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Clinical Investigation

CLINICAL INVESTIGATION

Comparison between thrombelastography and thromboelastometry in hyperfibrinolysis detection during adult liver transplantation

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Abstract

Background: Hyperfibrinolysis is one of the main causes of non-surgical bleeding during liver transplantation (LT). Viscoelastic haemostatic assays, including thromboelastometry (ROTEM®) and thrombelastography (TEG®), can detect hyperfibrinolysis at the bedside. No study has yet demonstrated which device or assay is more suitable for detecting hyperfibrinolysis.

Methods: This prospective observational study compared ROTEM® and TEG® in isolated adult LT. ROTEM® (EXTEM® [tissue factor activation], FIBTEM® [tissue factor activation with platelet inhibition], and APTEM® [tissue factor activation with tranexamic acid/aprotinin]) and TEG® (kaolin-TEG®) were simultaneously performed using arterial blood samples at eight time-points during LT: induction of general anaesthesia, 60 min after skin incision, 10 and 45 min after portal vein clamp, 15 min before graft reperfusion, and five, 30, and 90 min after graft reperfusion. Hyperfibrinolysis was identified per the manufacturers' definitions (maximum lysis >15% in ROTEM® or Lysis30>8% in TEG®) and confirmed with APTEM®; incidence was compared between assays McNemar's test.

Results: Among 296 possible measurement points from 376 consecutive LT recipients, 250 underwent final analysis: 46 measurement points were excluded because of missing assays or flat line. Hyperfibrinolysis was confirmed at 89 (36%) of 250 measurement points: FIBTEM®, EXTEM®, and kaolin-TEG® detected 84 (94%), 41 (46%), and 21 (24%) hyperfibrinolysis, respectively. These hyperfibrinolysis detection rates significantly differed from each other ($P<0.001$).

Conclusions: Tissue factor-triggered ROTEM® tests were more sensitive than contact-activated k-TEG® in identifying hyperfibrinolysis in LT patients. Inhibition of platelet-fibrin interaction in FIBTEM® enhanced sensitivity to hyperfibrinolysis detection compared with EXTEM®.

Key words: clinical laboratory techniques; fibrinolysis; liver transplantation; thrombelastography

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Editor's key points

- Hyperfibrinolysis is a leading cause of non-surgical bleeding during liver transplantation, and is detectable by point-of-care viscoelastic testing.
- In a prospective observational study, three assays were compared in 37 consecutive adult liver transplant patients.
- ROTEM® was more sensitive than TEG® in identifying hyperfibrinolysis, with FIBTEM® being the most sensitive assay.

Liver transplantation (LT) is frequently associated with hyperfibrinolysis, which is one of the main causes of non-surgical bleeding during LT.[1 2] Unfortunately, no standard laboratory test is currently available to rapidly and reliably detect hyperfibrinolysis.

Two widely-available viscoelastic haemostatic assays (VHAs), thrombelastography (TEG®; Haemonetics, Niles, IL, USA) and rotational thromboelastometry (ROTEM®; TEM International, Munich, Germany), are able to detect hyperfibrinolysis at the bedside in a timely manner. In ROTEM®, the combinational use of EXTEM® (tissue factor and phospholipids activations) and APTEM® (tissue factor and phospholipids activations with tranexamic acid/aprotinin) is able to confirm or rule out hyperfibrinolysis. ROTEM® also has a FIBTEM® (tissue factor and phospholipids activations with platelet inhibition) assay that provides a qualitative assessment of fibrinogen status. This assay has potential to better detect hyperfibrinolysis, since FIBTEM® can isolate fibrin polymerization from platelet-fibrin(ogen) interactions in the presence of cytochalasin D as a platelet inhibitor. No study has yet demonstrated which device (TEG® vs. ROTEM®) or assay [kaolin-TEG® (k-TEG®) vs. EXTEM® vs. FIBTEM®] is more suitable for detecting hyperfibrinolysis. The aim of this prospective observational study was to compare hyperfibrinolysis detection between TEG® and ROTEM®.

