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Preoperative Frailty Assessment and Outcomes at 6 Months or Later in Older Adults Undergoing Cardiac Surgical Procedures

A Systematic Review

Dae Hyun Kim, MD, MPH, ScD; Caroline A. Kim, MD, MS, MPH; Sebastian Placide, BA; Lewis A. Lipsitz, MD; and Edward R. Marcantonio, MD, ScM

Background: Frailty assessment may inform surgical risk and prognosis not captured by conventional surgical risk scores.

Purpose: To evaluate the evidence for various frailty instruments used to predict mortality, functional status, or major adverse cardiovascular and cerebrovascular events (MACCEs) in older adults undergoing cardiac surgical procedures.

Data Sources: MEDLINE and EMBASE (without language restrictions), from their inception to 2 May 2016.

Study Selection: Cohort studies evaluating the association between frailty and mortality or functional status at 6 months or later in patients aged 60 years or older undergoing major or minimally invasive cardiac surgical procedures.

Data Extraction: 2 reviewers independently extracted study data and assessed study quality.

Data Synthesis: Mobility, disability, and nutrition were frequently assessed domains of frailty in both types of procedures. In patients undergoing major procedures (n = 18 388; 8 studies), 9 frailty instruments were evaluated. There was moderate-quality evidence to assess mobility or disability and very-low- to low-quality evidence for using a multicomponent instrument to predict mortality or MACCEs. No studies examined functional status. In patients undergoing minimally invasive procedures (n = 5177; 17 studies), 13 frailty instruments were evaluated. There was moderate- to high-quality evidence for assessing mobility to predict mortality or functional status. Several multicomponent instruments predicted mortality, functional status, or MACCEs, but the quality of evidence was low to moderate. Multicomponent instruments that measure different frailty domains seemed to outperform single-component ones.

Limitation: Heterogeneity of frailty assessment, limited generalizability of multicomponent frailty instruments, few validated frailty instruments, and potential publication bias.

Conclusion: Frailty status, assessed by mobility, disability, and nutritional status, may predict mortality at 6 months or later after major cardiac surgical procedures and functional decline after minimally invasive cardiac surgery.

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For author affiliations, see end of text.
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Approximately 500 000 cardiac surgical procedures are performed each year in the United States, more than 50% of them in older adults (1). Because of the high burden of cardiovascular disease and evolution of minimally invasive surgical techniques, this number is expected to rise (2–4). Although older patients may benefit from these procedures, some die or have complications (5–10), functional decline (11, 12), and poor quality of life (13–15). Identifying patients who are most or least likely to benefit from surgical procedures remains a significant challenge.

One of the factors underlying the heterogeneity of health outcomes in older patients is frailty, which reflects an individual's reduced physiologic reserve, inability to tolerate stressful events (such as surgery), and vulnerability to adverse outcomes (16). Experts have developed several instruments to measure frailty by assessing gait speed, grip strength, or deficit accumulation (17–23), but there is no consensus on how to best measure this vulnerability (24, 25). Despite the lack of agreement, accumulating evidence suggests that assessment by using any validated measures provides additional information about surgical risk and prognosis not captured by traditional risk assessment (5–10). However, most surgical risk scores do not include measures of frailty (26–29). To incorporate frailty screening in the risk assessment before cardiac surgical procedures, it is essential to evaluate the feasibility and validity of frailty instruments in this setting. If preoperative frailty status predicts mortality, functional status, and quality of life, such information would be useful in making informed decisions about the procedures.

This review evaluates the evidence regarding the feasibility of frailty instruments and their validity in predicting mortality or functional status in older patients who are having major or minimally invasive cardiac surgical procedures. Because several previous reviews (30–35) reported short-term mortality and complications, we reviewed up-to-date literature on clinical outcomes at 6 months or later after cardiac procedures.

METHODS

We developed but did not register a protocol for the review (**Supplement 1**, available at www.annals.org) and prepared this report according to PRISMA (Pre-

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Web-Only

Supplement

ferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines (36).

Data Sources and Searches

We searched MEDLINE and EMBASE, without language restriction, for original research articles that evaluated any frailty measures in adults undergoing cardiac surgery, from the databases' inception to 2 May 2016, using the following keywords and their variations: "aged" and "cardiac surgery" and "frailty, geriatric assessment, mobility, gait speed, muscle strength, grip strength, physical activity, exhaustion, weight loss, nutrition, cognitive function, functional status, activities of daily living" (Supplement 1). We also examined reference lists of reviews (30–35) and articles meeting inclusion criteria.

Study Selection

Two investigators (C.A.K. and S.P.) independently screened titles and abstracts and then texts of full-length articles passing the title and abstract screen. Disagreement was resolved by consensus involving a third investigator (D.H.K.). Original research articles published in any language were eligible if the mean age of study participants was 60 years or older; the surgical procedure was coronary artery bypass grafting (CABG), open valve surgery, or transcatheter aortic valve replacement (TAVR); the research was a cohort study with 6 months or more of follow-up; and mortality or functional status was reported according to preoperative frailty status. We considered any measure of physical function (mobility, muscle strength, physical activity, exhaustion, nutrition, balance, or disability) or any combination of measures as an acceptable screening method for frailty. We did not consider comorbidity or cognitive function alone as a measure of frailty if it was not combined with measures of physical function. Although the 6-minute walk test (6MWT) is a measure of endurance, we classified it under mobility because it is highly correlated with mobility (37, 38). Articles were excluded if the research used a design other than a cohort study, sample size was less than 100, or frailty measures were not assessed before surgery. If 2 or more articles originated from the same population, the study with the larger sample size or longer follow-up was included.

