Chapter 9
Frailty and Surgery in the Elderly

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Introduction

Conventional surgical wisdom has long held that the elderly do not tolerate surgery as well as their younger counterparts. Numerous case series comparing outcomes such as morbidity and length of stay often corroborate that viewpoint. However, the older surgical population displays great heterogeneity, and that heterogeneity is not always obvious from preoperative morbidities and preoperative testing criteria. In fact, we have on numerous occasions been surprised by the elderly patient who beats the odds following surgery, and the patient who, ostensibly, should recover well, but does not.

Among older surgical patients, it can be quite challenging to predict who will thrive and who will develop a complication that can trigger a cascade of events that may lead to unexpected demise or permanent disability. In this chapter, we explore the emerging concept that frailty adds significant information to outcome prediction in elderly surgical candidates, beyond that of conventional preoperative criteria.

Limitations of Age as a Predictor

The effect of advanced age on surgical outcomes, independent of other patient-specific factors, is not well understood. The geriatric literature is replete with large series documenting comparable excellent surgical outcomes in the elderly [1–3]. Indeed, the risk factors for poor outcomes in the elderly are the same as for younger patients, namely comorbid illness and poor baseline functional status [4]. These factors have an increased prevalence in the elderly, though not uniformly across the entire elderly population. This varied distribution gives rise to the concept of the heterogeneity of aging.

Selection bias and the failure to account for a heterogeneous elderly population may explain why many other studies have shown that such good surgical outcomes are possible in older patients. This is particularly important because for many diseases, especially malignancies, age is often a major, if not the most important, risk factor for the development of the disease. With many groups publishing papers on their successful experience operating on octogenarians and nonagenarians, the indications for surgery in the elderly are expanding. For example, after adjusting for preoperative comorbidities, we found that age was not an independent risk factor for perioperative mortality and morbidity following pancreaticoduodenectomy [1]. Filsoufi and colleagues reached the same conclusion for patients over 80 years of age following aortic valve replacement [2]. Another group found that in elderly patients with minimal comorbid illness undergoing colon resection, there was no mortality difference in those over 70 years of age compared with younger patients [3]. In general, age is no longer an absolute contraindication to surgery.

Clinical Decision Making

A major challenge for surgeons in caring for the elderly is to determine which patients are good operative candidates. This estimation requires assessing potential operative candidates for a number of patient-specific factors, particularly comorbidities, disability, and frailty. These three factors, which are frequently used interchangeably in the common vernacular and might demonstrate overlap, are distinct clinical phenomena. In fact, there is near unanimous agreement in the gerontology community that disability and frailty are distinct clinical entities [5]. The conceptual model for frailty maintains that although disability and comorbidity may sometimes coexist with frailty, there is a significant group of frail individuals who present with neither disability nor comorbidity (Fig. 9.1). Disability is defined as difficulty in carrying out those activities that are essential for independent living, such as bathing, dressing, eating, shopping, and preparing meals. Comorbidity is the clinical manifestation of illness in an individual, such as congestive heart failure, osteoarthritis, or chronic obstructive pulmonary disease. The last factor, frailty, is a newer concept in the geriatrics literature.

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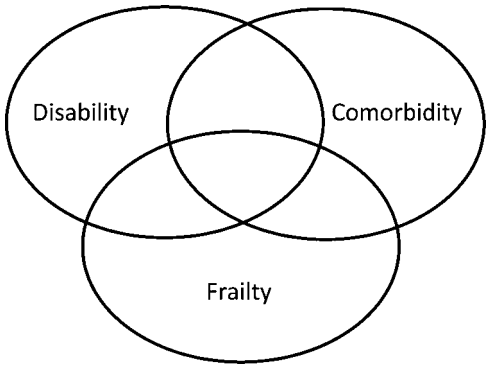

Figure 9.1 A conceptual framework for frailty, in the context of comorbidity and disability.

