⁷ The mortality rate in patients with cancer and VTE is greater than for those without VTE,³ with one study reporting VTE as the second leading cause of death in this population, along with infection.⁸ Finally, health care costs can almost double if a patient with cancer develops VTE.⁹

Advanced treatment options for VTE have been met with variable success and often require exposing patients to the increased bleeding risk associated with thrombolytic drugs.¹⁰⁻¹² Given the increased bleeding risk associated with cancer,⁷ this is of particular concern in the endovascular management of symptomatic VTE in the cancer population.

These factors demonstrate the prevalence, morbidity, and prognostic implications of cancer-related VTE, but they can also bias physicians against aggressive treatment due to a perception of overall limited benefit and higher risk.

To mitigate the elevated bleeding risk associated with thrombolytic drugs, Inari Medical has designed two mechanical thrombectomy devices to extract thrombus specifically within the venous system. First, the FlowTrierer System (Inari Medical)—comprising the Trierer20 (T20) aspiration guide catheter (Inari Medical) coupled with the add-on braided nitinol disks of the FlowTrierer catheter—has been used to successfully treat more than 2,000 patients with PE and inferior vena cava (IVC) thrombus. Second, the ClotTrierer System (Inari Medical), with a laser-cut nitinol coring element and attached woven nitinol collection bag for periprocedural embolic protection, has been used to successfully treat more than 2,000 patients with DVT. Importantly, both devices can effectively remove large amounts of thrombus in a single session.

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Although a rapid and thrombolysis-free thrombus removal system can be beneficial in many settings, this approach appears particularly compelling in cancer-associated VTE because it potentially expands candidacy for endovascular therapy in patients with a higher than average perioperative bleeding risk. Notable improvements in functional status associated with VTE intervention are either anecdotal or the subject of small case series in cancer patients. However, future prospective studies assessing improvements in quality of life and performance status are warranted and now feasible without the potential selection and reporting biases associated with thrombolytic contraindications in this understudied VTE population.

In this article, we present two case examples that highlight the potential early benefit of thrombolytic-free venous thrombectomy in cancer patients.

Successful Recanalization of a Malignant Occlusive DVT With ClotTrierer in a Patient With Metastatic Prostate Cancer

By Sirish A. Kishore, MD

PATIENT PRESENTATION

A 71-year-old man with high-grade, castration-sensitive, metastatic prostate cancer and extensive pelvic lymphadenopathy presented with 5 months of progressive right lower extremity swelling, pain, and heaviness, which was refractory to lymphedema physical therapy. He experienced a decline in performance status, primarily due to marked activity limitation from the condition of his right leg. He was unable to maintain employment or perform activities of daily living. He was also unable to climb stairs or exercise and required a walker to travel distances longer than 5 meters. All of this markedly affected his quality of life as well as his familial and professional relationships.

His case was referred to interventional radiology (IR) at a multidisciplinary tumor board, at which time a chronic, malignant, right ilioacaval venous stenosis and thrombotic right iliofemoral venous occlusion were incidentally diagnosed while assessing his candidacy for biopsy. Anticoagulation with enoxaparin was increased to therapeutic levels because of his elevated risk of recurrent right lower extremity DVT. His anticoagulation was ultimately interrupted due to massive retroperitoneal

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hemorrhage after a lymph node biopsy, necessitating coil embolization. His postprocedural course was further complicated by acute DVT extending from the right common femoral vein (CFV) through the central aspects of the femoral and profunda femoral veins, with worsening of his right lower extremity symptoms. At that time, he also began to experience additional swelling in his left ankle and foot. He was progressively titrated to a therapeutic dose of twice-daily enoxaparin over the next 3.5 weeks, with confirmation of therapeutic anti-Xa levels at the time of his postbiopsy IR appointment.

By the time his anticoagulation was therapeutic, approximately 3 to 4 weeks had elapsed between the new DVT diagnosis and the follow-up assessment, thus categorizing his thrombus as subacute to chronic. His CT venogram (CTV) showed persistent narrowing of the lower IVC, just central to the ilioacaval confluence, from nodal compression. In the right lower extremity, the common iliac vein (CIV) and central external iliac vein (EIV) were markedly stenotic from the infiltrative nodal mass, and the peripheral EIV through the CFV was occluded from chronic thrombus, which was exacerbated at that point by occlusive thrombus that propagated during his anticoagulation lapse (Figure 1A–C).

