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Frailty, Aging, and Cardiovascular Surgery

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Abstract

Older adults make up an ever-increasing number of patients presenting for surgery, and a significant percentage of these patients will be frail. Frailty is a geriatric syndrome that has been conceptualized as decreased reserve when confronted with stressors, although the precise definition of frailty has not been easy to standardize. The two most popular approaches to define frailty are the phenotypic approach and the deficit accumulation approach, although at least 20 tools have been developed, which has made comparison across studies difficult. In epidemiologic studies, baseline frailty has been associated with poor outcomes in both community cohorts and hospitalized patients. Specifically in cardiac surgery (including transcatheter valve implantation procedures), frailty has been strongly associated with postoperative mortality and morbidity, and thus frailty likely improves the identification of high-risk patients beyond known risk scores. For perioperative physicians then, the question arises of how to incorporate this information into perioperative care. To date, two thrusts of research and clinical practice have emerged: (1) preoperative identification of high risk-patients to guide both patient expectations and surgical decision-making, and (2) perioperative optimization strategies for frail patients. However, in spite of the strong association of frailty and poor outcomes, there is a lack of well-designed trials which have examined perioperative interventions with a specific focus on frail patients undergoing cardiac surgery. Thus, in many cases, principles of geriatric care may need to be applied. Further research is needed to standardize and implement feasible definitions of frailty and examine perioperative interventions for frail patients undergoing cardiac surgery.

Introduction

Older adults make up an ever-increasing number of patients presenting for surgery and a significant percentage of these patients will be frail, with decreased reserve when confronted with perioperative stressors. Frailty has become an important topic in cardiac surgery, as the

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average age and complexity of patients has increased, and treatment options for cardiac disease have diversified—from medical management to minimally invasive procedures to cardiac surgery. In an era that emphasizes value in medicine, identifying the most vulnerable patients, deciding an appropriate course of therapy, and targeting valuable resources are important priorities. The concept of frailty may play a key role in these processes. In this review, we summarize the current understanding of frailty in the perioperative period, as well as how this information might be used to improve outcomes for frail older adults, with a particular focus on cardiac surgery.

Understanding the Frailty Phenotype

Conceptualization of Frailty

The term frail is commonly used in medicine to describe the most vulnerable and weakest patients. In geriatric parlance, “frailty” is more specifically recognized as a geriatric syndrome characterized by “an excess vulnerability to stressors, with reduced ability to maintain or regain homeostasis after a destabilizing event.”¹ In a wide variety of community dwelling and hospitalized patients, frailty has been associated with an increased risk of disability, morbidity, and mortality, as further described in this review. Although commonly understood in concept, frailty may not be readily identified or managed by many clinicians, since it is not a “chief complaint” that can be reduced to a simple etiology in a single organ system.

Assessment of Frailty

Although perhaps easy to conceptualize, the precise definition of frailty has not been easy to standardize, with up to 20 tools having been developed to measure frailty.² Thus, in evaluating current literature, it is important to consider the exact definition of frailty that is used.

Two broad approaches to define frailty have emerged—the phenotypic definition of frailty and the deficit accumulation definition of frailty. First, the phenotypic definition was derived by Fried et al. using data on 5317 participants in the Cardiovascular Health Study.³ Based on prior work supporting the importance of sarcopenia, diminished muscle strength, and limited exertion, the authors defined frailty using the following criteria as described in Table 1: unintentional weight loss, exhaustion, weakness, slow walking speed, and low physical activity. A score of 3-5 was considered frail, while a score of 1-2 was considered pre-frail. The overall prevalence of frailty in this large cohort was 6.9%, and the frailty phenotype was independently associated over 3 years with incident falls, worsening mobility or disability, hospitalization, and death. There was a dose-response observed, with intermediate frailty being associated with a step-wise increase in risk of poor outcomes, as well as an increased risk of transitioning to frailty. These phenotypic criteria were soon validated in the Women's Health and Aging Study, in which the prevalence and outcomes associated with frailty were similar, and latent class analysis demonstrated strong internal validity of the criteria.⁴ Since the publication of these studies, the so called “Fried criteria” of frailty have been extensively used in other populations.

