JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2016 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER

VOL. 68, NO. 17, 2016
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2016.07.762

Prediction of Poor Outcome After Transcatheter Aortic Valve Replacement

Suzanne V. Arnold, MD, MHA,[a,b] Jonathan Afilalo, MD, MSc,[c] John A. Spertus, MD, MPH,[a,b] Yuanyuan Tang, PhD,[a] Suzanne J. Baron, MD, MSc,[a,b] Philip G. Jones, MS,[a] Michael J. Reardon, MD,[d] Steven J. Yakubov, MD,[e] David H. Adams, MD,[f] David J. Cohen, MD, MSc,[a,b] on behalf of the U.S. CoreValve Investigators

ABSTRACT

BACKGROUND A series of models have been developed to identify patients at high risk for poor outcomes after transcatheter aortic valve replacement (TAVR) to help guide treatment choices, offer patients realistic expectations of long-term outcomes, and support decision making.

OBJECTIVES This study examined the performance of the previously developed TAVR Poor Outcome risk models in an external dataset and explored the incremental contribution of geriatric domains to model performance.

METHODS Poor outcome after TAVR was defined as death, poor quality of life (QOL), or decline in QOL, as assessed using the Kansas City Cardiomyopathy Questionnaire. We tested 4 TAVR Poor Outcome risk models: 6-month and 1-year full and clinical (reduced) models. We examined each model's discrimination and calibration in the CoreValve trial dataset, and then tested the incremental contribution of frailty and disability markers to the model's discrimination using the incremental discrimination index.

RESULTS Among 2,830 patients who underwent TAVR in the CoreValve US Pivotal Extreme and High Risk trials and associated continued access registries, 31.2% experienced a poor outcome at 6 months following TAVR (death, 17.6%; very poor QOL, 11.6%; QOL decline, 2.0%) and 50.8% experienced a poor outcome at 1 year (death, 30.2%; poor QOL, 19.6%; QOL, decline 1.0%). The models demonstrated similar discrimination as in the Placement of Aortic Transcatheter Valves Trial cohorts (c-indexes, 0.637 to 0.665) and excellent calibration. Adding frailty as a syndrome increased the c-indexes by 0.000 to 0.004 (incremental discrimination index, $p < 0.01$ for all except the 1-year clinical model), with the most important individual components being disability and unintentional weight loss.

CONCLUSIONS Although discrimination of the TAVR Poor Outcome risk models was generally moderate, calibration was excellent among patients with different risk profiles and treated with a different TAVR device. These findings demonstrated the value of these models for individualizing outcome predictions in high-risk patients undergoing TAVR. (J Am Coll Cardiol 2016;68:1868–77) © 2016 by the American College of Cardiology Foundation.

From the [a]Saint Luke's Mid America Heart Institute, Kansas City, Missouri; [b]Department of Medicine, Saint Luke's Mid America Heart Institute, University of Missouri-Kansas City, Kansas City, Missouri; [c]Department of Medicine, Jewish General Hospital, McGill University, Montreal, Quebec, Canada; [d]Department of Cardiothoracic Surgery, Houston-Methodist-Debakey Heart and Vascular Center, Houston, Texas; [e]Riverside Methodist Hospital, Columbus, Ohio; and the [f]Department of Cardiothoracic Surgery, Mount Sinai Medical Center, New York, New York. The CoreValve U.S. Pivotal trials and associated continued access registries were sponsored by Medtronic. All analyses, the preparation of the manuscript, and the decision to submit the manuscript for publication were done independently of the study sponsor. Dr. Arnold is supported by a Career Development Grant Award (K23 HL116799) from the National Heart, Lung, and Blood Institute. Dr. Spertus has an equity interest in Health Outcomes Sciences; and owns the copyright for the Kansas City Cardiomyopathy Questionnaire. Dr. Baron has received speaker honoraria and consulting income from Edwards Lifesciences; and consulting income from St. Jude Medical. Dr. Reardon has received honoraria from Medtronic for participation on a surgical advisory board. Dr. Yakubov is on the advisory board for Boston Scientific, Medtronic, and Abbott Vascular; and is a consultant for Medtronic. Dr. Adams has received royalties through his institution from Medtronic for a patent related to a triscupid-valve annuloplasty ring and from Edwards Lifesciences for a patent related to degenerative valvular disease-specific annuloplasty rings. Dr. Cohen has received research support from Edwards Lifesciences, Medtronic, Boston Scientific, Abbott Vascular, Eli Lilly, Daiichi-Sankyo, and AstraZeneca; consulting income from Medtronic, Abbott Vascular, AstraZeneca, Eli Lilly, and Merck; and speaking honoraria from AstraZeneca. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Michael Mack, MD, served as Guest Editor for this paper.

