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EDITORIAL COMMENTARY

You can't get there from here without more robust data

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See related article on pages 3119-25.

Fiore and colleagues¹ report variability in the effectiveness of aspirin as a platelet-inhibitor measured by light-transmission aggregometry in patients after HeartMate II (Thoratec Corp, Pleasanton, Calif) ventricular-assist device (VAD) implantation. Like many centers performing VAD surgery, the investigators used a vitamin K pathway inhibitor to achieve an international normalized ratio of 2 to 3 along with oral aspirin to prevent thromboembolism. The clinical issue this study addresses is the value of platelet light-transmission aggregometry (LTA) for assessing the effectiveness of platelet inhibition by aspirin in patients with an axial VAD and reflects a long-standing need.²

Resistance to aspirin and anticoagulation management in patients with VAD are unresolved issues open to differing interpretation.³ Several factors drive local anticoagulation practices, including device type, pump flow, coagulation measurements used, and past experience. Tailoring anticoagulation to individual patients relies on having a measure or measures of anticoagulant effectiveness that are highly

associated with important patient outcomes. The clinical problem is complicated by uncertainty regarding which therapeutic targets to use to measure the multifaceted components of the coagulation cascade in patients with VAD.⁴ It is further complicated by temporal variation in coagulation status, from immediate postoperative coagulopathy to the procoagulant environment that is a nearly universal response to VAD placement, in part from VAD-induced loss of high-molecular-weight von Willebrand factor multimers.⁵ Individual variability in aspirin responsiveness, anticoagulant drug metabolism, circulating levels of coagulation factors, platelet count and fibrinolytic activity, and etiologic cardiac disease is seen in patients with a VAD and in cardiac populations and determines coagulation status and response to anticoagulants and antiplatelet agents.^{6,7} This variation predicts a failure of 1-size-fits-all anticoagulation strategies and drives the need for research such as this study to nail down this issue. Further, there is no proven advantage to steering either an anticoagulant or a procoagulant course—both are bad. Embolic stroke is an event feared by patients more than death and the physician response to bleeding is often to reduce the level of anticoagulation, resulting in a greater incidence of embolic events.⁸

This study has potential value for its reliance upon LTA to determine an appropriate long-term aspirin dosing in their patients over a period of more than 8 months but is limited by the small cohort size. The study observations of wide variability in aspirin dose required to achieve platelet inhibition measured by LTA, and that the majority of patients required aspirin doses several times higher than those required to achieve platelet inhibition in ambulatory coronary artery disease² are valuable. Although the authors state that adjustment of aspirin dosing according to LTA reduced the rate of

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bleeding episodes, this was not the case. Eight patients (33%) had a bleeding event and although the authors attempt to link these events to native coagulation dysfunction, the evidence is not convincing in my view. The observed bleeding rate is similar to that reported in larger observational and multicenter studies,⁹⁻¹² and fails to provide convincing evidence for effectiveness of LTA-based adjustment of aspirin dosing. Similarly, 3 of 24 patients experienced a thromboembolic event, an event rate similar to those seen in other HeartMate II registry studies,⁹⁻¹² and these events were seen in setting of optimal therapeutic anticoagulation. This disconnect between adjusting aspirin doses based on LTA measurement of platelet function, and a failure to reduce thromboembolic or bleeding events in their patients is disheartening and does not yet justify use of their proposed clinical algorithm of aspirin dosing based on LTA measurements.

Although ethical issues with randomized trials for established clinical practices complicate research upon optimal anticoagulant and dosing for patients with an axial-flow VAD, there is a critical need for improvement in the still-high rates of bleeding and thromboembolic disease. This article¹ emphasizes the need for clinical trials and a higher standard of registries of bleeding and thromboembolic events in patients with a VAD. To fulfill this need, bleeding and thromboembolic outcome definitions should be more inclusive and be specifically related to anticoagulation status and management. Major bleeding or hemorrhagic outcomes should be broadened from those centered around inpatient events and transfusion,¹² to include information about anticoagulant administration and coagulation testing before and at the time of the event, even if transfusion or rehospitalization are not required. Similarly, when identified, thromboembolic neurologic events should be more completely defined and provide information regarding

anticoagulant administration and coagulation testing. These reporting criteria should be uniformly adopted as a minimum standard to enhance direct comparison of study results.

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