



Preoperative Frailty Evaluation: A Promising Risk-stratification Tool in Older Adults Undergoing General Surgery

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ABSTRACT

Purpose: General surgical procedures are among the most commonly performed operations in the United States. Despite advances in surgical and anesthetic techniques and perioperative care, complications after general surgery in older adults remain a significant cause of increased morbidity, mortality, and health care costs. Frailty, a geriatric syndrome characterized by multisystem physiologic decline and increased vulnerability to stressors and adverse clinical outcomes, has emerged as a plausible predictor of adverse outcomes after surgery in older patients. Thus, the goal of this topical review is to evaluate the evidence on the association between preoperative frailty and clinical outcomes after general surgery and whether frailty evaluation may have a role in surgical risk-stratification in vulnerable older patients.

Methods: A PubMed database search was conducted between September and October 2018 to identify relevant studies evaluating the association between frailty and clinical outcomes after general surgery. Key words (*frailty* and *surgery*) and Medical Subject Heading term (*general surgery*) were used, and specific inclusion and exclusion criteria were applied.

Findings: The available evidence from meta-analyses and cohort studies suggest that preoperative frailty is significantly associated with adverse clinical outcomes after emergent or nonemergent general surgery in older patients. Although these studies are limited by a high degree of heterogeneity of frailty assessments, types of surgery, and primary outcomes, baseline frailty appears to increase risk of postoperative complications and morbidity, hospital length of stay, 30-day mortality, and long-term mortality after general surgical procedures in older adults.

Implications: Evidence supports the further development of preoperative frailty evaluation as a risk-stratification tool in older adults undergoing general surgery. Research is urgently needed to quantify and differentiate the predictive ability of validated frailty instruments in the context of different general surgical procedures and medical acuity and in conjunction with existing surgical risk indices widely used in clinical practice. Practical applicability of frailty instrument as well as geriatrics-centered outcomes need to be incorporated in future studies in this line of research. Furthermore, clinical care pathways that integrate frailty assessment, geriatric medicine focused perioperative and postoperative management, and patient-centered interdisciplinary care models should be investigated as a comprehensive intervention approach in older adults undergoing general surgery. Finally, early implementation of palliative care should occur at the outset of hospital encounter in frail older patients who present with indications for emergent general surgery. (*Clin Ther.* 2019;41:387–399) Published by Elsevier Inc.

Key words: frailty, general surgery, mortality, postoperative complications.

INTRODUCTION

The population in the United States is rapidly aging. Although the number of Americans aged ≥ 65 years was 43 million in 2012, this number is expected to

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be more than doubled by 2060.¹ Interestingly, this rapid rate of population aging has been outpaced by an increase in number of older patients who need surgical intervention as a main modality of treatment.^{2,3} It is estimated that more than half of the surgeries performed in the United States are provided to patients aged >65 years. Moreover, it is estimated that a surgeon's average caseload had increased by 14% to 47% from year 2000 to 2010 in all surgical fields because of an aging population.² Thus, the growth in demand for surgical services in older patients poses a new challenge for surgeons.

Postoperative complications in older adults remain a significant cause of increased costs, hospital length of stay (LOS), and patient distress and reported symptoms despite major advances in surgical and anesthetic techniques and perioperative care.³ By one estimate, 7% of patients who underwent non-cardiac surgery experienced at least 1 postoperative complication that led to a 78% increased hospital cost and 114% increased LOS.⁴ These complications after non-cardiac surgery frequently occurred within 30 days of the procedure.⁵ Moreover, postoperative complications were more common with increasing age, with 20% of patients aged ≥ 80 years experiencing ≥ 1 complications compared with 12.1% in patients aged <80 years.^{6,7} The high frequency of these surgery-induced complications are particularly alarming because they were more important determinants of mortality after major non-cardiac surgery than either preoperative or intraoperative risk factors.⁶ Given that postoperative complications are common and have significant medical and financial consequences and that surgical interventions are exceedingly common in an older population that is vulnerable to surgery-associated adverse sequelae, there is an urgent need to validate tools that accurately and reliably identify older adults at increased risk of surgical complications. Such validated tools would guide clinicians in risk-stratifying older patients before surgery with a goal to reduce surgery-induced morbidity and mortality and to improve quality of care.

