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REVIEW ARTICLE/BRIEF REVIEW

Frailty and perioperative outcomes: a narrative review
Fragilité et aboutissements périopératoires: une synthèse narrative

Thomas Beggs · Aresh Sepehri, BSc · Andrea Szwajcer, MLIS · Navdeep Tangri, MD, PhD · Rakesh C. Arora, MD, PhD

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Abstract

Background *Frailty has no single universally accepted definition or method for assessment. It is commonly defined from a physiological perspective as a disruption of homeostatic mechanisms ultimately leading to a vulnerable state. Numerous scoring indices and assessments exist to assist clinicians in determining the frailty status of a patient. The purpose of this review is to discuss the relationship between frailty and perioperative outcomes in surgical patients.*

Principal findings *We performed a review to determine the association of frailty with perioperative outcomes in patients undergoing a wide variety of surgical procedures. A scoping literature search was performed to capture studies from MEDLINE®, EMBASE™, and CENTRAL (Cochrane), which resulted in locating 175 studies across the three electronic databases. After an article screening process, 19 studies were found that examined frailty and perioperative outcomes. The studies used a range of assessments to determine frailty status and included patients in a variety of surgical fields. Regardless of surgical population and method of frailty assessment, a relationship existed between adverse perioperative outcomes and frailty status. Frail patients undergoing surgical procedures had a higher likelihood than non-frail patients of experiencing mortality, morbidity, complications, increased hospital length of stay, and discharge to an institution.*

Conclusions *Patients undergoing surgery who are deemed frail, regardless of the scoring assessment used, have a higher likelihood of experiencing adverse perioperative outcomes. With the lack of a unified definition for frailty, further research is needed to address which assessment method is most predictive of adverse postoperative outcomes.*

Co-first authors: Thomas Beggs and Aresh Sepehri
Co-senior authors: Navdeep Tangri and Rakesh C. Arora

T. Beggs
School of Medicine, Royal College of Surgeons in Ireland, Dublin, Ireland

T. Beggs · A. Sepehri, BSc
St. Boniface General Hospital and St. Boniface Hospital Research Centre, Winnipeg, MB, Canada

A. Sepehri, BSc
Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada

A. Szwajcer, MLIS
University of Manitoba Health Sciences Libraries, Winnipeg, MB, Canada

N. Tangri, MD, PhD
Seven Oaks General Hospital Renal Program, Winnipeg, MB, Canada

N. Tangri, MD, PhD
Section of Nephrology, Department of Internal Medicine, University of Manitoba, Winnipeg, MB, Canada

R. C. Arora, MD, PhD
Section of Cardiac Surgery, Department of Surgery, University of Manitoba, Winnipeg, MB, Canada

R. C. Arora, MD, PhD (✉)
St. Boniface Hospital/I.H. Asper Institute, CR3012 – 369 Tache Ave., Winnipeg, MB R2H 2A6, Canada
e-mail: rakeshcarora@gmail.com

Résumé

Contexte *La fragilité ne répond à aucune définition ou méthode d'évaluation universellement acceptée. Elle est couramment définie d'un point de vue physiologique comme une perturbation des mécanismes homéostatiques conduisant finalement à un état de vulnérabilité. De nombreux indices de cotation et d'évaluation existent pour aider les cliniciens à définir l'état de fragilité d'un patient. L'objectif de cette synthèse est de discuter les rapports existant entre la fragilité et les aboutissements périopératoires chez les patients chirurgicaux.*

Constatations principales *Nous avons effectué une étude de synthèse afin de préciser l'association entre fragilité et aboutissements périopératoires chez des patients devant subir une grande variété de procédures chirurgicales. Une recherche ciblée de la littérature a été menée dans les bases de données électroniques MEDLINE®, EMBASE™ et CENTRAL (Cochrane) pour identifier les études pertinentes: 175 études ont été localisées. Après un processus de sélection des articles, 19 études portant sur la fragilité et les aboutissements périopératoires ont été conservées. Ces études utilisaient différentes évaluations pour déterminer l'état de fragilité et incluaient des patients dans des domaines chirurgicaux variés. Indépendamment de la population chirurgicale et de la méthode d'évaluation de la fragilité, il existait une relation entre les évènements périopératoires indésirables et le statut de fragilité. Les patients fragiles subissant des procédures chirurgicales avaient une plus grande probabilité que les patients non fragiles d'être confrontés au décès, à une morbidité, à des complications, à un allongement de la durée de séjour et au congé vers un établissement de soins de longue durée.*

Conclusions *Les patients subissant une intervention chirurgicale et qui sont jugés fragiles, indépendamment du système d'évaluation utilisé ont une plus grande probabilité d'éprouver des évènements périopératoires indésirables. En l'absence de définition unique de la fragilité, des recherches supplémentaires sont nécessaires pour identifier quelle méthode d'évaluation prédit le mieux la survenue d'aboutissements postopératoires indésirables.*

Introduction

Overview and rationale

Frailty is a distinctive health state related to the aging process that results in a decrease in both reserve and resistance to stressors and ultimately, in vulnerability to adverse outcomes.[1] Frailty is estimated to be present in 10% of people over the age of 65 and increases to 25-50% of people over the age of 85.[2] Various frailty assessments have been shown to determine whether a patient will exhibit a decline in health in response to medical or surgical stressors.[2] Despite this, the multitude of definitions and scoring systems that have been developed for frailty make it difficult for healthcare practitioners to incorporate a standard assessment in clinical care.

In this review, we examine the literature and ultimately aim to determine the clinical utility of frailty as a preoperative assessment. In the Introduction, we discuss the definition of frailty and summarize common frailty assessments, and in the Methods section, we examine and analyze literature that explores the association of frailty with a range of perioperative and surgical outcomes. Lastly, in the Discussion section, we discuss the significance of considering frailty during preoperative assessment. Importantly, while not the main focus of this narrative review, we also provide a basic foundation to assist clinicians in developing an approach for the management of frail older adults undergoing surgery.

