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# Early Orthopedic Surgery in Intermediate-low and low-risk Pulmonary Embolism Patients: A Multi-centre study to determine the safety of Surgical Intervention

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## A B S T R A C T

**Background:** Globally, venous thromboembolism, which includes deep vein thrombosis and pulmonary embolism, is on the rise. Between twenty and thirty percent of all PE occurrences have other causes, such as recent immobilization, severe surgery, and trauma. Preoperative pulmonary embolism is a prevalent condition amongst patients with hip fracture.

**Objective:** To explore whether early orthopedic surgery is safe for individuals who have low-risk or intermediate-low-risk pulmonary emboli.

**Methodology:** The current study was conducted at the Orthopedic Department, Bacha Khan Medical Complex and Medical Teaching Institute (MTI), Mardan Medical Complex, Mardan from December 2018 to November 2020. The enrolled individuals in the current study were divided into PE group and non-PE group. The PE group comprises individuals who received a verified diagnosis of PE before undergoing surgery, whereas non-PE-group consists of those who did not get an official diagnosis of PE during their hospital stay. For comparison of categorical data, the chi-square or Fisher's exact test were employed whereas for continuous data the Mann-Whitney U-test was used. Approval of the study was taken from ethical committee of MTI Mardan Medical Complex, Mardan.

**Results:** Totally, 160 participants with hip fracture were enrolled in our study. All were diagnosed with pulmonary CT angiography. During the postoperative phase, 18 patients (11.25%) were diagnosed with PE. As a result, 92 participants (57.5%) were placed in the PE-group, whereas in non-PE-group, 52 patients (32.5%) were assigned. The baseline features of the PE and non-PE-groups and postoperative PE-group did not vary statistically. Within the PE-group, deep vein thrombosis (DVT) was identified in 39.1% of the individuals.

**Conclusion**: It was concluded from the current study that prompt surgical intervention may be clinically viable and reasonably safe for individuals with acute pulmonary embolism and hip fractures.

**Keywords:** Safety; Orthopedic Surgery; Pulmonary Embolism; Risk

## Introduction

Venous thromboembolism (VTE), which includes pulmonary embolism (PE) and deep vein thrombosis (DVT), is becoming more prevalent worldwide.[1,2] Despite the fact that novel medication classes, such direct oral anticoagulants have been shown useful in the management and prevention of it.[4,5] There is still a considerable morbidity and death rate linked to VTE.[6] Various risk factors are associated with VTE. Between twenty and thirty percent of all PE occurrences have other causes, such as recent immobilization, severe surgery, and trauma. One of these determinable risk factors is a fracture that necessitates surgery, which is linked to the occurrence of VTE both before and after surgery.[9-11] Because of the increased risk of return in the first four weeks following an acute PE incident, it is generally advised not to undergo elective surgery in month.[12-13] According to previous study, there is a >40% chance of recurrence if anticoagulation is stopped within a month following acute VTE.[13] If delaying surgery isn't an option, they also suggested postoperative vena cava inferior filters implantation.

One major cause of mortality for individuals with hip fractures is pulmonary embolisms (PE).[7] Preoperative deep vein thrombosis (DVT) has been diagnosed in 2.60%–34.98% individuals who receive preventative treatments because of trauma, prolonged bed rest, and underlying illnesses.[5] PE is seen in over one-third of DVT individuals, and in a majority of these individuals, the PE is asymptomatic.[8] This kind of PE may develop into more severe consequences in elderly individuals with hip fractures, such PE that is deadly during or after surgery. Thirteen percent of patients who die from hip fractures have PE.[2] Because they have multiple medical conditions and worse overall health, elderly patients with hip fractures need comprehensive preoperative examination and optimization, which often causes surgery to be postponed. In these individuals, surgical delay is a significant risk element in DVT and PE.[9] As a result, there is a greater chance of preoperative PE for these individuals. PE may worsen before and after surgery if it goes unnoticed and not addressed in a timely manner. Therefore, for older patients with hip fractures who have delayed surgery, it is crucial to avoid and diagnose preoperative PE, and more aggressive monitoring may be beneficial in these situations.[9]

One common condition that has to be treated quickly to lower mortality and perioperative complications is hip fracture.[14] However, little information is known on the optimal timing of surgery and the duration of care for patients suffering from hip fractures and PE. In our setting, no such study has been carried out. Therefore, this study was carried out to explore whether early orthopedic surgery is safe for individuals who have low-risk or intermediate-low-risk pulmonary emboli.

