ROUNDTABLE DISCUSSION

# Managing Post-PE Syndrome: Improving and Standardizing Post-PE Care

Insight into how post–pulmonary embolism syndrome is defined and treated, ideal standardized guidelines and protocols, improvement measurement, and more.

**With Geoffrey D. Barnes, MD, MSc; Sonia Jasuja, MD; and John M. Moriarty, MD, FSIR, FSVM**


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**Although post–pulmonary embolism syndrome (PPES) after acute pulmonary embolism (PE) is believed to be common, it lacks clinical validation and an agreed-upon definition. How do you define PPES and its causes, and what has it looked like for the patients you encounter at your institution?**

**Dr. Barnes:** To me, the PPES is a collection of physical and psychologic limitations after an acute PE. Traditionally, we have focused on chronic thromboembolic pulmonary hypertension (CTEPH) as the major long-term consequence of acute PE. However, more recent studies have focused on the patient experience after an acute PE, noting that more than one-third to one-half of patients will experience physical and/or psychologic limitations.

For many of these patients, they continue to experience breathlessness, dyspnea on exertion, or profound fatigue. However, when objective testing is performed (eg, echocardiogram, right heart cardiac catheterization), they do not exhibit evidence of pulmonary hypertension. Other patients experience psychologic distress that shares features with posttraumatic stress disorder (PTSD), including extreme fear of or anxiety about experiencing another acute PE.

**Drs. Jasuja and Moriarty:** PPES is defined as any symptoms or functional limitations that remain persistent after 6 to 12 weeks from a patient's initial PE event. Residual symptoms that signal the presence of PPES include ongoing dyspnea at rest or on exertion, chest pain, tachycardia, anxiety, or change in functional status. There is no direct correlation between the severity of the initial PE event and the incidence of PPES, and thus it is important to monitor for PPES in all patients after experiencing an acute PE. The severity of PPES can vary from mild to severe, and it exists on a spectrum. In its most severe forms, PPES can include chronic

thromboembolic disease (CTED) and CTEPH. There are no clear data to determine the cause of PPES, but it has been suggested that residual clot burden and residual abnormal pulmonary vascular hemodynamics contribute to ongoing symptoms after an initial PE event.

### How do you approach assessment and treatment for PPES? What outcomes have you seen?

**Drs. Jasuja and Moriarty:** In patients with signs and symptoms of PPES, it is recommended to start with a functional assessment by performing a 6-minute walk test (6MWT), followed by repeat echocardiography to assess for residual right ventricular (RV) dysfunction. In patients with functional limitation on 6MWT and normal residual RV function, the next steps are determined by the severity of the symptoms experienced and the timing after the acute event. In the subacute setting, an exercise program is recommended with cardiopulmonary rehabilitation. In the chronic setting, further testing is warranted, including level 3 cardiopulmonary exercise testing (CPET) for evaluation for the cause of exercise limitation. Conversely, in patients with an abnormal 6MWT and/or residual abnormal RV function on echocardiography 6 to 8 weeks after their initial PE event, further assessment for CTED or CTEPH should be completed. In terms of diagnosis and treatment of PPES, there are currently no consensus data or guidelines, and further research is needed in this realm. The data from long-term studies suggest that up to 50% of patients have residual symptoms for years after their initial episode of acute PE.

**Dr. Barnes:** The first step in assessing and treating PPES is to actually see the patient. This is one of many reasons that formal PE systems of care (eg, pulmonary embolism response teams [PERTs]) need to address both the acute treatment decisions as well as the outpatient, long-term follow-up. At my center, we try to have patients see their primary provider within 7 to 10 days after hospital discharge and then return to our dedicated PE follow-up clinic at 4 to 8 weeks after hospital discharge. At that time, we assess for any residual physical limitations and evidence of psychologic distress related to their acute PE. When appropriate, we perform repeat echocardiography to assess for RV dysfunction and/or evidence of ongoing elevated pulmonary artery pressures (PAPs). We also perform CPET for patients with persistent dyspnea or physical limitations.

We partner with our pulmonary hypertension colleagues for any patients with evidence of persistently elevated PAPs, RV dysfunction, or significant physical limitations > 3 months after an acute PE. Although evidence suggests that pulmonary rehabilitation may be highly effective at improving physical activity for patients with PPES, this is often not covered by insurance and therefore not available to many patients.

### What follow-up/tests need to be standardized for acute PE, and what might these standardized guidelines or protocols look like in your opinion?

**Dr. Barnes:** All patients with acute PE need close follow-up to assess for compliance to anticoagulation care, any complications related to anticoagulation, and mid- and long-term complications. For any patient with baseline RV abnormalities or elevated PAPs at the time of acute PE (usually identified on CT or echocardiogram), repeat echocardiography is appropriate to ensure that these abnormalities have normalized. At our center, these tests are typically ordered at 4 to 8 weeks after hospital discharge, but they definitely should be performed by 3 months postdischarge. For patients with persistent dyspnea or abnormal findings on echocardiography beyond 3 months, further workup should be initiated, including CPET, ventilation-perfusion imaging, and right heart cardiac catheterization. This is also an ideal time to reassess the need for extended phase anticoagulation (secondary prophylaxis) for patients without a strong, reversible provoking risk factor. For any patient who received an inferior vena cava (IVC) filter, determining when to have this filter removed is an important element of follow-up care.

