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Saddle pulmonary embolism diagnosed by CT angiography: Frequency, clinical features and outcome

Jay H. Ryu[a,*], Patricia A. Pellikka[b], David A. Froehling[c], Steve G. Peters[a], Gregory L. Aughenbaugh[d]

[a]*Division of Pulmonary and Critical Care Medicine, Mayo Clinic, 200 1st St. SW, Rochester, MN 55905, USA*
[b]*Division of Cardiovascular Diseases, Mayo Clinic, 200 1st St. SW, Rochester, MN 55905, USA*
[c]*Division of General Internal Medicine, Mayo Clinic, 200 1st St. SW, Rochester, MN 55905, USA*
[d]*Department of Radiology, Mayo Clinic, 200 1st St. SW, Rochester, MN 55905, USA*

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Summary
Objective: To assess the frequency, clinical presentation and outcome associated with saddle pulmonary embolism (PE) diagnosed by computed tomographic angiography (CTA).
Patients: Retrospective review of 546 consecutive patients diagnosed to have acute PE by CTA from 1 September 2002 to 31 December 2003.
Results: Fourteen of 546 patients (2.6%) had saddle PE; 10 were men (71%). None of these patients had pre-existing cardiopulmonary disease. Most common presenting symptoms included dyspnea (72%) and syncope (43%). Hypotension was documented in 2 patients (14%). The most common risk factor for PE was obesity (64%). CTA revealed saddle PE and additional filling defects in the main pulmonary arteries in all patients. Echocardiography was performed within 48 h of the PE diagnosis in 10 patients and revealed right ventricular dysfunction in 8 (80%). All patients were initially managed in the hospital, median length of stay of 4 days (range, 1–45 days). Standard anticoagulant therapy with heparin and warfarin was administered to all patients. Five patients (36%) received additional therapy; thrombolytic therapy was administered to 1 patient (7%) and 4 patients (29%) received an inferior vena cava filter. None of the patients died during their hospitalization. Four patients (29%) died following their hospitalization after intervals of 1, 5, 6, and 12 months, respectively. Causes of death were known in 3 patients, all of whom died from progressive malignancy.

Abbreviations: CTA, computed tomographic angiography; PE, pulmonary embolism; RV, right ventricle

*Corresponding author. Tel.: +1 507 284 2447; fax: +1 507 266 4372.
E-mail address: ryu.jay@mayo.edu (J.H. Ryu).

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Conclusion: Saddle PE in patients without pre-existing cardiopulmonary disease is associated with a relatively low in-hospital mortality rate and may not necessitate aggressive medical management.

Introduction

Pulmonary embolism (PE) remains a common cause of mortality and morbidity.[1–4] In particular, massive PE (defined by a systolic blood pressure <90 mmHg) has been associated with a 90-day mortality rate of 52.4% despite treatment.[5] Treatment options beyond anticoagulant therapy such as thrombolytic therapy, catheter-based interventions, and surgical embolectomy have been advocated for patients with massive PE.[5–9]

Saddle PE is defined as a visible thromboembolus straddling the bifurcation of the main pulmonary artery trunk (Fig. 1).[10] The diagnosis of saddle PE causes clinical alarm because it signals an unstable, large clot burden in the pulmonary artery, and the possibility of sudden hemodynamic collapse. However, there are relatively sparse data documenting clinical outcomes of patients with saddle PE and uncertainties remain regarding optimal management of these patients. In this study, we sought to determine the frequency, clinical presentation, and outcome of patients with saddle PE diagnosed by computed tomographic angiography (CTA), by far the most common tool used for diagnosing PE in recent years.[11–14]

