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Saddle vs Nonsaddle Pulmonary Embolism: Clinical Presentation, Hemodynamics, Management, and Outcomes

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Abstract

Objective: To understand the clinical significance, hemodynamic presentation, management, and outcomes of patients presenting with saddle pulmonary embolism (PE).

Methods: All patients with saddle PE diagnosed at Mayo Clinic in Rochester, Minnesota, from January 1, 1999, through December 31, 2014, were included in this study. These patients were age and simplified Pulmonary Embolism Severity Index (sPESI) matched (1:1) to a nonsaddle PE cohort. Both groups were then classified into massive, submassive, and low-risk PE based on established criteria and compared for clinical presentation, management, and outcomes.

Results: A total of 187 consecutive patients with saddle PE were identified. The saddle PE group presented more frequently with massive PE (31% vs 20%) and submassive PE (49% vs 32%), whereas low-risk PE was more common in the nonsaddle PE group (48% vs 20%). Systemic thrombolysis was used more frequently in the saddle PE group on admission (10% vs 4%; P=.04) and later during hospitalization (3.2% vs 0%; P=.03). Late major adverse events were similar in both groups except for mechanical ventilation (6% in saddle PE vs 1% in nonsaddle PE; P=.02). Overall in-hospital mortality did not differ between the 2 groups (4.3% in saddle PE vs 5.4% in nonsaddle PE; P=.81).

Conclusion: Although patients with saddle PE presented with higher rates of hemodynamic compromise and need for thrombolysis and mechanical ventilation, we found no difference in short-term outcomes compared with an age- and severity-matched nonsaddle PE cohort. Overall, in-hospital mortality was low in both groups.

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Acute pulmonary embolism (PE) is a potentially life-threatening disease and remains a leading cause of cardiovascular morbidity and mortality. Clinical outcomes differ widely depending on initial clinical presentation and presence of comorbidities, with mortality ranging from 2% to 11% in treated PE and up to 30% in untreated patients.[1-8] Often, PE is classified radiologically based on the most central extent of the clot burden.

Saddle PE is a radiologic definition and refers to thrombus that straddles the bifurcation of the pulmonary artery trunk often with extension into both the right and left main pulmonary arteries.[9] Saddle PE is found in 2.6% to 5.4% of patients with PE.[10,11] The large central clot burden seen in saddle PE often alarms clinicians, who often refer to saddle PE as massive PE and admit these patients to the intensive care unit (ICU). However, the term *massive PE* is actually a hemodynamic definition and refers to any PE that presents with shock and hemodynamic collapse.[12] Thus, it is incorrect to refer to patients with saddle PE as having massive PE because every clinician has encountered patients with saddle PE who present with stable hemodynamic values and a very benign clinical picture. Thus, saddle PE is a diverse entity with variable clinical features and eventual outcomes. There are relatively sparse data to guide clinicians on how to manage patients with saddle PE in general. A few small studies have shown that saddle PE does not confer an unfavorable clinical outcome, with mortality between 4.5% and 16%.[11,13] Only 1 study showed higher 1-year mortality rates in

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patients with saddle PE.[14] The wide variations in outcomes reflect the small sample sizes of these studies.

The aim of the present study was to better define the clinical presentation and outcomes of a large cohort of patients with saddle PE. Furthermore, we compared the clinical presentation and outcomes of patients with saddle PE with those of a matched nonsaddle PE cohort.

METHODS

The study was approved by the Mayo Clinic Institutional Review Board. We included all patients from January 1, 1999, through December 31, 2014, who had authorized the use of their medical records for research purposes. Data were obtained manually and from the Mayo Clinic Life Science Services and the Data Discovery and Query Builder, structured search software that interfaces with the Mayo Enterprise Data Trust and allows for detailed search results for all available data from the electronic medical record. Full technical details and other aspects of this tool are available elsewhere [15-17] Relevant clinical information extracted from the electronic medical record included vital signs, demographic characteristics, comorbidities, risk factors for PE, treatment on hospital admission (anticoagulation, thrombolytics, catheter-directed thrombectomy, surgical thrombectomy), laboratory data, echocardiographic and radiographic findings, and hospital course and outcomes.

