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Analysis of the prevalence and risk factors for venous thromboembolic complications in patients with proximal femoral fractures

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Due to the increasing incidence of PFA fractures and the associated morbidity and disability, the treatment and rehabilitation of patients with this pathology is a global problem of modern traumatology and orthopedics. Objective. To determine the incidence of venous thromboembolic complications in the setting of proximal femoral fractures, the presence of additional risk factors, and the possibility of using the Caprini score to identify surgical patients at "extremely high risk" of venous thromboembolism (VTE). Methods. The examination and treatment results of 153 (58 men, 95 women) patients aged 23 to 94 years (average 69.95±15.83 years) with proximal femoral fracture were studied. Results. The incidence of acute venous thromboembolic complications among patients with proximal femoral fractures is 13.7 %. The vast majority (98 %) of patients in this category have additional risk factors for VTE development, in addition to femoral fracture. A Caprini score of 10 points is associated with an increase in the risk of VTE development in patients with proximal femoral fractures by 11.7 times (95 % CI [1.25–109.3]), 11 points — by 23.7 times (95 % CI [2.25–250.2]), 12 points — by 45.1 times (95 % CI [4.42–461.0]), 13 and more points — by 79 times (95 % CI [8.95–697.4]) compared with the presence of 5–8 points. Conclusions. The Caprini score was found to identify patients at "extremely high risk" of developing VTE. The cut–off level of the Caprini score > 10 points allowed identifying patients at "extremely high risk" of thrombosis (AUROC 0.845; 95 % CI 0.769–0.922).

Через зростання частоти переломів ПВС й асоційованої з цим захворюваності й інвалідності, лікування та реабілітація пацієнтів із цією патологією є глобальною проблемою сучасної травматології та ортопедії. Мета. Визначити частоту розвитку венозних тромбоемболічних ускладнень у пацієнтів із переломами проксимального відділу стегна (ПВС), наявність додаткових факторів ризику та можливості використання шкали Caprini для ідентифікації хірургічних хворих із «вкрай високим ризиком» розвитку венозної тромбоемболії (ВТЕ). Методи. Досліджено результати обстеження та лікування 153 (58 чоловіків, 95 жінок) пацієнтів віком від 23 до 94 років (у середньому 69,95±15,83) із переломом ПВС. Результати. Частота гострих венозних тромбоемболічних ускладнень серед хворих із переломами ПВС становить 13,7 %. Переважна більшість (98 %) пацієнти цієї категорії мають додаткові фактори ризику розвитку ВТЕ, крім перелому стегнової кістки. Оцінка за шкалою Caprini 10 балів асоціюється із збільшенням ризику розвитку ВТЕ у хворих із переломами проксимального відділу стегна в 11,7 разів (95 % ДІ [1,25–109,3]), 11 балів — у 23,7 рази (95 % ДІ [2,25–250,2]), 12 балів — у 45,1 рази (95 % ДІ [4,42–461,0]), 13 і більше балів — у 79 разів (95 % ДІ [8,95-697,4]) порівняно з наявністю 5–8 балів. Висновки. Виявлено, що оцінка за шкалою Caprini дозволяє виявити пацієнтів «украй високого ризику» (extremely high risk) розвитку ВТЕ. Граничний рівень (cut-off) кількісної оцінки ризику за шкалою Caprini > 10 балів дозволяє виявити хворих «украй високого ризику» тромбозів (AUROC 0,845; 95 % ДІ 0,769–0,922). Ключові слова. Перелом проксимального відділу стегна, венозний тромбоз, фактори ризику, шкала Caprini.

Keywords. Proximal femoral fracture, venous thrombosis, risk factors, Caprini score

Introduction

According to the predictive data from the Danish National Register, the number of patients with proximal femur fractures (PFF) will increase by 2.5 times during the period from 2010 to 2040. Additionally, the number of affected individuals in the age groups over 60, 70, and especially 80 and 90 years old will rise significantly. This trend is largely related to the aging population [1]. Other reports have also identified an increase in the overall number of PFFs [2, 3], even though some indicated stable or decreasing age-adjusted incidence rates [4]. Due to the growing frequency of PFFs and the associated morbidity and disability, treatment and rehabilitation of patients with this condition have become a global problem in modern traumatology and orthopedics. Furthermore, the annual high number of new fractures (over 10 million) creates a significant physical, psychological, and financial burden on patients, their families, and significantly strains the healthcare system as a whole [5, 6].

