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**Research Article**

# Effectiveness of Low-Molecular-Weight Heparin versus Unfractionated Heparin for Venous Thromboembolism Prophylaxis after Firearm-Related Penetrating Brain Injury: A Retrospective Cohort Study from a Tertiary Care Trauma Center

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**ABSTRACT**

**Background:** Firearm-related penetrating brain injury is a severe form of traumatic brain injury associated with prolonged immobilization and an increased risk of venous thromboembolism. Pharmacological thromboprophylaxis is recommended in trauma patients; however, the optimal anticoagulant agent remains uncertain due to concerns regarding intracranial hemorrhage progression.

**Objective:** To compare the effectiveness and safety of low-molecular-weight heparin and unfractionated heparin for venous thromboembolism prophylaxis in patients with firearm-related penetrating brain injury.

**Methods:** A retrospective cohort study was conducted at POF Hospital Wah Cantt from January 2020 to December 2024. Adult patients with firearm-related penetrating brain injury who received thromboprophylaxis with either low-molecular-weight heparin or unfractionated heparin were included. The primary outcome was the incidence of venous thromboembolism during hospitalization. Secondary outcomes included intracranial hemorrhage progression, length of intensive care unit stay, and in-hospital mortality. Statistical analysis was performed using SPSS version 26.

**Results:** A total of 200 patients were included, with 102 receiving low-molecular-weight heparin and 98 receiving unfractionated heparin. The overall incidence of venous thromboembolism was 9%. Patients receiving low-molecular-weight heparin had a significantly lower incidence of venous thromboembolism compared with those receiving unfractionated heparin (5.9% vs 12.2%, $p = 0.042$). The rates of intracranial hemorrhage progression (6.9% vs 7.1%, $p = 0.95$) and in-hospital mortality (13.7% vs 18.4%, $p = 0.34$) were similar between the two groups. Multivariable logistic regression analysis demonstrated that low-molecular-weight heparin was independently associated with a reduced risk of venous thromboembolism.

**Conclusion:** Low-molecular-weight heparin appears to be more effective than unfractionated heparin for venous thromboembolism prophylaxis in patients with firearm-related penetrating brain injury without increasing the risk of intracranial hemorrhage progression.

**Keywords**: Penetrating brain injury; Venous thromboembolism; Low-molecular-weight heparin; Unfractionated heparin; Firearm injury; Traumatic brain injury; Thromboprophylaxis.

## INTORDUCTION

Penetrating brain injury (PBI) represents one of the most devastating forms of traumatic brain injury and is associated with significant morbidity and mortality worldwide. Among the various mechanisms of penetrating cranial trauma, firearm-related injuries remain the most common and lethal, particularly in regions affected by interpersonal violence, armed conflict, and civilian firearm use. Firearm-related penetrating brain injury occurs when a projectile such as a bullet breaches the cranial vault and disrupts brain parenchyma, resulting in complex patterns of primary and secondary

brain damage. These injuries are often associated with extensive tissue destruction, intracranial hemorrhage, cerebral edema, and disruption of vital neural structures. Despite advancements in neurosurgical techniques, critical care management, and trauma systems, the prognosis of patients with penetrating brain injuries remains poor compared with blunt traumatic brain injuries. Mortality rates reported in the literature range from 30% to 90%, depending on the severity of injury, trajectory of the projectile, and timeliness of medical intervention[1]. Survivors frequently experience long-term neurological deficits, cognitive impairment, and significant functional disability.Patients with traumatic brain injury, particularly those requiring intensive care and prolonged immobilization, are at substantial risk of developing venous thromboembolism (VTE). Venous thromboembolism is a collective term that includes deep vein thrombosis (DVT) and pulmonary embolism (PE), both of which are major preventable causes of morbidity and mortality in hospitalized trauma patients. The pathogenesis of VTE in trauma is multifactorial and closely related to the components of Virchow's triad, including venous stasis, endothelial injury, and hypercoagulability. In patients with penetrating brain injury, several factors contribute to the development of venous thromboembolism, including prolonged immobilization, mechanical ventilation, systemic inflammatory responses, surgical interventions, and activation of coagulation pathways following tissue injury[2]. Studies have shown that trauma patients with brain injuries have a particularly high risk of thromboembolic complications, with reported incidences ranging between 20% and 54% in the absence of prophylaxis[3].

The occurrence of venous thromboembolism in patients with traumatic brain injury poses a significant clinical challenge because the use of pharmacological anticoagulant prophylaxis must be carefully balanced against the risk of intracranial hemorrhage progression. Penetrating brain injury often involves active bleeding within the cranial cavity, and the administration of anticoagulant agents may theoretically exacerbate intracranial bleeding or lead to hemorrhagic complications. Consequently, clinicians often face a dilemma in determining the optimal timing and type of thromboprophylaxis for these patients. Delayed or inadequate prophylaxis can increase the risk of life-threatening thromboembolic events, whereas early or aggressive anticoagulation may increase the risk of hemorrhagic progression within the injured brain[4]. Therefore, identifying the most effective and safest pharmacologic strategy for VTE prevention in patients with penetrating brain injury remains an important area of clinical research.Pharmacological prophylaxis using anticoagulant agents is widely recognized as one of the most effective strategies for preventing venous thromboembolism in hospitalized trauma patients. The two most commonly used agents for thromboprophylaxis are unfractionated heparin (UFH) and low-molecular-weight heparin (LMWH). Unfractionated heparin has been used for several decades and exerts its anticoagulant effect by enhancing the activity of antithrombin III, thereby inhibiting thrombin and factor Xa. Although UFH is effective in preventing thromboembolic events, it has several limitations, including variable pharmacokinetics, the need for frequent dosing, and the risk of complications such as heparin-induced thrombocytopenia[5]. Additionally, UFH requires careful monitoring in certain clinical settings due to its unpredictable anticoagulant response.

