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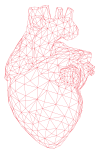
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ORIGINAL RESEARCH



## The “Eyeball Test” for Risk Assessment in Aortic Stenosis: Characterizing Subjective Frailty Using Objective Measures

Philip Green, MD<sup>a</sup>, Christine J. Chung, MD<sup>a</sup>, Brandon S. Oberweis, MD<sup>a</sup>, Isaac George, MD<sup>a</sup>, Torsten Vahl, MD<sup>a</sup>, Kishore Harjai, MD<sup>b</sup>, Ming Liao, MA<sup>a</sup>, Luz Jaquez, MS<sup>a</sup>, Marian Hawkey, RN<sup>a</sup>, Omar Khalique, MD<sup>a</sup>, Rebecca T. Hahn, MD<sup>a</sup>, Mathew R. Williams, MD<sup>c</sup>, Ajay J. Kirtane, MD, SM<sup>a</sup>, Martin B. Leon, MD<sup>a</sup>, Susheel K. Kodali, MD<sup>a</sup>, and Tamim M. Nazif, MD<sup>a</sup>

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### ABSTRACT

**Background:** Subjective frailty assessment is widely employed in risk stratification of patients with severe aortic stenosis (AS), but the association with objective frailty parameters is poorly characterized.

**Methods:** Frailty was subjectively assessed (dichotomously as frail or not frail) in high-risk patients with AS referred to a Heart Valve Clinic. An objectively derived composite frailty score was derived by summing quartiles of the following frailty measures: 15-foot walk time, grip strength, independence in activities of daily living (ADL), and serum albumin. The objective measures and composite score were compared between those considered frail and not frail by subjective assessment. The relationship between frailty status and outcomes was analyzed.

**Results:** Of 100 subjects, 31 were frail by subjective assessment. When compared to those considered not frail, there were no differences in age, sex, and BMI. However, frail subjects had higher STS scores and had significantly greater dependence in ADL, slower gait speed, weaker grip strength, and lower albumin than non-frail subjects. The composite frailty score was highly correlated with frailty designation by subjective assessment. Subjective and objective frailty were both highly predictive of treatment assignment to either medical therapy or aortic valve replacement, and of mortality.

**Conclusion:** Among patients with AS evaluated in a Heart Valve Clinic, those considered frail by subjective assessment were slower, weaker, more malnourished, and had greater ADL impairment. Subjective assessment of frailty and objective frailty measures were similarly predictive of treatment assignment and mortality.

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**KEYWORDS** Aortic stenosis; aortic valve replacement; frailty; risk assessment; eyeball test

### Introduction

Frailty is an age-associated syndrome of impaired physiological reserve and increased vulnerability to stressors.<sup>1</sup> It was originally defined by Fried and colleagues<sup>2</sup> as a clinical syndrome in which three or more of the following are manifest: unintentional weight loss, exhaustion, weakness, slow gait speed, and low physical activity. Frailty portends a poor prognosis in patients with severe aortic stenosis (AS), but controversy persists regarding how best to diagnose and characterize it in this population.

Historically, subjective frailty assessment, referred to colloquially as the “eyeball test,” has been employed as part of surgical preoperative assessment to predict a patient’s likelihood of surviving a planned procedure without major complications.<sup>3</sup> Formal assessment of frailty has since become part of the standard evaluation of older adults with severe AS being considered for aortic valve replacement (AVR).<sup>4</sup> National guidelines recommend consideration of frailty

when determining whether a patient is best served by a surgical or transcatheter approach, but do not specify which of myriad assessment tools should be utilized.<sup>5,6</sup>

Although no gold standard for frailty assessment has yet been established, the following domains are generally considered representative of physical frailty: slowness, weakness, malnutrition, fatigue, and inactivity.<sup>7</sup> Numerous studies have demonstrated the association between objectively measured markers of frailty and increased morbidity and mortality after surgical and transcatheter AVR.<sup>8–11</sup> However, since the “eyeball test” is quick and intuitive, it remains widely utilized in clinical practice although the relationship between subjective assessment of and objectively measured frailty with validated frailty parameters has not been well established. We therefore sought to characterize the relationship between subjective assessment of frailty and objective frailty measures, and to evaluate their association with clinical outcomes in older adults with AS at a high-volume Heart Valve Clinic.

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📎 Supplemental data for this article can be accessed [here](#).



