Frailty for Perioperative Clinicians: A Narrative Review

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Frailty is a multidimensional syndrome characterized by decreased reserve and diminished resistance to stressors. People with frailty are vulnerable to stressors, and exposure to the stress of surgery is associated with increased risk of adverse outcomes and higher levels of resource use. As Western populations age rapidly, older people with frailty are presenting for surgery with increasing frequency. This means that anesthesiologists and other perioperative clinicians need to be familiar with frailty, its assessment, manifestations, and strategies for optimization. We present a narrative review of frailty aimed at perioperative clinicians. The review will familiarize readers with the concept of frailty, will discuss common and feasible approaches to frailty assessment before surgery, and will describe the relative and absolute associations of frailty with commonly measured adverse outcomes, including morbidity and mortality, as well as patient-centered and reported outcomes related to function, disability, and quality of life. A proposed approach to optimization before surgery is presented, which includes frailty assessment followed by recommendations for identification of underlying physical disability, malnutrition, cognitive dysfunction, and mental health diagnoses. Overall, 30%–50% of older patients presenting for major surgery will be living with frailty, which results in a more than 2-fold increase in risk of morbidity, mortality, and development of new patient-reported disability. The Clinical Frailty Scale appears to be the most feasible frailty instrument for use before surgery; however, evidence suggests that predictive accuracy does not differ significantly between frailty instruments such as the Fried Phenotype, Edmonton Frail Scale, and Frailty Index. Identification of physical dysfunction may allow for optimization via exercise prehabilitation, while nutritional supplementation could be considered with a positive screen for malnutrition. The Hospital Elder Life Program shows promise for delirium prevention, while individuals with mental health and or other psychosocial stressors may derive particular benefit from multidisciplinary care and preadmission discharge planning. Robust trials are still required to provide definitive evidence supporting these interventions and minimal data are available to guide management during the intra- and postoperative phases. Improving the care and outcomes of older people with frailty represents a key opportunity for anesthesiologists and perioperative scientists. (Anesth Analg 2020;130:1450–60)

GLOSSARY

CFS = Clinical Frailty Scale; **CNST** = Canadian Nutrition Screening Test; **DASI** = Duke Activity Status Index; **EFS** = Edmonton Frail Scale; **FI** = Frailty Index; **FP** = Fried Phenotype; **IADL** = instrumental activities of daily living; **PHQ-2** = 2 question Personal Health Questionnaire; **TUGT** = Timed Up and Go Test

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Western populations are aging rapidly. Current census data suggest that by the year 2050, the number of people aged 65 years or older in the United States will double relative to this decade[1]; these data are closely mirrored in other jurisdictions such as Canada and Western Europe.[2,3] While rapid growth in the older age demographic has major impacts on all areas of medicine, it is especially relevant in the perioperative setting. Advanced age predicts a 2- to 4-fold increase in rates of morbidity and mortality,[4,5] and over 50% of people having major surgery are >65 years of age.[6,7]

Despite the increased relative risk associated with older age, however, most older people survive surgery without experiencing a serious complication (>95% survival and >75% without a major complication).[8,9] This suggests that identification of a high-risk stratum within the older surgical population may

allow for more targeted application of scarce health care resources to achieve value from perioperative enhanced care pathways and processes. While many risk stratification tools exist to help identify high-risk patients, few have been routinely operationalized in clinical practice.[10]

Over the past 10 years, frailty has emerged as a robust and clinically relevant entity that is commonly present in older people who experience adverse outcomes after surgery. As a multidimensional geriatric syndrome, the concept of frailty has been translated from geriatric medicine practice across many areas of acute care medicine. Interest in frailty in the perioperative setting has increased exponentially. However, many challenges exist regarding conceptualization of frailty, routine identification, and application of targeted interventions to improve outcomes. The objective of this review is to provide an overview of frailty relevant to perioperative clinicians, including defining frailty, reviewing techniques to operationalize frailty assessment before surgery, exploring pathways that may lead from frailty to adverse postoperative outcomes and discussing established and emerging interventions that may target these pathways to meaningfully improve outcomes for the growing number of older people with frailty who undergo surgery each year.

WHAT IS (OR ISN'T) FRAILTY?

Frailty is a multidimensional syndrome characterized by decreased reserves that leaves an individual vulnerable to adverse outcomes due to decreased tolerance of stressors (physical, physiologic, or psychosocial).[11–14] However, conceptualizing the specific features that underly frailty has eluded consensus. In general, experts agree that frailty is a multidimensional construct that includes deficits related to physical performance, nutritional status, mental health, and cognition.[14] Consensus has not been reached, however, on how to operationalize measurement of physical performance, nutrition, mental health, or cognition in clinical frailty assessments.

There is consensus, however, regarding what frailty isn't. First, although related, frailty is distinct from concepts such as disability and comorbidity.[11] Next, although investigators have occasionally defined frailty in research settings using single laboratory or diagnostic imaging values (eg, hypoalbuminemia, muscle cross-sectional area [a measure of sarcopenia]), these values on their own cannot allow direct measurement of an individual's frailty status.[14] Furthermore, although deficits will accumulate during the normal aging process, frailty is not directly synonymous with aging, but can instead be used to better identify individuals who are substantially more vulnerable relative to others of the same age.[13] Finally, the prevalence of frailty increases exponentially with increased age; however, frailty is not solely a geriatric syndrome. In fact, several studies in perioperative and critical care medicine have found that the presence of frailty at younger ages is associated with a greater relative risk of adverse outcome than frailty present in older individuals.[15,16]

In the perioperative setting, a useful definition is that frailty is an aggregate expression of risk that results from accumulation of age- and disease-related deficits across multiple domains.[17,18] This definition reflects the fact that frailty represents a global risk state (eg, it is not solely a risk factor for single organ complications), that frailty status can be impacted both by processes of aging (such as cellular and tissue breakdown) and disease-specific processes (eg, proinflammatory features of diabetes, or decreased cardiac function in coronary artery disease) and that frailty is a multidimensional entity that cannot be quantified by a single measurement.

Two leading frameworks are currently used to conceptualize frailty (Figure 1).[12] The first is the phenotype model,[17] where the presence of frailty is thought to be a primarily internal phenomenon occurring at the cellular level, caused by breakdown and dysregulation of energetics that are expressed phenotypically. This phenotype can then be identified through the measurement of gait speed, grip strength, energy levels, weight loss, and falls. The second conceptual framework is the accumulating deficits model.[13,19] In this approach, frailty is thought of as a measurement of the biologic (as opposed to chronologic) aging process; instead of counting calendar years, one counts the number of deficits present across multiple domains (≥30 deficits must be assessed).[20] The degree of frailty present can then be quantified by dividing the number of deficits present by the number of deficits assessed, which generates a score between 0 (no frailty) and 1 (completely frail). Regardless of the conceptual framework, however, it is crucial to recognize that frailty, although often described as being present or absent, is best used as a graded condition where higher levels of frailty equate to greater vulnerability and risk of adverse outcomes.

