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Preoperative thrombelastography maximum amplitude predicts massive transfusion in liver transplantation

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ABSTRACT

Background: Massive transfusion (MT) is frequently required during liver transplantation. Risk stratification of transplant patients at risk for MT is an appealing concept but remains poorly developed. Thrombelastography (TEG) has recently been shown to reduce mortality when used for trauma resuscitation. We hypothesize that preoperative TEG can be used to risk stratify patients for MT.

Material and methods: Liver transplant patients had blood drawn before surgical incision and assayed via TEG. Preoperative TEG measurements were collected in addition to standard laboratory coagulation tests. TEG variables including R-time (reaction time), angle, maximum amplitude (MA), and LY30 (clot lysis 30 min after MA) were correlated to red blood cell units, plasma (fresh frozen plasma), cryoprecipitate, and platelets during the first 24 h after surgery and tested for their performance using a receiver-operating characteristic curve.

Results: Twenty-eight patients were included in the analysis with a median Model for End-Stage Liver Disease score of 17; 36% received a MT. The TEG variables associated with MT (defined as $\geq$10 red blood cell units/24 h) were a low MA ($P < 0.001$) and low angle ($P = 0.014$). A high international normalized ratio of prothrombin time ($P = 0.003$) and low platelet count ($P = 0.007$) were also associated with MT. MA had the highest area under the curve (0.861) followed by international normalized ratio of prothrombin time (0.803). An MA of less than 47 mm has a sensitivity of 90% and specificity of 72% to predict a MT. MA was the only coagulation variable that correlated strongly to all blood products transfused.

Conclusions: TEG MA has a high predictability of MT during liver transplantation. The use of TEG preoperatively may help guide more cost effective blood bank preparation for this procedure as only a third of patients required a MT.

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Introduction

Early experience in liver transplant surgery was associated large volumes of blood products during the perioperative period. Starzl's first hundred transplants averaged 26 units of red blood cells (RBC) during the operation.[1] A more contemporary analysis of liver transplantation has demonstrated a marked reduction in blood product usage, averaging 14-17 units of RBC during the perioperative period.[2,3] In trauma, early identification of patients at risk of massive transfusion (MT) and implementation of a protocol to prepare transfusions have been associated with improved survival.[4] Conversely, in liver transplant, it is anticipated that most patients will undergo large blood product resuscitation; however, many patients may not require MT because liver transplantation in certain scenarios has become a virtually bloodless procedure.[5] Therefore, risk stratification for bleeding in these patients can lead to more optimal utilization of the blood bank and aid in patient education for anticipated postoperative outcomes.

Risk of blood product use in transplant has been associated with an elevated international normalized ratio of prothrombin time (INR) and low platelet (Plt) count,[6] but these have limitations for predicting bleeding risk in patients with liver disease.[7] The shortcoming of using these traditional coagulation assays is partitioning the coagulation system into plasma and cellular components. The cellular based model of hemostasis emphasizes the importance of retaining the cellular components of blood when assessing coagulation.[8] Thrombelastography (TEG) is a whole blood assay, which provides comparable coagulation information to five conventional laboratory assays.[9] TEG-guided transfusion for procedures in cirrhotic patients reduces unnecessary transfusions compared to traditional assays.[10] TEG-guided resuscitation in critically injured trauma patients also reduces blood product usage and reduces mortality by up to 50%.[11] The same benefit of fewer transfusions while using TEG-based resuscitation exists for liver transplantation.[12]

There is growing evidence supporting the use of TEG as a technique to guide transfusion strategies in patients with severe bleeding that are at risk for MT.[13,14] Currently, there are no consistent guidelines on predicting the risk of MT for patients undergoing liver transplant surgery. With refined technique, we can use devices to identify patients at risk for bleeding, guide and lessen the usage of blood products, and reduce MT. The objective of our study was to assess if preoperative TEG in patients undergoing liver transplant surgery can predict MT. We hypothesize that preoperative TEG can be used to risk stratify patients for MT.

Material and methods

Subjects

Liver transplant recipients were enrolled preoperatively in a Colorado Multi-Institutional Review Board study to prospectively collect blood samples for the first 24 h after surgery. All patients were transplanted at the University of Colorado Hospital; which averages ~100 liver transplants a year. Enrollment criteria were adult (>18 years) and cadaveric liver donor recipient. Patient demographics were recorded, including age, sex, and comorbidities, and model for end-stage liver disease calculated the day of surgery. TEG assays were not performed on these patients as part of their routine preoperative coagulation assessment, which is currently limited to international normalized ratio of prothrombin time (INR) and Plt count.

Thrombelastography

Preoperative blood samples were drawn in the operating room after intubation and before incision. Blood was collected in citrated tubes and assayed at room temperature between 20 min and 2 h after blood draw, per manufacturer's guidelines. The citrated samples were recalcified and assayed using the TEG 5000 Thrombelastograph Hemostasis Analyzer (Haemonetics, Niles, IL) per manufacturer instructions. Clot formation, strength, and fibrinolysis were measured using standard TEG measurements including reaction time (R-time), angle, maximum amplitude (MA), and clot lysis 30 min after MA (LY30). All TEG tracings were used for research purposes and not available to the surgeons or anesthesiologists.

Outcomes

Total blood product use was calculated at 24 h after the operation. MT was defined as ≥10 units of red blood cells transfused within 24 h of surgery,[15] and intraoperative mortality was also recorded as an outcome.

Statistical analysis

Statistical analysis was performed using SPSS 22 software (Microsoft, Armonk, NY). Normally distributed data were described as mean and standard deviation, and nonnormally distributed data were described as the median value within the 25th to 75th percentile values. Clinical variables and outcomes were contracted between patients who underwent a MT using a Mann-Whitney *U* test. Correlation between coagulation parameters and blood products was assessed with Spearman's Rho test, and a high correlation was considered a value > 0.5. Receiver-operating characteristic curves were generated with all coagulation tests that were significant between patients who underwent MT and patients who did not undergo MT (no-MT). Alpha was set to 0.05 for significance. Youden index was used to determine a threshold for predicting MT.

Results

There were 28 patients included in the analysis, 61% were male and the median age was 56 years (53-61). Median values for standard laboratory data were model for end-stage liver disease = 17 (10-27), INR = 1.9 (1.3-12.7), Plt count = 81 (56-110). Median values for total units transfused within 24 h of starting surgery were five units of RBC, four units of plasma, and one