

The impact of frailty on outcomes after cardiac surgery: A systematic review

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Objective: Current preoperative assessments for cardiac surgery, such as the European System for Cardiac Operative Risk Evaluation II and the Society of Thoracic Surgeons risk score, are limited in their ability to predict postoperative outcomes. This is thought to be due to the reliance on chronological age as a predictor of health. In geriatrics, frailty assessments have been developed as a tool in determining physiologic functioning capacity. Whether or not frailty predicts postoperative outcomes independent of existing cardiac preoperative risk scores remains unknown.

Methods: We performed a systematic review to determine the association of frailty with negative postoperative outcomes such as major adverse cardiac and cerebrovascular events (MACCE) in patients undergoing cardiac surgery. We searched PubMed, EMBASE, the Cochrane library, and Ageline from inception until July 2013 and screened 5913 abstracts for potential inclusion. Of these, 6 studies examined the relationship between objective frailty assessments and postoperative outcomes. Our included studies evaluated 4756 patients undergoing cardiac surgery.

Results: Frailty, defined using multiple criteria, had a strong positive relationship with the risk of MACCE (odds ratio, 4.89; 95% confidence interval, 1.64-14.60). Relationships were stronger in older patients undergoing transcatheter aortic valve replacement (TAVR) than younger patients undergoing coronary artery bypass grafting and valvular surgery (hazard ratio for frailty in TAVR, 3.31-4.89 vs hazard ratio for non-TAVR, 1.10-3.16).

Conclusions: Patients deemed frail, determined using an objective assessment tool, have a higher likelihood of experiencing mortality, morbidity, functional decline, and MACCE following cardiac surgery, regardless of definition. Further study is needed to determine which components of frailty are most predictive of negative postoperative outcomes before integration in risk prediction scores. (*J Thorac Cardiovasc Surg* 2014;148:3110-7)

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In the current era of cardiac surgery, more than half of procedures are being performed in patients aged 75 years and older.¹ These elderly and often frail patients represent the

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fastest growing demographic in North America² and are at increased risk of falls, prolonged hospitalization, and mortality after surgery.³ A comprehensive preoperative assessment is essential to determine the relative risk and benefit of the surgical intervention in this patient population. The European System for Cardiac Operative Risk Evaluation (EuroSCORE) II and Society of Thoracic Surgeons (STS) risk scores are widely used to evaluate perioperative mortality and morbidity in patients undergoing cardiac surgery.^{4,5} These risk assessment methods have limitations. The EuroSCORE II typically overestimates perioperative risk,⁵ whereas the STS score, which is considered to be the global standard,^{3,6} has been reported to underestimate perioperative risk in frail patients.^{3,7}

The limitations of these risk models may be tied to their weighting of chronological age and medical diagnoses without a standardized and/or comprehensive evaluation of the biological status of an elderly patient.^{3,8} The realization that age is not synonymous with vulnerability to adverse health outcomes has led to the development of the concept of frailty. Frailty is an umbrella term that encompasses the patient factors of malnutrition, wasting, weakness, slowness, and inactivity. Although frailty tends to increase with age, its assessment, measured through a

Abbreviations and Acronyms

CABG	= coronary artery bypass graft
EuroSCORE	= European System for Cardiac Operative Risk Evaluation
MACCE	= major adverse cardiac and cerebrovascular events
STS	= Society of Thoracic Surgeons
TAVR	= transcatheter aortic valve repair

variety of physical and cognitive tests, nutritional status, and self-reported functional deterioration,⁹ is independent of age or any specific medical condition.³ It can be thought of as a measure of an individual's vulnerability due to an inability to maintain homeostasis,¹⁰ where small insults, such as minor infections or surgeries, can have a disproportionate influence on health. Frailty has been linked to cardiovascular disease¹¹ and increased mortality and morbidity in the general population.¹²

To examine the effect of frailty on surgical outcomes, we performed a systematic review of relevant studies examining the association of frailty with major adverse cardiac and cerebrovascular events (MACCE) in patients undergoing cardiac surgery. We hypothesized that patients deemed frail by objective criteria would have a higher risk of MACCE after undergoing cardiac surgery. We also hypothesized that specific components (or domains) of the frailty assessment, may be more strongly associated with MACCE than others.