Frailty

Frailty in the elderly generally refers to patients with poor physiologic reserve who are at an increased risk of adverse events following exposure to stressors such as anesthesia and surgery. These clinically important adverse events include institutionalization in a long-term care facility, falls, and mortality. In 2001, Fried et al. published a standardized definition of frailty using five criteria (Table 9.1) [6]:

1. Slow gait speed
2. Low physical activity
3. Unintentional weight loss
4. Self-reported exhaustion
5. Muscle weakness

Frailty is defined as the presence of at least three of these five criteria. *Gait speed* is measured over a distance of 15 ft, with the criteria based on gender and height. The level of *physical activity* is based on the patient's kilocalorie expenditure over the prior 2 weeks using the Minnesota Leisure Time Activities Questionnaire [7]. *Unintentional weight loss* is present when the patient affirms that he or she has unintentionally lost more than 10 pounds over the preceding year. *Self-reported exhaustion* is based on the Center for Epidemiologic Studies Depression Scale (CES-D), and asks the patient to agree or disagree with these two statements: in the past week, "I felt that everything I did was an effort," and "I could not get going" [8]. Finally, *muscle weakness* is based on grip strength as measured by a hand-held dynamometer. This criterion varies by gender and body mass index. Of note, all of these criteria are quickly and inexpensively assessed in the clinic setting, lending them to easy adoption, even in a busy clinical practice.

Within the gerontology community, there remains considerable debate as to the appropriate definition of frailty. Some

Table 9.1 Frailty criteria

Criteria	Notes			
Slow gait speed	Timed 15 foot walk		*Height (cm)*	*Time (s)*
		Men		
			≤173	≥7
			≤173	≥6
		Women		
			≤159	≥7
			≤159	≥6
Low physical activity	Based on Minnesota Leisure Time Activity Questionnaire		*Weekly kcal expenditure*	
		Men	<343	
		Women	<270	
Unintentional weight loss	>10 lb weight loss in past year			
Self-reported exhaustion	Based on CES-D Depression Scale; quantifies the amount of time in the past week the patient felt the following		I felt that everything I did was an effort I could not get going	
Muscle weakness	Based on grip strength		*BMI*	*Force (kg)*
		Men		
			≤24	≤29
			24.1–26	≤30
			26.1–28	≤30
			>28	≤32
		Women		
			≤23	≤17
			23.1–26	≤17.3
			26.1–29	≤18
			>29	≤21

of the Fried criteria have been validated, while certain new ones have been proposed. Generally speaking, there is strong agreement amongst experts that the clinical syndrome represents a constellation of diseases, impairments, and/or symptoms, rather than simply the presence of one disease or condition [5]. Rothman and colleagues provided good preliminary evidence to support the use of slow gait speed, low physical activity, weight loss, and cognitive impairment as important indicators of frailty, but not self-reported exhaustion and muscle weakness [9]. In addition, they and others advocate including a number of different domains in the definition of frailty aside from just physical function, such as psychological characteristics and psychosocial factors. Rothman recommends integrating cognitive function into the frailty assessment as it is a strong predictor of adverse outcomes. While the exact definition of frailty may be in flux, there is no doubt that the presence of frailty portends a number of adverse clinical outcomes. We have found the above definition of frailty by Fried to be standardized and easy to implement.

Clinical Outcomes of Frailty

In the longitudinal Cardiovascular Health Study, which included over 5,000 community-dwelling Medicare-eligible people, subjects who met frailty criteria at baseline were more likely to be older, female, and African-American [6]. They also tended to have lower levels of education and income. Frail patients had a significantly higher mortality rate than their nonfrail counterparts at 3 and 7 years (18 vs. 3% and 43 vs. 12%, respectively). Frailty was also predictive of a number of other clinically relevant geriatric outcomes, including injurious falls, hospitalizations, and worsening disability, both in terms of performance of activities of daily living and in mobility.

In a separate longitudinal study of community-dwelling people over the age of 70 who were initially disability-free, frail individuals were also noted to experience increased mortality and incidence of chronic disability [9]. The study also found that 22% of frail patients had a long-term nursing home stay (>90 days) over 7.5 years of follow-up. Clearly, the presence of frailty has a number of ramifications in terms of clinical, economic, and quality-of-life outcomes.

