SSC Subcommittee Project/Collaborative Project

Standardized assessment of bleeding risk in patients treated with anticoagulants for venous thromboembolism.

Subcommittee: Predictive and Diagnostic Variables in Thrombotic Disease.

Person responsible (Chair / Principal Investigator): Geert-Jan Geersing, MD PhD

Description Abstract

Anticoagulant treatment is the cornerstone of the management of patients with venous thromboembolism (VTE). Since the landmark publication by Barritt and Jordon in the 60s there is no discussion that patients with an initial VTE event anticoagulant treatment needs to be prescribed to reduce VTE related morbidity and mortality. Later, studies confirmed that in all patients the initial treatment period should be at least 12 weeks, as shorter durations were associated with a higher risk of recurrence. After these 12 weeks, there is growing consensus that extending treatment for an indefinite time period needs to be considered in (i) patients with unprovoked events (in particular in male patients with extensive thrombosis at first presentation or persisting elevated D-dimer levels beyond the initial treatment phase), and in (ii) patients in the presence of a persisting strongly provoking risk factor (most notably active cancer). Similarly, prolonging anticoagulant treatment may also be considered in the presence of persisting of mildly provoking factors (e.g. thrombophilia is known or a family history of VTE), or an anticipated high risk of recurrence because of other clinical circumstances that currently may be quantified using available risk prediction scores.

Nevertheless, regardless of the exact reason why anticoagulant treatment is prolonged, the number of patients on extended anticoagulation after a first VTE event is clearly increasing. Albeit likely clinically effective in terms of reducing the occurrence of recurrent VTE, inevitably, this increases the risk of bleeding. Physicians caring for these patients thus are increasingly confronted with patients either experiencing a bleeding event under anticoagulant treatment, or they need to manage patients at (dynamically increasing) risk of experiencing such a bleeding event. Bleeding events are in a way thus an inevitable consequence of prolonging anticoagulant treatment, yet also have an important impact on treatment adherence, treatment persistence and overall quality of life for patients on these drugs. Assessing bleeding risk is thus more and more becoming an integral part of thrombosis medicine.

This SSC document proposal aims to aid physicians caring for these patients by providing guidance on the following questions:

1. What prediction scores or individual predictors are currently available for assessing bleeding risk in patients with VTE.

2. How are these prediction tools or individual predictors different in patients with active cancer, given that these patients are likely at highest risk for developing a bleeding event.
3. Based upon these prediction tools or individual predictors, is it possible to provide consensus amongst experts in the field on how patients on anticoagulant treatment should be assessed in terms of bleeding risk?

4. In particular, can we provide guidance on how to assess dynamic changes in potentially modifiable risk factors or circumstances increasing the risk for bleeding?

5. Finally, can we provide guidance based upon consensus on clinical scenarios that may warrant temporarily (and if so for how long?), or even permanent cessation of anticoagulant treatment in patients with VTE?

**Design and methodology:**

For questions 1 and 2, a systematic literature review on existing bleeding risk scores and predictors for bleeding in VTE patients using anticoagulants will be performed in PubMed. Based upon this literature review, a Table will be constructed to summarize existing prediction tools or individual predictors. Also, in text, we will summarize the existing literature on available methods to assess bleeding risk with a specific focus on venous thrombo-embolism.

Next, it is anticipated that for questions 3, 4, and 5 available evidence in the literature will be not informative enough. Therefore, we propose a Delphi approach amongst experts in the field from multiple countries. To focus of this Delphi procedure will be twofold. First, to construct a uniform research agenda on relevant questions that need to be addressed in novel research projects, preferably in prospective studies. Second, we aim to explore the possibility to arrive at a flow diagram on how bleeding risk should be assessed in clinical practice, building upon clinical consensus and ‘best practices’, with a specific focus on (i) assessment of potentially modifiable risk factors, (ii) clinical scenarios warranting (temporarily or permanent) cessation of anticoagulant treatment, and (iii) differences in these approaches in patients with or without cancer-associated thrombosis. It should be stressed that this should be regarded as defining the current state of clinical medicine in terms of assessing bleeding risk, highlighting areas of uncertainty that thus need to be addressed in future research.

**Study population:**

This project deliberately focusses on patients treated with anticoagulants for venous thrombo-embolism only, thus excluding other indications for anticoagulant treatment such as stroke prevention in atrial fibrillation. This is done given that the clinical circumstances differ amongst different indications, as well as the potential to identify and treat modifiable risk factors. Moreover, we also anticipate to bring specific attention to cancer-associated thrombosis, which is relatively unique to VTE or at least more prevalent with this indications than with other indications.
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Expected timeline:

- Project stage/set up: July-August 2019
- Launch: September – October 2019
- Duration: 12 months
- Finalization/analysis: 3 months
- Reporting: expected reporting late 2020 / early 2021

Expected outcomes:

We anticipate to publish our results as a SSC Communication in the *Journal of Thrombosis and Haemostasis*.

Description of project set up and management, needed infrastructure and resources (summary):

We expect to set-up a project team of 6 members from different backgrounds and settings.

Possible references: