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The Use of Frailty as a Surgical Risk Assessment Tool in Elderly Patients

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Abstract With the continued aging of the population, a rising proportion of surgical procedures will be performed in elderly patients. Current surgical decision-making tools rely on subjective judgments and were developed without special geriatric considerations. As a result, they have certain inadequacies that limit their utility in this population. Frailty, described for decades by the medical geriatric community, has just recently begun to be investigated as a surgical risk assessment tool. Identifying the frailty phenotype has been shown by multiple investigators to reliably predict which patients are at increased risk of adverse peri-operative outcomes. Perhaps, most importantly, it is a tool that can potentially discriminate among the elderly, identifying those that warrant heightened concern, "pre-habilitation", or special postoperative attention from those at no increased risk compared to the general population. Alternatively, some patients may be identified as "too frail" to undergo surgery, and alternative nonsurgical treatment options may be considered.

Keywords Urology · Surgery · Outcomes · Frailty · Preoperative assessment

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Introduction

As the "baby boomer" population ages, there has been a concomitant rise in the share of surgical procedures performed in the elderly, with over half of surgeries in the United States performed on patients 65 years or older [1]. Accompanying the dramatic increase in life expectancy over the last century is an increase in the life expectancy of the very old, with an 85-year-old man and woman expected to live another 5.5 and 7 years, respectively [2•]. These facts introduce nuance to a practicing surgeon's decision making: which elderly patients will benefit from lifesaving or life improving procedures, and which will be exposed to more harm than benefit? Exposing elderly frail patients to surgical procedures potentially puts them at risk for poor postoperative outcomes, while denying non-frail patients based on advanced age ("ageism") or inaccurate assessment tools may deny them the benefits of surgery.

Physiology of Aging

Although not the focus of this review, it is worthwhile to briefly discuss the physiologic derangements that accompany aging. As will be discussed in more detail later in the review, it is not the overt diagnosed comorbidities that present a challenge in preoperative risk assessment, but the subclinical deficits that are masked by compensatory mechanisms. Additionally, it is the inability to respond to the insults of surgery that may ultimately lead to adverse outcomes in the elderly following surgery.

Cardiac disease is most prevalent in the elderly. And, with 80 % of patients over 80 years of age showing evidence of cardiovascular disease, it also represents the most common cause of mortality in those 65 years and older [3]. In short, changes in cardiovascular physiology in the elderly are

characterized by an increase in arterial intimal thickness, increase in left ventricle thickness with a concomitant decrease in contractility and compliance, and an increase in left atrial volume and pressure [4–6]. Taken together, although these physiologic derangements may not result in symptomatic heart disease, they represent a decrease in functional reserve and an impairment in a patient's ability to respond to stressors, such as a surgical intervention.

Similarly, the elderly patient's pulmonary function is characterized by decreased elastic recoil of the lung parenchyma, decreased compliance of the chest wall, and diminished strength in respiratory muscles [3, 7, 8]. In combination with impaired response to hypoxia and hypercapnia, elderly patients are susceptible to risk and complications of general anesthesia and mechanical ventilation [9]. As such, while age itself is not an independent risk factor for needing mechanical ventilation after intensive care unit admission, there is an increased risk of an elderly patient being unable to wean off a ventilator due to these aforementioned age-related changes.

Independent of nephrotoxic comorbidities such as hypertension and diabetes mellitus, advancing age is inevitably accompanied by a steady decrease in glomerular filtration rate (GFR) and creatinine clearance [10]. Additionally, aging kidneys demonstrate vascular dysautonomia, altered tubular handling of creatinine, and impaired sodium reabsorption and potassium secretion, reflected by the inclusion of age as a variable in the MDRD formula for calculation of GFR [11]. Although clinically silent until a critical threshold is passed, the gradually decreased reserve in renal function predisposes the elderly to electrolyte imbalances, volume disturbances of overload and dehydration, and drug toxicity [11]. While important in all elderly patients, these concerns hold special importance in those subjected to the acute stress of surgery.

