LETTER TO THE EDITOR

World Thrombosis Day 2018 in Poland

To the Editor  Venous thromboembolism (VTE) is a major contributor to the burden caused by non-communicable diseases. Studies from different countries yielded consistent results, with annual incidence rates ranging from 0.75 to 2.69 per 1000 individuals in the population. The incidence increased to between 2 and 7 per 1000 among those aged 70 years or older.1 Up to 60% of all VTE cases are associated with hospitalization. Pulmonary embolism (PE) directly accounts for 5% to 10% of all in-hospital deaths and is the leading cause of preventable hospital death, ahead of infections. Considering the availability of effective VTE prophylaxis, many of these events and deaths could have been prevented. The estimated total number of symptomatic VTE events in Poland was ~57 000 DVT cases and ~35 000 PE cases per year.

The long-term complications of VTE include recurrent thrombosis, postthrombotic syndrome, and chronic thromboembolic pulmonary hypertension.

Launched in 2014 and held annually on October 13, the birthday of Rudolf Virchow, a scientist who developed the concept of “thrombosis” and was a pioneer in the pathophysiology of this disease, the World Thrombosis Day (WTD) aims to increase the awareness of thrombosis among the public, health care professionals, and health care systems.

Key messages for the WTD 2018 are as follows (www.worldthrombosisday.org):

1  VTE is often fatal but many, if not most, cases are preventable.
2  VTE risk factors include hospitalization, surgery, cancer, prolonged immobility, family history of VTE, estrogen-containing medications (birth control pills or hormone replacement therapy), pregnancy, and/or recent birth.
3  Cancer patients are at a higher risk than the general population of developing serious blood clots.
4  Surgery is one of the risk factors for VTE. While a clot can form after any type of the procedure, you are more likely to get one if you have had a major surgery.
5  Family history may increase the risk of VTE and genetic factors can contribute to VTE risk.
6  The signs and symptoms of deep vein thrombosis include pain and/or tenderness in the calf or thigh; swelling of the leg, foot, and/or ankle; redness and/or noticeable discoloration; warmth. 7  The signs and symptoms of PE include shortness of breath; rapid breathing; chest pain (may be worse upon deep breath); rapid heart rate; light headedness and/or passing out.
8  About 45% to 60% of VTE cases are associated with hospitalization, highlighting the troubling fact that VTE is the leading cause of preventable hospital death.
9  VTE adds billions to health care costs.

Nearly 1300 organizations in 98 countries were participating in the WTD in 2018, raising much-needed visibility of the condition through special events, educational forums, widespread media coverage, and social media. The Haemostasis Group of the Polish Society of Hematology and Transfusion Medicine, being a Global Partner of WTD, systematically implements initiatives dedicated to the increase of the global as well as medical staff awareness in the field of VTE prevention, diagnosis, and treatment. One of these initiatives is an annually organized educative WTD symposium. This year, it was the 5th Conference “Venous Thromboembolism – an underestimated problem,” which was held on October 13, 2018, in Warsaw. Some new data on the VTE prophylaxis and treatment have been presented by the Polish experts in these fields, for example, the draft recommendations for VTE prophylaxis for long distance (>4 hours) travelers, prepared by the American Society of Hematology/McMaster University GRADE Center.5

Much of the attention focused on direct oral anticoagulants (DOACs), which directly inhibit either thrombin (dabigatran) or factor Xa (apixaban, edoxaban, and rivaroxaban). DOACs have been approved for the treatment of VTE in general populations. However, in cancer patients, most guidelines continue to recommend low-molecular-weight heparin (LMWH) monotherapy for at least 3 to 6 months due to lack of cancer-specific data regarding the use of these agents.3,4 Currently, edoxaban and rivaroxaban are the only DOACs that have been compared with LMWH in randomized clinical trials in cancer populations. Nearly all studies reported lower rates of recurrent VTE for patients receiving DOACs than for those receiving LMWHs.3,4 However, patients receiving DOACs had a higher major bleeding rate than patients receiving LMWH. Therefore,
DOACs should be avoided in cancer patients with an acute diagnosis of VTE and a high risk of bleeding. The perceived benefits of DOACs (oral administration, lower recurrent VTE rate, and no monitoring) need to be considered against their perceived negative attributes (increased bleeding and drug–drug interactions) and the strength of value that an individual patient gives to each feature.\(^7\)

The remarkably complex subject of diagnostics and treatment of antiphospholipid syndrome, as well as of thrombotic complications in hematologic malignancies, has been presented by 2 lecturers, experts in these fields. Another interesting issue discussed during the conference was the management of patients with paroxysmal nocturnal hemoglobinuria—the most vicious acquired thrombophilic state known.