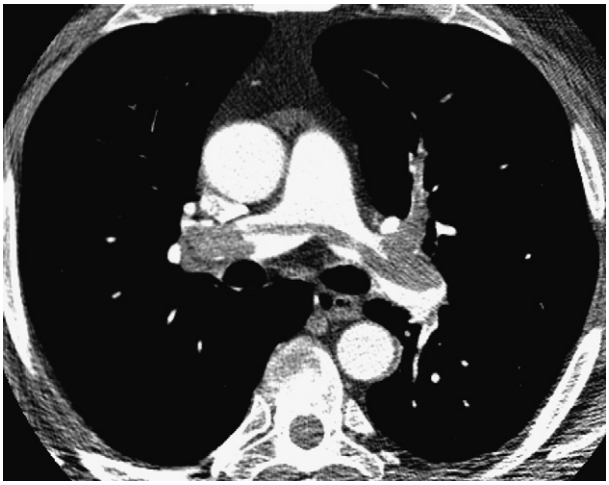

Figure 1 Computed tomographic angiography (CTA) demonstrating saddle pulmonary embolism (PE) as well as emboli partially obstructing both main pulmonary arteries. This was a 36-year-old man evaluated in the emergency department for progressive dyspnea of 8 days' duration. Risk factors for venous thromboembolism included obesity (BMI 41.5) and a previous history of deep vein thrombosis. He was not hypotensive and the oxygen saturation on room air was 93%. He was treated with heparin and warfarin only. He was doing well on warfarin therapy 36 months after this episode.

Methods

Patients who underwent CTA over a period of 16 months from 1 September 2002 to 31 December 2003 at Mayo Clinic Rochester, MN, were identified by a computer-assisted search of medical records. Of 3792 patients, 148 patients (3.9%) who did not authorize the use of their medical records for research were excluded resulting in a cohort of 3644 patients. Of these 3644 patients, 546 (15.0%) had evidence of acute PE on CTA. The scans of these 546 patients were reviewed with a particular focus on thromboembolism located in the central pulmonary vessels. Cases of saddle PE were identified by the presence of a filling defect extending across the bifurcation of the main pulmonary artery trunk.[10] We examined these cases of saddle PE in detail by extracting data regarding demographics, clinical presentation, clinical and radiologic features, as well as treatment and clinical outcome from the medical records. The 95% confidence interval for the in-hospital mortality rate was calculated using a method previously described.[15]

CTA was performed with a multidetector-row helical CT scanner using previously described methods.[16] The following CT scanners were used: a 16-slice scanner (Siemens Sensation 16; Siemens Medical Solutions, Forchheim, Germany), an 8-slice scanner (GE Lightspeed/QXl Ultra; General Electric, Milwaukee, Wisconsin), and a 4-slice scanner (GE Lightspeed/QXl Plus; General Electric, Milwaukee, Wisconsin). The findings on CTA were reviewed by one of us (GLA), an experienced chest radiologist, to confirm the presence of saddle PE.

Results

Among 546 patients diagnosed to have acute PE by CTA at our institution over a 16-month period we identified 14 patients with saddle PE (2.6%; 95% CI 1.41%, 4.26%); 10 were men (71%) (Table 1). The age at diagnosis ranged from 36 to 83 years. The most common symptoms at presentation were dyspnea (72%) followed by syncope (43%). Hypotension (systolic blood pressure <90 mmHg) was documented in 2 patients (14%) and hypoxemia ($PaO_2 \leqslant 55$ mmHg or $SaO_2 \leqslant 88\%$) in 1 patient (7%). None of the patients had pre-existing cardiopulmonary disease. At the time of the CTA, 9 were inpatients (64%), 2 were outpatients (14%), and 3 were being evaluated in the emergency department (21%). After the diagnosis of PE was established, initial management for all patients occurred in the hospital.

All patients had at least one risk factor for venous thromboembolism (VTE); 11 patients (79%) had 2 or more risk factors (Table 1). Obesity (BMI $>30\,kg/M^2$) was the most common risk factor (64%). Four patients (29%) were undergoing cancer therapy for metastatic gastrointestinal cancer (2 patients), metastatic melanoma (1 patient), or advanced

Table 1 Demographic and clinical features of 14 patients with saddle pulmonary embolism.