## Materials and methods

### Study population and design

Older adults with severe AS and elevated surgical risk who were referred to a Heart Valve Clinic at an academic medical center for consideration of transcatheter aortic valve replacement (TAVR) were prospectively enrolled in this cohort study from November 2012 through June 2013. All subjects were evaluated by a cardiologist or a physician assistant with specific expertise, training, and at least 2 years of experience in the management of heart valve disease. Clinicians performed an initial 30-minute clinical evaluation consisting of a focused medical history and physical examination, not including physical performance measures. Subjective frailty assessment (assessed dichotomously as either frail or not frail) was performed by the clinician during this initial clinical evaluation. A completely independent, trained research coordinator who was not present during the clinical evaluation of the patient, separately assessed objective measures of frailty. During the time period of this study, objective measures of frailty were routinely collected for all patients undergoing evaluation for TAVR at our center. The clinicians and research coordinator evaluated patients at different times and were blinded to each other's assessments at the time of patient evaluation.

Subsequently, treatment assignment (to AVR vs. medical therapy) was made through a Heart Team approach, including at least one interventional cardiologist and one cardiac surgeon in addition to the clinician performing the initial assessment. Results of objective frailty assessments were made available to the Heart Team at this time, as per routine clinical practice in this time period.

Baseline demographic, clinical, and echocardiographic information was collected for all subjects. Clinical outcomes, including mortality, were gathered through examination of medical records and telephone contact with subjects and referring physicians. This study was approved by the Columbia University Institutional Review Board.

### Frailty assessment

As described above, separate members of the Heart Team were responsible for performing subjective and objective assessments of frailty. Four objective measures of frailty were chosen to parallel the various dimensions of the frailty phenotype originally operationalized by Fried et al<sup>2</sup>: 15-foot walk time, hand grip strength, independence in activities of daily living (ADL), and serum albumin. The composite frailty score utilized in this study was previously validated by our group in high-risk patients with severe AS undergoing evaluation for TAVR, and shown to be independently associated with increased mortality after TAVR.<sup>4</sup> These four frailty metrics were subsequently studied in another cohort of high-risk patients with severe AS undergoing evaluation for TAVR from 2011 to 2015 and again shown to be associated with short- and long-term adverse outcomes including mortality.<sup>7</sup>

Gait speed was measured as the time in seconds required to walk 15 feet (4.57 meters) and reported in meters/second (m/s).<sup>12</sup> Patients were permitted to use walkers or canes, as needed. If

subjects were unable to walk 15 feet, gait speed was reported as 0 m/s. Grip strength was assessed by the maximal isometric grip of the dominant hand, measured in kilograms with a Jamar dynamometer (Sammons Preston) and reported as the average of three trials. Independence in ADL was determined using the Katz ADL survey.<sup>13</sup> Subjects were required to perform all six ADL without assistance to be considered independent. Serum albumin at the time of the initial clinical evaluation was collected as a marker of malnutrition. A composite frailty score was then calculated by summing quartiles of these four frailty measures as previously described.<sup>4</sup>

In brief, gait speed and serum albumin were divided into quartiles. Grip strength was divided into quartiles stratified by sex. Functional status was dichotomized into dependence in any activity of daily living and no dependence in all six ADL. With these quartiles, a frailty score was operationalized in the following manner: (1) quartiles of albumin, gait speed, and grip strength were assigned values of 0 to 3 in descending order; and (2) a score of 0 was assigned for complete independence in all ADL and a score of 3 for any degree of dependence in ADL. These component scores were then summed to derive a composite frailty score for each subject (possible range of values from 0 to 12), with the highest score representing the frailest subjects, and the lowest score representing the least frail. The cohort was dichotomized at the median frailty score.

### Definition of endpoints and statistical analyses

The primary endpoints were treatment assignment and all-cause mortality. Treatment assignment was classified as either medical therapy or AVR. Balloon aortic valvuloplasty (BAV) was considered medical therapy, consistent with the PARTNER trial definition.<sup>14</sup> Both surgical and transcatheter aortic valve replacement were classified as AVR.

The primary predictor variable was subjective frailty assessment. Individual objective frailty measures and the composite frailty score were compared between subjects considered frail and not frail by subjective assessment. The association of subjective and objective frailty status with clinical outcomes, including mortality, was analyzed.

Categorical baseline characteristics were presented as percentages and compared using  $\chi^2$  or the Fisher exact tests. Continuous characteristics were reported as mean  $\pm$  standard deviation and compared using the Student *t*-test or the Wilcoxon rank-sum test for non-normally distributed data. Clinical outcomes were represented as time-to-event variables using the Kaplan-Meier method and compared using the log-rank test. The association of objective frailty parameters and the composite frailty score with long-term survival after TAVR was assessed with Cox proportional hazards modeling. Receiver operating curves were used to compare the accuracy of subjective frailty and objective frailty status. The area under each curve was compared using the method of DeLong and Delong. All analyses were performed with SAS (version 9.2, SAS, Cary, NC, USA). A *p* value of 0.05 was considered to be statistically significant.

