

## Timely Diagnosis and Management of Pulmonary Embolism induced ischemic stroke in elderly patients

### Abstract

Timely diagnosis and management of pulmonary embolism-induced ischemic stroke in elderly patients pose significant challenges. Definitive diagnosis relies on comprehensive imaging studies like non-contrast brain MRI and computed tomography pulmonary angiography to identify and locate affected vascular territories. Transthoracic echocardiogram with agitated saline contrast proves valuable in understanding potential causes of acute ischemic stroke, aiding in detecting Patent Foramen Ovale (PFO) or intra-atrial thrombi, and providing insights into PE severity through right heart strain identification. TTE's prognostic value helps predict the condition's outcome, while Transesophageal echocardiogram accompanies TTE when results are inconclusive. Lower extremity ultrasound is crucial for comprehensive deep vein thrombosis evaluation in elderly patients, and considering occult malignancy workup (pan scan) and pelvic MR Venogram for May-Thurner syndrome is important. However, limited information on testing frequency for occult malignancy and MTS may contribute to the presence of both PFO and DVTs in multiple patients. Treatment approaches for PE-induced ischemic stroke vary based on severity and individual considerations. Acute thrombolysis with intravenous recombinant tissue plasminogen activator and mechanical thrombectomy effectively manage AIS. Intravenous heparin is a common choice for systemic anticoagulation in PE, necessitating prompt initiation to avoid worsening outcomes. However, anticoagulation alone for AIS does not improve prognosis or prevent future occurrences. Prompt IV rt-PA consideration in severe AIS cases with a high risk of hemorrhagic conversion is crucial. While having a stroke in the past six months is an absolute contraindication for PE thrombolytic therapy, it may be considered relative in life-threatening PE scenarios. In conclusion, timely diagnosis and appropriate management of PE-induced ischemic stroke in elderly patients necessitate a multidisciplinary approach. Integrating imaging studies, echocardiograms, and comprehensive thrombosis and malignancy evaluations is vital.

**Keywords:** Pulmonary embolism, ischemic stroke, Elderly patient

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8 .Commentaries / OpinionArticles:  
An opinion-based article on a topical issue of broad interest which is intended to engender discussion. We advise a length of 2500-3500 words, plus 2-3 figures and/or tables, and 15-20 key references.

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#### Comment [U2]: Abstract

The abstract should be concise and informative. It should not exceed 300 words in length. It should briefly describe the purpose of the work, techniques and methods used, major findings with important data and conclusions. Different subsections, as given below, should be used. No references should be cited in this part. Generally non-standard abbreviations should not be used. If necessary they should be clearly defined in the abstract, at first use.

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NÃO INDICA LOCAL DO ESTUDO  
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##### SAMPLE ABSTRACT:

**Aims:** Here clearly write the aims of this study.  
Sample: To correlate platelet count, splenic index (SI), platelet count/spleen diameter ratio and portal-systemic venous collaterals with the presence of esophageal varices in advanced liver disease to validate other screening parameters.

**Study design:** Mention the design of the study here

**Place and Duration of Study:** Sample: Department of Medicine (Medical Unit IV) and Department of Radiology, Services Institute of Medical Sciences (SIMS), Services Hospital Lahore, between June 2009 and July 2010.

**Methodology:** Please write main points of the research methodology applied. Sample: We included 63 patients (40 men, 23 women; age ...

## 1-Introduction

Stroke is considered to be one of the primary factors contributing to both mortality and physical impairment<sup>(1)</sup>. Medical complications that occur after an ischemic stroke play a significant role in causing unfavorable outcomes for stroke patients<sup>(2)</sup>. Pulmonary embolism (PE) is a very serious medical condition. It occurs in about 0.50 to 0.69 out of every 1000 people in the general population each year<sup>(3)</sup>. The mortality rate for PE in the 7-8 PE class is quite high, with a case fatality rate between 8.6% and 17% within a span of 3 months<sup>(4)</sup>. The mortality rate over a longer period of time can reach up to 24%<sup>(5)</sup>. The diagnosis of these two conditions is extremely challenging due to overlapping Symptoms such as shortness of breath, chest pain, and neurological deficits, making it challenging to differentiate between the two conditions<sup>(5)</sup>.

Additionally, managing these two conditions is also challenging because they require simultaneous attention: intravenous thrombolysis for acute ischemic stroke (AIS) within the first few hours of symptom onset, and systemic anticoagulation for pulmonary embolism (PE)<sup>(6)</sup>. However, administering anticoagulation after pharmacological thrombolysis in stroke is not recommended due to the heightened risk of intracranial bleeding<sup>(7)</sup>. Given the lack of specific guidelines for handling this uncommon presentation, a comprehensive review is warranted.