THE PREVALENCE OF FRAILTY BEFORE SURGERY

Risk factors may be considered important for prognostication and care planning for a variety of reasons.[21] Typically, one would consider a risk factor to have particular importance if (1) the risk factor is prevalent, (2) the risk factor is strongly predictive of outcome (eg, >50% relative risk increase), and/or (3) if the risk factor is potentially modifiable.[22] Below, we discuss the expected prevalence of frailty in surgical patients, while subsequent sections will address the strength of association and possible modifiability of frailty.

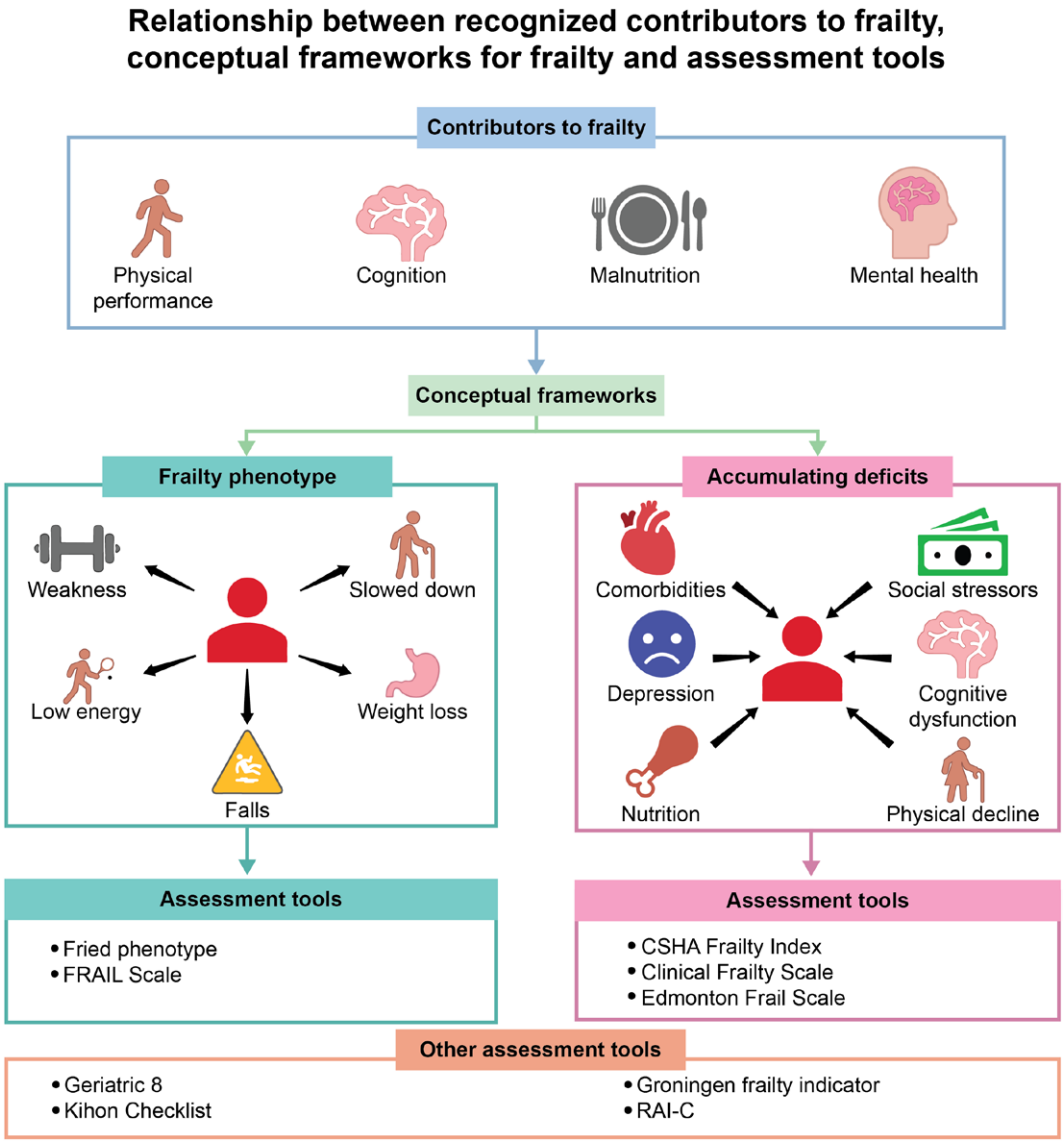

Figure 1. The relationship between domains contributing to frailty, conceptual frameworks, and commonly used frailty instruments (CSHA, FRAIL, RAI). (Terms of Use: This work is licensed under a Creative Commons Attribution-ShareAlike 4.0 International License. It is attributed to Daniel McIsaac.) CSHA indicates Canadian Study of Health and Ageing; FRAIL, Fatigue, Resistance, Ambulation, Illnesses, & Loss of weight; RAI, Risk Analysis Index.

In the general (ie, nonsurgical) population, frailty prevalence increases exponentially with age. At age 65 years, prevalence is typically <10%, while above age 85 years, prevalence typically exceeds 50%.[23] The prevalence of frailty in surgical populations differs substantially from the general population and is the product of several considerations. First, the prevalence of frailty is highly influenced by the instrument used to assess frailty (as well as the threshold used to define frailty when applying the instrument). For example, the frailty defining diagnosis approach (where the presence of one or more of a set of diagnoses typically associated with adverse aging is used to define frailty[24,25]) tends to estimate a relatively low prevalence (<10% in elective surgery[15]), whereas multidimensional clinical frailty assessments (eg, Fried Phenotype [FP], Clinical Frailty Scale [CFS]) tend to estimate a prevalence of 30%–40%.[26] The type and urgency of surgery is also an important predictor of prevalence. For example, prevalence of frailty in prostatectomy is much lower than cystectomy,[27] as surgically amenable prostate cancer has lower symptom burden than bladder cancer and prostatectomy is typically only considered for individuals with prolonged expected survival. Frailty prevalence also tends to be higher for emergency (versus elective) procedures. For example, a population-based study of major emergency surgery reported an 8-fold higher prevalence of frailty than a similar study of major elective surgery that used the same frailty definition

and data source.[15,28] Overall, age-stratified prevalence of frailty is higher in surgical populations compared to community-based samples. Using a clinically assessed multidimensional frailty instrument in the elective setting (where average age approximates 70 years), one would expect to identify frailty in approximately 30% of patients presenting for nononcologic surgery,[29] with prevalence approaching 50% in cancer surgery.[30] In a similarly aged community-based sample, frailty prevalence would approximate 10%–15%.[31] Higher prevalence and severity can be expected in emergency settings.