**Drs. Jasuja and Moriarty:** At our institution, we have standardized post-PE care with the development of a dedicated post-PE clinic. Patients are referred to this clinic for an initial visit between 4 and 8 weeks after hospital discharge, depending on the severity of their initial PE event. Each patient who initially had an intermediate- or high-risk PE undergoes repeat echocardiography just before their first follow-up visit in the post-PE clinic to assess for recovery of RV function. The PERT Consortium and the European Society of Cardiology/European Respiratory Society have published comprehensive guidelines for post-PE care that are an important first step in standardizing post-PE care.[1,2]

### If you are part of a PERT, who is involved in posttherapeutic care? What is the PERT's role in PPES, and how are management decisions communicated?

**Drs. Jasuja and Moriarty:** Our institution has a PERT that directly refers acute PE patients into the post-PE clinic, as described previously. The post-PE clinic is run primarily by the pulmonary vascular disease medicine group, often with input from our hematologists in certain circumstances. The existence of this clinic helps centralize care for the patient after their PE event, allowing for a streamlined approach to management and monitoring for PPES. One of the aims of this post-PE clinic is to identify PPES early and monitor its evolution in each patient, and especially watch for the most severe forms in CTED and CTEPH.

**Dr. Barnes:** It is critical for PERT programs to have well-established outpatient protocols. This includes referral to expert clinicians who can assist with anticoagulation management and assess for signs/symptoms of PPES. At many centers, members of the PERT run these dedicated post-PE clinics. Other centers may partner with hematology and/or pulmonary vascular specialists to perform this follow-up care. Importantly, engagement of the primary care providers is essential, with clear communication of the patient's hospital course, treatment plan, and recommendations for any future diagnostic testing.

## Are there any measures to be taken to aid in PPES prevention?

**Dr. Barnes:** At present, there are no proven strategies that reliably prevent the development of PPES in patients who experience an acute PE. However, it's likely that high-quality anticoagulation care is an important preventive strategy. There are some preliminary data suggesting that higher levels of pulmonary vascular obstruction correlate with PPES-related symptoms and patient quality of life. As such, there is a high level of interest in exploring the relationship between acute interventions that reduce thrombus burden (eg, catheter-directed thrombolysis, suction thrombectomy) and reductions in the risk of PPES. Although not yet proven, this is a promising area of ongoing research.

**Drs. Jasuja and Moriarty:** There are little data on this topic. So far, there have been trials aimed at the determination of whether intervention during an acute PE episode affects long-term mortality outcomes or long-term RV function; however, there have been no trials specifically aimed at evaluating whether intervention in acute PE affects the development of PPES. More research is needed in this area.

## What does improvement at long-term follow-up look like for you? How do you demonstrate/measure this?

**Drs. Jasuja and Moriarty:** One of the most useful ways to quantify improvement at long-term follow-up is to assess each patient's functional capacity. It is recommended that all patients maintain a regular physical activity routine, even just a daily walk, to monitor how much they can do and how much they improve with time. In the clinic, this improvement is measured with serial 6MWTs and subjective measures of improvement from the patient's perspective.

**Dr. Barnes:** Long-term follow-up for patients with acute PE should address anticoagulation care, as this is the bedrock of PE treatment. Specifically, clinicians need to assess the patient's access and adherence to anticoagulation, as well as any related side effects. Clinicians should also address the planned duration of anticoagulation and the eligibility for half-dose direct oral anticoagulants (eg, apixaban 2.5 mg twice daily, rivaroxaban 10 mg daily) after the primary treatment phase. To this end, measuring how many patients remain on anticoagulation for a minimum of 3 months is one key quality measure. Similarly, the number of patients without a reversible provoking factor who remain on anticoagulation beyond 1 year is another important care metric.

Another key element of follow-up is screening for PPES. This includes (1) follow-up echocardiography to look for RV dysfunction and elevated PAPs and (2) diagnostic testing for PPES (eg, CPET, 6MWT).

Lastly, for any patient in whom an IVC filter was placed, determining the optimal time for filter removal is key to preventing future complications. In patients with an IVC filter placed for an acute PE, an ongoing need for the filter should be reassessed within 3 months of hospital discharge. Rate of IVC filter retrieval is an important quality measure.

## What do we know about the origin of mental health issues post-PE (ie, PTSD, depression, anxiety) as well as the connection between mental health and PPES specifically? What needs improvement, and how do we combat this problem?

**Drs. Jasuja and Moriarty:** The association of mental health issues and acute PE is well established, with many studies citing an increase in depression, anxiety, and decreased quality of life after acute PE. There is much room for further research on this topic. One important step in addressing mental health issues post-PE is to identify and treat the issues, which should involve a multidisciplinary approach that could potentially be included in the post-PE clinic algorithm.

**Dr. Barnes:** We know that many patients with PPES experience signs and symptoms of psychological stress similar to PTSD. However, we are not yet able to predict which patients are most likely to experience these symptoms. Nonetheless, it is important to screen for these symptoms and refer patients to psychiatric care when these symptoms become debilitating. ■

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