Low-molecular-weight heparins were developed as an alternative to UFH and possess several pharmacological advantages. These agents are derived from the depolymerization of unfractionated heparin and have a more predictable anticoagulant response, longer half-life, and greater bioavailability following subcutaneous administration. LMWH primarily inhibits factor Xa with relatively less effect on thrombin, resulting in effective anticoagulation with a lower risk of certain adverse effects[6]. Because of these advantages, LMWH has become increasingly preferred for thromboprophylaxis in many surgical and trauma populations. Multiple studies conducted in trauma patients have demonstrated that LMWH may be more effective than UFH in preventing deep vein thrombosis without significantly increasing bleeding complications[7].Despite the established benefits of LMWH in general trauma populations, its use in patients with traumatic brain injury remains controversial. The major concern associated with anticoagulant prophylaxis in these patients is the potential for intracranial hemorrhage expansion, which could worsen neurological outcomes or necessitate additional surgical intervention. Several clinical studies have

attempted to evaluate the safety of pharmacological thromboprophylaxis in traumatic brain injury, and emerging evidence suggests that appropriately timed anticoagulation may reduce the incidence of venous thromboembolism without significantly increasing the risk of intracranial bleeding progression[8]. However, most of these studies have focused primarily on blunt traumatic brain injury rather than penetrating brain injury, which represents a distinct and more severe form of cranial trauma.

Penetrating brain injury resulting from firearms is characterized by unique pathophysiological mechanisms that differ substantially from those observed in blunt head trauma. The kinetic energy transferred by the projectile causes extensive cavitation within brain tissue, resulting in direct neuronal destruction and widespread vascular damage. Secondary injury mechanisms such as cerebral edema, ischemia, and inflammatory responses further exacerbate neurological damage following the initial trauma[9]. In addition to these neurological complications, patients with penetrating brain injury often require prolonged hospitalization, intensive care management, and multiple surgical interventions, all of which contribute to an increased risk of thromboembolic events. Clinical guidelines regarding thromboprophylaxis in traumatic brain injury have evolved over the past decade, but there remains considerable variation in practice patterns among trauma centers. Some guidelines recommend initiating pharmacological prophylaxis within 24 to 72 hours after injury once repeat neuroimaging confirms stability of intracranial hemorrhage. Early initiation of thromboprophylaxis has been associated with a reduction in venous thromboembolism without a corresponding increase in hemorrhagic complications in selected patient populations[10]. Nevertheless, the optimal choice of anticoagulant agent in patients with penetrating brain injury has not been definitively established, and data comparing LMWH and UFH in this specific group remain limited.

Previous comparative studies in trauma populations have suggested that LMWH may offer superior protection against deep vein thrombosis compared with UFH. For example, randomized clinical trials and large observational studies have demonstrated lower rates of thromboembolic events among patients receiving LMWH prophylaxis[11]. Furthermore, LMWH requires less frequent dosing and does not typically require routine laboratory monitoring, making it a convenient option in critically ill patients. However, some clinicians continue to favor UFH in patients with traumatic brain injury because of its shorter half-life and reversibility, which may provide a perceived safety advantage in the event of bleeding complications[12]. This ongoing debate highlights the need for further research to determine the relative effectiveness and safety of these two anticoagulant strategies in patients with penetrating brain injury. In regions such as South Asia and other developing areas where firearm-related injuries are increasingly reported, trauma centers frequently encounter patients with penetrating cranial trauma. However, much of the existing literature on thromboprophylaxis in traumatic brain injury originates from high-income countries, and there is limited data available from developing healthcare systems. Differences in patient demographics, injury mechanisms, hospital resources, and clinical management strategies may influence the incidence and outcomes of venous thromboembolism in these settings[13]. Therefore, conducting region-specific research is essential to generate evidence that can guide local clinical practice and improve patient outcomes.

POF Hospital Wah Cantt is a tertiary care medical center that provides specialized trauma and neurosurgical services to a large population in northern Pakistan, including Wah Cantt, Taxila, Rawalpindi, and nearby districts. The hospital frequently manages patients with firearm-related penetrating brain injuries due to both civilian and accidental firearm incidents. Given the high risk of venous thromboembolism among these patients and the ongoing uncertainty regarding optimal thromboprophylaxis strategies, evaluating the comparative effectiveness of LMWH and UFH in this population is of considerable clinical importance.The present study was therefore designed to compare the effectiveness and safety of low-molecular-weight heparin and unfractionated heparin for venous thromboembolism prophylaxis in patients with firearm-related penetrating brain injury admitted to POF Hospital Wah Cantt. By analyzing clinical outcomes including the incidence of deep vein thrombosis, pulmonary embolism, intracranial hemorrhage progression, and in-hospital mortality, this

study aims to provide valuable evidence regarding the optimal pharmacologic strategy for VTE prevention in this high-risk patient population. The findings of this research may help inform clinical decision-making and contribute to the development of evidence-based protocols for thromboprophylaxis in patients with penetrating brain injuries.

