The present issue of Seminars in Thrombosis & Hemostasis focuses on challenges related to hemostatic and thromboembolic complications in surgery or trauma. Multiple factors contribute to perioperative bleeding or thromboembolic risk. These factors might be related to the individual patient (e.g., bleeding disorders, cancer, or developmental hemostatic changes in pediatric patients), to anticoagulant medication or complications such as heparin-induced thrombocytopenia (HIT), or to inherent risks of a particular surgical procedure or affected organ (e.g., hepatobiliary surgery or renal transplantation). All of these factors can have a profound effect on expected outcomes.

Curnow provides, as the initial contribution to this issue, an in-depth review of how to manage and support patients with hereditary or acquired bleeding disorders undergoing surgery. In regard to hereditary bleeding disorders, patients with hemophilia are especially likely to undergo surgery during life due to arthropathy subsequent to repeating joint bleeds. Thorough interdisciplinary planning is crucial to manage the specialized treatment with specific factor concentrates. Curnow also addresses the need for an individualized venous thrombosis risk assessment following surgery, including evaluation of whether thromboprophylaxis is needed and safe in this setting. Another important aspect comprises pain management in patients with bleeding disorders, as the commonly used analgesic agents can be associated with an increased bleeding risk, and recommendations for handling this are therefore also provided in this review.

The risk of venous thromboembolism is considerably increased in cancer patients, and as major surgery in itself increases the risk, cancer patients undergoing surgery are particularly prone to development of thromboembolic complications. However, pharmacological thromboprophylaxis is complicated by the fact that cancer patients also have increased risk of bleeding during this treatment. Exploring these clinical dilemmas, Htun and Lee summarize the evidence on the efficacy and safety of primary thromboprophylaxis in cancer patients undergoing surgery, also taking into account the influence of cancer type on thromboembolic risk; they also present the current consensus recommendations in this setting.

Pediatric cardiac surgery affords special challenges in regard to management of hemostasis. First of all, hemostasis in children differs from that in adults, making interpretation of laboratory tests challenging. Although several methods exist for hemostatic evaluation, both plasma-based tests and dynamic whole blood coagulation tests, the use of reference values and decision limits for guidance of hemostatic treatment in children are sparsely documented. Ravn therefore summarizes and discusses studies evaluating viscoelastic tests such as ROTEM and TEG as well as platelet function tests in children undergoing cardiac surgery. Moreover, the review provides valuable information on heparin use and reversal in pediatric cardiopulmonary bypass, and finally, the potential use of antifibrinolytics in the pediatric population is challenged.

A new class of non–vitamin K oral anticoagulants (NOACs), also called direct oral anticoagulants (DOACs), and comprising direct anti-thrombin and anti-Xa agents, has now become available worldwide and is increasingly being used. One of the advantages of NOACs is that no regular laboratory monitoring is needed, but in case of emergency surgery anticoagulant assessment is warranted. As a result, a
variety of laboratory tests have been introduced, and in
the present issue of *Seminars in Thrombosis & Hemostasis*,
Blennerhassett and colleagues review and synthesize the
complexities of laboratory measurement of NOAC anticoag-
ulant effects. Furthermore, the recent advances in develop-
ment of specific NOAC reversal agents are discussed. The
review ends up providing tools for perioperative manage-
ment of patients taking NOACs based on the current
evidence.\(^7\)

Antiplatelet therapy is the cornerstone of primary
and secondary prevention of coronary artery disease.\(^8\) On
the other hand, antiplatelet therapy is also associated with
an increased risk for perioperative bleeding complications,
which is particularly the case in patients treated with acet-
ylsalicylic acid (aspirin) in combination with P2Y\(_{12}\) inhibitors
such as clopidogrel.\(^9\) Perioperative bleeding, with antiplatelet
therapy being one of the contributors, has been a serious
complication in cardiac surgery ever since its inception, with
severe bleeding complications contributing considerably to
operative mortality.\(^10\) To balance the competing needs of
reducing thromboembolic complications and minimizing
perioperative bleeding, several clinical questions arise, com-
monly including the timing of discontinuation of antiplatelet
therapy, the relevance of platelet function testing prior to
surgery, and the optimal time for restarting antiplatelet ther-
apy postoperatively. Hansson and Jeppsson comprehensively
address all these issues and provide a summary of evidence-
based recommendations on handling antiplatelet therapy in
patients undergoing cardiac surgery.\(^11\)

Nearly all patients undergoing cardiopulmonary bypass are
exposed to heparin intraoperatively. This heparin exposure is
associated with the risk of developing prothrombotic compli-
cations of HIT.\(^12\) Although unfractionated heparin, which
carries the highest risk for development of HIT,\(^12\) is increas-
ingly replaced by low molecular heparin in other clinical
settings, HIT remains a threat in cardiac surgery patients.
HIT arises in around 1 to 2% of cardiac surgery patients exposed
to heparin,\(^12\) and if left untreated, the initial rate of throm-
boembolism, amputation, and death is around 6% per day.\(^13\)
Thus, obtaining a timely and correct diagnosis is crucial.
However, the clinical diagnosis might be challenging because
the majority of patients experience a decrease in postoperative
platelet count, which can be difficult to distinguish from
development of the HIT. Herein, Pishko and Cuker review the
epidemiology of HIT after cardiac surgery and provide special
insight in the considerations needed regarding both clinical
and laboratory diagnosis of HIT.\(^14\) Finally, the difficult
task of anticoagulation in patients with previous HIT requiring
future cardiac surgery is addressed.\(^14\)