## Objective

The objective of our study was to explore whether early orthopedic surgery is safe for individuals who have low-risk or intermediate-low-risk pulmonary emboli.

## Methodology

The current study was conducted at the Orthopedic Department, Bacha Khan Medical Complex and MTI Mardan Medical Complex, Mardan from December 2018 to November 2020. Individuals who underwent surgery and had hip fractures were screened. This study only included the individuals who had pulmonary computed tomography (CT) angiography after it was suspected that they had PE. The enrolled individuals in the current study were divided into PE-group and non-PE-group. The PE group comprises individuals who received a verified diagnosis of pulmonary embolism before surgery, whereas the non-PE-group consists of those who did not get an official diagnosis of PE during their hospital stay. Participants who have received a diagnosis with pulmonary embolism in the postoperative period were not enrolled in this group. Lower-extremity venous Doppler ultrasonography, lower-extremity venography CT scans and pulmonary CT angiography all validated the diagnosis of pulmonary embolism and deep vein thrombosis (DVT). From the Asian Medical Center's computerized medical records, information on gender, age, BMI, threshold of D-dimer, past experiences with cancer, presence of DVT, and echocardiogram results was first gathered. The 2015 European Society of Cardiology recommendations and the streamlined Pulmonary Embolism Severity Index (PESI) were used to assess the severity of PE during the CT scan.[16,17]

At our hospital “the American College of Chest Physicians guidelines” [18] and a review paper of “O' Donnell and Kearon” [13] serve as the foundation for the perioperative care of patients with pulmonary embolism who need surgery. Therapeutic dosage bridging anticoagulation is advised for individuals whose surgery cannot be postponed for more than three months following the diagnosis of PE. Additionally, preoperative IVC filter implantation is advised for individuals whose surgery cannot be postponed for longer than two weeks following the diagnosis of PE. However, the responsible surgeon made the decision to undertake postoperative anticoagulation and preoperative IVC filter placement on a case-by-case basis.

Three months following the procedure, adverse results were assessed. Significant bleeding and symptomatic recurrent VTE were the study's main goals. Clinically relevant non major (CRNM) bleeding, the volume of

Table 1. Baseline features of the individuals

| Parameters | Total | PE-Group | Non-PE-Group | PE Group (Postoperative) | P value | P value |
|---|---|---|---|---|---|---|
| Numbers of individuals | 160 | 92 | 52 | 18 | | |
| Age (years) | 72.0 ± 14.8 | 72.0 ± 14.6 | 73.6 ± 11.0 | 66.8 ± 23.9 | 0.494 | 0.284 |
| Gender (Male) | 42 (26.3%) | 26 (28.9%) | 12 (24.0%) | 4 (22.2%) | 0.533 | 0.476 |
| BMI (kg/m$^{2)}$ | 22.8 ± 3.8 | 22.6 ± 3.3 | 23.4 ± 4.6 | 23.4 ± 4.5 | 0.494 | 0.960 |
| GFR (below 50 mL/min/1.73 m) | 19 (11.5%) | 12 (13.0%) | 6 (11.5%) | 1 (5.5%) | 0.533 | 0.545 |
| Hemoglobin (below10 g/dL) | 42 (27.6%) | 30 (32.6%) | 10 (19.2%) | 2 (11.11%) | 0.072 | 0.396 |
| Platelet count (less than 150,000/μL) | 34 (20.5%) | 18 (19.5%) | 13 (25%) | 3 (16.66%) | 0.475 | 0.476 |
| Liver cirrhosis | 3 (1.3%) | 0 | 0 | 0 | 0.538 | Not available |
| History of cancer | 25 (16%) | 18 (19.56%) | 6 (11.5%) | 1 (5.5%) | 0.462 | 0.372 |

