Calculating Risk for Poor Outcomes After Transcatheter Aortic Valve Replacement

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ABSTRACT

Objective: To outline the tools available to help understand the risk of transcatheter aortic valve replacement (TAVR) and the gaps in knowledge regarding TAVR risk estimation.

Methods: Review of the literature.

Results: Two models developed and validated by the American College of Cardiology can be used to estimate the risk of short-term mortality, a 6-variable in-hospital model designed for clinical use and a 41-variable 30-day model designed primarily for site comparisons and quality improvement. Importantly, neither model should be used to inform the choice of TAVR versus surgical aortic valve replacement. Regarding long-term outcomes, a risk model to estimate risk of dying or having a persistently poor quality of life at 1 year after TAVR has been developed and validated. Factors that most significantly increase a patient's risk for poor outcomes are very poor functional status prior to TAVR, requiring home oxygen, chronic renal insufficiency, atrial fibrillation, dependencies in activities of daily living, and dementia. If a patient has ≥ 2 or 3 major risk factors for a poor outcome, this risk and the uncertainty about the degree of recovery expected after TAVR should be discussed with the patient (and family).

Conclusion: It is important to understand the patient factors that most strongly drive risk of poor outcomes after TAVR and use this information to set appropriate expectations for recovery.

Keywords: aortic valve stenosis; risk factors; postoperative complications; TAVR.

Among patients with severe aortic stenosis, transcatheter aortic valve replacement (TAVR) has emerged as a less invasive option for aortic valve replacement. This procedure offers substantial reductions in mortality and improvement in quality of life compared with medical therapy[1,2] and at least similar long-term outcomes compared to surgical aortic valve replacement (SAVR).[3-9]

As with any emerging technology, selecting the appropriate patients for TAVR—a procedure with high initial costs[10]—has been an area of active investigation. As TAVR was first introduced in patients who were considered inoperable, initial efforts focused on trying to identify the patients who did not improve functionally or live longer following TAVR. Termed Cohort C patients, these patients were thought to have too many comorbidities, be too sick, and have too little reserve to recover from TAVR, and in the early trials, represented a substantial minority of the patients. For example, in pivotal clinical trials of patients at high or extreme surgical risk, approximately 1 in 4 patients who were treated with TAVR were dead at 1 year.[1,3,11] Furthermore, a number of patients who received TAVR were alive at 1 year but continued to have significant heart failure symptoms and functional limitations.[2,4] Practitioners,[12,13] regulators,[14] and third-party payers[15] have recommended that TAVR should not be offered to patients in whom valve replacement would not be expected to positively impact either their survival or quality of life, but how best to identify these patients has been less clear.

More recently, as the use of TAVR has moved down the risk spectrum, patient selection for TAVR has shifted to understanding which patients should be preferentially treated with TAVR versus SAVR. While patients often prefer a less invasive treatment option with faster recovery—which is what TAVR offers—there are lingering questions about valve longevity, need for a pacemaker (and the associated long-term implications), and the ability to treat

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other cardiovascular conditions (eg, Maze, mitral valve repair) that potentially make a patient a more appropriate candidate for valve surgery. This review outlines the tools currently available to help understand the risk of TAVR and the gaps in knowledge.

Short-Term Outcomes

When TAVR was initially introduced, the 30-day mortality rate was 5% to 8%.[1,11,16] This high mortality rate was a function of treating very ill patients and more invasive procedures with larger sheath sizes and routine use of general anesthesia, transesophageal echocardiography, pulmonary artery catheterization, and so on. Over time, however, this rate has gone down substantially, with the 30-day mortality rate in intermediate- and low-risk patients now ranging from 0.5% to 1%.[8,17-19] Although this low mortality rate indicates that the vast majority of patients will survive to discharge from the hospital, 2 models can be used to estimate the risk of short-term mortality: an in-hospital[20] and a 30-day model,[21] both developed and validated by the American College of Cardiology. The in-hospital model was developed for clinical use, as it includes only 6 variables (age, renal function, severe lung disease, non-femoral access, New York Heart Association class IV, and acuity of the procedure [elective versus urgent versus shock versus emergent])[20] and has an online calculator (http://tools.acc.org/tavrrisk/). The 30-day model was developed for risk adjustment (primarily for site comparisons and quality improvement) and includes 41 variables (including pre-TAVR patient health status and gait speed).[21]