The risk assessment of surgical outcomes in older adults has historically focused on age and preexisting medical comorbidities.^{3,6,8} Examples of surgery risk-stratification tools used by clinicians include the American Society of Anesthesiologists (ASA) Physical Status Classification System, Acute Physiology and

Chronic Health Evaluation, Physiologic and Severity Score for the Enumeration of Mortality and Morbidity, and Goldman Cardiac Risk Index.⁹ However, the predictive accuracy of these tools is quite variable among different patient populations, surgery indication and procedure performed, and age groups. A likely explanation for the limitation of these risk-stratification strategies may be their inability to capture physiologic compromise unique to older adults. For instance, these tools typically assess physiologic compromise of a few select end organs (ie, heart failure, renal failure); however, specific physiologic compromise of these organs likely do not capture a more global physiologic decline pertinent to the decrease in resilience to stress in older patients.^{10,11} Thus, the ability to better quantitate physiologic reserve in older patients may be key to improving the inexact science of preoperative risk assessment.

Frailty is a geriatric syndrome characterized by multisystem physiologic decline and increased vulnerability to stressors and adverse clinical outcomes.^{12,13} For example, frailty in the nonsurgical population was found to be independently predictive of incident falls, worsening mobility or disability, hospitalization, morbidity, and mortality in a large number of studies.^{14–16} Although frailty as a medical syndrome and its application as a measure of decreased physiologic reserve are well recognized, there is no gold standard definition of frailty that is universally used in the clinical and research setting. Buta et al¹⁷ recently systematically categorized the different purposes and contexts of use for frailty instruments frequently cited in the research literature and identified 67 such instruments. The Physical Frailty Phenotype (phenotype) was the most used instrument, followed by the Deficit Accumulation Index (Frailty Index; FI). In the phenotype model described by Fried et al,¹⁵ frailty is characterized by 5 clinical features—decline in lean body mass, grip strength, endurance, walking speed, and physical activity. Patients who display ≥ 3 features are deemed frail, 1 to 2 features are pre-frail, and 0 are non-frail. In the FI model developed by Rockwood et al¹⁸ in the Canadian Study of Health and Aging (CSHA), frailty is conceptualized as a multidimensional risk state quantifiable by the number of deficit accumulation. Regardless of the definition, frailty has emerged as an important assessment tool for

determining physiologic reserve and vulnerability in the geriatric population and has recently gained attention as a potential risk-stratification tool in surgical patients.

The relationship between frailty and postoperative outcomes in various surgical specialties has been a hot topic over the past few years.³ In a recent systematic review, Lin et al¹⁹ evaluated 23 studies that spanned cardiac, oncologic, general, vascular, and hip fracture surgeries in patients aged 75 to 87 years. Twenty-one different instruments were used to measure frailty in these studies. Regardless of how frailty was measured, strong evidence was noted in the association of frailty with increased 30-day, 90-day, and 1-year mortality; postoperative complications; and LOS. Similar findings from other studies strongly suggest that frailty assessment in the perioperative period would be helpful in identifying those patients who are more susceptible to adverse surgical outcomes, and that this line of investigation is warranted to better define these relationships and to further develop frailty instruments into preoperative risk stratification tools.^{20–22}

General surgical procedures are among the most commonly performed operations in the United States. By one estimate, 32.9% of all surgeries completed in patients aged ≥ 80 years were general surgical procedures.⁶ Among these procedures, colectomy (18.2%) and cholecystectomy (10.5%) comprised more than a quarter of general surgeries performed. Furthermore, older patients represented 28.8% of all major emergency general surgery cases, with partial colectomy, small-bowel resection, cholecystectomy, operative management of peptic ulcer disease, lysis of peritoneal adhesions, appendectomy, and laparotomy collectively accounting for 80% of all procedures, 80.3% of deaths, 78.9% of complications, and 80.2% of inpatient costs.^{23,24} Given the importance of general surgery as a common and main therapeutic intervention in older patients, its associated risk of complications and other adverse clinical outcomes, it is paramount to develop reliable risk-stratification tools to aptly guide clinicians and patients in medical decision making when general surgery is offered as a treatment. A critical first step to achieving this goal is to determine whether frailty, a measure of physiologic reserve and vulnerability in older patients, is predictive of adverse clinical outcomes after general surgery. Thus, the goal of this

narrative review is to summarize and evaluate recently published studies that investigated the association between preoperative frailty and clinical outcomes, including surgical complications, mortality, and hospital LOS, after general surgery in older patients.

MATERIALS AND METHODS

PubMed database was searched to identify relevant studies that evaluated the association between frailty and clinical outcomes after general surgery with the use of key words (including *frailty* and *surgery*) and Medical Subject Heading term (*general surgery*). The search was conducted between September and October 2018. Filters were applied to limit results to the English language and human research. No date restrictions were used. The criteria for inclusion in this topical review were (1) the patient population underwent a surgical procedure, (2) frailty was assessed using a validated method that included more than one domain of health deficit consistent with current conceptual idea of frailty,^{15,25} (3) frailty was a main variable of interest in the study, and (4) the association between frailty and postoperative clinical outcomes was evaluated. Exclusion criteria included conference abstracts, studies that assessed frailty as a single measure (eg, gait speed only), and studies that used large-scale database analysis to assess frailty and surgery outcomes. Large-scale database analysis studies were excluded because of issues such as incomplete data capture inherent to this type of study design. Search results and reference lists of identified articles were manually reviewed to further identify pertinent articles.

