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VENOUS THROMBOEMBOLISM IN MALIGNANT HEMATOLOGIC DISEASES (PILOT PROJECT)

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Abstract

Introduction: Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is a very common and potentially fatal disease. The incidence of VTE in cancer patients is about 4-7 times higher than in healthy individuals.

Aim: The motive for conducting this prospective cohort clinical study is to gain our experience regarding the incidence of VTE in malignant hemopathies, the association of VTE with the stage of the underlying disease, the possible impact of primary treatment on the incidence of VTE and the clinical outcome of the underlying disease.

Material and methods: This are a prospective cohort study involving 20 consecutive outpatients with malignant hemopathies. We conduct screening for deep vein thrombosis with Echo Color Doppler sonography.

Results: The study included 20 patients with a mean age of 58.35 years, of whom 13(65%) were male and 7(35%) females.18 patients were diagnosed with lymphoma and two were diagnosed with multiple myeloma. In 8 patients (45%) DVT was found, with occlusion of femoral vein in 4 (45%) , popliteal vein in 3 (33%), 1 (11%) patient had DVT of the subclavian vein, and 1 (11%) of the cerebral vein (confirmed by CT).

Conclusion: deep vein thrombosis is highly prevalent in patients with malignant hemopathies. Hospitalization, malignancy activity, and reception of therapy all contribute to the occurrence of venous thrombosis. Compressive ultrasound is a solid and sensitive tool for screening and diagnosis of deep vein thrombosis.

Keywords: malignant hemopathies, venous thromboembolism, anticoagulant therapy.

Introduction

Venous thromboembolism (VTE), encompassing deep vein thrombosis (DVT) and pulmonary embolism (PE), is a frequent and potentially life-threatening complication in patients with malignant hematologic disorders. It represents a major cause of morbidity and mortality and is recognized as the third leading cause of cardiovascular death worldwide, following acute coronary syndromes and stroke. In the context of cancer, approximately 20% of all VTE events are associated with malignancy, with a substantial proportion occurring in patients with hematologic cancers [1].

Patients with malignant hemopathies, including leukemias, lymphomas, and multiple myeloma, exhibit a markedly increased risk of thromboembolic events due to a complex interplay of disease-related, patient-related, and treatment-related factors.

The incidence of VTE in this population is estimated to be 4–7 times higher than in the general population, although the risk varies significantly depending on the specific type of hematologic malignancy. For instance, multiple myeloma and aggressive lymphomas are associated with particularly high thrombotic risk, especially in the setting of immunomodulatory therapy. VTE can occur at any time throughout the history of cancer and can even be the first sign of the disease [2].

The pathogenesis of VTE in malignant hemopathies is multifactorial and involves activation of coagulation pathways, endothelial dysfunction, and impaired fibrinolysis. Tumor cells can directly promote a procoagulant state through the expression of tissue factor and the release of procoagulant microparticles. In addition, systemic inflammation, cytokine release, and interactions between malignant cells and the vascular endothelium further amplify the thrombotic process.

Therapeutic interventions also play a crucial role in increasing thrombotic risk. Chemotherapy, immunomodulatory agents (such as thalidomide and lenalidomide), corticosteroids, and hematopoietic stem cell transplantation are all associated with an elevated incidence of VTE [3].

The use of central venous catheters, frequently required for treatment delivery, further contributes to the development of thrombosis, particularly in upper extremity veins.

Unlike solid tumors, where VTE most commonly presents as lower-extremity DVT or pulmonary embolism, patients with hematologic malignancies often develop thrombosis in atypical sites, including upper extremity veins, catheter-related thrombosis, cerebral venous sinuses, and splanchnic circulation [4].

VTE significantly impacts the clinical course of patients with malignant hemopathies, leading to treatment interruptions, increased risk of bleeding due to anticoagulation, prolonged hospitalization, and reduced quality of life. Importantly, the occurrence of VTE is associated with increased mortality, both directly and indirectly, by complicating cancer management [5,6].

Given the high thrombotic risk and its clinical consequences, early identification of high-risk patients and appropriate thromboprophylaxis strategies are essential components of modern management in malignant hematologic diseases.

Aims

The aim for conducting this clinical study is to gain our experience regarding the incidence of VTE in malignant haemopathies. Despite worldwide data that venous thromboembolism is a poor prognostic factor in patients with malignant diseases, there is currently no adequate data on these associated conditions at the level of our country [7,8].

