

## Review Article



# The Prognosis and New Treatments of Saddle Pulmonary Embolism: A Narrative Review

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**Abstract**

**Background:** A saddle pulmonary embolism (SPE) occurs when a blood clot blocks the main pulmonary artery or extends into both main pulmonary arteries. SPE is considered a non-fatal disease in some articles; however, recent research suggests that it could be a life-threatening condition. Treatment of patients with heparin or fibrinolytics depends on the prognostic evaluation of patients. This review study was conducted to address the controversy between different articles.

**Methods:** In this review, international databases, including PubMed, Scopus, and Web of Science, were searched for relevant studies. Finally, related articles were selected and included in the study using titles and abstracts.

**Results:** Based on the results, a total of 13 articles had prognostic evaluations for SPE. Among these articles, 5 articles suggested that SPE did not increase patient mortality, 5 articles suggested SPE as a prognostic factor for adverse events including higher mortality, and 3 articles did not show higher short-term mortality but reported some adverse events. Additionally, 9 articles were selected for new treatments. This review revealed a significant controversy between articles, indicating that further investigations should be conducted in this area, focusing on the size of the clot, its extension, and the comorbidities of patients.

**Conclusion:** It appears that hemodynamic changes on admission and during hospitalization are more important than the pure diagnosis of SPE in predicting patients' outcomes.

**Keywords:** Saddle pulmonary embolism, Mortality, Adverse events, Prognosis, Treatment

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**Introduction**

The outcome of acute pulmonary embolism (PE) can vary from a low-risk disease to a fatal disease. The mortality rate associated with PE in different studies varies depending on the initial clinical manifestations and the severity of the underlying pulmonary embolism. It has been shown that the in-hospital mortality of acute pulmonary embolism is about 12.7%, and the one-year mortality is 24.3%.<sup>1</sup>

In patients with unstable hemodynamics, removing the clot from the pulmonary arteries is very effective in preventing the worsening of the patient's condition. Thrombolytic therapy is recommended in patients with hemodynamic instability and severe right ventricular strain. There is also a general agreement that pulmonary embolism, which disturbs the patient's hemodynamics and causes a pressure drop, should be treated aggressively using fibrinolytic therapy or, in special cases, with surgical embolectomy.

**The Prognosis of Saddle Pulmonary Embolism**

In a study, Hajizadeh et al showed that out of 36 patients

who underwent surgical embolectomy, 10 patients (27.8%) died during the operation due to cardiopulmonary abnormalities before surgery (3 cases) and hemodynamic instability resulting in severe shock (2 cases). The mortality rate of surgical embolectomy was 27.7%. After excluding the above-mentioned 5 cases, the death rate decreased to 16.1%. Prolonged cardiopulmonary resuscitation (CPR), cardiogenic shock, and resultant ischemic state can lead to irreversible cardiac and hemodynamic conditions.<sup>2</sup>

Meanwhile, pulmonary embolism presenting a moderate risk of mortality continues to pose clinical challenges. Typically, these patients maintain normal blood pressure levels but may exhibit decreased oxygen saturation or present with an enlarged right ventricle. Given their compromised total lung capacity, even minimal increases in embolic burden can precipitate hemodynamic instability. The prognostic significance of saddle pulmonary embolism (SPE), along with its management and patient outcomes, remains an area requiring further elucidation.

SPE, a type of thromboembolism, is diagnosed by CT



angiography of the pulmonary vessels. It is characterized by a visible clot in the bifurcation of the trunk of the main pulmonary artery, which may extend to its right or left branch.<sup>3-5</sup> SPE has been reported in 3% to 5% of patients who undergo computed tomography pulmonary angiography (CTPA) and in 15% of patients who undergo transesophageal echocardiography with a definitive diagnosis of pulmonary embolism. Sometimes, in patients who are hemodynamically unstable and die before the diagnostic procedure is performed, the disease is confirmed at autopsy.<sup>6-8</sup>

While some studies recommend invasive treatment such as surgical embolectomy for patients with SPE, other studies have shown that invasive methods may not be useful and could increase the risk of complications and prolong hospitalization.