Characteristic	Value
Sex—no. (%)	
Male	10 (71)
Age (years)	
Median	54.5
Range	36–83
Presenting symptoms—no. (%)	
Dyspnea	10 (72)
Syncope	6 (43)
Chest pain	3 (21)
Nausea	2 (14)
Risk factors for venous thromboembolism—no. (%)	
Obesity (BMI $>30\,kg/M^2$)	9 (64)
Age >60 years	4 (29)
Malignancy	4 (29)
Cancer therapy	4 (29)
Surgery (within 3 months)	4 (29)
Previous venous thromboembolism	2 (14)
Oral contraceptive or estrogen use	2 (14)
Congenital thrombophilia	2 (14)

BMI = body mass index.

brain tumor (1 patient). Surgery had been performed within 3 months of the diagnostic CTA in 4 patients and consisted of hysterectomy (2 patients), repair of torn quadriceps tendon (1 patient), and open reduction/internal fixation of radial fracture (1 patient). Five patients underwent testing for thrombophilia and 3 were diagnosed to have thrombophilic conditions including heterozygosity for factor V Leiden (2 patients) and abnormal fibrinogen (1 patient).

In addition to the saddle PE in all patients (Fig. 1), CTA also revealed additional filling defects in the main pulmonary arteries in all patients. Leftward shift of the interventricular septum was present in 11 patients (79%). Pulmonary arteries were enlarged in 5 patients (36%). Small pleural effusions were noted in 6 patients (43%) and were bilateral in 3 patients.

Transthoracic echocardiography was performed in 10 patients (71%) within 48 h of the PE diagnosis and revealed mild to moderate right ventricular (RV) enlargement in 9 patients (90%), mild to severe RV dysfunction in 8 patients (80%). Estimated RV systolic pressure was obtainable in 8 patients with a median value of 50 mmHg (range, 32–62 mmHg).

All 14 patients received heparin and warfarin therapy. Heparin therapy was initiated with intravenous unfractionated heparin in 13 patients (93%) and low-molecular-weight heparin in the one remaining patient. Five patients (36%) received additional therapy; thrombolytic therapy (alteplase) was administered in 1 patient (7%) and inferior vena caval filter was deployed in 4 patients (29%).

All 14 patients survived their episode of saddle PE and were discharged from the hospital. The 95% confidence interval for the in-hospital mortality rate (given zero events in 14 patients) associated with saddle PE is 0–23%. Median duration of hospitalization was 4 days (range, 1–45 days) after the diagnosis of PE. Only one patient required hospitalization stay of >10 days; an 83-year-old man whose hospital course was complicated by gastrointestinal bleeding and respiratory failure requiring mechanical ventilation. This patient eventually died of unknown cause in a nursing home 5 months after dismissal from the hospital. One other patient experienced a complication during the hospital course and consisted of bleeding from a surgical wound that was managed by temporary discontinuation of anticoagulant therapy and inferior vena filter placement.

Follow-up information was available in all 14 patients with a median follow-up duration of 18 months (range, 1–40 months). Three patients discontinued their warfarin therapy after 6–12 months of treatment. The remaining 11 patients continued warfarin therapy indefinitely or up to the time of their death. Four patients (29%) had died following their hospitalization after intervals of 1, 5, 6, and 12 months, respectively. Causes of death were known in 3 patients all of whom died from progressive malignancy. There were no recurrences of venous thromboembolism documented during the follow-up period.

Follow-up CTA had been performed in 5 patients (36%) after a median interval of 26 months (range, 2–32 months) and revealed improvement in all patients (Fig. 2(a)–(d)). Four of these patients had evidence of residual chronic PE; CTA in one patient appeared normal at 32 months following saddle PE.

Follow-up transthoracic echocardiography was performed in 7 patients (50%) during the follow-up period with a median interval of 12 months (range, 1–32 months) after the diagnosis of saddle PE. All of these follow-up echocardiograms demonstrated normal RV size and function except in one patient who had borderline RV enlargement and mildly reduced RV function. RV systolic pressure could be estimated in 6 of these patients and the median value was 36 mmHg (range, 23–43 mmHg).

Discussion

Saddle PE represents a large and unstable clot load. Saddle PE accounted for 2.6% of 546 consecutive patients diagnosed to have acute PE by CTA at our institution. This finding is similar to that of Pruszczyk et al.[17] who described 5.2% of their 289 consecutive patients with acute PE to have a saddle component. Despite its ominous appearance on radiologic imaging, however, we did not observe any in-hospital mortality for our study cohort despite a relatively conservative treatment regimen for most patients. The results of our study are in agreement with the findings of Pruszczyk et al.,[17] who described 17 patients with saddle PE diagnosed by CTA in whom the 2-week mortality rate was 5.8%. These short-term mortality rates for patients with saddle PE are not any higher than in-hospital mortality rate for all patients with PE that has ranged from 8% to 10% in previous reports.[18–21]