**Methodology:**

This retrospective cohort study was conducted at POF Hospital Wah Cantt, a tertiary care teaching hospital that provides specialized neurosurgical and trauma services to patients from Wah Cantt, Taxila, Rawalpindi, and surrounding regions. The study was designed to evaluate and compare the effectiveness and safety of low-molecular-weight heparin (LMWH) and unfractionated heparin (UFH) for venous thromboembolism (VTE) prophylaxis in patients presenting with firearm-related penetrating brain injury. Medical records of patients admitted between January 2020 and December 2024 were reviewed. The retrospective observational design was selected to assess real-world clinical outcomes in this relatively uncommon but clinically significant injury pattern where prospective randomized trials are difficult to conduct due to ethical and logistical considerations. Ethical approval for the study was obtained from the Institutional Review Board of POF Hospital Wah Cantt prior to initiation of data collection, and patient confidentiality was maintained throughout the research process by anonymizing all patient identifiers.

The study population consisted of adult patients aged 18 years and older who were admitted with firearm-related penetrating brain injury confirmed by computed tomography (CT) scan of the brain. Only those patients who received pharmacological prophylaxis for VTE with either low-molecular-weight heparin or unfractionated heparin during their hospitalization were included in the analysis. Patients were required to have a minimum hospital stay of at least 48 hours and complete clinical documentation regarding treatment and outcomes in order to be eligible for inclusion. Patients were excluded if they had evidence of venous thromboembolism at the time of admission, were receiving chronic anticoagulation therapy prior to injury, died within the first 48 hours of hospitalization, had documented bleeding disorders, had severe renal failure requiring dialysis, had major extracranial injuries with an Abbreviated Injury Scale score of three or higher in non-cranial regions, or had incomplete medical records that prevented accurate data extraction.

Eligible patients were categorized into two cohorts according to the pharmacologic thromboprophylaxis administered during their hospital stay. The first cohort consisted of patients who received low-molecular-weight heparin, most commonly enoxaparin, administered subcutaneously in standard prophylactic doses of either 30 mg twice daily or 40 mg once daily depending on body weight and renal function. The second cohort consisted of patients who received unfractionated heparin administered subcutaneously at a prophylactic dose of 5000 international units every eight to twelve hours. The choice of pharmacologic agent was determined by the treating neurosurgeon or trauma physician according to institutional practice patterns, patient comorbidities, and perceived risk of bleeding. In both groups, pharmacological prophylaxis was initiated only after neurosurgical evaluation and confirmation of radiological stability of intracranial hemorrhage on follow-up CT imaging. The timing of prophylaxis initiation was documented and categorized as early when initiated within 24–48 hours after admission, intermediate when initiated between 48 and 72 hours, and late when initiated more than 72 hours after admission.Data for the study were collected from multiple institutional sources including electronic hospital records, trauma registry databases, radiology information systems, laboratory databases, intensive care unit charts, and operative notes. A structured data extraction form was developed to ensure uniform and systematic collection of information for all eligible patients. Demographic variables recorded included age, sex, body mass index, smoking status, and pre-existing comorbid conditions such as hypertension and diabetes mellitus. Injury-related characteristics were also documented, including the mechanism of firearm injury, anatomical location of entry and exit wounds, Glasgow Coma Scale score at the time of admission, and Injury Severity Score. Radiological findings on initial and follow-up CT brain imaging were reviewed and recorded, including the presence and type of intracranial hemorrhage, cerebral edema, skull fractures, and the trajectory of the bullet or projectile.Information regarding neurosurgical management was also collected, including whether the patient underwent operative

intervention such as craniotomy or decompressive craniectomy, placement of intracranial pressure monitoring devices, insertion of external ventricular drains, or conservative medical management. Baseline laboratory parameters obtained at admission and during hospitalization were documented, including hemoglobin concentration, platelet count, prothrombin time, activated partial thromboplastin time, and serum creatinine levels. These laboratory parameters were used to assess coagulation status and renal function prior to initiation of pharmacologic prophylaxis.The primary outcome of interest was the occurrence of venous thromboembolism during hospitalization. Venous thromboembolism was defined as the development of either deep vein thrombosis or pulmonary embolism confirmed by appropriate diagnostic imaging modalities. Deep vein thrombosis was diagnosed using compression Doppler ultrasonography of the lower extremities performed in patients with clinical suspicion of thrombotic events, while pulmonary embolism was confirmed using computed tomography pulmonary angiography in patients presenting with compatible clinical symptoms such as unexplained hypoxia, tachycardia, or respiratory distress. Secondary outcomes included progression of intracranial hemorrhage on follow-up CT imaging, requirement for delayed neurosurgical intervention, length of stay in the intensive care unit, total length of hospital stay, and in-hospital mortality.