Data Extraction

Two investigators (C.A.K. and D.H.K.) independently extracted data on patient characteristics, type of procedure (major vs. minimally invasive), frailty assessment domains (Table 1 of Supplement 2, available at www.annals.org), and outcomes (Supplement 1). Any disagreement was resolved by consensus. We classified CABG and open valve surgery as major procedures and TAVR as minimally invasive surgery. To determine the feasibility of a frailty assessment, we extracted the administration time for frailty measures or, if not reported, approximated it based on the literature or our own experience (Supplement 1). The prevalence of frailty was estimated according to the study-specific definition.

Our main outcome of interest was death or poor functional status at 6 months or later after surgery. We considered the following measures of functional status: activities of daily living (ADLs), instrumental ADLs, the Duke Activity Status Index (39), the Kansas City Cardiomyopathy Questionnaire (40), and New York Heart Association class. Our secondary outcome was major adverse cardiovascular and cerebrovascular events (MACCEs). We extracted the absolute risk and relative risk (RR) for each outcome and 95% CI according to frailty status, with or without adjustment for traditional surgical risk scores. If RR was not reported, we calculated it from the count data. Metrics to evaluate diagnostic tests or prediction models (such as sensitivity, specificity, calibration, and discrimination) were obtained, if reported. Data extracted from individual studies are provided in Table 2 of Supplement 2.

Quality Assessment

Two investigators (C.A.K and D.H.K.) independently evaluated each study for the following: representativeness of the study population, use of frailty measures that were validated in the general population of older adults, frailty status determination, loss to follow-up or amount of missing outcome data (death and functional status, separately), missing data on frailty measures, and validation of the risk prediction performance (Supplement 1). Any disagreement was resolved by consensus. We determined the overall quality of evidence for each frailty instrument–outcome pair as high, moderate, low, or very low on the basis of the representativeness of study populations, risk of bias, consistency in the results across studies, and strength of associations (Supplement 1).

Data Synthesis

We qualitatively summarized the evidence by type of cardiac procedure (major vs. minimally invasive) and type of frailty instrument (single component vs. multicomponent). One study included both major and minimally invasive procedures without data stratified by procedure type (41). Because only 15% of patients had minimally invasive procedures in this study, the cardiac surgeries were categorized as major procedures. Substantial variation in frailty assessment and patient characteristics across the studies prevented the pooling of individual study estimates into a summary result.

Role of the Funding Source

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RESULTS

We identified 25 studies that evaluated the association between frailty and death or functional status at 6 months or later in 18 388 patients undergoing major cardiac surgical procedures (9 frailty instruments in 8

Figure. Frailty assessment in cardiac procedures.

Study, Year (Reference)	Study Population						Frailty Assessment										
	Surgery	*N*	Mean Age, *y*	Mean STS, %	FU, *mo*	Frailty, %	Type	Mobility	Strength	Activity	Exhaustion	Nutrition	Cognition	Disability	Balance	Medical	Subjective
Major Cardiac Surgical Procedures (8 Studies)																	
Gardner et al, 2001 (45)	CABG	11 815	64	NR	7	16	Single-component							○			
Rapp-Kesek et al, 2004 (44)	CABG, AVR	886	67	NR	22	7	Single-component					○					
de Arenaza et al, 2010 (43)	AVR	208	70	NR	12	51	Single-component	●									
Lee et al, 2010 (46)	CABG, AVR	3254	66	NR	22	4	Multicomponent	○					○	○			
Cervera et al, 2012 (47)	CABG	1503	62	NR	65	21	Multicomponent							○		○	
Robinson et al, 2013 (42)	CABG, AVR	174	73	NR	12	70	Single-component	●									
Sündermann et al, 2014 (41)	CABG, AVR	450	79	4	12	49	Multicomponent	●	●	○	○	○		○	●	○	○
	(TAVR 15%)					63	Multicomponent	○	●		○			○		○	○
Ad et al, 2016 (49)	CABG, AVR	166	74	2	12	23	Multicomponent	●	●	○	○	○					
Studies, *n*								5	2	2	2	3	1	4	1	2	1
Minimally Invasive Cardiac Surgical Procedures (17 Studies)																	
Ewe et al, 2010 (59)	TAVR	147	80	NR	9	33	Multicomponent	●	●	○	○	○					
Rodés-Cabau et al, 2010 (56)	TAVR	339	81	10	8	25	Single-component										○
Rodés-Cabau et al, 2012 (57)	TAVR	339	81	10	42	25	Single-component										○
Muñoz-García et al, 2012 (54)	TAVR	133	79	7	11	85	Single-component							○			
						14	Multicomponent	●	●	○	○	○					
Stortecky et al, 2012 (58)	TAVR	100	84	6	12	49	Multicomponent	●				○	●	○			
Green et al, 2013 (52)	TAVR	484	85	11	24	73	Single-component	●									
Mok et al, 2013 (12)	TAVR	260	79	7	12	55	Single-component	●									
Mok et al, 2013 (53)	TAVR	319	80	6	12	NR	Single-component	●									
							Single-component										○
Schoenenberger et al, 2013 (11)	TAVR	119	83	6	6	49	Multicomponent	●				○	●	○			
Arnold et al, 2014 (13)	TAVR	2137	84	12	12	71	Multicomponent	●					●			○	
Dvir et al, 2014 (51)	TAVR	1108	83	12	12	NR	Single-component	●									
Puls et al, 2014 (55)	TAVR	300	82	7	18	48	Single-component							○			
Seiffert et al, 2014 (60)	TAVR	845	81	6	12	5	Single-component										○
Cockburn et al, 2015 (50)	TAVR	312	81	5	26	NR	Single-component	○						○			
							Single-component										
							Single-component										○
Codner et al, 2015 (61)	TAVR	360	82	8	23	NR	Multicomponent	●				○	●	○		○	○
Green et al, 2015 (14)	TAVR	244	86	11	12	55	Multicomponent	●	●			○		○			
Osnabrugge et al, 2015 (15)	TAVR	436	84	10	6	16	Single-component	○									
							Single-component					○					
Studies, *n*								13	3	2	2	7	4	7	0	2	6