Venous thromboembolism (VTE) is a serious complication of PFF due to a combination of factors related both to the trauma itself and the patient's immobilization. On the one hand, traumatic injury, especially in the case of complex fractures, is often accompanied by damage to blood vessels around the fracture site. This creates conditions for the formation of blood clots at the injury site. It is also important to remember that any traumatic stress to the body can trigger activation of the blood coagulation processes, which increases the risk of developing VTE, especially when combined with blood vessel damage and disrupted blood flow. On the other hand, post-trauma immobilization, particularly for the proximal parts of the limbs, leads to slowed blood flow in the veins, which also increases the likelihood of clot formation [7, 8]. At present, the issue is particularly serious when patients have to remain in the hospital for over three days while waiting for postponed surgery for a PFF, due to various objective reasons. Prolonging the time from the moment of injury to surgical intervention significantly increases the risk of thrombosis, multiplying the likelihood of its occurrence several times [9].

According to a systematic review and meta-analysis by Y. Hu et al. [8], the overall combined prevalence of preoperative deep vein thrombosis (DVT) in the thigh was 24.1 % (95 % CI: [19.3–28.8]). One study reported a two-fold higher prevalence of preoperative DVT, 52.5 %, in patients with PFF [10], while in another publication, the prevalence was only 5.3 % after hip fracture in elderly patients. On this basis, the authors concluded that routine venous thromboprophylaxis is not warranted for this patient population [11].

The development of DVT in the limbs increases the duration of hospitalization and healthcare costs [12]. Moreover, it can lead to pulmonary artery thromboembolism and subsequent post-thrombotic syndrome, which negatively affect the quality of life and are causes of hospital mortality [8]. According to existing data [12], about 50 % of patients with proximal venous thrombosis have asymptomatic pulmonary artery thromboembolism, and 80 % of cases with thromboembolism have asymptomatic DVT in the lower limbs. It is important to understand that the development of venous thromboembolism (VTE) in the preoperative period can result in delays in surgical intervention, shifting it from the optimal timing, which negatively affects the final treatment outcomes [8]. The use of anticoagulant therapy in patients with femoral fractures helps reduce the frequency of preoperative VTE and fatal complications [13].

A critical assessment of the existing literature reveals notable limitations and inconsistencies in the information related to preoperative VTE among individuals with PFFs. In response to these findings, this study was designed and implemented.

Objective: To reduce the incidence of deep vein thrombosis in patients with proximal femur fractures by determining the effectiveness of using the Caprini scale to identify individuals with a trauma surgery profile who belong to the "very high risk" group for developing venous thromboembolism.

We set the following main tasks:

1. To determine the frequency of preoperative deep vein thrombosis (DVT) in the lower limbs in patients with proximal femur fractures (PFF);

2. To identify additional risk factors for the development of venous thromboembolism (VTE) in this group of patients;

3. To investigate individual risk factors and the cumulative effect of these factors, and to determine whether the standard approach to thromboprophylaxis (e. g., using the Caprini scale to assess the risk of VTE) is appropriate.

Materials and Methods

The study was conducted in accordance with the principles of the Helsinki Declaration and the Council of Europe Convention on Human Rights and Biomedicine. The article materials were reviewed and approved by the Bioethics Committee of Shupyk

National University of Health of Ukraine (protocol No. 9, dated 22.11.2023). All patients gave informed consent to participate in the study.

The study was based on the results of examinations and treatment of 153 individuals aged 23 to 94 years (mean (M ± σ) — 69.95 ± 15.83) with PFF, who were hospitalized in the Trauma and Orthopedic Department of Kyiv City Clinical Hospital No. 8 during 2023. Among them, 58 (37.9 %) were men and 95 (62.1 %) were women.

Inclusion criteria: Age 18 years or older, presence of a proximal femur fracture, informed consent from the patient to participate in the study.

Exclusion criteria: Age under 18 years, the need for therapeutic doses of direct anticoagulants, thrombocytopenia, coagulopathy, hemorrhagic syndrome (unrelated to disseminated intravascular coagulation), blood disorders, decompensated cardiovascular and respiratory diseases (heart failure NYHA III or higher, significant arrhythmias, grade III respiratory failure), acute and chronic hepatitis B or C, severe renal or liver failure, malignancies, pregnancy, refusal to participate in the study.

Falls were the most common cause of PFF in the analyzed sample — 145 out of 153 patients (94.8 %). Less frequently, trauma was caused by combat actions — 6 cases (3.9 %) and road traffic accidents — 2 (1.3 %).