perioperative transfusion, the duration of hospitalization, and perioperative death were the secondary outcomes. Major and CRNM bleeding have been designated according to earlier research.[19,20] Major bleeding was characterized as bleeding that occurred within the brain, spinal cord, retroperitoneal, and heart; bleeding that was lethal or required a second therapy; bleeding that was obvious and resulted in a hemoglobin drop of at least two grams per deciliter after surgery; or bleeding that needed at least two units of packed red blood cells transfusion.[21] Overt bleeding that failed to fulfill the criteria for significant bleeding however required medical attention, unplanned hospital trips, stopping anticoagulants, or making everyday activities difficult was referred to as CRNM bleeding.[22] Categorical variables were shown as numbers (%), while continuous variables were given as mean ± standard deviation or median (interquartile range). Where applicable, the chi-square or Fisher's exact test were used to compare categorical data, and the Mann-Whitney U-test was used to compare continuous variables. $P<0.05$ was the threshold for statistical significance, and all P values were 2-tailed. IBM Corporation, Armonk, New York, USA's SPSS 20.0 was used for all the statistical analyses of the collected data.

Approval of the study was taken from ethical committee of MTI Mardan Medical Complex, Mardan.

## Results

Totally, 160 participants with hip fracture were enrolled in our study. All were diagnosed with pulmonary CT angiography. During the postoperative phase, 18 patients (11.25%) were diagnosed with PE. As a result, 92 participants (57.5%) were placed in the PE-group, whereas in non PE-group, 52 patients (32.5%) were assigned. The table shows the baseline features of the study participants in both groups. Among study cases, 26.3% of those examined were men, and the average age of the participants was 72 years. The baseline features of the PE and non-PE groups and postoperative PE group did not vary statistically. Within the PE group, deep vein thrombosis (DVT) was identified in 39.1% of the individuals (Table 2). Based on PESI categorization, the most common category of pulmonary embolism was class II in 42(45.6%) patients, class III in 28(30.4%) patients while class I was only observed in 15(16.3%) patients. Based on the guidelines of ESC (European Society of Cardiology), Intermediate-low risk PE was observed in (39.1%) participants whereas low risk PE was observed in (60.86%) patients in PE-group. Based on the level of artery involved, the segmental pulmonary artery involvement was observed in 47.8% of cases. The lobar pulmonary artery was involved in 23.3% of cases, and the

Table 2. Clinical features and pulmonary CT angiography results of the pulmonary embolism patients

| Variables | N=92 |
|---|---|
| **DVT (PE diagnosis time)** | |
| Yes | 36 (39.1%) |
| No | 35 (38.0%) |
| Not known | 21 (22.82%) |
| **PESI (classes)** | |
| I | 15 (16.3%) |
| II | 42 (45.6%) |
| III | 28 (30.4%) |
| IV | 6 (6.5%) |
| V | 1 (1.0%) |
| **Risk Stratification** | |
| High | 0 |
| Intermediate /high | 0 |
| Intermediate/low | 36 (39.1%) |
| Low | 56 (60.86%) |
| **findings of Pulmonary CT angiography** | |
| Involvement of single vessel | 52 (56.5%) |
| Involvement of multiple vessels | 40 (43.47%) |
| **Involvement of arteries** | |
| Pulmonary infarction | 1 (1.0%) |
| Main pulmonary artery | 10 (10.8%) |
| Segmental pulmonary artery | 43 (46.7%) |
| Lobar pulmonary artery | 22 (23.9%) |
| Sub segmental pulmonary artery | 17 (18.47%) |
| Trunk of pulmonary artery | 0 |