## Results

### Baseline patient characteristics

Baseline clinical characteristics are shown in **Table 1**. The median age was 85 [81, 89], 45% of the cohort was male, and the median STS score was 6.6 [4.5, 9.4]. Seven percent of patients had previously undergone a BAV, while 6% of patients had a history of prior aortic valve surgery.

When stratified by subjective frailty status, patients considered frail and those considered not frail were similar with respect to most demographic and clinical characteristics, including age, sex, left ventricular systolic function, severity of AS, and history of prior aortic valve surgery. There was no difference in the prevalence of common comorbid conditions such as atrial fibrillation or chronic kidney disease between groups. However, patients classified as frail by subjective assessment had significantly higher STS scores (8.3 [8.4, 12.8] vs. 6.2 [4.4, 8.2],  $p = 0.03$ ) and were more likely to have undergone a prior BAV (19% vs. 2%,  $p = 0.003$ ).

### Frailty assessment

Subjective frailty was present in 31% of patients. There was no significant difference in the subjective frailty assessments of physicians as compared to those of physician assistants. The objective correlates of subjective frailty status are shown in **Table 2**. Patients considered frail by subjective assessment were significantly more likely to be

dependent in ADL (74 vs. 33%,  $p < 0.001$ ), have slower gait speed (0.44 [0.27, 0.57] vs. 0.69 [0.59, 0.82] m/s,  $p < 0.001$ ), weaker grip strength (women: 12.0 [9.0, 15.3] vs. 15.5 [12.9, 20.0] kg,  $p = 0.02$ , men: 19.7 [14.8, 25.7] vs. 26.0 [19.7, 32.7] kg,  $p = 0.04$ ), and lower albumin (3.7 [3.4, 4.0] vs. 4.1 [3.9, 4.4] g/dL,  $p < 0.001$ ) than those considered not frail. The median composite frailty score was double among those considered subjectively frail than in those considered not frail (10 [8.0, 11.0] vs. 5.0 [3.0, 6.0],  $p < 0.001$ ). Patients classified as frail by subjective assessment were more likely to have a composite frailty score of 6 or greater compared to those classified as not frail (87% vs. 25%,  $p < 0.001$ ). The composite frailty score was highly predictive of frailty status as determined by subjective assessment (AUC = 0.88) (**Figure 1**).

### Clinical outcomes

Median follow-up was 686 [396, 1008] days. Of a total of 100 patients, 31 (31%) patients received medical therapy including BAV, 14 (14%) patients underwent SAVR and 47 (47%) underwent TAVR (**Table 3**). When patients were stratified by frailty status, those characterized as not frail by subjective assessment were more likely to undergo AVR rather than to receive medical therapy (76% TAVR or SAVR vs. 25% medical therapy including BAV). Similarly, patients characterized as not frail by objective assessment were also more likely to undergo AVR rather than to receive medical therapy (78%