Open circles indicate information obtained from self-report or medical records; solid circles indicate information obtained from performance tests. Prevalence of frailty was determined according to the study-specific definition. AVR = aortic valve replacement; CABG = coronary artery bypass grafting; FU = follow-up; NR = not reported; STS = Society of Thoracic Surgeons predicted risk for mortality; TAVR = transcatheter aortic valve replacement.

studies of CABG or open valve surgery) (41–49) and 5177 patients undergoing minimally invasive cardiac surgery (13 instruments in 17 studies of TAVR) (11–15, 50–61) (Figure 1 of Supplement 2).

Frailty Assessment in Major Cardiac Surgical Procedures

Eight studies evaluated 4 single-component and 5 multicomponent frailty instruments in patients undergoing major cardiac surgical procedures (Figure and Table 1). Studies varied widely in terms of sample size (166 to 11 815 patients), mean age (62 to 79 years), follow-up (7 to 65 months), and prevalence of frailty (4% to 70%). Mobility (5 studies), disability (4 studies), and nutrition (3 studies) were commonly assessed (Figure).

Single-Component Frailty Instruments

Except for the 6MWT, single-component instruments could be administered within 5 minutes (Table 1). Distance on 6MWT (43), low albumin levels (44), and ADL dependence (45) were statistically significantly associated with a 2.4- to 3.6-fold risk for death or MACCEs. The study by Robinson and colleagues (42) was underpowered to detect a clinically significant mortality difference by performance on the Timed Up and Go (TUG) test. No studies examined functional status. Only the 6MWT (43) and ADL dependence (45) were evaluated in highly representative samples of routine clinic patients (such as a multicenter study of consecutive patients); other measures were evaluated in less representative, single-center samples (Figure 2A of Supplement 2). None of the single-component instruments was validated in an independent sample of patients having major cardiac surgery. Accordingly, we judged the overall quality of evidence for predicting mortality to be moderate for mobility and ADL dependence and low for serum albumin (Figure 2B of Supplement 2).

Multicomponent Frailty Instruments

Five multicomponent frailty instruments required information from self-report or medical records alone (46, 47) (administration time less than 5 minutes) or ad-

Table 1. Frailty Assessment and Outcomes at ≥6 Months After Major Cardiac Procedures in Older Adults