In contrast, the frailty index is based on the underlying theory that aging results from lifelong accumulation of molecular damage which leads to impaired organ function. Beyond a certain threshold of age-related aggregate decline, frailty may result.⁵ Simplistically, this can be described as, “the more individuals have wrong with them, the more likely they are frail.”⁶ In a 2001 study from Dr. Ken Rockwood, the calculation of a frailty index was proposed, using data from a Canadian aging study investigating dementia in older adults. The frailty index was derived by adding the presence of 92 medical variables as a proportion of the total.⁷ Examples of these variables included medical symptoms, lab values, and disabilities. Further work showed that the number of variables could be decreased, and that the particular variables were not critical in and of themselves, as long as they were biologically sensitive, accumulated with age, and did not accumulate in totality too early.⁸ This conception of the frailty index has the attractive feature of being a continuous variable and easily adaptable to diverse settings. Additionally, the statistical distribution of this index is consistent with systems that have built in redundancy, as is evident in physiologic function.⁵ Although the phenotypic and deficit accumulation approaches to define frailty are different, it is noteworthy that each approach has shown overlap in identifying frail individuals with convergent predictive validity.⁹

In addition to these widely-used approaches, several investigators have reduced the characterization of frailty to single item measures, most notably gait speed or handgrip strength,^{10,11} or investigator-derived composite measures. These approaches have the advantage of simplicity, and in the perioperative population, have been correlated with increased risk after surgery. However, these approaches are more disparate, have been used less often individually, and have not been as widely validated as the phenotypic and frailty index approaches. Nevertheless, the existence of these alternate approaches highlight an important challenge in frailty research— there is no “gold standard” definition for frailty.¹²

Related Concept: Disability

While often used interchangeably with frailty, disability is a distinct concept. Disability can be broadly defined as difficulty or dependency in carrying out activities of daily living.¹³ Disability is often an unfortunate outcome in frail patients, or may even co-exist with frailty.¹⁴ Given the impact of frank disability on the lives of older adults, frailty assumes added importance because it may represent a pre-disability state that is amenable to intervention, or it may identify surgical patients with a high likelihood of progressing to disability. On the other hand, resilience has been conceptualized as opposite of frailty. In other words, resilience is the positive capacity to deal with stress and other detrimental challenges.¹⁵ It is likely that mechanisms that lead to frailty and promote resilience may be related.

Biologic Basis of Frailty

Although aging is not synonymous with frailty, common mechanisms may underlie both processes. Normal aging can be thought of as the deterioration of function at the cellular, tissue, and organ level,¹⁶ which leads to impaired homeostasis and decreased ability to adapt to stressors. The frailty phenotype specifically centers around dysfunction in energy

metabolism and muscle activity, while the processes of aging may be more widespread.¹⁶ Biologic processes which underlie both frailty and aging are further described below.

At the cellular and molecular level, the coordinated processes of apoptosis, senescence, autophagy, and mitochondrial dysfunction have been hypothesized to play key roles in aging biology. For instance, senescent cell populations that increase with age may no longer function normally, leading to organ dysfunction.¹⁷ Similarly, mitochondrial dysfunction may result in increased levels of free radicals and lower energy production.¹⁸ In animal models of frailty using IL-10 deficient mice, frail mice have abnormal mitochondria energy production,¹⁹ differential production of apoptosis and function genes,²⁰ and alterations in autophagy.²¹ The overall balance of these age-related cellular process likely influences the development of the frailty phenotype through changes in organ and system function.¹⁶

At an organ and system-level, changes in energy metabolism—including a cycle of decline in energy, skeletal muscle, and nutrition—are thought to be critical to the development of frailty.³ Dysfunction in energy metabolism is most evident by the sarcopenia that is common in frail patients. In a longitudinal study of aging women, the related symptom of weakness was the most common first manifestation among participants with frailty.²² Subsequently, weight loss and exhaustion were key components of progression to frailty.²² Energy-related hormones such as growth hormone, androgens, and insulin-like growth factor-2 decline with age and have been associated with frailty.^{23,24}