**Table 1.** Baseline characteristics.

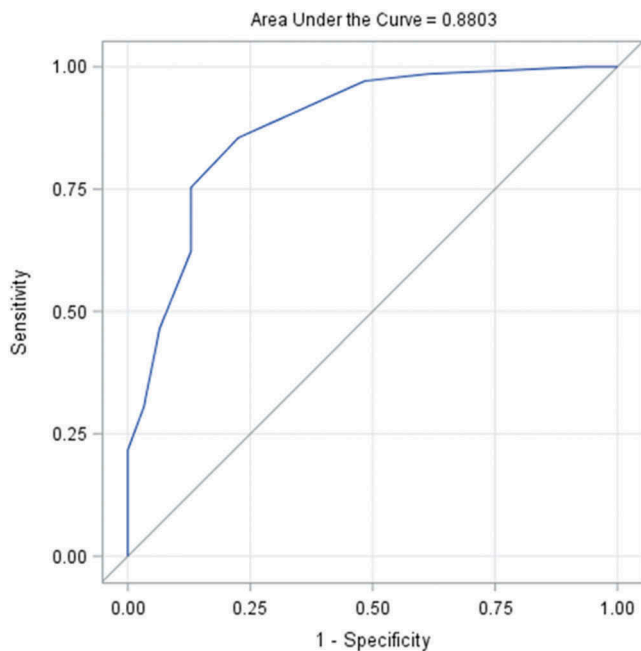
	Overall (N = 100)	Subjectively frail (n = 31)	Subjectively not frail (n = 69)	p-value
Age (yrs)	85 [81, 89]	88 [83, 91]	85 [81, 88]	0.10
Male gender	45 (45)	12 (39)	33 (48)	0.52
Body mass index (kg/m <sup>2</sup> )	25.20 [22.00, 28.75]	25.20 [21.50, 28.80]	25.20 [22.50, 28.70]	0.72
CAD	60 (60%)	20 (65%)	40 (58%)	0.66
CVA/TIA	17 (17%)	6 (19%)	11 (16%)	0.77
PAD	23 (23%)	10 (32%)	13 (19%)	0.20
A fib (missing n = 2)	39 (40%)	13 (43%)	26 (38%)	0.66
Cirrhosis	1 (1%)	1 (3%)	-	0.31
COPD	32 (32%)	9 (29%)	23 (33%)	0.82
CKD	28 (28%)	10 (33%)	18 (26%)	0.48
Prior MI	15 (15%)	6 (19%)	9 (13%)	0.55
Prior PCI	19 (19%)	6 (19%)	13 (19%)	1.00
Prior CABG	28 (28%)	6 (19%)	22 (32%)	0.24
Prior BAV	7 (7%)	6 (19%)	1 (2%)	<b>0.003*</b>
Prior valve surgery				
Aortic vs. none	6 (6)	1 (3)	5 (7)	0.66
Mitral vs. none	1 (1)	-	1 (2)	1.00
Tricuspid vs. none	-	-	-	
Previous PPM (missing n = 1)	16 (16)	7 (23)	9 (13)	0.25
LVEF (%)	59.00 [40.00, 65.00]	58.00 [43.00, 64.00]	60.00 [45.00, 65.00]	0.85
AVA (cm <sup>2</sup> )	0.70 [0.60, 0.90]	0.70 [0.60, 0.90]	0.70 [0.60, 0.87]	0.38
Mean gradient (mm Hg)	42.30 ± 16.10 [42.30, 51.45]	43.19 ± 16.91 [42.60, 50.60]	41.90 ± 15.83 [42.30, 52.40]	0.71 0.75
Peak velocity	4.20 [3.85, 4.60]	4.20 [4.00, 4.50]	4.20 [3.80, 4.70]	0.75
STS Score	6.55 [4.50, 9.40]	8.30 [5.40, 12.80]	6.20 [4.40, 8.20]	<b>0.03*</b>

Notes. \*The values in bold indicate  $p < 0.05$ . CAD, coronary artery disease; CVA, cerebrovascular accident; TIA, transient ischemic attack; PAD, peripheral artery disease; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; BAV, balloon aortic valvuloplasty; PPM, permanent pacemaker; LVEF, left ventricular ejection fraction; AVA, aortic valve area; STS, Society of Thoracic Surgeons.

**Table 2.** Objective frailty parameters in patients categorized by subjective frailty status.

	Subjectively frail (n = 31)	Subjectively not frail (n = 69)	p-value
Any ADL dependence (0–5/6)	23 (74%)	23 (33%)	<0.0001
Albumin, g/dL, median [IQR]	3.70 [3.40, 4.00]	4.10 [3.90, 4.40]	0.0001
Gait speed, m/s median [IQR]	0.43 ± 0.16 0.44 [0.27, 0.57]	0.69 ± 0.17 0.69 [0.59, 0.82]	<0.0001 <0.0001
Grip strength, kg (male), median [IQR]	19.70 [14.80, 25.65]	26.00 [19.70, 32.70]	0.04
Grip strength, kg (female), median [IQR]	12.00 [9.00, 15.30]	15.45 [12.85, 20.00]	0.02
Composite frailty score, median [IQR]	10.00 [8.00, 11.00]	5.00 [3.00, 6.00]	<0.0001
Composite frailty score, >6	27 (87%)	17 (25%)	<0.0001

Note. ADL, activities of daily living; IQR, interquartile range.

**Figure 1.** Correlation between subjective and objective frailty (as a continuous variable).

TAVR or SAVR vs. 22% medical therapy including BAV). Overall, subjective frailty and the objective composite frailty score were similarly predictive of treatment assignment (AUC = 0.66 vs. 0.65).

Over a median follow-up of nearly 2 years, the Kaplan-Meier estimate of all-cause mortality was 65% in those with an objective frailty score >6, compared to 35% in those with a score ≤ 6 (log-rank  $p < 0.001$ ) (Figure 2A). In subgroup analysis of patients undergoing AVR, an objective frailty score >6 was associated with significantly higher mortality (Figure 2B). Similarly, all-cause mortality was 56% in those who were characterized as subjectively frail, compared to 44% in those considered not frail (log-rank  $p < 0.001$ ) over the 2-year follow-up period (Figure 3A). In patients undergoing AVR, there was a trend toward higher mortality in those characterized as subjectively frail, but this did not reach statistical significance (Figure 3B). When outcomes were stratified by frailty status, the risk of mortality was significantly higher in those who were subjectively frail (HR 3.75, 95% CI

1.88–7.48,  $p = 0.001$ ) and objectively frail (HR 3.23, 95% CI 1.57–6.62,  $p < 0.001$ ), compared to those not frail (Table 4). Subjective and objective frailty scores were similarly predictive of mortality (AUC = 0.68 and 0.66, respectively).