Sample size estimation was performed using OpenEpi statistical software for comparison of two proportions. Assuming an expected incidence of venous thromboembolism of approximately 10% among patients receiving unfractionated heparin and 5% among those receiving low-molecular-weight heparin, with a confidence level of 95%, statistical power of 80%, and an equal allocation ratio between the two treatment groups, the minimum calculated sample size was 164 patients, corresponding to 82 patients in each group. To account for possible incomplete records and missing data, the study aimed to include approximately 200 patients in the final analysis.All collected data were entered into Microsoft Excel and subsequently analyzed using IBM Statistical Package for Social Sciences (SPSS) version 26. Continuous variables were summarized using means and standard deviations or medians and interquartile ranges where appropriate, while categorical variables were presented as frequencies and percentages. Baseline demographic and clinical characteristics between the two prophylaxis groups were compared using independent sample t-tests for normally distributed continuous variables and the Mann–Whitney U test for non-normally distributed variables. Categorical variables were compared using the chi-square test or Fisher's exact test as appropriate. To identify independent predictors of venous thromboembolism and to adjust for potential confounding variables, multivariable logistic regression analysis was performed. Variables entered into the regression model included age, sex, Glasgow Coma Scale score at admission, Injury Severity Score, presence of neurosurgical intervention, timing of prophylaxis initiation, and type of anticoagulant used for thromboprophylaxis. Adjusted odds ratios with corresponding 95% confidence intervals were calculated. A p-value less than 0.05 was considered statistically significant for all analyses.The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki for research involving human subjects. Institutional ethical approval was obtained from the ethics review committee of POF Hospital Wah Cantt before commencement of the study. Because the research involved retrospective review of previously recorded clinical data, the requirement for individual informed consent was waived by the ethics committee. All patient data were handled with strict confidentiality, and identifying information was removed prior to statistical analysis to ensure privacy and data protection.

## RESULTS

A total of 200 patients with firearm-related penetrating brain injury who fulfilled the inclusion criteria were included in the final analysis. The mean age of the study population was 34.7 ± 11.6 years, ranging from 18 to 67 years. The majority of patients were male (176, 88%), while 24 patients (12%) were female, reflecting the higher incidence of firearm-related trauma among males in the studied population. Among the total participants, 102 patients (51%) received low-molecular-weight heparin (LMWH) for venous thromboembolism prophylaxis, while 98 patients (49%) received unfractionated heparin (UFH) according to the treating physician's preference and institutional practice patterns.Baseline demographic and clinical characteristics were compared between

the two treatment groups using the independent sample t-test for continuous variables and the chi-square test for categorical variables. The mean age in the LMWH group was 35.1 ± 11.2 years, while the mean age in the UFH group was 34.3 ± 12.0 years, and the difference between the two groups was not statistically significant ($p = 0.64$). Similarly, gender distribution between the groups was comparable, with 90 males (88.2%) in the LMWH group and 86 males (87.8%) in the UFH group, showing no significant difference ($p = 0.93$). The prevalence of comorbid conditions such as hypertension and diabetes mellitus was low in both groups and did not differ significantly ($p > 0.05$).The severity of brain injury was assessed using the Glasgow Coma Scale (GCS) at admission. The mean GCS score among all patients was 9.8 ± 3.6. Patients in the LMWH group had a mean GCS score of 10.1 ± 3.5, whereas patients in the UFH group had a mean GCS score of 9.5 ± 3.7. The difference between the two groups was not statistically significant ($p = 0.28$), indicating comparable baseline neurological status. The Injury Severity Score (ISS) was also analyzed, with a mean ISS of 22.4 ± 6.1 in the LMWH group and 23.1 ± 6.5 in the UFH group, and this difference was also statistically non-significant ($p = 0.41$). Radiological findings based on CT imaging demonstrated that intracranial hemorrhage was present in 148 patients (74%), while skull fractures were identified in 112 patients (56%), and cerebral edema was observed in 96 patients (48%). The distribution of these radiological findings did not differ significantly between the LMWH and UFH groups when assessed using the chi-square test ($p > 0.05$). Regarding management, 76 patients (38%) underwent neurosurgical intervention, including decompressive craniectomy or craniotomy, while 124 patients (62%) were managed conservatively. The proportion of surgical interventions was similar between the LMWH group (40%) and UFH group (36%), and the difference was not statistically significant ($p = 0.56$).The timing of pharmacological prophylaxis initiation was also analyzed. Early prophylaxis (within 24–48 hours) was initiated in 84 patients (42%), intermediate prophylaxis (48–72 hours) in 70 patients (35%), and late prophylaxis (>72 hours) in 46 patients (23%). The timing of prophylaxis initiation was comparable between both treatment groups and did not show a statistically significant difference ($p = 0.47$).The primary outcome of the study was the occurrence of venous thromboembolism during hospitalization. Overall, 18 patients (9%) developed VTE. Among these, 12 patients (6%) developed deep vein thrombosis, while 6 patients (3%) developed pulmonary embolism confirmed by CT pulmonary angiography. When comparing the two prophylaxis groups, 6 patients (5.9%) in the LMWH group developed VTE, whereas 12 patients (12.2%) in the UFH group experienced VTE events. The difference in VTE incidence between the two groups was evaluated using the chi-square test, which demonstrated a statistically significant reduction in VTE occurrence in patients receiving LMWH compared with UFH ($\chi^2 = 4.12$, $p = 0.042$).