METHODS

Data Sources and Search Strategy

We aimed to systematically identify observational studies of human beings that explored the link between frailty, cardiac surgery, and postoperative outcomes. The primary question of interest was whether or not frailty demonstrated predictive value when determining risk of adverse outcomes following coronary artery bypass graft (CABG) and/or valve procedures. In collaboration with 2 medical librarians (K.M. and C.S.D.), a search strategy was designed and implemented to capture all relevant studies from the available literature. The following electronic databases were searched from their date of establishment to July 2013: PubMed, Cochrane library, AgeLine, and EMBASE. The search strategy was tailored to each database and used a combination of key words, including *frailty*, *elderly*, and *cardiac surgery*, as well as medical subject headings terms. The reference lists from any relevant review articles were cross-matched with the search results to ensure the search terms were broad and inclusive of all relevant studies, reducing the possibility of missing studies. The search resulted in 5913 articles.

Article Eligibility and Selection Criteria

From the 5913 articles 2 reviewers (A.S. and T.B.) selected 40 full-text citations for text review based on the title and abstract (Figure 1). To be included in the systematic review studies had to meet several inclusion criteria. First, frailty measurements needed to be based on comprehensive assessments of frailty, rather than on individual domains of frailty such as handgrip strength. Second, clear outcomes had to be measured. Finally, only studies that were based on a cardiac surgery population were included. Studies were finalized for inclusion in the systematic review after discussion with a third reviewer (N.T.). Disagreements were resolved by consensus.

Data Extraction

One reviewer (A.S.) conducted the data extraction, collecting the comparable and relevant information. Data extraction was then verified by a second reviewer (T.B.).

Evaluation of Risk of Bias

We evaluated each study for risk of bias using the Newcastle-Ottawa Scale¹³ to assess its quality (Table 1). The Newcastle-Ottawa Scale is a quality evaluation method for nonrandomized studies. Newcastle-Ottawa Scale criteria are split into 3 sections: selection, comparability, and outcome. Each study is designated a number of stars for each section, based on predetermined queries.

Statistical Analysis

Because of significant clinical heterogeneity in the patient population, definitions of frailty, study methodologies, and covariate adjustment were encountered; meta-analysis was not performed.

RESULTS

Study Characteristics

The individual study characteristics are outlined in Table 2. The 6 studies each looked at the relationship between frailty and postoperative outcomes for patients undergoing cardiac surgery. The cardiac surgeries included CABG, valve replacement, and transcatheter aortic valve replacement (TAVR). In total, the studies encompassed 4756 patients. Three of the studies were conducted in the United States and/or Canada and the remaining studies were conducted in Europe. All the studies were prospective and published after 2010. They each provided a definition and list of criteria for determining frailty. Each study also defined its own primary outcomes.

Measures of Frailty and Physical Function

Each study used different definitions of frailty, as outlined in Table 3. This resulted in varying methods for identification of frailty and physical function, based on currently accepted measurements. For example, in an American study looking at TAVR³ investigators used a modified Fried Scale, whereas a European study¹⁴ created an assessment using certain domains from previous assessments shown to have predictive value, which they referred to as the simplified Comprehensive Assessment of Frailty. Two studies^{14,15} used a modified geriatric baseline examination, whereas another looked at the Katz Index of Independence in Activities of Daily Living, independence in ambulation, and previous diagnosis of dementia.¹⁶ Afilalo and colleagues² looked at 4 scales for comparison. Frailty criteria for all the studies were determined through questionnaires, physical function tests, and lab investigations.

Four studies^{3,14-16} looked at frailty on a linear scale. Each study also dichotomized the data, creating a point on the scale that could definitively label patients as frail or not frail. The frailty measurements in the remaining 2

