Systemic Disease and Bleeding Disorders for the Oral and Maxillofacial Surgeon

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KEYWORDS

• Cirrhosis • Kidney disease • Coagulation • Hemostasis • Oral and maxillofacial surgery

KEY POINTS

- There are multiple systemic diseases that have an impact on coagulation of which oral and maxillofacial surgeons must be cognizant.
- Recent evidence has supported the potential for both hypocoagulable and hypercoagulable states in patients with liver and kidney disease with an even less understood impact on prolonged bleeding in the oral cavity.
- These systemic diseases are not limited to diseases affecting the liver, kidney, and bone marrow; however, these diseases are common among the patient population and surgeons must be capable of making appropriate judgment and modifying care appropriately.

Current treatment of patients with systemic diseases, such as liver and kidney disorders, often have the understanding that these patients are inherently at risk for impaired hemostasis and, therefore, altered bleeding. Currently, standard treatments are often based solely on expert opinion and are not evidence based. Recent evidence has supported the potential for both hypocoagulable and hypercoagulable states in patients with liver and kidney disease, with an even less understood impact on prolonged bleeding in the oral cavity. It is, therefore, prudent to understand the impact that these diseases have on patients and the potential effect on hemostasis when choosing treatment options.

LIVER

The liver is a vital player in coagulation and hemostasis. With the production of clotting factors, inhibitors, and proteins involved in the coagulation cascade as well as the ability to clear these products from circulation, hepatic diseases may significantly alter hemostasis. In liver disease processes, decreased production of clotting factors, thrombocytopenia, platelet dysfunction, and increased circulating fibrinolysis activity based on hepatocellular destruction are evident. It is, therefore, judicious to understand some of the more common hepatic disease processes and their role in coagulation.

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Cirrhosis

Cirrhosis is a chronic condition in which fibrous tissue replaces damaged hepatocytes. This results in a disruption of blood flow through the liver and hepatocellular failure. Blood flow disruption may lead to portal hypertension subsequently causing ascites, peripheral edema, splenomegaly, and varices in the gastrointestinal (GI) tract. Hepatocellular failure also results in decreased albumin and clotting factor synthesis.

The most common classification scheme for determining prognosis and bleeding risk in hepatic disease patients is the Child-Pugh classification with an updated modified Child-Pugh classification now in place. The classification assesses ascites, encephalopathy, bilirubin level, albumin level, and prothrombin time (PT) values as markers with different numeric scores given to each category based on disease progression. These values are added up and ranked as a Child-Pugh class A, B, or C, with class A patients having a better prognosis (estimated 100% 1-year survival) and class C patients having a worse prognosis (predicted 45% 1-year survival). A correlation between Child-Pugh class and increased bleeding time (BT) has not been identified, but it seems likely that higher Child-Pugh score relates to altered coagulopathy.

Another common scoring system used to assess liver disease is the Model for End-Stage Liver Disease (MELD) score, initially used to determine mortality rates in chronic liver disease patients but later found useful in prioritizing candidates for liver transplants rather than using the Child-Pugh score. It is based on a patient's serum bilirubin, creatinine, and international normalized ratio (INR) values to determine survivability. These components are combined into a formula to develop a score that predicts the 3-month mortality in hospitalized patients.

Cirrhosis may be caused by multiple disease processes, including alcoholic liver disease (most common), viral hepatitis, drug induced (eg, acetaminophen toxicity and chronic methotrexate therapy), autoimmune, dysfunction inherited metabolic diseases, and hepatic congestion.

Vitamin K is an essential cofactor in the production of factors II, VII, IX, and X and proteins C, S, and Z, enabling the binding of calcium to these proteins. Diet (green leafy vegetables) is a large source of vitamin K that is absorbed in the small bowel with the aid of bacteria. In some cases of coagulopathy, vitamin K can be used to increase the number of active coagulation factors. This coagulopathy is due to the decreased synthesis of clotting factors (I, II, V, VII, IX, X, XII, and XIII), resulting in increased PT/INR values.

Cirrhosis and Coagulation

Recent studies of coagulation and cirrhotic patients reveal that these patients may not be in a state of hypocoagulation even though bleeding is prolonged by up to 40% of all patients with cirrhosis.[1] Cirrhosis patients may have hypercoagulation or hypocoagulation. This is due to the nondiscrimination in the reduction of both procoagulants and anticoagulants that are synthesized in the liver. These patients typically have elevated levels of von Willebrand factor and factor VIII whereas protein C and antithrombin are reduced. In such cases of hypercoagulation, anticoagulant therapy may be necessary to prevent a hypercoagulable state. Current evidence also suggests that hypercoagulation contributes to hepatic fibrogenesis, where an association of hypercoagulation and increased progression of hepatic fibrosis has been made. It is theorized that microinfarcts from thrombi cause ischemia and hepatic parenchymal death that is eventually replaced with fibrotic tissue.[2,3] Coagulation as a therapeutic option in cirrhotic patients has been largely unexplored and therefore management recommendations have not yet been made.[4]

When measuring coagulation capacity in cirrhotic patients, clinicians often use PT testing in making their assessment. The inherent problem with this test is that it may not be accurate in vivo. PT primarily measures factor VII, the first factor to be depleted during episodes of bleeding (shortest half-life); therefore, the correct assessment of clotting time cannot be obtained through PT because it only primarily depicts a small portion of the coagulation cascade. There is a potential that decreases in coagulation factors and anticoagulation factors balance each other; therefore, PT may be reactive to decreased coagulants but not the decreased anticoagulants. Protein C, for instance, decreases thrombin formation by inhibiting factor V and VIII.[5] A deficiency in protein C makes patients hypercoagulable. It is hypothesized that the ratio of factor VIII to protein C is one of the determinants for hypercoagulability in cirrhotic patients. PT testing should be taken into consideration; however, a more appropriate in vivo test is necessary to obtain a correct depiction of the coagulation status of a patient. Testing, such as thromboelastography (TEG), is becoming increasingly popular in the determination of coagulation status. This is due to TEG's ability to determine platelet function, fibrinolysis, and clot strength. Unfortunately, TEG is only available in a few large institutions and is not readily available.

Platelet counts in cirrhotic patients are also severely affected. Many cirrhotic patients have