Venous thromboembolism (VTE) includes deep vein thrombosis (DVT) and pulmonary embolism (PE). It is the third most frequent cardiovascular disease, with an overall incidence of 100-200 per 100,000 individuals (1). VTE is responsible for the hospitalization of more than 250,000 patients annually in the United States (2).

Acute pulmonary embolism (PE) is the most serious presentation of VTE. PE is a potentially life-threatening disease and, in some cases, it presents as sudden death. Acute PE spans a wide spectrum of clinical outcomes, mainly based on the right ventricle’s capacity to tolerate strain. Increased right ventricular (RV) afterload causes RV dilation that then incites cardiac ischemia, coronary hypoperfusion, and hypotension that can progress to cardiogenic shock.

Massive or high-risk PE is defined as an acute PE with sustained hypotension (systolic blood pressure less than 90 mm Hg for at least 15 minutes or requiring inotropic support) (3,4). In the International Cooperative Pulmonary Embolism Registry (ICOPER), the 90-day mortality rate for patients with high-risk PE at presentation was 52 percent (4-6). Hemodynamically stable patients with preserved RV size and function are classified as low-risk PE and have excellent prognosis once anticoagulation therapy is established (4).

There is an intermediate category, however, that warrants further discussion, as these patients may have an increased risk of 30-day mortality. Approximately one quarter of non-massive PE patients are categorized as submassive or intermediate-risk PE, using a risk stratification score based on clinical variables known as the pulmonary embolism severity index (PESI) (3).

Within this category, risk delineation focuses on the presence of RV dysfunction (by echocardiography or CT angiography) and/or evidence of myocardial necrosis (by elevated cardiac biomarkers) (3,7). In patients who have evidence of both RV dysfunction and myocardial necrosis, 30-day mortality can reach 24.5 percent (8). Close monitoring of this group is recommended for early detection of hemodynamic decompensation and change in management.

Systemic thrombolysis, the recommended treatment for high-risk PE (3,4), improves hemodynamic parameters, reverses RV dysfunction, and improves survival in patients with acute PE; however it is associated with increased risk of major bleeding, including intracranial hemorrhage (9,10). In a recent study, in-hospital, all-cause mortality in hemodynamically unstable patients who received thrombolytic therapy was 15 percent, versus 47 percent without thrombolytic therapy (p less than 0.0001) (11).

The use of systemic thrombolysis for patients without hemodynamic compromise remains controversial. The recently published Pulmonary Embolism Thrombolysis (PEITHO) trial studied the role of fibrinolytic therapy in patients with intermediate-risk PE (12). Its primary outcome, a composite of all-cause death or hemodynamic decompensation within seven days after randomization, was significantly reduced with thrombolysis (2.6 percent versus 5.6 percent; odds ratio 0.44; 95 percent CI 0.23–0.87; p = 0.02). However, an increased risk of major hemorrhage (6.3 percent versus 1.5 percent; p less than 0.001) and stroke (2 percent versus 0.2 percent; p =0.003) was observed. An alternative strategy using reduced-dose tissue plasminogen activator (tPA) (50mg) in 121 patients with “moderate PE” reported no significant bleeding or differences in mortality (13). Current guidelines recommend against the routine use of systemic thrombolysis in these patients (3,14).

(Continued on Page 7)
The use of catheter-directed thrombolysis is emerging as an effective alternative in patients with intermediate or high-risk PE, using small doses of a thrombolytic agent (15). In a randomized, controlled clinical trial of 59 intermediate-risk patients, heparin plus ultrasound-guided catheter-directed thrombolysis was compared to heparin alone (16). Ultrasound-guided catheter-directed tPA significantly reversed RV dilatation at 24 hours by echocardiogram, without an increased risk of bleeding. For intermediate or high-risk PE, surgical embolectomy may be an alternative, especially if thrombolysis is contraindicated or has failed. A perioperative mortality of less than 6 percent has been reported for embolectomy before hemodynamic collapse (17). Extracorporeal membrane oxygenation (ECMO) may rescue those in critical situations, ensuring circulation and oxygenation until definitive management is provided. For a list of references to this article, other articles in this issue, and the Division of PACCM’s recent publications and suggested reading for this issue, visit UPMCPhysicianResources.com/Pulmonology.