

Research Article

# Frailty Phenotype and Deficit Accumulation Frailty Index in Predicting Recovery After Transcatheter and Surgical Aortic Valve Replacement

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## Abstract

**Background:** Frailty phenotype and deficit-accumulation frailty index (FI) are widely used measures of frailty. Their performance in predicting recovery after surgical aortic valve replacement (SAVR) and transcatheter aortic valve replacement (TAVR) has not been compared.

**Methods:** Patients undergoing SAVR ( $n = 91$ ) or TAVR ( $n = 137$ ) at an academic medical center were prospectively assessed for frailty phenotype and FI. Outcomes were death or poor recovery, defined as a decline in ability to perform 22 daily activities and New York Heart Association class 3 or 4 at 6 months after surgery. The predictive ability of frailty phenotype versus FI and their additive value to a traditional surgical risk model were evaluated using C-statistics, net reclassification improvement (NRI), and integrated discrimination improvement.

**Results:** TAVR patients had higher prevalence of phenotypic frailty (85% vs 38%,  $p < .001$ ) and greater mean FI (0.37 vs 0.24,  $p < .001$ ) than SAVR patients. In the overall cohort, FI had a higher C-statistic than frailty phenotype (0.74 vs 0.63,  $p = .01$ ) for predicting death or poor recovery. Adding FI to the traditional model improved prediction (NRI, 26.4%,  $p = .02$ ; integrated discrimination improvement, 7.7%,  $p < .001$ ), while adding phenotypic frailty did not (NRI, 4.0%,  $p = .70$ ; integrated discrimination improvement, 1.6%,  $p = .08$ ). The additive value of FI was evident in TAVR patients (NRI, 42.8%,  $p < .01$ ) but not in SAVR patients (NRI, 25.0%,  $p = .29$ ). Phenotypic frailty did not add significantly in either TAVR (NRI, 6.8%,  $p = .26$ ) or SAVR patients (NRI, 25.0%,  $p = .29$ ).

**Conclusions:** Deficit-accumulation FI provides better prediction of death or poor recovery than frailty phenotype in older patients undergoing SAVR and TAVR.

**Keywords:** Frailty, Aortic valve replacement, Functional status

Aortic stenosis (AS) is a disease of significant morbidity and mortality that affects approximately 290,000 older adults in the United States (1). While half of the patients with severe AS are referred for

aortic valve replacement, only about 40% of patients go on to have surgery due to high operative risk (2). Transcatheter aortic valve replacement (TAVR) has recently been established as an alternative

option with survival benefit for high-risk patients (3), but some patients die or live with poor quality of life (4). Traditional risk prediction models, such as the Society of Thoracic Surgeons predicted risk of mortality (STS-PROM), are suboptimal in predicting poor outcomes (5), failing to incorporate geriatric syndromes, such as frailty, which have been shown to be independently associated with poor outcomes after cardiac surgery (6).

Frailty is a syndrome that is characterized by “homeostenosis,” reduced physiologic reserve to tolerate stressors, which leads to increased vulnerability to adverse health outcomes (6). It is an independent risk factor of poor outcomes following cardiac surgery, including prolonged hospitalization (7), delirium (8), functional decline (9), or discharge to institution (10). However, studies in cardiac surgery have used various definitions of frailty, many of which have not been previously validated (6). Others adopted simple assessments (eg, gait speed (11)). Furthermore, outcomes have typically focused on mortality and major cardiovascular events rather than functional outcomes (6).

There are two widely accepted approaches to measuring frailty in geriatrics: the frailty phenotype (12) and deficit-accumulation frailty index (FI) (13–15). Frailty phenotype is defined based on weight loss, exhaustion, physical inactivity, slowness, and weakness (1). An FI quantifies a total burden of age-related health deficit across multiple domains (16). In community-dwelling older populations, an FI provides better risk prediction than phenotypic frailty (17), but the prognostic value of these approaches has not been compared in the setting of cardiac surgery.

We aimed to evaluate the performance of frailty phenotype and FI for prediction of mortality and poor functional recovery in older adults undergoing TAVR and surgical aortic valve replacement (SAVR). We hypothesized that, when added to a traditional surgical risk model based on age, sex, and STS-PROM, FI would improve prognostic accuracy more than frailty phenotype.

