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Outpatient Management of Pulmonary Embolism: Current Evidence and Future Perspectives

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Abstract: Pulmonary embolism(PE), a life-threatening manifestation of venous thromboembolism, is usually given meticulous care in hospitals. However, nowadays, due to the evolution of medicine, it has shifted to so-called outpatient management of this condition. To put this into practice in in-depth knowledge of the factors that support or hinder such management of patients is necessary. Global incidence of PE is rising as exposure to risk factors increases. It has become the 3rd cause of cardiovascular morbidity in Western countries. The review explores the advances in diagnostic tools like D-dimer testing and other tools, and risk stratification to identify low-risk PE patients needed for outpatient management. It also addresses different types of criteria that have to be met, and the anticoagulation regimens required to discharge patients. The review discusses future directions which is focused on telemedicine-guided anticoagulation services, technology-driven care models, all of which focus on improved patient care.

Keywords: *"Pulmonary Embolism" "Venous Thromboembolism" "Outpatient Management" "Diagnostic Tools" "Risk Stratification" "Anticoagulants" "Telemedicine".*

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I. INTRODUCTION

Pulmonary embolism(PE) is a life-threatening manifestation of venous thromboembolism, in which blood clots from deep veins in the body travel to the lungs and block the arteries[1]. Venous thromboembolism occurs mainly in the lower limbs, which begins with the formation of thrombi - attributed to Virchow's triad, which comprises stasis, endothelial injury, and hypercoagulability associated with risk factors like surgery, trauma, immobilisation, obesity, cancer, infection, and the risk factor list is being expanded to include additional considerations[2]. The usual approach is to provide care for patients within the hospital; however, new studies show that certain patients with low risk can be managed safely at home with the right treatment [1].

However, the definition of "outpatient management" varies considerably across studies, ranging from brief inpatient observation with advanced monitoring before discharge to entirely community-based and treatment without hospitalisation. On the other hand, it leaves an uncertainty about the scope of care, the intensity of monitoring required, and the applicability of these approaches to real clinical practice[3]. To apply this approach effectively, it is important to identify the factors that support or hinder its practicality. It also plays a role in lowering healthcare costs and reducing pressure on hospital resources[4]. Although research and guidelines support sending low-risk patients to PE, very few hospitals implement this in practice. The large differences between hospitals highlight a research gap in understanding the factors that influence these decisions and in finding practical ways to make outpatient care for PE more efficient[5].

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II. CLINICAL SIGNIFICANCE OF PULMONARY EMBOLISM

➢ *Introduction*

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III. CLINICAL SIGNIFICANCE OF PULMONARY EMBOLISM

Pulmonary embolism is an urgent condition that occurs without any specific symptoms. The global incidence of pulmonary embolism is on the rise, with key risk factors including recent surgical procedures, trauma, malignancy, and exposure to estrogen. The clinical presentation of pulmonary embolism varies with the location of the embolus. Peripheral emboli often manifest with pleuritic chest pain and/or hemoptysis, whereas larger central emboli more commonly present with isolated dyspnea [6].In Western countries, venous thromboembolism (VTE) ranks as the third leading cause of cardiovascular-related death, as shown by epidemiological studies Evidence from longitudinal studies further suggests that its prevalence is expected to rise due to increased life expectancy, the growing burden of comorbid conditions that serve as risk factors for VTE, and the enhanced sensitivity of modern diagnostic techniques [7].

In the context of pulmonary embolism, adverse clinical outcomes are predominantly determined by hemodynamic instability and right ventricular dysfunction or failure resulting from acute pressure overload [8]. Irrespective of left ventricular ejection fraction Right ventricular dysfunction has been identified as a predictor of sudden cardiac death [9]. It can be concluded that pulmonary embolism represents a potential precipitating factor for sudden cardiac death[7,8].

We have several therapeutic approaches that are available for pulmonary embolism, and management strategies are relatively well defined for high- and low-risk patients. However, the optimal approach for those classified as intermediate risk remains a subject of ongoing debate. Fibrinolytic therapy has been shown to lessen the risk of sudden death and hemodynamic decompensation in patients with intermediate-risk pulmonary embolism; however, its effect is neutralized in terms of mortality by an elevated risk of stroke and major hemorrhagic complications. In randomized trials, the apparent mortality benefit of thrombolytic therapy was negated once bias related to the inclusion of both hemodynamically stable and unstable pulmonary embolism cohorts was accounted for [9].

