Original Research Article

Pulmonary Embolism Post-Femoral Neck Fracture Surgery: A Critical Predictor of Five-Year Mortality

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Abstract

Objectives: This study examines the impact of pulmonary embolism (PE) on mortality among patients with femoral neck fractures, exploring the predictive value of preoperative PE for postoperative occurrences and associated mortality over a 5-year follow-up period. **Methods:** We analyzed 2256 patients over 60 years old admitted with femoral neck fractures, focusing on those who developed DVT or PE postoperatively. Surgical intervention aimed within 48 hours without pharmacological thromboprophylaxis, utilizing mechanical prophylaxis instead. Postoperative management included Enoxaparin administration. Data analysis employed SPSS 21, with chi-squared tests, T-tests, and multivariate logistic regression to explore mortality and PE incidence. **Results:** PE was diagnosed in 1.4% of patients, with a notable mortality contrast between patients with PE (87%) and those without (59.7%) over 5 years. A history of preoperative PE emerged as a significant risk factor for postoperative PE. Despite surgical variations, no significant correlation was found between surgery type and PE incidence. Early postoperative weight-bearing and institutional rehabilitation did not significantly alter PE incidence rates. **Conclusions:** The study underscores the significant mortality risk associated with preoperative PE in femoral neck fracture patients. It highlights the necessity for vigilant PE risk assessment and management, challenging assumptions about the protective role of early mobility and rehabilitation in PE incidence. Further research is essential to refine patient care strategies and improve outcomes.

Keywords

pulmonary embolism, femoral neck fractures, postoperative complications, mortality rate, surgical intervention, venous thromboembolism, deep vein thrombosis, rehabilitation, early weight-bearing, orthopedic surgery outcomes

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Introduction

Femoral neck fractures are a major health concern in the elderly. Annually, over 300 000 such cases occur in the United States alone, with global numbers even higher.[1,2] These fractures are not only prevalent but also carry a significant burden, both in terms of patient mortality and financial costs.[3] Recent data from a large-scale study in Lombardy involving 71 920 patients[4] highlighted the extensive nature of this issue. The study revealed a high incidence among the elderly, particularly in women, with a median age of 84 years. The financial impact is substantial, with the U.S. spending an estimated $20 billion annually on treating these fractures and their complications.[5]

The timing of surgical intervention post-fracture is crucial for patient outcomes. A recent review emphasized the importance of early surgery, ideally within 24 hours, to reduce mortality rates and hospital stay durations.[6] Delayed surgery, particularly beyond 48 hours, is associated with prolonged hospitalization and increased risk of complications such as pressure sores, pneumonia, and potentially venous thrombo-embolism (VTE).[7,8] This approach aligns with current guidelines that advocate for rapid surgery to enhance recovery and reduce mortality risks.

Pulmonary embolism, a potentially fatal complication of VTE, substantially affects patient survival post-surgery.[9] With a high incidence rate post-hip arthroplasty, PE significantly increases the risk of death.[10] The mortality rate for patients with postoperative PE is alarmingly high compared to those without PE.[11] This study aims to deepen our understanding the impact of PE on proximal femur fracture patients, focusing on a 5-year postoperative period. The objective of this study is to investigate whether preoperative PE is predictive of postoperative PE and its association with increased mortality.

Materials and Methods

Study Design

This is a retrospective, single-center study conducted over a 10-year period from January 2010 to December 2020. The study was approved by our institutional review board, and due to its retrospective nature, the requirement for obtaining consent from participants was waived.

Inclusion and Exclusion Criteria

Inclusion criteria:

1. Patients aged 60 years and older.
2. Admitted with femoral neck fractures.
3. Underwent surgical intervention within 48 hours of admission.
4. Patients with complete medical records available for review.

Exclusion Criteria:

1. Patients with incomplete medical records
2. Patients who did not undergo surgical intervention
3. Patients with pre-existing conditions that significantly impact mortality, such as:
   - Advanced malignancies
   - Severe liver disease
   - Severe chronic obstructive pulmonary disease (COPD)
   - End-stage renal disease
4. Patients who received pharmacological thromboprophylaxis preoperatively
5. Patients with a history of major trauma within the last 6 months

Outcome Measures

Primary Outcome Measures

1. Mortality Rate:
   - Mortality rate was defined as the percentage of patients who died within the 5-year follow-up period after surgery.
   - Mortality data were retrived from national death registries.
2. Incidence of Pulmonary Embolism (PE):
   - Incidence of PE was defined as the percentage of patients diagnosed with PE during the postoperative period.
   - PE diagnosis was based on clinical presentation and D-dimer testing. Any clinical and laboratory suspicion was confirmed with a CT pulmonary angiography.