While 30 days is a better time frame for assessment because outcome is less impacted by differences in local post-acute care facilities, we explicitly did not create a parsimonious 30-day mortality model for clinical use due to concern that having such a model would allow for indirect comparisons with estimated risk of SAVR using the Society of Thoracic Surgeons risk model (http://riskcalc.sts.org/stswebriskcalc). It would be tempting to estimate a patient's risk of mortality with the TAVR calculator and the SAVR calculator and use those risk estimates to inform the choice of treatment; however, these risk estimates should not be directly compared to make treatment selections, as they were built on entirely different patient populations. In real-world practice, there is minimal overlap in the characteristics of patients who are treated with TAVR and SAVR. For example, in an analysis that merged surgical and transcatheter databases, less than 25% of patients treated with TAVR could be matched to a clinically similar patient treated with SAVR.[22] As such, these TAVR models should be used to estimate a patient's risk for short-term mortality, but should not be used to contribute to the decision on TAVR versus SAVR.

The decision of selecting SAVR over TAVR is typically driven by factors other than short- or long-term mortality (eg, whether TAVR will be covered by insurance, very young age and concern about durability, need to treat concomitant mitral regurgitation or aortopathy), as clinical trials have shown that survival and quality of life outcomes are at least as good with TAVR compared with SAVR.[6,7,9,23] In fact, in an analysis that compared similar patients treated with TAVR versus SAVR and specifically looked for patient factors that might make one treatment preferable to the other, patients who had a prior cardiac operation and those on home oxygen were more likely to do better with TAVR, whereas no patient factors that favored SAVR were found.[24] The majority of patients, however, were expected to have similar long-term outcomes regardless of treatment choice, and as such, the benefit of TAVR appears mostly to be an earlier and easier recovery.

Long-Term Outcomes: Estimating the Risk for Failure to Recover

While many patients who undergo TAVR are quite ill prior to the procedure, with substantial limitations due to the fatigue and shortness of breath associated with severe aortic stenosis, most patients recover well after the procedure, with marked improvement in symptoms and functional capacity. Approximately 25% to 35% of patients currently treated with TAVR commercially (ie, intermediate- and high-surgical-risk patients) either die or do not recover a reasonable quality of life after the procedure. Identifying those patients prior to the procedure can be challenging. We have previously developed and externally validated a risk model to estimate risk of dying or having a persistently poor quality of life at 1 year after TAVR.[25,26] The factors that most significantly increase a patient's risk for poor outcomes are very poor functional status prior to

TAVR, requiring home oxygen, chronic renal insufficiency, atrial fibrillation, and dementia. For example, a patient who is short of breath at rest, is on home oxygen, has a serum creatinine of 2.5 mg/dL, and has atrial fibrillation has an estimated risk of poor outcome at 1 year of ~70%. However, it should be noted that ~25% of patients with no risk factors for poor outcomes (ie, those considered "low risk") still have a poor outcome at 1 year after TAVR, as the patients who undergo TAVR are typically at an advanced age with at least some comorbidities. Therefore, a 1-year mortality rate of 10% to 15% would not be unexpected in this population independent of the TAVR, although this will likely change over time as TAVR expands to patients at low surgical risk.

