A Decision-Making Framework for Objective Risk Assessment in Older Adults with Severe Symptomatic Aortic Stenosis

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A Decision-Making Framework for Objective Risk Assessment in Older Adults with Severe Symptomatic Aortic Stenosis

Decision-Making Framework in Severe AS

Ashok Krishnaswami1 · Daniel E. Forman2,3 · Mathew S. Maurer4 · Sei J. Lee5

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Abstract The increasing prevalence of severe symptomatic aortic stenosis (AS) in older adults is now considered a major public health concern. Since medical therapy has not been shown to improve prognosis, surgical aortic valve replacement (SAVR) and transcatheter aortic valve replacement (TAVR) are the best options currently available, yet not all patients benefit. Objective assessment of risk versus benefit for SAVR and TAVR is essential. Clinical prediction models (CPM) have been created to augment subjective physician estimates of risk and have been shown to improve the accuracy of risk predictions. This manuscript presents the rationale for a framework of objective evaluation of risk assessment and decision making by linking clinically relevant CPM (life expectancy, Society of Thoracic Surgery, and TAVR risk calculators) with two additional concepts of lag time to benefit and competing risks that are relatively novel to the clinical arena. We believe that such aggregate framework can improve the assessment of risk and benefit and thereby facilitate a more informed and standardized shared decision-making process in the care of older adults with severe symptomatic AS.

Keywords Age · Older adult · Risk stratification · Clinical prediction models · Life expectancy · Standard aortic valve replacement · Transcatheter aortic valve replacement · Lag time to benefit · Competing risks · Shared decision making

Case Presentation An 80-year-old male admitted to the hospital for shortness of breath and newly diagnosed aortic stenosis is referred to the cardiology clinic for further management. He and his family are interested in understanding the current options available and the associated benefits and risks with these options. His comorbidities include diet controlled type 2 diabetes mellitus, hypertension, hyperlipidemia, chronic kidney disease stage 3, prior renal cell cancer with resultant nephrectomy, severe chronic obstructive pulmonary disease on 3 l/min home oxygen, and chronic lymphocytic leukemia. His history, physical exam, and imaging studies are consistent with severe symptomatic degenerative, calcific aortic stenosis with no other conditions favoring toward either surgical or transcatheter aortic valve replacement such as prior radiation, hostile chest, porcelain aorta, or patient preference. He has associated mild valvular regurgitation of his tricuspid and mitral valve with mildly elevated pulmonary artery hypertension. Cardiac catheterization demonstrated mild obstructive coronary artery disease (with no indication for coronary revascularization).

Introduction

The increasing prevalence of severe symptomatic aortic stenosis (AS) in older adults in the USA and Europe is a major public health concern [1–3]. A recent meta-analysis and
modeling study found that the pooled prevalence among five studies of severe AS was 3.4% (1.1–5.7%), with symptomatic AS being 75.6% (65.8–85.4%) of the proportion of those with severe AS. This corresponded to approximately one million older adults in Europe and an additional half-million in North America with severe symptomatic AS that are eligible for consideration of either surgical aortic valve replacement (SAVR) or transcatheter aortic valve replacement (TAVR) [4•].

The introduction of TAVR has expanded the available therapeutic options for AS and in doing so, has also complicated the decision-making process. Prior to the introduction of TAVR, the primary determinant of clinical management was whether patients could successfully withstand the stress of surgery. For those who were deemed sufficiently resilient to survive SAVR, it was generally assumed that they would benefit with an improved long-term survival and quality of life. Unfortunately, even this single decision was associated with tacit bias; subsequent studies indicate that SAVR was frequently denied to many eligible patients in both the USA [5] and Europe [6]. This has been thought to be attributable to an inappropriate emphasis on advancing age [6] and increasing number of concomitant comorbidities [5]. Notably, in one study, approximately 20% of patients were thought to have inoperable AS by subjective evaluation; further, more objective evaluation led to subsequent SAVR with good outcomes [7]. Therefore, objective evaluation of patients for SAVR as well as TAVR holds the promise of improving and standardizing the decision-making process between physicians, patients, and their families. Clinical prediction models (CPM) and standardized algorithms provide a logical process to facilitate this goal [8•, 9]

In this review, we develop a seven-step CPM framework that is designed to link existing and novel CPM to optimize management choices for patients with symptomatic AS, i.e., helping clinicians and patients choose between SAVR, TAVR, or symptom management with medical therapy (Fig. 1). The entry point into this framework is only after a decision has been made that the patient has aortic stenosis of sufficient severity to warrant consideration of valve replacement.