RESULTS

The search strategy described in the section above identified a number of systematic reviews and meta-analyses and prospective cohort studies. In total, 1257 records were identified through database search and were screened. Full-text articles of 38 of these records were assessed for eligibility. Twenty-nine of these full-text articles were excluded according to selection criteria described in the section above (ie, frailty was not assessed using a validated method [n = 10], frailty was not a main variable of interest [n = 10], association between frailty and postoperative outcomes was not evaluated [n = 3], and large-scale database analysis was used [n = 6]).

No randomized controlled trials were identified. The major findings of these studies (ie, systematic review and meta-analysis [$n = 2$] and observational studies [$n = 7$]) are reported in this narrative review.

Systematic Review and Meta-analysis

The association between frailty and clinical outcomes after general surgery has been examined by Hewitt et al²⁶ in a recently published systematic review and meta-analysis. In this study, 9 prospective observational studies published from 2010 to 2017 were included in analysis. All studies used a validated method of frailty assessment (ie, Physical Frailty Phenotype, Deficit Accumulation Index, Groningen Frailty Indicator [GFI], 7-point clinical frailty score).¹⁷ In total, 2281 patients (49.3% men) with mean age ranging from 61 to 77 years were analyzed. Surgery types included elective and emergent upper and lower abdominal, colorectal cancer, and gastric cancer surgeries among others. The prevalence estimates for baseline frailty ranged from 10.4% to 37.0%, and pre-frailty ranged from 31.3% to 45.8%. Patients who were determined to be frail and pre-frail had higher 30-day mortality (8%; 95% CI, 4%–12%; $I^2 = 0\%$) than patients who were non-frail (1%; 95% CI, 0%–2%; $I^2 = 75\%$). Moreover, postoperative complications, assessed using the Accordion Severity Classification and the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) definitions,²⁷ were more common in patients who were frail (24%; 95% CI, 20%–31%; $I^2 = 92\%$) than in patients who were pre-frail (9%; 95% CI, 5%–14%; $I^2 = 82\%$) or non-frail (5%; 95% CI, 3%–7%; $I^2 = 70\%$). Finally, the mean LOS was longer in frail patients (9.6 days; 95% CI, 6.2–12.9 days) than in patients who were non-frail (6.4 days; 95% CI, 4.9–7.9 days). The researchers concluded that frailty in patients who underwent general surgery was associated with poorer postoperative clinical outcomes, including surgical complications, mortality, and hospital LOS.²⁶

A second systematic review and meta-analysis on this topic focused on preoperative frailty as a predictor of morbidity and mortality after major elective abdominal surgery.²⁸ In addition to the assessment of clinical outcomes after abdominal surgery, the researchers also evaluated the performance of different frailty metrics, given that a

multitude of frailty definitions and scoring systems have been used in this type of studies. Therefore, all possible definitions of frailty were considered, including studies that used measures other than a validated method of frailty assessment.¹⁷ In total, 12 different definitions of frailty that incorporated 1 to 70 domains in different combinations were included. Moreover, studies that used large-scale database analysis to assess frailty and surgery outcomes were included in addition to prospective cohort studies. In total, 35 studies with 1,153,684 patients with mean age ranging from 58 to 85 years and a frailty prevalence ranging from 0.5% to 67.2% were analyzed. Major abdominal surgery was defined as all gastrointestinal (colorectal, gastric, small bowel, hepatic, pancreatic resection), urologic (nephrectomy, cystectomy, prostatectomy), and gynecologic (uterus and ovary resection, pelvic floor reconstruction) operations, undertaken for any indication. The primary outcomes were 30-day major morbidity, defined by the Clavien–Dindo classification,²⁹ NSQIP,²⁷ or the Veterans Affairs Surgical Quality Improvement Program classification³⁰; short-term mortality, defined as death within 90 days after operation; and long-term mortality, defined as any death occurring before 1 year after surgery. With the use of random-effects meta-analysis, frailty was associated with increased risk of postoperative major morbidity (odds ratio [OR] = 2.56; 95% CI, 2.08–3.16), short-term mortality (OR = 5.77; 95% CI, 4.41–7.55), and long-term mortality (hazard ratio = 2.71; 95% CI, 1.63–4.49). Moreover, all domains of frailty measurements were associated with the occurrence of postoperative major morbidity (OR = 1.09; 95% CI, 1.00–1.18), and no moderator effect was observed according to the number of frailty components. Given these results, the researchers of this study concluded that baseline frailty was significantly associated with an increased risk of postoperative morbidity and mortality after major abdominal surgery regardless of the frailty definition.²⁸ Furthermore, data from this analysis did not support the superiority of one frailty definition or any particular domain of frailty instruments.

