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EDITORIAL COMMENT

Frailty in Patients Undergoing Transcatheter Aortic Valve Replacement

Frequently Measured, Seldom Managed*

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Transcatheter aortic valve replacement (TAVR) has transitioned from a fringe option for inoperable and high-risk patients facing an otherwise grave prognosis (1-3) to an established standard of care for the majority of patients with severe symptomatic aortic stenosis in little over 10 years (4-7). And yet, there remains marked heterogeneity in outcome at the individual patient level, with up to 30% experiencing little symptomatic benefit or death within 1 year of TAVR, despite 95% periprocedural success (8). Enhanced patient selection and risk stratification are therefore pressing requirements, demanding improved and integrated assessment of cardiac/noncardiac comorbidity and frailty.

Frailty has been defined as a clinical syndrome involving multisystem impairment that results in reduced physiological reserve and increased vulnerability to stressors (9). Related to (yet distinct from) comorbidity, it is of intuitive importance to elderly patients undergoing TAVR; and has rightly been the subject of increased research attention in recent years (**Figure 1**). Notable developments include: 1) the observation that integration of commonly employed frailty measures into conventional surgical risk scores augments their predictive accuracy (10,11); 2) development of frailty assessment tools for use in patients undergoing transcatheter therapies (**Figure 1**) (12-14); and 3) integration of objective frailty assessment in national guidelines (15). And yet, the optimal means of doing just that remain the subject of conjecture. The multitude of published frailty scores (n ≥35) exhibit marked inconsistency—ranging, for example, between 35% and 74% in the FRAILTY-AVR (Frailty Assessment Before Cardiac Surgery & Transcatheter Interventions) study (12)—while additional interobserver variability and the time-consuming nature of some manual assessments have hampered the clinical quest for a consensus metric to implement and inform practice.

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The work by Kiani et al. (16) featured in this issue of *JACC: Cardiovascular Interventions* is therefore a welcome contribution to the debate. In the largest study of frailty in TAVR patients to date, the investigators used Centers for Medicare & Medicaid Services-linked outcomes of 36,242 patients from the STS/ACC TVT (Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy) registry to examine the relationship between 3 commonly employed surrogates of frailty (hypoalbuminemia, anemia, and gait speed over a 5-m walk), and short- and long-term outcomes. In adjusted analyses, each surrogate of frailty was independently associated with an increase in 1-year mortality (the primary outcome), with an increasing number of adverse markers demonstrating additive effects. Adjusted hazard ratios for the presence of all 3 makers were 1.4 (95% confidence interval: 1.0 to 1.8; $p < 0.041$) and 2.5 (95% confidence interval: 2.1 to 3.0; $p < 0.001$) for 30-day and 1-year mortality, respectively. The relative contribution of each predictor variable was similar. Associations were also demonstrated with a number of important secondary

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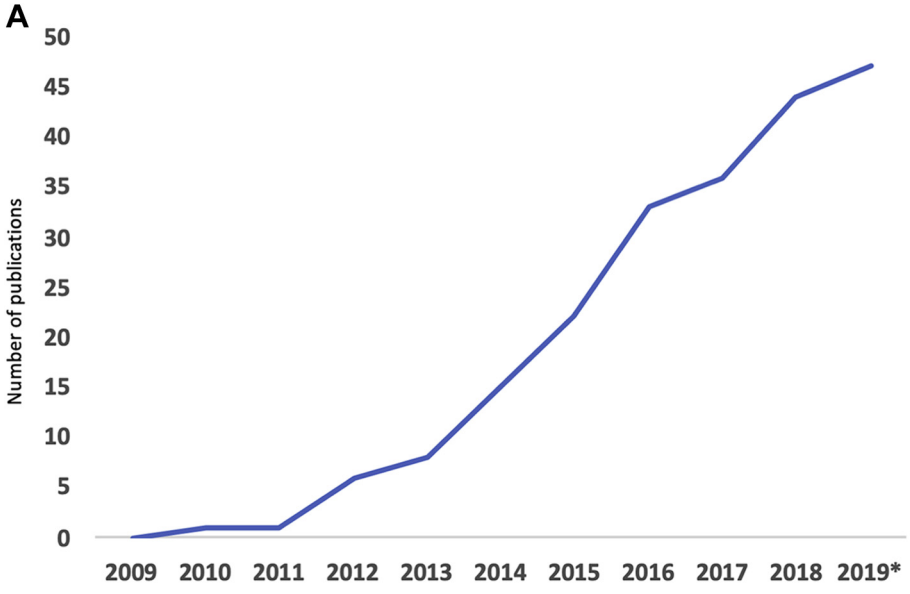
FIGURE 1 Frailty Publications in TAVR



B

Frailty score	Components	Study-type	n=
Essential frailty toolset[12]	Serum albumin, hemoglobin, chair raises, MMSE	Prospective	1020
Rogers *et al*[14]	BMI <20 kg/m^2, serum albumin, grip strength, gait speed, Katz ADL score ≤ 4/6	Prospective	554
Hospital frailty risk score[13]	Up to 109 ICD-10 concomitant diagnoses, present on admission	Retrospective	32277
Kiani *et al*[16]	Serum albumin, hemoglobin, gait speed	Retrospective	36242

(A) PubMed-cited articles on TAVR and frailty per year. **(B)** Summary of TAVR-related frailty scores. *Up until September 2019. BMI = body mass index; ICD-10 = International Classification of Diseases-Tenth Revision-Clinical Modification; Katz ADL = Katz Index of Independence in Activities of Daily Living; MMSE = Mini-Mental State Exam; TAVR = transcatheter aortic valve replacement.

outcomes, including periprocedural bleeding, length of stay, and readmission for heart failure. Interestingly, there was no significant interaction between age and the selected frailty predictors; highlighting the relevance of frailty to outcome irrespective of age.

Reflecting the variation in current practice, it is notable that frailty data were unavailable for over a third of records (n = 12,782). Although a supplementary sensitivity analysis suggested no difference in measured clinical characteristics between groups with or without frailty data, the investigators rightly acknowledge this as an important limitation. Those with prior valve surgery were similarly excluded. The absence of cognitive assessment (a demonstrably important factor in recovery) is also an important limitation (17). Nevertheless, the investigators correctly highlight considerable strength in the proposed model and its prospective use as a routine screening tool.

This work, therefore, represents a further important step forward in our ability to accurately identify frailty and its relevance to outcome in patients undergoing TAVR assessment. However, the most pressing question remains: once frailty is diagnosed, what do we do about it? Certainly, more accurate risk stratification should permit better informed discussions with patients (and their families) before TAVR, enable better targeted follow-up to prevent complications (e.g., heart failure readmission), and identify those who are unlikely to benefit. Whether TAVR *should* be performed in these patients will rightly remain an individualized decision based on heart team discussion and patient involvement. Meanwhile, further work is

clearly required to identify interventions that will render frailty a modifiable risk factor, rather than a passive harbinger of poor outcome. The outcomes of ongoing clinical trials investigating the effect of "prehabilitation" strategies (Pre-operative Rehabilitation for Reduction of Hospitalization After Coronary Bypass and Valvular Surgery [PREHAB], NCT02219815; Prehabilitation to Improve Functional and Clinical Outcomes in Patients With Aortic Stenosis [TAVR-FRAILTY], NCT02597985; Prehabilitation for Patients Undergoing Transcatheter Aortic Valve Replacement [TAVR-Prehab], NCT03107897) in this cohort are therefore awaited with keen interest.

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