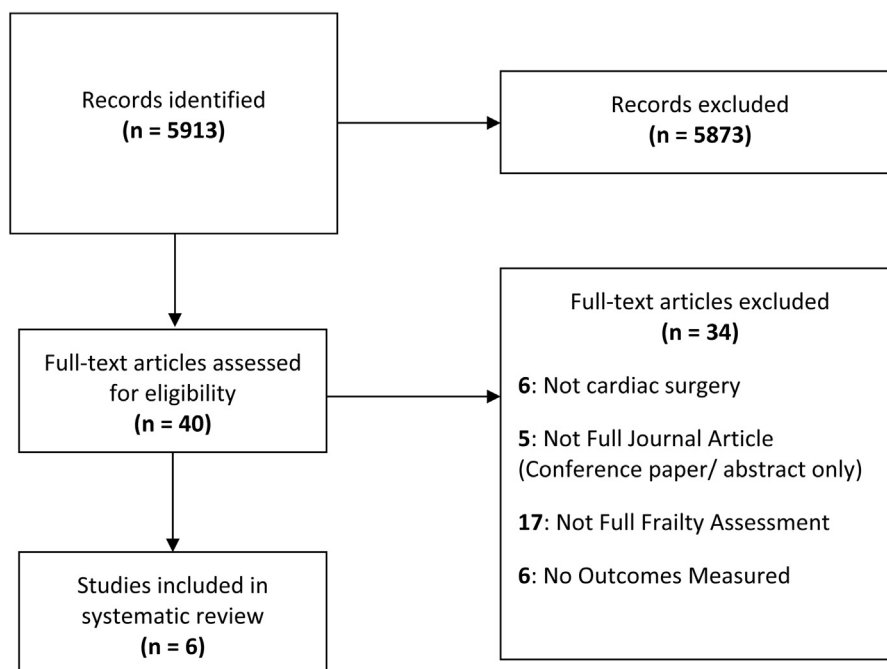


FIGURE 1. Flow diagram of reviewed studies.

studies^{2,17} were defined to determine either the presence or lack of frailty and did not have a correlating scale.

Association of Frailty With Postoperative Outcomes in Patients Undergoing Cardiac Surgery

All 6 published studies related frailty in patients undergoing cardiac surgery to an adverse clinical outcome (Table 4). A Canadian study¹⁷ looked at all-cause midterm mortality after cardiac surgery and defined frailty as any impairment in activities of daily living or ambulation, or a history of dementia. The study determined that patients who were deemed frail had a 1.5-fold higher risk of mortality compared with patients who were not frail (hazard ratio, 1.5; 95% confidence interval [CI], 1.1-2.2). The European study using their Comprehensive Assessment of Frailty definition¹⁴ found similar results, showing a relation between frailty and an increased 1-year mortality rate following cardiac surgery (odds ratio [OR], 1.097; 95% CI, 1.038-1.160).

Three studies examined the relationship between frailty and outcomes after TAVR. Two studies used a modified

Multidimensional Geriatric Assessment for determining frailty.^{15,16} Both studies had parallel results, with 1 study¹⁵ finding a significant association between frailty and functional decline (OR, 4.46; 95% CI, 1.85-10.75) and the other¹⁶ showing an association between frailty and increased mortality rates (OR, 3.68; 95% CI, 1.21-11.19). In line with these 2 studies, the Canadian study looking at TAVR³ found that using a modified Fried Scale, patients deemed frail had a more than 3-fold higher risk of mortality when compared with patients not deemed frail (hazard ratio, 3.16; 95% CI, 1.33-7.51).

Afilalo and colleagues² looked at 4 different scales to determine frailty: the 5-item Cardiovascular Health Study Frailty Scale, 7-item expanded Cardiovascular Health Study Frailty Scale, 4-item MacArthur Study of Successful Aging, and gait speed. The study looked at each scale independently when determining a patient's frailty. When looking for an association between the presence of frailty and mortality/major morbidity after CABG and/or valve surgery, it was found that only gait speed was significant (OR, 2.63; 95% CI, 1.17-5.90).

It is interesting to note that in patients undergoing traditional procedures such as CABG and/or valve procedures, frailty was associated with an increased OR of mortality ranging from 1.10 to 2.63, whereas in patients being referred for less invasive procedures such as TAVR, frailty was shown to be associated with a 3- to 5-fold increase in mortality, MACCE, or functional decline. One would speculate that the less invasive transcatheter aortic valve implantation procedure would result in better outcomes

TABLE 1. Newcastle-Ottawa Scale quality evaluations

First author, year	Selection	Comparability	Outcome	Total
Lee, 2010	3	0	2	5
Sundermann, 2011	4	1	1	6
Afilalo, 2012	3	1	2	6
Green, 2012	3	1	3	7
Stortecky, 2012	3	1	2	6
Schoenenberger, 2013	3	1	1	5

TABLE 2. Characteristics of included studies

First author, year	Population	n*	Frailty measurement	Outcomes measured	Association
Lee, 2010	Patients undergoing cardiac surgery	3826	Katz Index of Independence in Activities of Daily Living, independence in ambulation, and previous diagnosis of dementia	In-hospital mortality, midterm all-cause mortality, discharge to an institution, and secondary in-hospital outcomes	Frailty was linked to increased unadjusted in-hospital outcomes, increased in-hospital mortality, increased institutional discharge, and reduced midterm survival
Sundermann, 2011	Patients \geq 74 y undergoing cardiac surgery	400	Simplified CAF	1-y all-cause mortality, and MACCE	Frailty showed a good predictive ability concerning 1-y mortality
Afilalo, 2012	Patients \geq 70 y undergoing CABG and/or valve surgery	152	4 scales used: 5-item CHS 7-item expanded CHS 4-item MSSA Gait speed	Postoperative mortality or major morbidity	Only frailty measured through gait speed showed a statistically significant association with an increased mortality or major morbidity
Green, 2012	Patients \geq 60 y with advanced aortic disease undergoing TAVR	159	Modified Fried Frailty Criteria	All-cause mortality, and procedural outcomes	Frailty was independently associated with reduced long-term survival after TAVR
Stortecky, 2012	Patients \geq 70 y undergoing TAVI	100	Modified Multidimensional Geriatric Assessment	All-cause mortality, and MACCE	Strong evidence for an association between the frailty index with all-cause mortality and MACCE at 1 y post-TAVI
Schoenenberger, 2013	Patients \geq 70 y undergoing TAVI	119	Modified Geriatric Baseline Examination	Functional decline, and functional decline or death	Frailty index was strongly associated with functional decline as well as mortality