What is frailty?

A common theme in examining frailty as a syndrome is an increased vulnerability to stressors as a result of decreased physiological reserve.[3-5] This in turn increases the risk of adverse clinical consequences to stressors.[6] Indeed, Afilalo *et al.*[7] have classified stressors as falling into the categories of acute or chronic illness as well as due to iatrogenic processes.

There are several different models outlining the pathophysiology of how frailty develops and manifests; however, the two more commonly referenced models of frailty are the "phenotype" model described by Fried *et al.* and the "deficit" model used by Rockwood *et al.*[1,5] In the phenotype model, frailty manifests itself with "declines in lean body mass, strength, endurance, balance, walking performance and low activity".[1] The Fried phenotype assessment evaluates for the presence of such features. In the deficit model, such as in the Canadian Study of Health and Aging (CSHA),[5] it was found that "summing the number of impairments" and clinical deficits (which include a large range of symptoms, from an inability to perform activities of daily living to mood disorders) can also determine frailty.[5]

There is an overlap in management approaches for patients who are frail and for those with multimorbidities. The deficit model of frailty encompasses multimorbidity, as it incorporates disease and disability as well as cognitive, psychological, and social factors into the deficits. While not everyone with multimorbidities are labelled frail, once a certain number of morbidities have been reached, a patient can be classified as frail, with more deficits leading to an increased level of frailty.

Regardless of the model of frailty used, it is important for healthcare practitioners to be mindful that exposure to stressors has a profound impact on the health status of patients deemed frail and can be linked to poor outcomes. This is reflected in the fact that frail patients are at an increased risk of adverse events such as delirium,[8] procedural complications, disability, mortality, morbidity, slowed recovery,[5,7] cardiovascular events, and increased hospital length of stay (LOS).[9]

Frailty and an aging population

There is little doubt that the older adult population is growing at a rapid rate in North America and worldwide. In the United States, the population of adults aged 65 and older is expected to reach 80 million during the years 2010-2040.[10] According to Social Development Canada, approximately one quarter of the population in Canada will be over the age of 65 by the year 2041. Increasing age has a well-defined correlation with frailty status, but aging alone is not necessarily synonymous with frailty.[6] Nonetheless, similar features are shared by both frailty and aging. In both states, there is a loss of homeostatic mechanisms to respond to stressors and the manifestation of cellular responses such as apoptosis, cellular senescence, and cellular repair.[11] Some studies suggest that factors preceding a frail state come into play before a patient reaches old age.[12] As such, frailty can be considered a model for unsuccessful aging.

In a separate report, Rockwood *et al.* looked to investigate the influence of aging in relation to patients who are fit *vs* patients who are frail.[12] Their study used a frailty index based on an accumulation of deficits whereby a patient's frailty status was a component of the number of deficits. From this analysis, the authors observed that those who are relatively fit at all ages had a lower risk of death as well as less utilization of healthcare resources. In contrast, increasing frailty indices were associated with higher mortality and more utilization of healthcare services. Studies such as these indicate that, although frailty is often linked to age, there is variation within age groups due to the multifactorial nature of frailty.[13] In a prospective Canadian study examining frailty and intensive care unit (ICU) admission in patients aged 50 and older, it was shown that frailty can occur in a relatively younger patient demographic (i.e., those $\geq$ 50 yr of age).[14] It was determined that frailty status in ICU patients aged 50 and older was associated with a greater likelihood of experiencing adverse events such as nosocomial infection and re-intubation, greater in-hospital and ICU LOS, increased in-hospital mortality, and increased risk of mortality 12 months following ICU admission.[14]

With an increasingly older adult population, it can be assumed that there will be an increasing number of individuals who are frail. In a cohort study looking at frailty and adult lifespan in a Canadian population, it was determined that the prevalence of frailty exhibited an exponential pattern with age.[12] Another Canadian study using a Clinical Frailty Scale (CFS) determined that 43.3% of patients in a cohort of 2,305 patients aged 65 yr and older had a score of "vulnerable" or greater.[5,6] Interestingly, increased CFS scores were characteristic of being older, female, having problems with ambulation, cognitive impairment, as well as the presence of more comorbidities.[5,6]

Pathophysiology, association and interaction of factors leading to frailty

It is debatable whether frailty is a process incumbent with normal aging or if it is a distinct pathophysiological process.[15] The mechanism of frailty as a pathophysiological process is not fully understood.[16] It has been proposed that an interplay of inflammatory processes, endocrine changes, inactivity, and malnutrition leads to sarcopenia and ultimately to a frail status (Figure). Syndromes such as sarcopenia, as well as cachexia, disability, and comorbidity do "dip into the waters" of frailty, as these syndromes are commonly seen together.[15] Sarcopenia has a strong connection with a frail state as decreasing muscle mass in the elderly plays a role in the evolution of frailty.[1,17] From an endocrine point of view, an enhanced risk of sarcopenia and frailty is seen in relation to having low gonadal hormone levels and insulin-like growth factor-1 (IGF-1), along with high levels of inflammatory mediators, low vitamin D, and being in a pro-coagulative state.[16] Poor nutritional intake is also characteristic of both frailty and sarcopenia.[18] Clearly, there is an interaction among environmental, genetic, as well as age-related factors that determines frailty.

Frailty also appears to have an inflammatory component. It is known that preoperative inflammatory and coagulation markers are higher in frail patients.[6] These markers include interleukin-6 (IL-6), tumour necrosis factor-alpha, C-reactive protein, coagulation factor VIII, and D-dimer.[6,15] With respect to biomarkers, IL-6 may be an important factor, as increased plasma levels have the highest association with frailty.[18] Similarly, Afilalo *et al.* also mention other biomarkers that have a correlation with frailty,[7] some of them being markers of inflammation. These included lymphocyte count, memory/naïve CD8 T-cell count, plasminogen activator inhibitor-1, testosterone, insulin-like growth factor-1, albumin, and vitamin D.[7]

Why measure frailty?

