Acquired von Willebrand syndrome during mechanical circulatory support and extracorporeal membrane oxygenation: rapid onset and the demand for Point of Care Testing

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Introduction

Bleeding episodes are frequently observed in patients being treated with mechanical circulatory support (MCS) and extracorporeal membrane oxygenation (ECMO). Acquired von Willebrand syndrome (avWS) is caused by high shear stress inside ECMO and MCS and contributes to the ECMO- and MCS-associated coagulopathy (1,2). avWS is characterized by loss of high molecular weight multimers of von Willebrand factor (vWF) and decreased collagen binding to vWF. avWS can be diagnosed using vWF multimer analysis, and by assesment of vWF levels and function. However, these diagnostic methods are elaborate and can not provide quick results during acute bleeding. In this study we analyzed the management of MCS- and ECMO patients with suspected avWS with the aim to optimize diagnostic and therapeutic options.

Methods

Two groups of intensive care patients, who suffered from severe cardiovascular or respiratory failure and who were treated with either vvECMO, vaECMO or impella left ventricular assist devices were included in this study. In the first group 13 patients were retrospectively analysed. In these patients avWS had been suspected during the clinical course due to bleeding episodes on median day 6 of ECMO/impella treatment. vWF multimers had been measured in a specialized clinical laboratory using vWF multimer analysis to verify potential avWS.

In group two 11 patients were prospectively analyzed for the development of avWS during ECMO and impella treatment over time and to evaluate the potential of different diagnostic modalities. vWF-antigen and vWF:CBA were measured in a specialized clinical laboratoy. vWF multimers were measured using 1% agarose gel electrophoresis in blood samples of these patients before and 1h, 24 h and 48 h after device implantation.

Representative example of vWF-multimer analysis of a patient treated with vvECMO

Std: Standard human plasma

* HMW: High Molecular Weight multimers

Results

Patient characteristics

Group 1 – median age = 63 years		vvECMO (n=4)	vaECMO (n=5)	vaECMO + impella (n=3)	LVAD (n=1)
gender	w	3	1	2	1
	m	1	4	1	0
SOFA-Score		13	12	11	10

Hb-relevant bleeding occurred in all patients:

Group 1 bleeding	vvECMO	vaECMO	vaECMO+Impella	LVAD
intracranial	2	2		1
epistaxis		2	1	
Gastrointestinal		2	1	
catheters	2	3	1	1
Pulmonary		1	2	
hematothorax		1		1
retroperitoneal	1			
Perikardial effusion	1	2	1	

Bleeding in combination with thrombosis/embolism:

- 1x cardiac apex thrombus, 1x pulmonary embolism, 1x embolism of the
- A. femoralis

Average application of blood and coagulation products / patient in group 1

- Retrospective confirmation of avWS in 12/13 group 1 patients due to vWF multimer analysis.
- During the initial bleeding phase, when results of vWF multimer analysis were not yet available, calculated treatment with vWF and/or vWF/FVIII concentrates was performed in 10/13 patients. DDAVP was administered in 5/13 patients.

Patient characteristics

Group 2 – median age = 52 years		vvECMO (n=8)	vaECMO (n=2)	impella (n=1)
gender	w	6	1	0
	m	2	1	1
SOFA-Score		13	9	17

- In group 2 all patients developed avWS according vWF multimer analysis during 48 hours-this has been confirmed by the CBA/vWF ratio in all but one patients
- This was associated with Hb-relevant bleeding in 50% of these patients

Conclusion

avWS is a significant clinical problem, which can lead to Hb-relevant bleeding in intensive care patients being treated with ECMO and MCS. Due to heterogeneity of von Willebrand's disease and assay limitations, none of the currently available laboratory procedures is sufficient to diagnose avWS rapidly during acute bleeding. Therefore, avWS-specific blood product application cannot be guided sufficiently. Consequently, a Point of Care Test should be developed to improve early diagnosis and specific treatment of avWS.

Literature

- (1) Heilmann, Claudia, et al. "Acquired von Willebrand syndrome in patients with extracorporeal life support (ECLS)." *Intensive care medicine* 38.1 (2012): 62-68.
- (2) Kalbhenn, Johannes, et al. "Acquired von Willebrand syndrome and impaired platelet function during venovenous extracorporeal membrane oxygenation: Rapid onset and fast recovery." *The Journal of Heart and Lung Transplantation* (2018).