Secondary Outcome Measures

1. Incidence of Deep Vein Thrombosis (DVT):
   - Incidence of DVT was defined as the percentage of patients diagnosed with DVT during the postoperative period.
   - DVT diagnosis was based on clinical presentation and confirmed by Doppler ultrasound.
2. Length of Hospital Stay:
   - Length of hospital stay was measured in days from the date of admission to the date of discharge.

Description of Surgical Procedures

The surgical procedures performed on the study cohort included:

- Arthroplasty: hemiarthroplasty or total hip replacement.
- Internal fixation: Dynamic hip screw fixation, intramedullary nailing, or cannulated screw fixation.

Each procedure was chosen based on the patient's clinical condition and the surgeon's preference. All surgeries were conducted under standard aseptic conditions, and patients were monitored postoperatively in a specialized orthopedic ward.

Routine Management of Femoral Neck Fractures

Patients were comprehensively assessed pre-surgery. Mechanical prophylaxis using Sequential Compression Devices (SCDs) was applied during the preoperative period. Post-surgery, Enoxaparin (Sanofi Ltd, worldwide) was administered subcutaneously.

Distribution of Therapeutic and Prophylactic Anticoagulation

- Prophylactic Anticoagulation:
  - Enoxaparin was administered at a prophylactic dose of 40 mg once daily to patients without a prior history of thromboembolism or other high-risk factors for venous thromboembolism (VTE).
  - This dosage was chosen to balance the prevention of VTE while minimizing the risk of bleeding complications.
- Therapeutic Anticoagulation:
  - For patients with a history of thromboembolism or those diagnosed with deep vein thrombosis (DVT) or pulmonary embolism (PE) postoperatively, Enoxaparin was administered at a therapeutic dose of 1 mg/kg twice daily.
  - This therapeutic dose aimed to effectively treat existing thromboembolic events and prevent recurrence.

The identification of DVT and PE was based on clinical presentation, supplemented by Doppler ultrasound and D-dimer testing as needed. For suspicious cases, pulmonary CT angiography was performed to confirm the diagnosis of PE. Patients receiving therapeutic anticoagulation were closely monitored for signs of bleeding and other complications.

Data Collection and Analysis

Our study involved a detailed review of medical records focusing on patients who developed DVT or PE postoperatively. We particularly concentrated on the mortality of patients for a period of 5 years following their operation. Data were cross-referenced with variables like post-surgical mortality employing SPSS 21 for statistical analysis. Chi-squared tests, T-tests, and multivariate logistic regression were utilized with significance set at $P < .05$.

Multivariate Regression Analysis

We performed a multivariate regression analysis to assess the impact of various comorbidities on mortality. The comorbidities included in the analysis were obesity (defined as BMI >25), hypertension, diabetes, hypercholesterolemia, atrial fibrillation, ischemic heart disease, chronic heart failure, and chronic kidney failure. This analysis allowed us to identify and control for potential confounding factors that may influence the results.

Kaplan-Meier Estimators

Five-year survivorship was estimated using Kaplan-Meier estimators.

Odds Ratios and P-Values

- We employed multivariate logistic regression to calculate the odds ratios (OR) and their 95% confidence intervals (CI) to identify the risk factors for postoperative pulmonary embolism (PE). The significance of the ORs was determined using P-values, with a threshold of $P < .05P < .05P < .05$ indicating statistical significance.
- For example, the odds ratio for preoperative PE predicting postoperative PE was calculated to be 37.0 (95% CI, X–Y; $P = .045P = .045P = .045$), indicating a strong predictive value of preoperative PE for postoperative occurrences.
- We utilized Kaplan-Meier estimators to assess the 5-year survival rates of patients with and without postoperative PE. The Kaplan-Meier method is a non-parametric statistic used to estimate the survival function from the observed survival times.
- The survival curves generated by the Kaplan-Meier method illustrate the proportion of patients surviving over the specified period. In our study, the survival curves clearly indicate a significant difference in mortality between patients with PE (87% mortality) and those without PE (40.3% mortality) over 5 years.
- To interpret these curves: the y-axis represents the survival probability, while the x-axis represents the time in months post-surgery. The steep decline in the survival curve for patients with PE compared to those without PE underscores the severe impact of PE on long-term survival.