A new occlusive subacute-to-chronic component extended from the CFV through the profunda femoral vein and femoral vein without evidence of recanalization while anticoagulated. Additionally, there was moderate compression of his left CIV with new small nonocclusive thrombus in the peripheral aspect of the left CIV, suggesting that his left CIV stenosis may have also been hemodynamically significant.

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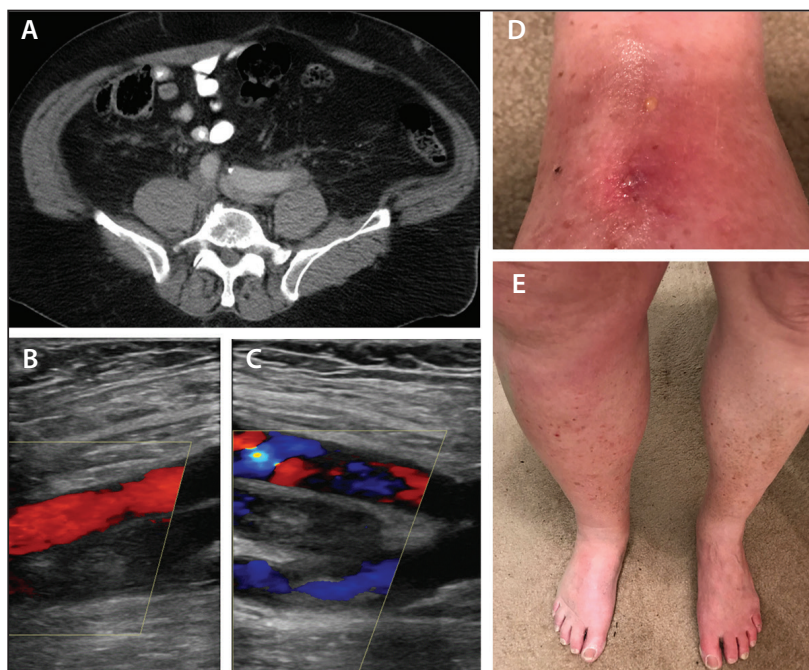


Figure 1. Preintervention assessment. CTV in a patient with prostate cancer revealed near-complete occlusion of the right CIV by several lymph nodes and a mild indentation of the left CIV by overlying left common iliac artery with small peripheral thrombus (A). On ultrasound, extension of occlusive thrombus into the central aspects of the CFV (B) and the femoral confluence (femoral vein and profunda femoral vein) was apparent (C). The patient showed early ulceration, weeping skin, lipodermatosclerosis, venous stasis changes (D), and size asymmetry of the legs (E).

The patient reported moderate pain and severe heaviness in his right leg, mild cramps, and paresthesia. The skin showed moderate induration, redness, and hyperpigmentation, with moderate venous ectasia and early venous ulceration present (Figure 1D). In his left leg, he noted new mild swelling, cramping, and heaviness with mild pitting edema—new since his lapse in anticoagulation. The right leg showed severe pretibial edema (Figure 1E) with a calf circumference of 52 cm, a thigh circumference of 74 cm, and an abnormal Villalta score of 30. For comparison, the left leg had a calf circumference of 39 cm, a thigh circumference of 59 cm, and a Villalta score of 4. The patient was scheduled for venography and an interventional procedure the next day.

PROCEDURAL OVERVIEW

The patient was positioned prone on the table. Both popliteal veins were accessed under direct ultrasound guidance, and two 10-F, 23-cm Brite Tip interventional sheaths (Cordis, a Cardinal Health company) were placed. Diagnostic venography confirmed thrombotic

chronic total occlusion of the right iliofemoral venous segment extending from the central aspect of the left femoral vein, with prominent collateral drainage arising from perforators and cross-filling pelvic collaterals. We also observed stenosis and extrinsic compression of the ilio caval and pelvic iliofemoral venous segments from multiple bulky retroperitoneal and pelvic lymph nodes.