Sardi et al demonstrated that most patients with SPE have stable hemodynamics and respond well to standard treatment with unfractionated heparin, without the need for invasive procedures.<sup>9</sup> In a case report, Biggs et al successfully treated a patient with COVID-19, deep vein thrombosis, SPE, and concomitant right ventricular enlargement with intravenous anticoagulants and non-invasive treatment.<sup>10</sup>

As mentioned earlier, the most important predictors of mortality and complications in patients with massive pulmonary embolism are hemodynamic instability and resistant hypotension.<sup>11</sup> Resistant hypotension, defined as a systolic blood pressure less than 90 mm Hg after proper treatment, can increase the 90-day mortality rate of patients with pulmonary embolism by 52.4%. On the other hand, right ventricular (RV) dysfunction has been shown to be an important predictor of adverse events in normotensive patients.<sup>12</sup> Therefore, excluding high-risk patients, especially those who die soon after admission, can significantly change the results.

In the study conducted by Ibrahim et al, 73 patients (16.9% of all patients diagnosed with pulmonary embolism) had SPE. This study showed that compared to other patients with non-SPE, patients with SPE had significantly more tachycardia, a greater need for admission to the intensive care unit (ICU), and were more prone to hypotension and cardiac arrest after hospitalization. Despite these findings, hypoxia, hypotension, and mortality rates were the same in both groups. Overall, this study showed that patients with SPE are prone to more adverse cardiovascular events.<sup>13</sup>

Although many experts believe that the presence of massive embolism in CTPA, defined as 50% of the pulmonary vessels being occupied by a clot, is an indication for aggressive treatment, the exact mortality rate of these patients is still a matter of debate.<sup>14</sup>

Jia et al studied 727 patients with acute pulmonary embolism who did not meet the high-risk criteria for 30 days. This study showed that patients with embolism in the main pulmonary artery who did not have SPE were at higher risk of hemodynamic deterioration, while patients with SPE were not. Finally, they concluded that low-risk

patients with SPE were not at a higher risk of worsening hemodynamic conditions.<sup>15</sup>

Ryu et al demonstrated that patients with SPE are not necessarily at a higher risk of death and disease complications compared to other patients.<sup>6</sup> Kaczyńska et al found that patients treated with SPE do not experience adverse clinical outcomes, and there are likely no long-term concerns about their health<sup>16</sup>. Alkinj et al discovered that while patients with SPE may experience a higher degree of hemodynamic instability and require aggressive treatment, their prognosis is not worse compared to other patients, with a low in-hospital mortality rate.<sup>17</sup>

Conversely, a study by Yusuf et al revealed that although patients with SPE do not have a worse short-term prognosis, they do have a higher mortality rate after one year.<sup>18</sup>

In patients presenting with shock, the majority of deaths occur within the first hour of hospitalization.<sup>19</sup> Some patients do not seek medical attention in the early stages of symptoms, often mistaking them for common colds or panic attacks, which delays their referral to cardiologists or lung disease experts. A study showed that 26% of patients with SPE were diagnosed more than 6 hours after hospitalization, indicating a continued delay in diagnosis despite admission to appropriate centers.<sup>20</sup>

In the study conducted by Wong et al,<sup>21</sup> 120 patients with SPE were examined, with only 4.2% showing symptoms indicative of massive embolism upon initial examination. The study reported an in-hospital mortality rate of 9.2% and a mortality rate of 8.6% within 6 months after discharge, with higher mortality rates observed in women. The study suggested that SPE is a significant risk factor for patient mortality and that stable hemodynamics on admission do not guarantee a low mortality rate in the following days. Simultaneous embolism in segmental pulmonary arteries and deep vein thrombosis can also significantly impact disease outcomes. The study conducted by Wong et al demonstrated that central pulmonary embolism, including the main pulmonary artery or left/right pulmonary arteries, was an independent predictor of adverse outcomes.<sup>21</sup>

Ghanima et al proposed that the location of the clot in the proximal part of the pulmonary artery is a valuable prognostic factor.<sup>19</sup> Kwak et al showed that cases of SPE had lower short-term mortality but higher rates of adverse events and were more likely to receive fibrinolytic therapy.<sup>22</sup>