Table 3. Management of the individuals with PE perioperatively

| **Mean duration (between diagnosis of PE diagnosis and surgery)** | **1-4 days** |
|---|---|
| Preoperative inferior vena cava filter insertion | 46 (50%) |
| **Anticoagulation before surgery** | |
| Heparin | 42 (45.65%) |
| low molecular weight heparin | 12 (13.0%) |
| Direct oral anticoagulant | 6 (6.5%) |
| Not performed | 32 (34.7%) |
| Operation duration /minute | 108 |
| Time (hours) without anticoagulation following surgery | 40 |
| **Initial anticoagulation after surgery** | |
| Heparin | 24 (26.0%) |
| low molecular weight heparin | 38 (41.3%) |
| Direct oral anticoagulant | 26 (28.2%) |
| Not done | 4 (4.34%) |

sub segmental pulmonary artery was involved in 46.7%. Only one participant was found to have pulmonary infarction. The mean duration between diagnosis of PE and surgery was two days. Surgical procedure was done by all the patients in the PE-group within one month following diagnosis of pulmonary embolism (Table 3).

Among study cases, 50% of the participants in the PE-group had undergone IVC filter implantation prior to surgery. The patients in the pulmonary embolism group were administered preoperatively for anticoagulation with heparin being the most frequently prescribed drug, accounting for 45.65% of cases. The typical duration of the procedure was 108 minutes, and the mean duration 40 hours without anticoagulation following surgery. The members of the PE group administered postoperative anticoagulation, mainly with low molecular weight heparin as the main prescribed medication (41.3%).

Postoperative anticoagulation was administered to more patients in the PE-group than the non-PE-group (treatment dosage in the PE-group, prophylactic dose in the non-PE-group). Nonetheless, there were no occurrences of symptomatic recurrent venous thromboembolism (VTE) or fatality within three months among the trial participants. Furthermore, no statistically significant differences were seen between the two groups in terms of severe bleeding, CRNM hemorrhage, transfusion quantity, bleeding location, or length of hospital stay.

The D-dimer levels were higher in the patients with pulmonary embolism who had IVC filter insertion (mean 19 vs 12.1g/mL, P=0.021) compared to those who did not (Table 5)**.** Additionally, at the PE diagnosis time, a greater number of individuals within the IVC filter group developed DVT (P=0.001) than those in the non-IVC filter group. Nevertheless, there were no statistically significant variations between the non-IVC filter group and the IVC filter group in terms of clinical outcomes like bleeding and hospital stay duration.

## Discussion

The present research looked at the clinical viability and safety of early orthopaedic surgery within 30 days in individuals with hip fractures and acute pulmonary embolism. Despite the fact that severe bleeding was observed in (21.7%) individuals of the PE group patients within three months following surgery, the clinical outcome of the PE & non-PE groups was same. According to our research, prompt surgery is clinically

possible for individuals having intermediate/low- as well as low-risk PE if the American College of Chest Physicians recommended perioperative treatment strategy is followed. While earlier research concentrated on the prevalence and prevention of Venous thromboembolism after surgery of hip fracture.[10,23,24] Before surgery VTE is also often seen among individuals with hip fractures, according to many studies (incidence varying from 2.6 percent to 62 percent).[11,25,28]

Regarding the scheduling of operation in patients with hip fractures and preoperative Venous thromboembolism, particularly in pulmonary embolism cases, there is, however, little data. Recurrence is a possibility for VTE patients, particularly in the first four weeks.[12] As a result, prior research recommended that elective surgery be postponed for a minimum of one month following the diagnosis of VTE.[13,28] But the kind of surgery was not taken into account in earlier research, which might have an impact on the clinical judgment. In general, hip fractures necessitate prompt surgery to minimize complications as well as to improve function and mortality.[14,15] Furthermore, individuals were admitted more than 72 hours after the accident had a greater frequency of Venous thromboembolism than participants whose were admitted within three days following the injury, according to research by Cho et al.[28] This highlights how crucial early surgery is. According to our recent research, patients with hip fractures and acute PE may have lower morbidity and death rates with appropriate care, particularly in low-risk situations. About 64.4% of patients in the PE category in the present investigation had anticoagulation before to surgery, and 95.6% of patients received it thereafter. Despite the fact that significant bleeding happened in the proportion of participants in the PE group was 21.7%, which is not in accordance with other studies.[30, 31] Nevertheless, there was no appreciable difference between the PE group and the non-PE group. To our knowledge, there has never been a consensus on when postoperative anticoagulation should be started for individuals who have both PE and a hip fracture. Our study's median duration without anticoagulation following surgery was two days, indicating that it is generally safe to start anticoagulant medication again in the early stages. It's interesting to note that the PE group's clinical history was unaffected by the preoperative IVC filter placement. Despite the fact that IVF filter use has grown over time.[32] IVC filters' function is still debatable, particularly in individuals receiving anticoagulant treatment who have VTE.[33-36]