Intravascular ultrasound (IVUS) also confirmed an approximate 70% narrowing of the left CIV due to compression from the overlying left common iliac artery, compatible with May-Thurner syndrome anatomy, as well as a nonocclusive subacute-to-chronic thrombus within the peripheral aspect of the left CIV. The chronically occluded right iliofemoral segment (Figure 2A and 2B) was recanalized using a curved 5-F, 45-cm curved Ansel sheath with Check-Flo valve (Cook Medical), a 4-F, 90-cm NaviCross catheter (Terumo Interventional Systems), and a 0.035-inch, 260-cm angled Glidewire Advantage (Terumo Interventional Systems). IVUS confirmed both the subacute-on-chronic iliofemoral

thrombus as well as the right ilio caval stenosis, which extended beyond the confluence to the lower IVC.

After crossing the lesion and IVUS assessment, angioplasty was performed on the affected segments to prepare for subsequent thrombectomy and to determine if the chronic thrombotic components could be resolved using angioplasty alone (Figure 2C). However, IVUS showed persistent luminal narrowing and residual subacute-to-chronic thrombus, which was now nearly occlusive, at the anticipated stent inflow site and extending through the central aspect of the femoral vein.

We then decided to address the thrombosis on his right side with the ClotTrieve System, which comprises a custom 13-F sheath that allows insertion of the ClotTrieve catheter over a 0.035-inch guidewire. The ClotTrieve catheter contains a laser-cut coring element that is collapsed in its native state and an integrated woven nitinol collection bag. The ClotTrieve catheter is inserted through the sheath and advanced and positioned beyond the thrombus. It is then unsheathed, deploying the coring element and allowing for wall

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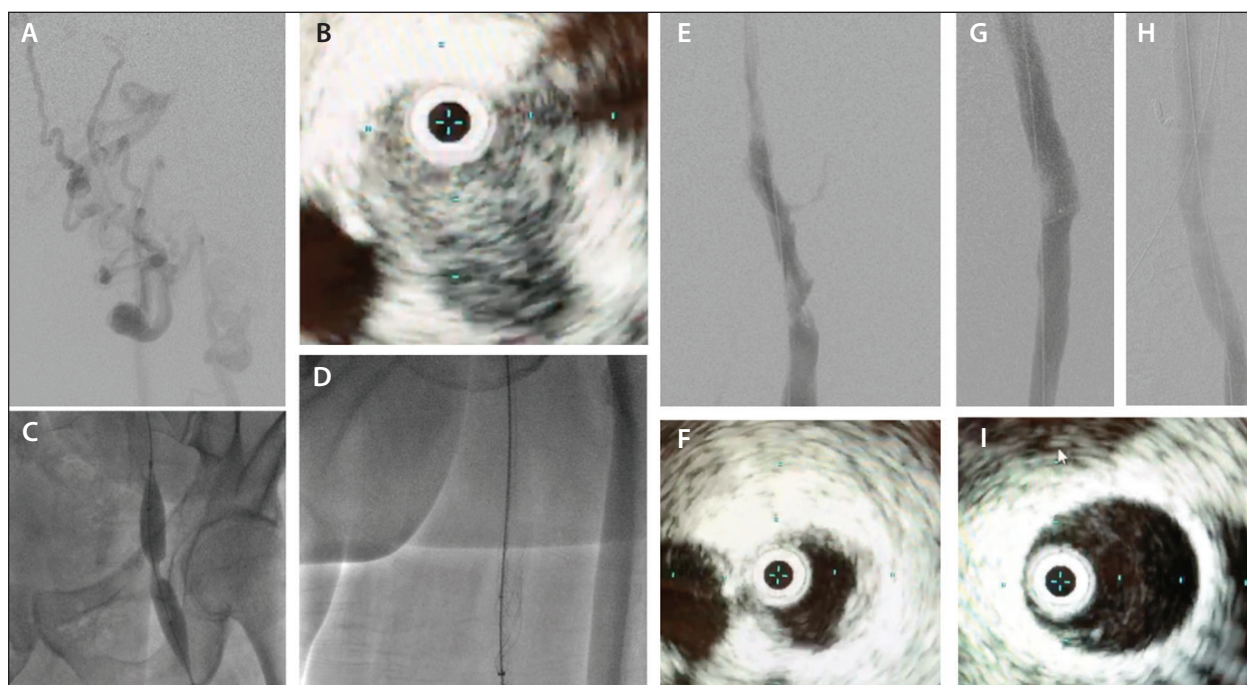


