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No bleeding complications during major surgery in subacute liver dysfunction patient with international normalized ratio within therapeutic range

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Introduction

A 45-year-old male was admitted to the intensive care unit due to septic shock in the course of intraabdominal infection. The patient had a 6-week history of liver dysfunction (discolored stools, dark urine, jaundice) which was classified as subacute [1]. To control the source of infection, a surgical consultation was requested, although due to illness severity initially a percutaneous abdominal drain was inserted, followed by an exploratory laparotomy the next day. Coagulation parameters pre-procedure were grossly abnormal: prothrombin time (PT) 32.6 (reference 9.4–12.5) s, international normalized ratio (INR) 2.75 (reference 0.80–1.20), prothrombin activity 25% (reference 80–120%), fibrinogen 254 (reference 200–393) mg/dL, thrombin time 16.1 (reference 10.3–16.6) s, activated partial thromboplastin time 46.1 (reference 25.4–36.9) s, D-dimers 14,188.0 (reference <500.0) ng/mL, platelets 315 (reference 130–400) × 10^3/μL, and hemoglobin (Hb) 104 (reference 135–165) g/L.

In order to examine the global hemostatic profile, point-of-care viscoelastic hemostatic assay (VHA) was performed (ROTEM delta, Werfen, Germany) (Figures 1A–D). Despite INR within the therapeutic range, VHA revealed balanced hemostasis. The VHA revealed some abnormal results of coagulation parameters assessing the intrinsic coagulation pathway (INTEM®), extrinsic coagulation pathway (EXTEM®), and fibrinogen function (FIBTEM®). Some of the abnormal ROTEM results suggested hypo-coagulation i.e. prolonged clotting time (depending on clotting factors and anticoagulants) in EXTEM® and FIBTEM®. Some abnormal ROTEM parameters suggested hyper-coagulation i.e. increased amplitude of the clot and maximal clot firmness (both parameters depending on platelets, fibrinogen, factor XIII, fibrinolysis) in INTEM® and EXTEM®. The remaining parameters were within the normal range. The patient underwent laparotomy with drainage of the peritoneal cavity and retroperitoneal space, segmental resection of proximal small intestine with side-to-side entero-enteric anastomosis, and segmental resection of distal small intestine with creation of a terminal ileostomy. There was no bleeding reported during this major surgical procedure.

Discussion

This case shows the possibility of balanced hemostasis despite highly abnormal results of standard coagulation tests. Hemostasis in acute liver failure (ALF) is characterized by imbalance between von Willebrand factor (vWF) and vWF-cleaving protease, and reduced fibrinolysis [2]. Attempts to correct spuriously elevated INR in non-bleeding ALF patients can lead to thromboembolic complications [2]. Our patient had already elevated D-dimers. This was why we decided to run VHA. The fact that there was no bleeding reported during surgery supports the appropriateness of hemostasis management.

The most recent iteration of guidelines on the management of severe peri-operative bleeding states that elevated INR does not predict bleeding in ALF patients [3]. The same guidelines state that mild-to-moderate prolongation of PT and INR does not predict bleeding in chronic liver disease (CLD) patients. Neither of these statements have been

