PE in DVT Roundtable

A panel of experts discusses treatment options, pitfalls, and unanswered questions.

PANEL

Kwame Amankwah, MD, MSc, FACS

Dr. Amankwah is a Vascular Surgeon and Assistant Professor of Surgery, Radiology, Cell and Developmental Biology at Upstate Medical University, and Chief of the Division of Vascular and Interventional Radiology, Veterans Administrative Hospital Upstate Healthcare Network, Syracuse, New York. He has disclosed that he holds no financial interest in any product or manufacturer mentioned herein. Dr. Amankwah may be reached at (315) 464-6241; amankwak@upstate.edu.

Peter A. Soukas, MD

Dr. Soukas is Director of Vascular Medicine and Director of Interventional Vascular & Noninvasive Vascular Laboratories, Caritas St. Elizabeth's Medical Center, and Assistant Professor of Medicine, Tufts University School of Medicine, Boston, Massachusetts. He has disclosed that he is a paid consultant for Possis Medical, Inc. Dr. Soukas may be reached at (617) 789-3202; peter.soukas@tufts.edu.

Anthony Venbrux, MD

Dr. Venbrux is a Professor of Radiology and Surgery and Director of Cardiovascular and Interventional Radiology at The George Washington University, Washington, DC. He has disclosed that he has received honoraria for lectures for Possis Medical, Inc., Cook Medical, Cordis Corporation, Terumo Medical Corporation, and Bard Peripheral Vascular. Dr. Venbrux may be reached at (202) 715-5155; avenbrux@mfa.gwu.edu.

***Endovascular Today*:** Do your institutions follow any diagnosis of pulmonary embolism (PE) with a scan for deep vein thrombosis (DVT)?

Dr. Amankwah: A few years ago, our institution did implement a protocol based on the PIOPED (Prospective Investigation of Pulmonary Embolism Diagnosis) study, and every patient who underwent a computed tomography pulmonary angiogram (CTPA) would also have a CT venogram (CTV) done. It was later determined that there was a low yield, especially in patients without symptoms of DVT and low Wells scores. Presently, patients suspected of PE will have a CTPA. If it is positive, these patients will have compression ultrasound examination to evaluate for DVT. If the study is equivocal and clinical suspicion is high for DVT, the patient may have a venogram done.

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Dr. Soukas: We do not have a specific protocol. It is usually managed on a case-by-case basis. We know that there is a relatively low yield of duplex ultrasound (10%-20%) in patients with PE without symptoms or signs of DVT, but a lot of our patients end up having a DVT study ordered by the primary service. We do like to emphasize to the ordering service that duplex is certainly accurate in symptomatic patients with suspected DVT, but normal results obviously do not rule out a PE. If there is a moderately high clinical suspicion, we recommend that they have a more definitive study, such as a CT angiogram.

Dr. Venbrux: At our institution, a contrast-enhanced chest CT scan for pulmonary embolism is often supplemented with limited slices at the level of the common femoral veins, the thighs, and the knees.

***Endovascular Today*:** Are D-dimer tests used in your practices to rule out DVT/PE? If so, when is the test ordered in the process?

Dr. Venbrux: D-dimer tests are not used in our practice to rule out DVT/PE.

Dr. Soukas: We use D-dimer early on in the evaluation for venous thromboembolism. A normal or low Well's score (clinical scoring system for PE), combined with a normal D-dimer, essentially rules out PE and may avoid the radiation and contrast exposures associated with performance of a CT pulmonary angiogram. An elevated D-dimer mandates further evaluation for venous thromboembolism.

Dr. Amankwah: There is extensive literature on the use of D-dimer testing for the diagnosis of PE/DVT. The enzyme-linked immunosorbent assay (ELISA)–based D-dimer tests have superior sensitivity (96%–98%). However, this test can cause a false positive due to things such as trauma, infection, and cancer. D-dimer testing is best considered together with clinical probability (ie, Wells or Revised Geneva scores). These scores are best used in patients who may present to the emergency room. It has been suggested, when patients have a low-to-moderate pretest probability and the D-dimer test is negative, the likelihood of PE or DVT is low. I would still be cautious with this patient group and perform some other tests to rule in or rule out DVT/PE. In patients with high pretest probability where clinical suspicion is high, imaging should be done in place of D-dimer testing. In my practice, I typically do not order D-dimer testing. Patients I may see in the office, as inpatients or in the emergency department, may have D-dimer testing done already. I will take that available information along with my evaluation to determine which appropriate imaging test I believe the patient will need.

