Preface

Recent Advances in Thrombosis and Hemostasis—Part IV

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> If one advances confidently in the direction of his dreams, and endeavors to live the life which he has imagined, he will meet with a success unexpected in common hours.
>
> Henry David Thoreau, 1817–1862

This is the fourth theme issue in the series of Recent Advances in Thrombosis and Hemostasis, for which I have had the honor to be the guest editor. When we think of advances in thrombosis, it is easy to associate with the recent developments of new oral anticoagulants that increasingly are replacing vitamin K antagonists. It is therefore appropriate that half of the contributions to this issue report on various aspects of the non-vitamin K antagonist oral anticoagulants (NOACs). In accordance with the previous issues in this series, the articles have been harmonized to use the term NOAC rather than any other term. This is, of course, a matter of style, but it is also the abbreviation consistently used by the European Society of Cardiology. It is also important to point out that NOAC does not stand for new/novel oral anticoagulant.[1] Nevertheless, even if these agents are not so new anymore, there are many new aspects to them that require studies.

Let us, however, start with a few more basic topics. South Africa has been hit hard by the human immunodeficiency virus (HIV) epidemic, and it is therefore pertinent to present a review by Jackson and Pretorius from South Africa on the effects of HIV on platelets, red blood cells, and fibrinogen.[2] They discuss how the inflammatory changes may increase the risk of deep vein thrombosis in patients infected by HIV and how some hematological markers could be of interest in the assessment of these patients. They also present the classes of antiretroviral therapy available in South Africa.

Autoimmune diseases also generate inflammatory responses and are associated with increased risk of venous thromboembolism (VTE). For patients with autoimmune disease and a VTE event, a common question is how long the anticoagulant treatment should continue. Is it more important to focus on immunosuppression or on anticoagulation in the long run? Borjas-Howard et al have here performed a systematic literature review to help us find some answers.[3]

Spinal cord injury activates multiple prothrombotic mechanisms, representing all three components of Virchow's triad and generates therefore probably the highest risk of VTE in patients admitted to hospital. The risk remains elevated for several months and requires extended thromboprophylaxis. Due to concomitant risk of bleeding, several questions regarding optimal prophylactic regimen and timing remain to be answered. Piran and Schulman present a narrative review of the topic together with suggestions for future research.[4] Prevention on the arterial side is important after myocardial infarction or stroke, but what is the risk/benefit ratio of primary prevention? This question has been further highlighted by the recently published ASPirin in Reducing Events in the Elderly (ASPREE) trial demonstrating not only lack of benefit but also harm with aspirin in healthy elderly people.[5] Lippi et al have reviewed the meta-analyses and the recent ASPREE data to try and tease out the benefits and harms of primary prophylaxis.[6]

The balance between high risk of thrombosis and bleeding is revisited in patients with hip fractures. They are usually elderly and frail and a substantial proportion of them are on an anticoagulant, mainly for stroke prophylaxis in atrial fibrillation. Grandone et al have performed a literature review to find answers to questions regarding reversal of anticoagulants and perioperative bridging of anticoagulants.[7] They summarize the available data in a narrative review, which includes both vitamin K antagonist and NOAC management. Conversely, for minor surgical procedures, there is growing evidence that oral anticoagulation does not have to be stopped. Brennan et al have reviewed the studies and also the recommendations from various societies and presented the results in another narrative review.[8]

NOACs have a favorable bleeding risk profile, especially regarding intracranial bleeding. In major surgery, there is always some blood loss, also unavoidable with the NOACs.

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Rivaroxaban was in a pooled analysis more effective than low-molecular-weight heparin in reducing symptomatic VTE after total hip or total knee replacement,[9] and has become the standard at many hospitals. Krauss et al performed a retrospective chart review of 1,241 arthroplasties at their center to investigate the risk of bleeding complications on rivaroxaban among obese and morbidly obese patients.[10] They found a significant increase in the risk of major bleeding with an interaction by sex. Likewise, there is an increased risk of bleeding and other complications shortly after discharge from hospital among patients started on anticoagulation. Identification of risk factors for bleeding, education, and intensive short-term follow-up may help reducing this risk. Lim et al describe a nurse-led pathway implemented at Monash Medical Centre in Australia to minimize adverse events after newly started rivaroxaban in the hospital.[11] They report low rates of bleeding and recurrence, and their model should be easy to replicate at other centers. Although bleeding is a well-recognized adverse event from anticoagulation therapy, other side effects have occasionally been reported or suspected, such as osteoporosis from vitamin K antagonists. Lobato et al investigated whether there is a difference in the signals of different adverse events between the vitamin K antagonists and the NOACs, using reports from a network of pharmacies in a Spanish region.[12] They were particularly interested in finding new signals of adverse drug reactions in clinical practice.

In the last contribution, Russo et al are seeking an answer to the question how NOACs perform in patients with atrial fibrillation and concomitant malignant disease.[13] We know now from two recently published trials that edoxaban and rivaroxaban appear at least as effective as low-molecular-weight heparin in patients with VTE and malignancy, albeit with increased risk of bleeding on the NOAC, driven by gastrointestinal hemorrhage in patients with cancer in this organ.[14,15] The presented systematic review did not identify any ad hoc designed trials and is based on cohort studies and subgroups from randomized trials. The authors could, however, not find any alarming data that would lead us to avoid NOACs in this context.

The reader can thus enjoy a compilation of articles on pathogenesis, prophylaxis, perioperative management, and adverse drug reactions. I hope that several, if not all, contributions will be of interest. Hopefully, the articles can also be useful as references.

Conflict of Interest
None.

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