There are also multiple studies suggesting that chronic diseases play a significant role in the development of frailty.²⁵ In addition to direct organ-specific effects, chronic disease states may activate widespread physiologic systems, including the innate immune system, the sympathetic nervous system, the hypothalamic-pituitary-axis, and the inflammatory response.²⁶ Indeed, several cross-sectional studies have found higher levels of the inflammatory cytokine IL-6²⁴ and C-reactive protein²⁷ in frail compared with non-frail patients. The altered inflammatory state has a pleiotropic effect and likely contributes to further changes seen in frailty, including in fatigability,²⁸ depression,²⁹ and cellular and immune responses.¹⁶

Beyond changes in cells, organs, and systems, the development of frailty represents a complex non-linear process, in which the combined manifestation of individual changes is thought to be greater than the sum of its parts. Using data from the Women's health and Aging study, Fried et al. found that the likelihood of frailty increased nonlinearly in relation to the number of abnormal physiologic systems, and that the aggregate number of systems was more predictive than individual systems.³⁰ With a decline in normal inter-connectedness and impaired redundancy of system components, frailty may represent a threshold of decline that is triggered by (and also triggers) a dysregulation in multiple physiologic systems.¹

Epidemiology and Outcomes Associated with Frailty

Epidemiology

The prevalence of frailty has generally been estimated to be <10% in community-dwelling populations in longitudinal cohort studies.³ However, among important subgroups of

patients, the prevalence is likely higher. Among patients with cardiovascular disease, studies have estimated the prevalence of frailty to range between 10-60%.³¹ Among patients specifically presenting for cardiac surgery, the presence of frailty has similarly been estimated to be between 20-50%,^{32,33} which is higher than prevalence estimates in non-cardiac surgery (10%, in one well-done study).³⁴

There has been particular interest in characterizing the epidemiology of frailty in the perioperative period for several reasons. First, transitions in frailty may occur in the perioperative period, and this has important implications for the decision to proceed to surgery. In the community, transitions in frailty are common and are generally deteriorations.³⁵ However, at least in the kidney transplant population, transitions in frailty have been shown to be bidirectional, with many patients initially declining in frailty status within the first month after surgery, but then improving in frailty status after the initial perioperative period.³⁶ Further research is needed to characterize these transitions after cardiac surgery. Second, the incidence of new disability after surgery is high, and disability significantly affects patient functional status and quality of life. Since frailty is often a precursor to disability, frailty may identify patients at high risk for the important patient-centered outcome of disability. Notably, while the prevalence of disability is generally low prior to cardiac surgery,³⁷ the prevalence of frailty may be as high as 50%, perhaps implying that frailty is not considered a relative contraindication for surgery, while frank disability is considered an important risk factor to guide a patient away from surgery.³¹ Finally, given the elective nature of many surgeries, there is the potential for interventions to improve outcomes that are seen in frail patients.

Outcomes

As would be expected, frailty has generally been associated with poor outcomes. In several studies of community-dwelling participants, frailty has consistently been associated with falls, hospitalizations, and mortality.^{3,4} The association of frailty and poor outcomes has been replicated in hospitalized patients. In a recent study of patients in the intensive care unit,³⁸ Clinical Frailty Scale score was associated with higher in-hospital and 1-year mortality, new functional dependence, more hospital readmissions, and lower quality of life. In non-cardiac elective surgery, Makary et al. prospectively enrolled close to 600 patients >65 y/o at a university hospital and found a 10% prevalence of frailty and 32% prevalence of intermediate frailty, using the Fried criteria.³⁴ Frailty was associated with increased complications, longer length of stay, and greater risk of not being discharged home. Importantly, the addition of frailty improved the predictive power of several well-validated risk models, including the ASA risk score. A recent population based Canadian study examined longer-term mortality in non-cardiac surgery patients >65 y/o.³⁹ In this study, frailty was defined using administrative data, with results showing an increased risk of 1-year mortality in frail (13.6%) compared with non-frail (4.8%) patients. There was a significant variation in increased risk of death for frail patients by surgery type (highest in joint arthroplasty) and by age category (the mortality impact of frailty was greater in the “younger” group of older adults compared to the “older” group).

