Management of Intraoperative Coagulopathy

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KEYWORDS

- Coagulopathy • Anticoagulant • Disseminated intravascular coagulation (DIC)
- Prothrombin complex concentrates (PCC) • Tranexamic acid/antifibrinolytics
- Recombinant factor VIIa (rFVIIa)

KEY POINTS

- Intraoperative hemorrhage can occur even in optimally prepared patients let alone during urgent procedures. Identifying the reason is crucial for appropriate and timely fashioned treatment.
- The cornerstone treatment of disseminated intravascular coagulation is transfusion therapy to correct the consumption of platelets and coagulation factors.
- Urgent reversal treatment of vitamin K antagonists–associated life-threatening bleeding includes vitamin K and prothrombin complex concentrate.
- Using recombinant factor VIIa should be considered for intractable bleeding when all other therapies have failed to achieve hemostasis.
- Antifibrinolytic therapy, such as tranexamic acid, should be considered as prophylaxis treatment before major surgery and to treat bleeding due to fibrinolysis.

Achieving and maintaining hemostasis during neurosurgical procedures is critical to their successful outcomes. Although the risk of hemorrhage can often be predicted with preoperative laboratory screening and a complete history and physical examination, there remain patients in whom intraoperative hemorrhage cannot be predicted.

The coagulation system is a complex interplay between cellular and molecular components. Hemostasis is a dynamic process that needs to be rapid, localized, and highly regulated. There is a balance between thrombus formation and lysis, and surgical trauma may disrupt this balance and cause abnormal bleeding or excessive thrombosis.

There is a difference between an elective procedure when preparation is optimal (good history, preoperative evaluation, and interruption of anticoagulant medications) versus urgent/emergent surgery when patients are often receiving antiplatelet agents, vitamin K antagonists (VKAs), or a direct oral anticoagulant (DOAC). In addition, in an emergency, no information about medications, concomitant medical conditions, or bleeding history may be available. Thus, the lack of reliable clinical information may contribute to unanticipated intraoperative hemorrhage.

Patients can bleed because of the surgical procedure or because of an impaired ability to establish hemostasis. In this review, the authors do not discuss technical factors that lead to intraoperative hemorrhage. The authors review potential causes for disrupted hemostasis, including a brief overview of the preparation for urgent procedures in patients on anticoagulants and the therapeutic options.

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It is extremely important to identify either acquired or inherited hemostatic defects if bleeding is encountered. The history should be reevaluated (if possible). In addition, the preoperative medications, including crystalloids, colloids, and blood products, should be reassessed. The laboratory evaluation that will screen for coagulation defects, including thrombocytopenia (or platelet dysfunction), should be reviewed in the context of intraoperative hemorrhage. It is also important to collect several tubes of citrated plasma before the administration of a blood product or other hemostatic agents in order to obtain a baseline assessment of hemostatic function.

Pharmacologic treatments for excessive bleeding include

- Topical hemostatics (eg, fibrin glue, thrombin gel)
- Transfusion of platelets
- Transfusion of coagulation factor concentrates: fresh frozen plasma (FFP), prothrombin complex concentrate (PCC), and recombinant factor VIIa (rFVIIa)
- Antifibrinolytics (ε-aminocaproic acid, tranexamic acid [TXA])
- Treatments for hypofibrinogenemia (cryoprecipitate, fibrinogen concentrate)
- Desmopressin (DDAVP).

INTRAOPERATIVE DISSEMINATED INTRAVASCULAR COAGULATION/ COAGULOPATHY

Disseminated intravascular coagulation (DIC) is a clinicopathologic condition in which there is intravascular activation of the coagulation system and regulators. This activation leads to the generation of soluble fibrin monomers, which deposit in the microvasculature and cause organ damage. There is simultaneous platelet and coagulation factor consumption and depletion, which may lead to bleeding. The pathophysiology of DIC is complex. It is well known that traumatic brain injury (TBI) is associated with severe coagulopathy, and existence of such at presentation is a predictor of unfavorable outcomes.[1] Multiple mechanisms are potentially linked to coagulopathy after TBI including disorders of platelet number and function, changes in endogenous procoagulant and anticoagulant factors, endothelial cell activation, hypoperfusion, and inflammation.

The causes of these hemostatic changes are not completely understood but likely include the release of tissue factor (TF) from the damaged brain, which binds extensively to factor VIIa triggering the extrinsic coagulation pathway, which results in thrombin generation. Platelets are activated by several mechanisms, first by local tissue or vessel injury (eg, exposed subendothelial matrix) and second by cytokine and TF release by systemically activated endothelial cells (eg, related to shock), possible platelet hyperactivity with subsequent platelet consumption, and secondary platelet depletion and dysfunction. Overactivation of clotting via TF has been suggested to drive hyperfibrinolysis. In addition, brain injury can promote clot dissolution by release of tissue-type and urokinase-type plasminogen activators. As multiple thrombi form, the systemic consumption of fibrinogen and platelets leads to bleeding complications.[1]

Even though very uncommon, there are case reports of DIC developing during neurosurgical removal of a tumor; this is associated with a high mortality rate.[2–4] It is thought to be related in part to tumor TF expression, a major actor in the activation of the coagulation cascade.

DIAGNOSIS

The diagnosis of DIC includes a combination of clinical and laboratory parameters. No single test can verify or exclude the diagnosis. It is also a dynamic situation that may necessitate serial clinical and laboratory evaluation.

An analysis of 5 reports of patient groups with DIC, with a total of more than 900 patients, suggests that the laboratory abnormalities reported in decreasing the order of frequency are thrombocytopenia, elevated fibrin degradation products, prolonged prothrombin time (PT), prolonged activated partial thromboplastin time (PTT), and low fibrinogen.[5]

The International Society of Thrombosis and Hemostasis recommended the use of a scoring system for overt DIC, whereby the presence of an underlying disorder known to be associated with DIC was a prerequisite for the use of the algorithm. It consists of simple tests (platelet number, PT, D-dimer, fibrin degradation products, and fibrinogen [**Table 1**]). It was found to be both sensitive (91%) and specific (97%) for the diagnosis of DIC, and an increased score correlated with an increase in the odds of mortality.[6,7]

Although the literature about the use of this scoring system during surgery is lacking, trauma was one of the specified prerequisites for an underlying disorder associated with DIC.

Other methods to identify coagulopathy during surgery include using viscoelastic hemostatic assays (VHAs), such as thromboelastography (TEG) or rotational thromboelastometry (ROTEM). These assays are point-of-care assays, capable of global assessments of coagulation based on the physical and kinetic properties of clot formation, that