



Comparative analysis of venous thromboembolic complications in diverse groups of orthopaedic patients

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Abstract

Introduction and Objective. Venous thromboembolism (VTE) is one of the most important and life-threatening complications in orthopaedic surgery. According to current scientific reports, there are several variables that can affect the severity of CVD, including the site of the pathology or the type of treatment implemented. The aim of the study was to analyze the risk of VTE depending on the location of the pathology, as well as to evaluate the impact of surgical treatment compared to conservative management.

Materials and method. Analysis of laboratory results and clinical picture of 276 patients hospitalized for orthopaedic reasons, admitted between January 2008 – December 2019, with suspected pulmonary embolism (PE).

Results. Among patients diagnosed with PE, the most common location of the disease was in the lower limb 59/116 (50.9%), followed by the pelvis location – 22/116 (19.0%), the spine – 19/116 (16.4%), disseminated lesions in oncological patients – 12/116 (10.3%), and a group of pathologies in the upper limb – 4/116 (3.5%). Significant statistical differences were found between the incidence of PE and the diagnosis of pathology in the lower limb and the pelvis. In the group of patients, there was no statistically significant relationship between the incidence of PE associated with surgical treatment, compared to conservative management.

Conclusions. The group with the highest risk of VTE were lower limb and pelvic pathologies. The results are largely consistent with numerous reports treating the risk of CVD among orthopaedic patient populations.

Key words

orthopaedic surgery, traumatology, venous thromboembolism, trauma complications, pulmonary embolism, pelvis fracture, spine fracture, lower limb fracture

INTRODUCTION AND OBJECTIVE

Venous thromboembolism (VTE) is one of the most serious complications affecting the orthopaedic population, including both patients with extensive trauma requiring urgent surgical interventions and those undergoing elective knee or hip replacement. This is a common phenomenon and in recent years has been taken into account in numerous publications [1]. Each year, there are more than 700,000 cases of VTE in reported Europe, 370,000 deaths related to its complications, and more than 60% of all VTE cases are associated with prior hospitalization [2]. Awareness of the potential serious health consequences for high-risk patients contributes to the implementation of thromboprophylaxis. In addition to anticoagulant pharmacotherapy, the methods of minimizing the risk include: reducing the duration of anaesthesia and surgery, reducing immobilization in the pre-operative period as much as possible, mobilizing the patient as quickly as

possible, using intermittent pneumatic compression and/or prophylactic graduated compression stockings.

Currently, thromboembolic complications are observed less and less frequently, but are still present in about 0.4 – 1.0% of patients despite the implementation of due prophylaxis [1, 2, 3, 4]. It should be borne in mind that there are many factors that significantly affect the degree of thromboembolic risk, such as age, long-term immobilization, multi-morbidity, previous history of VTE and a history of cancer. The study presents the results of a group of orthopaedic patients, and elaborates on a comparative analysis of the incidence of CCD, depending on the location of the disease and type of treatment.

MATERIALS AND METHOD

The results of laboratory tests and clinical features of patients hospitalized for orthopaedic reasons, in whom pulmonary embolism was suspected on the basis of clinical features and laboratory test results, and who were referred for pulmonary artery branch angio-CT for this reason, were analyzed in the

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study. The records of patients hospitalized from January 2008 to the end of December 2019 were studied.

In order to answer the research questions, statistical analyses were carried out using TIBCO Statistica software and Student's t-test analysis for independent samples, frequency analysis with the χ^2 test, ROC curve analysis, and standardized and adjusted residuals analysis. The significance level was considered to be the classic threshold acknowledged in the realm of medical sciences, $\alpha = 0.05$. The database and part of the calculations were done using Microsoft Excel.