The first step is to determine life expectancy [10, 11]. The second step is to utilize the Society of Thoracic Surgery (STS) risk calculator [12]. The third step is to utilize a TAVR risk calculator. The fourth step would be the incorporation of geriatric specific conditions or variables such as frailty, disability, and multiple chronic conditions into the aforementioned risk scores [13••, 14–18]. The fifth step is to determine the lag time to benefit of the procedure(s) that are chosen [19•]. The sixth step is a discussion of competing risks that may play an important role in the decision-making process [20•]. The seventh step is to engage patients and families in a shared decision-making (SDM) process [21••, 22••, 23••, 24••]. Although the current review is focused on patients with severe AS, these concepts can be readily translated to other clinical decisions, in regard to procedures or surgeries, which often present higher immediate risks for the promise of improved long-term outcomes.

### Seven-Step Clinical Prediction Model Framework

#### Assessment of Life Expectancy

In order for patients and their families to make a decision regarding their choices, physicians should be comfortable in a discussion of life expectancy and the natural history of their patient’s condition without any intervention. Many physicians have been asked by their patients contemplating surgical intervention “Doc, what if do nothing?” Although the original work of Ross and Braunwald [25] is often used as a reference for the natural history, its applicability to the modern era of the older patient with AS is limited. A recent 2006 study of 453 patients with severe AS who were managed nonsurgically, survival at 1, 5 and 10 years were 62%, 32, and 18% respectively [26]. Also, the original TAVR PARTNER trial noted that in the nonoperable cohort with severe symptomatic AS randomized to the medical arm, only 50% of patients were alive at 1 year [27]. Although these studies give a perspective regarding life expectancy in those with severe AS, the complex effects of severe AS and comorbidities that are commonly present are not incorporated into the risk analysis. Well-validated life expectancy calculators [28], created with support from the Division of Geriatrics at the University of California at San Francisco, that takes into consideration the location of the patient (community living, nursing home, hospitalized, or hospice) can be found on the world wide web at http://eprognosis.ucsf.edu/calculators.php. The site includes, but is not limited to, the Mazzaglia, Gagne, Carey, Lee, and Schonberg risk scores. As an example, the Lee mortality index which has a time frame of 4 [10] and 10 years was developed in approximately 12,000 community-dwelling adults from the Eastern, Western, and Central USA. It was then validated in 8009 Health Retirement Survey interviewees from the Southern USA with a good discriminative ability (c-statistic 0.82). The individual life expectancy calculators that are available at the site vary in the number and type of predictors as well as in the prognostic time frame (6 months, 15 months, 1, 2, 3, 4, 5, and 10 years). Examples of the variables that are included are baseline demographics (age, sex, body mass index), symptoms (shortness of breath, cognitive difficulties), comorbidities (diabetes, renal failure, heart failure), and many geriatric specific variables that include...
**STEP 4**
Incorporate Geriatric Specific Issues not Limited to the Following:

- Multiple Chronic Conditions
- Functional Status (Frailty, Disability)
- Cognitive Impairment
- Malnutrition
- Polypharmacy
- Fall Risk
- Mood Disorders (Depression, Anxiety)
- Social Isolation
- Quality of Life

**STEP 1**
Calculate Life Expectancy

**STEP 2**
Calculate STS Risk Score

**STEP 3**
Calculate TAVR Risk Score

**STEP 5**
Assess Lag time to Benefit

**STEP 6**
Assess for Competing Risks to Mortality

**STEP 7**
Shared Decision Making

- Acknowledging Benefits and Limitations of Current Method
- Addition of Clinical Acumen not specifically covered above