THE IMPACT OF FRAILTY ON PERIOPERATIVE OUTCOMES

Surgery induces substantial physiologic stress even for healthy individuals.[32] Therefore, it is not surprising that the presence of frailty before surgery is strongly associated with increased risk of adverse outcomes and higher resource utilization. Across an ever-expanding epidemiologic literature that now includes large studies using administrative data, prospective registries, primary prospective observational studies, and systematic reviews, frailty is consistently associated with at least a 2-fold increase in the risk of major morbidity, mortality, and readmissions.[33–35] Furthermore, given the increasing focus on patient-reported outcomes and the importance of functional measures for older surgical patients, it is of primary importance to recognize that frailty doubles the odds of new patient-reported disability,[26] impaired quality of life,[33,34] and increases the odds of nonhome discharge 5-fold among older people previously living in the community.[26,36] In addition, length of stay, costs, and other measures of resource use are consistently higher for older people with frailty, with a 15%–60% increase across a variety of studies.[26,36,37]

While relative increases in risk, as well as risk estimates adjusted for important confounders (such as surgery type, urgency, indication, etc) are important to clinicians and help to communicate expected outcomes to patients and their families, absolute risk estimates are typically better understood and more meaningful when providing prognostic information before surgery.[38,39] Fortunately, the absolute risk of death in the month after surgery is relatively low, even for individuals with frailty (typically <5% after major, elective noncardiac surgery).[8] However, 1-year mortality rates are often substantial and may exceed 40% after major elective surgery for cancer (which likely reflects the interplay between surgery, frailty, and the underlying oncologic process).[15,30,40] There is also a consistent dose-response relationship, where higher frailty scores (regardless of instrument) are associated with greater risk of death.[29,33]

Complications are common in people with frailty, with rates exceeding 50%.[41] Accordingly, a recent systematic review has identified frailty as the strongest risk factor for the development of postoperative morbidity in older patients.[41] Delirium is also common in older surgical patients, with rates estimated between 10% and 50% depending on the type and urgency of surgery.[42] Frailty is a strong risk factor for developing delirium after major surgery (odds ratio = 4.1),[43,44] and its strength of association with delirium incidence was exceeded only by a history of delirium in a recent systematic review.[44]

While older people place a high value on survival, expected function, and quality of life outcomes may be of even greater importance in the setting of acute illness.[45] Unfortunately, these patient-centered and patient-reported outcomes are rarely evaluated in perioperative frailty studies, and an even lower proportion provide clinically meaningful information.[34] Where these data do exist, evidence suggests that frailty is a strong predictor of adverse functional outcomes. In a multicenter cohort study of over 700 participants, our group found that 1 in 5 older people with frailty were experiencing a new or meaningfully worsened disability 3 months after major elective noncardiac surgery. We have also found that 15%–50% of older people with frailty who lived independently in the community before surgery were unable to achieve home discharge after elective procedures.[26,36] Overall, our prospective data suggest that 29% of people with frailty either die, are institutionalized, or go home with a new disability in the 90 days after major, elective noncardiac surgery.[26] These data are consistent with the cardiac literature, where older people with frailty face an approximately 20% absolute increase in the likelihood of dying or having reduced quality of life (compared to people without frailty) a year after surgery.[46]

Finally, while most studies describing the association of frailty with adverse outcomes focus on major inpatient surgery, it is also important to recognize that frailty predicts adverse outcomes in surgeries typically considered low risk. These include urgent and emergent appendectomy and cholecystectomy procedures, where the relative impact of frailty on mortality is stronger than for laparotomy or bowel resection.[28] Furthermore, after ambulatory hernia, breast, thyroid, or parathyroid surgery, frailty is associated with a greater than 3-fold increase in the odds of complications.[47]

PREOPERATIVE FRAILTY ASSESSMENT

To improve outcomes for older people with frailty, perioperative clinicians must first routinely identify frailty before surgery. However, despite guidelines from specialty societies, national institutions, and multidisciplinary groups that recommend frailty

assessment as a best practice,[48–50] there is currently little evidence that frailty assessment occurs routinely in preoperative care.[51,52] The urgent need to increase the application of routine frailty assessment is further highlighted by recent evidence linking preoperative frailty assessment (and subsequent communication to the perioperative team) with improved postoperative outcomes for older people with frailty.[53]

Many barriers to preoperative frailty assessment exist.[54] These include a lack of clarity on which frailty instrument to choose among the dozens described in the literature, time pressures that preclude the addition of further tests or assessments in an already busy preoperative clinic, the need for specialized assessments or instrument scoring for certain frailty scales, and other considerations. We suggest that the choice of frailty instrument should be informed by considerations of accuracy (ie, how well outcomes are predicted) and feasibility (ie, how practical it is to use in routine preoperative practice). Based on a careful review of the literature, we have identified at least 40 unique frailty instruments or proxy measures that have been used in clinical settings before surgery (Supplemental Digital Content, Appendix A, http://links.lww.com/AA/C985). The best-studied instruments include the FP (based on the frailty phenotype conceptual model[17]), the CFS (a clinically oriented adaptation of the accumulating deficits Frailty Index [FI][18]), the FI (direct application of the accumulating deficits frailty model[19]), and the Edmonton Frail Scale (EFS; a reduced version of the accumulating deficits FI[55]) (Table).[20,56–58] Other well-studied approaches include the use of a physical performance measure (eg, short physical performance battery[59] or 6-minute walk test[60]) or a modified FI (typically applied to the National Surgical Quality Improvement Program data[61]); however, these approaches are limited by a lack of multidimensionality. In other words, using an isolated measure of physical performance does not capture aspects of nutrition, cognition, or mental health, while the modified FI lacks adequate deficits (12 vs the recommended ≥30) and is more consistent with a modified comorbidity index.

Typically, the association of different frailty instruments with outcomes does not differ substantially. For example, systematic reviews generally find that all adequately powered studies find significantly higher rates of mortality in those with frailty than in people without frailty.[33,34] The consistent association of any frailty instrument with adverse outcomes can be demonstrated for most relevant outcomes. Unfortunately, the literature provides few studies that directly compare different frailty instruments head to head. Of those that have, authors have not found evidence of significantly different strengths of association between the instruments under study. The consistency of effect sizes found between different frailty instruments and outcomes is somewhat surprising, as different instruments typically identify the presence of preoperative frailty with only moderate agreement (Cohen's kappa = 0.4–0.6),[26,62] with much higher variation in agreement in nonoperative settings (Cohen's kappa = 0.1–0.8).[63,64] In comparing the ability of the CFS to the FP in identifying older individuals who go on to die or develop new disability after elective noncardiac surgery, we found no evidence of a difference in sensitivity, specificity, or odds ratios.[26] Similarly, Cooper et al[62] found no difference between the FP and FI when predicting prolonged length of stay, complications, or discharge disposition after orthopedic surgery, while Esses et al[65] found no difference between the modified FI, risk analysis index, and Ganapathi index in cardiac surgery. However, Wang et al[66] did find the CFS to be more strongly associated with length of stay and discharge disposition than the FRAIL Scale in orthopedics.