In an observational cohort study of patients presenting with right heart thrombus, 45% were found to have concomitant pulmonary embolism at admission. The presence of pulmonary embolism was further associated with increased in-hospital mortality and a higher risk of 90-day mortality [10]. In a cohort study of patients with subsegmental pulmonary embolism (SSPE), the incidence of recurrent symptomatic pulmonary embolism was comparable between symptomatic and asymptomatic groups, both during anticoagulation and after its discontinuation [11]. Together, these cohort studies demonstrate the prognostic and clinical significance of pulmonary embolism [10,11]. Pulmonary embolism is therefore associated with sudden death, and its diagnosis is often challenging due to non-specific clinical manifestations [6-10]

IV. ADVANCES IN DIAGNOSTIC TOOLS

Advances in diagnostic technology now enable the detection of pulmonary emboli that were previously undetectable, rather than being limited to identifying only large emboli that had already been recognized as a clinical risk. The acute onset of pleuritic dyspnea and chest pain typically prompts consideration of pulmonary embolism in the differential diagnosis, particularly when accompanied by symptoms such as cough, hemoptysis, signs of deep vein thrombosis, tachypnea, and tachycardia[12].

In the diagnostic approach to suspected acute pulmonary embolism, hemodynamically stable patients are stratified into low, intermediate, or high clinical probability categories using validated tools such as the Wells score, the modified Wells score, and the revised Geneva score[13].

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D-dimer testing is most valuable for ruling out pulmonary embolism, as positive results in low-risk patients are more often false positives than true positives. A D-dimer level below 500 ng/mL can help us in ruling out the diagnosis of pulmonary embolism [7-8]. The PERC criteria can improve the efficiency of diagnosing PE, while bedside echocardiography serves as a valuable tool in hemodynamically unstable patients [14].

A cross-sectional study conducted in patients with suspected PTE demonstrated the usefulness of pro-BNP and troponin I in identifying those at higher risk of PTE. The study results indicated that pro-BNP demonstrated higher specificity (80.2%) and sensitivity (85.2%) compared to troponin I, which showed lower specificity (42%) and sensitivity (65.5%). Because of its high sensitivity and specificity, pro-BNP can be used as a useful biomarker in the diagnosis of pulmonary thromboembolism (PTE)[15]. Data from 72 patients revealed that serum levels of BNP, D-dimer, and troponin I were significantly elevated in the high-risk groups in comparison to lower risk and moderate-risk groups. Significantly elevated serum levels of BNP, D-dimer, and troponin I were observed in patients who died compared to those who survived[16].

Echocardiography serves as a valuable diagnostic tool in patients for whom computed tomography is challenging to obtain and can aid in identifying high-risk pulmonary embolism even in those who appear hemodynamically stable. The risk of VTE is significantly higher in pregnant women when compared with non-pregnant ones of the same age. Given its lack of harmful effects on the fetus, echocardiography can be safely employed in pregnant women, among whom pulmonary embolism remains a leading cause of maternal mortality in developed countries[17].

Cross-sectional visualization of the pulmonary arteries, is provided with CT pulmonary angiography to make diagnosis of pulmonary embolism. It provides us with high-resolution imaging that facilitates the detection of even small emboli [18]. CT pulmonary angiography is extremely useful since it exhibits significant sensitivity and specificity in identifying pulmonary embolism in trauma patients [19]. CT continues to be a diagnostic technique that is always getting better [15-19].

V. RISK STRATIFICATION: IDENTIFYING LOW-RISK PE PATIENTS

Risk stratification for pulmonary embolism includes dividing patients into different categories, such as high-risk, intermediate-risk, and low-risk groups. Among them, the identification of the high-risk group is the first and most important step. Patients with a haemodtnamic insatbility are considered too be at high risk due to right ventricular dysfunction [20].

The PESI and sPESI scoring systems: The PESI evaluates 11 parameters for risk stratification wheras the sPESI was developed as a simpler method. The sPESI evaluates only six parameters, and patients with a score of 0 are considered suitable for outpatient management. The simplified Pulmonary Embolism Severity Index (sPESI) was developed for the identification of patients at low risk for early mortality [21]. The PESI score incorporates 11 independent predictors of mortality which includes factors such as age, sex, history of cancer, chronic lung disease, heart failure, systolic blood pressure, pulse rate, respiratory rate, body temperature, oxygenation status, and mental status alterations. Patients are classified into five risk categories and it helps us in identifying those with a low likelihood of mortality who may be suitable for outpatient management. In contrast, the sPESI consists of six components: one related to age, two reflecting comorbid conditions, and the remaining three representing the cardiopulmonary consequences of pulmonary embolism [22].

