PANEL DISCUSSION

PE in Prime Time: New Pathways, Devices, and Trials

A comprehensive conversation about the state of pulmonary embolism care today, including keys to a strong program, use of artificial intelligence, typical interventional pathways, approaches to trial enrollment, and more.

With Gregory Piazza, MD, MS; Akhilesh Sista, MD, FSIR, FAHA; Brent Keeling, MD; Saher Sabri, MD; and Mona Ranade, MD

Gregory Piazza, MD, MS
Director, Vascular Medicine Section
Brigham and Women's Hospital
Associate Professor of Medicine
Harvard Medical School
Boston, Massachusetts
gpiazza@partners.org

Akhilesh Sista, MD, FSIR, FAHA
Professor, Department of Radiology
Weill Cornell Medicine
New York, New York
aks9010@med.cornell.edu

Brent Keeling, MD
Professor of Surgery
Division of Cardiothoracic Surgery,
Department of Surgery
Emory University School of Medicine
Atlanta, Georgia
brent.keeling@emory.edu

Saher Sabri, MD
Professor of Radiology
Division of Interventional Radiology
MedStar Washington Hospital Center
MedStar Georgetown University Hospital
Washington, DC
saher.s.sabri@medstar.net

Mona Ranade, MD
Associate Professor of Interventional Radiology
Department of Radiology
UCLA Health
Los Angeles, California
mranade369@gmail.com

What are the keys to establishing—and maintaining—a strong pulmonary embolism (PE) interventional program?

Dr. Piazza:

- An active multidisciplinary PE response team (PERT) with diversity of proceduralists and non-proceduralists
- Flexibility of interventional approaches, including catheter-based fibrinolytic strategies and large-bore mechanical embolectomy
- Routine auditing and discussion of strategy utilization, treatment heterogeneity, and patient outcomes

Dr. Sista:

- Recognize where all physicians are coming from in their understanding of PE. Noninterventionalists see the full spectrum of PE and are involved in the longitudinal care of these patients, and it's important that the interventionalists respect that perspective and acknowledge their experience.
- Know the available data for interventions: their limitations, where the data need to go, and what can be learned from future studies. Be transparent about and critical of the current literature and what it does and doesn't show. From this you can glean what might be the appropriate interventional algorithm for your site.
- Rely on guidance documents, which are more helpful as PE care has become more sophisticated.

Dr. Keeling:

- Continued interest in PE care
- Strong leadership in the program
- Institutional support

Dr. Sabri:

- Multidisciplinary collaboration
- Expertise in catheter-directed therapy (CDT) for PE
- Access to escalate care to mechanical circulatory support (MCS) and an advanced intensive care unit (ICU)
- Longitudinal follow-up of PE patients

Dr. Ranade:

- Active interdisciplinary collaboration
- An efficient pathway or protocol for communication as well as rapid triage of patients with PE
- A database to monitor your own outcomes and data

Are you currently using an artificial intelligence (AI)–based detection/communication platform, and if so, what has the impact been?

Dr. Sista: There are a few AI programs out there that are being increasingly used. I think this is a real opportunity for sites to identify research patients who they wouldn't otherwise notice via their standard forms of notifications. This is particularly important for treating the next group of PE patients in this time of data generation and selection bias. I think AI has the ability to identify every single potential research patient who is entering the hospital. AI also gives us a more holistic understanding of the population that is coming through a hospital and can broaden one's perspective.

Dr. Ranade: The introduction of Aidoc as an AI tool has significantly enhanced our ability to rapidly and consistently triage patients with PE. Although UCLA has long maintained a strong PERT and an effective communication structure, the growing complexity of our academic health care system—spanning multiple community hospitals and continuously onboarding new physicians in training—posed challenges to maintaining uniformity. Aidoc has helped standardize our approach across sites, facilitating faster communication, more efficient decision-making, and a more consistent care pathway for PE patients throughout the system.

Dr. Keeling: Yes, we are using an AI-based platform. We've seen a mild increase in volume of interventional cases as well as many alerts.

Dr. Sabri: AI platforms have been very helpful in screening patients who are positive for PE on CT and for identifying patients with right ventricular (RV) dysfunction. AI has expedited delivery of care to these patients and coordination between team members, and it could potentially improve enrollment in clinical trials.