Effect sizes (eg, odds, risk, and hazard ratios) are only one aspect of predictive performance. For binary outcomes (such as death and complications), other measures of predictive performance must also be considered. These include discrimination (how well an instrument assigns a higher risk to people who truly go on to have the bad outcome), calibration (how well the instrument assigns an expected probability of bad outcome that matches with the observed rate of outcomes), and others.[67] Most studies do not provide these important measures. In those that do, frailty instruments typically have an area under the curve (a measure of discrimination where 0.5 represents chance and 1.0 represents perfection) of 0.65–0.85, depending on the outcome being predicted. Even fewer studies directly compare the discrimination and calibration of different instruments. However, a recently published study found that the CFS improved the discrimination of preoperative risk stratification models predicting death or new disability, prolonged length of stay, and institutional discharge to a greater extent that the FP or the FI, while also more meaningfully improving calibration than the other 2 comparators.[68]

While predictive accuracy must be a foundational consideration when choosing an instrument for risk stratification, if a frailty tool is to be used in clinical practice it must also be feasible.[69] Limited data are currently available that formally assess the feasibility of frailty instruments. Time is a primary consideration for busy clinicians. Based on available data, the CFS adds less than a minute to a preoperative assessment, while the EFS typically takes 5 minutes, the FP 5–20 minutes, and the FI approximately 10 minutes. A head-to-head comparison found the CFS to be significantly faster than the FP.[26] The CFS was also superior to the FP in terms of ease of use and logistical considerations in the same study. Further considerations that may limit the feasibility of certain frailty instruments

Table. Composition of Frailty Instruments Commonly Studied in the Perioperative Setting

Frailty Index			
Variable	**Fried Phenotype**	**Clinical Frailty Scale**	**Edmonton Frail Scale**
Anemia Albumin Sodium	Weight loss: >10 lbs unintentionally in the previous year	1. Very fit: People who are robust, very active, and motivated. These people commonly exercise regularly. They are among the fittest of their age	Cognition: Clock draw test
Low body mass index Obstructive sleep apnea Cerebrovascular disease	Grip strength: lowest 20% (by sex and body mass index)	2. Well: People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally	General health: Number of hospital admissions in the past year
Cancer Diabetes mellitus Cognitive impairment	Exhaustion: self-report	3. Managing well: People whose medical problems are well controlled, but they are rarely active beyond walking.	Functional independence: Number of activities of daily living requiring assistance
Alcohol abuse Falls history Heart failure	Slowness: 15-foot walking speed (by sex and height)	4. Vulnerable: While not dependent on others for daily help, often symptoms limit activities. A common complaint is being "slowed up," and/or being tired during the day	Social support: Availability of reliable help
Insulin use Liver disease Coronary artery disease	Low activity: Kilocalories per week (males <383, females <270)	5. Mildly frail: These people often have more evident slowing and need help in high order IADLs. Typically, this impairs shopping and walking outside alone, meal preparation, and housework	Medication use: Presence of polypharmacy
Peptic ulcer disease Peripheral vascular disease Renal disease			Medication use: Forgetting to take prescribed medications
Rheumatic disease Smoker Visual impairment		6. Moderately frail: People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal help with dressing	Nutrition: Unintentional weight loss
Hearing impairment			Mood: Feelings of sadness or depression
Assistance needed dressing Assistance needed meals Assistance needed shopping		7. Severely frail: Completely dependent for all personal care from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~6 mo)	Continence: Presence of urinary incontinence
Weight loss Multimorbidity Depression		9. Terminally ill: Approaching the end of life. This category applies to people with a life expectancy <6 mo, who are not evidently frail	Functional performance: Timed up and go test
Possibly inappropriate medication Polypharmacy			

AD8-Alzheimer's Disease in 8 questions questionnaire[57]; PHQ-2-Patient Health Questionnaire[56]; CAGE[58]; The Frailty Index is calculated as a number from 0 to 1 by dividing the number of deficits present by the number of deficits measured (ie, 30) as recommended by Searle et al.[20] One point is assigned for the presence of each feature of the phenotype, resulting in a score from 0 to 5. Following assessment, an individual is assigned a score on the scale. Zero to 2 points are assigned to each question, creating a score that ranges from 0 to 17.

Abbreviations: CAGE, cut down, annoyed, guilty, eye-opener; IADL, instrumental activities of daily living; PHQ-2, 2 question Personal Health Questionnaire.

include the need for space and timing of walk-based tests for the FP and EFS,[70] some difficulty in older patients understanding certain questions on the EFS (including people from differing backgrounds[71]), the need for a reliable and appropriately calibrated handheld dynamometer for the grip strength portion of the FP,[70] and the need to score subdomain questionnaires for the FP (activity questionnaire) and the EFS (clock draw test). Finally, the need to complete questionnaires and performance tests for the FP and EFS may limit their applicability in emergency surgery cases where patients are acutely ill at the time of assessment. For patients unable to actively participate in an assessment, a modification of the EFS (the reported EFS) has been described,[72] while a CFS assessment based on chart review and/or proxy history has been shown to be accurate in critically ill patients.[73]

In summary, perioperative clinicians must consider the specific characteristics of their preoperative assessment clinic and associated processes when selecting a frailty tool to implement because limited evidence supports the predictive superiority of a single instrument. However, available data do suggest that the CFS may provide some degree of improved discrimination and calibration when predicting patient- and system-important outcomes, while feasibility data consistently identify the CFS as a simple and practical instrument when used for preoperative assessment (see the Table for a detailed description of the CFS).

IMPROVING OUTCOMES FOR OLDER SURGICAL PATIENTS WITH FRAILTY

Preoperative frailty assessment provides an opportunity to identify a relatively homogenous and high-risk stratum of the older surgical population; early evidence suggests that the act of assessment and communication of frailty status to the perioperative team could improve outcomes on its own.[53] However, we suggest that frailty assessment most likely represents a first step linking risk stratification to perioperative optimization for high risk older surgical patients, a statement that reflects the underlying multidimensional nature of frailty. In fact, evidence from

nonsurgical older populations suggests that prognostic accuracy can be improved by differentiating the major underlying contributors to frailty.[74] Therefore, once frailty has been identified, contributors to frailty (ie, physical performance, nutrition, cognition, and mental health) can be highlighted using simple, validated screening tests (Figure 2). This should allow preoperative clinicians to link assessment to rational, evidence-based optimization strategies and support future research into optimization of older people with frailty before surgery.

Physical Performance

Surgical stress and postoperative immobility can substantially worsen physical performance in older people with frailty. Older people often experience immobilization after surgery, and when confined to bed rest, even healthy older adults lose 1.5 pounds of muscle mass per week.[75] This combination of preexisting physical vulnerability, surgical stress, and immobility can result in significant disability due to loss of lower limb function.[26] Therefore, identification of physical vulnerability before surgery could help to select individuals who might benefit from interventions to improve physical function, such as exercise prehabilitation.