Combined together, these decrements in physiologic reserve impair a patient's ability to respond to stressors, whether unintended medical illness or the intended stress of surgery. Importantly, they not only predispose patients to postoperative complications, but also prolong an elderly's patient recovery from seemingly minor events that would be less concerning in healthy, younger patients.

Traditional Risk Assessments

Although large retrospective studies have shown that advanced age carries a modestly increased risk of perioperative morbidity and mortality [1], others have demonstrated that mortality remains low and the elderly have outcomes similar to their younger counterparts for a variety of procedures [12–14]. The United States National Comprehensive Cancer Network (NCCN) and International Society of Geriatric Oncology (SIOG) both recommend that elderly cancer patients undergo some form of a geriatric assessment to help guide treatment decision making [15, 16]. Additionally, to avoid the pitfalls of ageism—offering or denying surgical procedures solely on the basis of age—many risk assessment tools and evaluations have been developed and currently exist in clinical practice. Unfortunately, the commonly employed risk assessment tools or comorbidity indices poorly capture the functional heterogeneity that characterizes the elderly. Aging is a very individualized phenomenon, and any comprehensive assessment must be multidimensional and multidisciplinary to fully characterize a patient's functional, physical, cognitive, and socio-environmental factors [16, 17].

The American Society of Anesthesiology Physical Status Classification System (ASA) is a widely employed risk assessment scale of surgical patients, and was developed in the 1940s as a standardization tool to allow accurate data collection and analysis, not to quantify operative risk [18]. Designation of a patient to a particular ASA score relies only on the degree of systemic illness and symptomatology and not actual operative risk. Although large studies have demonstrated that an increasing ASA classification carries modestly increased risk for morbidity and mortality [1, 19], the ASA's usefulness is limited by the subjective nature by which a patient's ASA score is assigned, as evidenced by its observed poor inter-observer consistency [20]. Similar to the ASA, the Eastern Cooperative Oncology Group Performance Status (ECOG) was developed as a tool not to estimate operative risk, but as a method to identify patients suitable for inclusion in clinical trials. It also relies on a subjective judgment of a patient's symptoms due to cancer and neglects subclinical deficits in physiologic reserve.

As cardiac disease is the most prevalent comorbidity in the elderly as well as the number one cause of mortality in this age group, the Eagle Criteria and subsequent Revised Cardiac Risk Index (RCRI) were developed to estimate the risk of cardiac complications in patients undergoing non-cardiac surgery. The obvious shortcomings of these risk indices are that they neglect non-cardiac organ systems and poorly capture the functional heterogeneity of the elderly surgical patient.

In an effort to remedy the deficiencies of the above mentioned risk assessment tools in the elderly, some investigators have advocated for the use of multidimensional assessments of the elderly, such as the Comprehensive Geriatric Assessment (CGA) [21]. The CGA encompasses physical, psychosocial, and environmental factors that impact outcomes, allowing a coordinated and optimized treatment plan [22]. Subsequently, the Preoperative Assessment of Cancer in the Elderly (PACE) was developed to predict postoperative outcomes, and incorporates the multifaceted CGA, Brief Fatigue Inventory (BFI), ECOG, and ASA [23]. In the original investigation, a multivariate analysis showed that Instrumental Activities of Daily Living (IADL), BFI, and ASA were significantly linked to comorbidities and useful for stratifying

patients according to fitness for surgery. Although the PACE demonstrates reliable identification of those patients at risk for poor outcomes, its practicality is limited by the extensive time and expertise required for administration.

Frailty

Definitions

The medical geriatric community has for many years recognized frailty as an entity independent of diagnosed comorbidities and chronologic age in community dwelling adults that places these adults at increased risk for hospitalization, falls, institutionalization, and mortality [24••, 25••]. No single definition has been agreed upon, but two models have emerged: a frailty index of accumulated deficits [24••] and a phenotype characterized by the constellation of weight loss, weakness, slowed gait speed, exhaustion in daily activities, and low activity [25••].

