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INVITED COMMENTARY

Because hemostasis and thrombosis share many of the same mechanisms, conventional wisdom dictates that the bleeding patient is at less risk for thromboembolism. However, ventricular assist device (VAD) recipients are often plagued by both of these events simultaneously [1]. Unfortunately, the tools to investigate this paradox of bleeding patients with clotted pumps are lacking because clinically available assays of coagulation are mostly ineffective at predicting bleeding or thromboembolism during VAD support.

To address this knowledge deficit, Steinlechner and colleagues [2] assessed coagulation and platelet function in 12 VAD patients, focusing their attention on von Willebrand factor (vWF), a multimeric protein that promotes hemostasis by facilitating platelet adhesion at the site of vascular injury. Because of its large size, vWF is uniquely responsive to cleavage under shear stress. An optimum size distribution between ultralarge vWF and smaller forms results from initial endothelial secretion balanced against subsequent intravascular cleavage. Prior groups have hypothesized that shear stress within the VAD promotes excessive vWF cleavage, thus altering

this balance and contributing to the risk of bleeding [3]. In this study, Steinlechner and colleagues demonstrated qualitative defects in vWF function (ie, abnormal platelet response to shear stress in the PFA-100 assay, reduced aggregation in response to ristocetin) as well as a deficiency of the high-molecular-weight multimers of vWF on Western blot analysis during VAD support.

Although these data add credence to an important hypothesis, a pathophysiologic link to either the presence of the VAD or the risk of postoperative bleeding was unable to be established in this small cohort, making the clinical significance of the findings unclear. A comparison group (eg, patients after heart transplant) would have been helpful to discriminate the confounding effects of chronic inflammation in postoperative patients, or the effects of diffuse atherosclerosis and multiple antithrombotic therapies on these hematologic assays. Establishing the relationship of a single variable to an adverse event such as bleeding is extremely challenging in small cohorts because of variations in baseline characteristics, response to surgical intervention, and postoperative management. This limitation was one of the reasons that

the National Heart Lung and Blood Institute funded a multicenter registry of VAD patients, the Interagency Registry for Mechanical Assisted Circulatory Support (INTERMACS) [4]. All registry enrollees are monitored for the need to reoperate for bleeding or to give transfusions. In addition, serum samples are routinely collected in the perioperative period and archived for future analysis. Therefore, this study is uniquely positioned to establish the link between defects in vWF or a variety of other inflammatory and hematologic pathways and the risk of bleeding during VAD support.

Although outcomes after VAD implantation have significantly improved during the last decade, bleeding episodes remain a serious complication that cannot be explained by the individual anticoagulation regimen alone in many cases. Perhaps through collaboration with the INTERMACS registry, the Steinlechner investigators may be poised to elucidate a relationship of vWF to bleeding and provide insight about the optimal device design and the utility of potential management strategies such as tranexamic acid, desmopressin, VWF-factor VIII concentrate, and recombinant factor VIIa.

Robert Poston, MD

*Division of Cardiac Surgery
Boston University
88 E Newton, Robinson 402
Boston, MA 02118
e-mail: robert.poston@bmc.org*

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