Biologic Basis of Frailty

While the biologic basis of frailty remains uncertain, it likely results from multiple etiologies, rather than from one underlying cause, and affects multiple physiologic systems (Fig. 9.2) [10]. A multifactorial basis for frailty is more probable given the broad spectrum of clinical manifestations of the frailty syndrome.

While a detailed review of the current understanding of the biological underpinnings of frailty is beyond the scope of this chapter, it appears that inflammation is central to its pathogenesis. C-reactive protein (CRP), a nonspecific serum marker of inflammation, has been shown to be elevated in frail elderly patients compared to their nonfrail counterparts [11]. This finding holds true across gender and racial lines, as well as across the age spectrum over 65, and is independent of diabetes mellitus and cardiovascular disease status, two disease states associated with chronic inflammation. That same report, part of the Cardiovascular Health Study, found that frail patients were significantly more likely to have congenital heart disease, congestive heart failure, diabetes, and hypertension (Table 9.2). There was no statistically significant increase in cancer rates amongst frail patients, though that likely has more to do with study exclusion criteria, as

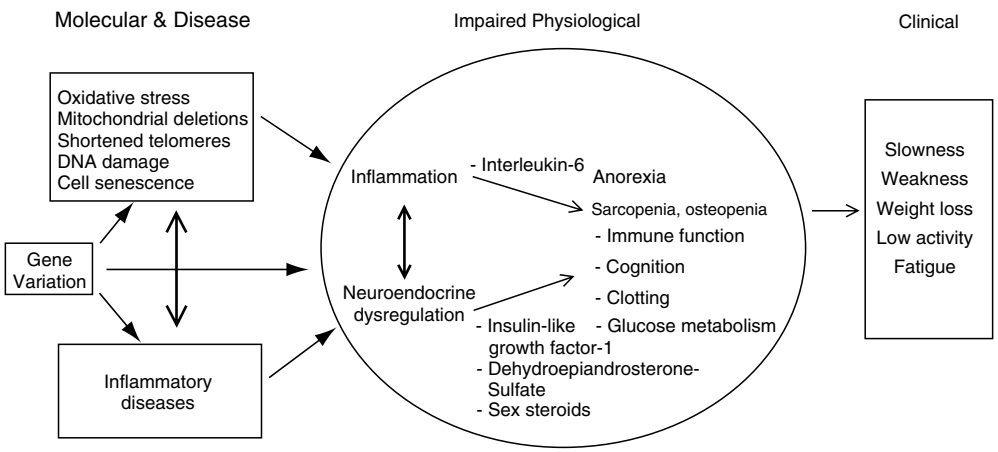

Figure 9.2 Overview of hypothesized molecular, physiological, and clinical pathway to frailty. *Arrows* pointing in both directions illustrate potential interactions between systems (from [5] reprinted with permission from The McGraw Hill Companies).

Table 9.2 Baseline disease status by frailty

Frailty indicator	Prevalence					
	Frailty	CHD[a]	CHF	Cancer	Diabetes[a]	Hypertension[a]
Not frail ($n=2289$)	48.3	15	1	14.8	18.8	37.9
Intermediate ($n=2147$)	45.3	21	4	15.5	24.5	43.9
Frail ($n=299$)	6.3	30.8	14	16.4	32.4	48.5

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patients actively being treated for a malignancy were not included in the study.

In addition to CRP, the major proinflammatory cytokine Interleukin-6 (IL-6) been shown to be predictive of mortality in the elderly [12]. IL-6 has also been extensively linked to, amongst other adverse clinical entities, osteopenia, sarcopenia (muscle loss), anemia, and insulin resistance, all of which contribute to the frailty syndrome [13] Leng et al. [29] demonstrated that elderly frail patients have significantly higher IL-6 levels than nonfrail elderly subjects, suggesting that IL-6 may also play a direct role in the pathogenesis of frailty.