## Methods

### Study Design and Participants

The FRAILTY-AVR Study was a prospective cohort study of older adults undergoing TAVR and SAVR at 14 academic centers in Canada, the United States, and France (NCT01845207). The design, conduct, and main results were published (18). Briefly, patients were eligible if they were 70 years or older and underwent TAVR or SAVR for severe AS. Exclusion criteria were (a) emergent surgery or surgery involving the aorta or another heart valve; (b) clinical instability precluding assessment; (c) severe neuropsychiatric impairment (eg, a Mini-Mental State Examination score <15 points or active psychosis); or (d) non-English speaking. The investigators at the Beth Israel Deaconess Medical Center, Boston, MA, conducted the FRAILTY-AVR Functional Outcomes Study to assess the longitudinal changes in functional status. Between 2014 and 2016, we screened 446 patients and enrolled 246 patients (103 SAVR and 143 TAVR patients) who met the selection criteria (Supplementary Figure 1). This analysis included 91 SAVR and 137 TAVR patients who had available functional status data at 6 months. This study was approved by the Institutional Review Board and a written consent was obtained.

### Preoperative Evaluation

A trained research assistant or nurse interviewed patients to obtain medical history, including the New York Heart Association (NYHA)

classification, geriatric conditions and functional limitations in 22 daily activities and physical tasks: seven activities of daily living, seven instrumental activities of daily living, five tasks in the Nagi scale (19), and three tasks in the Rosow-Breslau scale (Supplementary Table 1) (20). Minnesota Leisure Time Activity Questionnaire (21), Mini-Mental State Examination, 5-item Geriatric Depression Scale (22), and physical performance tests were also administered. The average gait speed (m/s) was calculated from five trials of 5-meter walk at usual pace and the average grip strength (kg) from three measurements using a Jamar hydraulic dynamometer in the dominant hand. A study geriatrician reviewed medical records to extract body mass index, comorbidities, medications, and test results. The STS-PROM (23) and Charlson comorbidity index were calculated (24).

### Frailty Assessment

We determined frailty status according to the frailty phenotype (12) and comprehensive geriatric assessment-based frailty index (CGA-FI) (13–15). Because modifications of the original criteria impact classification of frailty status and predictive ability (25), frailty phenotype was defined by cut-points reported in the original publication, based on weight loss, exhaustion, physical inactivity, slowness, and weakness (Supplementary Table 2) (12). Patients were classified as robust if they had no components, pre-frail if they had 1–2 components, and frail if they had  $\geq 3$  components. A CGA-FI was calculated by the proportion of deficits among 48 health-related items that were assessed on CGA (eg, symptoms, diagnoses, functional limitations, performance tests, and test results) (Supplementary Table 1). Patients were classified into three levels of frailty based on the CGA-FI distribution: mild (<0.23 [25th percentile]), moderate (0.23 [25th percentile] to <0.41 [75th percentile]), and severe ( $\geq 0.41$  [75th percentile]).

### Recovery Status

Trained research assistants interviewed patients or their proxies via telephone to assess vital status, NYHA class and functional limitations in 22 activities and physical tasks at 3 and 6 months after the surgery (Supplementary Table 1). A functional status score was calculated as the total number of activities that one could perform independently (range: 0–22). A hierarchical recovery profile was defined based on vital status, functional status score, and NYHA class at 6 months: (a) alive with a functional status score unchanged or improved from baseline, regardless of NYHA class (*good recovery*); (b) alive with functional decline, yet NYHA class 1 or 2 (*partial recovery*); (c) alive with functional decline and NYHA class 3 or 4 (*poor recovery*); and (d) death. Functional decline was defined by comparing baseline score with the average scores at 3 and 6 months. It was assumed that global functional status would be more important than disease-specific NYHA class, and that given the progressive nature of severe AS, stable (ie, no decline) functional status over 6 months would be acceptable.

