AN INTERVIEW WITH…

F.A. Klok, MD, PhD

The Leiden-based vascular medicine specialist offers insights into the necessity for routine use of patient-centered outcome measures for VTE and how that ties into post-PE syndrome, research into cancer-associated thrombosis, and more.

With the International Consortium for Health Outcomes Measurement (ICHOM), you and your colleagues developed a set of patient-relevant outcome measures for venous thromboembolism (VTE), which was a step toward your broader goal of shifting focus to a patient-centered, outcome-driven, value-based approach to VTE care.[1,2] Why is this shift from exclusively clinical outcomes needed now, and what would this approach ideally look like for VTE?

After pulmonary embolism (PE) or deep vein thrombosis (DVT), patients may face a broad spectrum of complications and long-term sequelae, beyond the usual quality-of-care indicators of recurrent VTE, bleeding complications, and survival. Although post-thrombotic syndrome (PTS) has long been recognized as a long-term complication of DVT, long-term complications of PE have only become apparent in the last decade with the first description of post-PE syndrome (PPES). PPES and PTS encompass well-defined clinical diagnoses such as venous ulcers or pulmonary hypertension but also a less well-defined and described burden of respiratory symptoms, pain, anxiety, and depression. The full impact of VTE on individual patients can only be captured by assessing all relevant health outcomes from the patient's perspective, in addition to the traditionally recognized and clinically defined VTE complications. Defining and measuring all important outcomes helps facilitate treatment tailored to the needs and preferences of patients and may improve health outcomes. The ICHOM-VTE standard set of outcomes highlights all outcomes that are relevant to all VTE patients, as well as the instruments to measure those. Wide implementation of the set would be a very big step forward in improving the health care outcomes of our VTE patients. After all, one cannot improve what isn't measured. This would truly allow for high-level, patient-centered care, with focused attention to the person surrounding the clot, rather than only to the clot itself.

Although you have said this requires an overarching strategy rather than a single step, what are some more immediate actions that can be taken?

Implementation of routine use of patient-reported outcome measures (PROMs) in clinical practice and clinical trials would be a very valuable step in the right direction, in particular when the full ICHOM set is implemented. To achieve this, several challenges should be overcome: further refinement of the set to lower the number of overlapping questions, integration of the PROM data into routine health care, and education of both the health care professionals involved in VTE care and patients in optimal use and interpretation of the PROM results.

As coordinator of the outpatient clinic for PPES at your institution and author of several papers on the topic, can you share your current algorithm for diagnosing and determining treatment for PPES?

We have implemented the ICHOM set in Leiden, and all PROMs are assessed shortly after the VTE diagnosis and after 3-month follow-up. During this follow-up, patients visit the thrombosis clinic at least twice to ensure they have received adequate disease-specific information, undergo additional tests where indicated (ie, screening for underlying cancer or thrombophilia), manage modifiable risk factors for bleeding, and establish the optimal duration and mode of anticoagulant

(Continued on page 79)

(Continued from page 82)
therapy. If patients still report dyspnea after 3 months, they are subjected to dedicated testing for the presence of pulmonary hypertension, starting with electrocardiogram reading and N-terminal-pro-brain natriuretic peptide measurement, followed by echocardiography if either of the two is abnormal. In addition, if pulmonary hypertension is not present and the patient reports functional limitations caused by dyspnea, cardiopulmonary exercise testing (CPET) is performed, followed by repeated imaging of the pulmonary vasculature and perfusion if the CPET is suggestive of chronic thromboembolic pulmonary disease. If no treatable causes of dyspnea are found, the patient is referred for an 8-week, PE-dedicated rehabilitation program. If the PROMs indicate relevant psychosocial burden, this will be discussed with the patients, and the general practitioner is asked to refer the patient to a local therapist.

DR. KLOK'S TIPS FOR MEDICAL RESIDENTS

01 **A day has only 24 hours. Prioritize what's most important to you, and don't forget all the important parts of life that happen *outside* the hospital.**

02 **A day is successful if you make a difference—recognize and cherish these moments.**

03 **Count your blessings—it will provide you with the correct perspectives.**

04 **Kids will enrich your life to an extent you could have never imagined. They will deprive you of sleep to the same level too.**

What are some of the ongoing research initiatives of the Leiden University Medical Center (LUMC) Good Research Practice Committee, for which you are Chair?