Our goals are:

1. To identify the incidence of venous thromboembolism (VTE) in patients with malignant haemopathies (lymphoproliferative diseases – malignant lymphomas, plasma cell dyscrasias – multiple myeloma).
2. To determine the association of VTE with the stage of the underlying disease
3. To determine the association of VTE with the primary treatment of malignant disease.
4. To assess the impact of VTE on clinical outcome and complications.

Materials and methods

Study Design and Population

This prospective cohort study included a total of 20 consecutive patients diagnosed with malignant hematologic diseases (malignant hemopathies), specifically lymphoproliferative disorders (malignant lymphomas) and plasma cell dyscrasias (multiple myeloma). All patients were referred from the University Clinic of Hematology to the University Clinic of Cardiology for outpatient screening of deep vein thrombosis (DVT) using color Doppler sonography.

Study Protocol

The study was conducted over a period of 18 months. During this time, patients with confirmed hematologic malignancies, including lymphoma, leukemia, and multiple myeloma, were evaluated on an outpatient basis in the vascular laboratory at the University Clinic of Cardiology.

All patients underwent echo color Doppler ultrasonographic examination of the deep veins of the lower and/or upper extremities. The indication for screening was established using the IMPROVE score [11], a validated risk assessment model designed to estimate the 3-month risk of venous thromboembolism (VTE) in hospitalized patients.

The IMPROVE score incorporates multiple clinical risk factors, including prior VTE, thrombophilia, lower limb paralysis or paresis, active malignancy, immobilization, intensive care unit stay, and age over 60 years. Patients with a cumulative score greater than 5 were considered at high risk, corresponding to a VTE risk exceeding 7%.

Table 1. IMPROVE Score for VTE Risk Assessment.

Risk Factor	**Score**
Previous episode of VTE	3
Thrombophilia	2
Paralysis/paresis of lower extremities	2
History of malignant disease	2
Stay in intensive/semi-intensive care unit	1
Complete immobilization >24 hours	1
Age >60 years	1

Ultrasonographic Examination

All patients underwent a comprehensive Doppler sonographic evaluation performed by experienced clinicians. The examination protocol included:

- Compression ultrasound (CUS) of the deep veins of the lower and/or upper extremities
- Compression ultrasound of the superficial veins of the lower and/or upper extremities
- Color Doppler ultrasound with pulsed-wave Doppler analysis of the deep venous system
- Color Doppler ultrasound with pulsed-wave Doppler analysis of the superficial venous system

This multimodal approach ensured high diagnostic accuracy for the detection of both symptomatic and asymptomatic DVT.

Data Collection

A total of 20 consecutive patients were screened for the presence of DVT and included in a dedicated study registry. The registry collected basic demographic and clinical data, including:

- Age
- Sex
- Current anticoagulant therapy

However, the registry did not include detailed information on:

- Type of hematologic malignancy
- Stage of the disease
- Type of primary hematologic treatment
- Presence of comorbid conditions

Laboratory Analysis

All patients underwent standard laboratory testing, including:

- Complete blood count (erythrocytes, hemoglobin, leukocytes, thrombocytes)
- D-dimer levels

These parameters were used to support the clinical and diagnostic evaluation of thrombotic risk.

Follow-Up

Patients were prospectively followed for a period of 12 months. During this follow-up period, adverse clinical events were recorded, including:

- Recurrent venous thromboembolism
- Bleeding complications

- Mortality
-

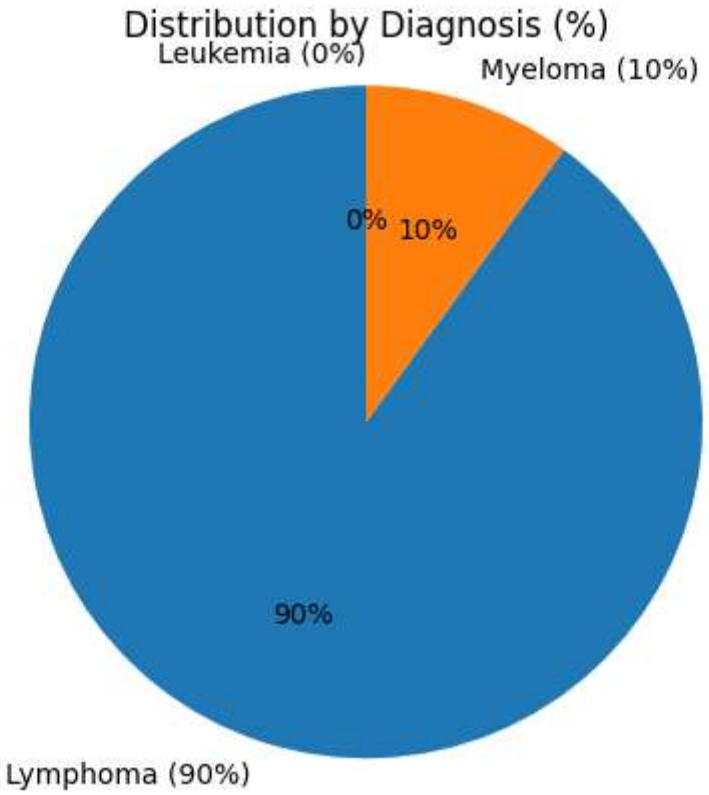
Statistical Analysis

Statistical analysis was performed during the final 6 months of the study period. The collected data were analyzed and summarized using appropriate descriptive statistical methods to evaluate the incidence of VTE and associated clinical outcomes in the study population.

Results

The study included 20 respondents with a mean age of 58.35 years, of whom 13(65%) were male and 7(35%) female.

Of the study population, 18 patients were diagnosed with lymphoma and two were diagnosed with multiple myeloma (Graphic No 1). Of these, six patients were currently undergoing chemotherapy protocol and the rest were in remission.



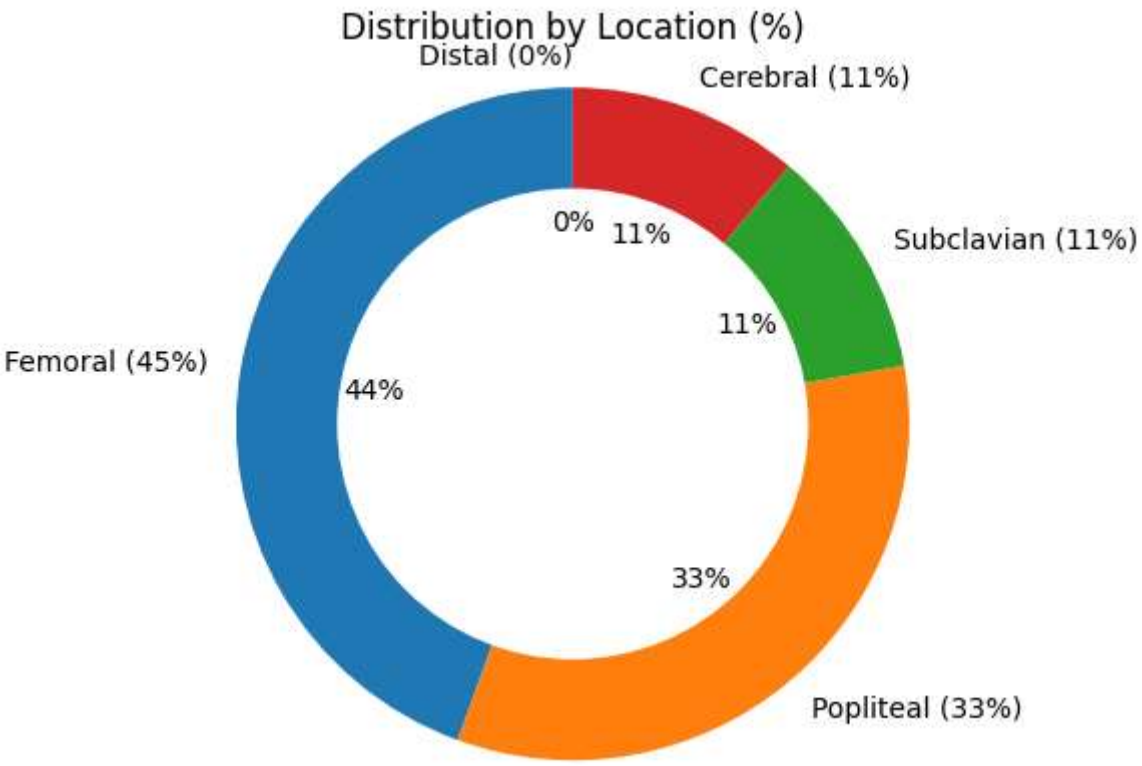
Graphic No 1: Distribution by malignant haemopathies.

Laboratory analyses found mean platelet values of 346.7/mL, Leukocytes 7.8 x109, Hemoglobin 14.3 g/L. D-dimers were not monitored in all patients, so they were not included in statistical analysis.

Ultrasound screening (Color Doppler sonography) was performed and previously patients were subjected to risk assessment for VTE after IMPROVE [12].