RESULTS

A total of 276 consecutive cases of patients were enrolled in the study, including 138 males and 138 females (both elective and emergency cases), whose set of findings allowed the planned analyses. Pulmonary embolism (PE), which is a dangerous manifestation of VTE, was confirmed on imaging in 116/276 (42.0%) patients, including 54 females (46.6%) and 62 males (53.4%), and excluded in 160/276 (58.0%) including 84 females (52.5%) and 76 males (47.5%). In the group with confirmed PE, the mean age for both sexes was 71.6 years (male: 63.9 years / female: 80.4 years). The difference between both sexes was not assumed as statistically significant (χ^2 test = 0.952 $p = 0.33$) (Table 1).

Table 1. Characteristics of patients in terms of gender and age

	No. of patients	% of patients	Age (years)
Total No. of Patients	276	100%	70.7
Female (F)	138	50%	78.8
Male (M)	138	50%	62.6
PE confirmed	116	100%	71.6
Female (F)	54	46.6%	80.4
Male (M)	62	53.4%	63.9
PE excluded	160	100%	68.9
Female (F)	84	52.5%	77.2
Male (M)	76	47.5%	61.6

Based on the analysis of ICD-10 codes and detailed descriptions, the patients' diagnoses were analyzed (Table 2).

The group of patients hospitalized for orthopaedic reasons included both patients referred on an elective basis and those admitted on emergency basis. Patients were divided into five subgroups according to the type or location of the disease: patients with diseases in the upper extremities, the lower extremities, spine, and pelvis (trauma), and patients with oncological diagnoses with disseminated lesions.

Pathologies in the lower extremity – 168/276 (60.9%) constituted the largest group in the total population, followed by the spine – 39/276 (14.1%) and pelvis – 37/276 (13.4%), patients with disseminated cancer – 24/276 (8.7%), and pathologies in the upper extremities – 8/276 (2.9%). Among patients diagnosed with pulmonary embolism, the most common location of the disease was in the lower limbs – 59/116 (50.9%), followed by the pelvis – 22/116 (19.0%), spine – 19/116 (16.4%), followed by oncology patients – 12/116 (10.3%) and a group of pathologies in the upper limb –

4/116 (3.5%). Detailed analysis using the standardized and adjusted residuals method indicated a significant statistical differences between the incidence of pulmonary embolism and the diagnosis of pathology in the lower extremity and the pelvis (Tab. 3).

The next stage of the study was devoted to analysis of the type of therapeutic management. Orthopaedic surgical treatment was implemented in 242 (87.7%) patients, while the remaining 34 (12.3%) individuals underwent conservative management, dispensing with surgery altogether. Of all those operated on, the suspicion of pulmonary embolism prior surgery occurred in 41 patients (16.9% of those operated on, 14.9% of the total population), while the remaining 201 patients (83.1% of those operated on, 72.8% of the total population) developed symptoms after surgical treatment (Tab. 4).

In the group of patients with confirmed pulmonary embolism (116 patients), surgical treatment was implemented in 106 (91.4%) cases, while the remaining 10 (8.6%) individuals were treated conservatively. Of all the operated patients in the group with confirmed pulmonary embolism (PE), the symptoms of became apparent even before surgery in 17 patients (16% of those operated on; 14.7% of the group with confirmed PE; 6.2% of the total population). In the remaining 89 (84% of those operated on; 76.2% of the study group; 32.2% of the total population), diagnosis was necessary after surgery. A total of 27 patients (23.3% of the group with confirmed PE) presented symptoms of the disease regardless of surgery – either before surgery or in those treated conservatively (Tab. 5). In 75 (27.2%) patients from both groups (confirmed and excluded PE), symptoms of pulmonary embolism occurred regardless of surgery. In the analyzed population, there were no statistically significant correlations in terms of a possible association of the implementation of surgical treatment alone with the occurrence of PE, compared to patients treated conservatively, or when the embolism occurred before surgery ($p = 0.215$) (Tab. 6).

