Von Willebrand factor as a predictor of mortality in acute-on-chronic liver failure

Lisman, Ton; van den Boom, Bente P.; Bernal, William; Patel, Vishal C.

Published in:
Liver International

DOI:
10.1111/liv.15820

Received: 4 December 2023 | Accepted: 4 December 2023

DOI: 10.1111/liv.15820

Liver INTERNATIONAL WILEY

LETTER TO THE EDITOR

Von Willebrand factor as a predictor of mortality in acute-on-chronic liver failure: Do not throw out the baby with the bathwater

Von Willebrand factor (VWF) has been identified as a marker of portal hypertension and as a reliable predictor of mortality in patients with cirrhosis. The predictive value of VWF for mortality may result from a combination of local endothelial cell activation by portal hypertension, and systemic endothelial cell activation because of systemic inflammation.

We recently reported that VWF levels are associated with mortality in 111 patients with acute decompensation of cirrhosis and in 106 patients with acute-on-chronic liver failure (ACLF).[1] These results align with a smaller study by Prasanna and coworkers in 50 patients.[2] Zanetto and coworkers now report a study of 51 patients in whom VWF levels are not associated with outcome.[3]

We concur with Zanetto and coworkers that a difference in methodology to assess VWF levels may underly discrepancies between studies. Indeed, both Prasanna and we used enzyme-linked immunosorbent assays (ELISA). Although it has been well established that ELISA results are interchangeable with test results on automated coagulation analysers for diagnosis of von Willebrand disease,[4] to our knowledge both assay types have not been extensively compared in samples with high VWF levels.

Another difference between both studies regards the mortality among patients with ACLF grade 3, which was substantially higher in our study (82% vs. 53%), whereas overall mortality in ACLF patients was comparable (32% vs. 29%). Importantly, both studies and the study by Prasanna and coworkers found VWF levels in ACLF grade 3 patients to be higher compared to VWF levels in ACLF grade 1 and 2 patients. Notably, the mortality in grade 3 ACLF patients in the Prasanna study was 63%.

In aggregate, VWF levels are substantially elevated in patients with ACLF, with higher values in grade 3 compared to grade 1/2 patients. The lack of an association between VWF levels and outcome in the Zanetto study may reflect differences in patient selection and/or VWF analysis methodology. Notwithstanding the negative result of the Zanetto study, we feel there is merit in further assessing VWF levels as a biomarker that associates with outcome as there is abundant data on the predictive value of VWF in patients with cirrhosis that are not critically ill,[5] and there is a clear biological explanation for the potential predictive value of VWF for outcome in these patients.[1] We, therefore, strongly encourage research in this area, evolving towards larger, multicentre cohorts of well-clinically phenotyped patients using uniform assay methodology.

FUNDING INFORMATION

None.

CONFLICT OF INTEREST STATEMENT

The authors do not have any disclosures to report.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Ton Lisman[1]
Bente P. van den Boom[1]
William Bernal[2]
Vishal C. Patel[2,3,4]

[1]*Surgical Research Laboratory and Section of Hepatobiliary Surgery and Liver Transplantation, Department of Surgery, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands*
[2]*Institute of Liver Studies & Transplantation, King's College Hospital, NHS Foundation Trust, London, UK*
[3]*The Roger Williams Institute of Hepatology, Foundation for Liver Research, London, UK*
[4]*Liver Sciences, School of Immunology & Microbial Sciences, Faculty of Life Sciences and Medicine, King's College London, London, UK*

Correspondence
Ton Lisman, Surgical Research Laboratory and Section of Hepatobiliary Surgery and Liver Transplantation, Department of Surgery, University of Groningen, University Medical Center Groningen, BA44, Hanzeplein 1, 9713 GZ, Groningen, The Netherlands.
Email: j.a.lisman@umcg.nl

ORCID

Ton Lisman https://orcid.org/0000-0002-3503-7140
Bente P. van den Boom https://orcid.org/0000-0003-3793-4176
William Bernal https://orcid.org/0000-0002-6508-3287
Vishal C. Patel https://orcid.org/0000-0001-6616-3628

REFERENCES

1. van den Boom BP, Stamouli M, Timon J, et al. Von Willebrand factor is an independent predictor of short-term mortality in acutely ill patients with cirrhosis. *Liver Int*. 2023;43(12):2752-2761.
2. Prasanna KS, Goel A, Amirtharaj GJ, et al. Plasma von Willebrand factor levels predict in-hospital survival in patients with acute-on-chronic liver failure. *Indian J Gastroenterol*. 2016;35(6):432-440.
3. Zanetto A, Campello E, Bulato C, Simioni P. von Willebrand factor does not predict short-term mortality in ACLF. *Liver Int*. 2023; in press. doi:10.1111/liv.15802
4. Favaloro EJ. Navigating the myriad of von Willebrand factor assays. *Hamostaseologie*. 2020;40(4):431-442.
5. Eidelberg A, Kirubakaran R, Nair SC, Eapen CE, Elias E, Goel A. Systematic review: role of elevated plasma von-Willebrand factor as predictor of mortality in patients with chronic liver disease. *Eur J Gastroenterol Hepatol*. 2019;31(10):1184-1191.