Figure 2. Preintervention venogram confirmed collateralized total occlusion of the right CFV, with delayed antegrade flow and no central iliac reconstitution (A); this was also confirmed via preintervention IVUS (B). Angioplasty with a 12-mm balloon was performed (C) to prepare for ClotTrievers thrombectomy and subsequent stenting (D). Post-ClotTrievers recanalization was confirmed on venography (E) and IVUS (F); the latter also confirmed underlying stenotic compression. Femoral vein inflow was present through a right iliofemoral 16-mm Venovo stent extending from the right EIV through the CFV across the inguinal ligament (G). The ilio caval segment poststenting with a 16-mm Vici stent showed efficient recanalization on venography (H) and IVUS (I) with a white arrow pointing to the nodal mass—displaced by the 16-mm Vici stent—adjacent to the reconstructed CIV lumen.

apposition. To extract thrombus, the catheter is slowly pulled back toward the sheath. This slow retraction allows the coring of thrombus off the vessel wall, collecting in the attached nitinol bag. After an initial pullback, the ClotTrievers is collapsed and removed from the body through its sheath. The extracted thrombus can be manually removed from the catheter to prepare for reinsertion. A ClotTrievers procedure can be repeated with the same device at the discretion of the operator until all thrombus is cleared.

We successfully performed the recanalization and endoluminal debulking of the subacute-to-chronic thrombosis of the right iliofemoral segments in this manner (Figure 2D and 2E). Three passes were performed, using sequential 90° rotation of the coring element with each pass. The extracted thrombus was largely organized with whitish-appearing fibrin. IVUS confirmed near-native luminal diameter with fully restored venous inflow (Figure 2F). After successfully extracting nearly all of the thrombus, we performed prolonged angioplasty of the right iliofemoral vein and the left ilio caval vein. However,

based on persistent focal stenoses on IVUS as well as known malignant venous obstruction, we performed stenting of the bilateral ilio caval and right iliofemoral veins (Figure 2G and 2H). We double-barreled overlapping 16-mm Vici stents (Boston Scientific Corporation) through the bilateral ilio caval segments and 16-mm Venovo nitinol stents (BD Interventional) extending from the right EIV through the right CFV across the inguinal ligament.

Final venography confirmed brisk central flow bilaterally and near-complete disappearance of the venous collaterals, with IVUS confirming the near-anatomic appearance of the reconstructed venous segments using the contralateral side for comparison (Figure 2I). The sheaths were removed, and closure was achieved via purse-string suture and manual compression. The patient was discharged the next day in stable condition, resuming therapeutic anticoagulation with 1 mg/kg of enoxaparin twice daily.

The patient returned for follow-up 4 weeks after thrombectomy and venous reconstruction (Figure 3). He report-