Ethical Considerations

The study was conducted in accordance with the ethical standards laid out in the 1964 Declaration of Helsinki and received approval from our institutional review board. Given its retrospective nature, the requirement for obtaining consent from participants was waived.

Results

In our extensive study involving 2256 patients who underwent surgery for femoral neck fractures, we discovered a notable incidence of pulmonary embolism (PE). Out of the entire cohort, 31 patients, equating to 1.4%, were diagnosed with PE.

This finding becomes even more relevant considering that only a fraction of these, precisely 6 patients, had a prior diagnosis of deep vein thrombosis (DVT), which highlights the complexity and unpredictability of PE development in this context. The study predominantly involved an elderly female demographic, with 1507 females (66.8%) and 749 males (33.2%). The average age of the patients was 79.4 ± 12 years (Table 1).

A vast majority, 98.6% of the patients, did not experience PE during the study period, underscoring the overall rarity of this complication in our patient population.

Upon analysis, we found no statistically significant differences in baseline demographic data between the two groups, except for the history of pulmonary embolism. Variables such as BMI, hypertension, diabetes, hypercholesterolemia, atrial fibrillation, ischemic heart disease, chronic heart failure, and chronic kidney failure did not show significant differences between participants with and without PE (Table 2). This indicates that the baseline characteristics were largely comparable across the groups, except for the prior history of PE, which was significantly higher in the PE group. Delving into the risk factors, our analysis revealed no significant gender or age-related differences in the likelihood of developing PE. Intriguingly, among those who did develop PE, 63.6% had a preexisting hypertension, which might suggest a potential link between hypertension and increased risk of postoperative PE. Notably, two patients who had preoperative PE also developed postoperative PE. This observation underlined a strong predictive value of preoperative PE for postoperative occurrences, with an odds ratio of 37.0, signaling a critical area for further investigation and patient monitoring (Figure 1).

Examining the surgical procedures, our data indicated no significant correlation between the type of surgery performed and the incidence of PE (Figure 2).

This observation was consistent across various treatment alternatives, including conservative treatment, arthroplasty, dynamic hip screw fixation, intramedullary nailing, and cannulated screw fixation. The uniformity of PE occurrence rates across these diverse surgical procedures suggests that the surgical method may not be a primary determinant in PE development.

Our mortality analysis conducted over a 5-year follow-up period post-surgery revealed a stark and concerning contrast in survival outcomes (Figure 3). Patients who developed PE had an alarmingly high mortality rate of 87% during this period, significantly exceeding the 59.7% mortality rate observed in patients who did not develop PE.

Table 1. Age and Gender Distribution Among Patients.

Age	Male	Female	Total
<65 years	135 (18.0%)	96 (6.4%)	231 (10.2%)
65-75 years	121 (16.2%)	216 (14.3%)	337 (14.9%)
>75 years	493 (65.8%)	1195 (79.3%)	1688 (74.9%)
Average age	76.4	80.9	79.4
Total	749	1507	2256

Multivariate Regression Analysis Results

The multivariate regression analysis showed that, after adjusting for various comorbidities, a history of preoperative PE remained a significant predictor of postoperative mortality (OR = 37.0, 95% CI = 22.0-62.0, $P = .045$). Other comorbidities, including obesity, hypertension, diabetes, hypercholesterolemia, atrial fibrillation, ischemic heart disease, chronic heart failure, and chronic kidney failure, were not found to be significant predictors of mortality in this model.

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Multivariate Regression Analysis Results

The multivariate regression analysis showed that, after adjusting for various comorbidities, a history of preoperative PE remained a significant predictor of postoperative mortality (OR = XX, 95% CI = XX, $P < .05$). Other comorbidities, including hypertension, diabetes, hypercholesterolemia, atrial fibrillation, ischemic heart disease, chronic heart failure, and chronic kidney failure, were not found to be significant predictors of mortality in this model (Figure 1). This striking difference not only underscores the severe impact of PE on patient survival but also highlights the critical need for vigilant monitoring and proactive management strategies in this vulnerable patient population.

Table 2. Baseline Characteristics and Comorbidities.