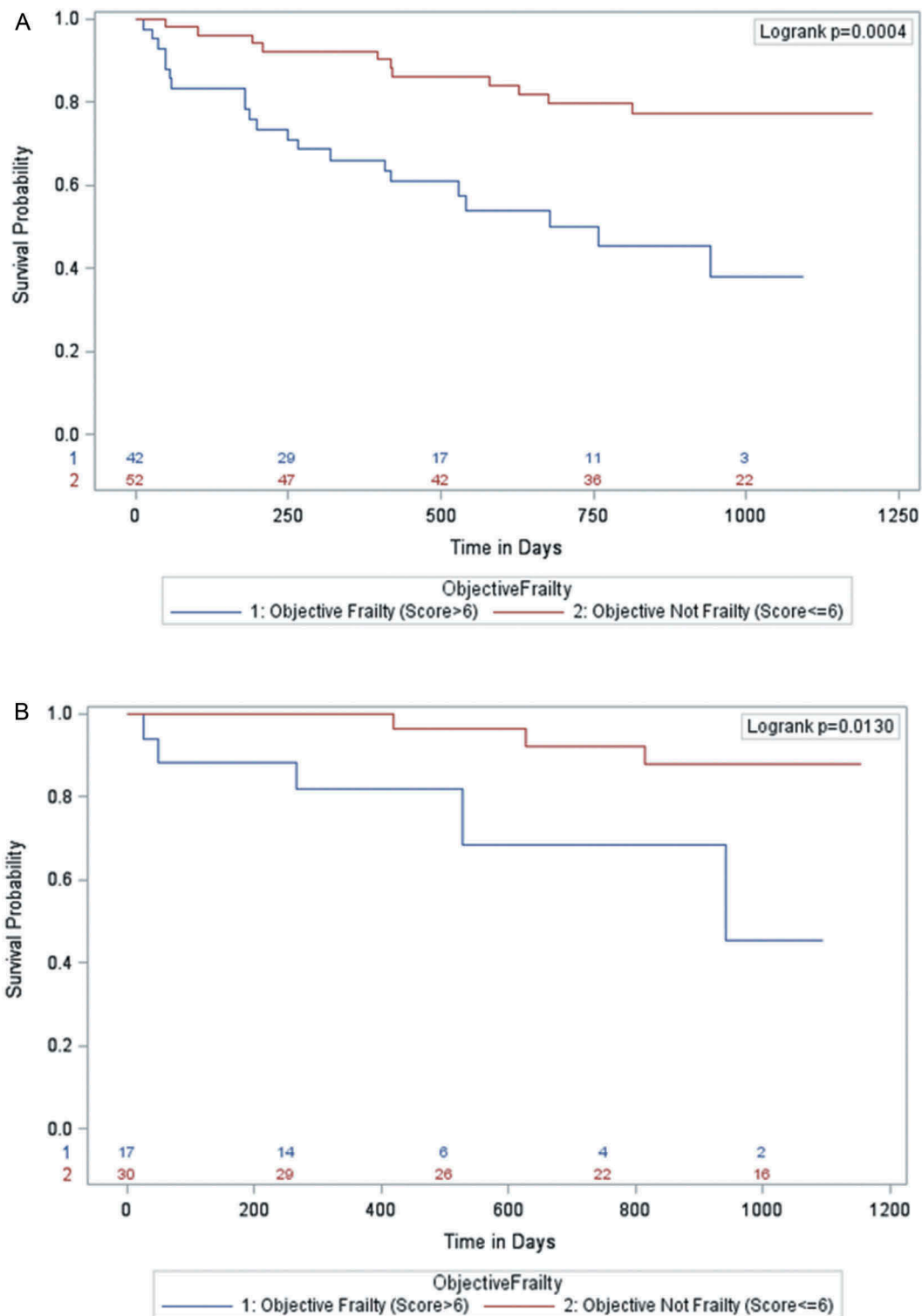
## Discussion

The principal findings of this study are: (1) Patients considered frail by subjective assessment have greater ADL dependence, slower gait speed, weaker grip strength, and lower albumin; (2) Subjective frailty has a strong correlation with an objective frailty score derived from measures of dependence in ADL, walking speed, grip strength, and malnutrition; (3) Subjective and objective frailty status are significantly associated with treatment assignment and late mortality in patients undergoing evaluation for AVR.