### Statistical Analysis

Preoperative characteristics were compared between SAVR and TAVR cohorts using Wilcoxon Rank Sum test or chi-square test. Because TAVR patients were clinically different from SAVR patients, we analyzed the total cohort as well as each cohort separately. Missing grip strength ( $n = 8$ ) and gait speed ( $n = 35$ ) were imputed using a conditional mean based on self-reported functional limitations in relevant physical tasks. We examined the distribution of the two frailty measures and their agreement using the Spearman correlation coefficient.

We first compared prediction of recovery status at 6 months between categorical frailty phenotype (robust, pre-frail, frail) versus categorical FI (mild, moderate, severe frailty), using chi-square test. As there were no robust patients, frailty phenotype only had two categories in this analysis (pre-frail and frail). Association of frailty measures as continuous variables with poor recovery or death was then compared using logistic regression to adjust for age, sex, and STS-PROM (as well as procedure type for the overall cohort analysis). The area under the receiver operating characteristic curves was compared between the two frailty measures treated as continuous variables using 2,000 bootstrap resampling. We also estimated sensitivity, specificity, positive predictive value, and negative predictive value at different cut-points and determined an optimal cut-point that maximized the sum of sensitivity and specificity for each frailty measure (26).

Lastly, we evaluated the performance of a continuous frailty phenotype and three-level CGA-FI, when added to a traditional risk model based on age, sex, and STS-PROM. Models were assessed in terms of (a) calibration using Hosmer-Lemeshow chi-square statistic, (b) C-statistics, (c) net reclassification improvement (NRI), and (d) integrated discrimination improvement (27). The NRI assesses the total proportion of subjects correctly moved between risk strata (ie, cases increases in risk strata and non-cases decreasing). The integrated discrimination improvement measures the separation of average predicted risk between cases and non-cases. The risk categories for NRI were defined as low (<13% [25th percentile]), moderate (13 [25th percentile] to <21% [75th percentile]), and high (≥21% [75th percentile]), based on the predicted risk from the traditional model.

Analyses were performed in Stata Release 14 (StataCorp., College Station, TX) and R software version 3.4.2. A 2-sided *p*-value < .05 was considered statistically significant.

## Results

### Cohort Characteristics

Compared with TAVR patients (Table 1), SAVR patients were younger (mean age: 78.1 vs 84.2 years) and had less symptoms (NYHA class 3 or 4: 62.1% vs 88.1%), lower STS-PROM (2.9% vs 5.8%), lower Charlson comorbidity index (2.1 vs 3.6), and higher MMSE score (26.9 vs 25.0). They also had faster gait speed (0.9 m/s vs 0.6 m/s), stronger grip strength (25.0 kg vs 16.7 kg), and less activity of daily living (5.8% vs 16.1%) and instrumental activity of daily living disability (48.5% vs 79.7%).

### Preoperative Frailty Assessment: Frailty Phenotype Versus CGA-FI

The overall prevalence of phenotypic frailty was 65.0% (the remaining 35.0% were pre-frail, and no patients were robust) and the mean CGA-FI was 0.32 (range: 0.02–0.66). The degree of frailty was greater among TAVR patients than SAVR patients according to the frailty phenotype (SAVR vs TAVR: 34.4% vs 82.5%) and CGA-FI (mean: 0.24 vs 0.37) (Table 1). Frailty phenotype was highly correlated with CGA-FI in SAVR patients (Spearman correlation coefficient: 0.73), and moderately correlated in TAVR patients (Spearman correlation coefficient: 0.48) (Supplementary Figure 2).

