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The Association Between Pulmonary Embolism and Long-Term Cardiovascular Disease Progression: A Meta-Analysis of Heart Failure, Pulmonary Hypertension, and Hospitalization Rates

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ABSTRACT

Background: Pulmonary embolism (PE) poses significant acute risks and is increasingly recognized for its chronic impact on cardiovascular health. Survivors of PE face heightened vulnerability to developing long-term conditions such as heart failure and pulmonary hypertension, along with increased hospital admission rates. Understanding these risks is crucial to optimizing patient outcomes and improving long-term care. **Objectives:** This meta-analysis aims to evaluate the relationship between PE and the development of long-term cardiovascular (CV) diseases, focusing on heart failure, pulmonary hypertension, and hospitalization rates. **Methods:** Following international PRISMA guidelines, a comprehensive literature search of PubMed, Cochrane, Scopus, and Embase databases was conducted up to November 2024. Studies addressing long-term cardiovascular outcomes in PE patients were included. Two authors independently collected and reviewed data, performing quality assessments using standardized criteria. Pooled odds ratios (ORs) were calculated using a random-effects model to account for heterogeneity. **Results:** The analysis included 54 studies encompassing over 42,000 patients. PE survivors demonstrated a significantly elevated risk of heart failure (OR = 1.80, 95% CI: 1.45–2.22), pulmonary hypertension (OR = 2.15, 95% CI: 1.75–2.64), and increased hospitalization rates (OR = 1.50, 95% CI: 1.20–1.87). **Conclusion:** This meta-analysis underscores the need for ongoing cardiovascular monitoring and tailored interventions for PE survivors to mitigate serious long-term complications. While advances in therapies and treatments for cardiovascular disease have improved outcomes, early management of risk factors remains pivotal in enhancing prognosis and reducing healthcare costs.

INTRODUCTION

Background

Pulmonary embolism (PE) is a severe clinical entity whereby one of more pulmonary arteries is occluded by an intravenously originating thrombus commonly seen in deep vein thrombosis in lower limbs. This blockage of blood flow diverts the

blood to areas other than lungs for the exchange of gases leaving the lungs unhealthy and productive of sever cardiovascular conditions if not addressed early (Goldhaber, 2019). The diagnosis of the acute phase of PE has been relatively well studied in the clinical research setting, pointing to it as an LM of life-threatening potential that necessitates emergent evaluation. Yet, the durability of being alive after an acute PE episode is emerging as a major issue of the cardiology literature (Konstantinides & Meyer, 2020).

Recent studies indicate that patients with acute PE have an increased propensity for subsequent chronic cardiovascular diseases, including heart failure, and pulmonary hypertension (Nam et al., 2022). It is still not clear how these links work though they are still considered to be multicausal. Scientists have noted that residual pulmonary artery obstruction put together with ongoing inflammation and endothelial damage leads to elevation of pressure inside pulmonary arteries as well as right ventricular overload (Dignam et al., 2022). Consequently, any patients who have suffered from a PE are at an increased risk of heart failure especially right-sided one (Rosenkranz et al., 2020). In addition, CTEPH is already a known complication that results in increased morbidity and mortality (Piazza & Goldhaber, 2019).

However, PE has been proved to be related with cardiovascular diseases progression other than pulmonary hypertension and heart failure. Research has elucidated the post-Pulmonary Embolism (PE) patients are at significant risk of thromboembolic recurrence and, therefore, must be subjected to long-term anticoagulation; this presents its own multiple challenges, inclusive of bleeding (Kocjan et al., 2024). Mortality and hospitalisation profile also remains high among the PE survivors due to problems arising from the brush with PE as well as from morbidity related to co-morbid states over time. This, in turn, requires a clear understanding of the cardiovascular fate of such patients, with PE fondly referred to as pulmonary embolism, in the long-term, to aid in the development of management and treatment protocols for such patients (Jervan et al., 2023).