With no widely universal definition of frailty[6] and the creation of many frailty scales, it is reasonable to question why frailty is measured. One reason is that frailty

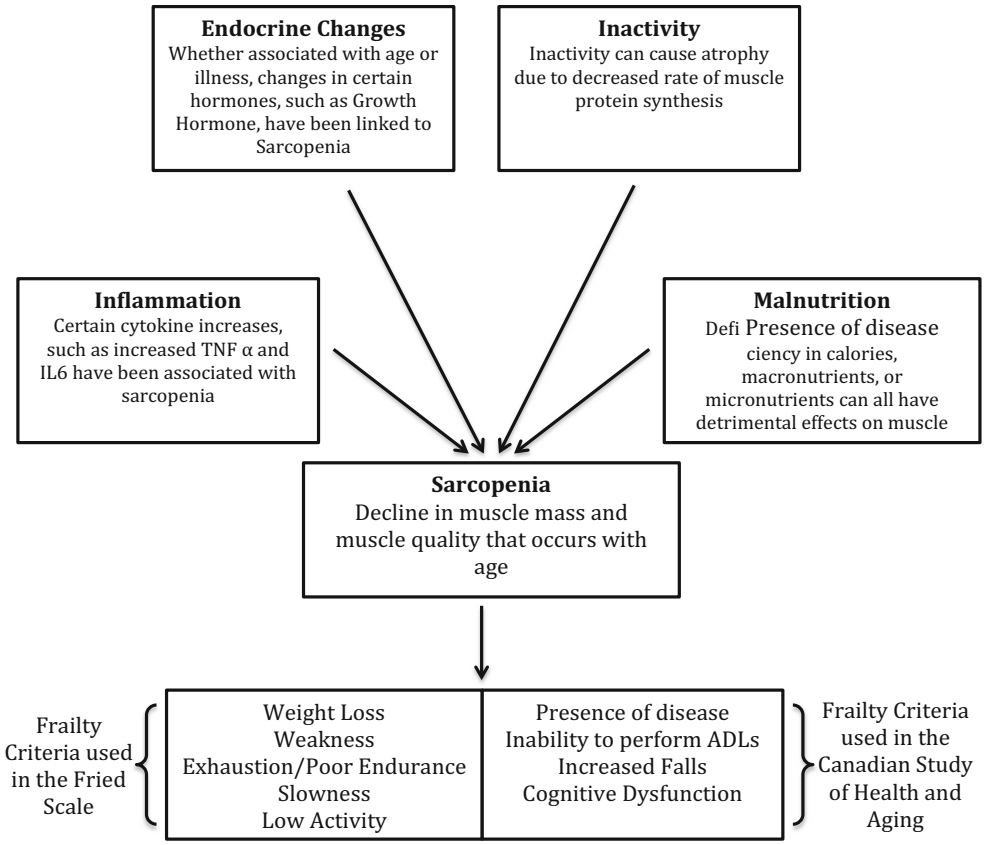

Figure Elements affecting frailty through sarcopenia

"identifies groups of people in need of extra medical attention".[19] Fulop *et al.* summated that "most important for the concept of frailty is the ability to predict it, so it can be modulated or even prevented".[18] Further rationale for the importance of assessing patient frailty is that such measures can be utilized as a clinical tool for optimizing healthcare policy planning.[5] Clinicians can use a patient's frailty status to help predict adverse consequences, such as the likelihood of mortality or if a patient is likely to require care in an institution.[5] In terms of healthcare policy, these measures can be used to help in identifying the need for healthcare services and their allocation.[5] The relationship of ICU resources and the older adult population may help support the usefulness of frailty measures, as they can help to determine ICU and long-term prognosis.[6]

What are common frailty assessments and their criteria?

With no universal criteria for what constitutes a frail patient, multiple frailty assessments and criteria have been generated. We tabulated what we consider to be some common frailty assessments and their respective criteria (Table 1).

Frailty in the surgical setting

Frail patients tend to have worse health in all illness settings.[20] Logically, a frail patient will likely not cope well with a major stressor such as surgery. Advanced age has already been shown to be a risk factor for poor surgical outcomes.[21] The association of frailty with both age and decreased physiological reserve leads to the opinion that frailty can be determined preoperatively in order to predict the risk of postoperative outcomes. Current preoperative assessments tend to focus on end-organ compromise, whereas frailty is a systemic indicator of overall health and physiological status.[20] This potentially makes characterizing frailty a useful tool for predicting both mortality and functional postoperative outcomes. The text that follows describes our search of the literature for studies analyzing frailty status in older adult surgical patients and the relationship of frailty with surgical outcomes.

Methods

In older adult patients about to undergo surgery, do postoperative outcomes differ between patients deemed frail and those deemed not frail?

Frailty has been shown to be a predictor of poor health and response to stressors. This literature search aimed to examine whether preoperative assessments of frailty are linked to worse postoperative outcome. We focused on studies describing an adult (18 years of age and older) surgical population. Studies to be considered had to have a well-defined frailty assessment performed preoperatively with comparisons made between patients deemed frail and those deemed not frail. Studies also had to report specific postoperative outcomes such as mortality, disability, or cost.

Data source and search strategy

In collaboration with a medical librarian (A.S.Z.), a scoping literature search was designed and conducted to capture best-evidence articles and literature regarding frailty, frailty assessments, and perioperative outcomes. The included studies were published during 2009-2014. The following electronic databases were used in the search: MEDLINE®, EMBASE™, and CENTRAL (Cochrane). The search resulted in 175 articles across the three databases.

