Evaluating TAVI outcomes—not just a matter of life and death

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Transcatherter aortic valve implantation (TAVI) has been widely adopted in Europe and in the USA as an alternative to surgical aortic valve replacement (SAVR) in patients with severe symptomatic aortic stenosis (AS) at high or prohibitive surgical risk. Unfortunately, although proven in many trials and registries as a safe and effective treatment, many of the patients undergoing TAVI are at the extremes of age and illness, thereby not deriving significant long-term benefit in terms of life expectancy or quality of life (QOL). For example, among patients at prohibitive surgical risk treated with TAVI in the PARTNER IB trial, 30% were dead at 1 year and approximately one-half were deceased or had less than moderate improvement in their quality of life or New York Heart Association (NYHA) functional class (1). Furthermore, the public expenditure has been enormous and is rapidly rising, mostly owing to therapy offered to patients who would not have been offered treatment in the pre-TAVI era. This has raised a continuing interest in strategies to improve pre-TAVI patient selection in order to minimize "futility" (i.e., ineffective TAVI procedures) and improve cost-effectiveness.

Although several models to identify patients at high risk for death after TAVR were constructed, QOL prediction models are lacking. Given the age and underlying burden of comorbidity among patients currently considered for TAVI, improved performance and QOL may be as important treatment goals as extending life (2,3). Consequently, integrating QOL outcomes into the definition of a poor (and, conversely, an acceptable) outcome is particularly relevant in these challenging and complex patients (4). Two questions arise when debating this subject: (I) how should we define poor outcome after TAVI? (II) What are the predictors of poor outcomes?

The current study by Arnold et al. published in the *Journal of the American College of Cardiology* vol. 68 No. 17 (5) sheds some new light on this important topic. It is an external validation of a model previously developed by the same authors to estimate risk of poor outcomes in the PARTNER patients (6), now implemented on a cohort consisting 2,830 patients who underwent TAVI in the CoreValve US Pivotal Extreme and High Risk trials and associated continued access registries. Poor clinical outcome at 6 months after TAVI were defined as death, poor QOL as defined by Kansas City Cardiomyopathy Questionnaire-overall summary score (KCCQ-OS) <45 (comparable to NYHA functional class IV), or a decrease of ≥10 points in the KCCQ-OS from baseline. A second model was constructed representing a slightly better outcome at 1 year after TAVI and included death, KCCQ-OS score <60, or a decline of ≥10 points in the KCCQ-OS score from baseline. Covariates included 6 minute walk test (6MWT), mean aortic valve gradient, home oxygen, serum creatinine, mini mental state examination (MMSE), atrial fibrillation, male sex, and BMI for both the 6-month and 1-year models, in addition to diabetes mellitus and mean arterial blood pressure solely for the 6-month model. For the sake of easy implementation two reduced ("clinical") models were also constructed excluding the 6MWT and using simplified KCCQ and cognitive assessment approach (moderate to severe impairment, mild

impairment, no impairment). At 6 months after attempted TAVI, 31.2% of patient had a poor outcome because of death in 17.6%, very poor QOL in 11.6%, and decline in QOL in 2.0% of treated AS patients. Among the 2,325 patients with 1-year outcomes data available, 50.8% had a poor outcome: death occurred in 30.2%, poor QOL was noticed in 19.6%, and decline in QOL in 1.0%. Model performance in terms of discrimination (i.e., its ability to separate patients with poor outcomes from patients with acceptable outcomes) was moderate with a c-index of 0.646 for the 6-year full model (Similar to the c-index of 0.661 in the PARTNER derivation cohort), and 0.637, 0.653, and 0.665 for the 6-month clinical model, 1-year full model, and 1-year clinical model respectively. Model calibration (i.e., agreement between observed and predicted risk) was excellent for all 4 models with R2 (assessing correlation) ranging between 0.969 and 0.979. Finally, the study intended to examine the incremental contribution of frailty (3 or more deficits in the following geriatric domains: slowness, weakness, unintentional weight loss, exhaustion, and inactivity) and its individual components [including all 5 individual frailty domains plus disability (defined as the need of assistance in bathing, dressing, toileting, transferring or feeding)] to the performance of the models. These were not included in the original model due to the lack of their systematic assessment in the PARTNER trial. Reaffirming previous data (7), frailty was associated with a modest improvement in discrimination of a poor outcome when added to the existing models ($P<0.01$ for all except the 1-year clinical model), with the most important individual components being disability and unintentional weight loss.

The authors conclude that by testing the performance of the prior risk models in a completely separate dataset, the current study provides critical evidence to support the validity of these models for predicting poor outcome post-TAVI, thereby increasing confidence in their generalizability and ability to provide useful information to physicians evaluating patients for TAVI.

The authors of the study undertook an epic task of defining poor outcomes in TAVI, building a solid model for predicting poor outcomes, and perhaps most importantly, they have performed an external validation of this model. Risk prediction models infrequently undergo external validation, restricting their performance and generalizability (8). An important and practical addition are the simplified 6-month and 1-year models built to facilitate easy implementation in the real world setting which preformed almost as good as the full model. The observation that more than 50% of patients did not benefit from TAVI at 1 year is disturbing. However, this data mostly reflects the early experience obtained in the Corvalve pivotal trials and combines the prohibitive and the high risk cohorts. Validation of this model on "real world data" derived from registries is therefore warranted because registries include patients of a wider spectrum of risk and of a more contemporary selection practice. The relatively modest incremental contribution in c-statistic offered by the frailty indices can be explained by the extensive overlap between the base covariates and the individual components of frailty (e.g., 6MWT and gait speed assessment).

Duly noted by the authors, the discriminative ability (as measured by the c-index) of the current model was only intermediate, reflecting the multifactorial nature of QOL indices. In other words, the models' ability to differentiate between patients who will benefit from the procedure and those who won't is questionable. In that respect, in order to minimize futility and avoid disappointment, patient selection for TAVI should be individualized, patient centered, and expectation driven. For example, a patient restrained to a wheel chair due to orthopedic disability would not achieve a significant gain in physical function, but may enjoy a reduction in dyspnea or chest pain. The model's excellent calibration translates to greater accuracy in the estimation of the risk of poor outcome. This can serve as a platform to counsel patients and their families as to the expected outcomes of care and could aid in decision making.

In summary, the current study looks at the quality of life as a desired outcome rather than merely life prolongation. It offers a simple and validated model for poor outcome prediction and can be used for patient consultation and to aid the clinical decision making process. Nevertheless, patient selection remains a highly individualized process in which a frank doctor-patient dialogue about the patient's expectations and needs is crucial. The importance of the experienced 'heart team' in the decision making process cannot be over emphasized.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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