	Participants without PE n = 2225	Participants with PE n = 31	*P*-value
History of pulmonary embolism	0	2	<0.05
BMI >25	89 (4.0%)	1 (3.2%)	NS
Comorbidities			
Hypertension	1416 (63.6%)	18 (58.1%)	NS
Diabetes	597 (26.8%)	9 (29.0%)	NS
Hypercholesterolemia	579 (26.0%)	7 (22.6%)	NS
Atrial fibrillation	330 (14.8%)	7 (22.6%)	NS
Ischemic heart disease	623 (28.0%)	8 (25.8%)	NS
Chronic heart failure	276 (12.4%)	7 (22.6%)	NS
Chronic kidney failure	244 (11.0%)	5 (16.1%)	NS

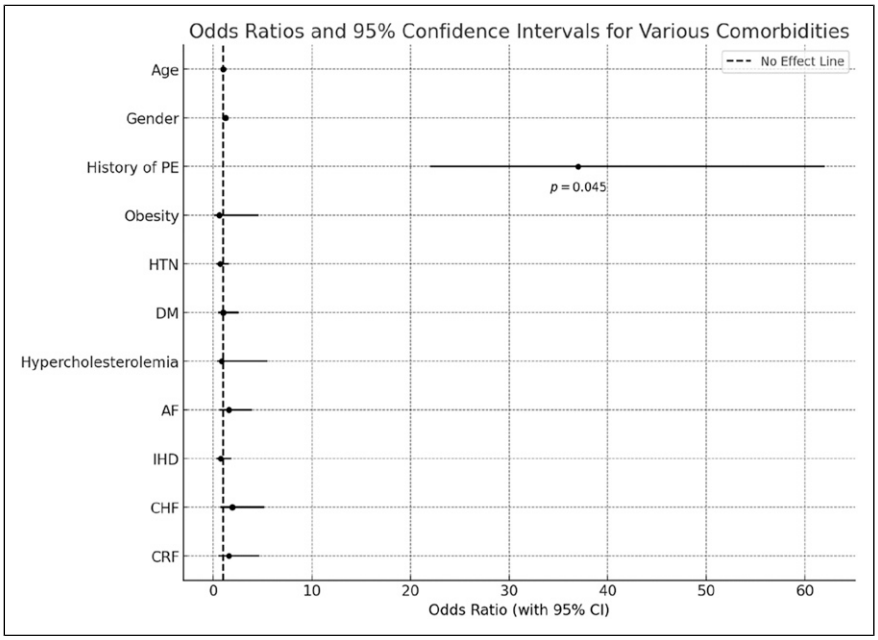

Figure 1. The forest plot illustrates the odds ratios (with 95% confidence intervals) for various comorbidities in relation to pulmonary embolism (PE) risk. Including in analysis are: age, gender, history of PE, obesity, hypertension (HTN), diabetes mellitus (DM), hypercholesterolemia, atrial fibrillation (AF), ischemic heart disease (IHD), chronic heart failure (CHF), and chronic renal failure (CRF). The dashed line at an odds ratio of 1.0 indicates no effect. A significant association is observed for history of PE ($P = .045$), highlighted below the corresponding line.

Despite anticipations, our analysis disclosed no significant variance in PE incidence among patients adhering to early weight-bearing protocols post-surgery vs those who did not, as well as between patients referred to institutional rehabilitation and their counterparts (Table 3). This revelation prompts a reevaluation of assumed protective strategies against PE, highlighting the imperative for intricate studies to decode the underlying complexities influencing PE risk post-orthopedic surgeries.

Odds Ratios and P-Values

- Our multivariate analysis revealed that preoperative PE is a significant predictor of postoperative PE, with an OR of 37.0 ($P = .045P = .045P = .045$). This suggests that patients with preoperative PE are 37 times more likely to develop postoperative PE compared to those without preoperative PE.
- The *P*-value indicates that this result is statistically significant, meaning the likelihood of observing such an association by chance is very low (less than 5%).

