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TO THE EDITOR

Frailty Scales in Transcatheter Aortic Valve Replacement

Incremental Body of Evidence

In a recent issue, Schoenenberger et al. (1) eloquently presented a post hoc analysis from their single-center cohort of 330 older adults undergoing transcatheter aortic valve replacement between 2009 and 2013, in which they assessed the predictive value of frailty alongside conventional risk scores. Given the modest number of events (52 deaths over 1 year), to avoid overfitting, the investigators selected 2 independent variables: a composite clinical risk score (logistic European System for Cardiac Operative Risk Evaluation score or Society of Thoracic Surgeons score) and a multidimensional geriatric assessment (MGA) score reflecting mobility, cognition, nutrition, and disability. By combining a clinical risk score with a frailty scale, they captured the use case of a practicing clinician who wishes to enrich his or her assessment of a complex older patient referred for transcatheter aortic valve replacement.

Frailty metrics provide unique information that is highly predictive and yet does not overlap with the realm of traditional risk factors that are encrusted in our cardiocentric vernacular; this may simultaneously be a strength of frailty scores and a limitation of current clinical risk scores. A small but salient caveat is that although the investigators used the older European System for Cardiac Operative Risk Evaluation I, the newer version (2) has added a question for "poor mobility" (broadly defined as severe impairment of mobility secondary to musculoskeletal or neurological dysfunction), borrowing from geriatricians' vernacular and initiating a paradigm shift from disease- or surgery-specific risk scores to much needed patient-centered risk scores.

The investigators of this study astutely used a bevy of model performance statistics to demonstrate that the MGA added incremental predictive value above the clinical risk scores. This finding is consistent with the 14-center FRAILTY-AVR (Frailty in Aortic Valve Replacement) cohort including >700 older adults undergoing transcatheter aortic valve replacement (119 deaths over 1 year), in which we had previously shown that the MGA added incremental value above the Society of Thoracic Surgeons score, achieving a C statistic of 0.70 (comparable with their reported C statistic of 0.68) and an integrated discrimination improvement statistic of 0.030.

The FRAILTY-AVR study (3) prospectively compared the incremental value of 7 different frailty scales, including the MGA, and ultimately found that the Essential Frailty Toolset was more predictive of 1-year mortality and disability and was shorter to administer. This leads us to respectfully question the omission of FRAILTY-AVR in the background and discussion of Schoenenberger et al.'s (1) study. Too often, readers are presented with the merits of frailty scale X without being presented data on frailty scales Y and Z. Alternatively, they are presented modified versions of frailty scales Y and Z constructed with one-off variables available in retrospective databases, leading them to believe that these scales perform poorly. This speaks to the clinical community's perplexity with the plethora of frailty scales being promulgated and the lack of consensus that has impeded frailty from going mainstream.

Although we cannot humbly assert a simple solution to this conundrum, pending external validation of the Essential Frailty Toolset, we would like to call on frailty researchers to take an inclusive view of frailty that acknowledges and compares the effectiveness of different scales to predict outcomes and affect care. Because the choice of frailty scale also depends on feasibility, expertise, and resources, relevant measures such as administration time and assessor training should be considered. Once we as frailty researchers show that we can advance a cohesive agenda, then clinicians will follow suit and carry our research forward to the ultimate stage of knowledge translation.

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REPLY: Frailty Scales in Transcatheter Aortic Valve Replacement Incremental Body of Evidence

We thank Dr. Afilalo and colleagues and Dr. Lantelme and colleagues for their interest in our paper (1).

Dr. Afilalo and colleagues refer to the results from the multicentric FRAILTY-AVR (Frailty Assessment Before Cardiac Surgery & Transcatheter Interventions) study (2), which they published after submission of the manuscript of our study. Their study investigated 7 frailty scales, including our own scale, to predict mortality and disability in patients undergoing transcatheter aortic valve replacement. We agree with Dr. Afilalo and colleagues that the huge variety of different frailty scales so far has impeded the implementation of frailty in clinical practice. Undoubtedly, the study from Afilalo et al. (2) is very comprehensive and helps clarify the situation.

To respond to the comment of Dr. Lantelme and colleagues about potential overoptimism and overfitting in our models, we re-analyzed the C-statistics of our main models using 1,000 bootstrap replications (Table 1). We conclude on the basis of these results that overfitting did not affect our conclusions.

Dr. Lantelme and colleagues also asked about clarification of our choice of confounders and predictors. We a priori chose a maximum of 4 variables in the modeling based on the recommended 10 events-per-variable (EPV) approach. Given the observed 52 deaths within 1 year of follow-up, we obtained an EPV of 17 (3 variables) and 13 (4 variables), which is even more than the recommended 10 EPV. Thus, based on our a priori variable selection approach and the observed EPV, we a priori minimized model overfitting and misspecification.

However, we agree with Dr. Lantelme and colleagues that our findings are limited to our observed data and study population, which need further validation. However, we adequately mentioned in the limitations section of our paper that external validation will be necessary to generalize our results.

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TO THE EDITOR

In Patients With Atrial Fibrillation Undergoing Percutaneous Coronary Intervention, One Size Cannot Fit All

I read with great interest the results of the post hoc analysis of the PIONEER AF-PCI (Open-Label, Randomized, Controlled, Multicenter Study Exploring Two Treatment Strategies of Rivaroxaban and a Dose-Adjusted Oral Vitamin K Antagonist Treatment Strategy in Subjects with Atrial Fibrillation who Undergo Percutaneous Coronary Intervention) trial (1) described in the report by Kerneis et al. (2) recently published in *JACC: Cardiovascular Interventions*. The investigators are to be congratulated on making this unquestionably important step in the search for

TABLE 1 Optimism-Corrected C-Statistic for Main Models		
	C-Statistic Original	C-Statistic Optimism-Corrected*
EuroSCORE	0.67	0.65
STS score	0.64	0.61
Frailty index	0.66	0.64
EuroSCORE + frailty	0.72	0.70
STS score + frailty	0.68	0.66

All models were adjusted for age and sex. *From 1,000 bootstrap replicates.