# "Periprocedural management of abnormal coagulation parameters and thrombocytopenia in patients with cirrhosis: Guidance from the SSC of the ISTH"

Roberts, Lara N.; Lisman, Ton; Stanworth, Simon; Hernandez-Gea, Virginia; Magnusson, Maria; Tripodi, Armando; Thachil, Jecko

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# "Periprocedural management of abnormal coagulation parameters and thrombocytopenia in patients with cirrhosis: Guidance from the SSC of the ISTH": Reply

We thank Hartmann and colleagues for their interest in this guidance document and for highlighting their further work with viscoelastic testing (VET) in patients with cirrhosis.[1] We agree the data presented suggest significant reductions in plasma and platelet transfusion for this patient group compared with inappropriate use of conventional hemostatic parameters to guide prophylactic blood component transfusion. However, it is important to acknowledge the limitations of VET in the evaluation of hemostasis in patients with cirrhosis. In particular, VET is insensitive to both protein C and von Willebrand factor (VWF), and therefore is unable to measure the 'rebalancing' effect of reduced protein C on reduced procoagulants or increased VWF on thrombocytopenia.[2]

Hartmann and colleagues suggest that multiple randomized controlled trials in patients with cirrhosis and gastrointestinal bleeding or undergoing liver transplantation, along with meta-analyses of five to seven studies involving 300 patients provide 'high quality' evidence supporting the use of VET to reduce transfusion requirements.[1] We contest this assertion and maintain there is currently low quality evidence for VET to guide transfusion in the periprocedural setting due to the limitations of the included studies. These limitations include the use of unvalidated thresholds for transfusion with VET, variable inclusion of low risk procedures, variable definition of the standard of care comparator, the lack of a 'no intervention' arm in all but one of these studies,[3] and most significantly, the lack of clinical endpoints along with only two of the seven studies considered as low risk of bias.[4]

A large observational cohort of 700 patients with cirrhosis undergoing liver transplantation demonstrates major surgery can be safely performed without transfusion to correct abnormal hemostatic parameters,[5] and published guidance supports this approach in the perioperative setting.[6] The single study evaluating a restrictive transfusion strategy in comparison to transfusion guided by VET or standard laboratory tests was performed in patients undergoing central venous catheterization (a low bleeding risk procedure). Whilst this study was underpowered to evaluate clinical outcomes (with no major bleeding events), it clearly demonstrates a restrictive approach is most effective in reducing blood component transfusion (OR 0.09, 95% CI 0.01 to 0.56 compared with the VET-guided arm), with superior cost effectiveness.[3] As the majority of procedures performed in patients with cirrhosis have a low bleeding risk, the routine use of VET will result in significant unnecessary blood component transfusion. Indeed, in the aforementioned study, 43% of participants received plasma in the VET-guided arm. Additionally, the larger of the two liver transplantation studies cited by Hartmann and colleagues reported a significant increase in the use of fibrinogen replacement (73% vs. 29%) with a VET-guided transfusion strategy.[7] Observational studies have also noted increased cryoprecipitate use with VET in liver transplantation, with a corresponding associated increase in thrombotic complications.[8] Importantly, a large retrospective study on cryoprecipitate use in patients who are critically ill with cirrhosis demonstrated no benefit on bleeding or mortality.[9] Furthermore, whilst the two RCTs in patients undergoing endoscopy of gastrointestinal bleeding demonstrated reduced use of plasma with VET, this is a low-risk procedure where centers adopting an evidence-based approach would not offer periprocedural plasma, particularly in view of the association between plasma transfusion and further increases in portal venous pressure. Recently updated EASL guidance and Baveno consensus recommended against the use of plasma in this setting due to the potential for fluid overload and worsened portal hypertension.[10,11] Hence we support the research recommendations proposed by these bodies for large prospective observational studies to clearly document the incidence of periprocedural bleeding, and for randomized controlled trials in high bleeding risk procedures to evaluate the impact of interventions (including VET) on clinically important outcomes such as bleeding and mortality, incorporating a restrictive transfusion strategy in which prophylactic transfusions are avoided and blood products are only administered when bleeding occurs as a comparator. Supporting the use of VET without such evidence risks continued unnecessary blood component use, with potential patient harm, and further perpetuates the dogma of abnormal hemostatic markers reflecting a bleeding tendency in patients with cirrhosis, rather than the severity of liver disease.

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## AUTHOR CONTRIBUTIONS

LNR and TL drafted the manuscript; all other authors provided intellectual input for revisions of the draft and approved the final version of the manuscript.

## CONFLICT OF INTEREST

We have no conflicts of interest to report.

Lara N. Roberts[1]
Ton Lisman[2]
Simon Stanworth[3]
Virginia Hernandez-Gea[4]
Maria Magnusson[5]
Armando Tripodi[6]
Jecko Thachil[7]

[1]*King's Thrombosis Centre, Department of Haematological Medicine, King's College Hospital, London, UK*
[2]*Surgical Research Laboratory and Section of Hepatobiliary Surgery and Liver Transplantation, Department of Surgery, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands*
[3]*Transfusion Medicine, NHS Blood and Transplant, Department of Haematology, Oxford University Hospitals, NHS Foundation Trust, Radcliffe Department of Medicine, University of Oxford and NIHR Oxford Biomedical Research Centre (Haematology), Oxford, UK*
[4]*Barcelona Hepatic Hemodynamic Laboratory, Liver Unit, Hospital Clínic, IDIBAPS, Red de Enfermedades Hepáticas y Digestivas (CIBEREHD), Health Care Provider of the European Reference Network on Rare Liver Disorders (ERN-Liver), University of Barcelona, Barcelona, Spain*
[5]*Clinical Chemistry and Blood Coagulation Research, MMK, Department of Pediatrics, CLINTEC, Karolinska Institutet, Department of Hematology, Karolinska University Hospital, Stockholm, Sweden*
[6]*IRCCS Ca' Granda Maggiore Hospital Foundation, Angelo Bianchi Bonomi Hemophilia and Thrombosis Center and Fondazione Luigi Villa, Milano, Italy*
[7]*Department of Haematology, Manchester Royal Infirmary, Manchester, UK*

**Correspondence**
Lara N. Roberts, King's Thrombosis Centre, Department of Haematological Medicine, King's College Hospital, Denmark Hill, London SE5 9RS, UK.
Email: lara.roberts@nhs.net

## ORCID

*Lara N. Roberts* https://orcid.org/0000-0003-3871-8491
*Ton Lisman* https://orcid.org/0000-0002-3503-7140
*Simon Stanworth* https://orcid.org/0000-0002-7414-4950
*Virginia Hernandez-Gea* https://orcid.org/0000-0001-7937-984X
*Maria Magnusson* https://orcid.org/0000-0001-5388-6608
*Armando Tripodi* https://orcid.org/0000-0003-1602-2776
*Jecko Thachil* https://orcid.org/0000-0001-7218-0993

## TWITTER

*Lara N. Roberts* @LaraNRoberts1

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