The analyses presented thus far have provided evidence that preoperative frailty is significantly associated with increased poor clinical outcomes after general surgery. Although these analyses were limited by a high degree of heterogeneity of frailty

assessments, types of surgery, and primary outcomes, baseline frailty appears to increase risk of postoperative complications and morbidity, hospital LOS, 30-day mortality, and long-term mortality after general surgical procedure in older adults. Given an absence of data from randomized trials, these meta-analyses have provided the most meaningful results to date in this area of research.

Observational Studies

A number of prospective studies have investigated the association of frailty and postoperative clinical outcomes.^{31–37} Because of a lack of data from randomized trials, well-conducted prospective studies exploring these associations may yield better insight into this clinically important question in geriatric medicine. Moreover, given the heterogeneity in the type of surgeries performed and clinical outcomes measured in studies of this type, high-quality observational studies can provide evidence specific to the acuity and severity of the surgical intervention performed. In the next section, we summarize findings from these studies, grouped by those that focused on emergent versus nonemergent surgeries. Key findings from these studies are summarized in the [Table 1](#).

Emergent Surgery

Emergent general surgery leads to significant morbidity and mortality in older patients. Although clinical outcomes after elective operations are similar in younger and older patients, the latter has higher rates of complications and mortality after emergency surgery.⁷ Abdominal surgical procedures such as colectomy, small-bowel resection, cholecystectomy, appendectomy, and others constitute ~80% of all emergent surgeries performed in older patients.^{23,24} The association of frailty and in-hospital complications after emergent general surgery in older patients was examined in a study published by Joseph et al.³¹ In this prospective study, 220 consecutive patients aged ≥ 65 years who presented to a single acute care surgery trauma center were enrolled. The mean age of the participants was 75.5 (7.7) years (56% men), and 37% were frail as determined by a modified 50-variable Rockwood Preadmission Frailty Index (ie, FI score ≥ 0.25). Surgeries that were performed included appendectomy, cholecystectomy, hernia repair, and

bowel resection. The in-hospital postoperative complications were categorized using NSQIP definitions to include major (eg, sepsis, intraabdominal abscess, enterocutaneous fistula, cholangitis, delirium, pneumonia, pulmonary emboli, deep venous thrombosis, hemorrhage/ischemia, acute kidney injury, deep surgical site infection) and minor (eg, urinary tract infection, superficial surgical site infection, gastroenteritis) complications. In this cohort, 35% of patients had postoperative complications and 19% had major complications. With the use of multivariate regression analysis, the FI independently predicted the development of in-hospital complications (OR = 2.13; 95% CI, 1.09–4.16; $P = 0.02$) and major complications (OR = 3.87; 95% CI, 1.69–8.84; $P = 0.001$) with 80% sensitivity and 72% specificity. Moreover, age and ASA score were not predictive of postoperative and major complications. Taken together, this study provided evidence that the use of frailty measurements may be superior to chronologic age in predicting outcomes and may provide added insight to postoperative hospital course in older patients who undergo emergent general surgery.³¹

The diagnostic accuracy of screening instruments for frailty in emergent general surgery is largely unknown. Kenig et al³² explored the predictive value of 6 screening instruments in geriatrics, several of which were validated frailty assessment tools, in a cohort of 184 consecutive older patients who underwent emergent abdominal surgery within 24 h after admission to a tertiary referral hospital. In this study, the patients' mean age was 76.9 (5.8) years (47% men). The prevalence of frailty as assessed by the following instruments were: Vulnerable Elderly Survey/VES-13 (70.7%),³⁸ Triage Risk Screening Tool (63.6%),³⁹ Geriatric-8 (79.9%),⁴⁰ GFI (54.3%),⁴¹ Rockwood FI (50%),⁴² and Balducci (50%).⁴³ The most common surgical indications were cholecystitis (27%), ileus (adhesions, incarcerated hernia; 20%), appendicitis (13%), and ulcer perforation (9%). The primary outcomes were 30-day mortality (24.5%) and 30-day morbidity (58.7%; 21.7% with minor complications and 37% with major complications) as defined by the Clavien–Dindo complications scale.²⁹ Multivariate regression analyses found that all screening instruments, except Triage Risk Screening Tool and Rockwood FI, were independent predictors of 30-day

Table 1. Cohort studies that evaluated association between preoperative frailty and postoperative adverse outcome.