Like serum IL-6 and CRP levels, plasma hypertonicity has been linked to adverse outcomes in the frail. Several theories have been proposed to explain this observation. Stookey et al. suggest that abnormalities in any of the myriad organs involved in regulating plasma homeostasis and thirst, from the pituitary to the kidneys, or states of glucose intolerance, as seen in such conditions as cancer, cachexia, diabetes, and chronic renal insufficiency, can lead to plasma hypertonicity [14]. These same underlying conditions may also play a simultaneous role in the development of frailty. As the understanding of frailty's pathogenesis improves, it is likely that biomarkers will become useful tools in screening patients and in predicting medical and surgical outcomes in the frail, similar to the MELD score for predicting 3-month mortality in surgical patients with end-stage liver disease [15].

Clinical Utility

A frailty index has many applications, including epidemiology, policy, and research. However, the most useful application may be at the bedside. In a prospective study of elderly surgical patients, we found that frail patients had a 2.5-fold increased odds of developing complications after surgery compared with their nonfrail counterparts [16]. Their hospital length of stay was twice as long as nonfrail patients for minor surgical procedures and over 80% longer for major operations. The odds of discharge to a skilled or assisted care facility were over 20 times higher in frail patients. Frailty also significantly augmented the predictive ability of other preoperative risk assessment systems, specifically the American Society of Anesthesiologists (ASA) score, and the Lee and Eagle [17–19] preoperative cardiac risk-stratification tools, in terms of postoperative complications, length of hospital stay, and discharge disposition.

Frailty may be helpful in selecting appropriate patients for surgery, particularly in settings where selection tools are vague and not validated. Clinicians have traditionally used age as a rough surrogate for triaging patients. For instance, the elderly are less likely to receive organ-directed surgery for malignancies of the breast, esophagus, stomach, pancreas, and rectum, as well as for sarcoma and non-small-cell lung cancer [20]. Moreover, a referral bias from nonsurgeons to surgeons has been observed for elective surgical procedures [21]. In a survey of Dutch cardiologists, age was the most important determinant of whether or not referrers would recommend surgery to patients with aortic stenosis 40% of the time [22]. Frailty status, rather than age, would be more helpful in the determination of overall fitness. Nonfrail individuals with resilient physiologic reserve could be selected for surgery, while frail ones could be identified to prevent operations in those patients at highest risk of a catastrophic clinical outcome.

In addition to aiding the selection of appropriate surgical candidates, a frailty index may identify patients who could, with additional interventions, become candidates for elective operations. One's frailty status is not a fixed, permanent entity; rather, frailty can have a waxing and waning course. Studenski and colleagues have developed a measure of change in frailty that quantifies patient mobility, balance, strength, endurance, nutrition, and neuromotor performance over time [23]. While its application for optimizing the timing of an operation has yet to be validated, the concept that frailty is a dynamic condition is an important one. One can imagine a related application as a measuring stick after completing a preoperative intervention aimed at medical optimization.

Indeed, there are a number of possible targets for preoperative intervention that may particularly benefit the frail elderly. Aggressive physical therapy may be of benefit. For major abdominal operations performed on the elderly, better preoperative physical performance status almost invariably predicts better recovery and a faster return to the activities of daily living (ADLs) and the instrumental activities of daily living (IADLs) [24]. While the study that demonstrated this finding was not exclusively focused on the frail, it seems logical that the frail may stand to gain the most from increased physical activity as the syndrome is characterized by low physical activity, slow gait speed, and muscle weakness.

Preoperative nutritional supplementation is another attractive preoperative intervention for the frail. In a Cochrane review of preoperative enteral supplementation in the elderly, there was an overall weight gain for participants in the 31 included trials, as well as a decrease in mortality and a shorter length of hospital stay for those patients who received preoperative supplementation [25]. Just as with preoperative physical therapy, it remains to be seen in clinical trials whether the frail elderly will benefit from this preoperative

intervention, though it does seem likely given the tight association between weight loss and the frailty syndrome.