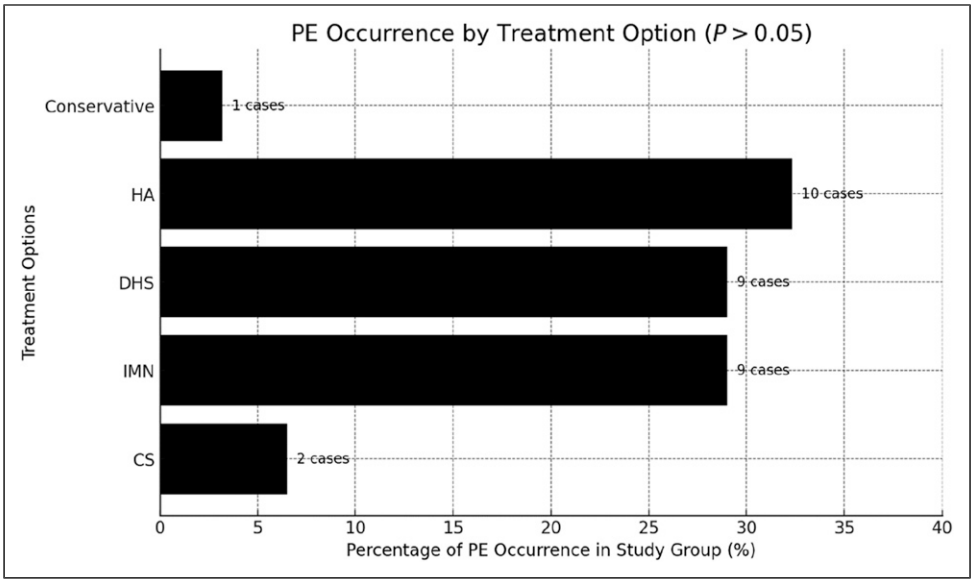

Figure 2. Pulmonary embolism (PE) occurrence by treatment type: conservative, hemiarthroplasty/arthroplasty (HA), dynamic hip screw (DHS), intramedullary nail (IMN), and cannulated screws (CS). The number of PE cases is shown next to each bar. All *P*-values are >.05, indicating no significant differences.

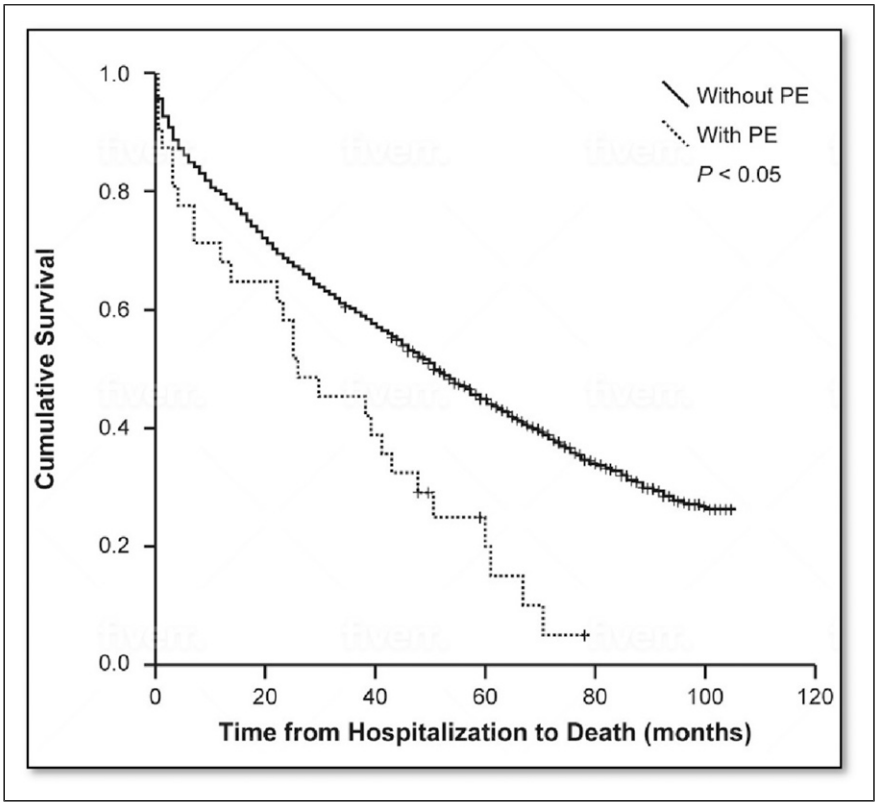

Figure 3. a Kaplan-Meier survivorship curve presents the significant difference in mortality rate between patients who had PE and those who hadn't.

Table 3. Incidence of Deep Vein Thrombosis (DVT) in Patients With Pulmonary Embolism (PE) Following Fracture Versus Those Who Underwent Surgery With Early Mobilization.