Article eligibility and selection criteria

From the 175 articles across the three databases, two reviewers (T.B. and A.S.) reviewed articles using a predetermined screening process. Articles were first screened on the basis of title, abstract, and whether or not they were full-text journal articles. In order to be included for data extraction into relevant tables, certain criteria had to be met as discussed previously by the authors. Firstly, articles had to use a well-defined frailty assessment/tool in a surgical population. Secondly, articles had to have a definitively measured perioperative surgical outcome. One author (T.B.) conducted the data extraction by collecting relevant and pertinent information, while another author (A.S.) verified the data extraction. While this review is not a systematic review *per se*, we adopted many of the PRISMA guidelines for systematic reviews and meta-analyses to strengthen our review.

Results

Basic study characteristics

Nineteen articles were used for the purposes of data extraction. The patient populations can be broken down based on type of surgical procedure performed. Four studies involved patients having cardiac valve surgery (including transcatheter aortic valve repplacement).[4,22-24] Five studies involved a mix of gastrointestinal surgical patients,[25-27] including abdominal[21] and other general surgery patients.[28] Two studies involved vascular surgical patients[29,30] and two involved surgical oncology patients with either gynecological neoplasms[31] or gastric adenocarcinoma.[32] Two of the studies involved comprehensive surgical populations,[33,34] one study involved thoracic surgical patients undergoing lobectomy;[35] two studies used a mix of patients undergoing a mix of surgical procedures,[20,36] and one study involved patients undergoing a mix of minimally invasive surgical procedures.[37] All studies were published during 2009-2014. Table 2 highlights the surgical populations and the association of frailty with perioperative outcomes for the articles included.

Frailty and perioperative surgical outcomes

All included studies showed an association between defined perioperative outcomes and frailty. In eight studies, mortality was a perioperative outcome associated with frailty.[4,22,24,25,29,32,33,35] There was a wide variety of odds ratios (OR) for mortality reported in these studies, likely due to the variation in surgical population and frailty assessment used. For example, one study involving cardiac surgical patients reported an OR of 1.10 (95% confidence interval [CI] 1.04 to 1.16),[22] while another study conducted in patients undergoing esophagectomy reported a very high OR of 31.84.[25] Eight studies showed an association between frailty and the development of postoperative complications.[20,21,26,27,31,34,36,37] As with mortality, a wide variety of ORs was reported for the development of complications, likely also due to the variation in surgical population and frailty assessment used. With respect to 30-day postoperative complications, the OR ranged from as low as 1.05 (95% CI 0.94 to 1.17) in older adult abdominal surgical patients[21] to as high as 11.70 in patients undergoing emergency general surgery.[28] One study using the Groningen Frailty Index (GFI) in vascular surgical patients found that a GFI of ≥ 4 had a significant relationship with the development of postoperative delirium.[30]

Various studies consistently listed infectious causes as the leading cause of postoperative complications.[21,26-28,30] Infection often manifested itself as surgical site infection but also included pneumonia, urinary tract infection (UTI), and septicemia. In addition, those deemed more frail using a modified frailty index (mFI) showed an increased incidence of prolonged ventilation (38.9%) and re-intubation (22.2%).[26] Delirium was another common

Table 1 Common frailty scales, components, and scoring methods

Frailty Scale and or Assessment	Components of Frailty Scale and Or Assessment	Scoring
Fried Frailty Phenotype	• Shrinking: defined as unintentional weight loss of ≥ 10 pounds in prior year or, at follow-up, ≥ 5% of body weight in the prior year • Weakness: defined as grip strength in the lowest 20% at baseline, adjusted for body mass index and sex • Poor Endurance and Energy: defined as self-reported exhaustion • Slowness: defined as a gait speed of > 6-7 seconds to walk 15 feet • Low Physical Activity: based on a weighted score of kilocalories expended per week based on a participant's report; men < 383 Kcal, women < 270 Kcal	• A positive frailty phenotype is indicated by ≥ 3 criteria fulfilled • An intermediate or pre-frail phenotype is indicated by 1 or 2 criteria fulfilled.
Rockwood – Canadian Study of Health and Aging – Frailty Index (CSHA – FI)	• Use of 70 variables (see Appendix 1) from Canadian Study of Health and Aging (CSHA), which includes signs, symptoms, disabilities, the presence of comorbidities, and frailty characteristics • Based on a model of accumulation of deficits	•Frailty is calculated based on an accumulation of deficits • Variables are dichotomized or trichotomized to give a score that ranges from 0-1 • Score is calculated by taking the total number of variables (i.e., deficits) present in a patient divided by the total number of variables • Example: a patient with 14 deficits would have a score of 0.2 (14/70)
Comprehensive Assessment of Frailty (CAF)	• Two parts make up the assessment Part One is taken and assessed based on parameters of the Fried Frailty Criteria, except for unintentional weight loss • Weakness: assessed via grip strength using dynamometer • Self-reported Exhaustion: assessed via questionnaire • Slow Gait Speed: time taken to walk 4 m (measured in meters/second) • Low Physical Activity: assessed via instrumental activities of daily living Part Two involves a battery of physical performance tests such as: • Standing Balance tests using a variety of stances (feet together, tandem, and semi-tandem); time recorded in ability to maintain position • Rising from chair 3 times • Picking up pen from floor • Putting on and removing jacket	• Results from the CAF scores are tabulated into a scale involving three groups • Scores of 1-10 are deemed "not frail" • 11-25 are deemed "moderately frail" • 26-36 are deemed "severely frail" • Lab tests for serum albumin, creatinine, brain natriuretic peptide, and forced expiratory volume in one second were also included in CAF score.