The management of AIS is focused on early administration of IV rt-PA and mechanical thrombectomy within specific timeframes after symptoms start<sup>(8)</sup>. Similarly, the treatment for PE involves promptly administering anticoagulants to impede the advancement of blood clots and prevent the formation of new clots<sup>(9)</sup>. While both therapies share a common physiological target and goal in theory, the intricacies of each treatment protocol present an additional layer of challenge. Even though rt-PA is generally considered safe and the chances of experiencing negative effects are low, when they do happen, they can have a severe impact, especially if there is symptomatic intracerebral hemorrhage and bleeding outside the brain<sup>(10)</sup>. Hence, it is crucial to meticulously choose appropriate candidates for this therapy. However, it is important to note that the occurrence of pulmonary hemorrhagic necrosis as a complication of rt-PA administration in patients with PE has not been thoroughly established<sup>(11)</sup>. In addition, it is important for patients who receive acute rt-PA treatment to not use antithrombotic medications at the same time. This goes against the guidelines for managing acute PE, which recommend starting patients on anticoagulation therapy as soon as possible<sup>(12)</sup>.

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### 1.1. Timely Diagnosis of Pulmonary embolism-induced ischemic stroke in Elderly patients

In order to make a definite and timely diagnosis of both pathologies in elderly patients, it is necessary to conduct imaging studies. Specifically, non-contrast brain MRI and CTPA are the standards used to identify and localize the injured vascular territory in both disorders. It is interesting to note that a transthoracic echocardiogram (TTE) with agitated saline contrast is a valuable tool for understanding the potential causes of AIS in elderly patients (12). This test helps determine if there is a presence of PFO (bubble study) or intra-atrial thrombi, which can shed light on the origin of the condition. Additionally, TTE with agitated saline contrast can also provide information on the severity of pulmonary embolism by identifying right heart strain in elderly patients (13). Lastly, this test can offer prognostic information, helping to predict the outcome of the condition in elderly patients. In addition, it has been found that the Transesophageal echocardiogram can improve the accuracy of detecting thrombi and PFO when the Transthoracic echocardiogram (TTE) results are not clear in elderly patients (14-16). It is also important to consider the inclusion of lower extremity ultrasound as a relevant test to identify the presence of deep vein thrombosis (DVTs) in elderly patients. In addition, it is important to consider performing additional tests for elderly individuals. These tests include an occult malignancy workup, such as a pan scan, and a pelvic MR Venogram to evaluate for May-Thurner syndrome (MTS).

A study examined the occurrence of venous thromboembolism in elderly patients with acute ischemic stroke who were prescribed aspirin and graded compression stockings for thromboprophylaxis (17). The study found that 11.8% of elderly patients developed pulmonary embolism. In additional research, such as studies on cryptogenic stroke and patent foramen ovale, it was discovered that PE was present in approximately 20% to 37% of elderly patients. However, it is important to note that the majority of these cases did not show any symptoms and were only identified through specific testing that was mandated by the research design (18).

### 1.2. Management of Pulmonary embolism-induced ischemic stroke in elderly patients

The existing guidelines are specific to different specialties and do not cover this unique situation in elderly patients. During the acute phase, the management options consist of anticoagulation,

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systemic intravenous thrombolysis, intra-arterial thrombolysis (if there is a high risk of systemic bleeding with intravenous thrombolysis), IVC filter placement, and endovascular pulmonary/cerebral embolectomy(19).

A study found that the treatment options can be divided into two categories: those that primarily focus on stimulating the brain and those that primarily target the lungs. In this study of elderly patients, it was discovered that 23.52% of the participants (n = 4) received intravenous recombinant tissue plasminogen activator (IV rt-PA) as a treatment for cerebral infarction. Additionally, an equal percentage of 23.52% underwent a procedure called mechanical thrombectomy (MT) to manage their condition. One elderly patient had both treatments(20), while the rest were treated with medical management and supportive measures because their injuries were severe and they were experiencing hemodynamic instability. In this analysis of elderly patients, the researchers found that the majority of patients who received IV rt-PA for PE management waited for 24 hours before starting the infusion with unfractionated heparin. This was the most commonly used therapeutic approach, accounting for 64.70% of elderly cases. However, one elderly patient experienced an intracranial hemorrhage as a complication after undergoing medical treatment (MT).The majority of elderly patients received treatment using intravenous heparin alone, even though their National Institutes of Health Stroke Scale (NIHSS) score was low, indicating a low risk of hemorrhagic conversion for recombinant tissue plasminogen activator (rt-PA). The use of acute thrombolysis has been found to be quite important in the treatment of acute ischemic stroke (AIS) in elderly patients. Based on the neurological perspective, the results were positive. They indicated that 75% of elderly patients (n = 3/4) who received rt-PA either fully recovered or experienced only minor disability symptoms. In contrast, elderly patients who were only given IV heparin experienced less positive neurological outcomes.