HESTIA criteria: The Hestia criteria which is designed to recognise patients suitable for outpatient treatment [23]. One major advantage of the Hestia criteria over the SPESI is that it takes into consideration the social factors in determining eligibility for outpatient care [21]. It takes into consideration multiple parameters and assigns a score of 1 for each factor present. These parameters include: Hemodynamic instability, Requirement for thrombectomy, Elevated risk of bleeding, Significant oxygen dependence, Severe pain necessitating intravenous analgesics, Pulmonary embolism occurring during anticoagulation therapy, Impaired renal function with creatinine clearance below 30 mL/min, Hepatic dysfunction, Pregnancy, and Presence of heparin-induced thrombocytopenia (HIT). Patients with a total score of zero are eligible for outpatient management, whereas any score above zero indicates the need for hospitalization [23]

Based on PESI or sPESI scores, patients with an sPESI of 0 or a PESI classification of I–II are categorized as low risk. Those with an sPESI >0 or evidence of elevated cardiac biomarkers or right ventricular dysfunction are considered intermediate–low risk. Patients with an sPESI >1 in combination with elevated cardiac biomarkers and right ventricular dysfunction are classified as intermediate-high–high risk [24]. High-risk patients are identified by the presence of cardiac arrest, hemodynamic instability—defined as a systolic blood pressure below 90 mmHg for more than 15 minutes without an alternative explanation—or the requirement for vasopressor support in association with end-organ hypoperfusion. Persistent hypotension not attributable to new-onset arrhythmia, hypovolemia, or sepsis is also considered a defining criterion [25]

Integrating imaging findings with laboratory results can markedly enhance risk stratification, given the established prognostic significance of biomarkers such as troponin and D-dimer, as well as the diagnostic value of echocardiography in detecting pulmonary embolism [16-20].

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VI. CRITERIA FOR OUTPATIENT MANAGEMENT

Outpatient management of pulmonary embolism may serve as a safe and effective alternative to traditional in-hospital care. The outpatient treatment outcomes for low-risk PE patients have been shown to have almost no difference when compared with those treated with in-hospital care. In a post-hoc analysis of the YEARS study, it was found that 46% of patients treated at home experienced very few adverse effects, further supporting the growing trend of managing PE patients in an outpatient setting [26]. A retrospective cohort study was conducted, through which we identified the eligibility criteria for outpatient treatment. Hemodynamically stable with normal vital signs, age below 65 years, limited clot burden, defined as no more than one embolus, no evidence of concomitant DVT, active malignancy, or pregnancy, absence of significant comorbidities or impaired cardiopulmonary reserve, classification within low-risk categories (PESI classes I–II), availability of reliable follow-up and adequate outpatient support [27].

Anticoagulant therapy should be initiated right after the diagnosis of pulmonary embolism is established. However, the patient's bleeding risk must be carefully assessed, as it is greatest during the first month of treatment and gradually decreases thereafter [28]. Outpatient management remains the standard approach for patients diagnosed with deep vein thrombosis (DVT), while hospitalization continues to be the primary strategy for those with pulmonary embolism (PE). The 2014 ESC criteria endorsed the feasibility of managing patients in outpatient settings. Furthermore, the 2019 ESC guidelines strongly recommended the continuation of anticoagulant therapy and home-based treatment. Similarly, the CHEST guideline and expert panel report recommend that patients be managed as outpatients, provided they have reliable access to medication, appropriate outpatient care, and suitable home conditions. The American College of Emergency Physicians also issues recommendations supporting the outpatient management of patients with low-risk pulmonary embolism [29].

Outpatient management of pulmonary embolism is now highly recommended when the requirements are met. Clinicians can therefore make treatment decisions based on specific criteria to determine the suitability of outpatient care for PE patients [26-29].

VII. OUTPATIENT ANTICOAGULATION REGIMENS

A study found that the treatment of pulmonary embolism (PE) with direct oral anticoagulants (DOACs) is both safe and effective in outpatient settings. The study, which included 245 patients, demonstrated favorable outcomes, with a mortality rate of only 0.4% and a major bleeding rate of 0.4% during the 6-month follow-up period [30].

The use of DOACs may be preferred over warfarin, as evidenced by a cohort study of 6,509 patients, which showed a lower incidence of pulmonary embolism among those treated with DOACs [31]. results from another retrospective analysis demonstrated that thromboembolic events occurred in 4.23% of patients treated with DOACs compared to 7.12% in the warfarin group, while bleeding events were reported in 8.85% of the DOAC group versus 10.1% in the warfarin group [32]. These findings further support the preference for DOACs over warfarin [25-27]. DOACs are more effective than warfarin in preventing left ventricular thrombus formation, thereby lowering the risk of sudden death. [33,9].