However, individuals with acute PE with a hip fracture may benefit from IVC filter placement. Due to the surgeon's assumption that patients with deep vein thrombosis (DVT) would get the most benefit from the therapy, our current study found a greater incidence of DVT in the group that received an inferior vena cava (IVC) filter compared to the group that did not receive one. In a previous study, Kim et al. found that 13.1% of patients who had preoperative IVC filter implant had caught thrombus during the recovery

Table 4. Evaluation of clinical course of PE and non-PE individuals

| Variable | Total | PE-Group | None PE-Group | P-value |
|---|---|---|---|---|
| No of individuals | 144 | 92 | 52 | |
| Recurrent venous thromboembolism | 0 | 0 | 0 | not available |
| Mortality during surgical procedure | 0 | 0 | 0 | not available |
| **Bleeding category** | | | | |
| Major bleeding | 29 (20.0%) | 20 (21.7%) | 9 | 0.463 |
| clinically relevant non-major bleeding | 18 (12.5%) | 12 (13.0%) | 6 (11.5%) | 0.342 |
| **Bleeding site** | | | | |
| Operation-site bleeding | 42 (29.1%) | 30 (32.6%) | 12 (23.0%) | 0.372 |
| Gastrointestinal tract bleeding | 4 (2.7%) | 0 | 0 | 0.538 |
| Urinary tract bleeding | 2 (1.3%) | 0 | 0 | >0.999 |

Table 5. Basic features and clinical findings according to inferior vena cava filter insertion in the pulmonary embolism individuals

| Variables | Inferior Vena Cava filter Group | Noninferior Vena Cava filter Group | p-value |
|---|---|---|---|
| No of individuals | 46 | 46 | |
| Age (years) | 71.6 ± 15.6 | 72.4 ± 13.8 | 0.791 |
| Gender (Male) | 14 (31.1) | 12 (26.7) | 0.642 |
| BMI (kg/m$^2$) | 22.7 ± 3.2 | 22.4 ± 3.4 | 0.659 |
| D-dimer (g/mL) | 19 | 12 | 0.021 |
| History of cancer | 8 (17.39%) | 10 (21.7%) | 0.419 |
| **DVT (PE Diagnosis time)** | | | |
| Yes | 27 (58.6%) | 10 (21.7%) | |
| No | 12 (26.0%) | 22 (47.8%) | |
| Symptomatic recurrent Venous thromboembolism | 0 | 0 | NA |
| Mortality during surgery | 0 | 0 | NA |
| **Bleeding** | | | |
| Major bleeding | 11 (23.9%) | 10 (21.7%) | 0.796 |
| CRNM bleeding | 9 (19.5%) | 3 (6.5%) | 0.063 |
| Length of hospital Stay (days) | 14 | 12 | 0.455 |

phase, out of 122 patients.[37] Still, more research is required to ascertain the function of IVC filter placement in individuals suffering from acute PE and hip fractures.

## Conclusion

The current study indicates that prompt surgical intervention may be a clinically viable and reasonably safe option for individuals suffering from acute pulmonary embolism and hip fractures. However, these findings should be interpreted with caution due to the study's limitations. To establish the safety and efficacy of this treatment approach, additional research with larger populations and prospective study designs is needed. This will provide a more robust evidence base for guiding clinical decisions in such complex cases.

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