We identified all consecutive patients with saddle PE diagnosed at Mayo Clinic in Rochester, Minnesota, from January 1, 1999, through December 31, 2014, using a well-validated, customized, in-house search tool called the Data Discovery and Query Builder. We confirmed the presence of saddle PE by reviewing the contrast-enhanced chest computed tomographic (CT) scans and the associated radiology report for each patient. A saddle PE was defined as any PE with a filling defect involving the bifurcation of the main pulmonary artery on chest CT.

Matching With the Nonsaddle PE Cohort

Each patient with saddle PE was matched in a 1:1 manner with a control (nonsaddle PE) diagnosed during the same period (January 1, 1999, through December 31, 2014). Nonsaddle PE was defined as any PE diagnosed by chest CT that did not involve the main pulmonary artery bifurcation area and included lobar, segmental, and subsegmental PE cases. Matching was based on age and the simplified Pulmonary Embolism Severity Index (sPESI). The sPESI is a validated bedside clinical score that allows for risk stratification of patients with PE into low- and high-risk groups in a binary manner.[18,19]

Hemodynamic Stratification of Patients With Saddle PE and Nonsaddle PE

Both cases (saddle PE) and controls (nonsaddle PE) were stratified as per initial clinical presentation into 1 of the following 3 hemodynamic categories:

1. Massive PE, defined as any PE requiring intubation or chest compressions/cardiopulmonary resuscitation (CPR) or presenting with persistent hypotension with systolic blood pressure less than 90 mm Hg for at least 15 minutes or requiring inotropic support, not due to another cause such as arrhythmia, hypovolemia, sepsis, or left ventricular dysfunction.[12]
2. Submassive PE, defined as any PE presenting without hypotension but with signs of either right ventricular (RV) dilatation/dysfunction on the echocardiogram or myocardial injury as indicated by an elevated cardiac troponin level AND not meeting the criteria for massive PE.[20]
3. Low-risk PE, defined as any PE not meeting the criteria for massive or submassive PE.

Outcomes Studied

We compared demographic characteristics, comorbidities, PE risk factors, hemodynamic values at presentation, echocardiographic results, and outcomes such as admission to the ICU, ICU length of stay (LOS), hospital LOS, and in-hospital mortality between the 2 groups. The RV dilation and dysfunction was graded as per the official echocardiography report. We also studied PE-related hospital complications and treatment decisions in both groups, including shock requiring inotropic support, respiratory failure requiring mechanical ventilation, hemodynamic collapse requiring CPR, and treatments such as

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thrombolysis, catheter-directed thrombectomy, and surgical thrombectomy. The PE-related complications and treatments were classified as acute if they occurred within 6 hours of hospital admission or as delayed if they occurred more than 6 hours after hospital admission.

All data analyses were performed using JMP software, version 9.0 (SAS Institute Inc). Continuous variables are presented as median and interquartile range, and a 2-sided *t* test was used to assess statistical significance. Categorical variables are presented as proportions, and the χ^2 test was used to assess statistical significance. A $P<.05$ was deemed to be statistically significant.

RESULTS

We identified 187 patients with saddle PE during a 15-year period (January 1, 1999, through December 31, 2014) and matched them in a 1:1 manner to 187 control patients with nonsaddle PE. The demographic characteristics, comorbidities, and risk factors for PE are summarized in Table 1. The median age at diagnosis in the saddle PE group was 66.3 years (interquartile range = 56-74.5 years). Most patients were white in both groups (>90%), and approximately half were males. The most frequent comorbidity was hypertension in both groups, and it was found more frequently in the nonsaddle PE group (53% vs 42%; $P=.04$). Patients with saddle PE had a higher body mass index (calculated as the weight in kilograms divided by the height in meters squared) (31.6 vs 29.6; $P=.01$). An active malignancy was found in similar numbers in both groups (28% in saddle PE vs 25% in nonsaddle PE; $P=.48$). The frequency of the risk factors for venous thromboembolism, such as recent surgery, a family or personal history of PE/deep vein thrombosis (DVT), recent trauma or immobilization, and a history of positive thrombophilia workup results, were not statistically significantly different between the 2 groups. Patients with saddle PE were more likely to have lower-extremity DVT at the time of diagnosis (72% vs 58%; $P=.01$) (Table 1).