Congestive heart failure (CHF) has been shown to be an independent predictor of postoperative complications in the elderly [26]. This suggests that, given a sufficiently lengthy window of opportunity preoperatively, frail patients, and elderly patients in general, who suffer from symptomatic CHF may benefit from pharmacologic optimization of their heart function prior to surgery in an effort to prevent postoperative complications.

Given that frail patients are more likely to suffer from postoperative, hospital-acquired complications, a frailty score may help identify which patients ought to be the subject of rigorous preventive measures to avoid the development of delirium, falls, infections, pressure sores, worsened malnutrition, and functional impairment. A number of strategies that are beyond the scope of this chapter have been described to prevent these complications, and identification of those most vulnerable to these complications using the frailty index will likely benefit from these measures.

Better risk assessment through the application of a frailty index has implications beyond just identifying opportunities to intervene: it also has implications for counseling of patients in the informed consent process. The decision to proceed with surgery should balance risk with the probability of survival and a meaningful quality of life as determined by the patient and the patient's family. Important to this discussion is the risk of discharge to a skilled nursing facility, as opposed to the patient's home. While not traditionally viewed as a surgical complication, discharge to a skilled nursing facility has a tremendous impact on patients and their families.

While a number of previously mentioned studies have demonstrated good surgical outcomes in elderly patients, a major criticism of these studies is their inherent selection bias. Patients who receive operations have been vetted by the referral process to a surgeon, as well as the surgeon's decision as to proceed with the surgery. Additionally, many of these results are from centers of excellence that have high patient volumes, as well as the resources, staff, and protocols necessary to care for these patients perioperatively.

It should be pointed out, however, that although frailty status can be an important aide in making decisions about management of patients, the heterogeneity of aging, the dearth of data regarding surgical outcomes in the frail, and the broad spectrum of patients' goals from surgery necessitate a highly individualized approach to care for the frail elderly.

Research Utility

Frailty may demonstrate particular utility in research, as its criteria become more standardized and its prognostic implications better defined. It has been well documented that the elderly are underrepresented in oncology clinical trials. In a study of 15 types of malignancies, Hutchins et al. found that while 63% of the US population comprises individuals over the age of 65, only 25% of cancer clinical trial participants are elderly [27]. While the reasons for this disparity are many, there is no doubt that clinician bias, at least in some part, is to blame. One half of surveyed oncologists stated that they deem elderly patients inappropriate for referral to clinical trials based on chronologic age alone [28]. A standardized frailty scoring system with predetermined cutoff points could be used as exclusion criteria in place of some of the more subjective and sometimes arbitrary considerations that are widely used, and thereby boost enrollment of elderly patients into clinical trials. Vulnerable elderly patients would still be excluded, while an important subgroup of suitable elderly candidates could be included.

Aside from using frailty to make clinical trial enrollment more equitable and representative of the population, knowledge about the aging process and frailty itself may be the endpoint of many future studies. An aging population and its incumbent economic considerations will likely drive research aimed at delaying or preventing the development of frailty, as well as trials to test interventions intended to minimize the effect of frailty on patient longevity, resource utilization, and quality of life.

Conclusion (Table 9.3)

Frailty is a multidomain syndrome that reflects poor physiologic and functional reserve and predicts a number of adverse clinical outcomes in surgery. We have found that the use of frailty as a clinical predictor adds significant value beyond other preoperative predictors, augmenting their ability to anticipate untoward postoperative events. Utilizing a standardized definition of frailty for future research in this highly vulnerable population may ultimately allow patients to be better risk-stratified for preoperative decision making. Increased awareness of the frailty syndrome and its clinical implications will undoubtedly improve care in older patients and improve their overall health outcomes.

Table 9.3 Frailty summary

Frailty is a multifactorial syndrome of poor physiologic reserve that puts patients at increased risk of adverse events following exposure to stressors
The standard definition of frailty uses the following five criteria slow gait speed, low physical activity, unintentional weight loss, self-reported exhaustion, and muscle weakness
Frailty is a better predictor of postoperative complications than a number of commonly used risk-stratification tools
Frailty can help with patient selection, risk stratification, and identification of patients who would benefit from preoperative risk-reduction interventions

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