Dr Miceli is a LivaNova consultant.

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REPLY: LOOK DEEPER INTO THROMBOCYTOPENIA

Reply to the Editor:

Transient periprocedural thrombocytopenia is common after biological aortic valve replacement (AVR) regardless of the prosthesis type or implant modality.[1] This phenomenon is more frequent in sutureless and stentless prostheses than in conventional sutured valves.[1] Many hypotheses have been raised, except in some cases of platelet transfusion, thrombocytopenia was never associated with poor outcomes.[2-4] Because it is not clinically relevant, Vendramin and Bortolotti[5] correctly pose the following questions: Do we really need to solve it and why should we still be worried? The Perceval S valve (LivaNova, London, UK) is considered the evolution of the Freedom SOLO (LivaNova) stentless valve, and both valves have been associated with postoperative thrombocytopenia.[2-4] There are 2 major issues that have never been addressed. First, Jiritano and colleagues[6] and my group[7] demonstrated that these valves were also associated with higher mean platelet volume and platelet distribution width compared with other prosthetic valves, indicating possible platelet activation. These platelets might be metabolically and enzymatically more active in comparison with smaller ones because they contain more alpha granules, produce more thromboxane A2, and feature high expression of adhesive glycoproteins.[8] Increased mean platelet volume and platelet distribution width have been identified as risk factors for thrombotic events, such as acute coronary syndromes and ischemic neurologic events.[9,10] To date, no study has investigated the 1-year follow-up of patients undergoing AVR with thrombocytopenia. Second, in the setting of multiorgan failure, thrombocytopenia after surgery might be clinically relevant and associated with worse outcomes.

Thrombocytopenia after surgical AVR is underestimated, and no study has been well designed to look at these issues. My suggestion is to look deeper into this phenomenon.

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REPLY: TRANSIENT THROMBOCYTOPENIA AFTER PERCEVAL S IMPLANTATION: A GOOD REASON TO CONTINUE WITH THE RESEARCH

Reply to the Editor:

We read with interest the letter by Vendramin and Bortolotti[1] regarding transient thrombocytopenia after surgical aortic valve replacement with the Freedom Solo stentless (FSS) prosthetic valve (LivaNova, London, United Kingdom) and with the Perceval S valve (LivaNova, London, United Kingdom). We note that the title of the letter suggests resignation about the enigma of thrombocytopenia because no valid scientific evidence has been demonstrated to date and awareness because, fortunately, transient thrombocytopenia is not associated with poor early prognosis and deleterious effects. Therefore, their question "Do we really need to solve it?" seems appropriate in this context.

In our commentary,[2] we pointed out that Steigmer and colleagues[3] failed to demonstrate statistically significant differences among groups in reoperation for bleeding and the lowest corrected platelet count, even though the worst values were reported for the Perceval S group. As we stated, the main reason for the absence of difference was the small sample size, rather than actual evidence of absence. Indeed, some

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authors[4] have reported significant increased transfusion rate after Perceval S implantation relative to other prosthetic valves, but without differences in terms of major cardiovascular events, whereas other authors[5] have reported no deleterious effects associated with the transient thrombocytopenia. On the basis of these recent results, the question of Vendramin and Bortolotti[1] would be correct.

Michael DeBakey[6] said, "The natural history of science is the study of the unknown. If you fear it, you're not going to study it and you're not going to make any progress." If we were to apply this concept to the Perceval-associated thrombocytopenia, great efforts must be made to fully understand this phenomenon because some potentially deleterious effects are reported in the literature and not fully explained. Having said that, we share the rhetorical question of Vendramin and Bortolotti,[1] but we also find that we deeply share DeBakey's sentiment. There are no studies focusing on the cellular, molecular, and biologic aspects of transient thrombocytopenia after Perceval S implantation. Such studies should be encouraged for better understanding of the biologic mechanism that would enable some useful changes in the device and in clinical practice. Because Steigmart and colleagues[3] compared the pericardial Perceval S valve with 2 other porcine prosthetic valves, Vendramin and Bortolotti[1] speculated that the pericardium itself might unintentionally cause thrombocytopenia. It is right to highlight this hypothesis. Several studies have compared the pericardial FSS or Perceval S with other pericardial prosthetic valves, and transient thrombocytopenia has been reported with significant statistical differences between the 2 models of biologic pericardial prosthesis.

We agree that we should not be so concerned about thrombocytopenia after Perceval S implantation, because it is now established that it does not carry major cardiovascular events. According to the principle that the absence of evidence is not the evidence of absence, however, we cannot overlook this phenomenon, and further large randomized clinical trials and biologic studies should be strongly encouraged. Otherwise, we are "not going to make any progress," as DeBakey[6] said.

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REPLY FROM AUTHORS: THROMBOCYTOPENIA AFTER IMPLANTATION OF A PERCEVAL S AORTIC BIOPROSTHESIS SHOULD BE STUDIED MORE VIGOROUSLY, NOT LESS:

Reply to the Editor:

We thank Vendramin and Bortolotti[1] for commenting on our article "Thrombocytopenia After Implantation of the Perceval S Aortic Bioprosthesis."[2] They criticize the retrospective nature of our study and wonder whether the thrombocytopenia after aortic valve implantation need be studied at all, given the many studies that have stated that postoperative thrombocytopenia is a common phenomenon with no apparent clinical consequences.

We do understand the critique regarding the retrospective design. When we started our investigation, however, there was not a single report linking the Perceval S aortic bioprosthesis (LivaNova PLC, London, UK) with postoperative thrombocytopenia. Because we had already stopped implantation of the Perceval S aortic bioprosthesis for other reasons at that time, we had no opportunity to do a prospective study. Unfortunately, we were not very fast in gathering the data, analyzing it, and submitting a manuscript.