CAF, Comprehensive Assessment of Frailty; MACCE, major adverse cardiac and cerebrovascular events; CABG, coronary artery bypass graft; CHS, Cardiovascular Health Study Frailty Scale; MSSA, MacArthur Study of Successful Aging; TAVR, transcatheter aortic valve repair; TAVI, transcatheter aortic valve implantation. *Study sample size.

for patients. However transcatheter aortic valve implantation is used to treat severe aortic stenosis and is reserved for older patients who are deemed inoperable.¹⁵ In the studies investigating TAVR and frailty, patients were older and had increased EuroSCOREs, which may account for the increase in the hazard ratios and ORs.^{15,16} Patients who are undergoing TAVR are typically selected with the notion that they would not fair well with a conventional surgical aortic valve replacement.³ This could lead to a discrepancy when trying to apply the studies findings to those in a lower risk demographic.³

Risk of Bias

The 6 studies had a similar risk of bias. All the studies have a relatively low risk of bias in the selection domains, but had a higher risk of bias in comparability. The risk of bias in outcome varied between studies.

DISCUSSION

In our systematic review, multiple studies identified a relationship between frailty and adverse postoperative outcomes following cardiac surgery. Although several assessments (ie, definitions) of frailty were used (Table 3),

these studies universally demonstrated that patients classified as being frail had a higher likelihood of experiencing mortality, morbidity, functional decline, and MACCE.

To our knowledge, our systematic review is the first to evaluate a range of frailty assessments and their relationship to adverse postoperative outcomes following cardiac surgery. A relevant systematic review was published in 2009 and examined the relationship between frailty and cardiovascular disease.⁵ Although this review was different from ours, both reviews shared similarities in that both used a comprehensive and clear assessment of frailty criteria. Together our results support our conclusion that frailty has an influence on mortality in operative or nonoperative patients with cardiovascular disease.⁵

Our review highlights some important similarities between the frailty assessments. Five studies incorporated a physical function assessment as part of the determination of frailty, including handgrip strength, Timed Up and Go test, gait speed, and climbing up stairs. Poor results in these physical function tests, in particular gait speed and handgrip strength, can be indicative of sarcopenia,¹⁸ which is defined as muscle loss independent of inflammation or disease.^{19,20} Previous studies have already linked