Frailty Assessment	Study, Year (Reference)	Time, *min*	Outcome	Frailty Category	Absolute Risk, %	Relative Risk (95% CI)	C-Statistic
Single-component frailty assessment							
TUG test	Robinson et al, 2013 (42)	<1*	1-y mortality	Fast: ≤10 s	2	Reference	NR
				Intermediate: 11–14 s	3	1.8 (0.2–17.0)	
				Slow: ≥15 s	12	6.4 (0.8–55.0)	
6MWT	de Arenaza et al, 2010 (43)	30*†	1-y mortality	Good mobility: ≥300 m	3	Reference	NR
				Poor mobility: <300 m	8	2.6 (0.7–9.4)	
			1-y mortality or MACCE	Good mobility	4	Reference	NR
				Poor mobility	14	3.6 (1.2–11.1)	
Serum albumin level	Rapp-Kesek et al, 2004 (44)	NA	1.8-y mortality	Normal nutrition: >37 g/L	6	Reference	NR
				Malnutrition: ≤37 g/L	14	2.5 (1.3–4.9)	
Katz Index of ADL	Gardner et al, 2001 (45)	5	7-mo mortality	Independent: 6	NR	Reference	NR
				Partially dependent: 1–5		1.5 (1.1–1.9)‡	
				Totally dependent: 0		2.4 (1.6–3.7)‡	
Multicomponent frailty assessment							
Lee index: ADL dependence Dependence in ambulation History of dementia	Lee et al, 2010 (46)	<5	1.8-y mortality	Nonfrail: 0	11	Reference	NR
				Frail: 1–3	30	1.5 (1.1–2.2)‡	
Cervera index: ADL dependence Nursing home residence Dialysis or oxygen therapy	Cervera et al, 2012 (47)	<5	5.4-y mortality	Nonfrail: 0	NR	Reference	NR
				Frail: 1–3		1.0 (0.7–1.4)‡§	
FORECAST: Chair rise Self-reported exhaustion Self-reported stair climbing Clinical Frailty Scale Serum creatinine level	Sündermann et al, 2014 (41) Sündermann et al, 2011 (48)	5*	1-y mortality	Nonfrail: 1–4	5	Reference	NR
				Moderately frail: 5–7	17	3.2 (1.6–6.7)	
				Severely frail: 8–13	21	3.9 (1.9–8.0)	
				Per 1-point increase (range: 1–13)		1.3 (1.1–1.4)‡	0.76
Frailty phenotype: 15-ft gait speed Grip strength Weight loss Self-reported exhaustion Low activity	Ad et al, 2016 (49)	15	1-y mortality	Nonfrail: 0–2	3	Reference	NR
				Frail: 3–5	6	2.3 (0.3–17.4)‡	
Comprehensive Assessment of Frailty: 4-m gait speed Grip strength Self-reported exhaustion Physical activity from instrumental ADL Standing balance Chair rise Put on and remove jacket Pick up a pen from the floor Turn 360 degrees Serum albumin level Serum creatinine level Serum brain-type natriuretic peptide level FEV_1 Clinical Frailty Scale	Sündermann et al, 2014 (41) Sündermann et al, 2011 (48)	20*	1-y mortality	Nonfrail: 1–10	8	Reference	NR
				Moderately frail: 11–25	17	2.1 (1.2–3.6)	
				Severely frail: 26–35	36	4.5 (2.4–8.7)	
				Per 1-point increase (range: 1–35)		1.1 (1.0–1.1)‡	0.70

6MWT = 6-minute walk test; ADL = activities of daily living; FORECAST = Frailty Predicts Death One Year after Elective Cardiac Surgery Test; MACCE = major adverse cardiovascular and cerebrovascular event; NA = not applicable; NR = not reported; TUG = Timed Up and Go.
* Reported by the authors.
† Includes explaining and performing the test and allowing the patient to recover according to a clinical trial protocol.
‡ Estimates were adjusted for clinical covariates.
§ The regression model simultaneously adjusted for other markers of frailty.

ministration of performance tests (41, 48, 49) (up to 20 minutes). Frequently included components were mobility (4 instruments) and disability (4 instruments). Lee and colleagues (46) and Sündermann and coworkers (41, 48) found a statistically significant 1.5- to 4.5-fold risk for death among frail patients. Such an association was not found for the Cervera index and frailty phenotype because of simultaneous adjustment for other frailty markers (47) or insufficient power (49). None of the studies examined functional status. All 4 studies of multicomponent instruments were conducted in single-center samples (**Figure 2A** of **Supplement 2**), and only Lee and colleagues (46) evaluated model performance after accounting for overfitting. Some studies did not use validated measures of frailty (46, 47), or they determined frailty status according to a previously validated definition or clinical cut points (41, 46–48). The overall quality of evidence for multicomponent instruments for mortality was low or very low (Figure 2B of Supplement 2).

Frailty Assessment in Minimally Invasive Cardiac Surgical Procedures

Seventeen studies evaluated 8 single-component and 5 multicomponent frailty instruments in patients undergoing TAVR (Figure and Table 2). The mean age of TAVR patients (79 to 86 years) was greater than that of patients undergoing major cardiac surgical procedures. Sample size (100 to 2137 patients), follow-up (6 to 42 months), and prevalence of frailty (5% to 85%) varied greatly across studies. Mobility (13 studies), nutrition (7 studies), disability (7 studies), and subjective assessment (6 studies) were frequently assessed domains (Figure).

Single-Component Frailty Instruments

Evidence of mobility impairment after a simple assessment (administration time less than 1 minute), such as a musculoskeletal or neurologic disorder (56), use of assistive devices (50), and distance on 6MWT (10 minutes) below various thresholds (12, 51–53) were statistically significantly associated with a 1.2- to 3.2-fold increase in mortality (Table 2). Dependence in ADLs (5 minutes) was statistically significantly associated with mortality in 2 of the 3 studies (54, 55). The Clinical Frailty Scale (3 minutes)—a global assessment based on medical problems, activity level, and disability—predicted mortality (50, 60), whereas subjective assessment without such a scale did not (12, 56, 57). Most studies of single-component instruments were done in highly representative samples, but the risk of bias was high because frailty status was determined without using previously validated or clinical cut points and validation was lacking (Figure 2A of Supplement 2). The overall quality of evidence was moderate for mobility, Clinical Frailty Scale, and subjective assessment and low for disability in predicting mortality (Figure 2B of Supplement 2). Three studies examined a composite outcome of death and poor functional status (Table 2). Being wheelchair-bound (15) and a 6MWT distance less than 170 m (among patients with chronic obstructive pulmonary disease) (12) were statistically significantly associated with a 2.6- to 2.8-fold risk for the composite outcome. Serum albumin was not associated with the outcome after adjustment for mobility impairment (15). Subjective assessment did not predict the outcome in patients with chronic obstructive pulmonary disease (12). All 3 studies were conducted in highly representative samples, but the risk of bias was moderate because of missing outcomes and a lack of validation (Figure 2A of Supplement 2). The quality of evidence was high for mobility and low for nutrition and subjective assessment (Figure 2B of Supplement 2).