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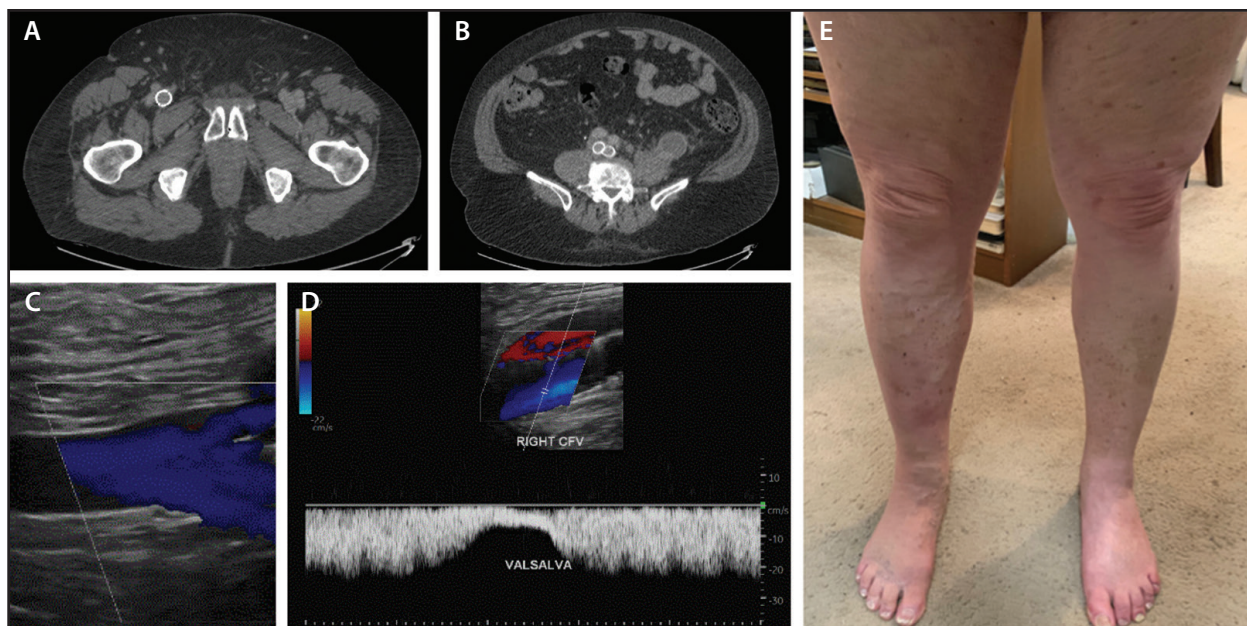


Figure 3. Follow-up assessment. CTV revealed resolution of occlusions in the CFV (A) and femoral confluence (B). Ultrasound confirmed a patent confluence (C) and right CFV stent, including the return of respiratory phasicity (D). The patient's right leg edema visually normalized 3 months postintervention (E).

ed dramatic improvement in his right lower extremity symptoms. He no longer required his walker for ambulation and could climb stairs in the subway station after a brief period of reconditioning. Most importantly to him, he could now play with his grandchildren and inquired about returning to his premalignancy exercise regimen.

On examination, his right leg showed marked improvement—now with mild residual cramping, pretibial edema, skin induration, hyperpigmentation, redness, venous ectasia, and a Villalta score of 6 (compared to 30 before intervention, an 80% reduction). The subjective heaviness had completely resolved. His right leg measured 42.5 cm at the calf and 60 cm at the thigh. Although much less severe on presentation, his left leg also improved, with resolution of swelling and heaviness and only mild cramping and venous ectasia (Villalta score, 2). His left calf circumference was now 40.5 cm, and his thigh circumference was 56.5 cm.

SUMMARY

We successfully treated a mixed-chronicity DVT in a patient with metastatic cancer and thrombolytic contraindications, a subacute-to-chronic thrombus, and combined benign and malignant venous obstruction. Mechanical thrombectomy with the ClotTrievers System

not only allowed us to intervene without the use of thrombolytic agents but also to expand the window of successful debulking of luminal thrombus beyond the standard 2-week window for pharmacologic thrombolysis. The latter can be especially beneficial in single-session treatment of mixed-chronicity thrombus secondary to recurrent DVT.

After thrombectomy, bilateral ilio caval venous reconstruction was necessary to address both the malignant obstruction and the thrombotic left CIV compression. The right ilio caval stent was extended through the ilio-femoral segment due to malignant obstruction and the sequelae of chronic DVT. The ClotTrievers coring element successfully cleared out organized thrombus to provide adequate stent inflow, which could not be achieved with angioplasty alone.

For the patient, the intervention provided great symptom relief and the ability to perform normal daily activities. Although this represents just one successful case, malignancy should not be considered a contraindication for aggressive intervention. By understanding the latest tools available in the realm of venous interventions, a vigilant interventional oncologist can greatly improve quality of life and restore function in oncologic patients with VTE.

Acute and Long-Term Clinical Benefit From Successful FlowTrieve Treatment of Cancer-Associated PE



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PATIENT PRESENTATION

A 70-year-old woman presented to the emergency department with complaints of acute left-sided chest pain and dyspnea that started that morning. Her medical history was notable for diabetes mellitus complicated by gastroparesis, coronary artery disease, morbid obesity, oxygen-dependent obstructive sleep apnea, and cancer. Three weeks before presentation, she underwent left nephrectomy for renal cell carcinoma.