**Patient Centered with Physician Recommendations**
variables representing activities of daily living, disability, and markers of frailty. Table 1 demonstrates the specific questions found in the Lee index. After assessing life expectancy using the appropriate risk score (with sensitivity to time frame, patient location and upon answering the specific questions), the results can be regarded as the proportion of adults (in a specific setting) that will die or survive over the duration of the prognostic model. This is displayed in the form of a pictograph to help physicians and patients comprehend the statistical benefit and risk. It is important to note that these online risk calculators do not take into consideration the dominant comorbidity of severe symptomatic aortic stenosis. Lastly, it is to be noted that life expectancy calculators address only mortality risk and do not attempt to address the quality of life for the remaining years.

### Assessment of Procedural Risk (SAVR) Using a Surgical Risk Calculator

The STS risk calculator is one of several tools available to assess surgical risk (The Euro SCORE or the Ambler risk score are also well-established). Although studies have validated the superiority of STS and other surgical predictive tools over subjective assessment of perioperative risks with the “eyeball test” [8••] or other subjective assessments [9], further work will need to be continued for maximal model validation and discrimination [30].

The mission of the STS is to “enhance the ability of cardiothoracic surgeons to provide the highest quality patient care through education, research and advocacy” (http://www.sts.org/about-sts). The STS risk calculator reflects this commitment to improved care. It is available on mobile applications and the web at http://riskcalc.sts.org/stswebriskcalc/#/calculate. The use of the STS risk calculator has been minimal until the recent advent of TAVR, possibly because it has been noted to predict SAVR perioperative and late outcomes risks relatively better than other scores [12] (i.e., higher than both the Euro SCORE or the Ambler risk scores). The use of the STS risk score has often been applied as a rationale for TAVR as a safer approach.

### Assessment of Procedural Risk (TAVR) Using a TAVR Risk Calculator

Whereas procedural aspects of TAVR are rapidly improving, risks are still substantial. Many of these risks relate to comorbidities and nonvalvular complexities. Currently, no formal risk score is available that takes into account baseline comorbidities and other variables to improve risk prediction for patients planning on TAVR to predict procedural success (as defined by short- and long-term mortality, quality of life, or other patient-centered outcomes). Several related studies are now underway [31].

### Incorporation of Geriatric Specific Variables into SAVR and TAVR Risk Scores

A comprehensive list of geriatric issues that impact outcomes in patients referred to SAVR or TAVR is beyond the scope of this review. However, we will highlight some of the key variables common in older adults that have the potential of being used in future clinical prediction models. Specific candidate variables include frailty, disability, cognitive impairment, mood disturbance, malnutrition, polypharmacy, fall risk, and social support [13••, 14, 15, 32, 33••]. Some of the concepts mentioned are modifiable while others are immutable and may act more of an obstacle to further care.

Frailty has been garnering considerable attention in the cardiovascular arena as it is now generally acknowledged to affect vulnerability to cardiovascular disease and also to confound cardiovascular disease management. The two main frailty models are the Fried phenotype model [14] and the cumulative deficit model [16–18]. Components of the more commonly used Fried scale include 5-m gait speed, handgrip strength test, physical activity questionnaire, depression questionnaire and assessment of weight loss has shown promise. Frailty is considered if the composite score is ≥3/5. Although frailty has been associated with suboptimal outcomes after cardiac surgery [13••, 34], formal risk scores incorporating some or all aspects of frailty are only now being developed and have not been fully implemented. A recent study brought attention to the cardiovascular community that assessment of frailty prior to TAVR is extremely important. It showed that while frailty did not affect periprocedural complications, it was associated with increased 1-year mortality. One important implication is that risk prediction for aortic valve management must extend well beyond the acute stress of the TAVR procedure. However, generalizability of this study is limited due to small sample size, limited number of outcomes, and lack of external model validation [35•].