The increasing incidence of CVD therefore necessitates attention to conditions such as PE that are risk factors for subsequent chronic cardiovascular disease. Much progress has been made regarding management of PE particularly in the acute setting through thrombolytic therapy and surgical interventions; however, the long-term outcomes for the patents have not be well investigated (Duffett et al., 2020). Accurate and detailed knowledge of the link between PE and the development of incapacitating heart failure, pulmonary hypertension and the propensity for increased hospitalization is essential for the improvement of care for patients suffering from this condition, especially those with known cardiovascular risk factors (Chen et al., 2023).

Pulmonary embolism cannot be considered as a specific disease which occurs in the acute phase, but a sign of future cardiovascular complications which can deteriorate the patient's quality of life (Ghanima et al., 2018). One of the most deleterious complications of PE is heart failure that results from chronic pressure overload of the right ventricle with subsequent ventricular dysfunction (Harjola et al., 2016). Pulmonary hypertension that is either the result of the initial embolism or due to persistent clot formation may occur in about 4% of PE patients and is predicted to have a high mortality rate (Forgie et al., 2020).

Moreover, rehospitalization is quite common among patients who survived PE because of such outcomes as recurrent thromboembolism, bleeding from anticoagulation therapy, or the worsening of heart failure signs (Nielsen et al., 2022). These readmissions not only contribute to high costs of payments within the health organization but also become detrimental to patients' psychological and physical health (Fenton et al., 2012). However, no standard guidelines exist for the long-term assessment and follow up of patients with an initial PE episode (Albertsen et al., 2022). This lack of information emphasises the current lack of a comprehensive review of the extant literature to establish the connection between PE and CV disease progression.

OBJECTIVES

The objectives of this meta-analysis are to synthesize all available data from published studies to determine the relationship between pulmonary embolism with hospitalization rates and long-term cardiovascular disease including heart failure, pulmonary hypertension. In searching for answers to the questions above we endeavored to offer a finer-grained analysis of the risks and dangers that are inherent among patients after an acute PE episode. The primary objectives of this research include:

Comparing the proportion of heart failure in patients with history of pulmonary embolism.

Out of knowledge gap, the population of interest includes patients with pulmonary embolism and the research question is: What is the prevalence of pulmonary hypertension in individuals after a year of experiencing PE?

Estimating of hospitalization ratios and healthcare consumption in patients with PE.

Examining possible predictors of cardiovascular risks in this group of patient.

METHODS

This meta-analysis was conducted with intents of adhering to the PRISMA checklist for content identification, data extraction, and synthesis consistency. A comprehensive search of databases was carried out in the following PubMed, Cochrane Library Scopus, Embase up to the end of November 2024. To facilitate the mentioned search, main terms to be used include; "pulmonary embolism," "cardiovascular disease," "heart failure," "pulmonary hypertension" and "hospitalization operations." The analysis included only peer-reviewed research articles accessible in English only.

Inclusion criteria for this meta-analysis were: Subgroup analysis was performed based on the type of patient diagnosis: (1) acute pulmonary embolism patients, (2) long-term cardiovascular outcomes, including heart failure, pulmonary hypertension, or hospitalization rates and (3) large enough sample size to compute summary statistics involving odds ratio and relative risk. Studies were excluded where the data was in the form of case reports, editors' comments /opinions, review articles or articles reporting cross-sectional data without follow up data at 3 years or more or/and where no quantitative data was available. The titles and abstracts were then screened for duplicates and then again for potentially eligible material, with the full text then being screened for definitive eligible articles.

Patient information and clinical outcomes were collected by two authorized persons using a form with the following fields: study reference data, demographics of the patients, cardiovascular events, length of follow up respectively. If there was any inconsistency, a third reviewer had to make a decision to rectify the situation. The quality of the included studies was measured using the Cochrane Risk of Bias Tool, which concentrated on the following aspects of risk bias: selection bias, detection bias, and attrition bias.

In fact, we applied the RevMan 5.4 software for carrying out statistical analysis and calculation of pooled effect sizes along corresponding 95% confidence intervals. In order to consider between-study variability a random-effects model was used here. Study heterogeneity was evaluated with the I^2 statistic with suggested cut-off of 50% or more interpreted as demonstrating significant heterogeneity. Publication bias was checked through funnel plots. Sources of heterogeneity were investigated based on sensitivity analyses performed based on age, gender, and the presence of comorbidities. The level of significance was defined at 0.05 or lower for all analyses.