Table 1 continued

Frailty Scale and or Assessment	Components of Frailty Scale and Or Assessment	Scoring
Modified Frailty Index (mFI)	• 11 variables present in both the National Surgical Quality Improvement Program (NSQIP) and CSHA-FI: These include: • Diabetes Mellitus • Functional Status of 2 or higher based on independence in activities of daily living (feeding, bathing, dressing, toileting, and mobility) • Chronic Obstructive Pulmonary Disease or Pneumonia • Congestive Heart Failure • Myocardial Infarction • Percutaneous Coronary Intervention and/or Stenting or Angina • Hypertension requiring medication • Peripheral Vascular Disease or Ischemic Rest PainImpaired Sensorium • Transient Ischemic Attack or Cerebrovascular Accident • Cerebrovascular Accident with neurological deficit	• The presence of each variable was scored as 1 point • Most variables were dichotomous, but if the variables had three categorical options, they were simplified to dichotomous • Score was calculated by taking total points scored by a patient and then dividing this by the number of variables present in the patient • mFI was calculated for each patient, giving a score from 0-11 (absence of frailty – maximum frailty).
Clinical Frailty Scale (CFS)	• A frailty scale that makes use of pictures and descriptions to assign a frailty score based on the subjective assessment of the user • When scoring frailty in patients with dementia, the degree of dementia corresponds to the degree of frailty	• The frailty score is assigned based on the subjective assessment of the user • Scores range from 1 (very fit) to 9 (terminally ill)

presentation of postoperative complications[28,37] and is itself a predictor of increased LOS. Cardiac complications were also noted. There was a significant correlation between myocardial infarctions and increased frailty scores.[26] Another common cardiac complication was arrhythmia,[27,28,37] which was present in up to 3.6% of patients in some studies.[28] These are important complications that anesthesiologists and intensivists may have to manage in the postoperative period.

Three studies looked at increased LOS in relation to frailty[26,34,36] as well as other perioperative outcomes. One study using a frailty assessment based on the Fried frailty criteria in older adult patients found that an association between increased LOS and frailty status existed in all types of surgical procedures.[34] For example, patients classified as intermediately frail in this study had an incident risk ratio (IRR) of 1.5 (95% CI 1.2 to 1.8) with respect to increased LOS, while those classified as frail had an IRR of 1.7 (95% CI 1.3 to 2.2) with respect to increased LOS. Two studies[24,34] examined institutionalization in addition to other perioperative outcomes. In older adult patients undergoing many types of surgeries, odds ratios for discharge to an institution were similar between frail cardiac surgery patients[24] and intermediately frail patients[34] (OR 3.7; 95% CI 1.8 to 7.7 and OR 3.2; 95% CI 1.0 to 10.0, respectively). Importantly, when an older adult patient was classified as "frail" in a study involving all types of surgeries,[34] the OR increased to 20.5 and had a wide 95% CI of 5.5 to 75.7.

Discussion and future directions

Frailty is associated with negative perioperative outcomes

In this review, multiple studies involving a variety of surgical populations identified a relationship between negative perioperative outcomes and frailty status. Even with a multitude of frailty assessments used and variation in surgical populations (Table 3), these studies collectively indicate a consensus that patients deemed to be frail have a higher likelihood of experiencing mortality, morbidity, complications, increased LOS, and discharge to a non-home institution.

Does this review mirror the findings of others?

It is important to emphasize that our findings accurately reflect the findings of previously published studies regarding frailty as an independent risk factor for negative surgical outcomes. Partridge *et al.*[15] also examined frailty definitions and methods of frailty assessment and their impact in the surgical population. Our review was similar in the sense that a number of frailty assessments were used in a variety of surgical populations. The present review included numerous studies pertaining to frailty assessments and perioperative outcomes in surgical populations.

Frailty assessments and the scoring indices of the included studies

Each study used a defined frailty assessment and/or scoring index in a surgical population (Table 3). Methods for obtaining frailty scores as part of an assessment tool or scoring index were collected through a variety of questionnaires, physical function tests, and laboratory biomarkers. The majority of the frailty assessments used were replicas or modifications of the more commonly used and validated frailty assessments that we have cited earlier (See Table 1). To highlight some of the more common assessments, five studies used a replica or modification of the Fried frailty criteria;[23,27,31,34,37] two studies used a replica or modification of the CSHA-FI based on an accumulation of deficits (where the more deficits accumulated the more frail the patient),[21,33] and four studies used a mFI.[25,28,29,35] The other studies utilized a range of frailty assessments, as outlined in Table 3. Clearly, there is a lack of consensus for a clear definition of frailty and for the best assessment tool to use in determining frailty status. More specifically, future research should focus on determining which assessment of frailty is best at predicting postoperative outcomes.

Clinical significance and future research directives

The results of our review provide important information for healthcare professionals in a variety of settings. Indeed, our findings are pertinent for healthcare providers involved in the care and evaluation of a patient before, during, and after surgery (perioperative period). It is of vital importance that perioperative healthcare providers understand that frailty has a link to the development of negative postoperative outcomes. As stated by authors in a paper regarding outcomes and their importance to perioperative elderly care, "increased healthcare usage by the elderly (particularly the frail "oldest old") requires reciprocal, coordinated continuity of care between community, hospital and rehabilitation services, if patients are to be managed safely, inexpensively and with dignity".[38] Our findings are also important for healthcare researchers. From our findings, it seems that, irrespective of the assessment of frailty used, frail patients are associated with more poor postoperative outcomes. Future research