Hemodynamic status and echocardiographic findings on hospital admission are presented in Table 2. As noted, the heart rate and systolic blood pressure on presentation were similar between the 2 groups ($P=.05$ for both). The saddle PE group had a higher proportion of patients with positive troponin

TABLE 1. Demographic Characteristics and Comorbidities[a]

Variable	Saddle PE (n=187)	Nonsaddle PE (n=187)	*P* value
Demographic characteristics			
Age (y), median (IQR)	66.3 (56-74.5)	66.3 (56-74.5)	.99
Male sex (No. [%])	98 (52)	90 (48)	0.47
White (No. [%])	180 (96)	172 (92)	0.12
BMI, median (IQR)	31.6 (27.5-37.8)	29.6 (26.2-35.5)	0.01
Comorbidities (No. [%])			
Hypertension	78 (42)	99 (53)	.04
Active malignancy	53 (28)	46 (25)	.48
DM	25 (13)	34 (18)	.26
COPD	9 (5)	15 (8)	.3
CHF	2 (1)	8 (4)	.1
Risk factors (No. [%])			
Lower-extremity DVT found at diagnosis[b]	128 (72)	84 (58)	.01
Recent immobilization	76 (41)	67 (36)	.4
Recent surgery or hospitalization	61 (33)	55 (29)	.58
History of PE/DVT	37 (20)	39 (21)	.9
Family history of PE/DVT	17 (9)	8 (4)	.1
Nursing home residents	8 (4)	12 (6)	.5
Positive thrombophilia work-up	6 (3)	10 (5)	.44

[a]BMI = body mass index; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; DVT = deep vein thrombosis; IQR = interquartile range; PE= pulmonary embolism.
[b]Lower-extremity ultrasound was performed in 178 patients with saddle PE and 144 with nonsaddle PE.

TABLE 2. Hemodynamic Status and Echocardiographic Findings on Presentation[a]

Variable	Saddle PE (n=187)	Nonsaddle PE (n=187)	*P* value
Highest HR on day of admission (beats/min), median (IQR)	108.5 (93-128.5)	103 (89-121)	.05
Lowest systolic blood pressure on day of admission (mm Hg), median (IQR)	100.5 (87.3-120)	107.5 (94-125.8)	.05
Lowest oxygen saturation on day of admission (%), median (IQR)	92 (87-94)	92 (88-95)	.13
Anatomic location of PE (most proximal) (No.)			
Saddle	187	0	
Main pulmonary arteries	0	60	
Segmental/subsegmental	0	127	
Troponin elevation within 24 h of admission ($\geq$0.01 ng/mL) (No. [%])[b]	97 (71)	50 (40)	<.001
Hemodynamic classification (No. [%])			
Massive	58 (31)	38 (20)	
Submassive	92 (49)	59 (32)	.01
Low risk	37 (20)	90 (48)	
Echocardiographic parameters at diagnosis			
RVSP (mm Hg), median (IQR)			
RV dilatation (No. [%])[c]	48 (40-57)	46 (36-60)	
Mild RV dilation	59 (41)	13 (15)	
Severe RV dilation	62 (43)	45 (52)	.46
No RV dilation	23 (16)	28 (33)	<.001
RV systolic dysfunction (No. [%])[d]			<.001
Mild RV systolic dysfunction	52 (36)	11 (13)	
Severe RV systolic dysfunction	67 (46	43 (50)	.30
No RV systolic dysfunction	26 (18)	32 (37)	
D-shaped left ventricle (No. [%])[d]	32 (22)	14 (16)	

[a]HR = heart rate; RV = right ventricle; RVSP = right ventricular systolic pressure.
[b]Data available in 136 patients with saddle PE and 126 with nonsaddle PE.
[c]Data available in 144 patients with saddle PE and 86 with nonsaddle PE.
[d]Data available in 145 patients with saddle PE and 86 with nonsaddle PE.

values indicative of RV injury/strain ($P<.001$). In the control group, two-thirds of patients had either segmental or subsegmental PE, confirming a clear distinction in the clot location compared with the saddle PE group.