Prentice et al conducted a study on 475 patients, 4.5% of whom had cancer and pulmonary embolism, and SPE was associated with a higher risk of mortality (odds ratio = 1.51; 95% confidence interval: 1.08-2.10).<sup>23</sup> However, Aramberri et al conducted a study on 66 patients (12% of all patients) with a history of cancer and pulmonary embolism. They showed that 58% were symptomatic, and right ventricular overload was more common in SPE cases. The study also found that the 30-day mortality rate was not significantly different between saddle and non-SPE groups.<sup>24</sup>

Hajizadeh et al showed that SPE is associated with higher adverse events. An O<sub>2</sub> saturation of <90%, systolic

blood pressure of <100 mm Hg, and the presence of SPE were independent prognostic factors for in-hospital mortality.<sup>25</sup> Given the critical nature of this topic and the extensive body of research dedicated to it, this review critically assessed the disparate findings reported in the literature regarding the mortality risk associated with SPE.

### New Treatments of Saddle PE

Treatment of saddle PE usually involves a combination of anticoagulant therapy, thrombolytic therapy, and sometimes surgical intervention.<sup>26</sup> Some new treatments and approaches that might be considered for saddle PE are summarized as follows:

**Catheter-directed thrombolysis:** It is a less invasive technique in which a thrombolytic agent is introduced directly into the blood vessels via a catheter in order to dissolve the clot in the artery.<sup>27</sup>

**Advantages:** When compared to traditional systemic thrombolysis, catheter-directed thrombolysis has been found to have certain benefits such as causing less bleeding complications, delivering medicine specifically to the site of clot formation, and enabling faster and better clot resolution.

**Disadvantages:** Though generally safe and effective, there are some risks with this type of treatment like bleeding at the site where they put in the catheters, allergic reactions to these drugs, as well as possibly detached pieces of clots going through other body parts.<sup>28</sup>

**Ultrasound-facilitated thrombolysis:** This procedure combines ultrasound with thrombolytic therapy to speed up the breakdown of blood clots in the arteries of the lungs. Ultrasound-facilitated thrombolysis might improve the efficacy of thrombolytic therapy and reduce the risk of bleeding.<sup>29</sup>

**Advantages:** This process offers a more focused method for removing blood clots using clot-dissolving medications combined with ultrasound technology. The breaking up of the clot by ultrasound waves helps the medication to penetrate through it, thereby hastening clot resolution. Additionally, compared to traditional forms of thrombolytic therapy, ultrasound-assisted thrombolysis is associated with lower bleeding incidence and may be safer for certain patients. The use of this technique results in improved blood circulation, symptomatic relief, and prevention of long-term sequelae related to venous obstruction.

**Disadvantages:** Ultrasound-guided thrombolysis is generally considered safe and effective; however, there are potential risks or complications that could occur during or after the procedure. These complications include bleeding in the area where a catheter is inserted into an artery or vein (the insertion site), hypersensitivity reactions to intravenous TPA (the drug used to break up clots), and distal embolization whereby bits of the clot can dislodge from their site of formation and travel elsewhere in the body. Additionally, there is a risk of damage to the blood vessel or surrounding tissues during the procedure.<sup>30</sup>

**Surgical embolectomy:** In some instances, when anticoagulants and thrombolytics fail or cannot be used, surgical embolectomy may be an option for treating saddle PE. This procedure involves the removal of a blood clot from the pulmonary artery by a surgeon to restore lung perfusion.<sup>31</sup>

**Advantages:** Surgical embolectomy has various advantages in cases of severe or life-threatening clots that include the removal of the blood clot from the affected artery or vein so as to enable uninterrupted circulation and avoid complications like tissue necrosis, as well as a tailor-made management plan directed at features peculiar to the obstructed vessel. Additionally, this technique can work hand-in-hand with other therapies, lower the risk of reoccurrence, and enhance future vascular health prospects.

**Disadvantages:** Surgical embolectomy is a major surgical procedure with risks such as bleeding, infection, damage to surrounding tissues or organs, and anesthesia-related problems.<sup>32</sup>

**Inferior vena cava (IVC) filter placement:** In some instances, an IVC filter can be put in place to prevent clots of blood from going to the lung and causing a saddle PE. An IVC filter is a tiny gadget that gets placed into the IVC, catches blood clots, and does not allow them into the pulmonary arteries.<sup>33</sup>

**Advantages:** The placement of an IVC filter can offer several benefits, the most important of which is trapping blood clots before they reach the lungs. This may help decrease the life-threatening risk of pulmonary embolism in patients who cannot take anticoagulants or continue developing thrombosis despite treatment. IVC filters are especially helpful in surgical patients, accident victims, and patients with certain diseases predisposing to clot formation. It is a non-invasive procedure that can be performed on outpatients; hence, it is a relatively fast and effective way of preventing pulmonary embolism among those at risk.