In previous reports, the clinical presentation of saddle PE has varied considerably from complete absence of symptoms to sudden death.[10,17,22–24] In the current study, clinical presentation associated with saddle PE was similarly

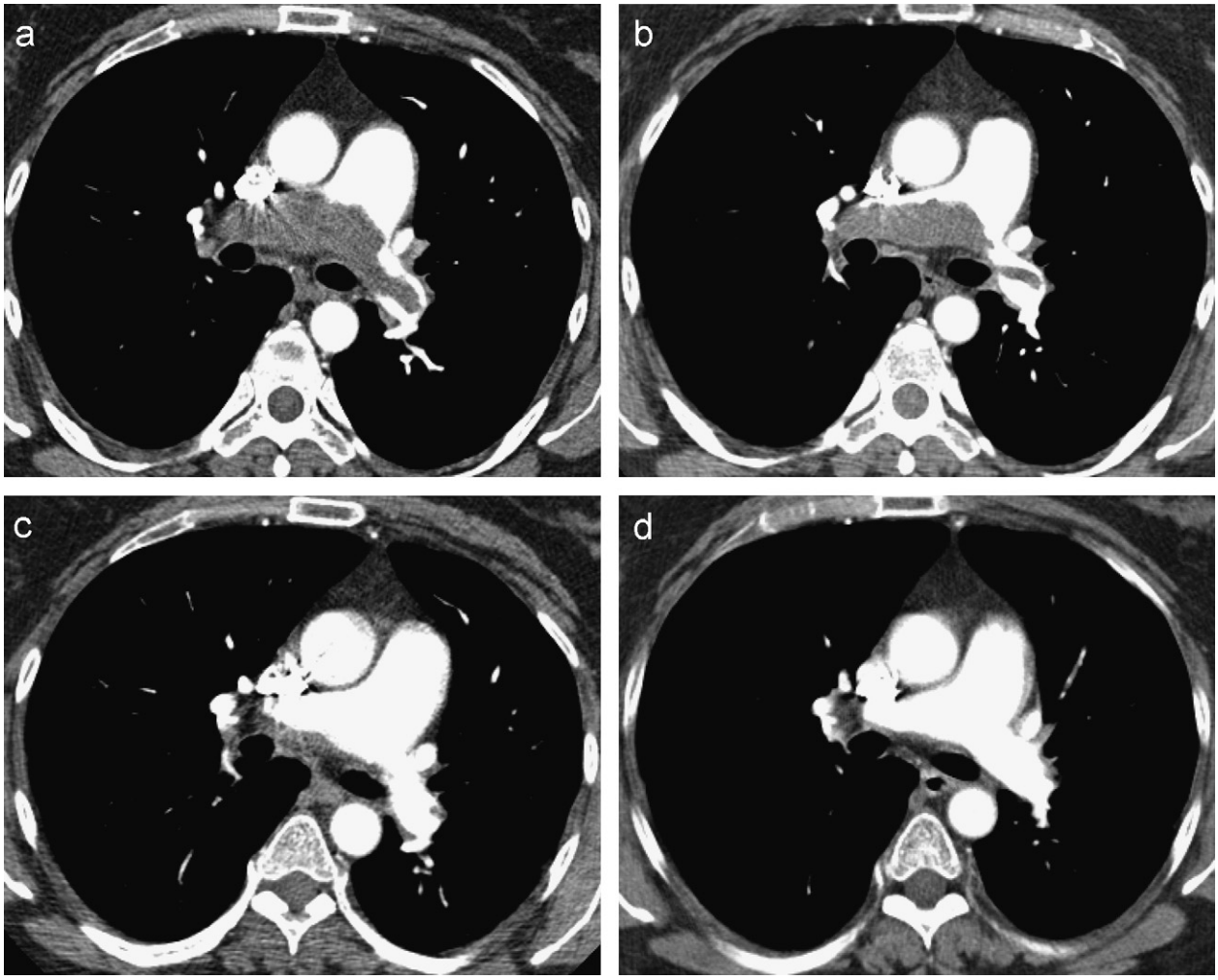

Figure 2 Serial CTA studies in a 52–year-old woman with saddle PE. At the time of the initial diagnosis (a) she was treated with heparin and warfarin. Subsequent studies performed at 4 months (b), 20 months (c), and 32 months (d) after the diagnosis demonstrated gradual improvement in the obstructing thromboembolus while continuing chronic warfarin therapy. Transthoracic echocardiography performed 32 months after the diagnosis of PE revealed normal right ventricular size and function; estimated right ventricular systolic pressure was 26 mmHg.