Table 2 Perioperative Outcomes of Included Studies

Measured Outcome	Author	Population	*n* (Frail / Total Population)	Association(s)	
Mortality	Afilalo *et al*., 2012	Cardiac surgical patients ≥ 70 yr of age undergoing CABG and/or valve Surgery	Depends on frailty scale used: ranged from 20% to 42% (*n*/152)	Frailty as measured through gait speed is associated with mortality or major morbidity after CABG and/or valve surgery	OR 2.63, 95% CI 1.17 to 5.90
	Sundermann *et al*., 2011	Patients ≥ 74 yr of age undergoing cardiac surgery	170/400 moderately frail 31/400 severely frail	Frailty is associated with one-year mortality after cardiac surgery	OR 1.097, 95% CI 1.038 to 1.160
	Green *et al*., 2012	Patients ≥ 60 yr of age with advanced aortic disease undergoing TAVR	76/159 frail	Frailty is associated with increased one-year mortality after TAVR	HR 3.16, 95% CI 1.33 to 7.51
	Farhat *et al*., 2012	Patients ≥ 60 yr of age undergoing emergency general surgery	*n*/ 35 344 depends on degree of frailty as assessed by mFI	Frailty index using mFI was strongest predictor of 30-day mortality	OR 11.70
	Ganapathi *et al*., 2014	Patients undergoing elective and non- elective proximal aortic arch surgery	148/574 frail	Frailty was associated with both 30-day mortality[1] and one-year mortality[2]	30-day: OR 5.0, 95% CI 2.4 to 9.7, $P < 0.01$ One-year: OR 4.5, 95% CI 2.1 to 9.6, $P < 0.01$
	Hodari *et al*., 2013	Patients undergoing esophagectomy	Depends on number of complications present using mFI (2 complications were 401/2,095)	Frailty and age were statistically significant predictors of mortality	Frail: OR 31.84, $P = 0.015$ Age: OR 1.05 $P = 0.001$
	Karam *et al*., 2013	In-patients undergoing vascular surgery	*n*/ 67 308 depends on degree of frailty as assessed by mFI	mFI shown to have highest OR for mortality using stepwise logistic regression	OR = 2.058, $P < 0.001$
	Revenig *et al*., 2014	Patients undergoing minimally invasive surgery	13/80 intermediately frail or frail	Frailty remained a statistically significant predictor of 30-day mortality	OR 5.914, 95% CI 1.25 to 27.96
	Tegels *et al*., 2014	Gastric adenocarcinoma patients undergoing surgical treatment	*n*/180	Multivariate analysis showed an association between increasing GFI score and in-hospital mortality independent of other factors (age, ASA classification, neoadjuvant chemotherapy, type of surgery, and stage of tumour)	OR 1.35, 95% CI 1.01 to 1.8
				Multivariate analysis showed a SNAQ ≥ 1 was independently associated with in-hospital mortality	OR 5.07, 95% CI 1.08 to 23.81
	Tsiouris *et al*., 2013	Patients undergoing lobectomy (thoracic surgery)	Depends on mFI score (mFI of 0.18 was 442/1,940)	Strongest predictors of mortality were mFI > 0.27 wound class of 3	OR 9.3, 95% CI 9.4 to 270 OR 4.0, 95% CI 1.07 to 24
	Velanovich *et al*., 2013	Patients undergoing all surgeries (Cardiac, general, gynecological, neurological, orthopedic, otolaryngological, plastic, general thoracic, urological, and vascular)	*n*/971 434; depends on degree of frailty as assessed by mFI	For each unit increase in Frailty Index there was a stepwise increase in mortality	OR 1.33-46.33

Table 2 continued

Measured Outcome	Author	Population	*n* (Frail / Total Population)	Association(s)	
Complication(s)	Dasgupta *et al*., 2009	Patients ≥ 70 yr of age undergoing a variety of surgical procedures (orthopedic knee surgery, carotid vascular surgery, spinal surgery, and abdominal surgery)	Depends on EFS score of >7 was 16/125)	EFS score of > 7 is associated with increased complications	OR 5.02, 95% CI 1.155 to 16.25, $P < 0.02$
	Courtney-Brooks *et al*., 2012	Gynecological oncology patients ≥ 65 yr of age undergoing various surgical procedures	10/37 intermediately frail and 6/37 frail	30-day surgical complications increased with frailty score	$P = 0.04$
	Cohen *et al*., 2012	Patients aged ≥ 65 yr of age who underwent abdominal surgery	*n*/102	Lower score on Braden scale was predictive of 30-day postoperative complications	OR 1.30, 95% CI 1.06 to 1.60
	Lasithiotakis *et al*., 2013	Patients > 65 yr of age undergoing elective laparoscopic cholecystectomy	32/57 frail	Frailty as measured by DAI was a predictor of 30-day postoperative complications	OR 1.05, 95% CI 0.94 to 1.17
	Makary *et al*., 2010	Patients ≥ 65 yr of age undergoing elective surgery (all types)	186/594 intermediately frail and 62/594 frail	Frail patients classified using CGA assessment had a higher incidence of postoperative complications	OR 6.0, 95% CI 1.2 to 30.4
				Preoperative intermediate frailty was associated with increased risk of postoperative complications	OR 2.06, 95% CI 1.18 to 3.60
	Pol *et al*., 2011	Patients undergoing vascular surgery	GFI ≥ 4 was 50/142	Preoperative frailty was associated with increased risk of postoperative complications	OR 2.54, 95% CI 1.12 to 5.77
	Robinson *et al*., 2013	Patients ≥ 65 yr of age undergoing cardiac and/or colorectal surgery	Colorectal: 24/72 frail	GFI score of ≥ 4 points was significantly related to development of postoperative delirium (POD)	$P = 0.03$
			Cardiac:32/129 frail	With every one-year increase in age, frail patients were 13.360 times as likely to have a complication when undergoing colorectal surgery	95% CI 2.557 to 68.803; $P = 0.002$
	Tan *et al*., 2012	Patients ≥ 75 yr of age undergoing colorectal surgery	23/83	With every one-year increase in age, frail patients were 6.697 times as likely to have a complication when undergoing cardiac surgery	95% CI 2.565 to 17.483; $P < 0.001$
Length of Stay (LOS)	Cohen *et al*., 2012	Listed Previously	Listed Previously	Frailty is associated with postoperative Type II complications and above, as defined by Clavien-Dindo Classification	OR 4.083, 95% CI 1.4333 to 11.6303
		Listed previously	Listed Previously	Lower score on Braden Scale was predictive of longer LOS	â = 1.44 (0.250 days, $P = \leq 0.0001$ OR 4.2, 95% CI 1.3 to 13.5
	Lasithiotakis *et al*., 2013	Listed Previously		Frail patients had a longer postoperative LOS compared with fit patients	IRR 1.49, 95% CI 1.24 to 1.80
	Makary *et al*., 2010	Listed Previously	Listed Previously	Preoperative intermediate frailty was associated with increased LOS	IRR 1.69, 95% CI 1.28 to 2.23
				Preoperative frailty was associated with increased LOS	OR 5.02, 95% CI 1.155 to 16.25, $P < 0.02$