In the emergency department, she had a heart rate of 96 bpm and blood pressure of 124/89 mm Hg. She required 4 L/min of oxygen via nasal cannula to achieve a saturation of 96%. Her troponin was elevated at 0.2 ng/mL and her brain natriuretic peptide was 248 pg/mL. CTA (Figure 1A) demonstrated a large

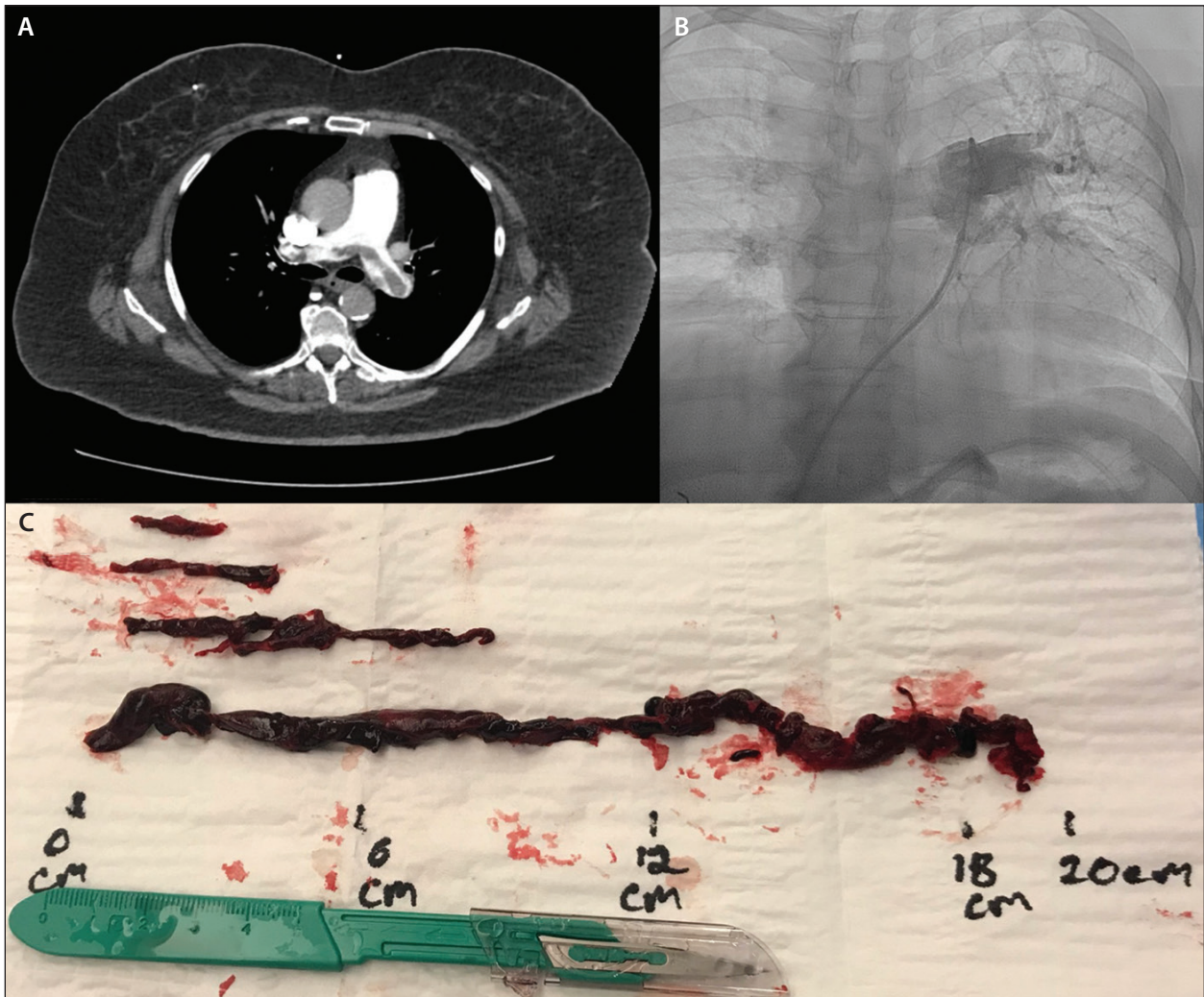


Figure 1. Diagnostic images and extracted clot. Preintervention CT showing the saddle PE (A). T20 placed in the left PA (B). Extracted clot (C).