**Table 1.** Characteristics of Patients Undergoing Aortic Valve Replacement

Characteristics	SAVR	TAVR	<i>p</i> -Value
	<i>N</i> (%) or Mean ± <i>SD</i>	<i>N</i> (%) or Mean ± <i>SD</i>	
Sample size	91	137	
Age, years	77.8 ± 5.3	84.5 ± 5.8	<.001
Female	44.0%	51.8%	.24
White race	95.6%	98.5%	.18
NYHA class 3/4	63.7%	88.3%	<.001
Aortic valve area, cm <sup>2</sup>	0.7 ± 0.2	0.7 ± 0.2	.091
STS predicted risk of mortality, %	2.8 ± 1.4	5.9 ± 3.0	<.001
Charlson comorbidity index	2.2 ± 1.7	3.6 ± 2.3	<.001
Atrial fibrillation	23.1%	48.2%	<.001
Chronic kidney disease	29.7%	37.2%	.24
Chronic lung disease	24.2%	34.3%	.10
Congestive heart failure	31.9%	57.7%	<.001
Diabetes	28.6%	27.7%	.89
Myocardial infarction	15.4%	25.6%	.07
Stroke or transient ischemic attack	6.6%	21.9%	.002
MMSE score, <sup>a</sup> points	27.1 ± 2.5	25.1 ± 3.2	<.001
Gait speed, <sup>a</sup> m/s	0.9 ± 0.3	0.6 ± 0.2	<.001
Grip strength, <sup>a</sup> kg	25.0 ± 1.0	16.8 ± 0.7	<.001
Frailty phenotype <sup>a</sup>	37.9%	84.6%	<.001
CGA-FI	0.24 ± 0.11	0.37 ± 0.11	<.001
ADL disability	5.5%	16.8%	.01
IADL disability	48.4%	79.6%	<.001

Notes: ADL = activity of daily living; CGA-FI = comprehensive geriatric assessment-based frailty index; IADL = instrumental activity of daily living; MMSE = Mini-Mental Status Examination; NA = not applicable; NYHA = New York Heart Association; SAVR = surgical aortic valve replacement; SD = standard deviation; STS = Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement.

<sup>a</sup>Missing information was imputed for MMSE (5 patients), gait speed (35 patients), grip strength (8 patients), and frailty phenotype (36 patients).

### Frailty and Recovery Status at 6 Months

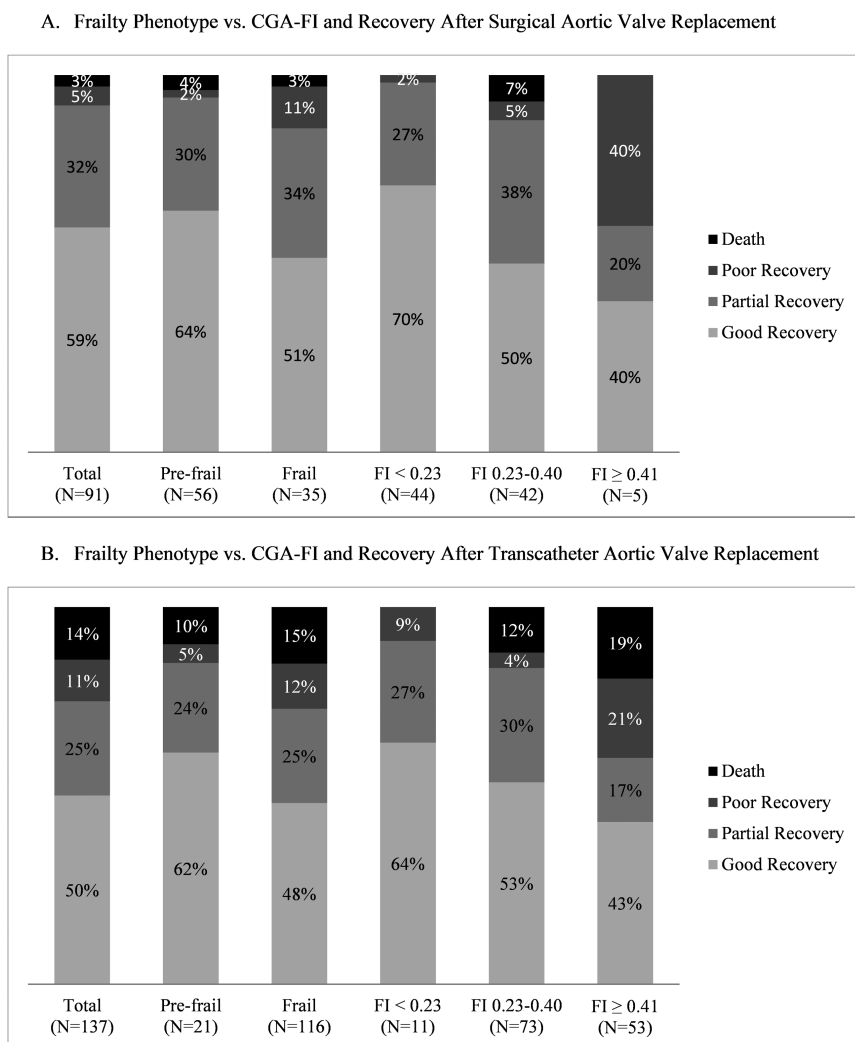
Of the 91 SAVR patients assessed at 6 months, 54 (59.3%) returned to functional baseline or improved (good recovery); 29 (31.9%) had functional decline with minimal symptoms (partial recovery); 5 (5.5%) had functional decline with severe symptoms (poor recovery); and 3 (3.3%) died (Figure 1). Of the 137 TAVR patients assessed at 6 months, the corresponding numbers were 69 (50.4%), 34 (24.8%), 15 (11.0%), and 19 (13.9%), respectively. As previously noted, no patients were robust, thus frailty phenotype was categorized into pre-frail and frail. Recovery status did not differ significantly by frailty phenotype in the SAVR cohort ( $p = .22$ ) and TAVR cohort ( $p = .60$ ) (Figure 1). In comparison, increasing CGA-FI was associated with lower risk of good recovery and greater risk of poor recovery or death in the SAVR cohort ( $p = .006$ ) and TAVR cohort ( $p = .03$ ).