Table 2 continued

Measured Outcome	Author	Population	*n* (Frail / Total Population)	Association(s)	
Discharge	Dasgupta *et al*., 2009	Listed Previously	Listed Previously	EFS score of > 7 is associated with lower chance of being discharged home	OR 1.23, 95% CI 1.02 to 1.48
	Cohen *et al*., 2012	Listed Previously	Listed Previously	Lower score on Braden Scale was predictive of discharge to an institution	OR 3.7, 95% CI 1.8 to 7.7, $P < 0.01$
	Ganapathi *et al*., 2014	Listed Previously	Listed Previously	Frailty is independently associated with discharge to an institution other than home	OR 3.16, 95% CI 1.0 to 9.99
	Makary *et al*., 2010	Listed Previously	Listed Previously	Preoperative intermediate frailty is associated with discharge to a skilled or assisted-living facility after previously being at home	OR 3.16, 95% CI 1.0 to 9.99
				Preoperative frailty is associated with discharge to a skill or assisted-living facility after previously being at home	OR 20.48, 95% CI 5.54 to 75.68
Morbidity	Afilalo *et al*., 2012	Listed Previously	Listed Previously	Frailty as measured through gait speed is associated with mortality and major morbidity after CABG and/or valve surgery	OR 2.63, 95% CI 1.17 to 5.90
	Velanovich *et al*., 2013		Listed Previously	Each unit increase in Frailty Index there was a stepwise increase in morbidity	OR 1.24 to 3.36

ASA = American Society of Anesthesiologists; OR = odds ratio; CI = confidence interval; CABG = coronary artery bypass graft; HR = heart rate; TAVR = transcatheter aortic valve replacement; mFI = modified Frailty Index; GFI = Groningen Frailty Index; IRR = incident risk ratio; SNAQ = Short Nutritional Assessment Questionnaire; EFS = Edmonton Frailty Scale; DAI = Deficit Accumulation Index; CGA = Comprehensive Geriatric Assessment

Table 3 Included studies, frailty scoring tool and/or frailty assessment

Author, Year	Frailty Scoring Tool and /or Frailty Assessment
Afilalo *et al.*, 2012	4 scales used:
	5-item Cardiovascular Health Study (CHS)
	7-item expanded CHS
	4-item McArthur Study of Successful Aging (MSSA)
	Gait Speed
Sundermann *et al.*, 2011	Simplified Comprehensive Assessment of Frailty (CAF)
Green *et al.*, 2012	Modified Fried Frailty Criteria
Dasgupta *et al.*, 2009	Edmonton Frailty Scale (EFS)
Courtney-Brooks *et al.*, 2012	Frailty Five-Domain Validated Scoring System based on Fried Criteria
Cohen *et al.*, 2012	2 scales used
	Braden Scale
	Deficit Accumulation Index (DAI) based on Rockwood's Frailty Index
Farhat *et al.*, 2012	Modified Frailty Index (mFI)
Ganapathi *et al.*, 2014	6-component frailty index
Hodari *et al.*, 2013	Modified Frailty Index (mFI)
Karam *et al.*, 2013	Modified Frailty Index (mFI)
Lasithiotakis *et al.*, 2013	Comprehensive Geriatric Assessment (CGA)
Makary *et al.*, 2010	Frailty Five-Domain Scoring System based on Fried Criteria
Pol *et al.*, 2011	Groningen Frailty Indicator
Revenig *et al.*, 2014	Fried Frailty Criteria
Robinson *et al.*, 2013	7 baseline frailty traits
Tan *et al.*, 2012	Fried Frailty Criteria
Tegels *et al.*, 2014	2 Assessments
	Groningen Frailty Scale
	Short Nutritional Assessment Questionnaire (SNAQ)
Tsiouris *et al.*, 2013	Modified Frailty Index (mFI)
Velanovich *et al.*, 2013	Accumulating Deficit Model of Frailty

should focus on evaluating how frailty can be modified in a patient once it is identified so that preventative strategies or minimization of negative perioperative adverse events can be achieved. An example of work in this field is the study by Arthur *et al.*[39] which shows that patients attending a preoperative exercise program prior to coronary artery bypass graft (CABG) procedures have better outcomes in quality of life (QoL) and hospital LOS. Similar research should be conducted on frail patients to determine if preoperative intervention can minimize, or even reverse, the effects of having a frail status.

A gold standard frailty assessment has yet to be established. This was clearly shown by the wide range of frailty assessments utilized in the articles examined. Creation of a unified frailty assessment methodology would prove invaluable in the hospital setting. Regarding surgery, research should examine which components of frailty are most associated with poor surgical outcome. For example, Afilalo *et al.*[9] compared various frailty assessments with postoperative outcomes, and determined that gait speed was the most statistically significant predictor of mortality and morbidity (OR 2.63; 95% CI 1.17 to 5.90). Continued research in this area could prove frailty status to be a valuable preoperative assessment tool in the future.