***Endovascular Today*:** Is there a consensus on the proportions of patients in the categories of massive pulmonary embolism, submassive PE (systemic normotensive patients with right heart dysfunction), and submassive PE with no right heart dysfunction? Do your institutions have standardized treatment protocols for each of the three diagnoses?

Dr. Soukas: There is not as much evidence-based medicine as one might think on this clinical entity. A lot of the data come from single-institution, retrospective studies, although there are a couple of papers that have merit. One is a paper from Grifoni et al[1] that was a retrospective clinical-outcomes study of 209 consecutive patients with documented PE. They looked at right ventricular (RV) dysfunction using echocardiography. RV dysfunction was defined as one or more of the following: (1) RV dilatation, (2) paradoxical septal systolic motion, and (3) Doppler evidence of pulmonary hyper-

tension. The authors described four groups: 13% of the patients had shock or cardiac arrest, 9% had hypotension without shock, 31% were normotensive with RV dysfunction, and 47% were normotensive without RV dysfunction. What they found was that 10% of patients with normotensive RV dysfunction experienced a clinical deterioration, and of those patients, 50% went on to die. I think the trend lately has been to be a bit more aggressive with those patients who, when you first see them, may be normotensive, but if they have evidence of RV dysfunction (ie, elevated troponin levels, look sick, and have no significant contraindications), we consider them very carefully for more aggressive therapy with intravenous tissue plasminogen activator (IV tPA) using the typical FDA protocol of 100 mg over 2 hours.

The MAPPED-3 study investigators looked at tPA plus heparin versus heparin alone. This was a double-blind study of 256 patients with PE and RV dysfunction, but without shock or hypotension. The primary endpoint in this study was death or escalation of therapy, the latter defined as the need for vasopressors, thrombolysis, intubation, CPR, or embolectomy. That specific endpoint was reached in 25% of patients with heparin alone versus only 10% in patients treated with both. Fortunately, in the randomized MAPPED-3 trial, there were no instances of intracranial hemorrhage, but in the registry, that incidence was as high as 3% .[2] In patients who had RV dysfunction, the in-hospital mortality rate was 22%, and almost all of those deaths were due to PE.

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In our institution, if patients present with hemodynamically life-threatening PE and they do not have a contraindication, we will typically give them the tPA protocol of 100 mg over 2 hours. Obviously, if they have a contraindication to thrombolysis, alternative therapies

such as mechanical thrombectomy will be considered. Submassive PE patients who are normotensive are considered on a case-by-case basis for thrombolysis, particularly if they have evidence of RV dysfunction and positive troponin values, and if their hemodynamics are borderline.

For patients who are completely normotensive, who do not look acutely ill and do not have RV dysfunction, we typically will not treat them with invasive embolectomy or with tPA.

Dr. Amankwah: If I understand you correctly, you are giving the patients who are normotensive and have no evidence of cardiac dysfunction only supportive measures (ie, fluid and heparin)?

Dr. Soukas: We are treating those patients conservatively, unless they have one or more high-risk criteria; we monitor those patients very closely with heparin therapy, eventually bridging them to warfarin. Certainly, the trend is moving toward more aggressive treatment of those patients.

Dr. Amankwah: I agree with Dr. Soukas; there is very little in the way of evidence-based medicine. We treat our patients similarly. In our patients with submassive PE who have no evidence of cardiac dysfunction, supportive measures are used. Those with submassive PE with cardiac dysfunction may receive IV tPA or catheter-directed thrombolytic therapy. The choice of therapy is on a case-by-case basis. Those patients with cardiac dysfunction who have contraindications to thrombolytic therapy will undergo some type of mechanical therapy.

Dr. Venbrux: There is no protocol at our institution. What we do have is a treatment algorithm in evolution. The only time that we tend to intervene much sooner is when there is massive PE with definite right heart dysfunction. We are becoming more liberal in applying different interventional techniques for treatment of patients with PE, instituting therapy early rather than waiting. We have had a couple of cases in which patients deteriorated, and, in hindsight, we probably should have acted sooner. These were patients with huge PEs who were stable initially. They may be young and have reasonably good heart function, but have evidence of right heart dysfunction.