The CGA-FI was more consistently associated with poor recovery or death than frailty phenotype (Table 2). In the combined cohort, patients with frailty phenotype had a greater risk of poor

recovery or death than those without; however, associations were attenuated after adjusting for age, sex, and STS-PROM (frail vs pre-frail: 23.8% vs 7.8%;  $p = .08$ ). In contrast, even after adjustment, increasing CGA-FI categories was associated with poor recovery or death in the combined cohort (mild, moderate, and severe frailty: 3.6%, 14.8%, and 39.7%;  $p = .002$ ). The results in each procedural cohort showed similar trends but had limited statistical power.

### Predicting Poor Recovery or Death at 6 Months Using Frailty Assessment

In predicting poor recovery or death, CGA-FI performed better than frailty phenotype (C-statistics for frailty phenotype vs CGA-FI: 0.63 vs 0.74;  $p = .01$ ) (Figure 2). The optimal cut-point was  $\geq 2$  for the frailty phenotype scale (sensitivity: 0.86, specificity: 0.38) and  $\geq 0.33$  for CGA-FI (sensitivity: 0.83, specificity: 0.63). The sensitivity, specificity, positive predictive value, and negative predictive value of the two frailty measures at alternative cut-points are presented in Supplementary Table 3. When each cohort was analyzed separately,



**Figure 1.** Frailty phenotype versus frailty index in predicting poor recovery or death after aortic valve replacement. (A) Frailty phenotype versus CGA-FI and recovery after surgical aortic valve replacement. (B) Frailty phenotype versus CGA-FI and recovery after transcatheter aortic valve replacement. CGA-FI, Comprehensive Geriatric Assessment – Frailty Index. Good recovery was defined as alive with functional status same as or improved from baseline; partial recovery was defined as alive with functional status lower than baseline and the New York Heart Association (NYHA) class 1 or 2; poor recovery was defined as being alive with functional status lower than baseline and the NYHA class 3 or 4. There were no robust patients according to the frailty phenotype in the study population.