Dr. Piazza: We are not using AI in our clinical care for PE. However, we have implemented AI for early detection of PE in one of our clinical trials, with an excellent impact on enrollment.

Who comprises your group's PE team? What specialties are involved and what does each contribute?

Dr. Sabri: Our PERT includes intensive care specialists, cardiologists, interventional radiologists, and vascular and cardiac surgeons. We also work closely with our pulmonary hypertension specialists for long-term care. We coordinate closely with our emergency department (ED) physicians as well.

Dr. Ranade: At UCLA, PERT consults are typically initiated by the ED or critical care team upon patient presentation. Interventional radiology (IR) leads catheter-based therapies, assesses imaging, and manages inferior

vena cava (IVC) filter placement. Cardiology provides echocardiographic evaluation, while pulmonary vascular specialists play a key role in case presentation and long-term follow-up. Postoperative care, especially for chronic thromboembolic pulmonary hypertension (CTEPH) patients, is coordinated through our dedicated Pulmonary Hypertension Clinic.

Dr. Keeling: Our PE team involves interventional cardiology, pulmonology, hematology, and surgery. Each specialty contributes a unique perspective in treating patients and brings a unique skill set to clinical decision-making.

Dr. Piazza: We split our multidisciplinary PERT leadership between cardiovascular medicine and pulmonary vascular disease. Our team approach also then integrates cardiac surgery for consideration of MCS (typically extracorporeal membrane oxygenation) and pulmonary embolectomy, as well as endovascular specialists for expertise in catheter-based thrombolysis and large-bore mechanical embolectomy.

Dr. Sista: The team at Weill Cornell includes IR or other interventionalists, cardiothoracic surgery, anesthesia, and pulmonary/critical care. We're very lucky to have Dr. Josh Goldberg, a very accomplished cardiothoracic surgeon who understands not only the open surgical management of PE patients but also the interventional management. We peripherally involve anesthesia in these decisions, especially when it comes to complexities around sedation and other management. The linchpin of the team is probably pulmonary/critical care; they take care of the patients from soup to nuts.

In cases selected for interventional therapy, what is the typical pathway from door to table?

Dr. Ranade: Typically, a patient with clinical suspicion for PE receives a CT. The AI platform alerts all members of the PERT regarding a positive PE and a Zoom call is coordinated between the team members within 1 to 2 hours of the alert. Depending on the patient's clinical presentation and characterization of PE as submassive or massive, the patient may be mobilized to the ICU or straight to the IR suite within 24 to 48 hours of the call.

Dr. Piazza: The typical pathway is activation of our multidisciplinary PERT for patients meeting criteria (either intermediate-high or high risk), with rapid evaluation (within 15 minutes) of the patient and imaging, followed by discussion of reperfusion options and circulatory support needs. Typically, this discussion considers the anatomy of the PE, along with comorbidities that may make one reperfusion technique preferred over others. The goal is to stabilize the patient and achieve rapid reperfusion depending on the acuity of the patient.

Dr. Sabri: Our pathway depends on the acuity of the presentation and the status of the patient. Patients with high-risk PE and hemodynamic compromise can be stabilized in the ICU before heading to an interventional suite for CDT. If the patient is in shock, they would potentially receive MCS first before entertaining an intervention. For intermediate-risk PE, patients are usually admitted to the ICU or an intermediate care unit and closely monitored on anticoagulation (AC). Depending on how symptomatic the patient is, intervention could be performed within the next 24 to 48 hours.

Dr. Keeling: Our typical pathway has patients presenting to the ED, followed by transfer to the ICU and then the cath lab. Most patients are intervened upon within 12 hours, while some go directly to the lab or operating room for intervention.

Dr. Sista: First is assessment of the severity of the PE. When someone presents with high-risk PE, teams need to quickly mobilize. All parties must be involved—surgeons, interventionalists, anesthesiologists, and critical care docs—and come together and ask where we should be treating the patient based on their vitals and other parameters. Do they need MCS? Do they need thrombus reduction, and if so, what method of thrombus reduction? Intermediate-risk PE patients typically do not deteriorate with prompt initiation of therapeutic AC. Early notification is not a bad thing in terms of reperfusion therapy.

Understanding where the patient started and where they're progressing is another important component of the interventional algorithm to determine the best approach and timing for treatment.