variable from absence of cardiorespiratory symptoms to that of syncope and hypotension. Although 6 of our patients (43%) had experienced syncope prior to the diagnosis of saddle PE, only 2 patients were documented to be hypotensive. In the study by Enzwelier et al.,[10] 6 of 17 patients (35%) with saddle PE had undergone CT scanning for reasons other than suspected PE and 3 of these 6 patients were asymptomatic. Pruszczyk et al.[17] found no difference in the initial clinical and echocardiographic parameters between patients with saddle and non-saddle PE. Specifically, systolic blood pressure did not differ between these two groups of patients. Thus, saddle PE is associated with a wide range of clinical presentations and hemodynamic instability appears to be relatively uncommon, at least in PE cases diagnosed by CTA.

The term ''massive PE'' has been used with varying connotations and has accounted for 4.2–10% of patients with PE.[5,7,21,25,26] An earlier use of this term referred to the presence of ''significant filling defects or obstruction of two or more lobar arteries'' identified on standard pulmonary angiography.[27] More recently, authors have used this term referring to PE associated with a large burden of clots in the central pulmonary vessels, the presence of systemic arterial hypotension, clinical signs of cardiogenic shock, or echocardiographic signs of right ventricular dysfunction.[5–7,28,29] Our study and previous studies suggest that saddle PE is uncommonly associated with hypotension or shock. Thus, whether saddle PE can be classified as a form of ''massive PE'' depends on the definition used.

Despite a large burden of thromboembolic material in the pulmonary vasculature, evidence of gradual resolution was demonstrated by subsequent echocardiographic and CTA studies. Our results are consistent with the findings of a recent systematic review on the resolution of PE suggesting that more than 50% of patients still have residual PE 6 months after the diagnosis.[30] Enzwelier et al.[10] described the short-term evolution of saddle PE in 12 patients in follow-up CT studies obtained at a mean interval of 7.5 days. In 8 patients, the saddle portion of the thromboembolus had resolved; thinning of the embolus at the bifurcation was

noted in the remaining 4 patients. These authors concluded that saddle PE is a "transient form" of acute PE.[10] Long-term follow-up was not provided.

There are conflicting data regarding the prognostic significance of the clot burden in the pulmonary vasculature.[25,27,31–33] Earlier studies found size of the emboli on standard pulmonary angiography to not correlate with mortality.[27] However, some recent studies utilizing CTA suggest that quantification of pulmonary vascular occlusion caused by thromboembolism can be a predictor of mortality.[25,31] These conflicting results may be explained by differences in study populations as demographic factors, comorbidities, and clinical features contribute to clinical outcome in patients with acute PE.[34]

To clinicians, the diagnosis of massive PE suggests possible need for aggressive treatment which may include thrombolytic therapy, surgical pulmonary embolectomy, catheter-based interventional techniques, and inferior vena caval filter.[5–9,35,36] Although all of our 14 patients survived, it is likely that some patients with acute saddle PE died suddenly without a diagnostic evaluation as we had previously documented in an autopsy study.[24] Short-term mortality associated with acute PE is likely determined by multiple factors including the physiologic status of the cardiopulmonary system at the time of the embolization, comorbid factors, age and overall condition of the patient, as well as the amount of clot load in the pulmonary vasculature.[29,30] The acute clinical consequences of saddle PE may be more serious in patients with pre-existing cardiopulmonary compromise or other comorbidities. The limitations in the current study including the retrospective design, small number of subjects, and limited follow-up data do not allow definitive conclusions regarding appropriate management of patients with saddle PE. Limited data available including the results described within suggest that the mortality rate associated with saddle PE diagnosed by CTA in patients without pre-existing cardiopulmonary disease may be similar to that associated with PE overall and may not necessitate aggressive management measures.

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