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PULMONARY EMBOLISM IN ICU PATIENTS

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Abstract:

Introduction: *Pulmonary embolism is a serious condition that, in some cases, can be fatal and lead to significant complications or mortality. A major pulmonary embolism generally manifests with rapid right ventricle failure along with severe hypoxia. The changes in pressure of the right ventricle are usually related to both the mechanical changes resulting from the vessels obstruction and the presence of abnormal cardiopulmonary condition. Management of pulmonary embolism must start as soon as possible, especially when dealing with patients with critical conditions, who must be immediately moved to the intensive care unit*

Aim of work: *In this review, we will discuss the most recent evidence regarding the management strategies for high-risk PE in recent years.*

Methodology: *We did a systematic search for the most recent evidence regarding the management strategies for high-risk PE in recent years using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). Our search also looked for the pathophysiology and prevention. All relevant studies were retrieved and discussed. We only included full articles.*

Conclusions: *Pulmonary embolism is an emergent condition that can be serious and life threatening. Diagnosis of pulmonary embolism can be confirmed using CT angiography, or echocardiograph. However, in high-risk patients, treatment should be immediately started without waiting for test results. Anticoagulation agents are the main line of treatment, and unfractionated heparin must be administrated as early as possible. Some studies have found benefits associated with the use of thrombolytics therapy. However, this should be applied with caution to prevent the development of associated complication, which can be fatal in some cases. Inferior vena cave filters are used when there is recurrence of pulmonary embolism or in patients who fail to achieve sufficient anticoagulation despite full treatment. These have been found to significantly improve mortality and recurrence of the disease, but do not provide treatment for the underlying DVT. Further studies are required to improve pulmonary embolism management and treatment protocols*

Key words: *Pulmonary embolism, DVT, critical patient, ICU, Management.*

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INTRODUCTION:

Pulmonary embolism is a serious condition that, in some cases, can be fatal and lead to significant complications or mortality [1]. Patients with pulmonary embolism are generally categorized into being high-risk or low-risk patients. Patients who have high-risk pulmonary embolism can die within few hours of the onset of the condition due to the development of severe shock. In fact, it is estimated that up to 25% of patients will develop a shock, which becomes 65% in patients with associated cardiovascular arrest [2]. Therefore, early diagnosis and proper management are crucial to prevent death in these patients.

A major pulmonary embolism generally manifests with rapid right ventricle failure along with severe hypoxia. The changes in pressure of the right ventricle are usually related to both the mechanical changes resulting from the vessels obstruction and the presence of abnormal cardiopulmonary condition. CT angiography provides an advanced method to efficiently visualize the emboli to the level of segment and the amount of enlargement of the right ventricle, which is considered an accurate indicator of the presence of right ventricular dysfunctions. Another used modality of imaging is echocardiography which can provide acceptable results when CT angiography is not available.

Most cases of pulmonary embolism result from the presence of a sudden obstruction of arteries within the pulmonary circulation. This obstruction occurs from an emboli that arises from a thrombus. In most cases, these thrombi originate from the lower extremities' deep veins [3]. Patients with other critical conditions or those who are hospitalized are considered at higher risk of developing pulmonary embolism [4].

Management of pulmonary embolism must start as soon as possible, especially when dealing with patients with critical conditions, who must be immediately moved to the intensive care unit [5]. In this review, we will discuss the most recent evidence regarding the management strategies for high-risk PE in recent years.

METHODOLOGY:

We did a systematic search for the most recent evidence regarding the management strategies for high-risk PE in recent years using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). Our search also looked for the pathophysiology and prevention. All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: pulmonary embolism, high risk, ICU, management, and prevention.

Pathophysiology

The most important clinical manifestation in patients with high-risk pulmonary embolism is the development of circulatory failure that results from the sudden right ventricular failure and lead to the development of severe hypoxia. The changes in pressure of the right ventricle are usually related to both the mechanical changes resulting from the vessels obstruction and the presence of abnormal cardiopulmonary condition. In addition, neural reflexes, and the development of systemic hypoxia will worsen the state of vasoconstriction of pulmonary vessels, which is also affected by the secretion of factors like serotonin, platelet-activating factor, thrombin, vasoactive peptides, C3a, C5a, and histamine from the platelets, plasma, and tissues [6]. In these cases, the consequence will be the development of heart failure that is the final result of higher wall stress and myocardial ischemia, which will further worsen right ventricular function and add left ventricular dysfunction [7].

