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EDITORIAL COMMENT

TAC for TAVR

What Is the Score?*

Michael Mack, MD, Mohanad Hamandi, MD, Ambarish Gopal, MD

Transcatheter aortic valve replacement (TAVR) has become a standard treatment for patients with aortic stenosis (AS) at prohibitive, high, and intermediate risk for surgical aortic valve replacement (1–3). Many predictive risk models have been used to help determine not only the ability of a patient to successfully undergo TAVR but also to receive benefit from the procedure. Those benefits include prolongation of life, improved quality of life, or ideally both. The most common models used to assess procedural risk include the Society of Thoracic Surgeons Predicted Risk of Mortality, the Logistic EuroSCORE, and the EuroSCORE II (4–6). These algorithms for predicting procedural mortality were developed and validated in patients undergoing surgical operations and thus have limited applicability and accuracy in TAVR populations. A TAVR-specific risk algorithm has been developed from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry but has had limited application and validation to date. All of these risk prediction algorithms are for in-hospital or 30-day mortality post-procedure. For TAVR currently, the 30-day procedural mortality has decreased significantly now approaching 1% in clinical trials and less than 4% in clinical practice (7).

Therefore, the focus of clinicians is now appropriately shifting toward identification of those patients who despite undergoing a successful procedure do not receive benefit from the correction of their AS. These patients have been characterized as dying *with* AS but not *from* AS. Current 1-year mortality is 26% meaning that 1 of 4 patients who received a TAVR valve are dead within 1 year (8). Can one accurately predict who are those patients that despite having survived TAVR will not be alive 1 year later (i.e., futility)? Numerous patient comorbidities have been identified as predictors of increased mortality and/or lack of improvement in quality of life at 1 year or longer post-procedure including oxygen-dependent chronic lung disease, chronic renal insufficiency especially when dialysis dependent, severe concomitant tricuspid regurgitation, and advanced stages of frailty among others (8). Clinical decision-making regarding recommendation for a patient to undergo a procedure is based on these factors and clinical judgement sometimes termed “the eyeball test.” It would help clinicians to have an objective, reproducible, and readily available tool that accurately predicts long-term outcomes that could serve as a decision aid in practice.

In this issue of *iJACC*, Lantelme et al. (9) report a new scoring system, the Calcification Prognostic Impact (CAPRI) score. The score is based on 4 domains including thoracic aortic calcification (TAC), patient demographics and comorbidities, atherosclerotic disease, and cardiac function to help predict 1-year cardiovascular and all-cause mortality in patients being considered for TAVR. The components of the latter 3 domains are patient demographics (age, sex, and renal and lung function), atherosclerotic disease (coronary artery and peripheral vascular disease, history of stroke), and cardiac function (ejection fraction, New York Heart Association functional class, pulmonary artery pressures, aortic valve gradient, and mitral regurgitation severity). Although the components of these domains are contained in other risk prediction scoring systems, the quantification of TAC is a unique characteristic of the CAPRI score.

TAC was obtained from a preoperative computerized tomographic scan using different scanners with at least 4-cm z-coverage of the whole thoracic aorta from the aortic sinus to the diaphragmatic hiatus excluding the aortic valve. Calcification was extracted

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From the Baylor Scott & White Health, Heart Hospital Baylor Plano, Dallas, Texas. Dr. Mack is Co-Principal Investigator of the Partner Trial of Edwards Lifesciences (uncompensated); and trial Co-Principal Investigator at Abbott Vascular and Medtronic. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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using a semiautomated, open source software and analyzed by 3 independent operators blinded to clinical outcomes. A score was developed based on the linear predictors of Cox models including TAC in addition to comorbidities and demographic, atherosclerotic disease, and cardiac function factors.

The model was derived from 1,425 patients treated between 2010 and 2014 as a derivation cohort and validated in 311 patients treated with TAVR in 2015. Cardiovascular and all-cause mortality at 1 year was 13.0% and 17.9%, respectively, in the training cohort and 8.2% and 11.8% in the test cohort. Adding TAC to the other factors improved significantly the prediction of cardiovascular and all-cause mortality ($p < 0.01$ and $p = 0.04$, respectively). An increase of 1 cm^3 in TAC was associated with a 6% increase in cardiovascular mortality (hazard ratio: 1.06; 95% confidence interval: 1.01 to 1.10) and a 4% increase in all-cause mortality (hazard ratio: 1.04; 95% confidence interval: 1.00 to 1.08). The predicted and observed survival probabilities were highly correlated (slopes >0.9 for both cardiovascular and all-cause mortality). The model's predictive power was moderate (area under the curve: 68%; 95% confidence interval: 64 to 72) for both cardiovascular and all-cause mortality. Perhaps most compelling is that patients with a CAPRI score above 0.70 and 0.78 for cardiovascular and all-cause mortality have a 50% chance of dying within the first year after TAVR. If a patient has a score under that threshold, the 1-year mortality is <10%.

So, what is the significance of TAC? Aortic calcification is likely a marker of vascular aging and a surrogate for aortic stiffening. Indeed, the authors have previously demonstrated an association with heart failure. As such, it may provide an objective marker of a patient's true age rather than chronologic age.

So, is TAC that "objective, reproducible and readily available tool" that will aid clinicians in determining who will benefit from TAVR long term and who are the "poor responders"? First, the CAPRI score that incorporates TAC does seem to be predictive of 1-year all-cause and cardiovascular mortality. Adding TAC to the more conventional predictors contained in the CAPRI can potentially identify with greater certainty poor TAVR responders who are likely to not benefit from the procedure. The CAPRI score was developed from 2 sets of patients in 2 different time periods at 4 different centers. Widespread adoption will require validation in other centers and in other populations.

Second, TAC was obtained from computed tomography scans, which are routinely performed before TAVR not requiring additional testing. The calculation of TAC is semiautomated but allows for case-based interpretation. This is an important part of any methodology because it does include input from the interpreting physician to delineate areas of calcification that have to be accurately included in study analysis and quantification. The limitation, however, is that the software for calculation of the calcium is not a commercial product and therefore is not widely available.

So, is TAC the final answer? Of course not. But it may provide an objective, reproducible, and potentially widely available objective tool that can help as a decision aid to define poor responders to TAVR at 1 year. The CAPRI score should thus be regarded as an objective tool to help the heart team make a decision on therapy and to inform the patient and family. Defining the futile patient who will not benefit from therapy is a critical goal as the treatment of AS progresses and matures.

ADDRESS FOR CORRESPONDENCE: Dr. Michael Mack, Baylor Scott & White Health, 1100 Allied Drive, Plano, Texas 75093. E-mail: Michael.mack@bswhealth.org.

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