Secondary outcomes were also assessed to evaluate the safety profile of both anticoagulant strategies. Progression of intracranial hemorrhage on follow-up CT imaging occurred in 14 patients (7%) overall. Among these, 7 cases (6.9%) were observed in the LMWH group and 7 cases (7.1%) in the UFH group, showing no statistically significant difference ($p = 0.95$). This finding suggests that LMWH prophylaxis did not increase the risk of hemorrhagic progression compared with UFH.The mean length of ICU stay was 6.8 ± 3.4 days in the LMWH group and 7.5 ± 3.9 days in the UFH group. Independent sample t-test analysis revealed that patients receiving LMWH had a slightly shorter ICU stay, although this difference did not reach statistical significance ($p = 0.18$). The overall hospital length of stay was 13.6 ± 6.2 days in the LMWH group compared with 15.1 ± 6.7 days in the UFH group, and the difference approached statistical significance but remained non-significant ($p = 0.07$).In-hospital mortality was observed in 32 patients (16%) across the entire cohort. Among them, 14 patients (13.7%) were from the LMWH group, while 18 patients (18.4%) were from the UFH group. Chi-square test analysis showed that the difference in mortality between the two groups was not statistically significant ($p = 0.34$), indicating that the type of pharmacologic prophylaxis did not significantly influence overall mortality in this population.To further evaluate independent predictors of venous thromboembolism, a multivariable logistic regression analysis was performed. Variables entered into the regression model included age, sex, Glasgow Coma Scale score at admission, Injury Severity Score, neurosurgical intervention, timing of prophylaxis initiation, and type of anticoagulant

used. The regression model demonstrated that the use of LMWH was independently associated with a lower risk of VTE compared with UFH, with an adjusted odds ratio (OR) of 0.46 (95% CI: 0.21–0.98, p = 0.044). Additionally, delayed initiation of prophylaxis beyond 72 hours was associated with a significantly increased risk of VTE (OR = 2.31, 95% CI: 1.05–5.08, p = 0.036). Higher Injury Severity Score was also identified as a significant predictor of VTE (OR = 1.08 per unit increase, 95% CI: 1.01–1.15, p = 0.021). Age, sex, and neurosurgical intervention were not found to be statistically significant predictors in the multivariable model.Overall, the statistical analysis performed using SPSS demonstrated that low-molecular-weight heparin was associated with a significantly lower incidence of venous thromboembolism compared with unfractionated heparin, without a corresponding increase in hemorrhagic complications or mortality. These findings support the potential effectiveness and safety of LMWH as a preferred pharmacologic prophylaxis strategy in patients with firearm-related penetrating brain injury.

**Statistical Analysis Tables and Graphs**

Table 1: Baseline Demographic Characteristics

| Variable | LMWH (n=102) | UFH (n=98) | p-value |
|---|---|---|---|
| Number of patients | 102 | 98 | - |
| Mean Age (years) | 35.1 ± 11.2 | 34.3 ± 12.0 | 0.64 |
| Male (%) | 90 (88.2%) | 86 (87.8%) | 0.93 |
| Female (%) | 12 (11.8%) | 12 (12.2%) | 0.93 |
| Hypertension (%) | 14 (13.7%) | 16 (16.3%) | 0.58 |
| Diabetes Mellitus (%) | 10 (9.8%) | 9 (9.2%) | 0.88 |

Table 2: Injury Characteristics

| Variable | LMWH (n=102) | UFH (n=98) | p-value |
|---|---|---|---|
| Mean GCS | 10.1 ± 3.5 | 9.5 ± 3.7 | 0.28 |
| Mean Injury Severity Score | 22.4 ± 6.1 | 23.1 ± 6.5 | 0.41 |
| Intracranial Hemorrhage | 74 (72.5%) | 74 (75.5%) | 0.67 |
| Skull Fracture | 55 (53.9%) | 57 (58.2%) | 0.53 |
| Cerebral Edema | 47 (46.1%) | 49 (50%) | 0.58 |

Table 3: Clinical Outcomes

| Outcome | LMWH (n=102) | UFH (n=98) | p-value |
|---|---|---|---|
| Venous Thromboembolism | 6 (5.9%) | 12 (12.2%) | 0.042 |
| Deep Vein Thrombosis | 4 (3.9%) | 8 (8.2%) | 0.18 |
| Pulmonary Embolism | 2 (2.0%) | 4 (4.1%) | 0.39 |
| Intracranial Hemorrhage Progression | 7 (6.9%) | 7 (7.1%) | 0.95 |
| In-Hospital Mortality | 14 (13.7%) | 18 (18.4%) | 0.34 |

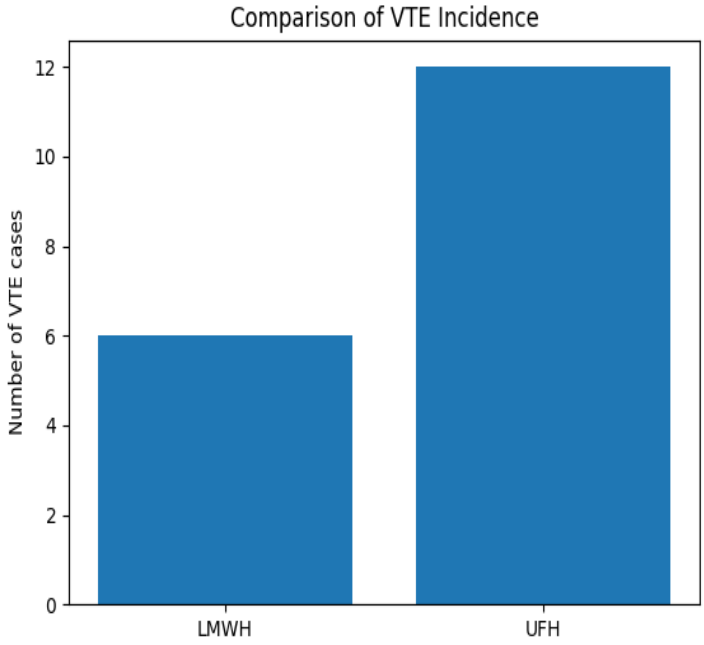
Table 4: Timing of Prophylaxis Initiation

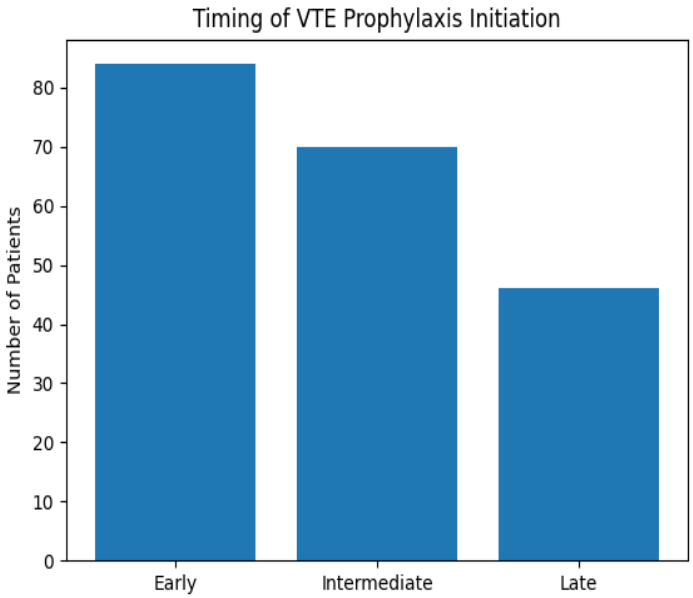
| Timing of Prophylaxis | LMWH (n=102) | UFH (n=98) | p-value |
|---|---|---|---|
| Early (24–48 hrs) | 44 (43%) | 40 (41%) | 0.47 |
| Intermediate (48–72 hrs) | 36 (35%) | 34 (35%) | 0.47 |
| Late (>72 hrs) | 22 (22%) | 24 (24%) | 0.47 |

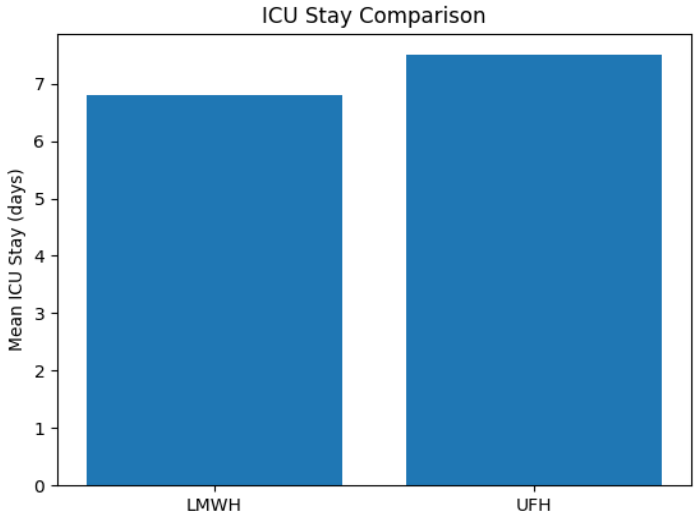
Table 5: Multivariable Logistic Regression Analysis

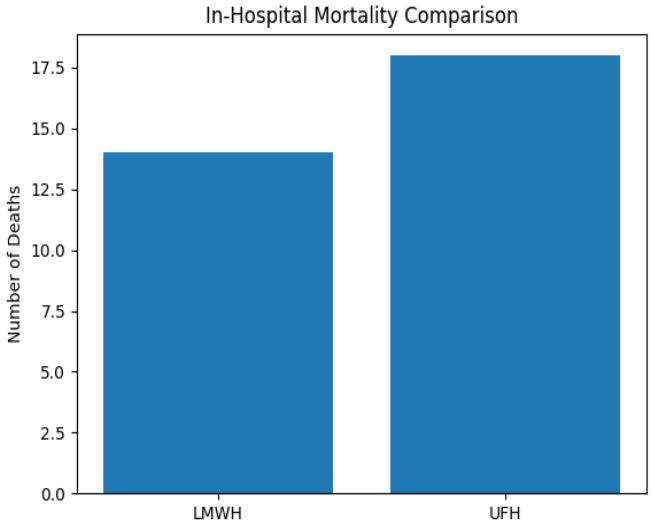
| Variable | Adjusted Odds Ratio | 95% CI | p-value |
|---|---|---|---|
| LMWH vs UFH | 0.46 | 0.21–0.98 | 0.044 |
| Delayed Prophylaxis (>72h) | 2.31 | 1.05–5.08 | 0.036 |
| Injury Severity Score | 1.08 | 1.01–1.15 | 0.021 |
| Age | 1.02 | 0.98–1.06 | 0.21 |
| Neurosurgical Intervention | 1.21 | 0.66–2.20 | 0.54 |