Cohort Study Variable				Association With Adverse Outcomes				
Author	Study Population	Type of Surgery	Frailty Measure	Postoperative Complications	Hospital Length of Stay	Discharge to Facility	30-day Mortality	90-day or long-term mortality
Emergent surgery								
Joseph et al ³¹	N = 220 Age: 75.5 (7.7) years Men: 56%	Abdominal	50-variable Rockwood Preadmission FI	+	ND	ND	ND	ND
Kenig et al ³²	N = 184 Age: 76.9 (5.8) years Men: 47%	Abdominal	VES-13 Geriatric-8 GFI Balducci	+	ND	ND	+	ND
Nonemergent surgery								
Makary et al ³³	N = 594 Age: 71.3 years (range, 65–94 years) Men: 40%	General	Fried phenotype	+	+	+	ND	ND
Hewitt et al ³⁴	N = 325 Age: 77.3 (8.2) years Men: 43%	General	CSHA 7-point scale	ND	+	ND	+	+
Robinson et al ³⁵	N = 201 Age: 74 (6) years Men: 98%	Abdominal	7-domain based score	+	+	ND	ND	ND
Saxton et al ³⁶	N = 226 Age: 61 (13) years; Men: 47%	General	CSHA 70-point scale	+	ND	ND	–	ND
Tegels et al ³⁷	N = 180 Age: 69.8 years (range, 73–88 years) Men: 59%	Abdominal	GFI	+	–	ND	+	–

CSHA = Canadian Study of Health and Ageing; FI = Frailty Index; GFI = Groningen Frailty Index; ND = not done; VES-13 = Vulnerable Elderly Survey; + = $P < 0.05$; – = P is not significant.

mortality and morbidity (OR = 1.4–2.4 and 1.5–2.4, respectively) in the frail compared with non-frail patients. Moreover, the sensitivity and negative predictive values in postoperative mortality ranged from 60% to 91% (Rockwood–VES-13) and from 30% to 93% (GFI–VES-13), respectively. In case of postoperative morbidity, these values were 52% to 85% (Rockwood–VES-13 and Geriatric-8) and 44% to 70% (Rockwood–VES-13), respectively. From these results, the researchers concluded that the VES-13 was the best screening instrument for adverse postoperative outcomes after emergent abdominal surgery in older adults.³²

The results of the studies described in the preceding paragraphs suggested that frailty assessment in the setting of emergent abdominal surgery in older patients may help to predict in-hospital complications and 30-day mortality. Moreover, preoperative frailty status may be a better predictor than chronologic age in this surgical setting. This finding is consistent with a large database analysis of >35,000 older Americans who underwent emergent general surgery in which a modified CSHA FI was deemed to be a superior predictor of 30-day mortality than ASA grading.⁴⁴ However, it is also evident that the discrepant findings in FI from the studies of Joseph et al³¹ and Kenig et al³² that much more research is needed to determine which frailty instrument is best suited for risk-stratification in emergent general surgeries.

Nonemergent Surgery

The first study to investigate frailty as a predictor of surgical complications and whether it enhances known perioperative risk models was conducted by Makary et al.³³ This study prospectively followed 594 patients aged ≥ 65 years who presented to a university hospital for elective surgery categorized as major procedure, intraabdominal procedure, open procedure, or procedure for cancer. Preoperative frailty status was assessed using the Fried phenotype determined by 5 measures (ie, weakness, weight loss, exhaustion, low physical activity, slowed walking speed), and the patients were categorized as frail (10.4%), pre-frail (31.3%), or non-frail (58.3%).¹⁵ The primary outcome measures were 30-day surgical complications as defined by NSQIP, LOS, and discharge disposition from acute hospitalization. With the use of regression analyses and after adjusting for known surgical risk indices,

preoperative frailty was found to be an independent predictor of these adverse outcomes. Specifically, frailty was associated with increased postoperative complications (OR = 2.54; 95% CI, 1.12–5.77), LOS (incidence rate ratio = 1.69; 95% CI, 1.28–2.23), and discharge to a skilled or assisted-living facility (OR = 20.48; 95% CI, 5.54–75.68). Pre-frailty was similarly associated with postoperative complications (OR = 2.06; 95% CI, 1.18–3.60), LOS (incidence rate ratio = 1.49; 95% CI, 1.24–1.80), and discharge to a skilled or assisted-living facility (OR = 3.16; 95% CI, 1.0–9.99). In addition, preoperative Fried phenotype improved predictive ability of known surgical risk indices, including the ASA, Lee, and Eagle scores ($P < 0.01$). These findings led the researchers to conclude that frailty status before surgery can independently predict adverse outcomes in older surgical patients and may enhance conventional risk-stratification models.³³