Pulmonary embolism	Diagnosed	Not Diagnosed	*P*-value	Odds Ratio	CI
DVT (following index fracture)	6 (19.4%)	51 (2.3%)	<.0001	4.292	1.21-15.1
Institutional rehabilitation	10 (32.3%)	728 (32.7%)	>.05	1.024	0.41-2.52
Early weight bearing (following surgery)	23 (74.2%)	1809 (81.2%)	>.05	0.965	0.20-5.20

Kaplan-Meier Survival Analysis

- The Kaplan-Meier survival curves demonstrated a stark contrast in the 5-year survival rates between the two groups. Patients with postoperative PE had a significantly higher mortality rate of 87% compared to 59.7% in those without PE.
- This significant difference ($P < .0001$) in survival outcomes highlights the critical need for vigilant monitoring and proactive management of PE in patients undergoing femoral neck fracture surgery.

Additionally, we observed a similar incidence of PE across different fracture types: including intra-capsular and extracapsular fractures. This finding suggests that the location of the fracture itself might not significantly influence the risk of developing PE post-surgery. The highest incidence of PE was found in 10 patients who had arthroplasty (hemi or total), compared to 9 patients who treated with a dynamic hip screw or proximal femoral nailing (Figure 2). Despite these variations in incidence rates among different surgical procedures, the overall statistical analysis did not reveal a significant difference in the occurrence of PE based on the surgical method, indicating that factors other than the type of surgery might play more crucial roles in PE development post-surgery.

Discussion

According to the literature, the 1-year mortality rate following a hip fracture ranges between 14% and 58%, irrespective of the treatment received.[12] Among the elderly population aged 65 years and older, this percentage increases by an additional 4% annually.[13] Our study's crucial finding that over a 5-year period, the mortality rate for patients who experienced PE was 87.1%, compared to 59.7% for patients without PE ($P = .001$), underscores the severity of PE as a complicating factor post-hip fracture. The mean time from admission for surgery to death was significantly shorter for patients with PE (33.5 months) compared to those without PE (57.1 months) ($P < .0001$), indicating a substantial impact on survival (Figure 3). The only significant predictors for postoperative PE were identified as preoperative PE ($P = .045$) and postoperative DVT ($P < .0001$), highlighting the critical need for vigilant management in these patients.[14] This aligns with findings from Ko et al,[15] which showed a 4.9% mortality rate at the first follow-up, with sociodemographic and nutritional factors being significant predictors of mortality. Similarly, the study on Swedish fracture register data pointed to higher mortality rates in males and those delayed beyond 36 hours for surgery, emphasizing timely interventions.[16]

Risk factors for PE in the elderly population following femoral neck surgery have been well-established throughout the literature. Memtsoudis et al[17] identified cerebrovascular and renal diseases, obesity, and dementia as factors linked to an increased risk of PE, whereas Mraovic et al[18] independently identified diabetes as a significant risk factor for PE.[17,18] However, our findings align with those of Zeng et al,[19] who also reported that a history of previous VTE was a predictive factor for postoperative VTE, while coronary artery disease did not show an increased risk. Zeng et al[20] also found an increased risk of VTE due to a history of VTE. In our study, this was among the few risk factors (1.1%) that predicted postoperative. This association can be attributed to venous stasis resulting from immobilization, hypercoagulability, and endothelial injury to blood vessels. The prevalence of preoperative PE in our study is also consistent with the findings of the recent studies,[21] highlighting the significance of thorough risk factor screening, including the new predictor model for DVT risk and the highlighted importance of recognizing preoperative conditions such as DVT to effectively manage and reduce the incidence of postoperative complications such as PE.

The debate regarding the impact of fracture and surgical types on the incidence of postoperative pulmonary embolism (PE) persists in academic circles. Our study's results reveal that the type of fracture, whether intracapsular or extracapsular, alongside the chosen surgical intervention—be it conservative methods, arthroplasty, dynamic hip screws (DHS), intramedullary nailing (IMN), or cannulated screws—exerts no discernible effect on the likelihood of postoperative PE development. This observation contrasts with Lin et al, [22] who noted an elevated PE risk in hemiarthroplasty patients, potentially attributed to their extensive comorbid conditions and compromised bone quality. Conversely, McNamara et al's[23] correlation between extracapsular fractures and increased blood loss, a

known PE risk factor, did not align with our findings; our analysis suggests that surgical technique advancements may neutralize risks associated with fracture types. This stance is bolstered by multiple studies that concur with our conclusion, indicating no significant variance in post-surgical PE rates among different hip fracture categories.[24,25]