While many screeners and questionnaires exist to quantify physical performance before surgery, the Duke Activity Status Index (DASI)[76] stands out as feasible and accurate tool. In an international multicenter study, the DASI was found to out-perform cardiopulmonary exercise testing when predicting adverse postoperative events[77] and outperformed the more time-intensive 6-minute walk test when predicting the occurrence of new disability.[78] Therefore, clinicians could consider the DASI as a screener for physical vulnerability among patients with frailty. One issue with the DASI, however, is that it has not been adequately tested in older people with frailty. Therefore, other standard measures of physical performance in older people, such as the timed up and go test, also deserve serious consideration.[79]

Once identified, such individuals may benefit from exercise prehabilitation, which has been shown to decrease complication rates[80,81] and possibly improve functional outcomes.[82,83] While generalizable multicenter randomized trials are still required, preliminary data suggest that people with frailty characteristics may benefit most from exercise before surgery,[84] and systematic reviews suggest that multimodal (ie, aerobic and strength training) exercise, performed at least

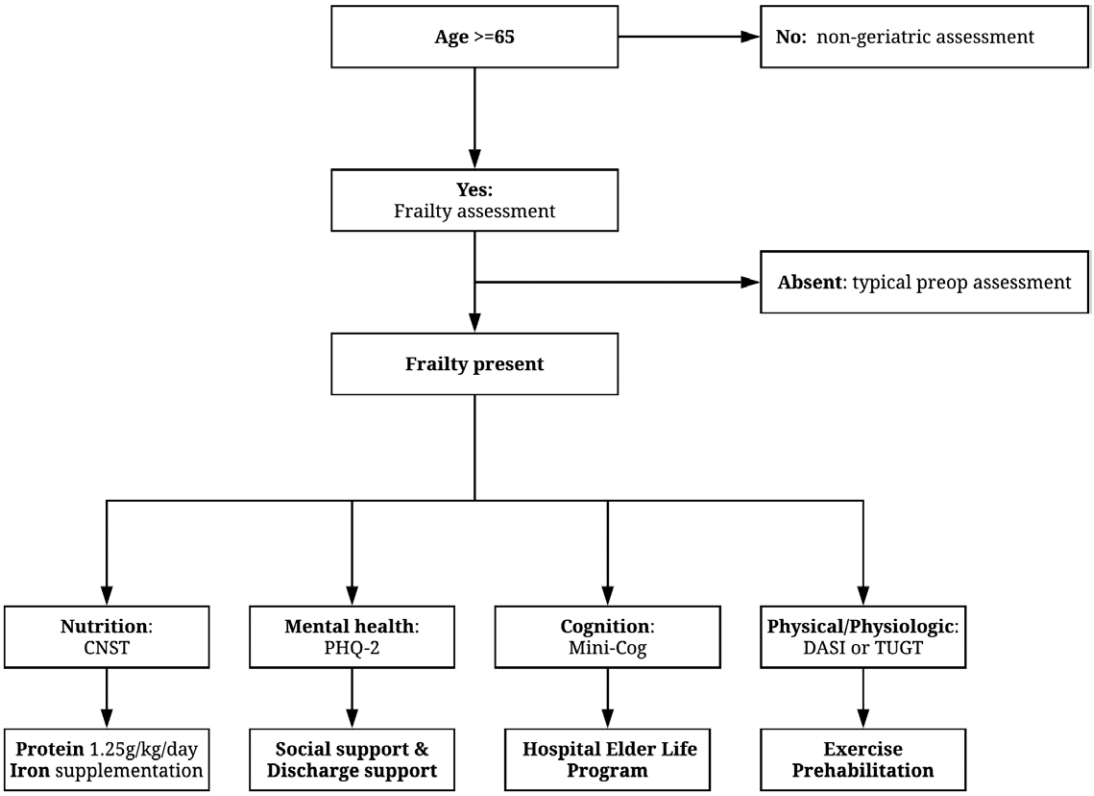

Figure 2. Proposed preoperative screening pathway for routine identification of frailty and underlying causal contributors to guide frailty-focused optimization before surgery (CNST, DASI, PHQ-2, TUGT). (Terms of Use: This work is licensed under a Creative Commons Attribution-ShareAlike 4.0 International License. It is attributed to Daniel McIsaac.) CNST indicates Canadian Nutrition Screening Tool; DASI, Duke Activity Status Index; PHQ-2, two question personal health questionnaire; TUGT, Timed Up and Go Test.

3 times per week,[85] for at least 2 weeks before surgery,[86] appears to be the most promising design.

Malnutrition

Malnutrition is prevalent in people with frailty (10%–20%)[87,88] as well as in older surgical patients (15%–60%, with higher rates seen in people with gastrointestinal and cancer diagnoses).[89,90] Malnutrition can leave older people vulnerable to physical and physiologic stressors, especially in the setting of surgery. Complications, prolonged length of stay, impaired functional recovery, and delirium are associated with malnutrition.[89,91,92] Therefore, addressing macro- and micronutrient deficits represents a promising means of optimizing the older person with frailty before surgery.

Similar to screening for physical performance, many tools are available to screen for malnutrition. These include calculation of body mass index, history of unintentional weight loss, or more specific nutritional screeners, such as the Canadian Nutrition Screening Tool (CNST)[93] or Mini Nutritional Assessment.[94] The CNST is a simple 2 question screener with good sensitivity (92%), specificity (75%), and interrater agreement (kappa = 0.88).[93]

While large studies of nutritional supplementation before surgery have not been performed in older people with frailty, protein supplementation has been a key component of several successful multimodal prehabilitation programs.[80–82,95] For people performing exercise prehabilitation, meeting protein requirements is especially important as these individuals will be attempting to address preexisting deficits while increasing demand through newly increased activity levels. Current perioperative guidelines recommend 1.5 g/kg/d (based on ideal body weight),[90] and it may be advisable to address malnutrition before commencing exercise therapy. Identification of iron deficiency anemia and treatment has also been included in prehabilitation programs and could be considered as well.[81]

Cognitive Dysfunction

Even among older people with frailty, clinically apparent dementia is uncommon.[96] However, mild neurocognitive dysfunction is prevalent and could contribute to the development of postoperative delirium and other adverse outcomes. The Mini-Cog test is currently recommended by best practice guidelines from the American College of Surgeons and American Geriatrics Society and can be considered as a cognitive screener before surgery.[48]

Once identified, the best available evidence suggests that environmental optimization and avoidance of delirium triggers can be used to reduce delirium after surgery.[97] The Hospital Elder Life Program[98] represents a bundled approach to delirium prevention (orientation, nutrition, mobilization) that is associated with lower delirium rates in surgical patients.[99] The role of cognitive prehabilitation, while promising, requires further study.[100,101]

Mental Health

Anxiety and depression are common in older surgical patients and can relate to underlying psychosocial stressors, the impact of the surgical diagnosis, or other organic causes of depression. Given the high absolute risk of nonhome discharge among older people with frailty, identifying underlying mental health issues and psychosocial stressors could help to pinpoint individuals who will have more complex discharge needs, reduced support for going home, or both. The 2 question Personal Health Questionnaire (PHQ-2) is 86% sensitive and 78% specific for identifying individuals with major depression and could be considered by preoperative clinicians as a screening tool for depression.[56] Unfortunately, to date, little interventional data are available to suggest specific strategies to intervene in this regard. However, well-designed multidisciplinary geriatric care pathways that include preadmission discharge planning show promise for decreasing adverse events and resource use among high-risk older patients.[102,103]

CONCLUSIONS

Frailty is a multidimensional syndrome that is prevalent among older surgical patients, is strongly associated with adverse outcomes, can be feasibly assessed and identified before surgery, and represents a potentially modifiable risk factor. Perioperative clinicians should consider routine frailty assessment using accurate and feasible instruments, while also considering the underlying contributors to frailty to identify specific targets for optimization. Future research will be needed to further refine interventions for preoperative optimization, while also addressing knowledge gaps related to intra- and postoperative care.