Multicomponent Frailty Instruments

Five multicomponent frailty instruments required 10 minutes (Green index) (14) to 25 minutes (Stortecky index) (11, 58) to administer (Table 2). Multicomponent tools frequently included an objective measure of mobility (5 instruments), nutrition (4 instruments), or disability (3 instruments). Ewe and colleagues (59) found that frailty phenotype was statistically significantly associated with a 4.2-fold risk for death or MACCEs, whereas Muñoz-García and coworkers (54) found no such association, probably because of overadjustment for postprocedure ADL dependence. Frailty defined by all other instruments (11, 14, 58, 61) was statistically significantly associated with a 1.9- to 5.6-fold risk for death. Only the Green index (14) was developed in a highly representative sample (Figure 2A of Supplement 2). Except for frailty phenotype, frailty status was defined according to the study population distribution. Validation was not performed. For predicting mortality, the overall quality of evidence was moderate for the Stortecky index (11, 58) and very low or low for the other instruments (Figure 2B of Supplement 2). Multicomponent instruments by Green and colleagues (14), Arnold and coworkers (13), and Schoenenberger and associates (11) examined a composite outcome of death and poor functional status (Table 2). Frailty determined by these indices was statistically significantly associated with a 2.2- to 4.2-fold increase in risk for the composite outcome at 6 or 12 months. The Green (14) and Arnold (13) indices were developed in highly representative samples (Figure 2A of Supplement 2). However, study-specific definitions of frailty have not been tested in an independent sample, and only the Arnold index (13) was internally validated by using split-sample validation. The quality of evidence was moderate for the Arnold index (13) and low for the other indices (11, 14) (Figure 2B Supplement 2).

Comparison of Frailty Instruments

Eight studies directly compared frailty instruments (Table 3 of Supplement 2). Objective measures of lower extremity performance (mobility and leg muscle strength), such as TUG (11, 58), 6MWT (12), and chair rise (48), seemed to have higher c-statistics or RRs than cognitive tests (11, 58), self-reported mobility impairment (11, 48, 58), disability (11, 58), or subjective assessment (12, 48). Among the non–performance-based measures, self-reported mobility impairment, such as stair climbing difficulty (48), preclinical mobility disability (11, 58), mobility impairment due to musculoskeletal or neurologic disorder (50), or wheelchair use (15), was more predictive than disability (11, 50, 58), serum albumin (15), and subjective assessment (48, 50). In comparing single-component with multicomponent frailty instruments, multicomponent ones seemed to provide better prediction, as shown by Green and colleagues (14) and Sündermann and coworkers (48). Similarly, the Mini Nutritional Assessment tool (62), which considered several risk factors of malnutrition in multiple domains, showed higher RR than disability or cognition alone (11, 58). However, a multicomponent instrument com-

Table 2. Frailty Assessment and Outcomes at ≥6 Months After Minimally Invasive Cardiac Procedures in Older Adults

