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Risk Framing in Cardiovascular Medicine II

To the Editor: We read with interest the commentary by Alkhouli and Rihal.[1] The authors accurately remark about the need of easily understood tools, available to clinicians and patients at point of care, that could simplify the assessment of individual patient risk benefit and harm of an intervention. In particular, they observed the paucity of intervention-specific, individualized risk/benefit scores that facilitate the identification of higher risk individuals that benefit the most from an intervention, with acceptable probability of harm. Such an example is provided by the TIMI Risk Score for Secondary Prevention,[2] a risk score that identifies those patients who benefit from the addition of ezetimibe to statin therapy after acute coronary syndrome. Although those patients who have 2 or more risk indicators derive some benefit, those who have 0 or 1 do not. In contrast, it could be interpreted from their statement on the Table that the likelihood of no benefit from an intervention, which they calculated as 1 minus the absolute risk reduction, means that most (>97 %) patients are not likely to benefit on the trials exemplified. It has been observed that the absolute risk reduction (or any other measure of risk reduction) represents the average risk reduction in the study group, and given the logarithmic distribution of risk in a disease with overall outcome rate < 50%, it translates that approximately *one-third* of patients in a randomized clinical trial benefit from an intervention, the so-called Lake Wobegon effect.[3] It is important then to distinguish between the magnitude of risk reduction and the percentage of individuals in a population likely to benefit. We completely agree with the authors that we need the tools to identify with ease and clarity those patients who lie in that area of risk to communicate effectively with patients and share the decision whether to apply a given intervention.

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In reply—Risk Framing in Cardiovascular Medicine I and II

We thank the authors for their insightful comments on our perspective published in the journal.[1] We agree with Dr Modarressi[1] that sodium-glucose cotransporter-2 inhibitors indeed represent an important new treatment for patients with heart failure. Although we used the trial definition of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction, or stroke) in the text and in the table's footnote, we acknowledge that this was a secondary and not a primary end point.[1,2] The purpose of our viewpoint was to illustrate the issue of risk in absolute vs relative terms. We agree that a 4.3% absolute risk reduction of the composite end point of end-stage kidney disease, doubling of the creatinine level for ≥30 days, and death due to cardiovascular or renal disease is substantial from a population health view; however, it may be less substantial to the individual patient, especially considering the marked out-of-

pocket costs. Economic studies measure cost-effectiveness from a society (and often payer) perspective, not from a patient perspective. We feel patients should be fully informed as to the magnitude of treatment benefit they may experience and the associated costs they may incur.

We concur with Dr Trejo-Gutiérrez that our presentation of "the likelihood of no benefit" in Table 1 may be overly simplistic considering that the benefit of a specific treatment reported in trials is a measure of the "average" effect for the whole study group. This is likely true for continuous variables; however, we respectfully point out that for a binary end point, such as death and stroke, the situation is likely different. All patients receiving a therapy may benefit; however, which specific individuals will realize an actual benefit is usually impossible to predict. This is analogous to purchasing insurance—any or all may benefit, but few will actually require it. More sophisticated and patient-specific risk analysis will be necessary to maximize the likelihood of benefit and minimize the risk of harm. Our nonconventional approach was meant to emphasize the need to clearly indicate absolute risk reduction values when reporting trial data and when discussing new therapies with patients.[1] It is well documented that patients and physicians tend to have overinflated impressions of treatment benefit. Decision aids have been developed to improve patient perception of risks/benefits, but those achieved variable success.[3,4] We as a community need to identify better methods to report and communicate scientific data to live up to the "advocate" role that our patients expect from us.