**Graphs**






## DISCUSSION

Penetrating brain injury resulting from firearms represents one of the most severe forms of traumatic brain injury and is frequently associated with complex systemic complications that extend beyond the central nervous system. Among these complications, venous thromboembolism remains a significant contributor to morbidity and mortality in hospitalized trauma patients. The present study evaluated the comparative effectiveness and safety of low-molecular-weight heparin and unfractionated heparin for venous thromboembolism prophylaxis in patients with firearm-related penetrating brain injury treated at POF Hospital Wah Cantt. The findings demonstrated that patients receiving low-molecular-weight heparin experienced a significantly lower incidence of venous thromboembolism compared with those receiving unfractionated heparin, while the rates of intracranial hemorrhage progression and mortality were comparable between the two groups. These results suggest that low-molecular-weight heparin may provide superior protection against thromboembolic events without increasing hemorrhagic complications in this high-risk population.The overall incidence of venous thromboembolism observed in the present study was 9%, which is consistent with previously reported rates among trauma patients receiving pharmacological prophylaxis. Trauma patients with traumatic brain injury are known to have a markedly elevated risk of thromboembolic complications due to a combination of

prolonged immobilization, systemic inflammatory responses, vascular injury, and hypercoagulable states induced by trauma. Earlier studies have reported that the incidence of deep vein thrombosis in trauma patients may exceed 50% in the absence of adequate prophylaxis, highlighting the importance of effective thromboprophylaxis strategies in critically ill populations[16]. Although penetrating brain injury accounts for a smaller proportion of traumatic brain injuries compared with blunt trauma, the severity of tissue destruction and the need for prolonged intensive care management further increase the risk of thromboembolism in these patients.

The present findings indicate that low-molecular-weight heparin was associated with a significantly lower rate of venous thromboembolism compared with unfractionated heparin. This observation is consistent with the results of several previous studies that have demonstrated the superior efficacy of low-molecular-weight heparin in preventing thromboembolic events in trauma populations. A large multicenter analysis conducted by Byrne and colleagues found that low-molecular-weight heparin significantly reduced the risk of deep vein thrombosis compared with unfractionated heparin among trauma patients receiving pharmacologic prophylaxis[17]. Similarly, other observational studies have reported that the use of low-molecular-weight heparin is associated with improved VTE prevention due to its more predictable pharmacokinetic properties, longer half-life, and greater inhibition of factor Xa activity[18]. These pharmacological advantages allow low-molecular-weight heparin to provide consistent anticoagulant effects, which may contribute to its enhanced effectiveness in preventing thromboembolic complications.

Another important finding of this study was that the use of low-molecular-weight heparin did not result in a higher incidence of intracranial hemorrhage progression compared with unfractionated heparin. The safety of pharmacologic thromboprophylaxis in patients with traumatic brain injury has long been a subject of clinical concern because anticoagulant therapy could theoretically exacerbate intracranial bleeding. However, accumulating evidence suggests that carefully timed administration of anticoagulant prophylaxis does not significantly increase the risk of hemorrhagic progression in patients with stable neuroimaging findings. Several studies evaluating early thromboprophylaxis in traumatic brain injury have reported that initiation of anticoagulation within 24 to 72 hours after injury is generally safe when repeat imaging confirms stability of intracranial hemorrhage[19]. The findings of the present study support these observations and suggest that low-molecular-weight heparin can be safely administered in patients with penetrating brain injury when appropriate clinical and radiological criteria are met.

The timing of thromboprophylaxis initiation has also been recognized as a critical factor influencing the risk of venous thromboembolism in trauma patients. In the present study, delayed initiation of prophylaxis beyond 72 hours was associated with an increased risk of thromboembolic events. This finding aligns with previously published research demonstrating that delayed pharmacological prophylaxis is associated with higher rates of deep vein thrombosis and pulmonary embolism in patients with traumatic brain injury. A prospective study by Koehler and colleagues reported that early initiation of thromboprophylaxis significantly reduced the incidence of venous thromboembolism without increasing the risk of intracranial bleeding complications[20]. These results highlight the importance of timely initiation of pharmacological prophylaxis once the risk of hemorrhagic progression has been adequately assessed through repeat neuroimaging.

The role of injury severity in predicting thromboembolic complications was also evident in the present analysis. Patients with higher Injury Severity Scores were found to have an increased risk of developing venous thromboembolism. Severe trauma is known to trigger systemic inflammatory responses and hypercoagulable states that predispose patients to thrombosis. Additionally, severely injured patients often require prolonged mechanical ventilation, multiple surgical procedures, and extended immobilization, all of which contribute to the development of venous stasis and thrombus formation[21]. These factors underscore the need for aggressive thromboprophylaxis strategies in patients with severe penetrating brain injury.In-hospital mortality observed in this study was 16%, which is comparable to mortality rates reported in other studies involving penetrating brain injury patients who survive initial resuscitation and hospital admission. Mortality in penetrating brain injury is influenced by several factors,

including the trajectory of the projectile, the extent of brain tissue destruction, the presence of major vascular injuries, and the initial neurological status of the patient. The absence of a significant difference in mortality between the low-molecular-weight heparin and unfractionated heparin groups suggests that the choice of thromboprophylactic agent did not directly influence survival outcomes in this cohort. Instead, mortality is more likely determined by the severity of the primary brain injury and associated complications[22].An additional observation from the present study was the slightly shorter intensive care unit stay among patients receiving low-molecular-weight heparin compared with those receiving unfractionated heparin, although this difference did not reach statistical significance. Shorter ICU stays in patients receiving effective thromboprophylaxis may reflect improved clinical stability and a lower incidence of thromboembolic complications requiring additional interventions. However, ICU length of stay is influenced by multiple factors including neurological recovery, infection, and the need for surgical procedures, which may explain the absence of a statistically significant difference between the two treatment groups[23].