The main aim of this committee is to support LUMC researchers in planning and performing studies. This involves establishing help desks for legal, budgetary, and ethical questions and methodologic and statistical support, as well as in-house monitoring of all clinical studies. We organize education for early career and established researchers on relevant topics and set the quality standards for all studies performed.

The association between oncology and VTE/antithrombotic therapy (ATT) has been another focus for you recently. What are the biggest research needs in this area?

Preventing and treating cancer-associated thrombosis is highly complex, not only because no cancer patient is the same but also because cancer patients are at high risk for bleeding and thrombotic complications and the cancer journey is often unpredictable and may ultimately lead to death. Throughout a patient's journey, their values, priorities, preferences, and risk profile change considerably. All these factors need to be taken into account when treatment decisions are made for individual patients. We desperately need more actionable knowledge on the mechanism of thrombosis and bleeding in cancer patients, ultimately accumulating to the development and validation of risk-prediction models that guide anticoagulant treatment throughout the course of disease.

Can you walk us through the main goals of SERENITY (Towards Cancer Patient Empowerment for Optimal Use of Antithrombotic Therapy at the End of Life) and why you chose to get involved?

Inspired by the clinical dilemmas we face in our daily practice and together with Professor Simon Noble from Cardiff University in the United Kingdom and a large pan-European consortium, I set out to provide a solution to the issue of inadequate management of ATT at the end of life in cancer patients. Despite the fact that ATT has little or even negative effects on the well-being of cancer patients during their last year of life, stopping ATT is rare in clinical practice. ATT is often continued until death, resulting in excess bleeding, higher health care costs, and increased disease burden. SERENITY will develop an information-driven, shared decision-making palliative care process enabled by a user-friendly, easily accessible, web-based shared decision support tool that will facilitate treatment decisions regarding appropriate use of ATT in cancer patients at the end of life. This shared decision tool will ultimately lead to (more) appropriate use of ATT, prevention of bleeding complications, and considerable cost savings, in addition to

improved quality of life and treatment satisfaction of patients, their carers, and involved health care professionals. This will empower cancer patients and their carers, enabling them to make their own choices.

What other research projects are you looking forward to in the coming months?

I am involved in HI-PEITHO, the first trial that investigates the efficacy and safety of catheter-directed treatment in patients with PE who are not in shock. Patients at elevated risk of early death or imminent hemodynamic collapse, based on very strict criteria, will be randomized 1:1 to treatment with a standardized protocol of ultrasound-facilitated, catheter-directed thrombolysis plus anticoagulation versus anticoagulation alone. The study will not only focus on a composite of PE-related mortality, cardiorespiratory decompensation or collapse, or nonfatal symptomatic and objectively confirmed PE recurrence but also on long-term quality of life and functional outcomes. I am very proud to be part of the steering committee of this game-changing trial.

What does a perfect day look like for you?

A perfect day for me could have many forms but includes at least the following components: dedicated time to spend with my wonderful (four) kids, even if just over breakfast or dinner; dedicated time to spend with my beautiful wife (same applies as above); and time to engage in sports and activities that are intellectual challenging, usually clinical duties and/or performing research activities. ■

1. Gwozdz AM, de Jong CMM, Fialho LS, et al. Development of an international standard set of outcome measures for patients with venous thromboembolism: an International Consortium for Health Outcomes Measurement consensus recommendation. Lancet Haematol. 2022;9:e698–e706. doi: 10.1016/S2352-3026(22)00215-0
2. de Jong CMM, Rosovsky RP, Klok FA. Outcomes of venous thromboembolism care: future directions. J Thromb Haemost. Published online February 28, 2023. doi: 10.1016/j.jtha.2023.02.015

F.A. Klok, MD, PhD
Department of Medicine–Thrombosis and Hemostasis
Leiden University Medical Center
Leiden, the Netherlands
f.a.klok@lumc.nl
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