Beyond clinical factors, frailty negatively impacts both survival and quality of life after TAVR. Frailty is a geriatric syndrome of impaired physiologic reserve and decreased resistance to stressors[27] that is characterized by weakness, slowness, exhaustion, wasting, and low activity level. Across a wide variety of clinical situations (eg, pneumonia,[28] myocardial infarction,[29] general[30,31] and cardiac surgery[32,33]), frailty increases the risk of morbidity and mortality after nearly any intervention[34] or clinical insult, independent of traditional demographic and clinical risk factors. Frail patients often do better with less invasive interventions such as TAVR compared with traditional surgery, but nonetheless remain at increased risk for death[35-37] or failure to recover quality of life and functional status[25,37] after TAVR. However, there are unique challenges in both assessing and managing frailty in patients who are considered potential candidates for TAVR. One challenge is the lack of a laboratory or radiologic test for frailty; instead, the lack of physiologic reserve of frailty is identified through a combination of factors, such as slow gait speed, weak grip strength, and unintentional weight loss. While these factors readily identify frail patients in general elderly populations, in patients with severe symptomatic aortic stenosis, these metrics can be impacted by the disease process itself. This distinction is important as slow gait speed that is due to aortic stenosis will be "fixed" by TAVR, but slow gait speed from frailty would identify a patient who will have a difficult time recovering from the procedure. For example, in the CoreValve High Risk Pivotal Trial, 80% of patients had a slow gait speed and 67% had a weak grip strength,[5] and yet 58% of patients in this trial were alive and with a reasonable quality of life 1 year after TAVR.[6] A number of studies have attempted to define true frailty within the pre-TAVR population, that which represents decreased physiologic reserve and an impaired ability to recover from an insult, and the factors that appear to be most prognostically important are malnutrition[38] or unintentional weight loss[25] and the inability to be independent in activities of daily living (eg, dressing, feeding, transferring).[25,37]

Table. **Estimation of Risk for Poor Outcome**[25,26]

Patient Factor	Approximate Increase in Absolute Risk[a]
New York Heart Association class III	8%
New York Heart Association class IV	15%
Atrial fibrillation/flutter	8%
Creatinine 2 mg/dL	4%
Creatinine 3 mg/dL	8%
Creatinine ≥ 4 mg/dL	12%
Home oxygen	15%
Dementia	15%
Activities of daily living (ADL) dependencies	5% per 1 ADL
Unintentional weight loss	15%

[a]Base case risk is ~25%, with a range up to ~80%.

Even with frailty assessments, the ability to predict who is or is not going to have a poor outcome after TAVR (ie, to use pre-procedural factors to identify patients who perhaps should not be offered TAVR because he or she will not recover from the procedure) is exceedingly difficult. The **Table** shows how to grossly estimate risk using the major factors that impact risk based on the more precise estimates from our models.[25,26]

The model shown in the Table can be used to estimate a patient's risk for a poor outcome, but it should be noted that even at the extreme high end of risk, there will be some patients who still do well after TAVR. Furthermore, being high risk for a poor outcome after TAVR does not imply anything about how the patient would do without TAVR, as many of these patients would likely die even

sooner or have worse quality of life with medical therapy only. However, if a patient has ≥ 2 or 3 major risk factors for a poor outcome, it may be worthwhile to have a serious conversation with the patient (and family) about this risk and the uncertainty about the degree of recovery expected after TAVR.

Conclusion

Calculating the risk of TAVR can be complicated. In patients who are electively treated using transfemoral access and a less invasive approach, the short-term risk of mortality is very low. Risk calculators can be used to estimate short-term risk, but the patients who are high risk for in-hospital mortality are often fairly easy to recognize, as the factors that drive that risk are not subtle (eg, the patient is in shock at the time of the procedure). The true risk of TAVR lies in the inability to recover from the procedure—being chronically ill, frail, or debilitated to a degree that the patient either dies or fails to recover a reasonable quality of life. Given the overlap of symptomatic aortic stenosis with true frailty, it is often difficult to identify these patients who will not thrive after TAVR. Understanding the patient factors that most strongly drive risk of poor outcomes after TAVR, and allowing this information to guide the conversation prior to TAVR so as to set appropriate expectations for recovery, can be a good place to start.

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