In the context of massive PE in elderly patients, it is evident that there is a need to address the increased pressure in the right ventricle and the risk of sudden and severe heart failure. This can be achieved by promptly restoring blood flow in the pulmonary blood vessels through either mechanical or pharmacological methods(7, 21). Hence, when dealing with significant cases of AIS and a high likelihood of hemorrhagic conversion in elderly patients, it is crucial to promptly consider the first option, which is IV rt-PA. According to the guidelines for thrombolytic therapy

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in PE, having a stroke in the past six months is considered an absolute contraindication<sup>(8)</sup>. However, additional consensus guidelines suggest that even though these contraindications are considered absolute, they should be seen as relative when there is a life-threatening situation related to PE in elderly patients<sup>(22)</sup>.

The management of systemic anticoagulation varies significantly between these two pathologies in elderly patients. There are specific recommendations for starting long-term anticoagulation after a stroke in elderly patients. These recommendations are based on the cause of the stroke and the prevention of future events<sup>(23, 24)</sup>. However, the initiation of the process is typically postponed until the subacute phase in elderly patients because there are potential risks of hemorrhagic conversion. On the other hand, it is important to note that anticoagulation plays a crucial role in the management of acute PE in elderly patients. Research has demonstrated that a delay in starting anticoagulation treatment can have negative consequences, leading to a poorer prognosis and worsening outcomes<sup>(25)</sup>. According to the current guidelines for elderly patients, it is recommended to start intravenous anticoagulation with unfractionated heparin right away after the event. This should be continued for a period of 5 to 10 days in elderly patients. After that, a transition to a vitamin K antagonist with a target international normalized ratio (INR) of 2 to 3 or a novel oral anticoagulant is advised for elderly patients<sup>(26-29)</sup>. However, it has been found that using anticoagulation alone for acute ischemic stroke (AIS) in elderly patients does not provide any advantages. It does not decrease the likelihood of future occurrences, improve the mortality rate, or have any effect on disability. In fact, it increases the risk of hemorrhagic conversion<sup>(30)</sup>.

According to another study, it was found that 70.5% of the participants were initiated on IV heparin<sup>(31)</sup>. Out of the total, eight elderly patients were promptly initiated, while four were postponed by 24 hours due to the administration of rt-PA. Out of the total of 8 elderly individuals, unfortunately, one elderly patient passed away, and an additional three elderly patients experienced significant long-term neurological effects, specifically aphasia and plegia. Out of the remaining four elderly patients, two experienced mild symptoms, but there is no information available regarding the outcomes for the other two elderly patients. Out of the four elderly patients who were administered rt-PA, one of them did not show any symptoms at all, while two experienced mild symptoms. The symptoms of the remaining elderly patient were not mentioned or reported. After being released, warfarin was the anticoagulant that most elderly

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subjects used, accounting for 41.7% of them. Additionally, 29.41% of elderly subjects were discharged with anticoagulation, but the specific agent was not specified. Only one elderly patient was released while taking Apixaban. Finally, in cases where elderly patients were not suitable for systemic anticoagulation, the medical team decided to proceed with the placement of an IVC filter.

## 2-Conclusion

In conclusion, the timely diagnosis and management of Pulmonary embolism (PE)-induced ischemic stroke in elderly patients pose considerable challenges. Imaging studies like non-contrast brain MRI and CTPA are essential for pinpointing the affected vascular territories. Transthoracic echocardiogram (TTE) with agitated saline contrast is valuable for understanding AIS causes in the elderly, detecting PFO or intra-atrial thrombi, and assessing PE severity through right heart strain. Lower extremity ultrasound is vital for detecting DVTs in elderly patients. Additional tests, such as occult malignancy workup and pelvic MR Venogram for evaluating MTS, should be considered. Treatment strategies vary depending on severity, with IV rt-PA and MT being effective for AIS in elderly patients. Prompt initiation of intravenous heparin is crucial for PE management. Consideration of IV rt-PA is essential for severe AIS cases with a high risk of hemorrhagic conversion. While a recent stroke is an absolute contraindication for thrombolytic therapy in PE, life-threatening situations in elderly patients may warrant relative consideration. The management of systemic anticoagulation differs significantly between the two pathologies in elderly patients, requiring individualized approaches. Timely anticoagulation initiation after PE is vital to prevent adverse outcomes. A multidisciplinary approach is necessary for the timely and appropriate management of PE-induced ischemic stroke in elderly patients, considering their unique characteristics and potential contraindications.

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