***Endovascular Today*:** What treatments (medical, drug, device) are emerging today, and what are you using?

Dr. Venbrux: FDA-approved treatments include anticoagulation and systemic lytic therapy. In terms of lytic agents for massive PE, the drug is usually tPA. All of the devices that are currently available, at least in the US, are used off-label. There are a number of trials being considered for devices. There is no labeled indication for PE for any of the mechanical devices. We use anticoagulation and lytic therapy, but when patients deteriorate, we go to mechanical thrombectomy, recognizing that it is an off-label application.

Dr. Soukas: In terms of medical therapy, the most recent addition is fondaparinux. The MATISSE study of approximately 2,200 patients with PE compared fondaparinux with unfractionated heparin.[3] There was a reduction in the number of recurrent thrombotic events (3.8% for fondaparinux vs 5% for unfractionated heparin). Massive bleeding was similar between the two groups (1.3% for fondaparinux vs 1.1% for unfractionated heparin). Although fondaparinux has been embraced by the orthopedic community for prophylaxis due to its long half-life, those of us who are considering an intervention are a bit more cautious about its use.

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With regard to mechanical approaches, our experience is similar to that of Dr. Venbrux. We do use the AngioJet (Possis Medical, Inc., Minneapolis, MN) in patients who deteriorate after tPA therapy or in patients who have contraindications to thrombolytic therapy.

There is an interesting technology that has only recently begun being used in PE patients who are hemodynamically stable and who have submassive PE. Granted, this is very anecdotal, but there are some investigators who believe that they achieve better clearing of central thrombi through the use of an ultrasound-assisted thrombolysis catheter. Obviously, these are patients who will require several hours of treatment to reduce the clot burden. It will also be necessary for these patients to be stable and cooperative if you are going to leave a catheter inserted in them for several hours.

In terms of following these patients, we do obtain pulmonary pressures on the way in. If we have a catheter in the pulmonary artery, we follow the pul-

monary artery diastolic pressure to give us an idea of what direction we are going in.

Dr. Venbrux: We have begun to use the Ekos ultrasound-assisted catheter (Ekos Corporation, Bothell, WA) in our patients, and, although I have limited experience, the concern about bradycardia is real when you are close to the right atrium and using the AngioJet.

Dr. Amankwah: In certain patients, usually patients who are failing thrombolytic therapy and deteriorating clinically, we will use the AngioJet. However, with the use of the AngioJet you have to be careful of events such as bradycardia and the possibility of vessel perforation. Recently, in patients with submassive PE and cardiac dysfunction we have used the Ekos catheter. We have had excellent outcomes and avoided the problems associated with the AngioJet. We recently had a patient with cardiac pacing wires with significant clot burden along the wires, who had submassive PE with cardiac dysfunction, and did well with catheter-directed thrombolytic therapy using the Ekos catheter.

Dr. Soukas: What has been your dose of lytic, and what length catheter have you used in those cases?

Dr. Amankwah: The dose that I use is 1 mg/h. The catheter infusion length varies, but usually it is the 18-cm infusion length. In the case of the patient with a pacemaker, we used a 50-cm length, with which we not only treated pulmonary artery clot but also the ventricular and atrial clot.

Dr. Venbrux: In a case of chronic PE, we have used simultaneous right and left groin access, placing one catheter in one pulmonary artery and another catheter in the other pulmonary artery. This way, we had two catheters simultaneously infusing at a dose of 0.5 mg/h. On each side, we used the 12-cm-sidehole Ekos catheter, which worked very well.

Dr. Amankwah: In our cases using the Ekos catheter we have used single puncture through which we have placed the end of the catheter at the bifurcation of the pulmonary artery within a saddle embolus and have had good results.

Dr. Venbrux: We have used the AngioJet device, and it has been lifesaving in some instances of acute decompensation. It is a tradeoff between a patient who is crashing and at least achieving some flow. I would like to ask the group if the bradycardia issue associated with AngioJet is so onerous that they are afraid to use it.

In our experience, bradycardia may occur, and some say that if atropine doesn't work you can use some of the theophylline derivatives to reduce the incidence of bradycardia. When bradycardia occurs, we usually slow down (ie, stop the AngioJet) for a while, and the patient's bradycardia tends to resolve on its own.