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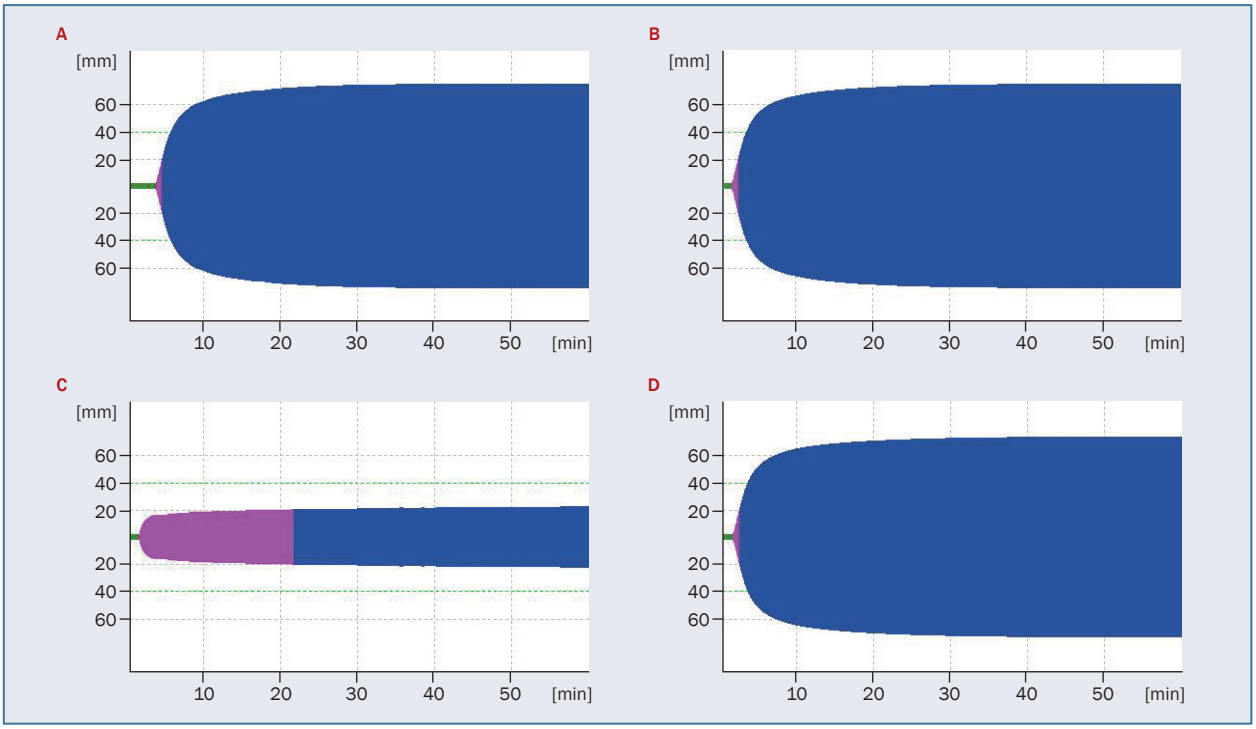

Figure 1. Rotational thromboelastometry pre-procedure: **A.** INTEM® tracing; **B.** EXTEM® tracing; **C.** FIBTEM® tracing; **D.** APTEM tracing

assigned strength, and the quality of scientific evidence was low. The aforementioned guidelines recommend that moderately elevated INR should not be corrected before invasive procedures in patients with ALF, although the quality of evidence was also low here. As 'moderately increased', we may assume INR 1.5–2.0 [4]. In a small pilot study (n = 57) investigating cirrhotic patients with a pre-procedure INR of 1.5–2.5, there was no difference in Hb concentration up to two days between a group that received fresh frozen plasma (FFP) (10–15 mL/kg) and a group that did not. Moreover, the mean drop in INR following FFP transfusion was only 0.24 [5].

Our patient's INR before major surgery was as high as 2.75. We suspect that many clinicians would try to correct such an abnormal result before a major invasive procedure with FFP. Our approach was to minimize the risks associated with procoagulant therapy. Transfusion of blood products can lead to numerous complications, the frequency of which depends on the blood product being transfused. These complications comprise febrile non-hemolytic transfusion reactions, acute hemolytic transfusion reactions, nosocomial infections, immunomodulation, transfusion-associated acute lung injury (TRALI), thromboembolic complications, allergic reactions, immunization, and blood-born pathogen transmission [6]. The leading cause of death following transfusion is transfusion-associated circulatory overload [7], particularly following high-volume (standard dose 20 mL/kg) FFP transfusions [8].

Guidance from VHA is recommended in order to reduce exposure to allogeneic blood products in cirrhotic patients undergoing invasive procedures. Observational studies show that VHAs are useful in ascertaining balanced hemostasis despite severely abnormal INR in patients with cirrhosis [9, 10].

Conclusions

Standard laboratory tests of coagulation in subacute liver dysfunction patients do not seem to predict bleeding during surgical procedures, irrespective of the degree of abnormality. Viscoelastic hemostatic assays may be extremely useful for ascertaining balanced hemostasis before invasive procedures in this patient population, potentially decreasing the risk associated with procoagulant therapy.

Article information and declarations

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Author contributions
PFC — concept, writing manuscript. JP — writing manuscript.

Conflict of interests
The authors declare no conflict of interests.

Ethics statement
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