Surgical intervention was performed in 76 patients (49.7 %) of the 153 participants in the study. Among them: 41 cases involved hip joint replacement, 33 cases involved metal osteosynthesis (MOS), and 2 cases involved external fixation devices with simultaneous use of a Vacuum-Assisted Closure (VAC) system. The remaining 77 individuals, who refused surgical intervention, were treated conservatively (skeletal traction).

Standard examination included taking disease and medical history, physical examination, palpation, assessment of the range of motion in the joints, evaluation of the condition of the venous system in the lower limbs according to the classification of chronic venous diseases: pain syndrome, if present — character and degree of pain, presence of peripheral edema, condition of the skin, functional tests, and the patient's level of physical activity. Prior to surgery, all patients underwent ultrasound examination of the veins in the lower limbs with the use of a compression test and color Doppler.

The risk of developing venous thromboembolism (VTE) was assessed using the validated Ukrainian-language Caprini scale (Caprini Risk Assessment Model), which includes a list of risk factors for venous thromboembolic complications in surgical patients. Each risk factor is assigned a score from 1 to 5. According to the total score, the risk of thrombosis development is classified as follows:

– Very low (less than 0.5 %) — 0;
– Low (around 1.5 %) — 1–2;
– Moderate (around 3 %) — 3–4;
– High (around 6 %) — 5 or more.

Statistical analysis of the data was performed using Microsoft Excel and the licensed IBM "Statistical Package for Social Science (SPSS) Statistics" software, version 20.0.0 for Windows. Descriptive statistics are presented as the mean value with the corresponding standard deviation (M ± σ). The statistical significance of differences in frequencies was analyzed using the Pearson χ^2 test. Additionally, odds ratios (OR) were calculated to assess the strength of the association between the factors studied.

The odds ratio (OR) was calculated as the ratio of the event frequency in the compared groups. For each indicator, a 95 % confidence interval (CI) was determined. A result was considered statistically significant if the confidence interval did not include the value 1.

The relationship between the variables studied was examined using correlation analysis and the Pearson correlation coefficient (r), whose significance was tested using the t-test. For multivariate analysis, the binomial logistic regression method was used. The predictive capacity of the model for assessing the risk of VTE was studied using ROC analysis. A result was considered statistically significant if the p-value was less than 0.05 (confidence level — 95 %).

Results

In the analyzed cohort of patients, the frequency of acute venous thromboembolic complications in cases of PFF was 13.7 % (21 out of 153 cases), with the vast majority (95.2 %) being lower limb deep vein thrombosis (DVT). At the same time, half of the patients (50.0 %) were found to have thrombotic occlusion of the calf vein.

Patients with PFF are classified into a high-risk group for the development of VTE, as according to the Caprini scale, a femoral fracture is assigned 5 points, and a score of ≥ 5 points stratifies the risk of thrombosis as high.

In addition to the fracture itself, which is assigned 5 points on the Caprini scale, the vast majority of patients with PFF (98 %) were shown to have numerous and varied additional risk factors for VTE (on

Table 1

Prevalence of individual risk factors for venous thromboembolism development

Age (years)	Patient number (n = 153)	
	abs.	%
Proximal femur fracture	153	100.0
Age ≥ 40 years	143	93.5
Previous major surgery in the medical history	41	26.8
Swelling of the lower limbs	35	22.9
Family history of VTE	29	19.0
Severe pulmonary disease, including pneumonia (< 1 month), impaired lung function	27	17.7
Varicose veins of the lower limbs	24	15.7
Obesity (BMI > 30 kg/m²)	23	15.0
History of VTE	21	13.7
Bed rest for > 72 hours	21	13.7
Inflammatory bowel diseases in the medical history	11	7.2
Thrombophilia	10	6.5
Acute cerebrovascular accident (< 1 month)	9	5.9
Malignant neoplasms in the medical history	4	2.6
History of VTE	3	2.0
Central venous catheterization	2	2.1
For women (n = 95): ≥ 3 spontaneous miscarriages Stillbirths / fetal death Premature delivery with toxemia during pregnancy or fetal growth restriction Hormone Replacement Therapy (HRT)	 6 4 7 9	 6.3 4.2 7.4 9.5

average (2.66 ± 1.48) factors per person). Information regarding these factors is provided in Table 1.