In cardiac surgery, the preoperative risk of operative mortality is commonly described using validated risk models, including the Society for Thoracic Surgeon (STS) risk score and several iterations of the EuroSCORE. Significant over- and underestimation of operative risk in each of these models⁴⁰ has led some to argue that these risk models do not account for the biologic status of patients, and that frailty may provide novel information important to risk prediction.⁴¹ Indeed, several studies have demonstrated a strong independent association of frailty and poor outcomes after cardiac surgery, although the definitions of frailty have been varied, as described in Table 2. In 3826 cardiac surgery patients in Canada, frailty was an independent predictor of in-hospital and midterm mortality, and institutional discharge.⁴² Similarly, in a smaller population of older adults undergoing cardiac surgery at 4 tertiary care centers, a single-item surrogate of frailty (slow gait speed) was independently associated with a composite outcome of in-hospital morbidity and mortality (OR 3.05; 95% CI 1.23-7.54).¹⁰ Further, the addition of gait speed to the STS risk model in this study resulted in improved model performance. This same group of investigators later examined the predictive ability of four different frailty scales, along with three disability scales and five cardiac risk scores. In this study, slow gait speed was the most predictive frailty scale for in-hospital mortality or morbidity and improved model discrimination of established risk scores.³² Finally, in a German cohort of patients assessed using a comprehensive assessment of frailty score, frailty was associated with one-year mortality.³³ Although the definition of frailty across studies has varied, the general results demonstrating an increased risk for frail surgical patients have been consistent. Recently, it has also been shown that frail patients have an increased risk of delirium after cardiac surgery.^{43,44}

A similar relationship between frailty and postoperative outcomes is evident among patients undergoing transcatheter aortic valve implantation (TAVI), as shown in Table 2. In a cohort study of 159 patients enrolled at Columbia University, the baseline prevalence of frailty (defined using gait speed, grip strength, albumin, and ADL) was close to 50% and was associated with an increased risk of 1-year mortality, but not peri-procedural complications or 30-day mortality.⁴⁵ Over 18% of patients could not walk 15 feet due to dyspnea, indicating the high degree of functional limitation in this cohort. Interestingly, gait speed by itself was not associated with survival in this study. A similarly-sized international study showed a 33% prevalence of frailty in TAVI patients with 4.2-fold increase in the hazard of major adverse cardiac events at 9-months.⁴⁶ Finally, a measure of frailty, as derived from assessment of cognition, mobility, nutrition, and ADL/IADL, was independently associated with both 1-year mortality⁴⁷ and functional decline⁴⁸ in a German population with a baseline frailty prevalence >50%. It is noteworthy that the prevalence of frailty in TAVI patients is generally higher than in cardiac surgery patients, although the definitions of frailty are quite varied, and in at least one study, frailty was defined using a cutoff of median values. Given the small number of patients in these studies, high prevalence of frailty, and conflicting results depending on the time frame of the outcome, the predictive value of frailty in TAVI patients remains to be better characterized and further studies are needed.

Utility of Frailty Assessment—"what can we do with this information"

Since the recognition and development of frailty as a syndrome, the number of studies describing the perioperative risk among frail patients has grown exponentially. For

perioperative physicians however, the question remains, “what can we do with this information?” and the number of studies that have demonstrated improvements in outcomes in frail patients is substantially smaller. To date, two thrusts of research and clinical practice have emerged: (1) preoperative identification of high risk-patients to guide both patient expectations and surgical decision-making, and (2) perioperative optimization strategies for frail patients. In the following sections, both of these areas will be discussed in more detail.

Utility of preoperative identification of frail patients

Patient Expectations and Preferences—Characterizing frailty status is an important first step to establish realistic expectations about postoperative outcomes and to elicit patient preferences. One prominent examples is anticipated discharge location, with frailty status strongly associated with failure to discharge home. A recent roundtable of VA surgeons emphasized the role of frailty in surgical management, and concluded that, “frailty measures...should provide the opportunity to discuss expectation and patient's wishes given a poor outcome during the postoperative period.”⁴⁹ Although frailty and old age are not synonymous, it is useful to step back and examine patient preferences in old age, and it is clear that maintaining cognitive and functional status are high priorities. In a landmark article examining preferences of older adults with limited life expectancy,⁵⁰ a vast majority of older adults reported that they would not choose treatment that would keep them alive, but with severe functional or cognitive impairments. (74% and 89% of participants respectively). Although these sentiments were derived from adults with limited life expectancy, it is important to consider functional status, disability, and cognitive impairment in guiding perioperative decisions for frail older adults.