Echocardiography was performed more frequently in the saddle PE group (77% vs 46%) and showed significant differences between the 2 groups. The most prominent difference was in the proportion of patients with normal vs mild abnormalities in RV dilation and systolic dysfunction. The saddle PE group had a much higher proportion with mild RV dilation, whereas the nonsaddle group showed a higher proportion with no RV dilation ($P<.001$ for overall comparison). Similar findings were also noted for mild vs no RV systolic dysfunction, with the saddle PE group showing a higher proportion of patients with mild RV systolic dysfunction ($P<.001$, overall comparison).

More patients in the saddle PE group were classified as having massive (31% vs 20%) or submassive (49% vs 32%) PE, whereas low-risk PE was more common in the nonsaddle PE group (20% vs 48%; $P=.01$).

Table 3 shows complications and treatments administered during the acute phase (within 6 hours of hospital admission). The use of vasopressors and the need for CPR along with mechanical ventilation were not statistically significantly different between groups in the acute phase; however, patients in the saddle PE group were more frequently treated with systemic thrombolysis (10% vs 4%; $P=.04$). The need for surgical thromboendarterectomy (3.7% in saddle PE vs 0.5% in nonsaddle PE; $P=.07$) and catheter-directed thrombectomy (1% in saddle PE vs 1% in nonsaddle PE; $P>.99$) were not different in both groups, likely due to small numbers of events. The saddle PE group had twice the rate of inferior vena cava (IVC) filter placement (40% vs 21%; $P<.001$).

During the delayed phase (>6 hours from hospital admission), the rates of decompensation resulting in PE-related shock, mechanical ventilation, and thrombolysis happened more

TABLE 3. Treatments Administered During the Acute Phase (Within 6 Hours of Hospital Admission)[a]

Variable	Saddle PE (n=187)	Nonsaddle PE (n=187)	*P* value
ICU admission (No. [%])	111 (59)	71 (38)	<.001
Vasopressor use (No. [%])	16 (9)	9 (5)	.2
CPR (No. [%])	3 (1.6)	5 (2.7)	.7
Mechanical ventilator (No. [%])	15 (8)	11 (6)	.5
Systemic thrombolysis (No. [%])	19 (10)	8 (4)	.04
Catheter-directed thrombectomy (No. [%])	2 (1)	2 (1)	>.99
Surgical thromboendarterectomy (No. [%])	7 (4)	1 (0.5)	.07
IVC filter placement (No. [%])[b]	74 (40)	39 (21)	<.001

[a]CPR = cardiopulmonary resuscitation; ICU = intensive care unit; IVC = inferior vena cava.
[b]Includes all IVC filters placed at any point during the PE-related hospitalization.

frequently in the saddle PE group. Twelve patients with saddle PE deteriorated after 6 hours of hospitalization compared with 6 patients in the nonsaddle PE group. The need for mechanical ventilation after the acute phase was higher in the saddle PE group (6% vs 1%; P=.02), and thrombolytic therapy was also used more frequently in this group (3.2% vs 0%; P=.03).

Table 4 shows similar hospital and ICU LOSs between the 2 groups. Overall in-hospital mortality was also similar in the 2 groups and low overall (4.3% in saddle PE vs 5.4% in nonsaddle PE; P=.81).