The accumulated deficits model provides a method to estimate stepwise increasing odds of poor outcomes, most notably mortality, as deficits are accrued [26]. Conversely, the phenotypic definition offers a simple-to-measure index that gives a dichotomous result: at increased risk over the average population of a similar age or not. Using the phenotypic definition, a large prospective observational study with long-term follow-up demonstrated that baseline frailty was an independent predictor for death, hip fracture, dependence in activities of daily living, and hospitalization [27].

Investigations in Surgical Patients

Recently, a number of surgical series have employed the measurement of frailty in their respective patient populations and correlated these findings with patient peri-operative outcomes. The mounting evidence from retrospective and prospective studies have shown that measuring frailty as an accumulation of deficits, as well as the frailty phenotype, specifically described by Fried et al., has a robust ability to identify patients at risk for adverse outcomes: morbidity, mortality, institutionalization, and extended length of stay. Recently published surgical frailty series are summarized in Table 1.

Accumulated Deficits

Rockwood et al. have published extensively on their development of a frailty index based on itemized variables from the complete geriatric assessment (FI-CGA) encompassing frailty characteristics of symptoms, signs, disabilities, disease, and lab values [24••]. Their results demonstrate a reliable estimation of the likelihood of death, hospitalization, and the development of disability in community-dwelling older adults [28, 29]. Although calculation of a frailty index from an extensive itemized list of variables may have a high degree of validity and reliability, the applicability to a busy surgical setting is limited.

Correspondingly, investigators have adapted the deficit accumulation model to the surgical setting. Robinson et al. operationalized an eight-item frailty index to patients≥ 65 years of age undergoing elective major surgery requiring intensive care unit (ICU) care postoperatively. Concordant with the geriatric community definition of frailty, the authors captured a multifactorial picture of their patients by measuring cognition, albumin, hematocrit, history of falls, dependence in activities of daily living, and comorbidities. Accumulation of these variables demonstrated stepwise increased risk of mortality and discharge to a nursing facility [30••].

In an effort to extend a currently practiced frailty assessment to a surgical population, Dasgupta et al. published their results utilizing the Edmonton Frail Scale (EFS) in a largely orthopedic surgical population. The EFS is a nine-item patient directed self-assessment that encompasses cognition, health status, functional independence, social support, medications, nutrition, mood, continence, and functional performance. Independent of age, the authors demonstrated increasing levels of frailty carried correspondingly increasing risk for postoperative complications, increased length-of-stay, and discharge to a nursing facility [31].

As further proof-of-concept of the accumulated deficit method of measuring frailty, Velanovich et al. undertook a large retrospective study matching 11 variables from the Canadian Study of Health and Aging Frailty Index (FI) to variables already captured in the National Surgical Quality Improvement Program (NSQIP) administrative database. A stepwise increase in the risk of morbidity and mortality was observed as patients accrued an increasing burden of frailty variables that was valid across a wide range of procedure and surgery types [32]. Despite the findings of these studies, the clinical utility of these results is limited by the lack of a single standard definition, and the complexity and extensiveness of measuring some of the frailty indices, limiting adoption into clinical practice.

Frailty Phenotype

Linda Fried first proposed the phenotypic definition of frailty, and it encapsulates the functional heterogeneity of the elderly population through an objective five-component scale that includes weight loss, poor grip strength, slowed gait speed, exhaustion, and low activity [25••]. In community dwelling adults, a designation of frailty using Fried's definition carries an increased risk for falls, hospitalizations, institutionalization, disability, and mortality [25••]. In 2010, Makary and