The findings of this research have important clinical implications for trauma centers managing patients with penetrating brain injuries. Given the significant morbidity associated with venous thromboembolism and the challenges involved in balancing thrombosis prevention with bleeding risk, identifying the most effective prophylactic strategy is essential for optimizing patient outcomes. The results of this study support the growing body of evidence favoring the use of low-molecular-weight heparin as the preferred pharmacological agent for thromboprophylaxis in trauma patients. Its predictable pharmacokinetic profile, convenient dosing regimen, and superior efficacy in preventing thromboembolic events make it an attractive option in critically ill patients with penetrating brain injuries[24].Despite the valuable insights provided by this study, several limitations should be acknowledged. The retrospective design may introduce potential biases related to patient selection and data completeness. Additionally, the study was conducted at a single tertiary care center, which may limit the generalizability of the findings to other healthcare settings. Variations in clinical management practices, imaging protocols, and patient demographics across institutions could influence the incidence of venous thromboembolism and treatment outcomes. Furthermore, the sample size, although adequate for statistical analysis, may not capture rare complications associated with anticoagulant therapy[25]. Future multicenter prospective studies with larger sample sizes would be valuable in confirming the findings of this research and establishing standardized guidelines for thromboprophylaxis in penetrating brain injury.

In summary, the present study demonstrated that low-molecular-weight heparin was associated with a significantly lower incidence of venous thromboembolism compared with unfractionated heparin in patients with firearm-related penetrating brain injury, without increasing the risk of intracranial hemorrhage progression or mortality. These findings support the use of low-molecular-weight heparin as an effective and safe option for thromboprophylaxis in this high-risk population when administered after confirmation of radiological stability. The results of this research contribute to the limited body of literature addressing thromboprophylaxis in penetrating brain injury and may help guide clinical decision-making in trauma centers managing these complex cases.

## CONCLUSION

This study evaluated the comparative effectiveness and safety of low-molecular-weight heparin and unfractionated heparin for venous thromboembolism prophylaxis in patients with firearm-related penetrating brain injury admitted to a tertiary care trauma center. The findings demonstrated that patients receiving low-molecular-weight heparin had a significantly lower incidence of venous thromboembolism compared with those receiving unfractionated heparin, while the rates of intracranial hemorrhage progression and in-hospital mortality were comparable between the two groups. These results suggest that low-molecular-weight heparin provides superior protection against thromboembolic complications without increasing the risk of hemorrhagic events in patients with penetrating brain injury. Additionally, delayed initiation of pharmacological prophylaxis was associated with a higher risk of venous thromboembolism, highlighting the importance of early thromboprophylaxis once radiological stability of intracranial injury is confirmed.

Overall, the findings support the use of low-molecular-weight heparin as a safe and effective strategy for preventing thromboembolic complications in patients with firearm-related penetrating brain injury.

**Recommendations**

Low-molecular-weight heparin should be considered the preferred pharmacological agent for venous thromboembolism prophylaxis in patients with penetrating brain injury once radiological stability is confirmed.Early initiation of thromboprophylaxis within 24–72 hours after injury should be encouraged when clinically appropriate.Trauma centers should develop standardized institutional protocols for venous thromboembolism prevention in traumatic brain injury patients.Multicenter prospective studies with larger sample sizes are recommended to further validate the findings of this study.Continuous monitoring for both thromboembolic and hemorrhagic complications should remain an essential component of patient management.

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**Ethical Approval**

Ethical approval for this study was obtained from the Institutional Review Board and Ethical Committee of POF Hospital Wah Cantt prior to the commencement of data collection. The study was conducted in accordance with the principles of the Declaration of Helsinki for research involving human subjects.

**Conflict of Interest**

The authors declare that there is no conflict of interest regarding the publication of this research.

**Funding Statement**

No external funding was received for this study.

**Data Availability Statement:**

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

**Consent for Publication**

Not applicable, as the study used anonymized retrospective clinical data without identifiable patient information.

**Limitations of the Study**

Although this study provides valuable insight into thromboprophylaxis strategies in patients with penetrating brain injury, several limitations should be acknowledged. First, the retrospective design of the study may introduce selection bias and limitations related to incomplete documentation in medical records. Second, the research was conducted at a single tertiary care center, which may limit the generalizability of the findings to other institutions with different patient populations and treatment protocols. Third, variations in clinical management, including timing of thromboprophylaxis initiation and neurosurgical interventions, may have influenced patient outcomes. Additionally, the sample size, although adequate for statistical analysis, may not capture rare adverse events associated with anticoagulant therapy. Future multicenter prospective studies with larger sample sizes are recommended to validate the findings of this study and establish standardized guidelines for venous thromboembolism prophylaxis in patients with penetrating brain injury.

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