A classic example would be a tachycardic and tachypneic patient who has bad RV dysfunction on echocardiography. Their lactate is up, and they're maintaining a systolic blood pressure in the low 100s. With time, they start to get more dyspneic, and their echocardiogram is unchanged. They have a lot of difficulty getting up and going to the bathroom. It doesn't seem like they're getting better on anticoagulants alone. This might cause concern for imminent RV failure. In this case, you'd almost be using the same team as for high-risk PE.

Thus, while we have a pathway established, trials will hopefully clarify this population in terms of timing, as well as when and whom. Also requiring further discussion and data is whether thrombus removal is ideal for patients in the medium to long term. I think we will see more sophis-

tication and interventional algorithms as we see data from some of the industry-sponsored trials.

When opting for intervention, what patient or clot factors influence your choice in therapy?

Dr. Keeling: The main factors for us for intervention are an acute presentation, no prior history of PE, and physiologic parameters. We attempt to avoid intervention in the acute-on-chronic patients if possible.

Dr. Sista: Clot location needs to be somewhat central; we haven't yet seen benefit in very peripheral clot. Patients with very large RV/left ventricular (LV) ratios and dysfunction on echocardiography would be considered "on alert." The ability to tolerate minimal or no sedation is also a factor. If a patient with cardiac disease with bundle branch block says, "I need to be completely out if you're going to do something," you might consider not doing an intervention if the patient is doing okay, because the risk of deep sedation or intubation and total cardiovascular collapse is higher than leaving this patient on anticoagulants and letting the anticoagulants do their job. Otherwise healthy patients who are not improving on anticoagulants, have a persistently high lactate, and could potentially tolerate minimal to no sedation would potentially benefit more from intervention.

Dr. Ranade: Patient characteristics, location, and quantity of the thrombus burden as well as bleeding risk dictate the type of interventional performed along with operator experience and comfort to a certain extent. In patients with signs of significant RV strain or failure or who are hemodynamically unstable, we ideally do mechanical thrombectomy immediately to debulk as much as possible. In others cases, we may opt to quickly drop lysis catheters and get out; this includes patients who may not tolerate laying flat on the interventional table for too long.

Dr. Sabri: Determining the status of the patient is the first step. Classifying the patient into high, intermediate, or low risk allows for choosing the appropriate pathway for treatment. CT imaging showing central clot and elevated RV/LV ratio is a key factor for determining candidacy for intervention. Other lab values such as cardiac biomarkers, lactate, and other basic lab work are also important in decision-making.

Dr. Piazza: Bleeding risk may favor a nonthrombolytic approach. Anatomic location of thrombus burden is also an important factor, with more distal disease favoring a thrombolytic-based catheter approach. I also look at clinical presentation severity measures, such as degree of pulmonary hypertension. Concerns about vascular access may complicate large-bore mechanical embolectomy; however, large-bore mechanical embolectomy may be chosen in a patient with a need for circulatory support. Lastly, I do factor in patient preference.

Which PE cases do you generally treat interventionally, and which do you avoid?

Dr. Sabri: Generally speaking, we offer CDT for high-risk and high-intermediate–risk patients. For high-risk patients with hemodynamic compromise, we do so urgently, with MCS available. For patients with RV dysfunction and elevated biomarkers (high-intermediate risk), we'll consider intervening if symptomatic. For patients who are asymptomatic, high-intermediate risk, and low-intermediate risk, we tend to observe after AC and intervene when they deteriorate. Part of monitoring patients on AC includes assessing their ability to walk and monitoring their oxygen saturation. Some patients become symptomatic when challenged physically, and these patients can be considered for intervention, especially if they are young and active. We generally avoid intervening on low-risk patients who are treated with AC primarily. Other patients to be cautious with are patients who have known chronic pulmonary hypertension who may be a higher risk for CDT and may not have the same desired postintervention improvement as acute PE patients.

Dr. Piazza: We typically treat high-risk PE interventionally or with systemic fibrinolysis, based on timing and clinical status. Intermediate-high–risk PE may be treated interventionally, but we typically monitor closely first to see if AC will be enough. We avoid treating intermediate-low– and low-risk patients with anything other than AC, if there are no contraindications.

Dr. Keeling: We tend to intervene on patients with intermediate-risk PE with central clot and signs of RV injury, either on echo or through serologic examination. We try to avoid intervention in patients with longevity-limiting comorbidities. We also tend to intervene on high-risk patients with stable hemodynamics and patients on MCS.