How best to manage the frail patient

Ultimately, clinicians want to be able to use this information to provide optimal healthcare for patients. Currently, however, definitive criteria are lacking on how best to manage the "frail patient". This is partly due to the heterogeneous nature of frailty. Nevertheless, treatments that address the conditions often associated and occurring with frailty can serve as guidelines for managing a frail patient.

Frailty is a multidimensional condition involving many organ systems.[40] Nutrition is an important factor in all aging patients, but seemingly more so in frail patients. Frail patients often exhibit anemia and hypoalbuminemia, two potential markers of poor nutrition.[40,41] In addition, nutrition plays a role in sarcopenia, which is often seen with frailty and tested in frailty assessments through physical function tests such as gait speed, get up and go, and grip strength. Literature recommendations have cited that increasing protein intake in community-dwelling older adults can combat the disability associated with sarcopenia,[40,41] which is a "surrogate marker of frailty".[40] The surgical literature has also recommended early enteric feeding for patients who are undergoing colorectal surgery or a cystectomy.[40,42,43] Postoperative nutrition guidelines such as this can also be applied to frail patients undergoing these types of operations.

Exercise is another proposed aspect of management that may help to improve perioperative and postoperative outcomes in frail surgical patients. Studies have shown that exercise intervention can improve functional outcomes, balance, and gait speed.[40] The concept of "prehabilitation" is likely to become an area of increasing interest within the frailty literature as it may optimize the risk profile of frail surgical patients. Preoperative exercise programs have already shown to be beneficial in regard to postoperative outcomes. In a pilot randomized controlled trial of prehabilitation for elective CABG patients, patients participating in the "prehab" exercise program improved their physical fitness as evaluated through a preoperative six-minute walk and 5-m gait speed test, and this improvement was preserved in the postoperative period.[44] In an orthopedic study, preoperative exercise programs prior to total joint arthroplasty improved physical function testing postoperatively compared with baseline.[45] Preoperative exercise programs address the physical components of frailty and sarcopenia and would seem to be beneficial. Research is beginning to emerge on the effects of prehabilitation in a variety of patients.[45,46] A randomized controlled trial, termed the PREHAB (Preoperative REhabilitation for reduction of Hospitalization After coronary Bypass and valvular surgery – NCT02219815) study is currently underway and looking at the effects of prehabilitation on frail patients undergoing cardiac surgery.

Exercise in the postoperative period also represents a window of opportunity that may help to improve outcomes associated with frailty in the surgical patient. In a review conducted by Jack *et al*. addressing postoperative exercise training in the older adult patient, they stated "…there is now convincing evidence that physical fitness is associated with outcome following major surgery; less-fit patients having a greater risk of complications and death".[47] While this is specific to the elderly, we deduce that early mobilization and postoperative exercise programs are just as, if not more, important in the recovery of a frail surgical patient.

We also recommend that clinicians, whether surgeon, anesthesiologist, nurse, or other therapist, seek out a comprehensive geriatric assessment and model of care in the appropriate patient population. Firstly, it is important that clinicians familiarize themselves with frailty and assessment criteria. As there is no single definition for frailty, we cannot recommend one specific assessment over another, as they will vary depending on location and resource availability. Nevertheless, we recommend including a physical function component in any assessment, particularly as gait speed was shown to have the highest association with mortality in postoperative CABG patients.[9] The multisystem nature of frailty appears to make management of this patient population challenging for the clinical team, as defined criteria are lacking that exemplify the gold standard model of care. Nevertheless, in a study by Ganz *et al.*, the authors proposed a model of care for providing high-quality care for vulnerable elders. This model aims to identify and improve outcomes such as health-related QoL, function, longevity, and disease control. In this model, there are three core realms to improve these outcomes: communication between the patient and caregiver, a personal care plan, and coordination of care between healthcare providers.[48] A co-management model where all providers of healthcare share responsibilities is useful for managing the frail patient who has undergone a major surgical stressor. This necessitates sufficient access to other clinical experts, such as geriatricians, rehabilitation therapists, nurse specialists, and case managers, while establishing links to the community.[48]

Conclusion

Our review shows that frailty, as measured using a variety of tools and assessments, shows a negative relationship with respect to perioperative adverse outcomes in a variety of surgical populations. Using some measurement of frailty is useful in a clinician's preoperative assessment as it can capture functional domains often missed by traditional preoperative risk scores. Frailty in a patient has consistently been shown to be an independent risk factor in the development of adverse postoperative outcomes such as mortality, morbidity, discharge to institution, and increased hospital LOS.[15] Perioperative knowledge of the frailty status of a very ill patient may also have implications for decision-making regarding end of life and palliative care[49] and may lead to more effective shared

decision-making among patients, their families, and the clinical team.[14] Frailty can thus have a prognostic value as medical interventions not considered beneficial for improving health can possibly be withdrawn or minimized if so desired by patients, loved ones, and caregivers.[49] Preoperative frailty measures can help to identify any modifiable factors in a patient that, if enhanced, are more likely to lead to a successful outcome.[15]

Further study is needed to evaluate how best to minimize frailty status in the older adult patient, whether via preoperative intervention or postoperative rehabilitation. Current suggestions for the management of frail patients include optimizing nutritional status, widespread use of preoperative and postoperative exercise programs, and a well-outlined model of care to familiarize the healthcare team with the frailty assessment being used.

Key points

- At present, frailty has no single universal definition or method for assessment/scoring.
- Frailty is a multifactorial and complex health state representing an interplay among physiologic, endocrine, genetic, inflammatory, and age-related factors.
- With age being a strong risk factor for frailty and an ever-increasing aging population presenting for surgery, it is important for perioperative clinicians to be knowledgeable about frailty as it is frequently seen in older adult patients.
- Frailty exists in patients undergoing many types of surgical interventions, and regardless of the method use in its assessment, it is linked to adverse perioperative outcomes.
- Future research is needed to determine if the evaluation of frailty status should be part of routine perioperative care and if the effects of being frail can be minimized.

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