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EDITORIAL COMMENTARY

A new spin on acquired von Willebrand factor deficiency during continuous-flow left ventricular assist device support

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See related article on pages 281-9.

In their article in this issue of the *Journal of Thoracic and Cardiovascular Surgery*, Bartoli and associates¹ have created a simple in vitro model that mimics left ventricular assist device (LVAD) shear forces to study the mechanisms of breakdown of von Willebrand factor (vWF). The effects of shear force and nonpulsatile blood flow in the setting of severe aortic stenosis have long been recognized to lead to formation of gastrointestinal arteriovenous malformations² and an acquired deficiency of vWF.³ In patients supported by continuous-flow LVADs who require aspirin and warfarin therapy to minimize the odds of device thrombosis, this pathophysiologic combination creates a difficult clinical scenario to navigate. Furthermore, a recently observed increase in early pump thrombosis⁴ has heightened concerns regarding balancing the risks of bleeding and thrombosis.

In this study, Bartoli and associates¹ demonstrated that the pattern of vWF breakdown into multimers, monomers, and partial fragments seen in the blood of patients with LVADs matches that seen in the blood of healthy volunteers after 4 hours in a vortexer. After validating the vortexer as an in vitro model for an LVAD, they conducted a series of

experiments in which they demonstrated shear force leads to breakdown of large-molecular weight vWF into smaller but functional polymers. In contrast, shear in combination with a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13 (ADAMTS-13), the vWF-cleaving metalloprotease, leads to a greater degree of breakdown and fragmentation of monomers, which matches the pattern seen in LVAD-supported patients. These fragments and monomers are not active, leading to vWF deficiency. Furthermore, shear force was observed to increase the activity of ADAMTS-13, thereby amplifying its effect on vWF breakdown. The implication is that pharmacologic antagonism of ADAMTS-13 may restore function of vWF. This is an easily tested hypothesis because of the simplicity of this model.

A well-known antagonist of ADAMTS-13 is doxycycline. Although prevention of infection would be a beneficial side effect of its use, it would be unwise to put this into clinical use before adequate confirmation first in the vortexer model then prospectively in a clinical trial. It is possible that acquired vWF deficiency is protective with regard to pump thrombosis and that alteration of this hematologic balancing act might be harmful.

The simplicity of this model is what makes it ingenious. Vortexers are ubiquitous in research laboratories worldwide. This model allows relatively quick and inexpensive experimentation that might have otherwise required significant time, laboratory animals, human subjects, or spare or salvaged LVADs. It is hoped that more valuable information will follow.

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