Frailty Assessment	Study, Year (Reference)	Time, *min**	Outcome	Frailty Category	Absolute Risk, %	Relative Risk (95% CI)	C-Statistic
Single-component frailty assessment							
Wheelchair-bound status	Osnabrugge et al, 2015 (15)	<1	6-mo mortality or poor QOL	Not wheelchair-bound	NR	Reference	0.72
				Wheelchair-bound		2.6 (1.3–5.2)†‡	
Mobility impairment due to musculoskeletal or neurologic disorder	Cockburn et al, 2015 (50)	<1	2.2-y mortality	No severe impairment	NR	Reference	NR
				Severe impairment		2.2 (1.3–2.5)	
Brighton Mobility Index	Cockburn et al, 2015 (50)	<1	2.2-y mortality	Per 1-category worsening (range: 0–6)	NR	1.2 (1.0–1.5)	NR
6MWT	Green et al, 2013 (52)	10	2-y mortality	Fast walker: >128.5 m	29	Reference	NR
				Slow walker: ≤128.5 m	31	1.2 (0.8–2.0)†	
				Unable to walk: 0 m	43	1.8 (1.2–2.7)†	
	Mok et al, 2013 (53)	10	1-y mortality	Good mobility: ≥182 m	9	Reference	NR
				Poor mobility: <182 m	25	2.8 (NR)	
				Per 10-m decrease		1.1 (1.0–1.1)†	NR
	Mok et al, 2013 (12)§	10	6-mo mortality or no symptom benefit	Good mobility: ≥170 m	29	Reference	NR
				Poor mobility: <170 m	59	2.8 (NR)	
				Per 20-m decrease		1.2 (1.0–1.2)†‡	0.67
			1-y mortality	Good mobility: ≥150 m	24	Reference	NR
				Poor mobility: <150 m	75	3.2 (NR)	
				Per 20-m decrease		1.2 (1.1–1.3)†	0.74
	Dvir et al, 2014 (51)§	10	1-y mortality	Good mobility: ≥50 m	NR	Reference	NR
				Poor mobility: <50 m		1.7 (1.2–2.2)†	
Serum albumin level	Osnabrugge et al, 2015 (15)	NA	6-mo mortality or poor QOL	Normal nutrition: ≥33 g/L	NR	Reference	0.72
				Malnutrition: <33 g/L		1.8 (0.9–3.5)†‡	
Barthel index of ADL	Muñoz-García et al, 2012 (54)	5	11-mo mortality	Per 1-point improvement (range: 0–100)	NR	1.0 (1.0–1.1)†	NR
Katz index of ADL	Puls et al, 2014 (55)	5	1.5-y mortality	Independent: 6	24	Reference	NR
				Dependent: 0–5	56	2.7 (1.8–3.9)†	
	Cockburn et al, 2015 (50)	5	2.2-y mortality	Per 1-point improvement (range: 0–6)	NR	0.9 (0.7–1.1)	NR
Subjective assessment	Rodés-Cabau et al, 2010 (56)	NA	1-y mortality	Nonfrail	23	Reference	NR
				Frail	30	1.4 (0.8–2.3)	
	Rodés-Cabau et al, 2012 (57)		3.5-y mortality	Nonfrail	NR	Reference	NR
				Frail		1.4 (1.0–2.0)†	
	Mok et al, 2013 (12)	NA	6-mo mortality or no symptom benefit	Nonfrail	42	Reference	NR
				Frail	45	1.1 (0.3–4.1)†‡	
			1-y mortality	Nonfrail	NR	Reference	NR
				Frail		0.6 (0.1–2.4)	
Clinical Frailty Scale	Seiffert et al, 2014 (60)	3	1-y mortality	Nonfrail: 1–5	24	Reference	0.71
				Frail: 6–7	63	3.6 (1.8–7.1)†	
	Cockburn et al, 2015 (50)	3	2.2-y mortality	Per 1-category worsening (range: 1–7)	NR	1.3 (1.1–1.6)	NR
Multicomponent frailty assessment							
Green index: 15-ft gait speed; Grip strength; Serum albumin level; ADL dependence	Green et al, 2015 (14)	10	6-mo mortality or poor QOL	Nonfrail: 0–5	28	Reference	NR
				Frail: 6–12	42	2.2 (1.1–4.5)†	
			1-y mortality or poor QOL	Nonfrail	32	Reference	NR
				Frail	50	2.4 (1.1–5.1)†	
			1-y mortality	Nonfrail	16	Reference	NR
				Frail	33	2.5 (1.4–4.4)†	
Frailty phenotype: 15-ft gait speed; Grip strength; Weight loss; Self-reported exhaustion; Low activity	Ewe et al, 2010 (59)	15	9-mo mortality or MACCE	Nonfrail: 0–2	NR	Reference	NR
				Frail: 3–5		4.2 (2.0–8.8)†	
	Muñoz-García et al, 2012 (54)	15	11-mo mortality	Nonfrail: 0–2	7	Reference	NR
				Frail: 3–5	25	1.0 (0.2–4.9)†‡	
Codner index: Gait speed; ADL dependence; Serum albumin level; Oxygen therapy; Cognitive function; General appearance; Subjective assessment	Codner et al, 2015 (61)	15	2.2-y mortality	Nonfrail: NR	NR	Reference	NR
				Frail: NR		1.9 (1.1–3.2)†	

Continued on following page

Table 2—Continued

Frailty Assessment	Study, Year (Reference)	Time, *min**	Outcome	Frailty Category	Absolute Risk, %	Relative Risk (95% CI)	C-Statistic
Arnold index: Diabetes Major arrhythmia Serum creatinine level Mean arterial pressure Body mass index Oxygen-dependent lung disease Mean aortic valve gradient Mini-Mental State Examination 6MWT	Arnold et al, 2014 (13)	20	6-mo mortality or poor QOL	Low: NR Intermediate: NR High: NR	18 37 55	Reference 2.1 (1.7–2.5) 3.1 (2.5–3.8)	0.64–0.66
			1-y mortality or poor QOL	Low: NR Intermediate NR High: NR Extremely high: NR	29 40 59 73	Reference 1.4 (0.9–2.0) 2.0 (1.4–2.9) 2.5 (1.7–3.7)	0.62–0.66
Stortecky index: TUG test Mini-Mental State Examination ADL dependence Instrumental ADL dependence Preclinical mobility disability Mini Nutritional Assessment	Stortecky et al, 2012 (58)	25	6-mo mortality or ADL decline	Nonfrail: 0–2 Frail: 3–7	15 44	Reference 4.2 (1.7–10.3)†	NR
	Schoenenberger et al, 2013 (11)		6-mo mortality	Nonfrail Frail	3 19	Reference 5.6 (1.3–24.2)	
			1-y mortality	Nonfrail Frail	NR	Reference 2.9 (0.9–9.2)†	
			1-y mortality or MACCE	Nonfrail Frail	NR	Reference 4.2 (1.4–12.7)†	

6MWT = 6-minute walk test; ADL = activities of daily living; MACCE = major adverse cardiovascular and cerebrovascular event; NA = not applicable; NR = not reported; QOL = quality of life; TUG = Timed Up and Go.
* Estimated from the literature or our experience.
† Adjusted for clinical covariates.
‡ The regression model simultaneously adjusted for other markers of frailty.
§ Patients with chronic obstructive pulmonary disease.

prising several measures assessing the same domain showed a lower c-statistic than its abbreviated version (48).