Methods

Study population, surgical technique, and anaesthetic management

Under local institutional review board approval (#PRO12120173), a prospective observational study was performed in a single institution on 37 consecutive adult patients who underwent LT from August 1, 2013 – November 30, 2013. Liver grafts from brain dead donors, donation after circulatory death donors, and live donors were included in the study. The surgical and anaesthetic management used have been previously described.[3] Briefly, organ procurement was performed using University of Wisconsin preservation solution. The piggyback technique was used for graft implantation. During the study period, percutaneous veno-venous bypass was only used for live donor LTs. Packed red blood cells (PRBCs) were administered to maintain a 26–30% haematocrit. A cell saver device was routinely used, except on recipients with hepatic malignant lesions. In the presence of microvascular bleeding, transfusions of fresh frozen plasma (FFP), platelets, and cryoprecipitate were considered by attending transplant anaesthetists based on TEG®. Kaolin-TEG® (k-TEG®) was performed using an arterial blood sample at eight standardized measurement points during LT per our institutional protocol.[3] Results of ROTEM® measurements were solely used for observational research and not for clinical management. I.V. ε-aminocaproic acid (125–500 mg) was only administered when both surgical bleeding and hyperfibrinolysis on k-TEG® were observed. No prophylactic antifibrinolytic therapy was used per our institutional protocol.

Coagulation study protocol

Blood samples were drawn simultaneously from an existing arterial catheter. ROTEM® (EXTEM®, FIBTEM®, and APTEM®) and TEG® (k-TEG®) were performed according to the manufacturer's instructions.[3] The minimum run time for 60 min was assured in both TEG® and ROTEM® assays in this study. These tests were performed at the following eight measurement points during LT: at induction of general anaesthesia, 60 min after skin incision, 10 and 45 min after portal vein clamp, 15 min before graft reperfusion, and five, 30, and 90 min after graft reperfusion . All TEG® tests were performed by a designated group of five anesthesiology technicians at a designated space at the hospital. These technicians had more than two years of experience in performing traditional TEG® assays. All ROTEM® tests were performed by one of the investigators (EA).

Diagnosis of hyperfibrinolysis

Hyperfibrinolysis was detected per the manufacturers' definitions (maximum lysis >15% in ROTEM® or Lysis30 >8% in TEG®), where maximum lysis is the reduction of clot firmness in relation to maximum clot firmness within the complete measurement period, and Lysis30 is the percentage reduction of amplitude compared with maximum amplitude (MA), which is measured at 30 min after the time of MA. None of the recently performed alternative hyperfibrinolysis thresholds was used in the current study.[4]

The diagnosis of hyperfibrinolysis was confirmed with normalization of maximum lysis in simultaneously performed APTEM® compared with maximum lysis measured in EXTEM®. APTEM® contains thromboplastin (recombinant tissue factor and phospholipids) as the activators with a fibrinolysis inhibitor (aprotinin or tranexamic acid) and a heparin inhibitor, so it can detect hyperfibrinolysis when compared with EXTEM®. 'An hyperfibrinolysis' pattern in EXTEM® and/or FIBTEM® without correction inAPTEM® was not considered as hyperfibrinolysis, nor was an isolated 'hyperfibrinolysis' pattern in k-TEG®.

Exclusion criteria for analysis

The entire set of VHA data performed simultaneously at each time point was excluded from analysis when any of the VHA measurements (1) were missed (not performed or not recorded as a result of technical reasons), or (2) showed a 'flat line' for more than 30 min. The latter is because of difficulty in differentiating hyperfibrinolysis from other causes (e.g., heparin administration) that lead to flat line.

Statistical analyses

Data are descriptively summarized as the number of measurement points or the number of LT patients with percentage. The sensitivities and specificities of three assays (k-TEG® vs. EXTEM® vs. FIBTEM®) for identification of hyperfibrinolysis were compared using McNemar's test. A P value <0.05 was considered statistically significant. Data were analysed using GraphPad Prism v4.0b (GraphPad Software, Inc. La Jolla, CA, USA).