Analysis of Additional Risk Factors

The analysis of the additional risk factors on the Caprini scale revealed a direct correlation between their number and the frequency of acute venous thrombosis ($r = 0.504$; $p < 0.001$). The data in Figure 1 show that the risk of developing acute venous thrombosis increases with the number of additional risk factors. Specifically, with 3 additional risk factors, the frequency of venous thromboembolism (VTE) in the studied cohort was 10.3 %, with 4 factors it increased to 28.6 %, with 5 factors it reached 50 %, with 6 factors it was 85.7 %, and with 7 factors, it was 100 %.

For the analysis of the frequency of verified acute venous thrombosis based on the Caprini score, the patients were divided into the following groups:

– Group I: 80 individuals with a score of 5–9 points;

– Group II: 31 cases with a score of 10 points;

– Group III: 13 cases with a score of 11 points;

– Group IV: 11 cases with a score of 12 points;

– Group V: 18 cases with a score of 13 or more points.

It was found that in Group I, acute VTE developed in 1 out of 80 cases; in Group II, in 4 out of 31 cases; in Group III, in 3 out of 13 cases; in Group IV, in 4 out of 11 cases; and in Group V, in 9 out of 18 cases. These frequencies were 1.3 %, 12.9 %, 23.1 %, 36.4 %, and 50.0 %, respectively ($p < 0.001$) (Figure 2).

It was established that an increase in the Caprini score was significantly associated with an increased risk of developing VTE in patients with proximal femur fractures. Specifically, a score of 10 points increases the risk of venous thromboembolism by 11.7 times (95 % CI: [1.25–109.3]; $p = 0.008$), 11 points increases the risk by 23.7 times (95 % CI: [2.25–250.2]; $p < 0.001$), 12 points increases the risk by 45.1 times (95 % CI: [4.42–461.0]; $p = 0.008$), and 13 or more points increases the risk by 79 times (95 % CI: [8.95–697.4]; $p < 0.001$), compared to patients with a score of 5–8 points.

The results of the ROC analysis confirmed the high predictive ability of the Caprini scale for the development of VTE: the area under the curve (AUC) was 0.845 (95% CI: [0.769–0.922]; $p < 0.001$).

During the ROC curve coordinate analysis, the cutoff point that significantly predicts the development of VTE in patients with proximal femur

fractures in the high-risk group was determined to be 10.5 points on the Caprini scale (sensitivity 76.2 %, specificity 80.3 %) (Table 2).

Therefore, the criterion that significantly increases the risk of VTE in patients with PFF in the high-risk group while receiving pharmacological thromboprophylaxis at the standard prophylactic dose is the presence of 11 or more points on the Caprini scale. Specifically, in patients with fewer than 11 points on the Caprini scale, the frequency of VTE in our study was 5/111 cases (4.5%) compared to 16/42 cases (38.1%) in patients with 11 or more points on this scale (OR 13.1; 95% CI [4.38–38.9], p < 0.001).

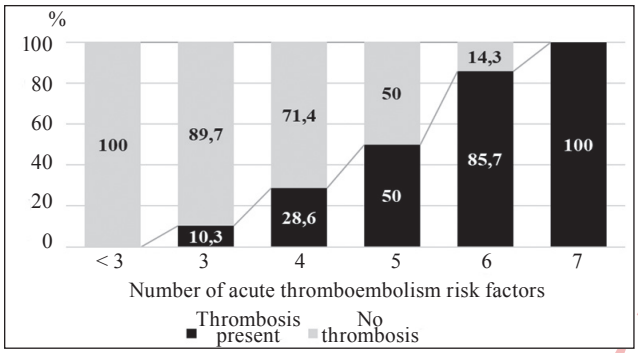

Fig. 1. Frequency of verified acute venous thromboembolism in patients (n = 153) with additional risk factors

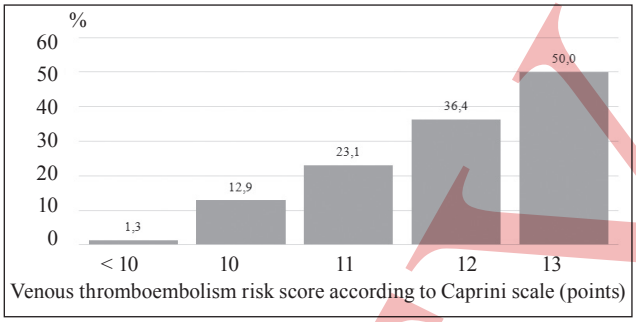

Fig. 2. Frequency of verified acute venous thromboembolism in patients (n = 153) with varying scores on the Caprini Risk Assessment Scale