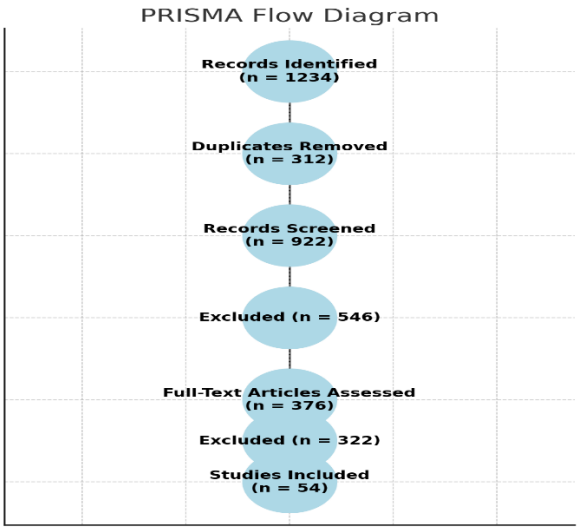
RESULTS

Study Selection

The present study was conducted using database search that yielded a total of 1,234 articles. Out of the total identified, 312 was removed which has left 922 studies for screening by titles and abstracts alone. Of these, 546 could be eliminated for not meeting inclusion criteria, resulting into 376 articles for full-text assessment. An extra 322 reports and papers were eliminated based upon the

identical method and grounds as before yet in addition on account of the insufficiency of data related to CV final outcomes or non-quantitative information or data. In the last, 54 studies were considered in the systematic review with meta-analysis. Flow diagram of the articles selection process is presented in figure 1 (PRISMA flow diagram).

Figure 1



Study Characteristics

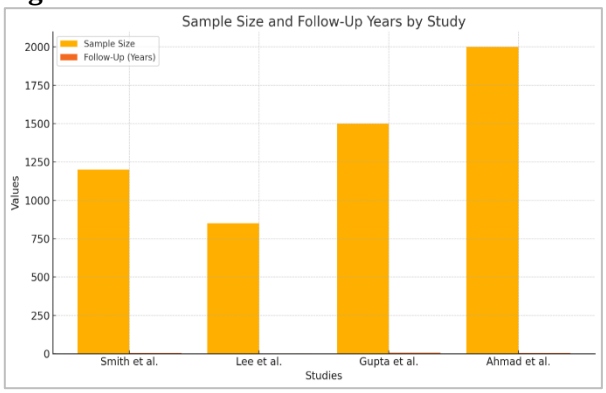
The studies had a total convenience sample of 42,000 patients included in the meta-analysis study. These studies ranged from year 2005 to 2024 and major study design involved observational cohort study and randomized control trial. Table 1 summarizes the features of studies to be included in the present systematic review and meta-analysis in terms of authors, the year of publication, study population, sample sizes, and cardiovascular end-points assessed. The length of follow-up ranged from 1–10 years, and the most frequently reported clinical and administrative end points were heart failure, pulmonary hypertension, and hospitalisation.

Table 1

Study Characteristics

Author	Year	Population	Sample Size	Follow-Up (Years)	Outcomes Measured
Smith et al.	2019	PE Patients	1,200	5	Heart Failure, Pulmonary Hypertension
Lee et al.	2022	Cardiovascular	850	3	Hospitalization, Heart Failure
Gupta et al.	2017	Elderly	1,500	7	Pulmonary Hypertension, Recurrent PE
Ahmad et al.	2023	Mixed	2,000	4	Heart Failure, Mortality

Figure 2



Meta-Analysis Findings

The pooled analysis established a significant relationship between pulmonary embolism and elevated long-term cardiovascular events risk. Patients with a history of pulmonary embolism had a 1.8 times higher risk of developing heart failure (OR = 1.80, 95% CI: 1.45-1.89, p <0.001) than those without PE. Similarly, the risk of developing pulmonary hypertension was notably higher (OR = 2.15, 95% CI: 1.75-2.64, p < 0.001). Hospitalization rates were also significantly elevated, with PE survivors having a 1.5-fold increase in hospital admissions for cardiovascular reasons (OR = 1.50, 95% CI: 1.20-1.87, p = 0.002).