**Table 2.** Frailty and Risk of Poor Recovery After Aortic Valve Replacement

	Poor Recovery <i>n/N</i> (%)	Unadjusted OR (95% CI)	Adjusted OR <sup>a</sup> (95% CI)
<b>Combined</b>			
Frailty phenotype <sup>b</sup>			
Pre-frail	6/77 (7.8%)	Reference	Reference
Frail	36/151 (23.8%)	3.7 (1.5–9.2)	2.5 (0.9–6.7)
<i>p</i> -value (df = 1)		0.005	0.08
CGA-FI			
Mild (<0.23)	2/55 (3.6%)	Reference	Reference
Moderate (0.23–0.40)	17/115 (14.8%)	4.6 (1.0–20.7)	3.8 (0.8–18.0)
Severe (≥0.41)	23/58 (39.7%)	17.4 (3.9–78.6)	12.2 (2.3–63.7)
<i>p</i> -value (df = 2)		<0.001	0.002
<b>SAVR</b>			
Frailty phenotype <sup>b</sup>			
Pre-frail	3/56 (5.4%)	Reference	Reference
Frail	5/35 (14.3%)	2.9 (0.7–13.2)	2.7 (0.6–13.6)
<i>p</i> -value (df = 1)		0.16	0.22
CGA-FI			
Mild (<0.23)	1/44 (2.3%)	Reference	Reference
Moderate (0.23–0.40)	5/42 (11.9%)	5.8 (0.7–52.0)	4.3 (0.4–42.1)
Severe (≥0.41)	2/5 (40.0%)	28.7 (2.0–414.2)	33.9 (1.8–657.8)
<i>p</i> -value (df = 2)		0.03	0.06
<b>TAVR</b>			
Frailty phenotype <sup>b</sup>			
Pre-frail	3/21 (14.3%)	Reference	Reference
Frail	31/116 (26.7%)	2.2 (0.6–7.9)	2.2 (0.6–8.0)
<i>p</i> -value (df=1)		0.23	0.24
CGA-FI			
Mild (<0.23)	1/11 (9.1%)	Reference	Reference
Moderate (0.23–0.40)	12/73 (16.4%)	2.0 (0.2–16.8)	2.0 (0.2–17.0)
Severe (≥0.41)	21/53 (39.6%)	6.6 (0.8–55.1)	5.5 (0.6–47.9)
<i>p</i> -value (df = 2)		0.006	0.03

Notes: CGA-FI = comprehensive geriatric assessment-based frailty index; CI = confidence interval; df = degree of freedom; OR = odds ratio; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

<sup>a</sup>Adjusted for age, sex, and Society of Thoracic Surgeons predicted risk of mortality (and procedure type for analysis of the combined cohort).

<sup>b</sup>No patients were robust according to frailty phenotype.

CGA-FI had higher C-statistics than frailty phenotype in SAVR patients (frailty phenotype vs CGA-FI: 0.69 vs. 0.81; *p* = .06) and TAVR patients (0.54 vs 0.65; *p* = .07), although these differences were not statistically significant.

Adding CGA-FI to a traditional model based on age, sex, and STS-PROM improved prediction more than adding frailty phenotype (Table 3). In the combined cohort, adding frailty phenotype correctly reclassified 4.0% of patients (*p* = .70) with an integrated discrimination improvement of 1.6% (*p* = .08). By comparison, incorporation of CGA-FI categories resulted an NRI of 26.4% (*p* = .02) and integrated discrimination improvement of 7.7% (*p* < .001). In the TAVR cohort, only 6.8% of patients with frailty phenotype (*p* = .26) versus 42.8% of patients were correctly reclassified with CGA-FI (*p* = .001). In the SAVR cohort, 21.4% of patients were correctly reclassified with frailty phenotype, in comparison to 25.0% correct reclassification with CGA-FI, although neither of these differences were statistically significant. Reclassification tables for frailty phenotype and CGA-FI in the total combined cohort are presented in Supplementary Table 4.

## Discussion

While measures of frailty improve preoperative risk assessment beyond traditional risk models in older patients undergoing SAVR and TAVR (28–31), the frailty phenotype and deficit accumulation FI

have not been directly compared in this setting. In our cohort in which frailty phenotype was highly prevalent, the frailty phenotype provided limited risk discrimination for poor recovery or death. By contrast, CGA-FI, which quantifies the severity of frailty based on a larger number of variables in multiple domains, improved prediction over a traditional cardiac surgery-specific assessment. These results suggest that selection of frailty measures should carefully consider characteristics of patient populations.