TABLE 3. Frailty criteria

First author, year	Frailty measurement	Measurement method	Criteria for frailty
Lee, 2010	Katz Index of Independence in Activities of Daily Living, independence in ambulation, and previous diagnosis of dementia	<ul style="list-style-type: none"> • Dependence in feeding, bathing, dressing, transferring, and toileting • Urinary incontinence • Walking aid or assist required • Previous diagnosis of dementia 	Defined as frail if any of the frailty elements were present
Sundermann, 2011	Simplified CAF	<ul style="list-style-type: none"> • Prolonged time for a patient to get up and down from a chair 3 times • Self-reported weakness • Patient is asked to climb as many stairs as they are able • Two physicians (1 being the cardiac surgeon) conduct a Clinical Frailty Scale as outlined by the Canadian Study of Health and Aging • High serum creatinine level 	Results from the CAF scores are tabulated into a scale from 1 to 35 points as outlined by the supplementary CAF Test Sheet. Scores between 1 and 10 are deemed not frail, between 11 and 25 are deemed moderately frail, and between 26 and 36 are deemed severely frail
Afilalo, 2012	4 scales used: 5-item CHS 7-item expanded CHS 4-item MSSA Gait speed	<ul style="list-style-type: none"> • 5-item CHS used gait speed, handgrip strength, inactivity, exhaustion, and weight loss • 7-item CHS used the above as well as cognitive impairment and depressed mood • 4-item MSSA used gait speed, handgrip strength, inactivity, and cognitive impairment • prolonged time for gait speed test (≥ 6 sec to walk 5 m) 	Defined as frail if any of the 4 scales deemed patient as frail
Green, 2012	Modified Fried Frailty Criteria	<ul style="list-style-type: none"> • Slow 15-m gait speed • Weak dominant handgrip strength • Assistance required in any of Katz Index of Independence in Activities of Daily Living criteria • Serum albumin as a measurement of malnutrition 	Defined frailty as a score > 5 on a scale from 0-12 where a higher score equated to more frail For gait speed, grip strength, and serum albumin, based on which quartile a patient was in, a value of 0-3 was given for each quartile in descending order. For activities of daily living, 0 points were given for independent and 3 for dependent
Stortecky, 2012	Modified Multidimensional Geriatric Assessment	<ul style="list-style-type: none"> • MMSE showing cognitive impairment • MNA shows malnutrition • TUG showing limitation of mobility • BADL and instrumental activities of daily living showed an activity with limitation • Preclinical mobility disability defined as decreased frequency of walking 200 m and/or climbing stairs in preceding 6 mo 	Defined frailty as ≥ 3 points, 2 points if MMSE < 21 , 1 point if MMSE ≥ 21 and < 27 , MNA < 12 , TUG ≥ 20 sec, BADL with at least 1 limited activity, instrumental activities of daily living with at least 1 limited activity, preclinical mobility disability
Schoenenberger, 2013	Modified Geriatric Baseline Examination	<ul style="list-style-type: none"> • MMSE showing cognitive impairment • MNA shows malnutrition • TUG showing limitation of mobility • BADL and instrumental activities of daily living showed an activity with limitation • Preclinical mobility disability defined as decreased frequency of walking 200 m and/or climbing stairs in preceding 6 mo 	Defined frailty as ≥ 3 points, 2 points if MMSE < 21 , 1 point if MMSE ≥ 21 , and < 27 , MNA < 12 , TUG ≥ 20 sec, BADL with at least 1 limited activity, instrumental activities of daily living with at least 1 limited activity, preclinical mobility disability

CAF, Comprehensive Assessment of Frailty; CHS, Cardiovascular Health Study; MSSA, MacArthur Study of Successful Aging; MMSE, Mini Mental State Exam; MNA, Mini Nutritional Assessment; TUG, Timed Up and Go test; BADL, basic activities of daily living.

sarcopenia to the frailty syndrome.^{18,19,21} We speculate that physical function tests and sarcopenia measurements, which seem to be significant in frailty assessments, may have a potential role in risk assessments for

cardiac surgery and should be an area of further research. Significant measurements could potentially be incorporated into existing operative risk assessments, such as the EuroSCORE and STS risk score, allowing better

TABLE 4. Associations reported within included studies

First author, year	Association	Odds ratio (OR) or hazard ratio (HR) and 95% confidence interval (CI)
Lee, 2010	After cardiac surgery, frailty is associated with in-hospital mortality	OR, 1.8; 95% CI, 1.1-3.0
	After cardiac surgery, frailty is associated with prolonged institutional care	OR, 6.3; 95% CI, 4.2-9.4
	After cardiac surgery, frailty is associated with midterm mortality	HR, 1.5; 95% CI, 1.1-2.2
Sundermann, 2011	Frailty is associated with 1-y mortality after cardiac surgery	OR, 1.097; 95% CI, 1.038-1.160
Afilalo, 2012	Frailty as measured through gait speed is associated with mortality or major morbidity after coronary artery bypass graft and/or valve surgery	OR, 2.63; 95% CI, 1.17-5.90
Green, 2012	Frailty is associated with increased 1-y mortality after transcatheter aortic valve repair	HR, 3.16; 95% CI, 1.33-7.51
Stortecky, 2012	Frailty is associated with increased all-cause mortality 1-y after transcatheter aortic valve implantation	OR, 3.68; 95% CI, 1.21-11.19
	Frailty is associated with increased major adverse cardiac and cerebrovascular events 1 y after transcatheter aortic valve implantation	OR, 4.89; 95% CI, 1.64-14.60
Schoenenberger, 2013	After transcatheter aortic valve implantation, frailty is associated with functional decline	OR, 3.31; 95% CI, 1.21-9.03
	After transcatheter aortic valve implantation, frailty is associated functional decline or death	OR, 4.46; 95% CI, 1.85-10.75

preoperative risk stratification of patients. In addition, protocols need to adopt scoring systems for evaluating frailty that do not exclude patients who cannot complete the performance measures. In other settings, nonperformance of performance measures, as well as inability or unwillingness to undertake the test, is associated with worse outcomes.²²

