Authors have nothing to disclose with regard to commercial support.

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TRANSCATHETER AORTIC VALVE REPLACEMENT IN INTERMEDIATE-RISK PATIENTS

Reply to the Editor:

We appreciate the letter by Benedetto and Uva regarding our study comparing use of the Sapien 3 Transcatheter Aortic Valve (TAV) (Edwards Lifesciences, Inc, Irvine, Calif) in intermediate-risk patients with results of patients undergoing surgery in the Placement of Aortic Transcatheter Valves 2 randomized trial.^{1,2}

The authors are completely correct that a propensity score analysis does not replace or compare with a true randomized trial, although the authors have commonly used propensity score matching in their own research endeavors. Furthermore, we agree that observational studies by nature are more prone to selection bias and cannot be equated to randomized trials. However, propensity score analysis is not trying to make apples into oranges or compare them, rather it is trying to make 2 fruit salad bowls have roughly equal proportions of apples, oranges, and pears so that they may taste similar and be comparable to a discerning palate. The authors note that the major challenge to observational studies is their vulnerability to selection bias and that despite statistical adjustments, including propensity scores (ie, analysis), apples and oranges will never be the same. The authors note that the 2 enrollment periods of the 2 cohorts were different (mainly 2011 and 2012 for the surgical aortic valve replacement [SAVR] cohort and 2014 for the Sapien 3 cohort), and this might have translated

into different patterns of practice, including improvement in case selection. We argue that absolutely nothing changed in the performance of SAVR from 2012 to 2014. If analysis compared TAV replacement (TAVR) with SAVR from the 1970s, then the authors would have a valid argument; but that is not the case in this analysis. Furthermore, patients undergoing TAVR and SAVR had an almost identical case selection committee, inclusion and exclusion criteria, event adjudication committee, echocardiographic core laboratory, and clinical sites (to keep 2 two fruit salads tasting roughly the same).

We also pose a question to the authors: When a new version of SAVR valve is introduced for clinical use, is a randomized trial performed to show superiority? No. In the past 12 years, more than 4 new surgical valves have been introduced worldwide with none of them approved or used widely under the auspices of a randomized trial. A retrospective analysis or prospective single-arm registry was performed and reported.

The authors argue that the surgical group was defined according to the as-treated principle, potentially including the higher-risk subgroup of patients initially allocated to TAVR who received surgery, biasing the results in favor of TAVR. A close look at Figure 1 in the article by Thourani and colleagues² demonstrates that this is not true. From the patients who were randomly allocated to surgery in the Placement of Aortic Transcatheter Valves 2A trial, 68 patients withdrew before treatment, 4 were ineligible due to aortic calcification, and 5 died before treatment, leaving 944 patients (ie, the as-treated group who initiated surgery). None of these patients were TAVR patients who received surgery. The reason for choosing this group was to compare TAVR using a Sapien 3 valve with patients who actually received SAVR, rather than patients who did not undergo a procedure whatsoever. The median Society of Thoracic Surgeons score was 5.2% in the TAVR group and 5.4% in the SAVR group. The authors note the statistically different Society of Thoracic Surgery scores between the 2 groups as a significant limitation. We used propensity score analysis to address and adjust for this and other differences between the groups.

The authors question how a small change like adding a skirt to the Sapien 3 valve can translate into hard clinical end points. The authors should consider in addition to the skirt a more reliable positioning and deployment of the Sapien 3 valve due to the balloon inflation mechanism; the more maneuverable delivery system, which minimizes interaction with the aortic wall and aids in coaxial positioning; and smaller sheaths through which the valve can be introduced, leading to nearly 90% use of the transfemoral route. One can imagine that the so-called simple addition of a skirt, which reduces paravalvular leak, may lead to decreased need for dilation of the valve, with implications related to aortic root ruptures and strokes.

Authors have nothing to disclose with regard to commercial support.

Although we agree that observational studies should not have the same weight as randomized trials, they can provide vital information for the advancement of medicine, especially when randomized trials are lacking. We performed a prespecified, adjudicated, rigorous, US Food and Drug Administration-approved analysis amounting to high-quality and peer-reviewed conclusions that up to this point are the best-available evidence comparing use of the Sapien 3 TAV in intermediate-risk patients with use of SAVR.

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