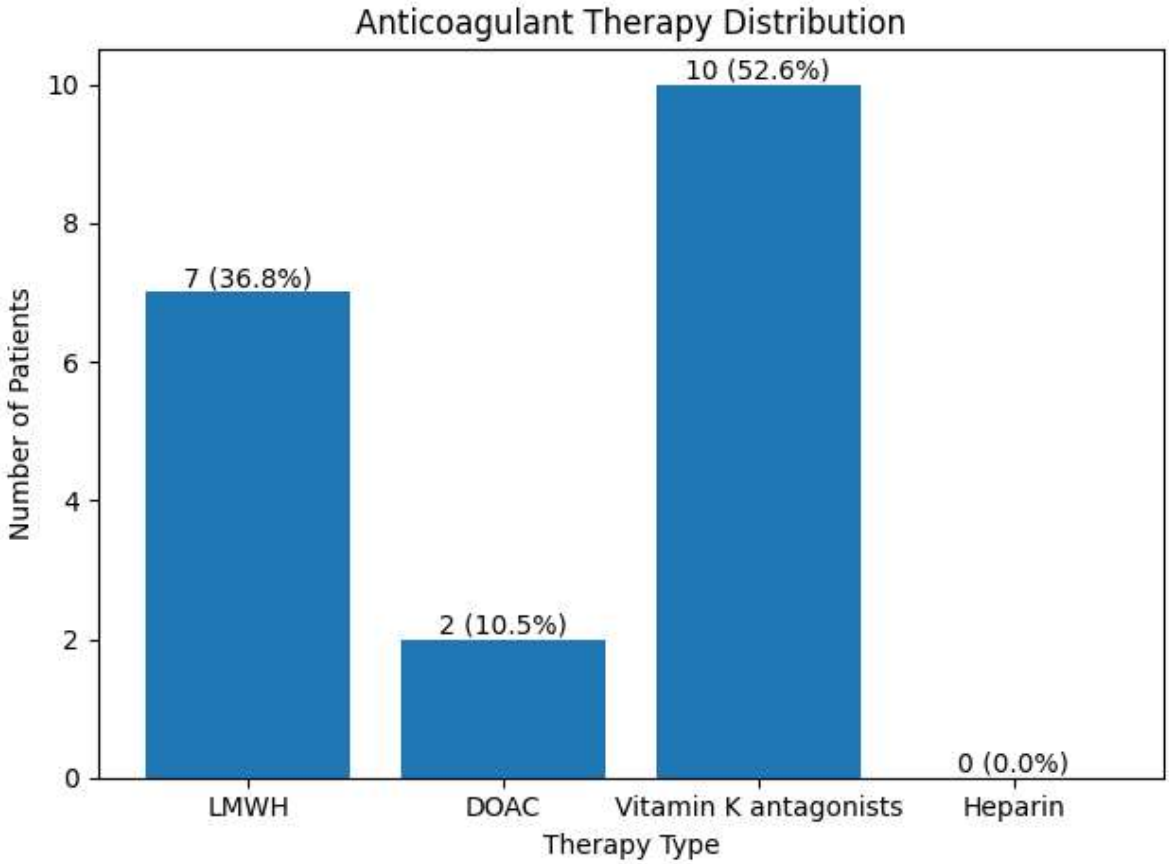
Following screening in 8 patients (45%), DVT was found. The most common location was the femoral vein in 4 (45%) patients, the popliteal vein in 3 (33%) patients, 1 (11%) patient had DVT of the subclavian vein, and 1 (11%) of the cerebral vein (Graphic No 2). A CT angiography was also performed on the last patient.

Chart 2



Graphic No 2: Location of thrombosis.

Seven patients were treated with low molecular weight heparin and two with direct oral anticoagulants (DOACs) in the acute phase. In all, anticoagulation with vitamin K antagonists is prolonged in the chronic phase (Graphic No 3).



Graphic No 3: Anticoagulant therapy type.

The median duration of anticoagulation was 5.6 months. It wasn't noted
bleeding complication in the study population during anticoagulation. After discontinuation of therapy, there were no recurring episodes of DVT.

By the end of the project, there were no fatal outcomes regarding the eventual impact of VTE on the prognosis of these patients.

Discussion

The results of this study provide a comprehensive overview of the incidence and clinical characteristics of venous thromboembolism (VTE) in patients with malignant hemopathies, with a particular focus on lymphoproliferative diseases, including malignant lymphomas and plasma cell dyscrasias such as multiple myeloma.

In our study population, the incidence of VTE was 45%, indicating a substantial thrombotic burden among patients with hematologic malignancies. This finding is consistent with previously

published data suggesting an increased risk of thromboembolic events in this patient population, particularly in those with active disease and ongoing treatment.