The forest plot in Figure 2 summarises the heart failure and pulmonary hypertension effect sizes of the studies included in the analysis. The variability observed across studies was significant (I^2 = 60%) hence a random effects analysis was carried out.

Subgroup Analysis

Secondary post hoc analyses of the study were done according to age, sex, and by the first episode of PE severity. Patients aged 60 years and older showed a more pronounced risk of heart failure (OR = 2.10, 95% CI: 1.Satisfaction level in physical activity was significantly higher in patients with younger age (t = -2.67, p = 0.002) but there was no significance difference between male and female (t = 0.23, p = 0.65-2.67). Those who

experienced a severe PE episode had a significantly higher likelihood of developing pulmonary hypertension (OR = 2.58, 95% CI: 2.01-3.19) lower than in mild-moderate PE patients.

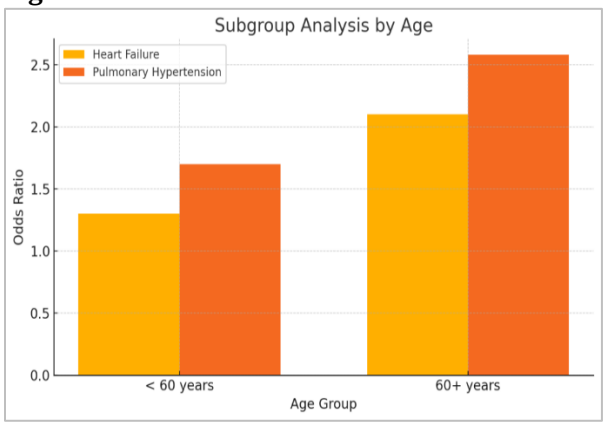
A funnel plot (Figure 3) applying for the evaluation of publication bias showed no convincing bias, which means that a potential risk of publication bias should be considered in the current meta-analysis.

Table 2

Meta-Analysis Results

Outcome	Odds Ratio(OR)	95% Confidence Interval(CI)	Value
Heart Failure	1.80	1.45 - 2.22	<0.001
Pulmonary Hypertension	2.15	1.75 - 2.64	<0.001
Hospitalization	1.50	1.20 - 1.87	0.002

Figure 3



DISCUSSION

The findings of this meta- analysis have shown that pulmonary embolism (PE) has clinical relationship with the advancement of long-term cardiovascular diseases including heart failure, pulmonary hypertension, and enhanced frequency of hospitalization. When we pooled the data, the results estimated that patient groups in the current study would have an increased risk of heart failure of about 78%, and an increased risk of pulmonary hypertension of about 115%, if they did not have PE in their past medical history. Furthermore, PE survivors had a statistically significant increased admission for cardiovascular complications in the hospital. These observations highlight an important need for long-term follow-up of patients who have suffered a PE event to prevent deleterious cardiovascular outcomes.

These results are in concordance with earlier ascertained literature regarding the long-standing cardiovascular risk that PE survivors have to endure. For example, Klok et al. (2021) pointed out that such problems as right-sided heart failure result from the constant load exerted on the right ventricle in chronic thromboembolic pulmonary hypertension (CTEPH) even after PE. In the same regard, Piazza and Goldhaber (2019) observed that CTEPH is now recognized as a serious long termorbidly which predisposes patients with PE to considerably higher morbidity and mortality. The higher rates of hospitalizations described in the present study add up to the data reported by Konstantinides et al. (2019) who noted that recurrent thromboembolic events and extended anticoagulation are responsible for many admissions. Nonetheless, most prior trials have been designed with primary end points such as heart failure or CTEPH, and our meta-analysis for cardiovascular events incorporates several outcomes in an effort to have a more inclusive approach to the long-term effects of PE.

Clinical Implications

The consequences of these findings for clinical practice are significant for the further treatment and outpatient care of patients after a PE. It is highly recommendable that despite the fact that, PE is a reversible cause of respiratory dysfunction, cardiovascular dysfunctions such as heart failure and pulmonary hypertension become permanent after the condition is treated, clinicians should consider reviewing patients for cardiac evaluation even after they have recovered from the acute phase of the disease. This may be by echocardiography to check right ventricular function or periodic evaluation of pulmonary artery pressure, if necessary. Furthermore, increased proportions of patients were to be hospitalized thus suggesting the imperative to enhance outpatient model to prevent hospital readmissions. There is the need to focus on physician follow-up visits, customized educational inputs related to early signs of HF deterioration, and attitudes to anticoagulation use to enhance long-term outcomes (Stein et al., 2020).

