

Transcatheter aortic valve replacement (TAVR) has revolutionized the treatment of patients with severe and symptomatic aortic stenosis. Patients at extreme risk for open surgery (inoperable) have an absolute benefit in 1-year survival that exceeds 20%,1,2 and high-risk patients have outcomes that are noninferior to surgery for 2 years.3 Nonetheless, the 1- and 3-year mortality in extreme-risk patients who undergo TAVR is ≈30% and 50%, respectively.1 These patients did not derive the anticipated survival benefit from TAVR, and it would be beneficial to be able to predict this adverse outcome preprocedure.

Analyses of individual predictive factors are helpful in risk stratifying patients but have the weakness that they offer little practical help in the complex decision making of whether to offer TAVR to individual high-risk patients.

For example, in the recently reported Italian multicenter registry of >1000 patients receiving TAVR with the CoreValve device, patients with moderate or severe mitral regurgitation (MR) had an ≈2-fold higher mortality at both 30 days and 1 year than those without significant MR.12 Modest improvement in MR occurred in close to half the patients and was predicted by a functional cause and the absence of severe pulmonary hypertension and atrial fibrillation. However, the improvement in MR did not predict better survival.12 In an observational analysis of the Partner trial database, Dvir et al13 reported that patients with chronic lung disease have higher mortality after TAVR. Combining 5 measures in a score raised the risk of 1-year mortality after TAVR from 8% to >40%.

However, despite an increased mortality relative to patients without lung disease, these patients experienced a 34% improvement in 2-year survival relative to standard therapy and fared as well with TAVR as with open surgery.13 Should we, therefore, not offer TAVR to patients with aortic stenosis with lung disease or significant MR?

In this issue of Circulation: Cardiovascular Interventions, investigators from the France 2 Registry confirm other reports that demonstrate that more than moderate pulmonary hypertension is another dichotomous risk factor that is associated with worse outcome after TAVR.14 Patients with systolic pulmonary artery pressure (PASP) ≥40 mm Hg had a 1-year mortality of 28% compared with a mortality of 22% in those with pressure <40 mm Hg. As with other similar studies, functional status of survivors improved, regardless of the preprocedure level of pulmonary pressure.

Pulmonary hypertension, estimated by adding the tricuspid regurgitation gradient and estimated right atrial pressure, does not distinguish between causes of left ventricular systolic or diastolic dysfunction, MR, pulmonary disease, or right ventricular (RV) dysfunction, all of which are prevalent in the TAVR population. Nonetheless, it seems to be a marker of worse outcome in a variety of conditions. In 1 community study of >1000 patients with heart failure, the odds ratio for death was 2.07 for patients in the highest tertile of PASP compared with the lowest tertile.15 Sinning et al16 reported similar findings in patients with TAVR in whom the 2-year mortality was 48.4% with PASP >60 mm Hg compared with 13.9% in patients with PASP <30 mm Hg. Although useful for informing both patients and clinicians about prognosis, this information is of limited value in deciding whether to offer TAVR to an individual patient.

In the France 2 Registry, the survivors with the highest PASP had a greater reduction in PASP post-TAVR (a reduction of 16 mm Hg in median pressure compared with no change in the lowest PASP group and 5 mm Hg in the intermediate group).14 Sinning et al16 demonstrated that a reduction of PASP to <60 mm Hg 90 days after TAVR was associated with improved 2-year survival. These patients likely had reversible pulmonary venous hypertension that was relieved by TAVR, possibly because of MR or left ventricular systolic dysfunction.

How can we improve the usefulness of this risk factor to predict the outcome for individual patients? Although a good noninvasive measure of pulmonary pressure, PASP may be underestimated in patients with severe tricuspid regurgitation because of rapid equilibration of RV and right atrial pressures. We are not provided with any information on the degree or distribution of tricuspid regurgitation in the patients studied. PASP also does not reflect RV function. RV function estimated by tricuspid annular plane excursion or by the fractional area change has been studied in conjunction with PASP.
in patients with heart failure in which the combination of RV dysfunction and high PASP conferred the worst prognosis.\textsuperscript{17–19} Perhaps, teasing out the underestimation of PASP because of concomitant tricuspid regurgitation and adding RV functional estimates to PASP would enhance the discrimination between survivors and nonsurvivors after TAVR. As a result of the limitations of any single factor as a litmus test to discern benefit for patients with aortic stenosis who need therapy, one might surmise that combining factors into a score would be more helpful. Data from the Partner 1B trial demonstrated that patients with a Society for Thoracic Surgery risk score \textgreater 15\% for predicted operative mortality at 30 days derived no survival benefit from TAVR at 1 year compared with standard therapy.\textsuperscript{1} The Society for Thoracic Surgery risk calculation is not perfect and has limitations. It only includes operated patients for comparison, data are voluntarily submitted and not independently audited, and it does not include several risk factors that influence survival, such as porcelain aorta, hostile chest, advanced liver disease, frailty (both physical and mental), debility, and immobility.

Recently, much attention has focused on frailty as a risk factor for poor outcome after both TAVR and surgery. Defining frailty as an impairment of physiological reserve and decreased resistance to stressors, Green et al\textsuperscript{10} demonstrated in a TAVR population that a combination of frailty measures of slowness, weakness, malnutrition, and inactivity was associated with a 3.5-fold increase in 1-year mortality. Impairment in mental and cognitive ability, mood, and mental health would likely add even greater risk.

As we continue to apply TAVR to sicker and older patients, we must also consider whether mortality is the right outcome. Quality of life in many elderly patients may be even more important. Arnold et al\textsuperscript{20} used the Kansas City Cardiomyopathy Questionnaire to identify 16\% of patients with a poor-quality-of-life outcome 6 months after TAVR, in addition to 19\% who died. In a recent study of 106 survivors after TAVR, functional decline occurred in 21\% and was much better predicted by measures of frailty (including cognitive impairment) than by Society for Thoracic Surgery score or EuroSCORE.\textsuperscript{21} For our sickest patients with aortic stenosis being considered for TAVR, we desperately need scores that not only combine multiple risk factors that are each properly assessed but which also use the factors to predict a combination of mortality and quality-of-life outcome to avoid Oscar Wilde’s potential tragedy in life of getting what one wants.

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**References**


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**Table. Factors Associated With Poor Outcome After Transcatheter Aortic Valve Replacement**

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<th>Factor</th>
<th>Noncardiac</th>
<th>Cardiac</th>
<th>Procedural</th>
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<td>COPD</td>
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<td>CKD</td>
<td>Pulmonary</td>
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<tr>
<td>High BMI</td>
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<td>Male sex</td>
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<tr>
<td>Frailty</td>
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AKI indicates acute kidney injury; AR, aortic regurgitation; BMI, body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CPS, cardiopulmonary support; CVA, cerebral vascular accident; DM, diabetes mellitus; EF, ejection fraction; HTN, hypertension; and MR, mitral regurgitation.
Identifying Patients Who Do Not Benefit From Transcatheter Aortic Valve Replacement
Howard C. Herrmann and Yuchi Han

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