Discussion

In this review, we critically appraised heterogeneous literature on the role of frailty assessment in predicting mortality and functional status at 6 months or later after cardiac surgery. Nine frailty instruments were evaluated in major surgical procedures and 13 in minimally invasive ones. Despite various ways of measuring frailty, we found strong evidence that it predicts mortality at 6 months or later after major or minimally invasive procedures. Some evidence indicated that frailty may predict functional decline, poor quality of life, or lack of symptomatic benefit after minimally invasive procedures.

Current evidence best supports mobility assessment as a single-component frailty instrument before cardiac surgical procedures. In the general population, gait speed is a highly sensitive marker of frailty (63, 64) and a strong predictor of institutionalization, disability, and death (65). Gait speed predicts short-term mortality and complications after cardiac surgery or TAVR (6–8). We found a large body of evidence to support the use of mobility assessment to predict mortality at 6 months or later after major or minimally invasive procedures and functional status after minimally invasive surgery. Although 6MWT was evaluated most frequently, a simple gait speed or TUG test might be as useful, given its high correlation with 6MWT performance (0.70 to 0.73) (37, 38). If an objective assessment is not feasible, asking a patient about his or her ability to climb stairs, any difficulty walking due to musculoskeletal or neurologic disorders, or wheelchair use may be an alternative screening method. Although disability, nutritional status, and the Clinical Frailty Scale may be useful, the evidence for these assessments is not as robust as for mobility assessment. There is sufficient evidence that a clinician's subjective assessment does not predict outcomes (12, 56, 57); such an assessment without standardized criteria is prone to personal bias and low reproducibility (66).

Several multicomponent frailty instruments predicted mortality at 6 months or later after major or minimally invasive cardiac surgery and functional status after minimally invasive procedures. These instruments included assessments of mobility (based on a performance test), disability, and nutrition. Although a widely validated frailty phenotype (17) predicted mortality and MACCEs after TAVR (59), this finding was not consistent with other studies (49, 54). The frailty index of deficit accumulation also is validated (18, 67), but its association with clinical outcomes has not been tested in patients having cardiac surgery.

Some evidence suggests that, in major or minimally invasive cardiac procedures, multicomponent frailty instruments may offer better risk discrimination than single-component ones. Green and colleagues (14) and Sündermann and coworkers (48) showed that combining measures in different frailty domains might improve risk prediction. Stortecky and colleagues (58) and Schoenenberger and coworkers (11) found that the Mini Nutritional Assessment (62), a multicomponent screening tool for malnutrition, was associated more strongly with mortality and functional decline than disability or cognitive function alone. Moreover, information from multicomponent frailty instruments may inform clinicians of each patient's vulnerability and need for perioperative management.

We searched MEDLINE using the keywords "cardiovascular surgical procedures" and "frailty" on 1 June 2016 and identified 6 reviews (30–35) highlighting the high prevalence of frailty and its prognostic power in predicting short- and long-term clinical outcomes after cardiac surgery. The authors of these reviews called for the development and validation of a standardized frailty instrument for preoperative risk assessment. Our work adds to previous reviews by summarizing up-to-date literature and evaluating the strength of evidence by type of frailty instrument and cardiac procedures. We summarized the definition and feasibility of the frailty instruments, along with the absolute risk and RR for death and poor functional status by frailty status. We focused on the outcomes at 6 months or later after cardiac surgery, because death and functional status beyond the early postoperative period are better aligned with the patient's values than surviving the first 30 days after the procedure (68). Our review may facilitate adoption of evidence-based frailty assessment, objective assessment of prognosis, and transparent decision making regarding cardiac surgery.

Our evidence synthesis is limited by the heterogeneity of frailty instruments and low to moderate quality of the included studies. Most multicomponent frailty instruments were evaluated in single-center samples. Population-specific cut points were commonly used to define frailty status, and procedures to minimize model overfitting were used rarely. These limitations make it difficult to generalize predicted risks derived from 1 instrument (particularly a multicomponent frailty instrument) to typical clinic patients. We found only 5 studies on functional status (11–15); even when it was measured, the measurement interval was not adequate to capture the fluctuation in functional status of frail older patients. Our screening may have missed relevant studies in which the frailty–outcome association was not the main focus of analysis (that is, frailty as a covariate), and publication bias due to selective reporting is possible.