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Dr. Soukas: I have gotten into the habit of prophylactically placing a temporary pacemaker in everybody. That seems to remove a lot of the nuisance bradycardia when you are repeatedly stopping and starting. We have tried atropine and theophylline, but if these patients are compromised, I try to avoid using them if I can.

We typically use the Xpeedior device (Possis). Have any of you used the AngioJet DVX for PE, and what has been your experience?

Dr. Venbrux: We have used both, and I do not see a great difference between the two, but I do not have a huge series to support that statement.

Dr. Amankwah: I have used both and cannot comment that one is different from the other.

Dr. Soukas: We have not noticed much of a difference either, other than perhaps the bradycardia in transient hypotension seems to be a bit more profound with the DVX.

***Endovascular Today*:** How do you know when your treatment is done? Do you need to know pulmonary pressure?

Dr. Amankwah: I do not obtain pressures any more. Since I am not treating the numbers, I am looking for some improvement in the patient's clinical parameters (ie, improved oxygen saturation, heart rate, blood pressure). In some of these cases an echocardiogram was done prior to the procedure, possibly demonstrating

some type of cardiac dysfunction such as septal deviation, increased pulmonary artery pressure, or wall motion abnormality. I will get a follow-up as another measure to see whether cardiac function has improved.

Dr. Soukas: If I am already in the process of performing an invasive procedure, I will obtain the right heart pressures on the way in, and when I think I am finished, I will measure those pressures again. If there has not been a decrease in the pulmonary pressures, I do not necessarily use that as my benchmark to go on to further intervention. These patients are frequently very sick. You want to get enough blood flow to save their life; you are not looking for perfection. In such situations, the pulmonary artery pressure may be worse or the same, hopefully a little bit better. However, it is the other clinical parameters (ie, oxygen saturation, blood pressure, heart rate, and overall patient status) that guide me in determining if therapy is complete. Also, I do like the follow-up echocardiogram to compare the pre- and post-pulmonary artery systolic pressures.

Additionally, if there is less flattening of the septum, less pulmonary hypertension, and if the RV is contracting better and is less dilated, I know that the patient is improving.

Dr. Venbrux: For follow-up, I completely agree. Most of our patients will get an echocardiogram before hand, and that helps us decide when we are to intervene. I measure pressures on the way in if there is time and on the way out, but it is not the pressures that dictate when to stop. It is my firm belief that it is "perfusion, not perfection," which is what I keep teaching the fellows. You just want to get flow into the patient's lungs.

***Endovascular Today*:** In the absence of definitive literature, do you believe that angiographic evidence of the completeness of clot clearance is important to prevent chronic thromboembolic pulmonary hypertension (CTPH), PE recurrence, and to improve 5-year survival?

Dr. Amankwah: I would like to know if the panel, when performing catheter-directed therapy, repeats the CT of the chest besides repeating the echocardiography?

Dr. Venbrux: I think it is a good idea, but from a practical point of view, at least in our institution, which has a busy trauma service, the CT scanner is heavily used.

Dr. Amankwah: I was curious because we have done this with a couple of our patients when their clinical parameters have improved. I have found it to be beneficial because then I know that we are at least on the right path and can determine whether or not to make adjustments to our treatment.

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Dr. Soukas: We do not have a specific protocol for that. I think it depends on the individual circumstances and the patient's clinical picture. Also, there are the practical issues, such as the patient's renal function and if the patient can tolerate an additional 75 to 100 mL of contrast. If you decided to intervene on a saddle embolus seen on CT angiogram, it certainly seems logical to repeat the CT angiography to document that you improved the situation. If there was any question about what the next therapeutic step should be, it would certainly be a valuable piece of information.

Unfortunately, there is not a lot of literature to answer this question. I know of one article by Wan et al[4], which concluded that lytics accelerate clot dissolution, more rapidly resolve diffusion defects, and perhaps reduce the PA pressures and normalize the RV function. But by no means is this an answered question. There is a trial in Europe that just began, randomizing 1,000 patients to heparin alone versus bolus tenectaplase with heparin. I believe CT angiography is one of the parameters that the study will follow to quantify the dissolution of the clot burden. I think that trial, if commenced and completed, will go a long way toward answering this question. ■

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