The advent of TAVR has revolutionized the management of patients with severe AS. Growing numbers of patients at increased risk for surgical aortic valve replacement (SAVR) are now being routinely treated with TAVR. As the adoption of TAVR continues to expand, it has become increasingly important to develop and validate tools for risk stratification in this population that enable optimal patient selection. Surgical risk assessment algorithms such as the Society of Thoracic Surgeons Predicted Risk of Mortality (STS PROM) score and European System for Cardiac Operative Risk Evaluation (EuroSCORE) were developed and validated in surgical populations.<sup>15,16</sup> Though these tools are widely utilized to assess risk in patients being considered for TAVR, they were neither developed nor validated for this purpose.<sup>3</sup> In fact, the performance of traditional surgical risk calculators has been shown to be particularly poor in the TAVR population,<sup>4,17,18</sup> likely at least in part due to their omission of assessments of frailty and functional disability, factors that are especially relevant in the prognosis of older adults with symptomatic severe AS.<sup>19</sup>

There has been growing recognition of the interplay between frailty and cardiovascular morbidity and mortality. Studies have shown that women with coronary artery disease are more likely to develop frailty<sup>20</sup> and that older adults with markers of frailty are more likely to develop cardiovascular disease.<sup>21</sup> Of nearly 5000 patients aged greater than 65 years with an acute coronary syndrome managed medically in the Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes (TRILOGY-ACS) trial, the 5% who were considered frail (as determined by a questionnaire based on the Fried frailty score) were more likely to experience cardiovascular death, MI or stroke.<sup>22</sup> Both frailty and severe AS are increasingly prevalent with advancing age, raising the question of the degree to which frailty may impact management and outcomes of AS in the elderly.

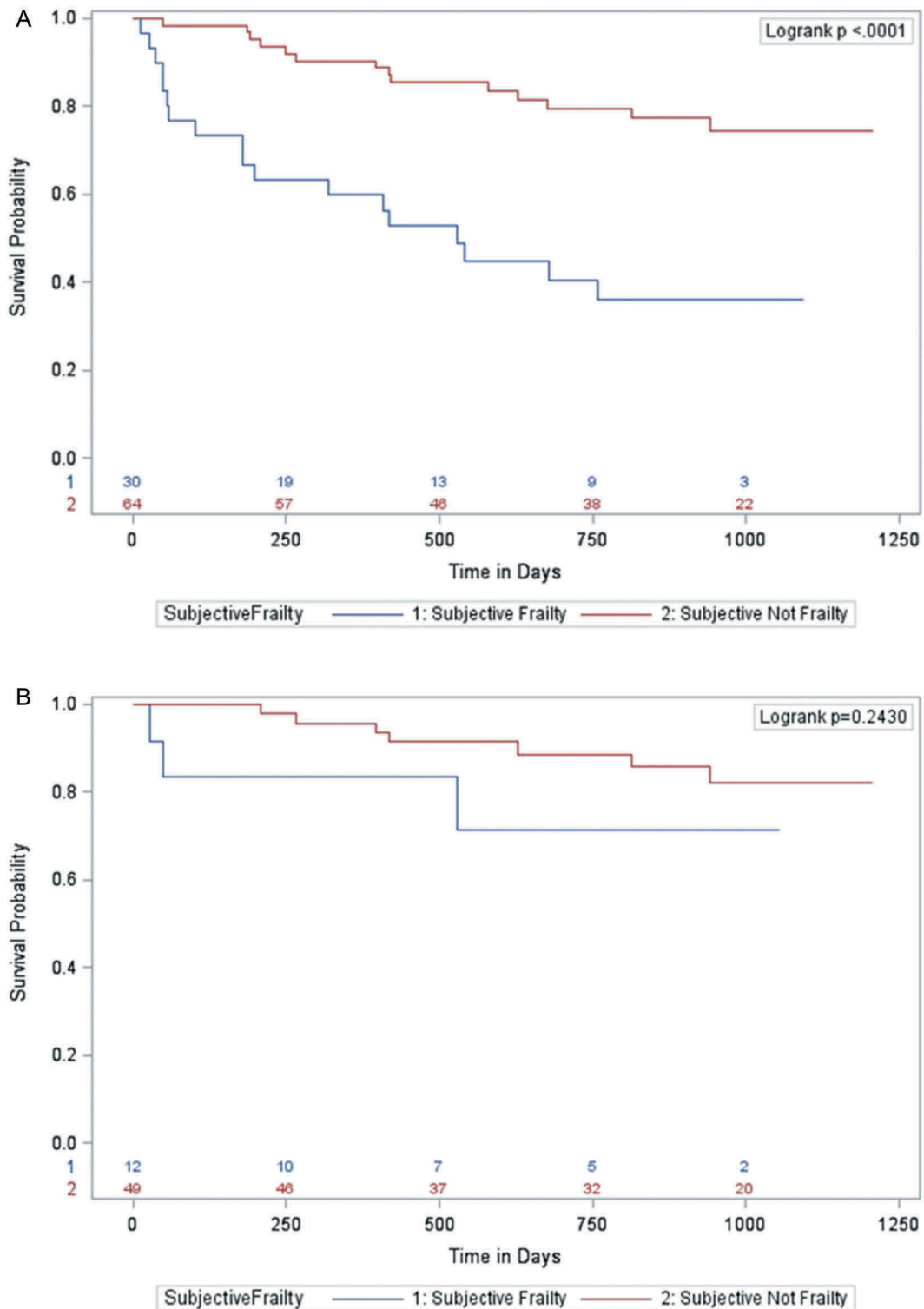
An analysis by Rodés-Cabau and colleagues<sup>23</sup> of a Canadian cohort in the early era of TAVR suggested that frailty, as assessed subjectively by the treating physician, was not an independent predictor of outcomes. Our group, however, subsequently demonstrated that baseline frailty, when assessed objectively by a composite of multiple physiologic domains, as in the current study, was associated with increased mortality at 1 year after TAVR, even after