There is clinical and research relevance to the findings of our systematic review. Health care systems will have to plan for the large increase in aging among the world's population. Evidence to support this includes an estimate that by the year 2050 the population of those aged 65 years will grow to 2 billion.¹⁰ It is important to note that heart failure is the leading cause of hospitalization in those aged ≥ 65 years.²³ In addition, frailty has been found to be quite prevalent among community-dwelling adults with heart failure and could play a role in heart failure development and management.²³ Interestingly, obese patients with heart failure fair better than leaner patients with heart failure, including those who are frail and cachectic, despite obesity being a major risk factor for coronary heart disease and hypertension, 2 of the most compelling risk factors for heart failure.²⁴ This obesity paradox, as it is described, likely has many potential mechanisms. Relating to frailty, 1 explanation for this paradox is that patients who experience weight loss are at a very high risk for developing frailty, whereas obese patients have a lesser but still significant risk.²⁵ Obese patients have more metabolic reserve, and combined with the lower rate of frailty, can likely cope better with the catabolic effects of heart failure.²⁴

The syndrome of frailty is important from a cardiac rehabilitation perspective because cardiac rehabilitation programs can help to increase normal functional abilities, as well as improve psychosocial well-being and exercise capacity.²⁶ These rehabilitation programs seem to address

some components of frailty. In addition, a study looking at cardiac patients undergoing cardiac rehabilitation and exercise training found that participants of this program had a decrease in mortality and that increased attendance led to increased positive outcomes.^{26,27} Elderly patients participating in cardiac rehabilitation programs can improve their level of independence as well as decrease their mortality,²⁶ which leads to speculation that frailty is a reversible process.

Although our study establishes the importance of frailty in operative risk assessment, it also reveals the need for further studies to establish which criteria are best in deeming patients frail and are most predictive of clinical outcomes. We found significant heterogeneity in the criteria for frailty and in the ascertainment of postoperative outcomes. As such, it was not possible to meta-analyze our findings, nor compare and determine which frailty assessment is superior in evaluating elderly surgical patients. Two of the studies used the same frailty criteria^{15,16} but examined different postoperative outcomes (mortality vs functional decline). Nonetheless, both still showed that frailty was predictive of adverse outcomes. The Canadian study² compared different frailty assessments within its own study and determined gait speed to be most significant. We believe that further large, prospective studies must be done to directly compare and validate the performance of different frailty measures in the prediction of relevant clinical outcomes after cardiac surgery.²⁸ Once an optimum frailty tool is validated, frailty and its components may help guide patient selection for surgery, as well as informing studies of pre- and postoperative interventions aimed at improving outcomes in patients at highest risk of adverse sequelae. In the absence of a widely accepted tool, the Clinical Frailty Scale (CFS) is a potentially practical instrument that could be used at bedsides. A potential practical solution

could be the implementation of the CFS. The CFS, a tool born from a mathematical accumulation of deficit model of frailty, can function as a standardized eyeball test for determining frailty status based on a categorized, subjective clinical judgment of the evaluator and may be a reasonable first choice in making assessments.²⁸ Frailty status according to the CFS (score ≥ 4) could be an indication to a clinician that treatment should be applied.

Our study has several strengths. First, we developed a structured protocol incorporating detailed background knowledge, as well as study-specific inclusion criteria and quality assessment based on our research question. This allowed us to be stringent in reviewing and evaluating the results of our search. Second, our search strategy incorporated very broad medical subject heading terms applied to multiple electronic databases to ensure the most complete capture possible of the published literature on frailty, postoperative outcomes, and cardiac surgery. Third, we strategically cross-referenced the bibliographies of included articles in an effort to further maximize our search strategy.

Our study also has some limitations. First, our search strategy included only English language studies and it is possible that relevant non-English publications were missed. Second, we included only published full-text journal articles. This could introduce an element of publication bias to our review, because some studies may only have been published in abstract form. Third, when choosing articles for our review, we did not include articles evaluating individual elements of frailty, but only those that included a comprehensive assessment of frailty. With significant heterogeneity in the data collection methods of the primary studies used, it is difficult to ascertain which frailty measurements are superior.

CONCLUSIONS

Our systematic review demonstrated that a negative relationship exists between frailty and major adverse postoperative outcome following cardiac surgery, such that patients who are deemed frail, regardless of definition used, have a higher likelihood of experiencing mortality, morbidity, functional decline, and MACCE. Further study is needed in forming a standardized assessment of frailty and in determining which components of frailty correlate best with negative postoperative outcomes.