Exploring the relationship between early postoperative outcomes and pulmonary embolism (PE), our analysis discerned no significant disparities in early weight-bearing initiation, duration of hospital stay, or the latency to surgical intervention between patients afflicted with PE and their counterparts. This observation aligns with findings by Klestil et al,[26] who posited that surgical intervention within a 72-hour window mitigates complication risks, resonating with our data wherein surgical delays averaged beneath 48 hours. Contrarily, Lin et al [22] reported extended hospitalizations for PE patients compared to non-PE patients, without delving into surgical timing—a factor previously correlated with hospitalization length.[27] Despite associations between non-weight-bearing status and elevated PE risk, primarily due to immobilization,[28] our study noted substantial adherence to weight-bearing in both cohorts. This parity in outcomes across cohorts may be attributed to our hospital's rigorous anticoagulation protocol,[29] perioperative strategies,[30] and patient-specific factors (Tables 1 and 2).

The impact of pulmonary embolism (PE) on mortality rates and the period from surgery to death has been notably significant in this study. Lin et al[22] have documented considerably elevated cumulative mortality rates at 1, 3, and 6 months post-surgery in the PE cohort, distinctly higher than those in the non-PE group. Previous research by our group[31] established a significant link between postoperative cerebrovascular accidents (CVA) and diminished median survival times at a 5-year follow-up, albeit without considering PE as a variable. Despite the lack of a statistically significant correlation between postoperative PE and CVA in the present analysis, it is plausible that these factors independently influence mortality rates. This hypothesis is corroborated by a multicenter study in France[32] and research by Tran et al, [33] both highlighting the sustained increase in mortality risk following a hip fracture, with gender-specific risk durations extending up to 10 years.

Our investigation revealed a striking 5-year mortality rate differential, with 87.1% in the pulmonary embolism (PE) cohort vs 59.7% in those without PE. The median duration from surgical intervention to mortality notably diverged between groups: 33.5 months for PE patients (range: 3-70 months), as opposed to 57.1 months in the non-PE group (range: 2-72 months). Although not exclusively attributable to PE, the significant variance in survival times, in the absence of other major risk factors, perioperative, or postoperative complications beyond deep vein thrombosis (DVT), strongly suggests a linkage. This underscores the imperative for a broader inquiry into the roles of preoperative and postoperative PE in shaping mortality outcomes post-hip fracture, advocating for expanded research endeavors.[21,34]

Limitations

Inherent to its retrospective design, our study, while robust with a cohort of 2256 patients, acknowledges certain limitations. The absence of a non-hip fracture control group presents a clear direction for future research. Areas such as malignancy, myocardial infarction, and concurrent injuries remain unaddressed, signaling a gap in the current hip fracture literature. Variability in surgical interventions, influenced by individual health and fracture specifics, alongside unmeasured factors like pre-surgical mobility and post-discharge rehabilitation compliance, mark areas for further investigation. Despite these constraints, the study stands out for its extensive follow-up period and exploration of critical yet underreported phenomena.

Conclusion

Our study highlights the heightened mortality risk for patients with a preoperative history of pulmonary embolism (PE) following proximal femoral fracture, presenting a 37-fold increased risk for postoperative PE. It emphasizes the criticality of recognizing preoperative PE alongside postoperative occurrences, advocating for a comprehensive approach in patient assessment and management to mitigate mortality risks. This underscores the need for vigilant screening and proactive interventions in the perioperative care of these high-risk patients.

Author Contributions

R.A. conceptualized and designed the study; J.D. and S.S. collected the data; E.T., E.Y., and E.P. analyzed and interpreted the data; M.D. drafted the manuscript; N.O. supervision, critically final revised the manuscript for important intellectual content.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Statement

Ethical Approval

This study was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. Ethical approval was waived by the local Ethics Committee of Meir medical center (approval number: MMC 0290-18), as this is a retrospective study without identifiable patient data.

Informed Consent/Patient Consent

This study is retrospective, involving the analysis of existing patient records for which individual consent for inclusion in the study was waived by the ethical standards committee.

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Data Availability Statement

All data generated or analyzed during this study are included in this published article.

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