**Figure 2.** (A) Long-term survival stratified by objective frailty status (as a binary variable). (B) Long-term survival in patients undergoing aortic valve replacement (AVR) stratified by objective frailty status (as a binary variable).

adjustment for STS score and other baseline characteristics.<sup>4</sup> Since then, numerous additional studies have demonstrated a consistent relationship between objectively assessed frailty parameters and increased morbidity and mortality after AVR.<sup>24–26</sup> Furthermore, using a multi-dimensional index to characterize frailty, investigators in Germany showed that frailty, but neither the EuroSCORE nor the STS score, was

predictive of functional decline after TAVR.<sup>26</sup> The discordant results of the earliest study likely reflect the era of the study and the incomplete understanding of frailty at that time, but also raise the possibility that subjective assessment of frailty may not be as accurate as objective measurement of frailty parameters, particularly when evaluating a population with a high prevalence of the condition.



**Figure 3.** (A) Long-term survival stratified by subjective frailty status. (B) Long-term survival in patients undergoing aortic valve replacement (AVR) stratified by subjective frailty status.

The current study sought to investigate the performance of a subjective global assessment of frailty, or the “eyeball test,” in predicting outcomes of patients undergoing evaluation for severe AS. We found that subjective assessment of frailty by an experienced clinician was strongly correlated with an objective frailty score, and that both subjective and objective

frailty status were correlated with treatment assignment and late all-cause mortality. The finding of prognostic relevance of subjective frailty assessment conflicts with the results of the earlier Canadian study, most likely due to the fact that that study included patients from an earlier time period (2005–2009). This includes a time when TAVR was first being used

**Table 3.** Treatment assignment by frailty status.

	Subjectively frail		Subjectively not frail	
Objectively frail (score >6)	25 <sup>a</sup> (27%)		17 (17%)	
	Medical+BAV	15 (60%)	Medical+BAV	6 (35%)
	TAVR+SAVR	10 (40%)	TAVR+SAVR	11 (65%)
Objectively not frail (score ≤6)	4 (4%)		51 <sup>b</sup> (52%)	
	Medical+BAV	2 (50%)	Medical+BAV	10 (20%)
	TAVR+SAVR	2 (50%)	TAVR+SAVR	41 (80%)

Note. <sup>a</sup>Treatment assignment status missing n = 2.

<sup>b</sup>Treatment assignment status missing n = 1.

BAV, balloon aortic valvuloplasty; TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement.

**Table 4.** Risk of mortality stratified by frailty status in the overall population and according to treatment assignment.

	Death <sup>a</sup>	HR [95% CI]	p-value
Overall			
Subjective frailty (Yes)	19/34 (56%)	3.75 [1.88, 7.48]	0.001
Objective frailty score >6	22/34 (65%)	3.23 [1.57, 6.62]	0.0002
AVR (TAVR+SAVR) <sup>b</sup>			
Subjective frailty (Yes)	3/11 (27%)	2.20 (0.57, 8.54)	0.2550
Objective frailty score >6	5/11 (46%)	3.08 (0.87, 10.87)	0.0802
Medical therapy			
Subjective frailty (Yes)	14/21 (67%)	2.52 (1.00, 6.33)	0.0500
Objective frailty score >6	15/21 (71%)	1.65 (0.63, 4.31)	0.3054

Note. <sup>a</sup>Mortality status missing n = 3.