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References

1. Afilalo J, Eisenberg MJ, Morin JF, Bergman H, Monette J, Noiseux N, et al. Gait speed as an incremental predictor of mortality and major morbidity in

elderly patients undergoing cardiac surgery. *J Am Coll Cardiol*. 2010;56:1668-76.

2. Afilalo J, Mottillo S, Eisenberg MJ, Alexander KP, Noiseux N, Perrault LP, et al. Addition of frailty and disability to cardiac surgery risk scores identifies elderly patients at high risk of mortality or major morbidity. *Circ Cardiovasc Qual Outcomes*. 2012;5:222-8.
3. Green P, Woglom AE, Genereux P, Daneault B, Paradis JM, Schnell S, et al. The impact of frailty status on survival after transcatheter aortic valve replacement in older adults with severe aortic stenosis: a single-center experience. *J Am Coll Cardiol Cardiovasc Interv*. 2012;5:974-81.
4. Nilsson J, Algotsson L, Högglund P, Luhrs C, Brandt J. Comparison of 19 preoperative risk stratification models in open-heart surgery. *Eur Heart J*. 2006;27:867-74.
5. Barili F, Pacini D, Capo A, Rasovic O, Grossi C, Alamanni F, et al. Does EuroSCORE II perform better than its original versions? A multicentre validation study. *Eur Heart J*. 2013;34:22-9.
6. Puskas JD, Kilgo PD, Thourani VH, Lattouf OM, Chen E, Vega JD, et al. The society of thoracic surgeons 30-day predicted risk of mortality score also predicts long-term survival. *Ann Thorac Surg*. 2012;93:26-33; discussion 33-5.
7. Wendt D, Osswald BR, Kayser K, Thielmann M, Tossios P, Massoudy P, et al. Society of Thoracic Surgeons score is superior to the EuroSCORE determining mortality in high risk patients undergoing isolated aortic valve replacement. *Ann Thorac Surg*. 2009;88:468-74; discussion 474-5.
8. Sundermann S, Dademasch A, Rastan A, Praetorius J, Rodriguez H, Walther T, et al. One-year follow-up of patients undergoing elective cardiac surgery assessed with the comprehensive assessment of frailty test and its simplified form. *Interact Cardiovasc Thorac Surg*. 2011;13:119-23.
9. Fulop T, Larbi A, Witkowski JM, McElhaney J, Loeb M, Mitnitski A, et al. Aging, frailty and age-related diseases. *Biogerontology*. 2010;11:547-63.
10. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet*. 2013;381:752-62.
11. Afilalo J, Karunanathan S, Eisenberg MJ, Alexander KP, Bergman H. Role of frailty in patients with cardiovascular disease. *Am J Cardiol*. 2009;103:1616-21.
12. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: Evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56:M146-56.
13. Ottawa Hospital Research Institute http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed February 24, 2014.
14. Sundermann S, Dademasch A, Praetorius J, Kempfert J, Dewey T, Falk V, et al. Comprehensive assessment of frailty for elderly high-risk patients undergoing cardiac surgery. *Eur J Cardiothorac Surg*. 2011;39:33-7.
15. Stortecky S, Schoenenberger AW, Moser A, Kalesan B, Juni P, Carrel T, et al. Evaluation of multidimensional geriatric assessment as a predictor of mortality and cardiovascular events after transcatheter aortic valve implantation. *J Am Coll Cardiol Cardiovasc Interv*. 2012;5:489-96.
16. Schoenenberger AW, Stortecky S, Neumann S, Moser A, Juni P, Carrel T, et al. Predictors of functional decline in elderly patients undergoing transcatheter aortic valve implantation (TAVI). *Eur Heart J*. 2013;34:684-92.
17. Lee DH, Buth KJ, Martin BJ, Yip AM, Hirsch GM. Frail patients are at increased risk for mortality and prolonged institutional care after cardiac surgery. *Circulation*. 2010;121:973-8.
18. Viana JU, Silva SL, Torres JL, Dias JM, Pereira LS, Dias RC. Influence of sarcopenia and functionality indicators on the frailty profile of community-dwelling elderly subjects: a cross-sectional study. *Braz J Phys Ther*. 2013;17:373-81.
19. Roubenoff R. Sarcopenia and its implications for the elderly. *Eur J Clin Nutr*. 2000;54(Suppl 3):S40-7.
20. Carter CS, Marzetti E, Leeuwenburgh C, Manini T, Foster TC, Groban L, et al. Usefulness of preclinical models for assessing the efficacy of late-life interventions for sarcopenia. *J Gerontol A Biol Sci Med Sci*. 2012;67:17-27.
21. Marzetti E, Leeuwenburgh C. Skeletal muscle apoptosis, sarcopenia and frailty at old age. *Exp Gerontol*. 2006;41:1234-8.
22. Rockwood K, Jones D, Wang Y, Carver D, Mitnitski A. Failure to complete performance-based measures is associated with poor health status and an increased risk of death. *Age Ageing*. 2007;36:225-8.
23. McNallan SM, Singh M, Chamberlain AM, Kane RL, Dunlay SM, Redfield MM, et al. Frailty and healthcare utilization among patients with heart failure in the community. *J Am Coll Cardiol Heart Fail*. 2013;1:135-41.