DISCUSSION

Regardless of the location and type of surgery, this type of procedure always carries a higher thromboembolic risk. As for orthopaedic surgery, in which there is a constant interference with bone tissue through repositioning or resection of bone fragments, the risk of thromboembolism increases significantly. In recent years, a number of studies have been conducted to assess the risk of thromboembolic complications in patients after major joint surgery, such as knee or hip endoprosthesis. These have proven to be one of the most common and serious complications after this type of surgery, which has led to the establishment of a common position of many societies and the recommendation to introduce thromboprophylaxis in these patients. In trauma surgery, prophylactic measures should also be recommended, especially for patients hospitalized as a result of high-energy trauma, with vascular and nerve damage, and extensive soft tissue contusions that require immobilization [3, 5, 6, 7]. The risk of VTE does not apply only to cases of major multi-joint and multi-organ injuries, but it also can affect patients with isolated injuries in locations often overlooked, relatively rarely elaborated on in the literature, and increases significantly in patients with multi-morbidity [8, 9].

Table 2. List of preliminary diagnoses of patients according to ICD-10 codes.

ICD-10 Code	Total No. of patients	PE confirmed	PE excluded	Descriptive diagnosis
C40	5	3	2	Malignant neoplasm of bone and articular cartilage of limbs
C41	1	1	1	Malignant neoplasm of bone and articular cartilage. unspecified site
C49	2	1	1	Malignant neoplasms of connective and soft tissue
C64	1	1	0	Malignant neoplasm of kidney
C79	10	3	7	Secondary malignant neoplasm of other sites
D16	3	2	1	Benign neoplasms of bone and articular cartilage
D43	1	1	0	Tumour of uncertain or unknown behaviour of the central nervous system
I71	2	1	1	Aneurysm and dissecting aneurysm of the main artery
I72	2	1	1	Aneurysm of other arteries
L08	1	0	1	Other localized infections of skin and subcutaneous tissue
M13	1	0	1	Other joint inflammations
M16	31	13	18	Degenerative joint disease of the hip
M17	24	12	12	Degenerative joint disease of the knee (Gonarthrosis)
M20	1	0	1	Acquired deformities of fingers and toes
M46	2	0	2	Other inflammatory diseases of the spine
M51	1	0	1	Other intervertebral disc disorders
M71	1	0	1	Other synovial joint disorders
M84	3	2	1	Disorders of bone continuity - pathological fracture
S06	1	1	0	Brain contusion
S12	7	2	5	Fractures of the neck
S22	12	7	5	Fracture of rib(s), sternum, and thoracic spine
S25	1	1	0	Chest vascular injury
S27	1	1	0	Injury of other and unspecified organs of the thorax
S27	1	1	0	Injury of other and unspecified organs of the thorax
S30	1	0	1	Contusion of lower back and pelvis
S32	12	6	6	Fracture of the lumbar spine and pelvis
S36	2	2	0	Abdominal organ injury
S40	2	0	2	Bruised shoulder and arm
S42	4	4	0	Fracture of the shoulder and arm
S43	1	0	1	Dislocation, sprain, and tear of the shoulder joint and rotator cuff
S52	1	0	1	Fracture of the forearm
S70	1	0	1	Superficial injury of the hip and thigh
S72	80	28	52	Fracture of the femur
S78	1	1	0	Traumatic hip disarticulation with amputation of the thigh
S82	9	2	7	Fracture of the lower leg including the ankle joint
S85	1	0	1	Vascular injury at the level of the lower leg
T01	1	0	1	Open wounds involving multiple body areas
T02	6	4	2	Fractures involving multiple body areas - fractures of multiple body regions
T06	20	11	9	Other injuries involving multiple body areas, not classified elsewhere - multiple injuries.
T84	13	4	9	Complications of prosthetic, implant, and orthopaedic graft - complications of orthopaedic prostheses, implants, and grafts.
T92	1	1	0	Consequences of upper limb injuries.
T93	2	0	2	Consequences of lower limb injuries.
T94	1	1	0	Consequences of injuries involving multiple body regions.
W06	1	0	1	Fall
Total	276			

Several papers are cited below, both original and review articles analyzing particular groups of orthopaedic patients with differential thromboembolic risks, depending on the location of the pathology or type of treatment.