VIII. EVIDENCE FROM RECENT CLINICAL TRIALS

We have already established the effectiveness of rivaroxaban and similar DOACs, with minimal adverse effects [25-28]. We have also gained a clear understanding of the purpose of the sPESI and Hestia scores [21-23]. Evidence from clinical trials conducted gives further satisfaction. The HoT-PE trial demonstrated that early discharge of low-risk PE patients was associated with very low rates of VTE recurrence or PE-related death. Although fragile patients (advanced age, renal dysfunction, or low BMI) had a slightly higher bleeding risk, recurrence remained low. These findings give us confidence regarding the safety of rivaroxaban-based early discharge, even in fragile individuals [34].

In another study involving 2,694 acute PE patients discharged within 24 hours, early discharge was shown to be safe, with rivaroxaban use further showing its effectiveness in outpatient management. Rates of all-cause mortality, recurrent VTE, and major bleeding was below 1% at both 14 and 30 days. It was only the combined endpoint of these outcomes that slightly exceeded 1%, reaching about 1.2% at 30 days [35]. The Hestia study was able to prove the safety of outpatient management, showing that the rate of adverse events among patients treated at home was remarkably low [36]. The safety of outpatient treatment was demonstrated in patients with cancer-associated pulmonary embolism consolidates belief in this approach [37]. In summary, outpatient care can be confirmed as a safe and effective approach for appropriately selected patients [34-37].

IX. FUTURE DIRECTIONS

Outpatient care of pulmonary embolism in future may rely on individual probability rather than population-based algorithms. Such an approach could improve the safety and personalization of care, but requires further validation and development of practice tools before it is widely adopted [38]. the role of artificial intelligence (AI) is evolving To make a decision on the care provided to the patient. AI tools play a role in identifying patients with a higher rate of recurrence, bleeding, or mortality, thereby informing decisions on

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anticoagulation duration, monitoring intensity, and the level of inpatient versus outpatient care [39].

Telemedicine-guided anticoagulation services, as demonstrated by the thrombo EVAL program, resulted in improved treatment quality of VTE patients and also offered dosing accuracy. This suggests that technology-driven care models could be expanded to direct anticoagulant therapy and can be integrated with emerging digital tools. Adapting such systems across diverse and resource-limited settings in the upcoming decade may help establish more standardized pathways for VTE management [40]. Future anticoagulation therapies focus on safer agents targeting novel pathways, such as aptamers and nanoparticle delivery, to improve efficacy while minimizing bleeding risk. Pharmacogenomics may enable personalized dosing and risk prediction, moving toward more precise and patient-centred therapy[41].

Future research should explore the long-term sustainability, scalability, and cost-effectiveness of virtual anticoagulation clinics, particularly in low-resource and rural settings. Studies based on telehealth models pointed most effective strategies for different patient populations. Integration of digital tools like mobile health applications, AI-based risk prediction, and remote monitoring systems can result in improved patient care[42].

X. CONCLUSION

Pulmonary embolism (PE) is a common and potentially fatal cardiovascular condition that frequently presents with non-specific symptoms, making its diagnosis challenging for clinicians. Advancements in diagnostic methods have now made it possible to detect large emboli that were previously undetectable. Risk stratification can be performed using the PESI, sPESI, and Hestia criteria, which help us in identifying low-risk patients. Evidence supports that outpatient management should be considered and encouraged for these low-risk patients. D-dimer, pro- BNP, and troponin I serve as valuable biomarkers in the diagnosis of PE; however, their sensitivity and specificity vary. Risk stratification, along with these can contribute to improved patient outcomes. It should also be noted that echocardiography is recommended for patients with limited access to CT imaging. The Hestia score, PESI and sPESI scores, identifies low-risk patients and ensures appropriate risk stratification. Outpatient management of low-risk patients is safe when the necessary criteria are met. While reviewing anticoagulation regimens for outpatient management, it was found that DOACs are preferred over warfarin. The safety of early discharge is supported by evidence from recent clinical trials, such as the HoT-PE trial.

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➢ *Author Contributions:*
- A.K.K.R. conceptualized the study, designed the structure, coordinated the literature review process, and edited the full manuscript.
- S.S.L. contributed to the literature review and drafting of assigned sections.
- A.K.K.R. reviewed and finalized the entire manuscript.

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