

The 2016 World Thrombosis Day in Poland

To the Editor In 2012, the World Health Assembly set a global target to reduce premature deaths from noninfectious disease, including venous thromboembolism (VTE), by 25% by 2025. VTE, which encompasses deep vein thrombosis (DVT) and pulmonary embolism (PE), causes significant morbidity and mortality in hospitalized and nonhospitalized patients. The estimated total number of symptomatic VTE events (range based on probabilistic sensitivity analysis) per annum within the 25 European Union (EU) countries with a population of 454.4 million, was ~680 000 DVT events, and ~430 000 PE events. The number of VTE-related deaths was estimated at ~540 000 across the EU per annum, which is more than double the number of combined deaths due to AIDS, breast cancer, prostate cancer, and transport accidents.¹ Almost three-quarters of all VTE-related deaths were from hospital-acquired VTE, and according to available evidence, PE directly accounts for 5% to 10% of all in-hospital deaths. Given the availability of effective VTE prophylaxis, many of these events and deaths could have been prevented. In the United States, of the more than 900 000 annual cases of VTE, at least 300 000 deaths (directly or indirectly) are related to VTE, and these numbers are expected to increase, because of population aging.² The long-term complications of VTE include recurrent thrombosis, postthrombotic syndrome, and chronic thromboembolic pulmonary hypertension.

The estimated total number of symptomatic VTE events in Poland was ~56 000 DVT cases, and ~35 000 PE cases per annum.

The most comprehensive systematic review of the literature on the global disease burden caused by VTE, including over 8000 citations, was published in 2014 by the International Society on Thrombosis and Haemostasis (ISTH), the leading worldwide not-for-profit organization dedicated to advancing the understanding, prevention, diagnosis, and treatment of thrombotic and bleeding disorders.³ Studies from Western Europe, North America, Australia, and southern Latin America (Argentina) yielded consistent results, with annual incidence of VTE 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. In response to requests for

a focused global awareness day on thrombosis, in 2014 ISTH founded the World Thrombosis Day (WTD), which takes place every year on October 13, the birthday of Rudolf Virchow. This scientist developed the concept of “thrombosis”, and was a pioneer in the pathophysiology of this disease. WTD places a global spotlight on thrombosis as an urgent and growing health problem, and focuses attention on the following aims:

- 1 Highlight the burden of disease (thrombosis in general) and highlight the need for action, specifically underscoring the unrecognized threat and serious consequences (morbidity and mortality) related to VTE and atrial fibrillation (AF).
- 2 Increase public awareness of the significance, risks, and signs and symptoms of thrombosis, specifically VTE and AF as an important cause of thromboembolic stroke.
- 3 Empower individuals to talk with their health-care providers about their risk for thrombosis and appropriate prevention. Empower individuals to seek immediate medical attention if they have signs and symptoms.
- 4 Galvanize organizations in countries across the globe to conduct appropriate and aligned campaigns in their countries and regions.
- 5 Begin the process of advocating for “systems of care” to properly prevent, diagnose, and treat VTE and AF.

Nearly 675 organizations in 80 countries were participating in WTD in 2016, 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, together with the Polish Society of Phlebology, 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 this initiatives is an annually organized educative WTD symposium: this year the 3rd Conference “Venous Thromboembolism – an underestimated problem” was held on October 13, 2016, in Warsaw, Poland (www.chorobykrwi.pl).

The discussions covered different aspects of VTE diagnosis and treatment, with much of the attention focused on direct oral anticoagulants (DOACs), which directly inhibit either thrombin (dabigatran) or factor Xa (apixaban,

edoxaban, and rivaroxaban). Slowly but steadily, there has been an increased preference for DOACs over vitamin K antagonists (VKAs). However, pending further evidence of safety and efficacy, DOACs should be avoided in patients with cancer-associated VTE, where low-molecular-weight heparin is the treatment of choice. A DOAC might be administered in patients with VTE due to antiphospholipid antibodies, as an off-label indication in the light of the observation that thrombosis still occurs in 5% to 20% of cases despite adequate use of VKAs, but these observations require further prospective, randomized studies.⁴

All patients contemplating DOAC use must weigh the benefit of treatment against the risk of bleeding. These risk-benefit considerations are particularly important for special populations, such as the elderly and those with severely compromised renal function. The different options of DOAC-related bleeding complication treatment were also discussed, including information about reversal agents such as idarucizumab, andexanet alfa, and ciraparantag. The reversal agent for dabigatran, idarucizumab, is approved in Europe and available in Poland. Alternatively, andexanet alfa is being developed as a universal reversal agent for patients anticoagulated with an oral or injectable factor Xa inhibitor who experience a serious uncontrolled bleeding event or who require urgent or emergent surgery, and is currently in the process of future regulatory approval by the US Food & Drug Administration.

Patients who have had an unprovoked DVT or PE are at a high risk for recurrent VTE. Risk factor for recurrent VTE were discussed, and extended "lifelong" anticoagulation has been recommended in patients with high risk of recurrence. VKAs, DOACs, aspirin, and sulodexide significantly reduced the risk of recurrent VTE, with DOACs and VKA being more effective than aspirin. The decision regarding life-long anticoagulation following an unprovoked DVT or PE should depend on the patients' risk of VTE recurrence, risk of bleeding complication, as well as the patients' values and preferences.