Lower limb. Trauma, surgery and other interventions involving the lower extremities are associated with an increased risk of VTE, making it an absolute recommendation to implement thromboprophylaxis. The aging process of the

Table 3. Classification of patients based on the type or site of the disease

Location	Total	% of patients	PE confirmed	% of patients with PE	PE excluded	% of patients without PE
Upper limbs	8	2.9	4	3.5	4	2.5
Lower limbs	168	60.9	59	50.9	109	68.1
Spine	39	14.1	19	16.4	20	12.5
Pelvis	37	13.4	22	19.0	15	9.4
Diffuse neoplastic lesions	24	8.7	12	10.3	12	7.5

Table 4. Associations between occurrence of PE symptoms and type of treatment

Parameters for entire population (both groups)	No. of patients	% of patients (entire population)
Non-surgical treatment	34	12.3
Surgical treatment	242	87.0
a) preoperative symptoms	a) 41	a) 14.9
b) postoperative symptoms	b) 201	b) 72.8
Occurrence of VTE symptoms after surgical treatment	201	72.8
Occurrence of VTE symptoms unrelated to surgical treatment	75	27.2

Table 5. Comparison of surgically and non-surgically treated patients in the confirmed PE group

Patients with confirmed PE	No. of patients	% of patients
Non-surgical treatment	10	8.6%
Surgical treatment	106	91.4%
a) preoperative symptoms	a) 17	a) 14.7%
b) postoperative symptoms	b) 89	b) 76.7%
Occurrence of VTE symptoms unrelated to surgical procedure or pre-operative symptoms	27	23.3%

Table 6. Overall comparison of patient groups based on location of pathology and surgical intervention

	PE excluded (n = 160)	PE confirmed (n = 116)	p
Upper limb	4 (2.50%)	4 (3.45%)	
Lower limb	109 (68.13%)	59 (50.86%)	
Spine	20 (12.50%)	19 (16.38%)	p = 0.051
Pelvis	15 (9.38%)	22 (18.97%)	
Diffuse metastatic lesions	12 (7.50%)	12 (10.34%)	
After surgical treatment	112 (70.00%)	89 (76.72%)	
Unrelated to surgical treatment	48 (30.00%)	27 (23.28%)	p = 0.215

global population means that an increasing number of patients will undergo major orthopaedic surgery in the region of the lower extremities. For major procedures, not only hip and knee endoprosthesis, but also for femoral fracture, anti-coagulant management is a priority, and post-operative pharmacotherapy should be prolonged up to the 35th day after surgery. For less extensive interventions, such as arthroscopic procedures, the implementation of prophylaxis is also required but often takes much less time. There is a wealth of literature available describing multicentre studies

involving large groups of patients with confirmed pulmonary embolism after surgery and traumatic incidents.

Gade et al. [2] analyzed the data of 1,012,823 patients (hospitalized between 1996 – 2017) who had undergone their first ever orthopaedic surgery on the lower extremity. During the 180-day post-operative period, 0.71% of patients had confirmed VTE, compared to 0.11% in an age-, gender- and history-matched control group. The majority of patients were those after hip/femur surgery – 1.15%, and the least common after foot/ankle surgery – 0.49%. It was noted that the type of surgery associated with the highest risk of thromboembolism were: endoprosthesis, fracture repositioning and stabilization and amputation, while biopsies/arthroscopy were associated with the lowest risk. The researchers estimated that the highest risk of VTE for all sites was within the first 30 days after surgery.

Majima et al. [3] conducted a detailed review of the literature analyzing, among others, the risk of VTE after hip fracture. Based on an analysis of studies conducted between 1980 – 2002, the researchers noticed that during the 3-month post-operative period, 'full-blown' VTE was confirmed in 1.3 – 8.2% of patients, despite the application of an anti-coagulant pharmacotherapy.

In 2022, Galsklint et al. [10] conducted a data review of 1,172 patients who had undergone lower extremity surgery between 2009 – 2019 at the North Denmark Region Hospital in Aalborg. The mean age was 68.6 years, and 48 (11.4%) patients presented a history of VTE. During the 180-day post-operative period, a diagnosis of VTE was made among 420/1172 (35.8%) patients, where the most commonly operated anatomical locations were the hip joint and femur (47.9%), followed by the knee joint and shin (40.7%), ankle joint, foot (10.7%), and pelvis (0.7%).

Samama et al. [8] reviewed the most current literature in which they paid particular attention to the probability of VTE occurrence and the validity of thromboprophylaxis, excluding from the analysis the highest-risk surgeries, such as hip and knee replacement procedures. Among the publications analyzed, one should mention the study of Warren et al. in which data from 120,521 patients (2008–2016) with lower limb trauma were analyzed. VTE was most common after fractures of the femur (2.4%) and hip (1.7%), and to a lesser extent after fractures of the shinbone (1.1%) or the patella (0.9%).

Other studies have indicated a noticeably lower thromboembolic risk in patients undergoing diagnostic arthroscopy. In a single-centre study by Krych et al. of 12,595 patients of whom only 0.34% had reported VTE, prophylaxis was not routinely implemented; Hetsroni et al. – in 374,033 patients also undergoing diagnostic arthroscopy of the knee joint, PE was observed in 0.028%. The results obtained in the current analysis based on own material confirm a significant association between pathology in the lower limb and thromboembolic disease.

Pelvis. The mechanism of injury to the pelvic ring is most often an effect of a high-energy trauma resulting from a traffic accident, and fractures within it are associated with a high risk of thromboembolic complications, which significantly increases mortality in this group of patients. As with extensive endoprostheses of the large joints of the lower limb or fractures of the femur, traumatology of the pelvic bone requires anti-coagulant protection [11, 12].

Thromboembolic complications after fractures of the pelvic bone or hip acetabulum are observed in up to 18% of patients, and PE is a not uncommon cause of death within the first 24 hours after injury [13].

In 2021, Kirchner et al. [13] published the results of their study in which they analyzed the thromboembolic risk of 10,634 patients after pelvic or hip acetabular fracture. Among the 521/10,634 (4.9%), VTE was confirmed, while 502/521 (96.4%) had mechanical or pharmacological anti-coagulant prophylaxis. 8,935/10,634 (84.02%) patients were treated by surgery, the rest in a conservative mode. In a group with VTE, surgical treatment was implemented in 88.9%, compared to 83.8% among patients without VTE. The rate of thromboembolic complications in the operated group was 5.2%, compared to 3.4% in the group treated conservatively.

The study by Lowe et al [14] included 510 patients undergoing surgical management after pelvic bone fracture and 240 after hip acetabular injury. For the group with a pelvic fracture, the rate of VTE was 1.70% (9/510), while the other group had a lower result of 0.42% (1/240).

In the literature, there is a considerable difference of the opinion addressing the issue of pelvic rim injuries and their impact on thromboembolic risk. Many factors influence this, including the type of therapeutic management, the mechanism of injury or the implementation of appropriate thromboprophylaxis. The current study showed convergent results compared to other authors, and confirmed a significantly increased thromboembolic risk for pelvic pathologies.

Spine. Thromboprophylaxis is not routinely implemented in patients following spinal surgery and, as with other locations, requires individualized approach. Among other things, this management is linked to concerns about potential serious haemorrhagic complications, such as the development of an epidural haematoma, which can contribute to irreversible changes in the central nervous system. This is a rare complication (<0.3% of spinal procedures); however, it has been reported in the literature that more than 1/3 of cases do require anti-coagulant pharmacotherapy. The current literature relating to thromboembolic risk in this group of patients does not report convergent results; it states a wide range from 0.2% to as high as 31%, highlighting the fact that patients with spinal cord injuries present the highest risk [15, 16].

In 2020, Solaru et al. [17] performed an extensive analysis of the current literature treating thromboembolic complications associated with spinal surgery. In one paper which included 5,766 patients, there were 89/5,766 (1.5%) cases of VTE without anti-coagulant pharmacotherapy implementation. In another publication involving 838,507 patients, VTE was confirmed in a small number – 3,499 (0.42%) patients after 30 days, and 4,321 (0.62%) patients after 90 days were readmitted to hospital.