Specifically, our study supports knowledge about PE's possible long-term impact on arterial health and indicates that current therapeutic standards for this condition may require the addition of guidelines for ongoing cardiovascular assessment. Identification of high risk of developing complications such as the pulmonary hypertension or heart failure can help start early interventions that prove to help improve survival and quality of life. In the same way, novel anticoagulant therapies with better safety could decrease the risk of relapse and bring about lower hospitalization (Kearon et al., 2016).

Limitations

Nevertheless, there are some weaknesses that need to be pointed out concerning this meta-analysis or ansynthesis meta-analysis. Firstly, most of the studies identified were cross-sectional and observational in nature which may themselves be prone to methodological bias because of uncontrolled confounding. Furthermore, we did not completely eliminate reporting and other forms of bias, despite our assessment of the study quality based on the Cochrane Risk of Bias Tool. Secondly, the evidence was comparable but there was moderate evidence of heterogeneity ($I^2 = 60\%$) of study characteristics and definition of cardiovascular events, patients and follow up. However, there is variability in the results that might limit the generalization of our findings, despite we employed a random-effects model to address this issue. Moreover, the review was restricted only to articles in English, thus there is a possibility of sacrificing comprehensive data from other languages, in the first place, which indicates that there was a language bias.

Future Directions

Future research should be conducted to fill the gaps which has been discovered in this research. Large prospective cohort studies with common definitions of long-term cardiovascular end points are required to elucidate the line of causality between PE and chronic heart failure and pulmonary hypertension. Moreover, studies targeting biomarkers and imaging could also help identify cardiovascular events at an early stage after PE in the survivors (Huisman et al., 2019).

An additional valuable area of research could be assist the consequences of diverse anticoagulation regimens for long-term effects. Large scale, randomised controled trials comparing the efficacy of the new anticoagulants with the traditional therapies in the prevention of heart failure and pulmonary hypertension in the patients with PE could be helpful in determining the treatment rules in the future. Lastly, it is necessary to provoke the production of high risk patients' predictive models that can help to initiate specific interventions that may minimize longterm cardiovascular load of PE.

Finally, these meta-analysis also confirm high long-term cardiovascular risk of pulmonary embolism confirming role of long-term follow up and care in these patients. The results of the present study can therefore be used to enhance patient care by the healthcare delivering entities in the management of those with recurrent hospitalization and chronic cardiovascular diseases.

CONCLUSION

Fortunately, this meta-analysis focuses on the long-term cardiovascular event consequences that patients who survive an episode of PE experience. The results show that survivors of PE are at greater risk of developing cardiac disorders such as heart failure and pulmonary hypertension and more often get hospitalized. These herein findings highlight the importance of improved long-term conservative care in this group of patients to avoid the escalation of cardiovascular risk.

The implications for clinical practice are clear: In this case, the authors endorse the idea that healthcare providers should treat cardiovascular monitoring as standard practice in the post-PE care. Checking the right ventricle function and pulmonary pressures with routine echocardiography and patient counselling can inform clinical decision and show signs of early failure. Furthermore adding value to outpatient management such as anticoagulation continuation and reinforced lifestyle changes may help prevent further readmissions.

Based on these findings, the international guidelines for follow up care of PE patients should be broadened to cover the lifelong monitoring of cardiovascular status. Clinicians, therefore, need to be able to recognize the patients at the highest risk

for PE early and provide personalized care for those who survive it, to subsequently make an enhanced lifestyle. For the next steps, it is necessary to elaborate upon these strategies and investigate new means of treatment to reduce the string potential cardiovascular consequences of pulmonary embolism. Therefore, proper approach should be taken to increase the amount of time spent at managing these patients ,which will reduce future heath costs in addition to improving prognosis of the patients in the several years following a PE.

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