VTE is increasingly recognized in pediatric practice, and the annual incidence of VTE in children has been estimated at 0.7 to 1.0 per 100 000 population. Advances in technology have improved the survival of infants who are born prematurely and of children in intensive care units. The incidence of VTE peaks in newborns and infants younger than 1 year, then remains very low until adolescence, when the incidence begins to increase. In children, over 90% of events are related to underlying medical or surgical risk factors, of which central venous lines are the most important. In keeping with this, there is a high incidence of upper extremity thrombosis in children. Few clinical trials have been performed in this area in this patient group, and management is largely extrapolated from adult practice. Recently, the British Committee for Standards in Haematology has published guidelines with the aim

to provide a rational basis for the investigation and management of children aged from 1 month to 16 years with VTE, including cerebral venous thrombosis.⁵

The remarkably complex subject of pathophysiology of thrombotic complications in antiphospholipid syndrome, and in paroxysmal nocturnal hemoglobinuria has been presented by 2 lecturers, experts in these fields.

For years, a venous thrombectomy as well as fibrinolytic treatment were dedicated mostly to the patients with life-threatening leg ischemia of the venous origin (*phlegmasia coerulea dolens*). In recent years, the growing interest dedicated to the rapid vein lumen patency restoration methods has been observed. Despite the fact that in the most current guidelines the main way of DVT treatment remains conservative treatment (anticoagulation), the hypothesis of so called "open vein concept" to restore not only the vein patency but also proper valve function is currently more and more widely discussed. Among the methods used in this indication, the surgical venous thrombectomy seems to have rather historical value. In the current treatment, mostly the catheter directed as well as other percutaneous pharmacomechanical or mechanical methods are proposed. According to the Guidelines of Society of Vascular Surgery and American Venous Forum as well as American Heart Association Guidelines in patients with proximal (iliofemoral) DVT with short disease duration (no more than 14 days), in good functional condition and with low risk of bleeding, such a treatment can be proposed, if performed by experienced physicians in the experienced center.^{6,7} After the vein patency restoration all underlying lesions should be subsequently corrected by venous stent implantation. The grade of recommendation dedicated to local thrombolysis remains still very low and further studies are needed especially focusing on the possibilities of avoiding postthrombotic syndrome (PTS) in this type of therapy. In the CAVENT study based on a 2-year follow-up in patients treated with catheter-directed thrombolysis (CDT) or anticoagulation, the reduction of the PTS occurrence in CDT group was 14.4%.⁸ The new ongoing study (ATTRACT, CAVA trials) should bring more data about the efficacy and safety of such a treatment. In the current daily clinical practice, the patient undergoing invasive DVT treatment should be strictly selected and followed during the treatment. The new treatment modalities such as rheolytic thrombectomy (AngioJet), ultrasound enhanced CDT (EKOS) or mechanical thrombectomy devices allow to restore the vein patency in the very rapid way, limiting often the treatment of the proximal DVT to the single session or 1-day therapy.

PTS as a chronic sequela of acute DVT concerns the large part of patients with DVT. Beside the vein valve injury, in many cases the post-thrombotic obstructive changes can be observed. The technical progress of the endovascular medicine gives the chance for the successful

endovascular revascularization even in the cases of the complete occlusion of a long vein segment, with satisfactory early and long-term results. The venous stent implantation procedures are currently dedicated mostly to patients with proximal ilocaval obstruction of thrombotic or nonthrombotic origin. The new dedicated venous stents and further technical progress as well as the growing experience in this field (also in Poland) will open the new treatment possibilities for patients with significant quality of life worsening related to obstructive PTS changes in the proximal vein segment. In this context, the role of the proper proximal vein diagnostic workup in patients with PTS symptoms or severe chronic venous disease complains should be emphasized.

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REFERENCES

- 1 Cohen AT, Agnelli G, Anderson FA, et al. Venous thromboembolism (VTE) in Europe. The number of VTE events and associated morbidity and mortality. *Thromb Haemost.* 2007; 98: 756-764.
- 2 Deitelzweig SB, Johnson BH, Lin J, Schulman KL. Prevalence of clinical venous thromboembolism in the USA: current trends and future projections. *Am J Hematol.* 2011; 86: 217-220.
- 3 ISTH Steering Committee for World Thrombosis Day. Thrombosis: a major contributor to the global disease burden. *J Thromb Haemost.* 2014; 12: 1580-1590.
- 4 Son M, Wypasek E, Celinska-Lowenhoff M, Undas A. The use of rivaroxaban in patients with antiphospholipid syndrome: a series of 12 cases. *Thromb Res.* 2015; 135: 1035-1036.
- 5 Chalmers EA, Ganesen VJ, Liesner R, et al. Guideline on the investigation, management and prevention of venous thrombosis in children. British Committee for Standards in Haematology. www.bcsghguidelines.com. Date for Guideline review: December 2015.
- 6 Meissner MH, Gloviczki P, Comerota AJ, et al. Society for Vascular Surgery Surgery, American Venous Forum. Early thrombus removal strategies for acute deep venous thrombosis: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. *J Vasc Surg.* 2012; 55: 1449-1462.
- 7 Kahn SR, Comerota AJ, Cushman M, et al; American Heart Association Council on Peripheral Vascular Disease, Council on Clinical Cardiology, and Council on Cardiovascular and Stroke Nursing. The postthrombotic syndrome: evidence-based prevention, diagnosis, and treatment strategies: a scientific statement from the American Heart Association. *Circulation.* 2014; 130: 1636-1661.
- 8 Ender T, Haig Y, Klöw NE, et al. CaVenT Study Group. Long-term outcome after additional catheter-directed thrombolysis versus standard treatment for acute iliofemoral deep vein thrombosis (the CaVenT study): a randomised controlled trial. *Lancet.* 2012; 379: 31-38.