Authors have nothing to disclose with regard to commercial support.

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Reply to the Editor:

We are pleased that our study on cyclic guanosine monophosphate (cGMP) and gastrointestinal (GI) bleeding in recipients of a continuous-flow left ventricular assist device (CF-LVAD)¹ gained interest by Spiliopoulos. Postoperative GI bleeding continues to be a major challenge for recipients of a CF-LVAD.²⁻⁴ We strongly agree with Spiliopoulos' comment that comorbidities at the time of surgery and factors related to the preoperative state such as INTERMACS level, New York Heart Association class, patients' age, history of coronary artery bypass grafting

and dialysis should be carefully considered when selecting patients for CF-LVAD implantation.

However, our goal was to identify biochemical markers of risk in patients who were already carefully selected for CF-LVAD support, and their preoperative state and comorbidities were considered. We focus our investigation on the reason for a higher rate of postoperative GI bleeding events in CF-LVAD recipients compared with preoperative GI bleeding events in patients with heart failure who may be eligible for CF-LVAD. We propose that if cGMP is confirmed prospectively as an important marker, then anticoagulation therapy should be adjusted appropriately. It is important to emphasize that we believe that the cGMP pathway might not be the sole mechanism responsible for the increase in GI bleeding, but that the synergistic effects of several pathways contribute to the increased risk of GI bleeding in CF-LVAD recipients, as noted in the comprehensive editorial commentary by Crestanello.⁵ Thus, we need a deeper understanding of the mechanisms and the complex interactions among them, and to explore future therapeutic targets. Our study makes the important observation that biochemical markers, such as cGMP, may be used to detect those CF-LVAD recipients at the greatest risk for GI bleeding, thereby allowing clinicians to modify the intensity of anticoagulation if possible (Figure 1).

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FIGURE 1. Future research directions should focus on: (1) Strategies to improve patient assessment and selection for continuous-flow left ventricular assist device (CF-LVAD) therapy and (2) the mechanisms of gastrointestinal (GI) bleeding and the complex interactions among them to evaluate the risk for GI bleeding and explore future therapeutic targets.

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