

DEFINITION OF GERIATRIC DOMAINS OF FRAILITY

The 5 geriatric domains of frailty are slowness, weakness, unintentional weight loss (sometimes referred to as “wasting”), exhaustion, and inactivity, and were defined as follows. Gait speed was measured using the 5-meter walk test; slowness was defined as gait speed ≤ 0.65 m/s (height ≤ 159 cm) or ≤ 0.76 m/s (height > 159 cm) or inability to complete the test. Grip strength was assessed using the average of 3 trials of maximal isometric grip with the dominant hand, measured in kilograms with a dynamometer. Weakness was defined as grip strength ≤ 17 kg (for patients with body mass index [BMI] ≤ 23 kg/m²), ≤ 17.3 kg (BMI > 23 and ≤ 26 kg/m²), ≤ 18 kg (BMI > 26 and < 29 kg/m²), or ≤ 21 kg (BMI ≥ 29 kg/m²).

Unintentional weight loss was defined as a self-report of unintentional weight loss of ≥ 5 pounds in the prior 6 months. Exhaustion was assessed using the second part of the sixth question on the SF-12 questionnaire, which asks patients “How much of the time during the past 4 weeks did you have a lot of energy?” with the responses recorded on a 5-category Likert scale ranging from “none of the time” to “all of the time.” The lowest 2 responses (“none” or “a little of the time”) were used to indicate self-reported exhaustion. Inactivity was assessed using the first part of the second question on the SF-12 questionnaire, which asks patients “Does your health now limit you in moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf?” Patients who answered “Yes, limited a lot” were deemed to have inactivity. Frailty, as a syndrome, was defined as 3 or more deficits in these 5 geriatric domains (slowness, weakness, unintentional weight loss, exhaustion, and inactivity).

Reference: Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56:M146-56.

DETAILS OF FRAILTY AND DISABILITY STATISTICAL ANALYSIS

We first added frailty, as a dichotomous syndrome, to the model and assessed its independent association with poor outcome by chi-square value, adjusting for other model covariates. We evaluated the improvement in model discrimination by comparison of c-statistics and by the integrated discrimination improvement (IDI) statistics, which can be interpreted as the average increase in predicted risks for those having a poor outcome minus the average increase for those not having a poor outcome (31). Individual geriatric domains, including all 5 factors of the frailty syndrome and disability (considered as a continuous variable, with a range from 0 (no dependencies) to 6 (fully dependent)), were tested using a modified forward selection method. The domain with the highest chi-square value was added individually to the model, and the incremental contribution tested with a combination of the chi-square value of the domain in the multivariable model and the IDI. Based on these factors, the domain was either retained or discarded, and the next variable was then tested. All 6 domains (slowness, weakness, unintentional weight loss, exhaustion, inactivity, and disability) were tested in order to identify the optimally performing model, and this process was repeated for all 4 models.

Reference: Pencina MJ, D'Agostino RB, Sr, D'Agostino RB Jr, Vasan RS. Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. *Stat Med* 2008;27:157-72; discussion 207-12.

Supplemental Table 1. Baseline characteristics of patients with and without KCCQ data

	Missing Data n=460	Analytic Cohort n=2830	p-value
Demographic and clinical characteristics			
Age (years)	82.7±7.9	83.3±7.8	0.177
Male sex	47.4%	54.6%	0.004
Coronary artery disease	75.9%	79.8%	0.054
Cerebrovascular disease	23.5%	26.7%	0.151
Peripheral vascular disease	44.2%	46.3%	0.397
Diabetes mellitus	40.7%	36.6%	0.098
Atrial fibrillation/flutter	49.6%	43.8%	0.021
Home oxygen	24.1%	22.9%	0.563
Creatinine (mg/dL)	1.2±0.5	1.2±1.2	0.289
Hemoglobin (g/dL)	11.8±1.8	11.8±2.1	0.821
Mean arterial pressure (mmHg)	89.1±12.8	88.2±12.6	0.124
Body mass index	28.2±6.9	27.8±6.4	0.143
Mini mental status exam	26.1±3.0	26.5±2.8	0.004
Disease severity			
Left ventricular ejection fraction (%)	54.6±13.8	54.1±13.7	0.445
Mean aortic valve gradient (mmHg)	46.9±14.4	47.3±13.4	0.564
STS mortality risk score (%)	9.1±4.6	9.0±4.9	0.585
6-Minute Walk Test distance (m)	114.4±122.8	123.1±118.0	0.146
KCCQ overall summary	40.8±23.4	43.0±23.2	0.066

STS, Society of Thoracic Surgeons; KCCQ, Kansas City Cardiomyopathy Questionnaire

Supplemental Table 2. Incremental contribution of frailty and geriatric domains to the discrimination of the poor outcome models

	<u>6-months</u>			<u>1-year</u>		
	Domain p-value	c-index	IDI p-value	Domain p-value	c-index	IDI p-value
Full model (base)		0.6463			0.6531	
Base + frailty syndrome	0.002	0.6506	0.002	<0.001	0.6575	0.001
Base + disability	<0.001	0.6586	<0.001	<0.001	0.6612	<0.001
Base + disability + unintentional weight loss	0.002	0.6625	0.007	0.002	0.6645	0.003
Base + disability + unintentional weight loss + exhaustion ¹	0.003	0.6673	0.002	0.002	0.6659	0.021
Base + disability + unintentional weight loss + exhaustion + slowness	0.471	0.6672	0.802	0.343	0.6662	0.366
Base + disability + unintentional weight loss + exhaustion + weakness	0.503	0.6684	0.024	0.374	0.6672	0.105
Base + disability + unintentional weight loss + exhaustion + inactivity	0.518	0.6666	0.402	0.057	0.6672	0.023
Clinical model (base)		0.6371			0.6651	
Base + frailty syndrome	0.004	0.6407	0.005	0.209	0.6652	0.218
Base + disability	<0.001	0.6534	<0.001	<0.001	0.6736	<0.001
Base + disability + unintentional weight loss ¹	0.001	0.6563	0.007	0.003	0.6755	0.008
Base + disability + unintentional weight loss + exhaustion	0.058	0.6591	0.019	0.981	0.6744	0.001
Base + disability + unintentional weight loss + slowness	0.059	0.6601	0.119	0.168	0.6751	0.194
Base + disability + unintentional weight loss + weakness	0.560	0.6603	0.009	0.534	0.6759	0.006
Base + disability + unintentional weight loss + inactivity	0.881	0.6589	0.036	0.534	0.6760	<0.001

¹Represents the final model

Supplemental Figure 1. Outcomes of patients by their predicted risk of poor outcome. Panel A: 6 month full model. Panel B: 1 year full model. Panel C: 6 month clinical model. Panel D: 1 year clinical model. The numbers below the x-axis categories indicate the percentage of the cohort that fall into each category of risk.