### Table 1 Lee mortality index questions

<table>
<thead>
<tr>
<th>Question</th>
<th>Source: [10]. Adapted from <a href="http://eprognosis.ucsf.edu/">http://eprognosis.ucsf.edu/</a></th>
</tr>
</thead>
<tbody>
<tr>
<td>How old is your patient?</td>
<td></td>
</tr>
<tr>
<td>What is your patient’s biological sex?</td>
<td></td>
</tr>
<tr>
<td>What is your patient’s BMI?</td>
<td></td>
</tr>
<tr>
<td>Does your patient have diabetes?</td>
<td></td>
</tr>
<tr>
<td>Has your patient ever had cancer (excluding minor skin cancers)?</td>
<td></td>
</tr>
<tr>
<td>Does your patient have COPD that limits their usual activities at home?</td>
<td></td>
</tr>
<tr>
<td>Does your patient have congestive heart failure?</td>
<td></td>
</tr>
<tr>
<td>Does your patient currently smoke cigarettes?</td>
<td></td>
</tr>
<tr>
<td>Does your patient have difficulty walking several blocks?</td>
<td></td>
</tr>
<tr>
<td>Does your patient have difficulty with managing their finances on their own?</td>
<td></td>
</tr>
<tr>
<td>Does your patient have difficulty with bathing or showering without help from other people?</td>
<td></td>
</tr>
<tr>
<td>Does your patient have difficulty pulling or pushing large objects such as a living room chair?</td>
<td></td>
</tr>
</tbody>
</table>
Although numerous geriatric specific variables are known, the integration into risk models is often limited by the lack of their routine availability. Furthermore, selecting the variable(s) to be included is rarely straightforward. A recent study that compared the ability of risk scores, frailty, and disability to predict downstream mortality or major morbidity noted that the single variable gait speed had an acceptable area under the curve with a c-statistic of 0.64 along with the lowest Aikake information criterion (AIC) of 0.54 with the revised Parsonnet surgical risk score [36] having a c-statistic of 0.72 and an AIC of 0.55 [33••]. This accentuates the fact that many geriatric-oriented variables are likely correlated (collinearity in statistical literature) and therefore may conceptually be measuring things similarly. Therefore, future studies will need to decide on an optimum single variable or a specific family of variables that represent geriatric specific variables that can be used to optimize the discrimination of risk. Until geriatric specific variable(s) for risk prediction are better refined, the assessment of geriatric syndromes will have to be reported as an additive assessment of risk in a manner that is still often subjective [15, 32].

Assessment of Lag Time to Benefit

Lag time to benefit has been used to determine the time that it would take for preventive measures to yield fruition in terms of improving mortality [19•]. If life expectancy is less than the lag time to benefit, then the intervention will expose the patient to the risks of the intervention with little chance that the patient will survive to benefit from the intervention. These concepts can also be extrapolated to invasive procedures such as TAVR. Makkar et al. reported on 2-year outcomes after TAVR from the original PARTNER trial and showed via four Kaplan-Meier graphs that the time of onset of separation of the curves (TAVR vs standard therapy) is from 3 to 6 months for the outcomes all-cause mortality, cardiac mortality, rehospitalization, or combined outcome of death or stroke. They improved on this analysis and showed three separate Kaplan-Meier curves (Fig. 2) by patient entry STS scores [37]. In patients with STS <5 %, the curves quickly diverged with no apparent lag time to benefit. Intermediate risk STS scores of 5–14.9 % noted a lag time to benefit of 6 months. Finally, when STS scores were ≥15 %, there was no benefit with TAVR (p=0.31). Incorporating lag time to benefit with life expectancy calculators, STS scores, and eventually TAVR scores can aid the referring physician in understanding the time needed for complex procedures and surgeries to yield benefit. In the high-risk patients with STS≥15 %, physicians should convey that the survival benefits with TAVR are not seen. In intermediate risk STS, consideration of proceeding with TAVR may be entertained with further discussion of patient wishes incorporating competing risks.