Clinical outcomes such as 30- and 90-day mortality and hospital readmission, in addition to LOS in frail older patients after general surgery, were investigated in a United Kingdom study.³⁴ The researchers of this prospective study assessed 325 consecutive patients with a mean age of 77.3 (8.2) years (43% men) who were admitted to 3 acute surgical admission units with diagnoses in keeping with acute general surgical conditions. Frailty status measured with the use of a 7-point clinical frailty score derived from CSHA was severe (6%), moderate (13%), or mild (8%).¹⁸ The patients underwent general surgery procedures that were categorized as minor, intermediate, major, or complex major operations. Compared with the non-frail group, patients in the frail group had higher mortality at 30 days (OR = 4.0; 95% CI, 1.1–15.2; $P = 0.04$) and 90 days (OR = 3.0; 95% CI, 1.3–7.4; $P = 0.02$). The LOS in the frail group was longer than that in the non-frail group (11.1 days [95% CI, 7.2–15.0 days] versus 7.6 days [95% CI, 6.1–9.2 days]; $P = 0.03$), consistent with that reported by Makary et al.³³ Hospital readmission between the frail and non-frail groups did not differ (OR = 1.1; 95% CI, 0.5–2.3). These findings added evidence that morbidity and mortality after acute general surgery are increased in older adults who are frail.³⁴

The association of baseline frailty and clinical outcomes after elective colorectal surgery in older adults was examined in a study published by Robinson et al.³⁵ This prospective cohort study

conducted at the Denver Veterans Affairs Medical Center included 201 patients aged 74 (6 years (98% were men), 72 of whom underwent colorectal operations. Surgical procedures performed for the colorectal group included right colectomies (36%), left colectomies (22%), sigmoid colectomies (31%), and colostomy takedowns (11%). Preoperative frailty status was ascertained with the use of 7 baseline traits, which were Katz Score ≤ 5 , Timed Up-and-Go ≥ 15 seconds, Charlson Index ≥ 3 , anemia defined as hematocrit $< 35\%$, Mini-Cog score ≤ 3 , albumin < 3.4 gm/dL, and ≥ 1 fall within past 6 months. A 7-domain-based score was then calculated as the total number of positive traits—frail (≥ 4 traits), pre-frail (2–3 traits), and non-frail (0–1 trait). The Veterans Affairs Surgical Quality Improvement Program definitions were used to determine postoperative complications.³⁰ Categories of complications included cardiac (cardiac arrest, myocardial infarction), respiratory (pneumonia, pulmonary embolism, reintubation), renal insufficiency, neurologic (cerebral vascular accident, coma), postoperative infection (deep or superficial surgical site wound infection, urinary tract infection, sepsis), deep vein thrombosis, and re-operation. In this cohort, preoperative frailty was associated with higher rates of complications after colorectal surgery (frail, 58%; pre-frail, 40%; non-frail, 21%; $P = 0.016$) independent of age. Compared with the non-frail group, frail patients were 13.36 times more likely to have a complication (95% CI, 2.56–69.81; $P = 0.002$) and pre-frail patients were 3.4 times more likely to have a complication (95% CI, 0.77–14.97; $P = 0.106$). Moreover, the receiver operating characteristic curves examining frailty's ability to forecast complications was 0.7 (95% CI, 0.58–0.83; $P = 0.004$) for colorectal surgery. In addition to postoperative complications, patients who were frail also had longer hospital stays (frail, 14 [11.0] days; non-frail, 6 [3.6] days; $P < 0.001$) and higher 30-day readmission rates (frail, 29%; non-frail, 6%; $P = 0.046$). Thus, these findings added to the rationale that preoperative frailty evaluation may be a plausible risk-stratification tool in older adults subjected to general surgery.^{33,35}

The association between preoperative frailty and complications after elective general surgery of different complexity was also explored in a study reported by Saxton et al.³⁶ In this prospective study,

226 patients aged 61 (13) years (47% men) admitted to the hospital for general surgical operations were enrolled. Preoperative frailty was determined by CSHA FI and patients with a FI score > 0.12 was defined as frail.¹⁸ Surgical procedures the patients underwent were divided into 3 categories: (1) 31% had superficial or laparoscopic procedures for benign disease (eg, hernia repair, cholecystectomy, appendectomy), (2) 17% had open or intraabdominal procedures for benign disease (eg, pancreatectomy, enterostomy), and (3) 52% had open or laparoscopic procedures for malignant disease (eg, esophagectomy, gastrectomy, colectomy, Whipple). Primary outcomes ascertained were occurrence and number of 30-day complications and severity of complications determined by the Clavien–Dindo classification (ie, none or minor [Clavien class I] versus severe [Clavien class II–V] complications).²⁹ In this cohort, patients who had ≥ 1 postoperative complications had higher median preoperative FI than patients without complications (0.075 [interquartile range, 0.046–0.118] versus 0.059 [interquartile range, 0.045–0.089]; $P = 0.007$). Moreover, multiple logistic regression analysis found that FI > 0.12 was associated with increased risk of postoperative complications (OR = 2.71; 95% CI, 1.08–6.78; $P = 0.03$) but not mortality (OR = 0.42; 95% CI, 0.04–4.20; $P = 0.5$). Hence, results from this study suggested that preoperative frailty status as measured by CSHA FI may help identify patients at higher risk of postoperative complications.