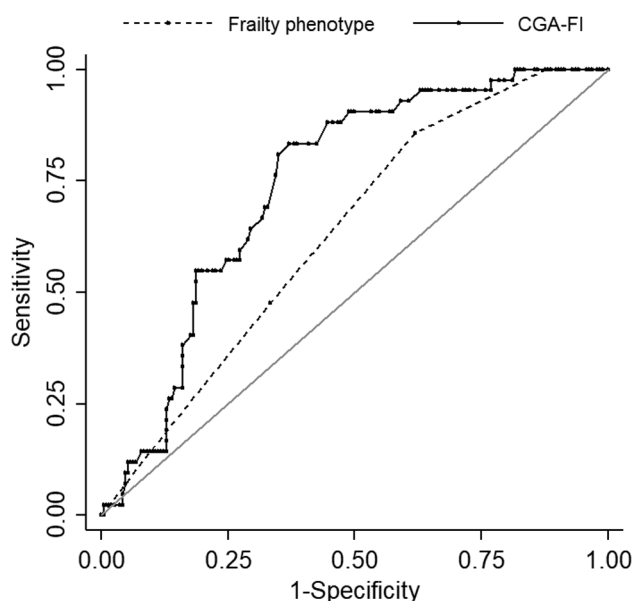
Research on frailty assessment in cardiac surgical procedures has thus far focused on devising disease-specific frailty instruments, rather than validating well-established frailty instruments in current use. In a recent systematic review (6), we found that numerous disease-specific frailty assessments were developed, but very few have been validated in an independent sample (9,30–33). It remains uncertain whether the predicted risk calculated using weights from the original study population is generalizable to a different population. While several validated frailty measures exist in geriatrics (12,14,15,34), little attention has been paid to assess the comparative performance of existing measures in aortic valve replacement. Moreover, previous studies have emphasized prediction of mortality or cardiovascular events rather than functional recovery, which may be more meaningful to patients (35).

Our results are consistent with previous studies in general populations which demonstrated better prediction of mortality with a more comprehensive deficit-accumulation FI than frailty phenotype,



which largely focuses on physical frailty (36,37). Incorporating CGA-FI to a traditional risk model resulted in improved prediction, while adding frailty phenotype did not. In particular, additional improvement over the traditional risk model with CGA-FI was evident in TAVR cohort. This suggests that frailty phenotype may not effectively capture multisystem impairments in TAVR patients. The frailty phenotype classified 82.5% of TAVR patients as frail, limiting further risk stratification among the frailest patients.

As in previous studies (2,3), we observed that the maximum value of CGA-FI was 0.66. This limit is typically around 0.6–0.7,



**Figure 2.** Receiver operating characteristic curves of frailty phenotype and frailty index to predict poor recovery or death at 6 months after aortic valve replacement. The C-statistic for CGA-FI was significantly higher than that for frailty phenotype (0.74 vs 0.63;  $p = .01$ ). The optimal cut-point was  $\geq 2$  for the frailty phenotype scale (sensitivity: 0.86, specificity: 0.38) and  $\geq 0.33$  for CGA-FI (sensitivity: 0.83, specificity: 0.63). CGA-FI, comprehensive geriatric assessment-based frailty index.

suggesting that survival may not be possible beyond this limit. Such feature offers a useful framework of preoperative risk assessment and decision-making. For instance, a patient with a CGA-FI of 0.5 has little reserve to tolerate additional stress; thus potential benefits should be carefully weighed against the risk of poor recovery and death from new deficits. While such interpretation is intuitive, our ability to quantify frailty from a one-time preoperative evaluation might have been limited. Prediction was more difficult in medically complex TAVR patients than SAVR patients, reflecting the inherent variability and heterogeneity in TAVR patients. The risk of poor recovery or death was 40% among severely frail patients by CGA-FI, suggesting that a high value of CGA-FI alone is not deterministic of futility. Functional impairment mainly driven by severe AS may recover post-procedure. One recent study found that phenotypically frail patients had greater improvement in patient-centered outcomes following TAVR and SAVR (38). Thus, while frailty assessment may serve to inform expected clinical outcomes, multidisciplinary efforts and shared decision-making remain a critical part of the evaluation process.