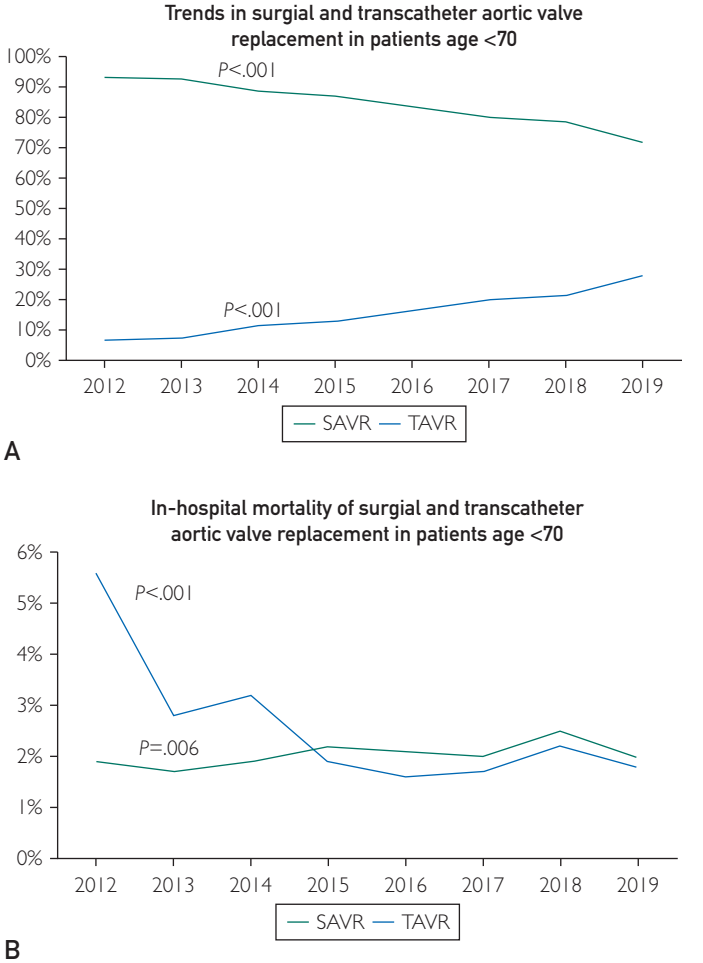

FIGURE. Trends in the utilization and outcomes of isolated aortic valve replacement in patients <70 years of age. A, Trends in use. B, Trends in in-hospital mortality.

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Trends in the Use of Isolated Surgical and Transcatheter Aortic Valve Replacement in Patients Younger Than 70 Years of Age

To The Editor: The demonstrated safety and efficacy of transcatheter aortic valve replacement (TAVR) in low-risk patients led to its growing acceptance as a standard therapy for aortic stenosis (AS), regardless of patients' surgical risks.[1] However, concerns arose on expanding TAVR to younger patients (<70 years of age), considering the scarce long-term data in this age group and the remaining questions of transcatheter valve durability, coronary reaccess, impact of long-term permanent pacing, and the risk of future surgical aortic valve replacement (SAVR).[2-5] In this focused analysis, we examined contemporary utilization trends and in-hospital mortality of AVR in patients aged <70 years.

The Vizient Clinical Data Base (CDB) (Vizient Inc., Irving, Texas) was queried to select patients who underwent isolated SAVR or TAVR between 2012 and 2019, using International Classification of Diseases (ICD)-9/10-CM codes.[1] The CDB contains deidentified data of 100% of index hospitalizations at >400 US academic centers and their affiliates. The primary end point was the trend in the proportion of TAVR to all AVRs. Secondary end points were trends in unadjusted in-hospital mortality. Trends were assessed using the nonparametric Mann-Kendal method. The study was deemed Institutional Review Board exempt because the study uses publicly available deidentified data.

A total of 140,104 patients who underwent isolated AVR were identified, of whom 54,174 were <70 years old (45,093 SAVR; 9081 TAVR). The proportion of TAVR to all AVRs in this age group increased from 6.8% in 2012, to 28.2% in 2019 (P trend<.001) (Figure). Patients who underwent TAVR were older (63.0±7.3 vs 56.2±11.6 years; P<.001) and more likely to be women (39.4% vs 28.7%, P<.001). In the TAVR group, transfemoral access was used in 95.2% of patients. In the SAVR group, bioprosthetic valves were used in 71.4%. In-hospital mortality decreased over time with TAVR (5.6% in 2012, to 1.8% in 2019; P trend<.001) but remained stable with SAVR (1.9% in 2012, to 2.0% in 2019, P trend=.06) (Figure).

This key finding in this focused analysis is the marked increase in the use of TAVR among patients <70 years of age. Nearly 3 in 10 patients aged <70 who were referred for interventions for isolated severe AS in 2019 received TAVR. It is likely that these trends will continue to grow, considering the recent Food and Drug Administration decision to approve TAVR for suitable patients regardless of estimated surgical risk. Although the continuously improving in-hospital mortality for TAVR in this analysis is reassuring, the increasing trends to offer TAVR in patients younger than 70 years of age warrants additional studies with long-term follow-up. Currently available long-term data are derived from the original pivotal TAVR trials in intermediate- and high-risk patients, in which the mean age was ~80 years.[2]

The interpretation of these data also needs to consider the inherent limitation of administrative datasets including potential coding inaccuracies, lack of echocardiographic data, and selection bias. Nonetheless, considering that the purpose of this study is to assess trends in major procedures and in-hospital mortality, those limitations are unlikely to have impact on its results. In conclusion, we document a considerable temporal increase in adoption of TAVR in patients aged <70 years. Long-term follow-up is needed before making TAVR the default strategy in these patients.

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