<sup>b</sup>Treatment assignment status missing n = 3.

AVR, aortic valve replacement; TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement.

in patients at very high or prohibitive surgical risk, consistent with the mean STS score of 9.8%. That only 25% of their cohort was subjectively determined to be frail likely reflects under-recognition of the frailty syndrome at a time when clinicians were just beginning to appreciate its importance and learn how to diagnose it. Furthermore, there were likely overall worse outcomes in that early era and multiple competing risks for mortality due to an inherently sicker population, less sophisticated technology, operator inexperience, and increased procedural complications. Interpreted within the context of more recent investigations in the current era of TAVR, our findings further support the routine incorporation of a formal frailty assessment in the evaluation for TAVR and suggest that both subjective assessment of frailty by experienced clinicians and objective frailty measures may play a role in Heart Team decisions. Furthermore, in busy, high volume centers where routine assessment of multiple objective frailty parameters may not be feasible, it may still be valuable to incorporate a quicker subjective frailty assessment.

As clinical experience with TAVR and the body of evidence demonstrating the impact of frailty on post-procedural outcomes continue to accrue, it may become possible to delineate the specific domains best suited for pre-procedural evaluation of this population. Since there is currently no gold standard for the assessment of frailty, there is widespread variation in how it is characterized and defined, resulting in inherent limitations in the ability to compare

findings of the present study to those of others in this field of investigation. Most of the available tools developed to assess frailty focus on one or more of the following domains: slowness, weakness, low physical activity, fatigue, and shrinking.<sup>18</sup> Some investigators have used gait speed alone, as a representation of slowness, to identify frailty because it has been shown to predict morbidity and mortality in patients with cardiovascular disease as well as in the general population.<sup>12,27-29</sup> However, previous work by our group has demonstrated that gait speed alone is not predictive of mortality in patients undergoing TAVR,<sup>4,11</sup> a finding that highlights the limitations of substituting a single performance measure for the complex phenotype of frailty.

Though the composite frailty score used in the current study encompasses multiple domains, a formal cognitive assessment was not included. Impairment on baseline cognitive testing has been linked to increased risk of stroke, congestive heart failure and mortality in adults at high risk of cardiovascular events,<sup>30</sup> and with adverse outcomes after surgery.<sup>31</sup> The relationship between pre-existing cognitive impairment and outcomes after TAVR has not been well-established. However, it has recently been shown that frailty, defined using a multi-dimensional score including a Mini-Mental State Exam to assess cognition, is associated with significantly increased mortality after TAVR.<sup>25</sup> These results suggest that an assessment of cognitive function may also be an important element in the risk stratification of patients undergoing evaluation for TAVR, and raise the question of whether impairment in this domain is part of the frailty phenotype or an independent risk factor. Further research will be required to refine the optimal measures of frailty that best characterize the complex, elderly population that comprises the majority of patients with symptomatic severe AS.

The current analysis has several important limitations. It is a relatively small, single-center study that reflects the patient population and clinical practice patterns at a tertiary academic medical center. Further research will be required to determine the generalizability and applicability of these findings to routine, real-world clinical practice. The clinicians involved in this study were very experienced in the care of patients with valvular heart disease, and there is likely a learning curve in the subjective assessment of frailty. However, the strong correlation between subjective and objective frailty assessment suggests that Heart Teams at less experienced centers may be able to replicate the frailty assessment of more experienced clinicians by utilizing objective metrics of frailty. Finally, there have been significant advances in TAVR device technology, as well as operator experience, in the years since this cohort was assessed, presumably resulting in lower complication rates and improved outcomes that may impact the observed results.

## Conclusion

In high-risk older adults with severe AS undergoing assessment at a specialized Heart Valve Clinic, subjective frailty assessment was found to have a strong association with



objective measures of frailty, including 15-foot walk time, grip strength, dependence in ADL, and serum albumin. Both subjective and objective frailty assessment predicted treatment assignment and late all-cause mortality.

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## Disclosure statements

Tamim Nazif reports consulting for Edwards LifeSciences, Medtronic, and Boston Scientific. Susheel Kodali reports consulting for Abbott Vascular and serves on the advisory boards of Thubrikar Aortic Valve, Inc. and Dura Biotech. Omar Khaliq is on the speakers' bureau of Edwards Lifesciences. Martin Leon reports that he is a member of the PARTNER Trial Executive Committee (no direct compensation). The authors report institutional funding to Columbia University and/or the Cardiovascular Research Foundation from Edwards LifeSciences, Medtronic, Boston Scientific, Abbott Vascular, Abiomed, CSI, CathWorks, Siemens, Philips, and ReCor Medical. The remaining authors have no conflicts of interest to disclose.

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