Right-heart failure will eventually lead to an increase in the right ventricular load, which will act with increased wall stress to further worsen the symptoms of heart failure, leading to the development of left-heart failure from the significantly decreased left ventricular preload. This will cause a significant reduction in systemic blood pressure which will lead to more systemic hypoxia, poor tissue perfusion, and eventually death.

The average pressure in the pulmonary artery that can be caused by the right ventricle is 40 mmHg in healthy individuals [8]. Therefore, it is thought that if the pressure of the pulmonary artery becomes more than 40 mmHg during an acute pulmonary embolism, the clinician must suspect the presence of recurrence, or chronic thromboembolic pulmonary hypertension.
In addition to circulatory failure, patients with high-risk pulmonary embolism are at higher risk of developing respiratory failure, which is also a serious complication of the condition. Generally, the development of abnormalities during gas exchange in pulmonary embolism patients is associated mainly with the size of the emboli, its characteristics, the extent of obstruction caused by it, the overall cardiovascular status, and the duration of pulmonary obstruction [7].

Hypoxia can result from the increase in the dead space volume, the presence of shunting from right to left, the development of ventilation-perfusion mismatch, and the presence of low levels of mixed venous oxygen [9]. The persistence of hypocapnia and hypoxia even following treatment is thought to be a result of these mechanisms.

Diagnosis

In any patient with a suspected high-risk pulmonary embolism, following the admission to the intensive care unit and the resuscitation, undergoing CT angiography is considered the best diagnostic next step. CT angiography provides an advanced method to efficiently visualize the emboli to the level of segment and the amount of enlargement of the right ventricle, which is considered an accurate indicator of the presence of right ventricular dysfunctions [10].

Another imaging modality is CT venography which can be used to diagnose the presence of a DVT in patients in case they are hemodynamically stable, and the diagnosis of pulmonary embolism is not yet confirmed. CT venography is usually used together with CT angiography using only one dose of the contrast dye [11].

In settings where CT angiography is not readily available, or cannot be performed due to the clinical status of the patient, the use of bedside echocardiogram is preferred as it provides an acceptable visualization of the presence of increased pulmonary blood pressure and right ventricular dysfunctions. In severely ill patients with unstable vital signs, positive echocardiography results are considered enough to immediately start treatment without waiting for further test results. Bilateral venous ultrasound could sometimes be used to confirm the presence of a deep venous thrombus, especially in stable patients where the diagnosis of pulmonary embolism is not clear. Ultrasound techniques are generally useful in emergency settings [9].

Treatment:

Resuscitation is considered the single most important step in the management of a patients with pulmonary embolism. The first step is to correct abnormalities in the vital signs and maintain sufficient breathing and circulation. This becomes of higher importance in patients who are already in a state of shock at presentation. Patients with hypoxia can significantly benefit from oxygen administration. In cases where mechanical ventilation is needed, patients must be strictly monitored to prevent the development of its associated adverse events. More specifically, mechanical ventilation leads to the induction of a positive intrathoracic pressure which can potentially decrease the venous return and lead to significant worsening of the right ventricular failure in patients who have shock. To prevent this, clinicians could use low tidal volumes.

Previous studies have shown the administration of large volumes of fluid will lead to worsening symptoms of right ventricular failure, which is most likely due to the mechanical stretching of the heart that will induce depressing reflexes. However, a single trial has found that the administration of 500 millimeters of dextran within fifteen minutes in a patient with pulmonary embolism, normal blood pressure, and decreased cardiac index, led to the significant improvement of cardiac index from 1.7 l/min/m2 to 2.1 l/min/m2 [12]. Results of this trial suggest that the administration of moderate amounts of fluids can in fact improve the cardiac index in patients with pulmonary embolism, given they have normal blood pressure. The administration of large volumes is still not preferred [9]k. In summary, the amount of fluid preferred is between 500 ml to 1000 ml.