In surgical patients, the focus has been on pharmacological
prophylaxis to reduce the intra- and postoperative throm-
boembolic risk. Nonetheless, increasing attention is being paid
to other modalities such as ischemic conditioning, which has
been shown to attenuate ischemia–reperfusion injury.\(^15\)
Hence, this intervention has been suggested as a possible
future additional intervention during surgery to prevent
ischemia–reperfusion injury. However, the mechanisms be-
hind the tissue-protective effect of ischemic conditioning are
still not clarified. The review by Krag and Hvas summarizes the
existing evidence of the effects of local or remote ischemic
conditioning on laboratory hemostasis measures as well as the
incidence of thromboembolism and bleeding in patients
undergoing surgery or cardiac procedures.\(^16\) This systematic
review points to the fact that although conditioning consis-
tently reduced platelet activation in patients undergoing
cardiac procedures, the intervention did not increase bleeding
risk, but notably the majority of studies also indicated that the
intervention did not reduce arterial thromboembolic risk in
surgery or other cardiac procedures.\(^16\) Thus, the possible role
of ischemic conditioning during surgery still needs further
investigations.

Hepatobiliary surgery is associated with an increased risk
of both substantial perioperative bleeding and thrombotic
complications. Bos and colleagues highlight the complex
nature of changes in both primary and secondary hemostasis
as well as fibrinolysis in patients with liver disease under-
going hepatobiliary surgery.\(^17\) The hemorrhagic and throm-
botic complications are reviewed and risk factors and
possible predictors of hemostatic complications in the peri-
operative period of hepatobiliary surgery are discussed. Finally,
the need for pharmacological thromboprophylaxis following
liver surgery is emphasized due to the hypercoag-
ulable postoperative state.\(^17\) The authors stress the need for
further research within this area, as the prevalence of venous
thromboembolic events in patients undergoing hepatobiliary
surgery continues to be relatively high.

During recent years, more effective immunosuppressive
drugs and advances in surgical techniques have led to
improvement in patient and graft survival after renal trans-
plantation.\(^18\) Still, perioperative bleeding and thrombosis
affect both patient and graft survival.\(^19\) Patients with chronic
kidney disease, especially those with end-stage renal dis-
 ease, exhibit hemostatic changes conferring both a pro-
thrombotic state and coagulopathy leading to increased
bleeding risk.\(^19,20\) These hemostatic changes, including
the role of thrombophilia, are reviewed by Poli et al., followed by
the recommendations for prophylaxis of graft thrombosis
and prophylaxis and treatment of venous thromboembolism
following renal transplantation.\(^21\)

The case fatality in subarachnoid hemorrhage is high,\(^22\) and
half of the survivors are left with permanent disabilities.\(^23\)
Rebleeding contributes to further increased mortality\(^24\) and
neurosurgery does not prevent all cases of rebleeding.\(^25\) As
subarachnoid hemorrhage has been shown to be associated
with increased fibrinolysis, antifibrinolytics could potentially
reduce the risk of rebleeding. However, available guidelines
differ on this particular issue.\(^26,27\) In the present issue of
*Seminars in Thrombosis & Hemostasis*, Anker-Møller et al. pro-
vide a systematic review on the effect of the use of antifibrin-
olytics following subarachnoid hemorrhage.\(^28\) They conclude
that tranexamic acid reduced the overall risk of rebleeding
following nontraumatic subarachnoid hemorrhage. Moreover,
a statistically nonsignificant reduction in mortality was found
in both nontraumatic and traumatic subarachnoid hemor-
Rhage, still without substantial indication of increased risk of
ischemic lesions.\(^28\)
Trauma is one of the leading causes of mortality in the world, and hemorrhage is one of the most frequent causes of death in trauma patients. As presented by Fries et al, overall two different transfusion strategies exist for management of massive bleeding after trauma: a guided and a nonguided treatment strategy, respectively. First, Fries et al provide a review of different transfusion regimens. Second, the authors address the ongoing debate about which transfusion strategy is superior by reviewing their effect on mortality in trauma patients. The current evidence indicates a trend toward lower mortality in studies where guided treatment was used, but the studies published so far are mainly retrospective and show a high degree of heterogeneity. Thus, as concluded by Fries et al, randomized controlled trials are strongly needed to ascertain optimal transfusion approaches in trauma patients.

At least some of the aforementioned challenges could be met if coagulation tests had high predictive values in terms of ability to predict perioperative bleeding. Larsen and Hvas present a comprehensive systematic review on the predictive value of plasma and whole blood coagulation tests as well as platelet function tests. They conclude that while these laboratory tests are useful in the diagnosis and management of perioperative bleeding, they have only limited ability to predict perioperative bleeding in unselected patients. Therefore, neither plasma-based coagulation tests nor whole blood tests provide valid predictive information when used for screening in unselected patients prior to surgery and should primarily be used for the management of bleeding patients.

In summary, this issue of Seminars in Thrombosis & Hemostasis highlights several patient-, drug-, and surgery-related factors that influence bleeding and thrombosis risk and thus have to be taken into account in the perioperative setting or trauma. The reviews presented also point to the research needed to further expand the scope and improve the quality of data in this area. We hope you will enjoy reading and discussing the variety of topics presented herein.

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