Among the patients diagnosed with VTE, the majority (six patients) were receiving active chemotherapy at the time of thrombotic event occurrence, while two patients were in remission. This observation highlights the strong association between active malignancy, systemic anticancer therapy, and thrombotic risk. All patients included in the study were classified as high-risk for VTE according to the IMPROVE risk assessment model, originally developed by Gregory V. Spyropoulos and subsequently validated by David Rosenberg [11].

These findings further support the clinical utility of validated risk assessment models in identifying patients at increased risk for thromboembolic complications.

The results emphasize the critical role of hospitalization, active malignant disease, and exposure to anticancer therapy as key contributors to the development of venous thrombosis. Hospitalization itself is a well-recognized risk factor due to reduced mobility, acute illness, and the frequent use of invasive procedures.

Diagnosis of VTE in this study was established by venous ultrasonography, a widely accepted and reliable imaging modality. Previous studies have demonstrated that venous ultrasound has a sensitivity and specificity exceeding 95% for the detection of deep vein thrombosis (DVT), confirming its diagnostic accuracy and clinical utility [9].

All patients diagnosed with VTE were promptly initiated on anticoagulant therapy. The treatment approach included low molecular weight heparin (LMWH) and direct oral anticoagulants (DOACs), in accordance with current clinical guidelines. The applied anticoagulation strategy demonstrated both efficacy and safety in the acute phase of treatment, as evidenced by the absence of recurrent thromboembolic events and documented venous recanalization during follow-up [10]. These findings are in line with contemporary evidence supporting the use of LMWH and DOACs in cancer-associated thrombosis.

It is important to note that the study design and statistical analysis did not include patients in whom VTE represented the initial clinical manifestation leading to the diagnosis of malignancy. Specifically, two such cases were identified, one subsequently diagnosed with Hodgkin lymphoma and the other with non-Hodgkin lymphoma [12].

The exclusion of these patients may have led to a slight underestimation of the true incidence of VTE in this population.

From a preventive perspective, current evidence and guidelines suggest that most hospitalized patients with active cancer should receive thromboprophylaxis, unless contraindicated. In contrast, routine thromboprophylaxis is not universally recommended for ambulatory cancer patients but may be considered in selected high-risk individuals based on validated risk assessment models.

Special consideration is required for patients with multiple myeloma receiving immunomodulatory and antiangiogenic therapies in combination with corticosteroids or chemotherapy, as these regimens are associated with a particularly high thrombotic risk. In such cases, prophylaxis with LMWH or low-dose aspirin is recommended.

In the perioperative setting, patients undergoing major oncologic surgery should receive thromboprophylaxis initiated preoperatively and continued for at least 7–10 days. Extended prophylaxis for up to 4 weeks should be considered in patients undergoing major abdominal or pelvic surgery with additional high-risk features.

For the treatment of established VTE, LMWH remains the recommended standard during the initial 5–10 days and for long-term therapy up to 6 months. However, direct oral anticoagulants have emerged as an effective alternative in selected patients with malignancy, provided that an individualized assessment of bleeding risk is performed. Prolonged anticoagulation beyond 6 months is recommended in patients with persistent risk factors, including active cancer or ongoing treatment [13].

The present study was conducted in accordance with the recommendations of the American Society of Clinical Oncology, which advocate for periodic assessment of thrombotic risk in patients with cancer and the implementation of individualized prevention and treatment strategies [14,15].

Conclusion

Based on the results of this study, it can be concluded that deep vein thrombosis (DVT) is highly prevalent among patients with malignant hematologic diseases.

The occurrence of venous thromboembolism in this population is strongly influenced by multiple interrelated factors, including hospitalization, the presence of active malignancy, and the administration of anticancer therapy. These findings underscore the multifactorial nature of thrombotic risk in patients with malignant hemopathies.

Venous ultrasonography has proven to be a reliable, sensitive, and non-invasive diagnostic modality for the detection of DVT, supporting its role as a primary tool for both screening and diagnosis in clinical practice.

Timely initiation of anticoagulant therapy is essential for the effective management of DVT in this high-risk population. In addition to reducing acute morbidity, appropriate anticoagulation significantly contributes to improved patient outcomes by preventing thrombotic complications, recurrence, and disease progression. Consequently, early recognition and prompt treatment of VTE are critical components in the overall management and prognosis of patients with malignant hematologic disorders.

However, despite the insights gained from this study, there remains a need for further large-scale, prospective clinical investigations involving more extensive and diverse patient populations. Such studies would enable more robust subgroup analyses, improve risk stratification, and contribute to the development of optimized, individualized strategies for the prevention and treatment of venous thromboembolism in patients with hematologic malignancies.

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