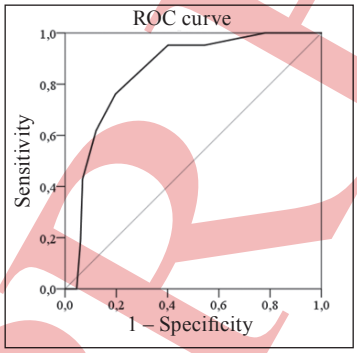

Fig. 3. ROC curve showing the correlation between the probability of VTE development in patients with proximal femoral shaft fractures and their risk score according to the Caprini scale

Discussion

VTE, specifically DVT, is a common complication in patients with proximal femur fractures (PFF) [8]. The majority of scientific publications report on the prevalence of postoperative DVT in patients in this category [7, 14]. However, there is insufficient data on the frequency and localization of preoperative DVT in patients with fractures of long tubular bones (including femur, tibia, and fibula) of the lower limbs. It should also be acknowledged that existing clinical guidelines do not distinguish between preoperative and postoperative thrombosis in terms of screening and diagnostic strategies. In fact, much more attention is given to the prevention and treatment of postoperative VTE than to preoperative thrombosis [8].

Our data indicate that the prevalence of this complication in patients with PFF was 13.7 %, with the vast majority (95.2 %) being lower limb DVT. This rate is twice as low as the overall pooled prevalence of preoperative DVT, which was 24.1 % (95 % CI 19.3–28.8 %) in a systematic review and meta-analysis published in 2023 [8]. This discrepancy likely reflects population characteristics, particularly differences in baseline risk. At the same time, there are studies showing a DVT rate (16.3 %) similar to the one we found [15].

As noted by other authors, we believe that the relatively high prevalence of preoperative DVT deserves more attention, as this complication is closely associated with negative treatment outcomes. It is crucial to highlight that preoperative thrombosis can delay surgical treatment. More seriously, if a thrombus is not detected in time before surgery, orthopedic interventions may cause fragmentation of the thrombus, increasing the risk of pulmonary embolism and other adverse outcomes [16].

Existing studies involving patients with lower limb fractures have repeatedly shown statistically significant differences between the groups of patients with and without DVT, with various risk

Table 2

Results of ROC analysis for the number of points on the Caprini scale as a prognostic criterion for the development of VTE

Criterion	AUROC	p	95 % CI	Cut-off point	Sensitivity %	Specificity %
Caprini Risk Assessment Score	0.845	< 0.001	0.769–0.922	> 10 points	56.3	55.6

factors such as age, presence of diabetes, hypertension, fracture location, and preoperative plasma D-dimer levels [17]. According to our data, the vast majority (98 %) of patients with PFF have multiple and diverse additional risk factors for VTE, beyond the femoral fracture itself (on average, 2.66 ± 1.48 factors per patient). This suggests that the standard approach, such as using the Caprini scale, to assess the risk of developing VTE does not account for individual risk factors and their cumulative effects. However, we have established a direct correlation between the number of additional risk factors and the frequency of acute venous thrombosis ($r = 0.504$; $p < 0.001$). In our opinion, this indicates the need to optimize VTE risk analysis in patients with PFF, as well as the likely importance of personalizing their preoperative thromboprophylaxis.

Conclusions

The overall frequency of acute venous thromboembolic complications among patients with proximal femur fractures (PFF) is 13.7 %, with the majority (95.2 %) being deep vein thrombosis (DVT) of the lower limb.

The vast majority (98 %) of patients with PFF have multiple and varied additional risk factors for venous thromboembolism (on average, 2.66 ± 1.48 per patient).

ROC analysis has shown that a cutoff level of > 10 points on the Caprini scale allows for the prediction of "extremely high risk" of thrombosis (AUROC 0.845; 95 % CI 0.769–0.922). We believe that a score of 11 or more points on the Caprini scale requires the personalization of thromboprophylaxis for patients with PFF.

Conflicts of Interest. The authors declare no conflicts of interest.

Prospects for Further Research. We consider the development and study of the effectiveness and safety of personalized preoperative thromboprophylaxis in patients with PFF as a promising direction for our future research.

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ANALYSIS OF THE PREVALENCE AND RISK FACTORS FOR VENOUS THROMBOEMBOLIC COMPLICATIONS IN PATIENTS WITH PROXIMAL FEMORAL FRACTURES

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