Several key issues must be resolved for frailty assessment to be adopted in preoperative evaluation and decision making. First, criteria should be established for selecting a multi- versus single-component frailty instrument, as well as for which domains should be measured. Instead of developing a new instrument, we believe that risk prediction based on a common set of frailty domains that can inform clinical care (such as mobility, nutrition, disability, and cognition) may streamline assessment and interventions. Such standardization also may facilitate validation in different populations. Second, frailty may be reversed with cardiac procedures in some patients, but none of the studies assessed postsurgical change in frailty. Third, although most studies on frailty assessment aimed to improve surgical risk stratification, more research is needed for patient-centered outcomes, such as functional status and quality of life. Fourth, making decisions about cardiac surgery is challenging without knowing the expected outcome of alternative treatment options (for example, TAVR vs. surgical aortic valve replacement or TAVR vs. palliative care). Secondary analyses of clinical trial data may be useful in addressing this key question. A core set of frailty measures should be obtained in future clinical trials in older adults. Finally, when reporting the results of analysis, investigators should include absolute risks in addition to RRs. When the background risk is low, RRs may be misleading (69). Metrics of prognostic models, such as sensitivity, specificity, calibration, and discrimination, also should be reported.

Clinicians should attempt to classify patients into 3 groups: extreme-risk patients, whose predicted health status after the procedure is unlikely to be meaningfully better than it would without the procedure; high-risk patients, whose predicted health status after the procedure is likely to be better than it would be without the procedure, albeit with a high yet not prohibitive risk for harms; and low-risk patients, who are likely to benefit from the procedure with a low risk for harms. Health status should not be confined to the risk for short-term complications or death; functional status may be as important, depending on the patient's values.

The ideal screening test would be practical, sensitive, and validated in a broad spectrum of patients. Gait speed or TUG test is a reasonable screening tool, because it is highly correlated with 6MWT and highly sensitive for frailty (sensitivity is 0.99 if gait speed is <0.8 m/s [63] and 0.93 if TUG is >10 seconds [64]). If an objective assessment of mobility is not feasible, self-reported mobility, disability, nutritional status, or the Clinical Frailty Scale may be used. The American Heart Association and American College of Cardiology recommend assessments of mobility and ADL disability (70). Patients with positive screening results should have a comprehensive geriatric assessment that provides a benchmark for evaluating and managing frail older adults (71). The purpose of comprehensive assessment is to refine surgical risk stratification and to deliver individualized care to prevent complications and promote recovery and independence after cardiac surgery.

Case Example

An 87-year-old patient with severe aortic stenosis is evaluated for TAVR after a recent heart failure exacerbation. His medical history includes systolic heart failure, coronary artery disease, chronic lung disease, chronic kidney disease, and spinal stenosis. He has been using a walker at home and a wheelchair outside for the past 5 years. His aide helps him with bathing and dressing, and family members provide assistance with all instrumental ADLs. It took 30 seconds for him to complete the TUG test. A comprehensive assessment reveals moderate to severe impairment in mobility (gait speed is 0.3 m/s), nutrition (at risk for malnutrition), and cognition (Mini-Mental State Examination is 17 of 30 points). His risk for in-hospital death after TAVR is 8% (the national average is 4%) (29). The patient's risk probably is underestimated, because frailty is not included in the risk calculator. Given his severe mobility impairment, frailty, and chronic lung disease, his risk for death or functional decline after TAVR is greater than 40% to 50% at 6 months (11, 12, 58). These risks should be presented to the patient against the potential benefits of TAVR in an unbiased fashion. If the likelihood of benefit is unclear and the risk for harms is high, the decision should be guided by his personal values and preferences.

Conclusion

Frailty status, assessed as mobility, disability, and nutritional status, may predict the risk for death at 6 months or later in older patients after major cardiac surgery and the risk for death and functional decline after minimally invasive cardiac procedures.

From Harvard Medical School, Boston, Massachusetts, and Albert Einstein College of Medicine, Bronx, New York.

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Requests for Single Reprints: Dae Hyun Kim, MD, MPH, ScD, Beth Israel Deaconess Medical Center, 110 Francis Street, Suite 1A, Boston, MA 02215; e-mail, dkim2@bidmc.harvard.edu.

Current author addresses and author contributions are available at www.annals.org.

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Current Author Addresses: Drs. D.H. Kim, C.A. Kim, and Lipsitz: Beth Israel Deaconess Medical Center, 110 Francis Street, Suite 1A, Boston, MA 02215.
Mr. Placide: Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461.
Dr. Marcantonio: Division of General Medicine and Primary Care, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, CO-216, Boston, MA 02215.

Author Contributions: Conception and design: D.H. Kim, C.A. Kim, E.R. Marcantonio.
Analysis and interpretation of the data: D.H. Kim, C.A. Kim.
Drafting of the article: D.H. Kim, C.A. Kim, L.A. Lipsitz.
Critical revision for important intellectual content: D.H. Kim, C.A. Kim, L.A. Lipsitz, E.R. Marcantonio.
Final approval of the article: D.H. Kim, C.A. Kim, L.A. Lipsitz, S. Placide, E.R. Marcantonio.
Provision of study materials or patients: C.A. Kim.
Obtaining of funding: C.A. Kim, L.A. Lipsitz.
Administrative, technical, or logistic support: C.A. Kim, S. Placide.
Collection and assembly of data: D.H. Kim, C.A. Kim, S. Placide.