Another dimension to this aspect of the decision process is whether or not cardiac rehabilitation or other rehabilitation process can be used to accelerate recovery (and benefit) for patient who undergo SAVR or TAVR [38, 39]. Whereas cardiac rehabilitation is notoriously underused by eligible older cardiac patients, the potential benefit for older adults referred for valve replacement is particularly compelling. Many elderly candidates for valve replacement suffer from disability and even frailty that becomes exacerbated by their valvular disease (primarily due to exercise intolerance due to impaired cardiac output). Their theoretical potential to regain functional capacity after valve replacement is often quite high, but their time to benefit is delayed amidst sarcopenia, multimorbidity, and other impediments to recovery. Cardiac rehabilitation and other aspects of care may impact the speed of improvement. Therefore, pre-procedural assessment of each patient’s willingness and capacity to attend rehabilitation after TAVR or SAVR is also relevant.

Assessment of Competing Risks

An understanding of the concept of competing risks [20•] is essential for any physician or patient [40] who is balancing the possibility of treatment of one condition detrimentally affecting another condition. Nowhere is this more evident than in the current scenario of the older adult with severe symptomatic AS and multiple chronic conditions with the choices they face. A competing risk can be defined as “an alternative outcome that is of equal or more significant clinical importance than the primary outcome and alters the probability of the outcome of interest” [20•, 41]. In the current scenario, competing risks are risks other than mortality such as stroke, kidney injury, and vascular complications. Although many feel that competing risks results should routinely be reported in the study of older adults, the methodology is infrequently used in the cardiovascular and geriatrics clinical research with the nonuse well-known to often result in biased estimates [20•, 42].

Holmes et al. recently reported 1-year real-world outcomes from the Transcatheter Valve Therapies Registry [43]. Using a competing risk analysis, they graphed a cumulative incidence function demonstrating the incidence of heart failure, stroke, or aortic valve reintervention, respectively, at 14.3, 4.1, and 1.4 % (prior to mortality) with the competing risk of mortality of 23.7 % at 1 year. As the registry included only those patients that have undergone TAVR, the competing risks of heart failure, stroke, or aortic valve reintervention with mortality is not known between SAVR and TAVR or between SAVR and medical therapy. It has been suggested that routine reporting of competing risks should be considered standard in reporting out pragmatic comparative effectiveness trials that address the elderly or those with multiple chronic conditions [44].
Shared Decision Making

The last step in the proposed decision-making framework is a coordinated discussion between physicians, patients, and their families of the benefits and risks of the proposed procedure(s), a concept that has been called shared decision making. Shared decision making came into light with the Presidents’ Commission in 1982. Subsequently, it has bloomed into a discipline of its own [21] with a goal toward improving patient-centered outcomes [22]. It has been described as “a way to improve clinical care for patients by encouraging the production and dissemination of accurate, balanced, understandable health information and increasing patient participation in care” [21]. There are well-founded rationales of SDM requirements, participants, measurements, and process [23]. Unfortunately, there have been challenges in the uptake of the implementation of SDM by clinical providers [24].

Decision aids have been demonstrated to better match patient understanding and wishes with physician suggested treatment to maximize the appropriateness of the treatment delivered [45]. Decision aids in the SDM process have been shown to be of immense help in patients presenting to the emergency room with chest pain [46] and access site choices prior to coronary angiography [47]. Furthermore, a Cochrane review demonstrated that decision aids improve patients knowledge regarding their options, improve the feeling of being more informed, improve the ability to have an appropriate expectation of the benefits and harms, and increase participation in the decision making process [48]. A full discussion of SDM is beyond the scope of this review, and it is hoped that readers will review the references provided here to improve their knowledge on SDM with future application into the management of severe aortic stenosis as well as other disease states.

Case Presentation Results

In approaching our 80-year-old case study, a man with severe AS, we can apply our CPM framework to achieve a logical and effective approach to management.

1. **Life expectancy** by the Lee 4-year mortality risk showed that “out of 100 community-dwelling adults aged 50 and older with similar answers, 74 will die, and 26 will survive over the next 4 years.” However, it is to be noted that this does not account for quality of life and other possible pertinent patient-centered outcomes.

2. **STS risk score for SAVR** was 6.5% for mortality with a combined risk of morbidity or mortality of 30.5%.