Postthrombotic syndrome (PTS) is a chronic complication of DVT that develops in 20% to 50% of patients. Its overall estimated incidence is 0.7 to 2 per 1000 person-years, and increases with age.\(^8\) The evidence-based statement has been recently created by a panel of Polish experts with the aim to provide practical recommendations for the optimal prevention, diagnosis, and management of PTS.\(^9\) Patients with iliofemoral DVT have 2-year PTS rates of 50% or more, despite anticoagulation. These patients are also more likely to develop severe PTS manifestations, such as disabling venous claudication and venous ulcers. Early clot removal can prevent persistent venous obstruction and damage to the vein valves. Catheter-directed thrombolysis (CDT), a direct intrathrombus administration of a fibrinolytic drug via a catheter embedded within the thrombus, induces a successful lysis of the thrombus in 80% to 90% of patients with DVT symptom duration of less than 14 days. However, 41% of CDT patients still developed PTS by 2 years, indicating that CDT does not eliminate the risk of PTS. Pharmacomechanical CDT (PCDT) involves the use of catheter-mounted thrombectomy devices along with intrathrombus delivery of fibrinolytic drugs. It is suggested that CDT/PCDT with or without balloon angioplasty and stenting might be considered in patients with extensive (eg, iliofemoral) thrombosis with recent onset (ie, \(\leq 14\) days) of symptoms, a low risk of bleeding, life expectancy of at least 1 year, and surgical thrombectomy—in patients who are not candidates for PCDT/CDT.

Recent years have brought progress in our understanding of the role of endovascular techniques (venous bypass procedures and/or stenting) in the treatment of PTS and the subgroups of patients who may benefit from these modalities when conservative treatment fails. Intractable pain, massive edema, progression of skin changes, and venous ulcer formation are among the better-justified indications for intervention. Stenting is generally accepted as the treatment for residual deep venous obstructions located between the common femoral vein and inferior vena cava. To date, the quality of evidence to support its use is weak, but consistent effects and marked changes in a disease course with potential impact on the quality of life are promising. Patients with postthrombotic ulcers should be managed with a multidisciplinary team approach.

Thrombophilias are defined as inherited or acquired abnormalities of hemostasis predisposing to thrombosis. The most important inherited thrombophilic defects are inborn deficiencies of naturally occurring inhibitors of coagulation: antithrombin (AT), protein C (PC) and protein S (PS), and 2 point mutations: a) single substitution in the gene of factor V (FV) at nucleotide position 1691, resulting in an amino acid change at position 506 (FV Q506 or FV Leiden (FVL)) and b) G to A nucleotide polymorphism at position 20210 in the 3' untranslated region of the prothrombin gene (PTG20210A).

In contrast to an inherited deficiency of AT, PC, and PS, which are very rare in the general population, heterozygous FVL and PTG20210A are common, with the prevalence among Caucasians of 5% and 2%, respectively. A relative risk of initial VTE increases about 3 to 4 times in subjects with heterozygous FVL or PTG20210A, about 10 times in patients with PC or PS deficiency, and 10 to 30 times in the case of AT deficiency.\(^10\)\(^11\) Interestingly, in contrast to the initial VTE episode, a relative risk for recurrent VTE in subjects with inherited thrombophilic defects is only mildly increased and ranges from 1.4 for FVL and PTG20210A to 2.6 for AT deficiency.\(^11\)

Testing for thrombophilia should only be performed when results will be used to improve or modify management. Potential reasons to test for inherited thrombophilia are: 1) identifying thrombophilic defects in asymptomatic family members of patients with VTE and inherited thrombophilia to decide on preventive measures, for example, not to take an oral contraceptive; 2) identifying antithrombin deficiency in a patient with resistance to heparin may indicate the need for antithrombin supplementation during an acute episode of VTE; 3) identifying inherited deficiency of PC or PS may affect anticoagulation strategy when initiating vitamin K antagonist (VKA) therapy (risk of skin necrosis); 4) identifying patients who may benefit from a specific anticoagulant therapy; for example, for patients with high-risk antiphospholipid syndrome, VKA is probably the treatment of choice; 5) VTE at a young age, particularly if associated with no or weak provoking factors or a strong family history of VTE or recurrent VTE or VTE in unusual sites (eg, cerebral or splanchinic veins) since identification of high-risk thrombophilia in such cases may influence the decision on extended anticoagulation.\(^12\)\(^13\)

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**Conflict of interest**  The authors declare no conflict of interest.


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**REFERENCES**