Submassive Pulmonary Embolism

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KEYWORDS

• Pulmonary embolism • Submassive • Risk stratification • Thrombolysis
• Intermediate-risk pulmonary embolism • Right ventricular dysfunction

KEY POINTS

- Acute pulmonary embolism (PE) is common and associated with a high degree of morbidity and mortality.
- PE can present silently or with hemodynamic collapse and cardiac arrest, is difficult to diagnose, and treatment options depend on accurate and timely risk stratification.
- Severity in PE depends on the amount of clot burden as well as physiologic response to the clot, and is stratified into low risk, submassive, and massive, with increasing levels of mortality.

INTRODUCTION

Acute pulmonary embolism (PE) is part of the spectrum comprising venous thromboembolic disease. In the United States alone there are estimated to be 350,000 to 600,000 cases of venous thromboembolism (VTE) annually with 100,000 to 200,000 related deaths.[1,2] PE is associated with a high rate of morbidity and mortality, depending on the clinical presentation and underlying cardiopulmonary status. Mortality ranges from low in the hemodynamically stable patient to being almost a certainty in severe cases. In all risk groups, combined in-hospital mortality is estimated at 15%.[3] Arguably the single biggest contributor to mortality in PE is failure of diagnosis.[4] Long-term morbidity including recurrence, chronic venous insufficiency, and chronic thromboembolic pulmonary hypertension can occur in up to 12.9%, 7.3%, and 35% of patients, respectively, at 1 year.[5–7]

VTE is common in the critical care setting. The frequency depends on the method of surveillance. Systematic screening for deep vein thrombosis (DVT) by ultrasonography identifies thrombus in as many as 40% of patients.[8–10] Patel and colleagues[11]

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conducted a multicenter, retrospective study of VTE incidence in patients in established intensive care units (ICUs) based on clinical diagnosis. The incidence of DVT was 1.0% and the incidence of PE was 0.5%, despite most patients having received pharmacologic prophylaxis. ICU admission is an independent risk factor for the presence of VTE.[12] The economic burden of VTE is considerable, contributing an average additional hospital cost of $8763 per patient (not accounting for severity of PE) and an attributable length of stay increase of 3 to 4 days.[13] PE is considered preventable and in 2008 the Centers for Medicare and Medicaid Services (CMS) stopped reimbursing hospitals for nosocomial VTE following certain orthopedic procedures. The Federal Agency for Healthcare Quality and Research adopted postoperative VTE as patient safety indicator, which requires mandatory reporting of all such events. Given such scrutiny and emphasis, much effort has been spent on identifying risk factors, educating patients and health care providers, and putting into place procedures and protocols designed to minimize the occurrence of VTE.

The presentation of PE is complex and variable, and can range from asymptomatic to fatal. Therefore, much research has gone into the development of clinical decision tools to aid in the diagnosis of PE. Given the heterogeneity of outcomes, similar attention has been given to the development of risk stratification tools and treatment algorithms that take into account the estimated morbidity and mortality.

DEFINITIONS

PE can be categorized into low-risk, submassive, and massive PE, which correlate well with increasing levels of mortality and are readily identified with available technology. Massive PE, which accounts for 5% of all PE-related admissions, is characterized by shock, typically defined as systolic blood pressure less than 90 mm Hg or a reduction of 40 mm Hg in systolic blood pressure from baseline for at least 15 minutes.[14] Patients manifest typical signs of organ hypoperfusion including encephalopathy, oliguria, cold and clammy extremities, or frank cardiac arrest.[15,16]

Submassive PE denotes the important subset of patients who seem hemodynamically stable, but have evidence of right ventricular strain or dysfunction. Right ventricular dysfunction results from right ventricular pressure overload, and findings include hypokinesis and dilatation of the right ventricle, flattening and paradoxical motion of the interventricular septum toward the left ventricle, tricuspid regurgitation, severe right ventricular free wall hypokinesis and apical sparing (McConnell sign), loss of respiratory variation in the diameter of the inferior vena cava, and pulmonary hypertension as identified by a peak tricuspid valve pressure gradient greater than 30 mm Hg or tricuspid regurgitant peak flow velocity greater than 2.5 m/s.[17–19] These findings are supported by varying levels of evidence, and no single finding can predict death. Hence, a combination of findings is routinely used to diagnose right ventricular dysfunction.[20,21] Transthoracic echocardiography has long been established as a valid tool in determining evidence of right ventricular dysfunction, as has computed tomography (CT) angiography (CTA).[19,22] Right ventricular strain is a function of increased wall tension, which results in myocardial cell damage and necrosis. Myocardial damage can be elucidated by several different criteria, with varying levels of supporting evidence. Electrocardiographic findings (including complete and incomplete right bundle branch block and $S_1Q_3T_3$ pattern) as well as several biomarkers (troponin, brain natriuretic peptide [BNP] and N-terminal proBNP [NT-proBNP], heart-type fatty acid binding protein [H-FABP]) have been studied. Although right ventricular dysfunction and strain can be identified easily with the