Table 1 Summary of relevant surgical frailty studies

Author	Patients	Definition of Frailty	Outcomes
Robinson et al. [30••]	≥ 65 years, major operation requiring ICU admission	Accumulated deficits (cognition, albumin, hematocrit, weight loss, BMI, falls, dependence in ADLs, depression)	6-month mortality
Dasgupta et al. [31]	≥ 70 years, elective major surgery (82 % orthopedic)	Edmonton Frail Scale —nine-item assessment	Post-operative complications, extended LOS, and discharge to facility
Makary et al. [33••]	≥ 65 years, all types of surgery	Fried Criteria	Complications, mortality, extended LOS, and discharge to facility
Lee et al. [50]	Cardiac surgery patients	Frailty = ADL impairment, ambulation impairment, OR dementia	Mortality and discharge to a facility
Robinson et al. [51]	≥ 65 years, major operation requiring ICU admission	Six domains with 14 items	older age, CCI≥3, Hct<35 %, any functional dependence, up-and-go≥15 seconds, albumin<3.4 mg/dL, Mini-Cog≤3, fall w/in 6 months predicted discharge to a nursing facility
Tan et al. [52]	≥ 75 years, colorectal surgery	Fried Criteria	Occurrence of major complications
Courtney-Brooks et al. [53]	≥ 65 years, gynecologic oncology	Fried Criteria	Occurrence of any 30-day complication
Revenig et al. [34]	Patients undergoing major intra-abdominal operations	Fried Criteria	Occurrence of any 30-day complication
Velanovich et al. [32]	All surgical procedures	11 variables matched to NSQIP data	Morbidity and mortality

ADL activities of daily living, *CCI* Charlson Comorbidity Index, *LOS* length of stay, *NSQIP* National Surgical Quality Improvement Program

colleagues published their experience measuring the Fried Frailty Criteria in a surgical population and correlating these measurements with peri-operative outcomes. Assessed during the preoperative anesthesia clinic, the study prospectively analyzed a large cohort of patients undergoing a wide variety of surgical procedures. After controlling for surgery type, demographic factors, and traditional risk assessments, frailty was shown to identify patients at increased risk for morbidity, mortality, extended length of stay, and discharge to a long-term care facility. Notably, although the frailty assessment independently outperformed the traditional risk assessments, the authors also demonstrated the additive value of combining frailty with the ASA, Lee score, and Eagle score [33••].

To further characterize the phenotypic definition of frailty and its use as a surgical risk assessment tool, our group undertook a large prospective trial evaluating patients undergoing major intra-abdominal surgery. Our data showed that when adjusted for age and traditional risk assessments, a designation of "intermediately frail" or "frail" places a patient at increased risk for any 30-day complication (OR=2.07, 95 % CI 1.05 to 4.08, p=0.036) [34]. Furthermore, a subset analysis also demonstrated that the risk conferred by frailty remained a statistically significant predictor of 30-day morbidity in patients undergoing minimally invasive surgery (OR=5.914, 95 % CI=1.25 – 27.96, p=0.025) [35]. While our results reinforced others' conclusions, we also evaluated a variety of other laboratory values and patient self-assessments not previously investigated in surgical patients. As a predictor for postoperative outcomes, we found no utility for the Katz Activities of Daily Living, Mini Nutritional Short Form, or the Center for Epidemiologic Studies Depression Scale [34].

Another unique aspect of our study was the inclusion of all patients aged 18 years or older, in contrast to others who have only investigated surgical frailty in patients 65 years or older. As illustrated in Fig. 1 the incidence of frailty increased with age; however, we also discovered a significant portion of patients in their 40s and 50s who were deemed intermediately frail or frail [34]. Our findings highlight the importance of considering patients of all ages with these types of risk assessments. Although numbers in our study were too small for subset analyses, other investigators have shown that even patients in their 40s who are frail have higher rates of mortality compared to their non-frail peers [36].

