EDITORIAL COMMENT

Working Toward a Frailty Index in Transcatheter Aortic Valve Replacement

A Major Move Away From the “Eyeball Test”*

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Transcatheter aortic valve replacement (TAVR) has become an alternative treatment option for patients with severe symptomatic aortic stenosis considered to be at high or prohibitive surgical risk (1). However, despite TAVR being associated with a very high procedural success rate (>95%), associated mortality rates at 1- and 2-year follow-up remain ≥15% and >30%, respectively (1-3). Central to the success of any medical treatment is performance of the correct procedure on the correct patient. Cardiac surgical risk scores and subjective clinical impression have in general guided the patient selection process and risk prediction in TAVR. Cardiac risk scores, however, do not take into account some important factors such as frailty, likely to be prevalent among elderly persons and high-risk profile patients undergoing TAVR. The awareness of the concept of frailty in cardiology and cardiac surgery parallels its increasing awareness in fields of medicine outside gerontology (4,5) and now has extended to TAVR. Frailty assessment of TAVR candidates to date has been mainly based on the traditional “eyeball” test, which is limited by its empirical nature, leading to major personal biases, low reproducibility among physicians and centers, and a lack of a scientifically proven methodology.

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Frailty syndrome might be best described as a multidimensional series of limitations characterized by diminished reserves and incapacity to adequately tolerate stressors. However, as simplistic as the word “frailty” might seem, there is neither a currently universally accepted definition of frailty nor a consensus about specific clinical measures or laboratory markers for its diagnosis (6). Furthermore, extensive overlap and interactions occur in a nonlinear fashion between disability, comorbidity, and frailty. The most commonly used definition of frailty is based on the criteria of Fried et al. (7), which assess up to 5 domains—nutritional status (weight loss), energy (exhaustion), physical activity (leisure time activity), mobility (gait speed), and strength (grip strength)—to define a frail phenotype and identify older people at high risk for adverse outcomes. What is agreed upon is the need to assess, in addition to physical status, other domains such as cognitive ability, mood, and mental health to obtain a more complete assessment of frailty (6).

Although some studies provided some preliminary data on the importance of the functional impairment pre-TAVR as evaluated by the Karnofsky index (8) and the Duke Activity Score index (9), Stortecky et al. (10) were the first to use a multidimensional geriatric assessment for TAVR candidates and found it to be associated with all-cause mortality and major cardiovascular events at 30 days and at 1-year follow-up. This group also proposed a frailty index from predetermined summary scores of instruments that assessed pre-procedural nutritional, cognition, mobility, and activities of daily living (ADL). In the same direction, in this issue of JACC: Cardiovascular Interventions, Green et al. (11) assessed frailty in 159 patients who received TAVR as part of the PARTNER (Placement of AoRTic TraNs cathet ER Valve Trial). The authors aimed to use some measures of the original components of criteria of Fried et al. for frailty (7). At an undefined time before TAVR, 4 factors were measured: pre-procedural gait speed with a 15-ft timed walk test, weakness by dominant hand-grip strength test, decline in independence in ADL as evaluated by the Katz Index of Independence in ADL survey, and measured serum albumin as a surrogate for malnutrition and wasting. Domains as defined by Fried et al. (7) that were not measured in this study were: weight loss of 10 lbs or more in 1 year, self-reported exhaustion, and decline in physical activity of 15 tasks of daily life. Green et al. divided the results of their 4 markers into quartiles and assigned scores (0 to 3) to each quartile, thus deriving a frailty score, where highest (maximum score = 12) represented the most frail and lowest score represented the least frail in their cohort. Those patients with a score >5 had—dichotomizing the median-derived frailty score—a higher 1-year mortality (hazard ratio: 3.5, 95% confidence interval: 1.4 to 8.5, p = 0.007) after TAVR. In fact, after the periprocedural period (>30 days), the mortality rate at 1-year follow-up was as low as 3% among patients with low frailty scores, as compared with 13% among patients with high frailty scores. The authors also derived a simple comorbidity score in an attempt to correlate frailty and comorbidity, finding no association between comorbidities or Society of Thoracic Surgeons (STS) score

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and frailty in TAVR patients. In addition when serum albumin was analyzed in quartiles, it was found to correlate with increased mortality in this high-risk cohort. However, it is unclear as to the significance of this serum marker, because hypoalbuminemia could also reflect the presence of liver synthetic impairment, nephrotic syndrome, or malabsorption rather than a specific marker for malnutrition and caloric wasting.

The most important message coming from this study is that a simple and objective evaluation of the frailty status can provide important prognostic information for TAVR candidates. In addition, the prognostic value of a frailty index was independent of other important comorbidities and the STS score. Interestingly, a more advanced age and lower body mass index, commonly used in the subjective “eyeball” evaluation of frailty, were not associated with a higher frailty score, highlighting once again the importance of using objective tools for the evaluation of this complex syndrome.

Although the work of Green et al. (11) represents an important step forward in the assessment of frailty and in the global evaluation of TAVR patients, there are many unresolved issues. Although the prognostic value of a multi-item assessment tool of frailty would probably surpass that of a single-item assessment, the usefulness of each individual component of the frailty score in predicting outcomes after TAVR merits further evaluation in a larger series of patients. Establishing TAVR-specific cutoffs for each individual measure of frailty, which will ultimately contribute to a TAVR frailty index, would probably provide a better estimate of acute and late outcomes. Also, much data exist on the prognostic value of several comorbidities and procedural complications in patients undergoing TAVR (1). However, no information was provided by the authors on the selection criteria for the comorbidity factors used in their comorbidity score, and further analyses using validated comorbidity indexes are needed to confirm the lack of significant interaction between frailty and other comorbidities in TAVR candidates. Also, it would be important to determine whether or not similar frailty index cutoffs can be applied in transfemoral versus other routes of access, especially those requiring a thoracotomy (transapical, transaortic). The inclusion of domains such as cognitive status, mood, or other aspects of mental health would probably have high clinical relevance in the evaluation of frailty pre-TAVR. Finally, improvements in health status and quality of life after TAVR might be even more important than improvements in longevity. Although TAVR has been usually associated with marked improvements in functional status and quality of life, a significant proportion of patients experience mild or no improvement within the months after the procedure (9,12). The potential impact of frailty on the lack of significant functional status increase and quality-of-life improvement after TAVR is an important point that will also need to be addressed in future studies.

The frailty syndrome is becoming a major factor in the evaluation of cardiac patients, due to the increasing age of the population. This is particularly true in the cohort of patients with aortic stenosis considered to be at high or prohibitive surgical risk undergoing TAVR. The work of Green et al. (11) represents one of the first and a very important step in the right direction toward establishing objective tools for the evaluation of the frailty syndrome in the setting of TAVR. The prospective validation of frailty scores for the prediction of outcomes (survival and quality of life) after TAVR might assist in determining the patients who might or might not benefit from this procedure. Ultimately, the incorporation of the frailty status into algorithms for clinical decision making among TAVR candidates would be a much-needed step toward providing the best care for this complex and vulnerable group of patients.

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