Management of acute-on-chronic liver failure: rotational thromboelastometry may reduce substitution of coagulation factors in liver cirrhosis

With great interest we have read the manuscript by Angeli *et al*,[1] demonstrating development of acute-on-chronic liver failure (ACLF) as an accurate predictor for mortality in hospitalised patients with decompensated liver cirrhosis. The authors show that assessment of the chronic liver failure-sequential organ failure assessment (CLIF-SOFA) score improves prognostic accuracy and is superior to the acute kidney injury (AKI) classification, when taken at 48 h after hospitalisation. Patients with acutely decompensated cirrhosis are in a severe condition and the manuscript shows that mortality is extremely high in patients with ACLF grade 3 (three or more organ failures). In a previous study, Reiberger *et al*[2] showed that therapy with β-blockers for variceal bleedings can effectively reduce decompensation of liver cirrhosis. Though, not all patients respond to this treatment. We would like to add a small contribution, which may improve management of these difficult to treat patients at high risk.

One major difficulty in clinical management of patients with cirrhosis is impaired coagulation and consequently the risk for bleeding.[2 3] Indeed, one of the potential causes of AKI in the study of Angeli *et al* was volume depletion due to GI bleeding (ref. 1, table 3). Moreover, the authors demonstrated that hypovolemic shock (ref. 1, table 6) was the cause of death in 16% of the patients with ACLF. Thus, bleeding and impaired coagulation seem to contribute significantly to the prognosis of patients with acutely decompensated liver cirrhosis. In these patients, even minor interventions may constitute a significant risk due to increased bleeding diathesis. This is usually corrected for by administering coagulation factors to adjust classical parameters of coagulation to certain threshold values (ie, 50×10^9 platelets/L or prothrombin time of 50%).[4] Though, transfusion of coagulation factors is costly and may also induce complications as portal vein thrombosis and other thrombotic events. To improve clinical management of patients with advanced cirrhosis in our centre, we employed rotational thromboelastometry (RTE) to assess coagulopathy, in addition to classic parameters prior minimally invasive procedures (MIPs). We were already able to show that this method can improve management in a surgical setting.[5] Demographic and clinical baseline data of the 37 recruited patients with advanced cirrhosis and coagulopathy according to conventional parameters (international normalised ratio, INR >1.5 or platelet counts $<50\times10^9$/L) are given in table 1. Supplementation of coagulation factors (prothrombin complex concentrates (PCCs), fresh frozen plasma (FFP) and fibrinogen) was performed according to an algorithm based on RTE measurements and MIPs were conducted as clinically indicated. No adverse events related to the MIPs or bleeding complications were observed. Moreover, no thrombotic complications occurred. The amount of coagulation factors which would have been supplemented according to conventional parameters was calculated and compared with the actually transfused coagulation factors. As RTE detected a deficit of fibrinogen, more fibrinogen (16 g vs 2 g, figure1B) was transfused than it would have been, based on conventional

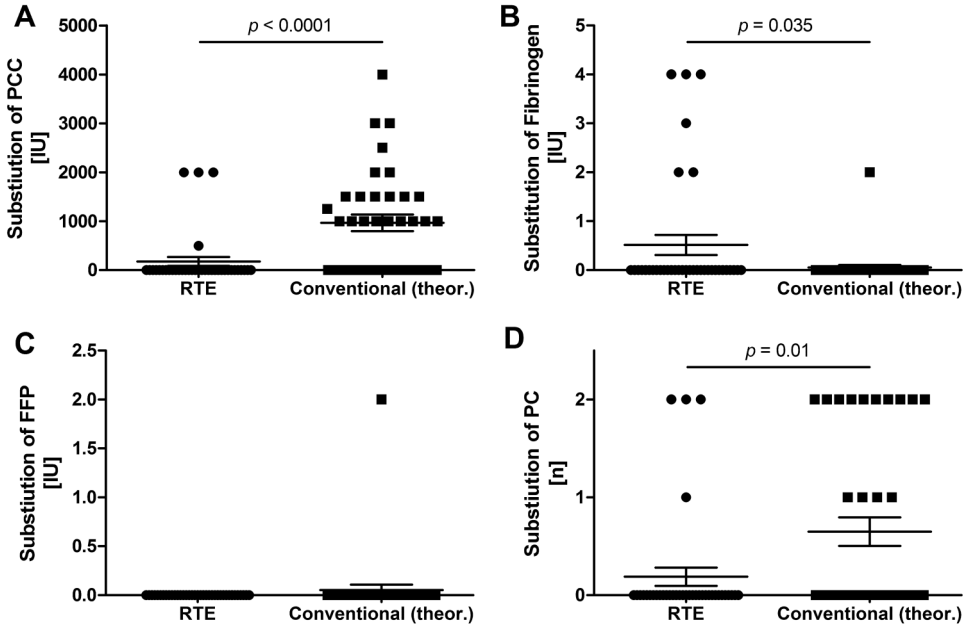

Figure 1 Savings of coagulation factors due to rotational thromboelastometry (RTE) guided transfusion. Depicted are the amounts of actually substituted coagulation factors based on RTE measurements and amounts that would have been substituted under a regime of conventional assessment/transfusion protocols. Significant reduction was achieved for prothrombin complex concentrates (PCCs; A) and platelet concentrates (PCs; D). Fibrinogen was substituted in significantly more cases by the RTE-guided protocol than under conventional assessment (B), while no difference was found for substitution of fresh frozen plasma (FFP; C). IU, international units.

coagulation assessment. In contrast, much less PCC (6500 IU vs 35 750 IU; figure 1A) and FFP (0 vs 2 units; figure 1C) were transfused than under a conventional regime. Since it is already difficult to manage patients with advanced cirrhosis, especially in situations of ACLF, every option to reduce potential causes for complication (ie, prophylaxis of variceal bleeding) should be evaluated. In the described cohort, supplementation of coagulation factors according to RTE assessment of coagulopathy significantly reduced transfused coagulation factors compared with conventional methods. This procedure was not associated with any bleeding or thrombotic complications and reduced effective cost in patient management, releasing resources for other measures. We hope to stimulate further study of this topic and encourage other hepatological centres to adopt this procedure for improved safety of patients and improvement of economic strain on the healthcare system.

Table 1 Demographic and clinical parameters of patients with LC

Parameter	LC with RTE (n=37)	Normal range
Age (years)	54.4±1.9 (25–76)	
Sex (male/female)	25/12	
BMI (kg/m^2)	26.4±0.8	
MELD	18.1±1.4	
Child-Pugh points	8.1±2.3	
INR	1.59±0.07	
aPTT (s)	38.5±2.0	24.4–32.4
TPT (%)	51.5±3.58	70–130
Fibrinogen (mg/dL)	197.6±17.3	200–400
Platelets (n/L)	102.8×10^9±22.3×10^9	140–320
Bilirubin (mg/dL)	5.7±1.1	0.3–1.2
Serum creatinine (mg/dL)	1.4±0.2	0.67–1.17

aPTT, activated partial thromboplastin time; BMI, body mass index; INR, international normalised ratio; LC, liver cirrhosis; MELD, model for end-stage liver disease; RTE, Rotational thromboelastometry; TPT, thromboplastin time.

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Competing interests SB, J-PS, GG, FHS and AC declare that they have no competing interests in the research.

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