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REFERENCES

1. He W, Goodkind D, Kowal P. An Aging World. Washington, DC, 2015. Available at: https://www.census.gov/content/dam/Census/library/publications/2016/demo/p95-16-1.pdf. Accessed October 1, 2019.
2. Statistics Canada: The Canadian Population in 2011: Age and Sex. Ottawa, ON, 2011. Available at: http://www12.statcan.gc.ca/census-recensement/2011/as-sa/98-311-x/98-311-x2011001-eng.cfm#a2. Accessed October 1, 2019.
3. Organization for Economic Co-operation and Development. Elderly population (indicator). Available at: https://data.oecd.org/pop/elderly-population.htm. Accessed October 1, 2019.
4. Finlayson EV, Birkmeyer JD. Operative mortality with elective surgery in older adults. *Eff Clin Pract*. 2001;4:172–177.
5. Turrentine FE, Wang H, Simpson VB, Jones RS. Surgical risk factors, morbidity, and mortality in elderly patients. *J Am Coll Surg*. 2006;203:865–877.
6. Etzioni DA, Liu JH, Maggard MA, Ko CY. The aging population and its impact on the surgery workforce. *Ann Surg*. 2003;238:170–177.
7. Fowler AJ, Abbott TEF, Prowle J, Pearse RM. Age of patients undergoing surgery. *Br J Surg*. 2019;106:1012–1018.
8. McIsaac DI, Wijeysundera DN, Huang A, Bryson GL, van Walraven C. Association of the hospital volume of frail surgical patients cared for with outcomes after elective, major noncardiac surgery: a Retrospective Population-based Cohort Study. *Anesthesiology*. 2017;126:602–613.
9. King A, Bottle A, Faiz O, Aylin P. Investigating adverse event free admissions in medicare inpatients as a patient safety indicator. *Ann Surg*. 2017;265:910–915.
10. Harris EP, MacDonald DB, Boland L, Boet S, Lalu MM, McIsaac DI. Personalized perioperative medicine: a scoping review of personalized assessment and communication of risk before surgery. *Can J Anaesth*. 2019;66:1026–1037.
11. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci*. 2004;59:255–263.
12. Robinson TN, Walston JD, Brummel NE, et al. Frailty for surgeons: review of a national institute on aging conference on frailty for specialists. *J Am Coll Surg*. 2015;221:1083–1092.
13. Rockwood K, Song X, Mitnitski A. Changes in relative fitness and frailty across the adult lifespan: evidence from the Canadian National Population Health Survey. *CMAJ*. 2011;183:E487–E494.
14. Rodríguez-Mañas L, Féart C, Mann G, et al; FOD-CC group (Appendix 1). Searching for an operational definition of frailty: a Delphi method based consensus statement: the frailty operative definition-consensus conference project. *J Gerontol A Biol Sci Med Sci*. 2013;68:62–67.
15. McIsaac DI, Bryson GL, van Walraven C. Association of frailty and 1-year postoperative mortality following major elective noncardiac surgery: a Population-Based Cohort Study. *JAMA Surg*. 2016;151:538–545.
16. Bagshaw M, Majumdar SR, Rolfson DB, Ibrahim Q, McDermid RC, Stelfox HT. A prospective multicenter cohort study of frailty in younger critically ill patients. *Crit Care*. 2016;20:175.
17. Fried LP, Tangen CM, Walston J, et al; Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56:M146–M156.
18. Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. *CMAJ*. 2005;173:489–495.
19. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. *ScientificWorldJournal*. 2001;1:323–336.
20. Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K. A standard procedure for creating a frailty index. *BMC Geriatr*. 2008;8:24.
21. Rose G. Sick individuals and sick populations. 1985. *Bull World Health Organ*. 2001;79:990–996.
22. Monson R. *Occupational Epidemiology*. 2nd ed. Boca Raton, FL: CRC Press; 1990.
23. Gale CR, Cooper C, Sayer AA. Prevalence of frailty and disability: findings from the English Longitudinal Study of Ageing. *Age Ageing*. 2015;44:162–165.
24. Sternberg SA, Bentur N, Abrams C, et al. Identifying frail older people using predictive modeling. *Am J Manag Care*. 2012;18:e392–e397.
25. Technical Reference Guide 9.0. Baltimore, MD, 2009. Available at: acg.jhsph.org. Accessed September 17, 2019.
26. McIsaac DI, Taljaard M, Bryson GL, et al. Frailty as a predictor of death or new disability after surgery: a Prospective Cohort Study. *Ann Surg*. 2018 July 24 [Epub ahead of print].
27. Lascano D, Pak JS, Kates M, et al. Validation of a frailty index in patients undergoing curative surgery for urologic malignancy and comparison with other risk stratification tools. *Urol Oncol*. 2015;33:426.e1–426.12.
28. McIsaac DI, Moloo H, Bryson GL, van Walraven C. The association of frailty with outcomes and resource use after emergency general surgery: a Population-Based Cohort Study. *Anesth Analg*. 2017;124:1653–1661.
29. McIsaac DI, Wong CA, Huang A, Moloo H, van Walraven C. Derivation and validation of a generalizable preoperative frailty index using population-based health administrative data. *Ann Surg*. 2019;270:102–108.
30. Handforth C, Clegg A, Young C, et al. The prevalence and outcomes of frailty in older cancer patients: a systematic review. *Ann Oncol*. 2015;26:1091–1101.
31. Gale CR, Cooper C, Sayer AA. Prevalence of frailty and disability: findings from the English Longitudinal Study of Ageing. *Age Ageing*. 2014;0:1–4.
32. Gerhard-Herman MD, Gornik HL, Barrett C, et al; Writing Committee Members. 2016 AHA / ACC guideline on the management of patients with lower extremity peripheral artery disease. *Vasc Med*. 2017;22:NP1–NP43.
33. Lin HS, Watts JN, Peel NM, Hubbard RE. Frailty and postoperative outcomes in older surgical patients: a systematic review. *BMC Geriatr*. 2016;16:157.
34. Kim DH, Kim CA, Placide S, Lipsitz LA, Marcantonio ER. Preoperative frailty assessment and outcomes at 6 months or later in older adults undergoing cardiac surgical procedures: a systematic review. *Ann Intern Med*. 2016;165:650–660.
35. Beggs T, Sepehri A, Szwajcer A, Tangri N, Arora RC. Frailty and perioperative outcomes: a narrative review. *Can J Anaesth*. 2015;62:143–157.
36. McIsaac DI, Beaulé PE, Bryson GL, Van Walraven C. The impact of frailty on outcomes and healthcare resource usage after total joint arthroplasty: a population-based cohort study. *Bone Joint J*. 2016;98-B:799–805.
37. Robinson TN, Wu DS, Stiegmann GV, Moss M. Frailty predicts increased hospital and six-month healthcare cost following colorectal surgery in older adults. *Am J Surg*. 2011;202:511–514.
38. Ahmed H, Naik G, Willoughby H, Edwards AG. Communicating risk. *BMJ*. 2012;344:e3996.
39. Trevena LJ, Davey HM, Barratt A, Butow P, Caldwell P. A systematic review on communicating with patients about evidence. *J Eval Clin Pract*. 2006;12:13–23.