Surgical Decision-Making—There are several areas in which frailty can guide surgical decision-making. First, frailty may impact goals of therapy. At a recent NIH-sponsored U13 conference convened to discuss frailty in the context of specialty care, a consensus emerged that the goals of surgical interventions for frail older adults are to improve quality of life, prevent worsening chronic disease, reduce the risk of catastrophic outcomes, and provide risk assessment to guide therapeutic decisions.⁵¹ Unfortunately, these goals are not always reflected in current quality metrics, which emphasize easily-measured outcomes such as 30-day mortality.⁵² There is a push to recognize and measure important patient-centered outcomes for older adults, with great implications for frail surgical patients.

Second, the incorporation of frailty measures generally improves current risk prediction models,^{32,34} and thus may change decision-making on treatment options. An example is how frailty status might be considered when deciding between interventions for aortic stenosis—Transcatheter Aortic Valve Implantation (TAVI) vs. surgical aortic valve replacement vs. medical management.⁵³ Although the high prevalence of frailty in these patients limits the ability of frailty to predict meaningful outcomes, frailty might help identify patients at the extremes—those patients who are *not frail* and would be surgical candidates, or conversely, those patients who are *too frail* for any intervention and might benefit from medical management.³¹ Incorporation of frailty measures may be most important in settings where resources are limited—such as allocation of transplants or expensive therapies. Similarly, improved risk prediction may identify patients with high risk

of postoperative complications, who might be appropriate for targeted strategies, including enhanced monitoring or mobility protocols. Finally, frail patients may benefit from team-based approaches to care, as advocated by a recent editorial in the New England Journal of Medicine.⁵⁴

Perioperative Optimization and Management

Frailty identifies patients who might benefit from targeted strategies to enhance perioperative care, and the following sections discuss strategies for preoperative, intraoperative, and postoperative management of frail older adults. In this regard, the success of bundled interventions, such as Enhanced Recovery After Surgery (ERAS) programs, may be a model to guide approaches for frail patients.⁵⁵ However, to date, no clinical trials have demonstrated that a bundle of targeted strategies for frail patients can improve outcomes.

Preoperative—The preoperative period is an ideal time for baseline assessment to guide both perioperative optimization and management. The American Geriatric Society and American College of Surgeons recently released guidelines on the optimal preoperative assessment for older adults, and stress the importance of assessing frailty, cognitive status, functional status, and nutrition, among others.⁵⁶ However, implementation of these guidelines may require additional resources, and so adoption has been varied.

A key question is whether the preoperative time can be used for “pre-habilitation”. There may be benefit to structured exercise programs in the preoperative period, although the risk/benefits need to be considered, and no studies have been conducted in frail patients specifically. In a randomized trial of low-risk patients undergoing CABG surgery in Canada, a 10-week program of twice weekly supervised exercise training was associated with a reduction in length of stay by one day and less time in the ICU after surgery.⁵⁷ Preoperative inspiratory muscle training (IMT) may also be beneficial prior to cardiac surgery, with a recent Cochrane review demonstrating that preoperative IMT +/- exercise reduced length of stay and the risk of pneumonia (RR 0.45; 95% CI 0.24-0.83) and atelectasis (0.52; 95% CI 0.32-0.87), but not mechanical ventilation >48 hours.⁵⁸ An ongoing randomized trial in cardiac surgery patients using structured exercise protocols will provide further insight into this question and help define questions of safety and “dose” of exercises.⁵⁹

Incorporating interdisciplinary geriatric teams and approaches is important. In community-dwelling frail older adults, use of the Comprehensive Geriatric Assessment (CGA) has shown long-term improvement in survival and functional status.⁶⁰ In the hospital setting, similar programs exist, and a recent Cochrane review supported the benefit of these programs.⁶¹ The evidence in surgical patients is more limited, but the conclusions of a smaller systematic review showed a positive impact on postoperative outcomes (medical complications and length of stay) in older patients undergoing elective surgery.⁶²

Approaches to enhance nutrition may be beneficial, as nicely summarized by a recent review for anesthesiologists.⁶³ The prevalence of some degree of malnutrition prior to general surgery has been estimated to be upwards of 40%,^{63,64} and frail patients may be at higher risk.⁶⁵ Oral carbohydrates prior to surgery may be beneficial to reduce postoperative catabolism,⁶⁶ and small reductions in length of stay have been observed with this strategy

after elective surgery.⁶⁷ Additionally, early resumption of oral feeding after surgery should be encouraged.