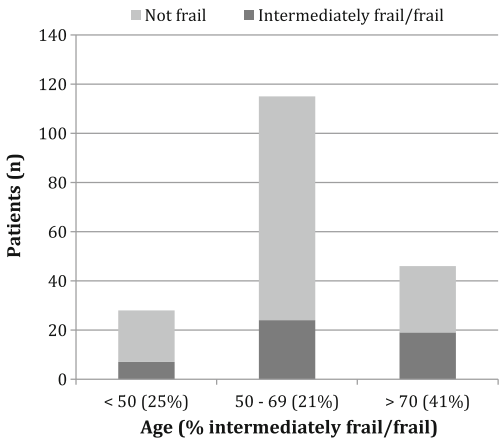

Fig. 1 Patients stratified by decade of life and frailty status

In contrast to the accumulated deficits model, the five-component Fried criteria may be more appropriate for the pre-operative setting. Although not thoroughly investigated in surgical patients at this point, each of the five components conceivably highlights an area amenable to optimization before surgery. Weight loss could be curbed with a nutrition program; poor grip strength, slow walking speed, and low activity may benefit from an exercise regimen; and exhaustion is likely co-linear with depression and may respond to appropriate psychiatric treatment. A summary of the literature on these considerations in non-surgical patients is below.

Interventions on Frailty

Nutrition

While frailty is certainly multifactorial with contributions across a wide range of organ systems, improving nutritional status is an attractive avenue to pursue improvement in patient outcomes. Anemia and hypoalbuminemia can be considered surrogates for poor nutrition and represent well-defined treatment targets in surgical patients [37, 38]. For elective orthopedic procedures, guideline concordant management includes treating anemic patients by replenishing iron, B12, and folate. Specifically, the Network for Advancement of Transfusion Alternatives (NATA) recommends that “anemia should be viewed as a serious and treatable medical condition, rather than simply an abnormal laboratory value” [39].

Similarly, sarcopenia is a well-recognized phenomenon that co-exists with hypoalbuminemia and often occurs in frail elderly patients. To counteract the muscle-wasting and disability that characterize sarcopenic patients, there are recommendations for increased protein intake in community dwelling adults [40]. These interventions could also be instituted pre-operatively. Also, although not a preoperative intervention, the colorectal and urology communities have recommended early enteral feeding with a carbohydrate and protein rich diet in colorectal resection and cystectomy patients, to promote healing, convalescence, and the prevention of disability [41–44].

Exercise

Several large, high-quality trials have demonstrated that exercise interventions in frail patients improve gait speed, balance, and functional abilities [45]. Furthermore, although yet to be investigated as a modifiable risk factor, cardiopulmonary exercise capacity has been shown to hold prognostic implications in patients undergoing major vascular surgery, even outperforming traditional risk indices [46]. Although no studies have evaluated the impact that preoperative exercise programs would have on postoperative adverse outcomes, it seems likely that "pre-habilitation" with exercise would improve the risk profile of surgical patients. Clearly, a "pre-habilitation" program that is low-cost and applicable across a wide range of socio-economic classes would be optimal.

Hypogonadism

Low serum testosterone levels have been observed in frail older men and may represent one of the few opportunities for pharmacologic intervention on the frailty phenotype [47, 48]. In a study of hypogonadal men who received 6 months of testosterone supplementation, these patients showed improvement in body mass index (BMI), waist circumference, fasting plasma glucose, and insulin resistance. Notably, these patients also exhibited an improvement their frailty scores, specifically grip strength, physical activity, and gait speed [49]. Further research is needed to assess the impact treatment of hypogonadism has on the outcomes of surgical patients.

Conclusions and Future Directions

Regardless of the approach, frailty is a dependable method to identify and distinguish between those patients at increased risk for adverse outcomes compared to the general population, regardless of age. Deficit accumulation and phenotypic frailty have proved useful for a variety of investigators, but perhaps there is a role for a combination of features of both, and even inclusion of biochemical variables. Ultimately, for a frailty assessment to prove valuable enough for wide dissemination into clinical practice it must fulfill two criteria. First, it must accurately estimate a patient’s risk for post-operative outcomes to facilitate patient counseling and shared decision-making. Secondly, a worthwhile frailty assessment will offer an opportunity for patient pre-habilitation to minimize risk and optimize outcomes.

Compliance with Ethics Guidelines

Conflict of Interest Louis M. Revenig, Kenneth Ogan, Thomas J. Guzzo, and Daniel J. Canter declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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