DISCUSSION

We report on the first large study of patients with saddle PE compared with a contemporary cohort of age- and sPESI-matched patients with nonsaddle PE. Although patients with saddle PE were more likely to present with massive or submassive PE, they did not seem to carry a higher risk of in-hospital mortality compared with this severity-adjusted nonsaddle PE cohort. In addition, rates of vasopressor use or need for CPR within 6 hours of hospital admission were not significantly higher compared with the nonsaddle PE cohort. However, we did find that patients with saddle PE had a slightly higher risk of delayed decompensation, with higher rates of mechanical ventilation and delayed thrombolytic use (>6 hours from hospital admission). Patients with saddle PE were also more likely to be diagnosed as having a lower-extremity DVT and were twice as likely to undergo IVC filter placement. Thus, patients with saddle PE seem to have some specific in-hospital morbidity risks but not necessarily a higher mortality rate.

Importance of Hemodynamic vs Anatomic Stratification of PE

In previous studies and in clinical practice, the term *saddle PE* has often been used interchangeably with *massive PE*. However, the term *massive PE* is a hemodynamic definition and should refer only to a PE presenting with severe hemodynamic compromise, including shock, vasopressor use, or the need for CPR. Patients with saddle PE, on the other hand, can (and often do) present with completely stable hemodynamic findings and minimal symptoms. This is confirmed by the fact that less than one-third of patients with saddle PE in the present study presented with massive PE features. Thus, the terms *massive PE* and *saddle PE* should not be used

TABLE 4. Outcomes

Variable	Saddle PE (n=187)	Nonsaddle PE (n=187)	*P* value
ICU LOS (d), median (IQR)	1.72 (0.89-2.94)	1.99 (0.89-4.1)	.25
Hospital LOS (d), median (IQR)	5 (3-7)	4 (2-8)	.09
In-hospital mortality (No. [%])	8 (4)	10 (5)	.81

ICU = intensive care unit; IQR = interquartile range; LOS = length of stay.

interchangeably. In fact, 20% of patients with nonsaddle PE also presented with massive PE features despite the fact that two-thirds of them had anatomic clot burden only in a segmental/subsegmental location. This clearly reinforces the notion that PE should be managed and triaged based on hemodynamic values and clinical presentation rather than on the location of the anatomic clot burden. We used the same criteria for massive PE as described in the 2011 American Heart Association scientific statement[21] but added "respiratory failure requiring mechanical ventilation" as an additional criterion to classify patients as having massive PE based on our observations from clinical practice.

Higher Rates of Thrombolysis and DVT in the Saddle PE Cohort

The saddle PE group received more systemic thrombolytic therapy than the nonsaddle PE group (n=19, 10% vs n=8, 4%; *P*=.04). Of the 19 patients who received thrombolytic therapy in the saddle PE group, 10 presented with massive PE and 9 with submassive PE. Another 6 patients with saddle PE underwent surgical thromboendarterectomy, and all of them presented as having massive PE. Catheter-directed thrombolysis was used in only 2 patients in each group. Thrombolytic use for saddle PE has varied widely in previous studies, with Ryu et al[10] and Sardi et al[11] reporting similar findings to the present study (7% and 11%, respectively), whereas Pruszczyk et al[13] and Yusuf et al[14] reported significantly higher rates (29% and 27.8%, respectively). However, the small number of patients with saddle PE in those studies limits their external validity. Thrombolytic use in submassive PE is more controversial, with recent randomized controlled trials showing no clear mortality benefit, although there does seem to be a decreased risk of secondary decompensation.[20]

Patients with saddle PE presented more frequently with concurrent DVT on hospital admission. This finding may reflect the higher rates of leg ultrasound examinations performed in patients with saddle PE (detection bias) but may also point toward a higher lower-extremity clot burden in these patients. The higher rate of IVC filter placement in the saddle PE group is not surprising given these findings. Echocardiography was also performed more frequently in patients with saddle PE compared with patients with nonsaddle PE (145 vs 86). The frequency of RV enlargement and dysfunction in the present study is similar to that in other studies: Ryu et al[10] and Sardi et al[11] found 90% and 78% RV enlargement, respectively, in patients with saddle PE.