3. **TAVR risk score**. There is no equivalent risk calculator for TAVR.

4. **Frailty evaluation** with the Fried scale showed four of the five frailty measures (slowness, low physical activity, exhaustion, and weight loss). This is notable, but it is not clear how much of this may be modifiable from the effects of valve replacement and associated cardiac rehabilitation.

5. **Lag time to benefit** is approximately 6 months based on his STS risk of mortality of slightly greater than 6% (i.e., intermediate risk SAVR). However, this may be protracted by the pre-procedural frailty, but also possibly decreased by cardiac rehabilitation.
6. **Competing risks.** Although there are no graphs clearly distinguishing the course and sequelae of SAVR, TAVR, or medical management, a discussion was had with the patient and family regarding the travails of each within the contexts of underlying risks of mortality and quality of life.

7. **Shared decision making.** Further discussion with the patient and family was had regarding his advanced COPD, sarcopenia (as noted by his weight loss), and general frailty with accompanying pictographs of risks.

In this case, the patient and family have decided that they will continue with medical therapy and eventual palliative care and not pursue TAVR. Their basis for this decision was on a personal emphasis on severity of COPD and the concerns that intervention would not lead to long-term benefits even if the procedure was perfect and even if he pursued cardiac rehabilitation.

**Limitations**

There are some limitations of the current proposed framework. First, there are only a few currently available CPM combinations that are well known and routinely used. The CHADS2-VASc and the HAS-BLED scores are examples of risk scores that have been successfully combined to assess thromboembolic and bleeding risk as an aggregate. Physicians caring for patients with nonvalvular atrial fibrillation can use these combined assessments in steps to achieve SDM [49]. Unfortunately, the impact of this combination has not been well studied. This manuscript formalizes a process to link available CPM to approach procedural risk as an aggregate in patients with severe AS. Secondly, the current proposed framework is based on an assumption that each patient will be delegated to a risk state based on the above steps, i.e., a static patient status. However, it is hypothesized by many that therapeutic interventions in the frail older adult may benefit and enable them to increase their life expectancy along with an improved quality of life; resulting in a change in their patient status. Numerous interventions including exercise training, nutritional supplements (+ exercise training), pharmacological agents, multidimensional programs, and home-based programs have been studied to determine whether they can improve the frailty and functional status [39]. Some are currently undergoing evaluation and have not been published [38]. How these interventions along with the referral to cardiac rehabilitation [50, 51] can alter the evolution of patients with symptomatic AS will need to be determined. Third, although there are over 500 current cardiovascular CPM [52••], the potential benefit [53••], limitations, and impact are important concepts to consider but are beyond the scope of this review. Therefore, we point you to a series of articles and books related to prognostic research that discuss the importance of CPM that specifically discuss the development, validation, impact of newly developed CPM, as well as the recalibration or adaption of prior CPM [54–59]. Lastly, the validity of this proposed framework will need to be tested in future studies.

**Conclusion**

Cardiac valvular diseases are now considered a major public health issue with aortic stenosis having the highest burden. Although the introduction of TAVR has expanded the available therapeutic options for patients with aortic stenosis, it has also complicated the decision-making process. An objective, standardized evaluation of risk and benefit is needed to streamline this process. Clinical prediction models and standardized algorithms provide a logical process to facilitate this goal. In this review, we propose a seven-step framework for objective evaluation of risk assessment and decision making by linking clinically relevant clinical prevention models (life expectancy, Society of Thoracic Surgery, and TAVR risk calculators) with two additional concepts of lag time to benefit and competing risks that are relatively novel to the clinical arena. We believe that the use of this framework will initially improve the care of older adults with symptomatic aortic stenosis and can later be translated to other clinical decisions, in regard to procedures or surgeries, which often present higher immediate risks for the promise of improved long-term outcomes.

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**Compliance with Ethics Guidelines**

**Conflict of Interest** Ashok Krishnaswami, Daniel E. Forman, Mathew S. Maurer, and Sei J. Lee declare that they have no conflict of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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- Of importance
- Of major importance


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