Preface

Hemostatic Dysfunction in Liver Diseases

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The liver plays a central role in hemostasis, as it is the site of
synthesis of most procoagulant and anticoagulant factors. It
also synthesizes many fibrinolytic proteins, and is an impor-
tant source of thrombopoietin. Furthermore, it is involved in
clearance of many hemostatic and fibrinolytic components.
Consequently, patients with a decreased synthetic capacity of
the liver acquire a complex coagulopathy, with decreased
plasma levels of hepatocyte-derived hemostatic proteins and
a decreased platelet count.1 In addition, chronic and acute
liver diseases are characterized by chronic endothelial cell
activation resulting in additional hemostatic changes such as
substantially elevated plasma levels of von Willebrand factor
(VWF).2,3 Finally, systemic or intrahepatic activation of coag-
ulation results in consumption of platelets and hemostatic
proteins.4,5

These hemostatic changes accompanying liver diseases are
among the most complex acquired hemostatic changes, and
the net effects of these changes have, therefore, long been
unclear. Historically, patients with liver diseases were con-
sidered to have a significant bleeding risk. This belief arose
primarily from observations of prolonged coagulation
screening test results, especially the prothrombin time/intern-
national normalized ratio (PT/INR), the apparent reduction of
many liver-derived coagulation factors (e.g., II, V, VII, IX, X,
and XI), and reduction in platelet count, leading to a perceived
“hypocoagulable” state. Careful clinical observation and
extensive laboratory studies, however, have led to the concept
of a rebalanced hemostasis.6 The notion that the hemostatic
balance in liver disease is reset because of a concomitant
decline in both prohemostatic (as noted earlier) and anti-
hemostatic (e.g., proteins C and S) components and conse-
quent processes is therefore rapidly gaining acceptance.7,8

Furthermore, it is increasingly recognized that the hemostatic
status of patients with liver disease comprises hypercoagula-
able components (e.g., increases in VWF, factor VIII, and
decreases in anticoagulant proteins).9–12 These hypercoagu-
able features explain, at least partly, why systemic and local
thrombotic events in patients with liver diseases are common.13,14

In total, the hemostatic balance in liver disease appears
more fragile compared with that of healthy individuals, and
this explains why both bleeding and thrombotic complica-
tions can occur in these patients. The current clinical chal-
enges include the prediction and management of bleeding
and thrombotic events in patients with both chronic and
acute liver diseases. Thus, we have assembled in this issue of
Seminars in Thrombosis and Hemostasis several articles on the
pathophysiology and clinical management of the coagulop-
athy of liver diseases by prominent investigators in this field,
and thus providing our readers with updated information on
this important clinical field.

To begin, Hoffman outlines the central role of the liver in
hemostasis, citing the concept of the cell-based hemostasis
model to show the limited value of common tests such as the
PT.15 Next, Giannini and Peck-Radosavljevic discuss how
thrombopoietin with thrombocytopenia may be affected in
the different liver diseases.16 This is followed by an article by
Tripodi and Mannucci who describe the imbalance between
the procoagulant and anticoagulant effects in the chronic liver
diseases.17 Lisman and Stravitz then discuss hemostatic
changes in patients with acute liver failure, which are similar,
but not identical to the changes in patients with cirrhosis,
and provide evidence for hemostatic rebalance in this particular
type of liver disease.18 Excessive fibrinolysis, another major
abnormality in liver dysfunction, is then reviewed by Leebeek
and Rijken, who present findings of hyperfibrinolysis in
various liver diseases and provide critical analysis of different
laboratory tests for fibrinolytic activity.19 Barrera et al then
show the link between hemostatic alterations and the risk for
variceal bleeding in patients with cirrhosis.20

The increased risk for cardiovascular events in patients with
diabetes, obesity, and the metabolic syndrome have
been well established, and the increased risk has been partly
ascribed to prohemostatic changes. However, less is known
on the hemostatic changes in patients with nonalcoholic fatty liver disease (NAFLD), particularly, when it has advanced to cirrhosis. Potze et al discuss the incidence and risk factors for vascular disease in NAFLD and explore the potential role of hemostatic changes therein.\(^{21}\) Valla then outlines risk factors, diagnosis, and treatment of splanchnic vein thrombosis,\(^{22}\) after which Derman and Kwaan provide additional data from their single institutional findings.\(^{23}\) Intagliata and Northup then discuss opportunities and pitfalls for prevention and treatment of thrombotic disease in patients with liver diseases using anticoagulant therapy.\(^ {24}\) A pragmatic approach to prevention and treatment of bleeding and thrombosis in critically ill patients with liver disease is then provided by Roberts and Bernal,\(^ {25}\) and Mallett subsequently outlines how viscoelastic tests of coagulation help in management decisions on bleeding and thrombosis in patients with liver disease and during liver transplantation.\(^ {26}\) Finally, Massicotte et al present data from their institution which uses state-of-the-art approaches to prevention of blood loss during liver transplantation.\(^ {27}\)

In total, the contributions to this issue of Seminars in Thrombosis and Hemostasis amply illustrate that the field of coagulopathy in liver diseases has been rapidly evolving over the last decade, with novel concepts that truly impact on our understanding of this disorder and on the clinical consequences that are changing the way we are managing patients with liver disease. We trust that our readers will be as excited to be updated with this remarkable progress as we are.

References