Following oxygen and fluids administration, vasopressors can be administrated while waiting for the administration of definitive treatment. The use of norepinephrine has been shown to significantly improve the functions of the right ventricle by its direct inotropic effect and increasing the perfusion of the right coronary arteries. However, no clinical trials have studied the effects of norepinephrine in patients with shock that specifically resulted from pulmonary embolism. Therefore, its use in these patients is not recommended unless the patient has severe hypotension.

A previous study has examined patients who developed high-risk pulmonary embolism and were admitted to the intensive care unit, and found that the administration of dobutamine in these patients led to significant improvements in the cardiac output and the oxygen transport, which correlated with improved tissue perfusion and oxygenation. Another study was conducted and included ten pulmonary embolism patients with decreased cardiac index and normotensive status showed that the administration of dobutamine intravenously lead to a 35% elevation of the cardiac index without significant alterations in the systemic blood pressure, the heart rate, and the pulmonary pressure [13]. Therefore, dobutamine is recommended for use in normotensive patients with pulmonary embolism given they have decreased cardiac index [14].

However, caution should be present as the elevation of cardiac index higher than normal values will lead to significant worsening of ventilation-perfusion mismatch. Epinephrine has both the advantages of epinephrine and dobutamine but does not induce vasodilation. Therefore, it could be beneficial for the use in patients with shock due to pulmonary embolism.

The use of inhaled nitric oxide can lead to improvement in the ventilation-perfusion mismatch those results from pulmonary embolism. This effect is due to its ability to selectively dilate the pulmonary vessels without dilating systemic vessels. Therefore, it is considered the best line of treatment in patients with pulmonary embolism that is not responding to other lines of treatment [15].

Some evidence has suggested that extracorporeal membrane oxygenation can be used for support in patients with pulmonary embolism resulting in circulatory collapse. This was first observed in a trial that included ten massive pulmonary embolism patients who showed improved clinical status following the initiation of extracorporeal membrane oxygenation support [16].

Pharmacological treatment

Treatment with anticoagulants is considered essential in the management of pulmonary embolism patients. In 1960, the landmark study was performed and concluded that the immediate use of unfractionated heparin leads to significant reduction in the rates of pulmonary embolism propagation and recurrence. Since then, unfractionated heparin has been recommended to be immediately used in any patient with pulmonary embolism. Immediate use of unfractionated heparin is important as rates of recurrence of pulmonary embolism are higher in the early course of the disease. The failure of early achieving therapeutic aPTT level and sufficient anticoagulation is associated with significantly higher rates of pulmonary embolism recurrence [17].

In high-risk pulmonary embolism patients, the use of unfractionated heparin should start as early as possible, and should not wait for the confirmation of diagnosis, as these cases have a higher risk of mortality. Exceptions of this include the presence of any contraindication for unfractionated heparin. Following the admisntration of heparin, the aPTT should be measured after about 6 hours, with further adjusting the dose of heparin according to aPTT results. When therapeutic aPTT is reached, its measurement once daily becomes enough.

After the patient becomes clinically and hemodynamically stable, the use of oral anticoagulants can be started. Following the initiation of warfarin, the administration of heparin must continue until the INR becomes therapeutic for two days. The uses of direct oral agents has not been assessed in trials for patients with high risk pulmonary embolism, and thus are not preferred.

Patient with acute pulmonary embolism can sometimes benefit from the use of thrombolytic therapy, which can achieve improved and more rapid perfusion when compared to the use of unfractionated heparin alone [18]. A previous study has found that patients with pulmonary embolism who received early thrombolytic therapy had better diffusing capacity than patients who did not.

However, the potential benefits of thrombolytic therapy will only occur if the patients receive treatment early and within the first two to three days. Previous studies have found that the administration of thrombolytic therapy after more than a week of presentation was not associated with any apparent benefits. In patients with acute pulmonary embolism, monteplase has been recommended to be used in cases with unstable hemodynamic status[19]. It has been found that following its use, up to 90% of cases will show improvements of hemodynamic status within the first two days [20]. Efficacy can be even better when treatment is started earlier at the course of the disease [21].

On the other hand, the use of thrombolytic therapy should be only applied with extreme caution as it could be associated with significant complications that could be fatal. Bleeding and intracranial hemorrhage are examples of possible consequences that can follow the use of thrombolytic therapy. A previously published meta-analysis concluded that about 1.5% of patients who underwent thrombolytic therapy developed intracranial hemorrhage [22], which is significantly higher than patients who only receive anticoagulants therapy [23]. The used of smaller doses of t-PA led to less rates of complications in patients with unstable hemodynamic status. In addition, the benefits of using thrombolytic therapy in patients who have thrombi in the right ventricles are still debatable [24].

Thrombolytics therapy is absolutely contraindicated in patients who have current bleeding, ischemic attack within the last two months, and any history of a prior hemorrhagic stroke. Other relative contraindications are undergoing a surgical operation within the last ten days, the presence of multiple

traumatic injuries within the last fourteen days, undergoing any neurological surgery within the last month, and undergoing any ophthalmological surgery within the last month. In the presence of these relative contraindications, thrombolytic therapy is only recommended in patients with severe pulmonary embolism and with extreme caution. In addition, any patient with cardiac arrest from a suspected pulmonary embolism is recommended to receive thrombolytic therapy, unless an absolute contraindication is present [25].

In patients who have contraindications that prevent them from receiving thrombolytics therapy, the use of catheter-directed treatment could be an acceptable alternative. Catheter-directed treatment can also be used in patients where thrombolytic therapy could not achieve sufficient improvement in hemodynamic status. Catheter- directed treatment aims at removing the thrombus that is causing the obstruction of the pulmonary circulation to induce recovery of the right ventricular function and thus decrease mortality [26].

Surgical interventions:

Embolectomy is generally used in patients with severe pulmonary embolism who need resuscitation. In addition, patients who have contraindications to thrombolytic therapy or those who did not improve sufficiently can also undergo surgical embolectomy to improve their condition. Surgical embolectomy of pulmonary embolism is considered to be a relatively simple procedure that can potentially provide rapid improvement of circulation and clinical picture [27].

Undergoing surgical embolectomy for pulmonary embolism before the occurrence of circulatory collapse has been associated with a significant decrease in mortality. The prior use of thrombolytics therapy was found to increase the risk of bleeding during embolectomy, but this is not considered a contraindication [28].

In patients with pulmonary embolism who are contraindicated to use anticoagulation therapy, or in those who could not achieve sufficient anticoagulation despite full therapeutic dose, inferior vena cava filters can be used to prevent the recurrence of pulmonary embolism. The use of inferior vena cava filters in patients with pulmonary embolism has been shown to significantly decrease mortality [29]. However, inferior vena cava filters do not provide treatment for the underlying deep venous thrombosis. In fact, filters may lead to worsening of the DVT [30]. This is still considered acceptable as complications of DVT are milder than pulmonary embolism and not associated with high mortality rates [31].

CONCLUSIONS:

Pulmonary embolism is an emergent condition that can be serious and life threatening in some patients. Pulmonary embolism cab be associated with low-risk of mortality or high-risk. In patients with high-risk pulmonary embolism, many patients develop severe shock within the first few hours, leading to death. Therefore, it is essential to properly address and manage pulmonary embolism to prevent severe consequences. the first step in the management of pulmonary embolism is the resuscitation of patients with hemodynamic instability by administrating oxygen and fluid replacements. Patients with severe shock may also benefit from the use of vasopressors. Diagnosis of pulmonary embolism can be confirmed using CT angiography, or echocardiograph. However, in high-risk patients, treatment should be immediately started without waiting for test results. Anticoagulation agents are the main line of treatment, and unfractionated heparin must be administrated as early as possible. Some studies have found benefits associated with the use of thrombolytics therapy. However, this should be applied with caution to prevent the development of associated complication, which can be fatal in some cases. Inferior vena cave filters are used when there is recurrence of pulmonary embolism or in patients who fail to achieve sufficient anticoagulation despite full treatment. These have been found to significantly improve mortality and recurrence of the disease, but do not provide treatment for the underlying DVT. Further studies are required to improve pulmonary embolism management and treatment protocols

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