Logistical considerations in choosing a frailty measure include time, resources, and expertise to conduct the assessment. CGA is longer to administer and requires expertise in geriatrics; in exchange, it provides a multi-faceted quantitative assessment to deliver more individualized perioperative and post-acute care. Frailty phenotype, which does not include assessments of cognitive function and functional limitations, may be less useful for this purpose. Nonetheless, how to practically implement CGA-FI in the busy workflow of preoperative clinics remains a challenge. A more feasible approach may be to apply a simple screening, such as gait speed, to identify high-risk patients for CGA and perioperative co-management (11). Calculation of CGA-FI can be also be automated in electronic medical records or web-based calculators.

Strengths of our study include prospective assessment of frailty using the original frailty phenotype criteria and the deficit-accumulation FI; adoption of a patient-centered outcome that combines mortality, functional status, and NYHA class; and a high retention rate ( $>90\%$ ). Our study has limitations that deserve mention. We aimed to compare the performance of the two frailty measures, not the outcomes of SAVR versus TAVR. Although the comparison of outcomes

**Table 3.** Contribution of Frailty Phenotype and Comprehensive Geriatric Assessment-Frailty Index to a Traditional Surgical Risk Assessment Model in Predicting Poor Recovery or Death at 6 mo After Aortic Valve Replacement

Population	Model Performance	Traditional Model <sup>a</sup>	Traditional Model + FP	Traditional Model + CGA-FI
Combined	Hosmer-Lemeshow chi-square	7.83	12.35	9.98
Total N = 228	C-Statistic	0.66	0.67; $p = .48^b$	0.75; $p = .02^c$
Poor recovery or	NRI, %	NA	4.0; $p = .70^b$	26.4; $p = .02^c$
Death N = 42	IDI, %	NA	1.6; $p = .08^b$	7.7; $p < .001^c$
SAVR	Hosmer-Lemeshow chi-square	6.06	10.40	5.12
Total N = 91	C-Statistic	0.79	0.82; $p = .41^b$	0.87; $p = .24^c$
Poor recovery or	NRI, %	NA	25.0; $p = .29^b$	25.0; $p = .29^c$
Death N = 8	IDI, %	NA	4.5; $p = .28^b$	9.1; $p = .23^c$
TAVR	Hosmer-Lemeshow chi-square	7.41	6.21	8.59
Total N = 137	C-Statistic	0.63	0.64; $p = .64^b$	0.70; $p = .18^c$
Poor recovery or	NRI, %	NA	6.8; $p = .26^b$	42.8; $p = .001^c$
Death N = 34	IDI, %	NA	0.2; $p = .63^b$	4.7; $p = .03^c$

Notes: CGA-FI = comprehensive geriatric assessment-based frailty index; FP = frailty phenotype; IDI = integrated discrimination improvement; NA = not applicable; NRI = net reclassification index; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

<sup>a</sup>The traditional surgical risk assessment model is based on age, sex, and Society of Thoracic Surgeons predicted risk of mortality.

<sup>b</sup> $p$ -value compares traditional model plus frailty phenotype vs traditional model alone.

<sup>c</sup> $p$ -value compares traditional model plus comprehensive geriatric assessment-based frailty index vs traditional model alone.

between SAVR and TAVR by different levels of frailty is crucial for decision-making, such interpretation is subject to bias in the absence of randomization. Our study was underpowered to evaluate the performance of frailty measures within each procedural cohort. For instance, a non-significant NRI of 25.0% in SAVR cohort may be clinically important. In addition, the 18 patients whose recovery status was missing tended to be less frail at baseline (frailty phenotype: 50% vs 67%; mean CGA-FI: 0.28 vs 0.32). Thus, the risk of poor recovery or death might have been overestimated. Finally, the outcome risk in our study reflects our institution's earlier experience with high-risk patients. Absolute risks may not generalize to patients treated at other institutions or to a more contemporary cohort.

In conclusion, our study shows that preoperative frailty status is associated with death or poor functional recovery at 6 months after SAVR and TAVR. In this population with high prevalence of frailty, a CGA-FI, which incorporates multiple dimensions of health, has an advantage over the frailty phenotype in preoperative risk prediction. Further research is needed to determine how CGA-FI can be practically incorporated in routine care.

### Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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### Conflict of Interest

L.A.L. holds the Irving and Edyth S. Usen and Family Chair in Geriatric Medicine at Hebrew SeniorLife. J.J.P. reports receiving institutional grants

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