Brief Communication

Fibrinolysis after reperfusion of liver graft

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Abstract

From September 2012 to March 2013, a total of 63 adult-to-adult living donor liver transplantations were performed at our institution. All the patients were monitored for their coagulation functions using rotation thromboelastometry (ROTEM, Tem Innovations GmbH) during the procedure at the following points: preoperative baseline, 5 minutes, 30 minutes, and 120 minutes, respectively, after reperfusion of the liver graft. A total of 84.13% of cases (n = 53) revealed fibrinolysis after reperfusion of the graft and the condition was reversed after 30 minutes without any need for additional treatment. No significant coagulopathy was observed during this period in all of the cases. The result of the ROTEM finding must correlate with the clinical situation before instituting any management to avoid the risk of thrombosis of the hepatic artery.

1. Introduction

Liver transplantation has been accepted as an effective treatment for patients suffering from end-stage liver disease (ESLD) and certain hepatocellular carcinomas which are not resectable due to underlying poor liver conditions. Liver transplant recipients, especially those with ESLD, often have underlying coagulopathy and such an altered hemostatic state often continues for a few days after liver transplantation. Careful and discreet monitoring of a patient’s coagulation profile constitutes an essential part of management of this problem. The thromboelastometry system is a useful diagnostic tool that is intended to provide a quantitative and qualitative assessment of a patient’s coagulation profile during surgery.1 Thromboelastography reflects various physiological results that help in understanding the interactions between various coagulation factors and inhibitors. The effectiveness of the thromboelastograph-guided transfusion replacement therapy is considered to be helpful in improving the management of coagulopathy during liver transplant surgery.1,2

The aim of our observation was to evaluate the cause of hyperfibrinolysis as depicted by rotation thromboelastometry (ROTEM Tem Innovations GmbH) after reperfusion of the liver graft and its importance in the management of coagulopathy in living donor liver transplantation (LDLT).

2. Materials and methods

From September 2012 to March 2013, a total of 63 adult-to-adult LDLTs were performed at our institute of China Medical University Hospital, Taichung, Taiwan. After obtaining approval from the Institutional Review Board, all 63 recipients were included in the retrospective analysis. All patients were monitored for their coagulation profile using rotation thromboelastometry (ROTEM, Tem Innovations GmbH) during the transplant surgery regularly at the following points: preoperative baseline, 5 minutes, 30 minutes, and 120 minutes, respectively, after reperfusion of the liver graft. Additional blood samples were collected to perform the ROTEM analysis at any point of time if the clinical differential diagnosis required more sampling. Rotem in-TEM (composition: partial thromboplastin phospholipid) and Rotem ex-TEM (composition: recombinant tissue factor and phospholipids) tests were checked routinely in every blood sample to evaluate the intrinsic and extrinsic coagulation pathways. The Rotem ap-TEM (composition: Aprotinin) test was added at the point of reperfusion of the liver graft.
graft, 5 minutes after we observed hyperfibrinolysis which occurred at this period.

3. Results

A total of 84.13% (n = 53) of the studied cohort revealed hyperfibrinolysis using the Rotem ex-TEM test in reperfusion of the liver graft at 5 minutes (Fig. 1). The blood samples of reperfusion at 5 minutes were evaluated using the Rotem ap-TEM test at the same time. The hyperfibrinolysis was not observed when plasmin inhibitor (aprotinin) was added (Fig. 1). The hyperfibrinolysis that occurred in 53 of the studied recipients was reversed to normal pattern after 30 minutes of reperfusion. Transfusion or any other additional management were not required in any of the recipients (Fig. 1). No significant bleeding diathesis was observed during this period.

4. Discussion

According to the results of the Rotem ex-TEM and Rotem ap-TEM tests, the hyperfibrinolysis of our cases in reperfusion of the liver graft has been attributed to the increased activity of plasmin. The aprotinin in Rotem ap-TEM inhibited the fibrinolytic process of plasmin and reversed the phenomenon.

After reperfusion of the graft, transient coagulopathy often results that may be due to a decrease in coagulation factor levels, a sudden increase in tissue plasminogen activator (tPA), thrombocytopenia, and fibrinolysis, and a moderate increase in fibrin degradation products. Although, the exact mechanism of the increased fibrinolytic activity during the reperfusion of the liver graft remains obscure, it is thought to be due to increased tPA levels in the anhepatic phase due to lack of hepatic clearance and its enhanced release after reperfusion. Other observations had pointed out that the hyperfibrinolysis was most pronounced during

![Thromboelastograph change during intraoperative course](#)

**Fig. 1.** Thromboelastograph change during intraoperative course. The time of clot formation in minutes is plotted on the x-axis. The amplitude of the clot firmness in mm is plotted on the y-axis. **Aptem** – the APTEM assay of rotation thromboelastometry (ROTEM, Tem Innovations GmbH); Over 80% of cases (53/63 patients) revealed fibrinolysis after reperfusion of the graft and the condition was reversed after 30 minutes without any management. No significant bleeding tendency was observed during this period in all of the cases; **Extem** – the EXTEM assay of rotation thromboelastometry (ROTEM, Tem Innovations GmbH); **Intem** – the INTEM assay of rotation thromboelastometry (ROTEM, Tem Innovations GmbH).
the anhepatic phase of surgery. However, in our study cohort we did not encounter any increased fibrinolytic activity during the anhepatic phase. We had performed the Rotem analysis during the anhepatic phase in the first 20 recipients and no fibrinolysis was observed. However, fibrinolytic activity was transiently increased during the reperfusion phase as demonstrated by the ROTEM study that recovered without any additional management. This finding can be correlated with our short anhepatic phase which was < 30 minutes in all the studied patients. Our outflow reconstruction methods and variations are previously discussed. For the recipient, we employed a continuous single running suture during the anhepatic phase of surgery.4 However, in our study cohort we did not encounter any increased anticoagulant therapy in recipients before and after reperfusion to avoid such complications, many centers prefer to use anticoagulant therapy in recipients before and after reperfusion to minimize vascular complications. To avoid such complications, many centers prefer to use anticoagulant therapy in recipients before and after reperfusion to minimize vascular complications. Hence, coagulation profiles should be meticulously scrutinized intraoperatively. However, in our study cohort we did not use the anticoagulation and/or apro- tinin therapy.

The transient hyperfibrinolysis evidenced in our study during reperfusion was dealt with through observations without any additional treatment and the coagulation profile was checked at intervals to note any major swings. The thromboelastographs had no significant differences when compared with 30 minutes and 120 minutes after reperfusion of the liver graft.

In conclusion, the result of thromboelastographs can be correlated clinically with intraoperative events. The hyperfibrinolysis that we observed in the reperfusion phase is usually transient in nature and no additional therapy is needed. However, repeated coagulation profile checks using ROTEM are mandatory to ensure normalization of coagulation profiles. However, if hyperfibrinolytic states persist longer leading to increased intraoperative blood loss, administration of antifibrinolytic agents is necessary taking due care of any possible vascular complications.

Acknowledgments

This work was supported by research grants from the China Medical University Hospital (DMR-95-057).

References