A review published by Zhang et al [18] included 26 papers and the meta-analyzed data of 3,216,187 patients. The rate of VTE associated with spinal surgery was estimated at 0.35%. The authors noted, among other factors, that higher incidence of thromboembolic complications was associated with age, gender, history of VTE, and the duration of surgery.

Disseminated neoplastic lesions of the musculoskeletal system. The neoplastic process is one of the most common

and important thromboembolic risk factors, with up to seven times greater the risk compared to the general population. In addition, in orthopaedic oncology, patients often undergo lengthy surgeries, suffer from pathological fractures, prolonged immobilization, and loss of contractile skeletal muscle tissue that supports venous recovery. The incidence of VTE in this group of patients is discrepant, ranging from 1% to as high as 28%, according to some reports [19, 20].

Lex et al. [19] reviewed the literature, based on 17 papers from 1998 – 2018, in which they found the incidence of VTE in orthopaedic-oncology patients to average 10.7% (1.1 – 27.7%). This was reduced to 7.9% (1.1 – 21.8%) with thromboprophylaxis, compared to 8.7% (2–23.4%) without pharmacotherapy.

In 2021, You et al. [21] analyzed 29 publications from 2000 – 2020 which included 11,491 patients. The majority of the study population underwent surgery due to an acute pathologic fracture (64.8%), and the most common disease locations were the femur (82.1%), humerus (8.9% and tibia (0.7%), respectively. The overall incidence of VTE was reported at 4.7%. However, there exist many reports that do not coincide with the results of the current study, and confirm a statistically significant association with the incidence of VTE and oncologic diagnosis.

Upper limb. Thromboembolic complications, following orthopaedic interventions in the upper limb, are a relatively rare complication. As a result, anti-coagulant pharmacotherapy is not routinely implemented. A procedure with a potentially increased risk of VTE and requiring the inclusion of prophylaxis is shoulder endoprosthesis in elderly patients with comorbidities. Current estimates put the average incidence of VTE for shoulder arthroplasty at <1%, and <0.4% for arthroscopy. Few scientific publications describe the risk of thromboembolic complications in patients with upper extremity pathology [22]. Melman et al. [5] conducted a comparative analysis of 56,884 (including 19,981 with upper limb trauma) trauma patients requiring surgery in which they present a differential incidence of symptomatic thromboembolism depending on the location of the injury. The most common types of upper limb trauma were: fracture of the distal root of the radius bone (0.003% of the VTE), fractures of the proximal root or shaft of the humerus (0.005% of the VTE), fracture of the distal root of the humerus (0.002% of the VTE) and fracture of the ulnar process of the ulna (0.001% of the VTE). The thromboembolic risk was the lowest compared to other trauma sites.

Another study by Haque et al. [9] conducted between 2010 – 2012, evaluated the thromboembolic risk of patients after surgery of the hand which involved only elective and emergency procedures. The analysis included 334,211 surgeries, among which the occurrence of CVD was recorded in only 40 cases (0.006%).

Statistical analysis of the results of the current study showed no significant association between the occurrence of thromboembolic events and the location of the pathology in the upper limb. These results are consistent with literature reports.

CONCLUSIONS

The results of this study and the current literature addressing the issue discussed are largely consistent. The greatest and undeniable thromboembolic risk is associated with the pathology of the lower limb and the pelvis. The most vulnerable group are patients undergoing extensive surgery of their musculoskeletal system, such as endoprostheses of large joints (hip or knee), as well as after fractures of the femur and the pelvis.

The implementation of thromboprophylaxis and observation of patients at high thromboembolic risk seems mandatory. For procedures of smaller scope, minor trauma or locations associated with a lower chance of thromboembolic incidents, such as the upper limb or spine, an individualized risk assessment should be undertaken to evaluate age and comorbidities, or history of CVD, among other factors. More effort addressing the topic of thromboembolic risk assessment in orthopaedic patients is required to optimize management in these groups and minimize the risk of complications.

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