With the continued call to develop more robust data support, how are you approaching enrolling PE patients in clinical trials?

Dr. Keeling: We approach every patient as if they may potentially be a trial patient.

Dr. Sabri: There has been an established need for randomized controlled trial (RCTs) in the PE space, and we have been prioritizing enrolling here. Our next focus is

enrolling in trials that include longitudinal follow-up beyond immediate change in patient status or RV dysfunction. Such studies look into longer-term outcomes at 3 months and 1 year to evaluate quality of life (QOL) and walking distance. Lastly, we enroll in investigational device exemption trials to evaluate newer technologies in the PE space.

Dr. Sista: Clinical trial enrollment issue is a big issue, and it has been difficult to generate data in randomized trials. I'm speaking as the architect of the PE-TRACT trial, but I think we need to go back in time to when we didn't know what a PE algorithm should look like. There have been a lot of factors going into which patient gets which intervention, but much has yet to be proven and is based on personal experience or anecdotes. There is a certain amount of confirmation bias associated with this approach.

I would argue that every patient who comes in with intermediate- or high-risk PE and is appropriate for a clinical trial should be enrolled in or considered for a clinical trial. The patient would ultimately decide, but the opportunity to be in a trial needs to be presented to them, with balance and care and with a lot of support for the need for generation of data. As part of clinical trial leadership, I've seen different approaches from different sites, and the ones that take the need for data seriously are the ones that enroll successfully.

Dr. Piazza: We prioritize enrollment in clinical trials as much as we can within the construct of our multidisciplinary PERT.

Dr. Ranade: Everyone is screened for clinical trials and subsequently approached for an informed consent. All members of the IR and pulmonary teams at UCLA are very familiar with the inclusion/exclusion criteria, so everyone is aware of the need to enroll a patient if they fit into a trial's criteria. UCLA is specifically part of PE-TRACT; we prioritize screening all patients into an RCT and specifically for this National Institutes of Health–funded effort.

What are the opportunities and challenges with enrolling PE patients in clinical trials?

Dr. Piazza: The main opportunities and challenges are (1) the expectation that the patient will undergo a procedure and hesitance to allow the patient to be randomized to AC alone; (2) the incredible number of active enrolling trials; and (3) limited data for each technology, such that we are still learning about safety and efficacy.

Dr. Keeling: One challenge and potential opportunity is the absence of RCTs without industry funding. This may be addressed by PE-TRACT. It is also my own bias that none of the current or proposed RCTs have a surgery arm included. Surgery remains an excellent therapy for well-selected patients with intermediate- to high-risk PEs, but all of the data surrounding surgery come from observational studies.

Dr. Ranade: This presents an opportunity to collect data that can help answer long-standing questions: Which patients are ideal candidates for catheter-based therapy? Which patients benefit most from specific types of catheter-based interventions? What are the long-term outcomes beyond hospital stay and 30-day mortality? Additionally, we aim to explore broader impacts—particularly how these procedures affect patients' QOL.

There is an immense opportunity to collect data to answer these questions and thus provide more nuanced care for patients with PE. Upcoming updated PE guidelines will also be key to having good data-based, catheter-based therapies.

We know there is immediate benefit to the patient with catheter-based therapies, and a lot of us are now over the learning curve. With increased volumes and increased procedures, clinicians are getting better at performing these cases and stabilizing patients. We see the benefits in decreased hospital stay and decreased use of lytic.

The challenge is thus an inherent bias for catheter-based therapies in the procedural community. This is also true from a patient standpoint in my experience. Typically, when patients are discussing consent, they ask the questions such as, "How many of these procedures are happening? What is the technical success rate? How quickly can I get discharged?" I think the patients also feel that if there is something that can be done, they want it all done. If the data are out there, patients can go on Google and search it. Thus, a lot of our patients come in ready to ask for catheter-based therapy. This can be a challenge to navigate when doing an informed consent for an RCT for example. A lot of patients will drop out when they hear they may be randomized to an AC arm.