Tegels et al³⁷ published a study specifically evaluating the relationship between gastric cancer surgical complications and mortality and preoperative assessment of frailty. In this study, 180 patients (58.9% men), aged 69.8 years (range, 73–88 years) with histologically proven gastric adenocarcinoma underwent surgical treatment in a community teaching hospital that was a referral center for surgical treatment of gastric malignancy. Frailty was assessed with the use of the GFI, a 15-item (scored 0 or 1 point) questionnaire that evaluates mobility, self-perceived physical fitness, nourishment (ie, weight loss), morbidity (ie, polypharmacy), and cognition.⁴⁵ Surgical procedures performed were total gastrectomy (23.9%), subtotal gastrectomy (57.8%), gastroenterostomy (9.4%), and explorative laparotomy (8.9%) with an overall in-hospital mortality of 8.3%. Patients who were more frail (ie,

GFI ≥ 3) had a higher mortality rate of 23.3% compared with 5.2% in patients with GFI < 3 (OR = 4.0; 95% CI, 1.1–14.1; $P = 0.03$). In addition, patients with GFI ≥ 3 had increased risk of serious adverse events (Clavien–Dindo grade $\geq 3a$) compared with patients with GFI < 3 (OR = 3.62; 95% CI, 1.53–8.58; $P = 0.04$) independent of age, type of surgery, tumor stage, ASA classification, and neoadjuvant chemotherapy in multivariate analysis.²⁹ Higher GFI score was not associated with 6-month mortality or hospital LOS. In a subset of 125 patients who underwent surgery with curative intent, in-hospital mortality was 27.3% in patients with GFI ≥ 3 compared with 5.7% in patients with GFI < 3 (OR = 4.6; 95% CI, 1.0–20.9; $P = 0.05$). Thus, these findings suggested that frailty assessment that used GFI can help to identify individuals at risk for higher adverse events and in-hospital mortality after gastric cancer surgery.³⁷

Although these studies were limited by heterogeneity of surgical interventions and frailty measures and outcome assessments, they added to the evidence base that frailty in older patients may influence clinical outcomes after nonemergent general surgery. The finding that preoperative Fried phenotype improved predictive ability of known surgical risk indices further suggested that frailty instruments have a role in improving the clinicians' ability to perform risk assessment before nonemergent general surgery in older patients.

RECOMMENDATIONS FOR FUTURE DIRECTIONS

In summary, the studies presented in this topical review strongly suggest that preoperative frailty is associated with increased poor clinical outcomes after emergent or nonemergent general surgery in older adults. The outcomes that may be adversely influenced by baseline frailty include postoperative complications and morbidity, hospital LOS, 30-day mortality, and long-term mortality. These findings have several implications for future research and clinical care as outlined in the paragraph below.

Considerable gaps remain in knowledge about frailty as a predictive indicator for outcomes after general surgery.^{19,28} First, it is unclear if one frailty instrument is superior to another in this setting, given that different types of surgical procedures (eg, degree of invasiveness, duration of surgery) likely would

induce variable extent of stress responses. Moreover, the high acuity nature of emergent general surgery, frequently complicated by associated infection, bleeding, and cardiovascular decline, likely would further compromise the limited physiologic reserve in vulnerable older patients. Thus, although the identification of a single unified frailty assessment tool in the setting of general surgery would greatly enhance its adaptability and ease of use, this may not be a feasible or pragmatic approach. Future research will be needed to better quantify and differentiate the predictive ability of existing frailty instruments in the context of different surgical procedures and medical acuity in older patients undergoing general surgery. A potential approach to this type of investigation is to simultaneously administer multiple candidate frailty instruments that are based on best-available evidence, in large cohorts of older patients who undergo specific categories of surgical procedures (eg, open versus laparoscopic) and medical acuity (eg, emergency versus elective). Second, considerations should be given to the selection of frailty instruments for future investigations depending on practical applications. For instance, a short questionnaire-based instrument may be better suited for preoperative assessment before emergent surgery, given the feasibility and rapidity of its administration. Moreover, a phenotype-based instrument may not be an optimal tool in older patients who are severely deconditioned or physically incapacitated because of their inability to participate in performance-based assessment (eg, walking speed). In contrast, a frailty instrument grounded in the Deficit Accumulation Index, if robust and valid, may be well suited for elective general surgery evaluation administered in a preoperative evaluation clinic. Third, the predictive values of frailty instruments must be investigated in conjunction with existing surgical risk indices widely used in clinical practice (eg, ASA, Goldman Cardiac Risk Index). This study design will help to determine whether preoperative frailty assessment enhances known conventional risk-stratification models and whether it should be an added component, or a stand-alone tool, in preoperative risk assessment in older adults. Finally, although postoperative complications, hospital LOS, and mortality are important factors to consider in the care of older adults, other key aspects of geriatric care, including postoperative functional and cognitive decline and

quality of life, are issues that should not be overlooked. Thus, these geriatrics-centered outcomes need to be included in future studies in this line of research.