**Disadvantages:** There is a possibility that the filter can move from its original position, leading to complications such as perforation of the filter, migration to other organs, or blockage of the IVC. Sometimes blood clots may be trapped in the IVC filter, which may lead to blockage in the vein. The risk of infection at the site where it is placed or allergic reactions to materials used in constructing the filter also exists. In addition, long-term use of an IVC filter might lead to complications such as DVT or fracture of the filter. Patients undergoing IVC filter placement should be closely monitored for any signs of complications, and the decision to use an IVC filter should be carefully considered based on the individual's risk factors and medical history.<sup>34</sup>

### Methods

PubMed, Scopus, and Web of Science databases were searched for related articles published from 2005 to 2024 using the following keywords: saddle pulmonary embolism, mortality, prognosis, and treatment. Subsequently, review

articles were excluded, and the language of the articles was limited to English. Finally, related articles were selected using the title and abstract.

## Results

A total of 13 articles had prognostic evaluation for SPE. Among these articles, 5 articles suggested that SPE do not increase the mortality of patients, 5 articles suggested SPE as a prognostic factor for adverse events including higher

mortality, and 3 articles did not show higher short-term mortality but reported some adverse events (Table 1). Moreover, 9 articles were selected for new treatments of SPE. This review reveals that there is a great controversy between articles and more investigations should be done in this era with a focus on the size of the clot, its extension, and comorbidities of patients. It is important that the treatment approach chosen for saddle PE should depend on the patient's condition, size and location of the blood

**Table 1.** Effect of Saddle Pulmonary Embolism on Mortality and Morbidity of Patients

Study	SPE Patients	Average Duration of Hospitalization	Mortality	Systemic Diseases	Conclusion
Sardi et al <sup>9</sup>	37	9	2	No	The study reported that unfractionated heparin was administered to 87% of the patients, while thrombolytics were given to 11%. Most patients were stable and heparin therapy was useful.
Biggs et al <sup>10</sup>	1	Unknown	0	COVID-19	The case study underscored the importance of maintaining a high clinical suspicion for pulmonary embolism in individuals diagnosed with COVID-19, especially in those with resolving symptoms of the viral infection. Successful treatment with anticoagulants alone was achieved and non-invasive method was preferred.
Ibrahim et al <sup>13</sup>	73	Unknown	2	Diabetes, hypertension, heart failure	Patients with saddle pulmonary embolism had a higher prevalence of hypotension and cardiac arrest but the overall mortality was not higher compared to the PE.
Jia et al <sup>15</sup>	51	Unknown	4	Unknown	The thrombus location in the main pulmonary artery (MPA) is a key factor indicating a higher risk of deterioration in acute pulmonary embolism (PE) patients. Saddle pulmonary embolism does not necessarily pose a higher risk than non-MPA embolism. Effective management and treatment of acute PE should integrate thrombus location with other risk predictors.
Ryu et al <sup>6</sup>	14	4	0	No	Saddle PE was not correlated with increased in-hospital mortality, making its prognostic significance unclear. It exhibited diverse clinical symptoms, often without hemodynamic instability.
Kaczyńska et al <sup>16</sup>	22	Unknown	1	Unknown	Saddle PE often occurs in patients showing echocardiographic evidence of reduced pulmonary function. However, it does not necessarily lead to worse clinical outcomes and should not be the sole factor in choosing a treatment approach.
Alkinj et al <sup>17</sup>	187	5	8	Hypertension, COPD, Congestive heart failure, malignancy, diabetes	Patients with saddle pulmonary embolism may experience a higher degree of hemodynamic instability. However, their short-term outcomes, including in-hospital mortality, are similar to those of patients with non-saddle PE. The study emphasized the need to focus on the hemodynamic status rather than the location of the clot in managing patients with saddle PE.
Yusuf et al <sup>18</sup>	18	Unknown	2 (1 month) 15 (1 year)	Cancer	This study was conducted on cancer patients and found that large pulmonary embolism (PE) identified by CT scans increased mortality rates. The presence of a saddle pulmonary embolism was linked to a poorer one-year prognosis. CT imaging could effectively differentiate between saddle and non-saddle PE for risk assessment for up to a year after the initial PE event.
Wong et al <sup>21</sup>	120	9	11 (in-hospital)	Malignancy, sepsis	SPE was linked to high inpatient mortality, especially in diverse urban populations. Traditional scans could not effectively diagnose SPE, and right heart thromboembolism, in particular, had a high mortality rate, suggesting a need for more intensive treatment strategies.
Kwak et al <sup>22</sup>	27	Unknown	5 (30 days)	Diabetes, heart failure, cancer	While saddle embolism (SE), detected via CT angiography, was not correlated with mortality in non-high risk pulmonary embolism (PE) patients in the emergency department, it predicted the occurrence of major adverse events (MAEs) related to PE within 30 days. Hence, close monitoring of SE patients for any MAEs is crucial.
Prentice et al <sup>23</sup>	475	5	41 (in-hospital)	Cancer	This study associated saddle pulmonary embolism with a higher risk of mortality, especially in patients with cancer.
Aramberri et al <sup>24</sup>	36	Unknown	5 (30 days)	Cancer	The findings of the study contrasted with those of Prentice et al, showing no significant difference in 30-day mortality rates between saddle and non-saddle PE groups.
Hajizadeh et al <sup>25</sup>	70	Unknown	20 (in-hospital)	Congestive heart failure, diabetes, COPD	The findings of the study indicated that the presence of SPE was statistically significant in predicting both in-hospital mortality and side effects among PE patients, a result that contradicts numerous prior studies.



