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Can We Predict Who Will Be Alive and Well After TAVR? Is That Useful to Individual Patients?

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The goal of health care is to optimize both quantity and quality of life for patients. Among select patients with severe symptomatic aortic stenosis, transcatheter aortic valve replacement (TAVR) can, on average, improve both survival and health status (i.e. symptoms, functional status, and quality of life).[1,2] Yet, the technology is currently limited to patients who are either ineligible or at high risk for open surgical AVR. The result is that TAVR is used in older patients with multi-morbidity and frailty. As such, success is far from guaranteed for each of these complex cases. Indeed, despite the overall benefits seen in the Placement of AoRTic TraNscathetER Valve (PARTNER) trial, approximately 1 in 5 patients undergoing TAVR died within 6-months.[3] An unmet need is to better determine, prior to TAVR, which individual patients are unlikely to achieve a "good" outcome.

Risk models offer the potential to move beyond the average effects presented in summary trial results by further risk stratifying patients based on their individual characteristics.[4] A number of TAVR risk models have been constructed, primarily to predict risk for death. Yet, for many of these patients (the average TAVR recipient is in his or her ninth decade of life), survival alone may not constitute a "victory". Persistently poor or worsening patient health status, even among longer-term survivors, is unlikely to be perceived as a success for most patients and their families. Fortunately, the PARTNER trial collected data on a wide range of anticipated benefits and risks of treatment, including formal measures of health status.[2,5]

In this issue of *Circulation*, Arnold and colleagues tackle the critical question, "*Can we predict who will be 'alive and well' after TAVR?*"[6] Using the cohort of patients who underwent TAVR in the PARTNER trial or continued access registry, they derived and

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validated a risk model to predict poor outcome after TAVR. Poor outcome was defined as death OR poor patient health status OR a decline in patient health status 6 months following the procedure.

The novelty of this risk model is noteworthy. It is a true patient outcome model, predicting both survival and patient health status. Despite the obvious relevance to patients, few models of this type exist in the medical literature.[7] A key to the creation of such models is the increasing availability of standardized tools to measure patient health status. These instruments, such as the Kansas City Cardiomyopathy Questionnaire (KCCQ) used in this study, are reproducible, valid, and clinically interpretable.[5] The era of measuring and predicting patient-reported outcomes as part of clinical practice is just dawning, and is bolstered by the study by Arnold and colleagues.

The results presented in the current study are eye-opening.[6] Overall, one-third of the patients had a poor outcome at 6 months after TAVR: 19% had died, 12% had poor health status, and 2% had worsened health status. These individuals were more likely to have low body weights, low mean aortic valve gradients, oxygen-dependent lung disease, and poor baseline functional and cognitive status. When patients were categorized by the risk model using these characteristics, poor outcome at 6 months after TAVR was seen in 55% of high-risk patients, 37% of intermediate-risk patients, and 18% of low-risk patients. Thus, the risk model was able to stratify risk of poor outcome following TAVR using pre-procedural patient factors.

This directly leads to the next critical question, "*Is this risk model useful?*" This is an open question. The vast majority of risk models—for any outcome and for any condition or procedure—have not been clinically applied. They remain more academic than practical. For risk models like the one developed by Arnold and colleagues to be helpful in clinical practice, the 3 'I's' must be embraced: *Integration*, *Interpretation*, and *Interaction*.

Integration

Risk model results for individual patients must become integrated with routine clinical workflow. They cannot inhibit or add significant time to patient care. Electronic health records (EHRs) should support this, but only rare examples of effective integration of clinical decision support tools exist. Most current EHRs are largely electronic versions of paper records, with critical clinical information not available as structured data. Additionally, patient health status measures such as the KCCQ are rarely captured in routine care.[5] To integrate the Arnold TAVR risk model in clinical practice and monitor outcomes, EHRs will need to have risk factors and patient health status measures available in a usable form, automatically calculate risk model scores based on the most up-to-date model, and display results back at the point of care in a way that is clinically meaningful..

Interpretation

Clinicians will need to become familiar with the interpretation of risk model results, and understand the limitations of model predictions. This is analogous to interpreting other clinical test results that inform treatment recommendations (e.g. labs or diagnostic studies).

However, interpretation of risk model estimates and patient health status data such as the KCCQ have not yet become as familiar as creatinine clearance. Furthermore, the inherent uncertainty for any future event must be incorporated into the practical use of risk models. In split-sample validation, the c-index for the Arnold TAVR model was 0.64, with nearly one in five “low risk” patients having a poor outcome and nearly half of “high-risk” patients having a good outcome. The Holy Grail of such risk models could be the ability to determine pre-procedural futility, thereby avoiding hopeless procedures and simplifying treatment decisions. The truth is that risk models will never say that an individual patient will or will not derive benefit from a procedure. In the case of TAVR, where the alternative of medical therapy has a very high rates of poor outcome, even a risk model predicting a >50% chance of adverse outcome after TAVR may not change the decision by many patients and clinicians to move forward with the procedure. What such risk models can do is objectively calibrate expectations and help anticipate possible future events.

Interaction

The most important aspect of risk models is the way they interact with patients and their families. Even the best risk models cannot supplant the process of communicating prognosis. And clinicians cannot let models outweigh clinical sense and consideration of patient preferences. This defines the need for shared decision making, which integrates evidence-based medicine and tailored risk estimates with individual patient preferences. There are increasingly available shared decision making tools to effectively display a patient’s estimated risk and benefit for a given therapy.[8] The TAVR risk model developed by Arnold and colleagues can become clinically useful if it is implemented as part of a meaningful shared decision making process.

In the final analysis, the creation of the TAVR risk model by Arnold and colleagues is an important step forward. It rightly focuses attention on quality of life outcomes in addition to mortality. And it could become a tool to support decision making prior to TAVR. But for the risk model to move from academic to clinical practice relevance, the 3 ‘I’s’ will need to be accomplished: *integration* with clinical workflow; appropriate *interpretation* by clinicians at the point of care; and, most critically, meaningful *interaction* with patients and families. For TAVR and other medical treatment decisions, shared decision making that is supported by risk model estimates for individual patients is a path to higher quality of care through better decision quality. This is the promise of personalized medicine—a promise that remains unfulfilled in contemporary medical practice.

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