Dr. Sabri: Like any field, enrollment in clinical trials has its hurdles. We generally approach the patient first with the RCT and explain that we do not have sufficient level 1 evidence for the benefit of CDT for PE. If the patient is not a candidate or not interested in enrolling in an RCT, we present one of the other single-arm trials. We need more data for the safety and efficacy of pulmonary interventions, and we should approach each PE patient as a trial candidate if they meet eligibility criteria. Screening imaging studies with positive PE findings and having buy-in from the entire team, including the ED and ICU, would help in increasing enrollment.

What advice do you have to encourage trial enrollment in the wider interventional community? What would you say to centers not enrolling patients?

Dr. Piazza: We must prioritize enrollment in trials as much as possible in lieu of simply making a decision to intervene. We really do not yet know the role of intervention in intermediate-high–risk PE and should feed trials so we can move the field forward.

Dr. Keeling: Screen. Enroll. Repeat. Approach every patient as a trial patient; more robust data are still needed in the field, despite existing results from prior trials.

Dr. Sista: The research arm of medicine can be quite bureaucratic and expensive, and not every site necessarily has the resources to be involved in clinical research—that's just reality. However, I do think every PE team should be aware of ongoing trials, examining the trial in detail and understanding the inclusion criteria as well as the rationale behind each trial. Then, they can incorporate this information into their own algorithm and have some amount of equipoise in terms of patients.

Even if you aren't directly involved in a clinical trial, there is readily available information that one can examine carefully and adjust until the data come out.

What is your role in follow-up care? What questions would you most like to see answered in the follow-up of PE patients to help guide your practice?

Dr. Sista: Interventionalists should stay involved with their patients postintervention for several reasons. I've noticed that the interventionalist often ends up being a care coordinator, ensuring the patient gets follow-up imaging, looking for residual symptoms and other health issues. The interventionalist can almost become that patient's primary care doctor for venous thromboembolism (VTE) in the months following the PE. This an opportunity for great care for VTE patients.

We need to find out the markers for concern among the follow-up population (eg, poor performance on a cardiopulmonary exercise test, a correlation with 6-minute walk distance). Then we need a standardized way of approaching these patients in the follow-up period and finding the parameters to actually predict someone going on to CTEPH or exercise dysfunction, for example, in the following months. I hope this is where some data will be generated to get us a clearer picture of that group of patients.

I'd like to see future data giving us direction in the follow-up population, and that is the sincere attempt from PE-TRACT.

Dr. Keeling: We have a multidisciplinary PE clinic. This clinic helps identify CTEPH patients and guide long-term AC management.

I would most like to see the true incidence of chronic thromboembolic disease and/or CTEPH emerge from long-term follow-up data and a comparison of patients over the long term based on initial therapy.

Dr. Ranade: As mentioned, UCLA has a CTEPH clinic that sees all patients postoperatively. Typically, if we have seen a patient for PE and that patient is enrolled in a clinical trial, the interventionalist or procedural team will also do the assessment that is required by the trial, which is typically either 30 days or 30 and 90 days. We have patients fill out the QOL questionnaires and do a 6-minute walk test.

Dr. Piazza: We see patients in follow-up around 4 to 6 weeks after discharge. We typically focus on questions of why the PE happened, what risk factors are present for recurrence, how we mitigate risk, how to successful treat PE, and how to lead a healthy lifestyle.

Dr. Sabri: We bring all of our patients to the IR clinic at 1-month postprocedure. We obtain the necessary images and review them with the patient. We conduct PE QOL surveys and perform a 6-minute walk test if part of the study protocol. If the patient continues to be symptomatic, we arrange for them to follow up with the pulmonary hypertension clinic. Some of the trials we enroll in require more advanced follow-up, such as cardiopulmonary exercise testing. We coordinate that with our pulmonary hypertension specialists, who are part of the trial. ■

Disclosures
Dr. Piazza: Research support paid to institution from Bristol-Myers Squibb/Pfizer Alliance, Bayer, Janssen, Alexion, Regeneron, Esperion, Amgen, and Boston Scientific Corporation; consulting fees from Bristol-Myers Squibb/Pfizer Alliance, Boston Scientific Corporation, Janssen, NAMSA, and Thrombolex.
Dr. Sista: None.
Dr. Keeling: Consultant to AngioDynamics, Inc.
Dr. Sabri: Consultant to Boston Scientific Corporation and Medtronic; receives research support from Inquis Medical.
Dr. Ranade: Consultant to Boston Scientific Corporation, AngioDynamics, Inc., Inari Medical, and Medtronic.