40. Shen Y, Hao Q, Zhou J, Dong B. The impact of frailty and sarcopenia on postoperative outcomes in older patients undergoing gastrectomy surgery: a systematic review and meta-analysis. *BMC Geriatr*. 2017;17:188.
41. Watt J, Tricco AC, Talbot-Hamon C, et al. Identifying older adults at risk of harm following elective surgery: a systematic review and meta-analysis. *BMC Med*. 2018;16:2.
42. Scholz AF, Oldroyd C, McCarthy K, Quinn TJ, Hewitt J. Systematic review and meta-analysis of risk factors for postoperative delirium among older patients undergoing gastrointestinal surgery. *Br J Surg*. 2016;103:e21–e28.
43. Brown CH IV, Max L, LaFlam A, et al. The association between preoperative frailty and postoperative delirium after cardiac surgery. *Anesth Analg*. 2016;123:430–435.
44. Watt J, Tricco AC, Talbot-Hamon C, et al. Identifying older adults at risk of delirium following elective surgery: a systematic review and meta-analysis. *J Gen Intern Med*. 2018;33:500–509.
45. Fried TR, Bradley EH, Towle VR, Allore H. Understanding the treatment preferences of seriously ill patients. *N Engl J Med*. 2002;346:1061–1066.
46. Green P, Arnold SV, Cohen DJ, et al. Relation of frailty to outcomes after transcatheter aortic valve replacement (from the PARTNER trial). *Am J Cardiol*. 2015;116:264–269.
47. Seib CD, Rochefort H, Chomsky-Higgins K, et al. Association of patient frailty with increased morbidity after common ambulatory general surgery operations. *JAMA Surg*. 2018;153:160–168.
48. Chow WB, Rosenthal RA, Merkow RP, Ko CY, Esnaola NF; American College of Surgeons National Surgical Quality Improvement Program; American Geriatrics Society. Optimal preoperative assessment of the geriatric surgical patient: a best practices guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society. *J Am Coll Surg*. 2012;215:453–466.
49. Beech F, Brown A, Dhesi J, et al. Peri-operative care of the elderly 2014. *Anaesthesia*. 2014;69:81–98.
50. Alvarez-Nebreda ML, Bentov N, Urman RD, et al. Recommendations for preoperative management of frailty from the Society for Perioperative Assessment and Quality Improvement (SPAQI). *J Clin Anesth*. 2018;47:33–42.
51. Eamer G, Taheri A, Chen SS, et al. Comprehensive geriatric assessment for older people admitted to a surgical service. *Cochrane Database Syst Rev*. 2018;1:CD012485.
52. Eamer G, Gibson JA, Gillis C, et al. Surgical frailty assessment: a missed opportunity. *BMC Anesthesiol*. 2017;17:99.
53. Hall DE, Arya S, Schmid KK, et al. Association of a frailty screening initiative with postoperative survival at 30, 180, and 365 days. *JAMA Surg*. 2017;152:233–240.
54. Rockwood K, Theou O, Mitnitski A. What are frailty instruments for ? *Age Ageing*. 2015;44:545–547.
55. Rolfson DB, Majumdar SR, Tsuyuki RT, Tahir A, Rockwood K. Validity and reliability of the Edmonton Frail Scale. *Age Ageing*. 2006;35:526–529.
56. Arroll B, Goodyear-Smith F, Crengle S, et al. Validation of PHQ-2 and PHQ-9 to screen for major depression in the primary care population. *Ann Fam Med*. 2010;8:348–353.
57. Galvin JE, Roe CM, Powlishta KK, et al. The AD8: a brief informant interview to detect dementia. *Neurology*. 2005;65:599–564.
58. Ewing J. Detecting alcoholism. The CAGE questionnaire. *JAMA*. 1984;252:1905–1907.
59. Freire AN, Guerra RO, Alvarado B, Guralnik JM, Zunzunegui MV. Validity and reliability of the short physical performance battery in two diverse older adult populations in Quebec and Brazil. *J Aging Health*. 2012;24:863–878.
60. Moriello C, Mayo NE, Feldman L, Carli F. Validating the six-minute walk test as a measure of recovery after elective colon resection surgery. *Arch Phys Med Rehabil*. 2008;89:1083–1089.
61. Antoine HJ, Velanovich V, Watson PY, Farooq M, Swartz A, Rubinfeld IS. A simplified frailty index tested in the National Surgical Quality Improvement Program (NSQIP) predicts perioperative risk in orthopedic populations. *JACS*. 2011;213S72.
62. Cooper Z, Rogers SO Jr, Ngo L, et al. Comparison of frailty measures as predictors of outcomes after orthopedic surgery. *J Am Geriatr Soc*. 2016;64:2464–2471.
63. Theou O, Brothers TD, Mitnitski A, Rockwood K. Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. *J Am Geriatr Soc*. 2013;61:1537–1551.
64. Aguayo GA, Donneau AF, Vaillant MT, et al. Agreement between 35 published frailty scores in the general population. *Am J Epidemiol*. 2017;186:420–434.
65. Esses G, Andreopoulos E, Lin HM, Arya S, Deiner S. A comparison of three frailty indices in predicting morbidity and mortality after on-pump aortic valve replacement. *Anesth Analg*. 2018;126:39–45.
66. Wang HT, Fafard J, Ahern S, Vendittoli PA, Hebert P. Frailty as a predictor of hospital length of stay after elective total joint replacements in elderly patients. *BMC Musculoskelet Disord*. 2018;19:14.
67. Steyerberg EW, Vickers AJ, Cook NR, et al. Assessing the performance of prediction models: a framework for traditional and novel measures. *Epidemiology*. 2010;21:128–138.
68. McIsaac DI, Harris EP, Hladkowicz E, et al. Prospective comparison of preoperative predictive performance between 3 leading frailty instruments. *Anesth Analg*. 2019 [Epub ahead of print].
69. Bowen DJ, Kreuter M, Spring B, et al. How we design feasibility studies. *Am J Prev Med*. 2009;36:452–457.
70. Kapoor A, Matheos T, Walz M, et al. Self-reported function more informative than frailty phenotype in predicting adverse postoperative course in older adults. *J Am Geriatr Soc*. 2017;65:2522–2528.
71. Kovacs J, Moraru L, Antal K, Cioc A, Voidazan S, Szabo A. Are frailty scales better than anesthesia or surgical scales to determine risk in cardiac surgery? *Korean J Anesthesiol*. 2017;70:157–162.
72. Hilmer SN, Perera V, Mitchell S, et al. The assessment of frailty in older people in acute care. *Australas J Ageing*. 2009;28:182–188.
73. Shears M, Takaoka A, Rochwerg B, et al; Canadian Critical Care Trials Group. Assessing frailty in the intensive care unit: a reliability and validity study. *J Crit Care*. 2018;45:197–203.
74. Looman WM, Fabbricotti IN, Blom JW, et al; TOPICS-MDS Research Consortium. The frail older person does not exist: development of frailty profiles with latent class analysis. *BMC Geriatr*. 2018;18:84.
75. English KL, Paddon-Jones D. Protecting muscle mass and function in older adults during bed rest. *Curr Opin Clin Nutr Metab Care*. 2010;13:34–39.
76. Hlatky MA, Boineau RE, Higginbotham MB, et al. A brief self-administered questionnaire to determine functional capacity (the Duke Activity Status Index). *Am J Cardiol*. 1989;64:651–654.
77. Wijeysundera DN, Pearse RM, Shulman MA, et al; METS study investigators. Assessment of functional capacity before major non-cardiac surgery: an international, prospective cohort study. *Lancet*. 2018;391:2631–2640.