The utility of frailty assessment should extend beyond its role in preoperative risk-stratification. In fact, the positive identification of frailty in an older surgical patient should trigger the initiation of a set of interventions that may reduce morbidity and enhance functional recovery after surgery.²⁸ Potential types of interventions to be considered include (1) the Enhanced Recovery After Surgery pathways, an integrated clinical care delivery program recently found to improve clinical and functional outcomes in older patients after colorectal surgery^{46,47}; (2) prehabilitation programs that aim to optimize physical function and comorbidity preoperatively⁴⁸; and (3) geriatric interdisciplinary assessment and treatment models that have been found to improve clinical outcomes of frail older adults.¹² Although further investigation is needed, clinical care pathways that integrate frailty assessment, geriatric medicine—focused perioperative and postoperative management, and patient-centered interdisciplinary care models should be delivered as a comprehensive intervention in frail older adults undergoing surgery.

A fundamental principle in geriatric medicine is that standard indications for medical and surgical interventions may not be generalizable to older adults because age-associated changes in physiologic reserve and associated multi-morbidity could alter the risk-to-benefit ratio. Frailty, as presented in this review, was found to have promise as an important assessment tool to determine physiologic reserve and vulnerability in older surgical patients. Thus, the use of a validated frailty instrument that accurately

predicts adverse outcomes after general surgery can provide key information to help guide medical decision making for patients and their families. Emergent general surgery, given its high morbidity and mortality in older patients, is a clinical scenario in which risk-to-benefit ratio of surgical intervention could be significantly influenced by early assessment and diagnosis of frailty. Here, we propose a model of care for emergent general surgery in frail older patients that incorporates early frailty assessment and palliative care (Figure 1). Palliative care is an interdisciplinary specialty that focuses on improving quality of life for patients by providing an added layer of support (eg, pain and symptom management, goals of care discussions, care coordination) in the setting of serious illness and is provided concurrently with other disease-directed or curative treatments. In this model, frailty assessment with a validated tool is to be completed when an older patient presents to the emergency department for a condition that requires emergent general surgical intervention as the primary means of treatment. If the patient is found to be frail and the risk-to-benefit ratio of an emergent surgery increases, the medical and surgical team should introduce and include palliative care in the medical decision discussions with the patient and his or her proxy and integrate palliative care in the patient's management. Thus, palliative care is implemented at the outset of emergency department presentation and can be scaled up for patients who are highly frail. Finally, hospice care needs to be considered and administered if appropriate in patients who are severely frail and present with other advanced comorbidity and acute multi-system decompensation.

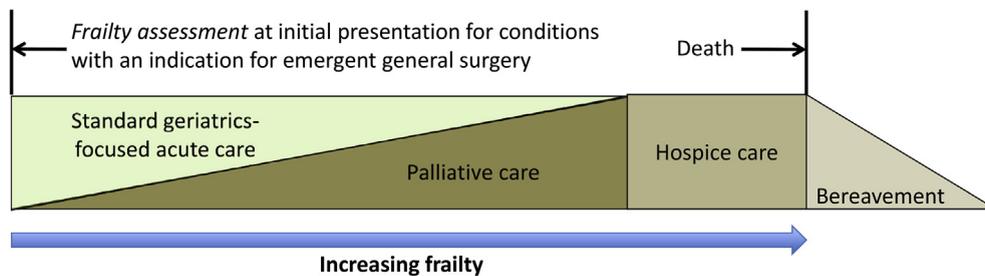


Figure 1. A model of care for emergent general surgery in frail older patients.

CONCLUSIONS

Evidence is growing that preoperative frailty is associated with increased adverse clinical outcomes after emergent or nonemergent general surgery in older adults. Although more research is critically needed in this field, frailty assessment holds promise as a preoperative risk-stratification tool in geriatric and perioperative medicine. The validation of frailty instruments in the surgical setting will likely improve patient-centered, comprehensive intervention in older adults undergoing general surgery across the spectrum of frailty syndrome.

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CONFLICTS OF INTEREST

The author has indicated no conflicts of interest regarding the content of this article.

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