clot, as well as any underlying health conditions.

### Discussion

The prognostic implications of SPE have been a subject of considerable debate in the medical community. The divergence in findings from various studies underscores the complexity of SPE as a clinical entity and its impact on patient outcomes. While some studies suggest that SPE does not inherently increase mortality, others associate it with a higher risk of adverse events, including death.<sup>19</sup>

One of the primary challenges in reaching a consensus is the heterogeneity of study populations. Many studies have varied in their inclusion criteria, with some focusing solely on stable patients and others including those with immediate post-admission mortality. This discrepancy can significantly skew results and interpretations, leading to conflicting conclusions about the true impact of SPE on patient prognosis.

Moreover, the current body of literature often lacks granularity concerning the size and extension of the clot, as well as the presence of concurrent deep vein thrombosis. These factors are crucial in understanding the pathophysiology of SPE and its potential to precipitate hemodynamic compromise. Without this detailed information, it is challenging to formulate a comprehensive risk profile for patients with SPE.

The advent of artificial intelligence (AI) in medical imaging presents a promising avenue for addressing these gaps. AI algorithms have the potential to provide more nuanced analyses of imaging studies, correlating the physical characteristics of embolism with clinical data such as laboratory results and hemodynamic parameters. Consequently, this integration could lead to better prognostication and personalized treatment methods which will ultimately improve patient outcomes.

Clearly, SPE may not be an independent predictor of mortality but still remains important in the clinical assessment of pulmonary embolism. It should prompt a thorough evaluation of the patient's hemodynamic status and consideration for aggressive treatment modalities when needed. As the field moves forward, it is imperative that future studies incorporate more detailed analyses of clot characteristics and leverage advanced technologies such as AI to enhance our understanding of SPE. Only through such concerted efforts can we hope to resolve the current controversies and provide clear guidance for the management of this complex condition.<sup>35</sup>

The management of SPE is intricate and necessitates a comprehensive approach. The treatments mentioned in the article offer promising avenues for managing SPE, they also come with their own set of challenges and risks. Healthcare practitioners must weigh several factors such as the patient's specific condition, severity of the PE, and potential benefits/drawbacks associated with each approach before making their choice. Further studies will improve these therapies, minimizing potential hazards and enhancing prognosis among patients with SPE.

### Conclusion

Saddle pulmonary embolism may not be an independent predictor of mortality but still remains important in clinical assessment of patients, especially in intermediate risk patients. New treatments may reduce mortality in these patients.

### Ethics statement

Not applicable.

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### Conflict of interests declaration

The author declares that he has no conflict of interests.

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### Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

### Author contributions

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