Low Rates of Thrombolysis and Interventional Therapies in Massive PE

A high proportion of patients (80%) in the saddle PE group were classified as having either massive or submassive PE vs 52% in the nonsaddle PE group. Given that the 2 cohorts were matched based on age and sPESI, it does seem that central clot burden is an independent risk factor for hemodynamic compromise. Nonetheless, most patients classified as having massive PE did not receive thrombolysis or other interventional therapies. Among patients with massive PE, only 16 (28%) in the saddle PE group and 7 (18%) in the nonsaddle PE group received thrombolytics or embolectomy (surgical or catheter directed). This finding was consistent with the findings of a previous study by Kucher et al[22] in which only one-third of the patients with massive PE received thrombolytics or embolectomy. This finding is likely related to the definition of massive PE because most of the studies, including the present study, considered a systolic blood pressure less than 90 mm Hg for 15 minutes as a cutoff point to define massive PE. This likely overestimated massive PE cases owing to inclusion of patients with an immediate and sustained hemodynamic improvement to fluid boluses alone. In the present study, only 16 patients (9%) in the saddle PE group and 9 (5%) in the nonsaddle PE group received vasopressors as a treatment for persistent shock. The remaining patients who met the definition of massive PE had only transient hypotension with an adequate response to fluid resuscitation alone. These findings are in agreement with those of Sardi et al,[11] who described hypotension for more than 15 minutes in 16% of the patients with saddle PE in their study; however, only 8% of those patients had persistent shock that required vasopressor use. Given the low mortality rates overall, the use of transient hypotension as a criterion to define massive PE may need to be revisited, and only patients who receive vasopressor therapy for persistent hypotension could be considered to meet this criterion.

Late Decompensation in the Saddle PE Group

Systemic thrombolysis therapy for late (>6 hours after admission) decompensation was used more frequently in the saddle PE group compared with the nonsaddle PE group (n=6, 3.2% vs 0%; *P*=.03). These findings are similar to the findings of Kwak et al,[23] who found that saddle PE was an independent predictor of the development of major adverse events within 30 days of diagnosis. Delayed decompensation should be considered by clinicians taking care of patients with saddle PE, and close clinical and hemodynamic monitoring is recommended within the first 12 to 24 hours of admission.

One of the most important findings of the present study is that there is no difference in outcomes such as mortality or hospital or ICU LOS when patients with saddle PE are compared with an age- and sPESI-matched cohort of patients with nonsaddle PE. This, again, points toward a hemodynamic presentation and comorbidities being the primary drivers of PE outcomes rather than the location or extent of the anatomic clot burden.

Limitations of the present study include the retrospective nature and its associated shortcomings, including selection bias and hidden confounders. Strengths of the present study include the large number of consecutive patients with saddle PE studied in a systematic manner from a single center. We also had access to detailed hemodynamic, laboratory, and imaging studies in each patient via the electronic medical record. In addition, this study is unique in the use of an age- and sPESI-matched cohort of patients with nonsaddle PE for comparison. This allowed us to adjust for the most important factors influencing PE outcome and to more precisely isolate the effect of the saddle location on outcomes.

CONCLUSION

Although patients with saddle PE tend to present with greater hemodynamic compromise, they have a low in-hospital mortality rate, which is similar to that of an age- and severity-matched nonsaddle PE cohort. Patients with saddle PE do seem to have higher rates of DVT and a higher risk of late decompensation. Thus, optimal clinical management of patients with saddle PE should be based on the initial and delayed hemodynamic status rather than on the location and extent of the anatomic clot burden.

Abbreviations and Acronyms: **BMI** = body mass index; **CHF** = congestive heart failure; **COPD** = chronic obstructive pulmonary disease; **CPR** = cardiopulmonary resuscitation; **CT** = computed tomographic; **DM** = diabetes mellitus; **DVT** = deep vein thrombosis; **HR** = heart rate; **HTN** = hypertension; **ICU** = intensive care unit; **IQR** = interquartile range; **IVC** = inferior vena cava; **LOS** = length of stay; **PE** = pulmonary embolism; **RV** = right ventricle; **RVSP** = right ventricular systolic pressure; **sPESI** = simplified Pulmonary Embolism Severity Index

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