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saddle PE extending from the distal main pulmonary artery (PA) into the bilateral upper and lower lobar PAs. The right ventricular (RV)-to-left ventricular diameter ratio was 2:3, indicating severe RV dysfunction.

Additional clinical assessment included echocardiography, which showed RV dilatation and hypokinesis. The estimated PA systolic pressure was 47 mm Hg. There was no clot in transit noted. Lower extremity Doppler ultrasound demonstrated an acute left lower extremity DVT in the distal femoral and popliteal veins. She remained dyspneic despite continuous treatment with parenteral anticoagulation.

The patient was stratified as having a high-risk sub-massive PE because of clinical factors of symptomatic hypoxemia and relative tachycardia, as well as evidence of significant right heart strain with elevated troponin and RV dilatation on echocardiography and CT scan. A more aggressive invasive approach was thought to be warranted. Because the embolus was located in the proximal pulmonary vessels, the best treatment was to remove the embolus using the FlowTrieve System.

PROCEDURAL OVERVIEW

The patient was brought to the cardiac catheterization lab and was given mild conscious sedation with midazolam and fentanyl. Intravenous heparin was continued, and an additional bolus was given to achieve an activated clotting time of 250 seconds.

Using ultrasound guidance and a micropuncture technique, access was achieved in the right femoral vein, and an 8-F Preface sheath (Biosense Webster, Inc.) was inserted. Right heart catheterization was performed using a 7-F pulmonary capillary wedge (PCW) catheter. The catheter was placed in the right PA and exchanged for a Grollman pigtail catheter (Cook Medical). Diagnostic pulmonary angiography was performed using 20 mL of contrast to identify the thrombus location. Using a 0.035-inch Amplatz Super Stiff guidewire (Boston Scientific Corporation) for support, the catheter and sheath were removed, and a 22-F DrySeal sheath (Gore & Associates) was inserted. Through this, the FlowTrieve T20 aspiration catheter was advanced through the right heart into the right PA. Two aspirations were performed, yielding a large amount of thrombus.

The PCW catheter was then used to redirect to the left PA. Over the Amplatz guidewire, the T20 was advanced to the left PA. Aspiration did not yield any thrombus. Additional angiography was performed to clarify the location of the residual thrombus (Figure 1B). It was decided that a more distal guidewire position would be needed to advance the T20 to the correct position in the interlobar artery. Using a Supra Core guidewire (Abbott Vascular), the PCW was carefully advanced into the left lower lobe and exchanged for the Amplatz guidewire. Using this distal support, the T20 could then be advanced to a location just adjacent to the residual clot. Aspiration yielded a large amount of thrombus, including a continuous 20-cm-long segment (Figure 1C).

The patient tolerated the procedure without difficulty. Her initial elevated PA pressure (42/19 mm Hg; mean, 23 mm Hg) normalized at the end of the procedure (23/9 mm Hg; mean, 15 mm Hg), and her symptoms and oxygen requirement immediately improved. The catheter and sheath were removed, and hemostasis was achieved using a figure-of-eight suture. She was started on oral apixaban and was discharged 2 days postprocedure.

The patient continues to do well 7 months post-procedure, without dyspnea or PE recurrence. She had a follow-up echocardiogram at 1 month that revealed normal RV function and size. She also had normal pulmonary pressures estimated by echocardiography. A follow-up lower extremity Doppler study 3 months after hospitalization demonstrated resolution of her residual left DVT.

SUMMARY

The FlowTrieve System can be used to successfully extract thrombus and rapidly resolve RV strain in patients with PE, providing patients with cancer a treatment option that eliminates the bleeding risk inherent to thrombolytics. Given the magnitude of clinical improvement seen with a low-risk percutaneous procedure, a diagnosis of malignancy should not preclude treatment in appropriately selected patients. ■