Intraoperative—There is no anesthetic approach in the literature that has been shown to modify the risk of surgery specifically for frail older adults. Thus, in the absence of evidence, it is reasonable to apply geriatric principles of anesthetic care to the management of frail older adults. Benzodiazepine usage (especially long-acting benzodiazepines) should be minimized. Other common anesthetic drugs that are on the Beers list of inappropriate medications for older adults include Benadryl, scopolamine, and promethazine. Optimizing depth of anesthesia has been proposed as an intraoperative strategy.⁶⁸ Four observational studies have demonstrated an association between increased depth of anesthesia and mortality,⁶⁹⁻⁷² although this result has not been consistent.⁷³ Several randomized trials have also demonstrated a reduction in delirium in patients randomized to reduced depth of anesthesia.⁷⁴⁻⁷⁶ However, these results need to be repeated, in particular in the cardiac surgery population. Lung protective ventilation has been shown to be effective in critically ill patients with acute lung injury, and recent evidence has shown benefit during the intraoperative period as well.⁷⁷ Given the high risk of postoperative pulmonary complications in frail older adults, it is reasonable to employ lung protective strategies in the operating room. Temperature management during cardiopulmonary bypass should be monitored closely, since excessively fast rates of rewarming have been associated with postoperative neurological complications⁷⁸ as well as the release of biomarkers of brain injury.⁷⁹

Postoperative—The literature on postoperative care specific to frail older adults is limited, and thus principles of care for older adults need to be extrapolated. Particular emphasis should be paid to evaluation of cognitive status, function and mobility, pain control, and nutritional status, in addition to general postoperative concerns.⁸⁰ Avoidance of complications is important, as frail patients have less reserve to deal with further stressors. There may be a role for geriatric specific teams in optimizing long-term outcomes, with one study in older trauma patients showing preserved activities of daily living at 1-year for patients who received a geriatric consult compared to usual care.⁸¹

Delirium prevention is an important goal in the postoperative period, and guidelines from the American Geriatric Society focus on perioperative management strategies.⁸² Although there is no magic bullet for delirium prevention, the best evidence is for multi-modal non-pharmacological methods, such as the Hospital Elderly Life Program.⁸³ Principles of this program include increased mobility, sleep-enhancement, orientation protocols, hearing and vision optimization, and avoidance of dehydration. Although this protocol has been effective in general surgery patients,⁸⁴ there are no studies examining implementation after cardiac surgery. Sedation practices continue to be investigated. There is some evidence to suggest that dexmedetomidine may reduce the risk of delirium,^{85,86} and that the use of benzodiazepines should be avoided.⁸⁷ Trials investigating pharmacologic methods for delirium prevention, including steroids⁸⁸ and anti-cholinergic agents,⁸⁹ have generally shown no benefit in cardiac surgery patients, while trials investigating the use of prophylactic anti-psychotic drugs have been mixed. Return to functional status is a key goal

of frail older adults, and this process begins in the hospital. Early mobilization and early physical therapy involvement as indicated should be emphasized.⁸⁷ Pain control should be optimized, since both excessive pain and excessive pain medications have been associated with postoperative delirium in older adults. While regional techniques have shown benefit in non-cardiac surgery, the role of regional techniques after cardiac surgery is generally more limited. Multi-modal analgesia should be considered, including Tylenol, with a goal of reducing opioid consumption. There is limited evidence supporting the use of other adjuncts, such as pregabalin.⁹⁰

Future Directions

There are several gaps in knowledge moving forward. First, a frailty assessment that is feasible in the preoperative setting and shows clear relationships to important postoperative outcomes would be valuable. Second, strategies are needed to determine how to manage frail patients in the preoperative, intraoperative, and postoperative areas to improve outcomes. Third, large national registries should incorporate important geriatric exposures and outcomes into existing databases. NSQIP has piloted this approach in a subset of hospitals, and the STS registry is incorporating baseline gait speed into data collection. Finally, a better understanding of the biology of frailty is needed in order to target appropriate therapies.