78. Shulman MA, Cuthbertson BH, Wijeysundera DN, et al; Measurement of Exercise Tolerance for Surgery Study Investigators. Using the 6-minute walk test to predict disability-free survival after major surgery. *Br J Anaesth*. 2019;122:111–119.
79. Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc*. 1991;39:142–148.
80. Minnella EM, Awasthi R, Loiselle SE, Agnihotram RV, Ferri LE, Carli F. Effect of exercise and nutrition prehabilitation on functional capacity in esophagogastric cancer surgery: a Randomized Clinical Trial. *JAMA Surg*. 2018;153:1081–1089.
81. Barberan-Garcia A, Ubré M, Roca J, et al. Personalised prehabilitation in high-risk patients undergoing elective major abdominal surgery: a Randomized Blinded Controlled Trial. *Ann Surg*. 2018;267:50–56.
82. Gillis C, Li C, Lee L, et al. Prehabilitation versus rehabilitation: a randomized control trial in patients undergoing colorectal resection for cancer. *Anesthesiology*. 2014;121:937–947.
83. McIsaac DI, Jen T, Mookerji N, Patel A, Lalu MM. Interventions to improve the outcomes of frail people having surgery: a systematic review. *PLoS One*. 2017;12:e0190071.
84. Minnella EM, Awasthi R, Gillis C, et al. Patients with poor baseline walking capacity are most likely to improve their functional status with multimodal prehabilitation. *Surgery*. 2016;160:1070–1079.
85. Theou O, Stathokostas L, Roland KP, et al. The effectiveness of exercise interventions for the management of frailty: a systematic review. *J Aging Res*. 2011;2011:569194.
86. Mainini C, Rebelo PF, Bardelli R, et al. Perioperative physical exercise interventions for patients undergoing lung cancer surgery: what is the evidence? *SAGE Open Med*. 2016;4:2050312116673855.
87. Wei K, Nyunt MSZ, Gao Q, Wee SL, Ng TP. Frailty and malnutrition: related and distinct syndrome prevalence and association among community-dwelling older adults: Singapore Longitudinal Ageing Studies. *J Am Med Dir Assoc*. 2017;18:1019–1028.
88. Wei K, Nyunt MS, Gao Q, Wee SL, Yap KB, Ng TP. Association of frailty and malnutrition with long-term functional and mortality outcomes among community-dwelling older adults: results from the Singapore Longitudinal Aging Study 1. *JAMA Netw Open*. 2018;1:e180650.
89. Tobert CM, Hamilton-Reeves JM, Norian LA, et al. Emerging impact of malnutrition on surgical patients: literature review and potential implications for cystectomy in bladder cancer. *J Urol*. 2017;198:511–519.
90. Weimann A, Braga M, Carli F, et al. ESPEN guideline: clinical nutrition in surgery. *Clin Nutr*. 2017;36:623–650.
91. Goisser S, Schrader E, Singler K, et al. Malnutrition according to mini nutritional assessment is associated with severe functional impairment in geriatric patients before and up to 6 months after hip fracture. *J Am Med Dir Assoc*. 2015;16:661–667.
92. Mazzola P, Ward L, Zazzetta S, et al. Association between preoperative malnutrition and postoperative delirium after hip fracture surgery in older adults. *J Am Geriatr Soc*. 2017;65:1222–1228.
93. Laporte M, Keller HH, Payette H, et al. Validity and reliability of the new Canadian Nutrition Screening Tool in the 'real-world' hospital setting. *Eur J Clin Nutr*. 2015;69:558–564.
94. Vellas B, Guigoz Y, Garry PJ, et al. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. *Nutrition*. 1999;15:116–122.
95. Gillis C, Buhler K, Bresee L, et al. Effects of nutritional prehabilitation, with and without exercise, on outcomes of patients who undergo colorectal surgery: a systematic review and meta-analysis. *Gastroenterology*. 2018;155:391–410.e4.
96. Hui Y, van Walraven C, McIsaac DI. How do common comorbidities modify the association of frailty with survival after elective noncardiac surgery? A Population-Based Cohort Study. *Anesth Analg*. 2019;129:1699–1706.
97. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. *Lancet*. 2014;383:911–922.
98. Hospital Elder Life Program. Available at: www.hospitalelderlifeprogram.org. Accessed October 1, 2019.
99. Chen CC, Li HC, Liang JT, et al. Effect of a modified hospital elder life program on delirium and length of hospital stay in patients undergoing abdominal surgery: a Cluster Randomized Clinical Trial. *JAMA Surg*. 2017;152:827–834.
100. Borrell-Vega J, Esparza Gutierrez AG, Humeidan ML. Multimodal prehabilitation programs for older surgical patients. *Anesthesiol Clin*. 2019;37:437–452.
101. Humeidan ML, Otey A, Zuleta-Alarcon A, Mavarez-Martinez A, Stoicea N, Bergese S. Perioperative cognitive protection-cognitive exercise and cognitive reserve (The Neurobics Trial): a Single-blind Randomized Trial. *Clin Ther*. 2015;37:2641–2650.
102. Harari D, Hopper A, Dhesi J, Babic-Illman G, Lockwood L, Martin F. Proactive care of older people undergoing surgery ('POPS'): designing, embedding, evaluating and funding a comprehensive geriatric assessment service for older elective surgical patients. *Age Ageing*. 2007;36:190–196.
103. McDonald SR, Heflin MT, Whitson HE, et al. Association of integrated care coordination with postsurgical outcomes in high-risk older adults: the Perioperative Optimization of Senior Health (POSH) initiative. *JAMA Surg*. 2018;153:454–462.