Manuscript received May 17, 2016; revised manuscript received July 8, 2016, accepted July 22, 2016.

Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

Over the past decade, transcatheter aortic valve replacement (TAVR) has emerged as a less invasive option for aortic valve replacement and is currently approved in the United States for patients at high or extreme risk of morbidity or mortality with conventional surgical aortic valve replacement. Several randomized trials have demonstrated that TAVR substantially reduces mortality and improves quality of life (QOL) as compared with medical therapy among patients considered to be inoperable (1), outcomes that are similar or superior to those of surgical aortic valve replacement in high-risk patients (2,3). Nonetheless, some patients do not improve functionally or live long following TAVR, with approximately 1 in 4 patients treated with TAVR dying within 1 year (4). Moreover, despite substantial improvement in QOL for many patients, a sizeable minority continues to experience significant heart failure symptoms, with associated functional limitation and poor QOL (5–9).

SEE PAGE 1878

Consequently, there is considerable interest in developing methods to identify patients at high risk of poor outcomes post-TAVR (10–13). A series of TAVR poor outcome risk models have been developed using data from the PARTNER (Placement of Aortic Transcatheter Valve) trials. Based on pre-procedural characteristics, these models were designed to identify such individuals (7) to help guide treatment choices and offer patients realistic expectations of outcomes based on their personal characteristics. Unlike previous studies that focused solely on mortality (14,15), these models integrated both mortality and health status into a single construct (16). This outcome is particularly relevant in this elderly population, because one of the principal benefits of treatment is to improve patient health status. Although these models had moderate discrimination and good calibration with the observed data, external validation could not be performed, nor were other potentially important predictors examined, such as frailty and disability, which have demonstrated prognostic importance (17).

To address these knowledge gaps, we used data from the CoreValve U.S. Pivotal Extreme and High Risk trials and their associated continued access registries to examine the performance of the prior models in a distinct and broader patient population. Additionally, we sought to determine the incremental contribution of integrating geriatric domains, such as gait speed and disability, in the risk models. Our ultimate goal was to develop models that could be deployed at the bedside.

METHODS

The specific details of the CoreValve trials have been published previously (18,19). Briefly, patients had severe, symptomatic aortic stenosis (AS) and were estimated to be at high (estimated 30-day risk of mortality of ≥15%) or extreme (estimated 30-day risk of mortality or irreversible morbidity of ≥50%) surgical risk. Patients in the high-risk trial were randomized to TAVR versus surgical aortic valve replacement; after the randomized trial was enrolled, subsequent patients underwent TAVR as part of a continued access registry. All patients in the extreme-risk cohort underwent TAVR. Our study included only patients who underwent an attempted TAVR procedure, performed using the self-expanding system (CoreValve, Medtronic, Inc., Minneapolis, Minnesota). The study was approved by the institutional review board at each site, and all patients provided written informed consent before participation.

HEALTH STATUS, FUNCTIONAL STATUS, AND MEMORY. Disease-specific health status was assessed at baseline, 1 month, 6 months, and 1 year after enrollment using the Kansas City Cardiomyopathy Questionnaire (KCCQ) (20). The overall KCCQ summary score (KCCQ-OS) was the primary health status outcome for this study. KCCQ-OS values ranged from 0 to 100; higher scores indicated fewer symptoms and better QOL. The KCCQ-OS score generally correlated with New York Heart Association functional class as follows: class I, KCCQ-OS 75 to 100; class II, 60 to 74; class III, 45 to 59; and class IV, 0 to 44 (21,22). Changes in the KCCQ-OS of 5, 10, and 20 points correspond with small, moderate, or large clinical improvements, respectively (22).

Generic health status was assessed with the Medical Outcomes Study Short Form-12 Health Survey (23). Functional status was assessed using a 6-min walk test (6MWT), with patients permitted to use assist devices (e.g., walkers, canes), if needed (24). If a patient could not perform the test, the value for the 6MWT distance was set to 0 m. Memory was tested using the Mini-Mental State Examination (MMSE) and scores were categorized as normal, mild dementia, or severe dementia (MMSE 28 to 30, 19 to 27, 0 to 18, respectively) (25).

FRAILTY AND DISABILITY. A syndrome of decreased physiologic reserve, frailty is generally assessed through a range of geriatric domains including slowness, weakness, unintentional weight loss, exhaustion, and inactivity (26). Frailty, as a syndrome,

ABBREVIATIONS AND ACRONYMS

6MWT = 6-min walk test

ADLs = activities of daily living

AS = aortic stenosis

IDI = integrated discrimination improvement

KCCQ-OS = Kansas City Cardiomyopathy Questionnaire-overall summary score

MMSE = Mini-Mental State Examination

TAVR = transcatheter aortic valve replacement