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Table 1
Frailty Measurement According to the Cardiovascular Health Study-Derived Criteria
(“Fried” Criteria)

Domain	Measurement
Shrinking	>10 lbs unintentional weight loss in last year
Weakness	Gender and BMI-stratified cutoffs using a Jamar hand dynamometer
Exhaustion	Self-report of either: <ul style="list-style-type: none"> a. I felt that everything I did was an effort in the last week, or b. I could not get going in the last week
Slowness	Gender and height-stratified cutoffs (generally >6-7 seconds for 15 feet)
Low activity	Energy expenditure using the Minnesota Leisure Time Activity Questionnaire (men < 383 kcal/week, women <270 kcal/week)

Abbreviations: BMI—Body Mass Index; kcal—kilocalories

Table 2
Important Studies Examining the Association of Frailty and Post-operative Outcomes in Cardiac Surgery and TAVI Patients

First author, year	Population	Frailty Definition	Outcome	Finding
Cardiac Surgery (predominantly)				
Lee, 2010 ⁴²	All cardiac surgery; Canadian; n=3826	Any deficit in ADL or ambulation, or history of dementia	In-hospital and midterm mortality (median 1.8 year follow-up), discharge to an institution	Baseline frailty was present in 4.1% and was independently associated with in-hospital mortality, midterm mortality, and discharge to an institution
Afilalo, 2010 ¹⁰	CABG and/or valve, >70 y/o; 4 U.S. and Canadian centers; n=131	Gait speed (5 m) 6 seconds	Composite of in-hospital mortality and STS morbidity	Baseline frailty was present in 46% and was a predictor of the composite outcome, even after adjusting for STS risk score.
Sundermann, 2011 ³³	Elective cardiac surgery; 74 y/o; n=400 in cohort, but follow-up data only on n=213	Multi-item Comprehensive Assessment of Frailty score (CAF)	1-year mortality	Severe frailty was present in 8.9% at baseline, and was associated with 1-year mortality, adjusted for EuroSCORE.
Afilalo, 2012 ³²	CABG and/or valve, >70 y/o; 4 U.S. and Canadian centers; n=152	4 different scales: 1 Gait speed 2 “Fried” criteria 3 “Fried” criteria + cognition and mood criteria 4 MacArthur aging scale	Composite of in-hospital mortality and STS morbidity	Depending on the scale, 20%-46% were frail. The most predictive frailty scale was 5m gait speed, which improved the model compared to STS risk score
TAVI				
Green, 2012 ⁴⁵	High-risk patients with aortic stenosis and 60 y/o undergoing TAVI. Substudy of the PARTNER study; n=159	Gait speed, grip strength, albumin, ADL; frailty defined based on median score	1-year mortality, procedural outcomes (bleeding, vascular injury, stroke, acute kidney injury, 30-day mortality)	Frailty was associated with 1-year mortality, but not with the composite of procedural outcomes.
Stortecky, 2012 ⁴⁷	70 y/o undergoing TAVI; n=100	Investigator-derived, included cognition, nutrition, TUG ADL, IADL	30-day and 1-year mortality, major adverse cardiac and cerebral events	Baseline frailty was present in 49% and was associated with mortality and complications, independent of STS and EuroSCORE
Schoenenberger, 2013 ⁴⁸	70 y/o undergoing TAVI; n=119	Investigator-derived, included cognition, nutrition, TUG ADL, IADL,	Decline in ADL 1 point at 6 months	Baseline frailty was present in 50% and was strongly associated with functional decline

Abbreviations: TAVI—transcatheter aortic valve implantation, CABG—coronary artery bypass graft, STS—Society for Thoracic Surgeons, ADL—activities of daily living, IADL—instrumental activities of daily living, TUG—timed up and go