24. Lavie CJ, De Schutter A, Alpert MA, Mehra MR, Milani RV, Ventura HO. Obesity paradox, cachexia, frailty, and heart failure. *Heart Fail Clin*. 2014;10:319-26.
25. Strandberg TE, Stenholm S, Strandberg AY, Salomaa VV, Pitkala KH, Tilvis RS. The “obesity paradox,” frailty, disability, and mortality in older men: a prospective, longitudinal cohort study. *Am J Epidemiol*. 2013;178:1452-60.
26. Menezes AR, Lavie CJ, Milani RV, Forman DE, King M, Williams MA. Cardiac rehabilitation in the United States. *Prog Cardiovasc Dis*. 2014;56:522-9.
27. Suaya JA, Stason WB, Ades PA, Normand SL, Shepard DS. Cardiac rehabilitation and survival in older coronary patients. *J Am Coll Cardiol*. 2009;54:25-33.
28. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. *Can Med Assoc J*. 2005;173:489-95.

EDITORIAL COMMENTARY

Frailty: It's hard to define, but you know it when you see it

Keith B. Allen, MD

See related article on pages 3110-7.

In their article in this issue of the *Journal* entitled, “The impact of frailty on outcomes after cardiac surgery: A systematic review,” Sepehri and colleagues¹ analyze the influence that “frailty” has on predicting poor outcomes after cardiac surgery. In their review of 6 contemporary, prospective studies published during the last 4 years and encompassing more than 4500 patients, Sepehri and colleagues¹ conclude, not surprisingly, that patients deemed frail by an objective assessment tool have a higher likelihood of mortality, morbidity, functional decline, and major adverse cardiac and cerebrovascular events after cardiac surgery, regardless of how frailty is defined. Sepehri and colleagues¹ are to be complimented for highlighting the adverse impact that frailty has on cardiac surgical outcomes; however, a key question is whether the concept of frailty is based on a matrix of several standardized tests or there is one test alone that would be most predictive. To paraphrase former Supreme Court Justice Potter Stewart, frailty is hard to define but I know it when I see it.

Current risk models either overestimate (euroSCORE) or underestimate (Society of Thoracic Surgeons) perioperative risk; discrepancies between predicted and observed outcomes may be confounded by a disproportionate weight placed on chronologic age alone without taking into account the biology of the aged. Advanced age is not necessarily synonymous with vulnerability to adverse health

outcomes; furthermore, the potential to use age alone inappropriately to ration increasingly expensive and technologically advanced health care, such as transcatheter aortic valve replacement, has made the concept of frailty very timely. In surgical parlance, frailty is an ambiguous but well understood phrase that encompasses a patient's inability to withstand and successfully recover from surgery. Surgeons, whether consciously or unconsciously, have always evaluated frailty. Watching the patient get out of bed and walk across the room and testing the firmness of the handshake are all part of a seasoned surgeon's “eyeball” test for frailty. Of the 6 studies in this systematic review, 5 incorporated a physical function assessment as part of the determination of frailty, including hand grip strength, timed get up and go test, and gait speed. Although Sepehri and colleagues¹ were unable to determine which frailty test is best, it's clear from their review that a more “standardized eyeball” test, such as the Clinical Frailty Scale, may better predict postoperative outcomes.

Although standardized frailty scores may be predictive of poor surgical outcomes, the use of them to justify less-invasive procedures with the hope of achieving better outcomes may be misguided. It is clear that frailty predicts worse outcomes with either surgical or nonsurgical procedures (frail patients have worse outcomes than nonfrail patients even without subjecting them to a procedure). The critical question that needs to be asked is this: Does frailty identify a group of patients who would derive preferential benefit from one or another form of treatment? Within the review of Sepehri and colleagues,¹ patients labeled as frail had a higher hazard ratio for death when undergoing less-invasive procedures, such as transcatheter aortic valve replacement, than when undergoing more-invasive open procedures. Given the same frailty definition within each study, one would expect to be able to perform less-invasive procedures on more frail patients and have better outcomes—not worse. This paradox might be

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