Published in final edited form as:

J Surg Oncol. 2017 June ; 115(8): 997–1003. doi:10.1002/jso.24617.

Modified frailty index predicts postoperative outcomes in older gastrointestinal cancer patients

Sarah A. Vermillion¹, Fang-Chi Hsu², Robert D. Dorrell¹, Perry Shen³, Clancy J. Clark³

¹Wake Forest School of Medicine, Wake Forest Baptist Health, Winston Salem, North Carolina

²Division of Public Health Sciences, Wake Forest Baptist Health, Winston Salem, North Carolina

³Division of Surgical Oncology, Department of General Surgery, Wake Forest Baptist Health, Winston Salem, North Carolina

Abstract

Background and Objectives—Frailty disproportionately impacts older patients with gastrointestinal cancer, rendering them at increased risk for poor outcomes. A frailty index may aid in preoperative risk stratification. We hypothesized that high modified frailty index (mFI) scores are associated with adverse outcomes after tumor resection in older, gastrointestinal cancer patients.

Methods—Patients (60–90 years old) who underwent gastrointestinal tumor resection were identified in the 2005–2012 NSQIP Participant Use File. mFI was defined by 11 previously described, preoperative variables. Frailty was defined by an mFI score >0.27 . The postoperative course was evaluated using univariate and multivariate analysis.

Results—41 455 patients (mean age 72.4 years, 47.4% female) were identified. The most prevalent form of cancer was colorectal (69.3%, $n = 28\,708$) and 2.8% of patients were frail ($n = 1,164$). Frail patients were significantly more likely to have increased length of stay (11.7 vs 9.0 days), major complications (29.1% vs 17.9%), and 30-day mortality (5.6% vs 2.5%), (all $P < 0.001$). Multivariate analysis identified mFI as an independent predictor of major complications (OR 1.52, 95% CI 1.39–1.65, $P < 0.001$) and 30-day mortality (OR 1.48, 95% CI 1.24–1.75, $P < 0.001$).

Conclusions—mFI was associated with the incidence of postoperative complications and mortality in older surgical patients with gastrointestinal cancer.

Keywords

frailty; gastrointestinal cancer; modified frailty index; NSQIP; preoperative risk stratification

Correspondence: Clancy J. Clark, MD, FACS, Division of Surgical Oncology, Department of General Surgery, Medical Center Blvd., Winston-Salem, North Carolina 27157, cjclark@wakehealth.edu.

CONFLICT OF INTERESTS

The authors have no conflicts of interest.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

1 | INTRODUCTION

The worldwide population is rapidly aging—a fact that presents several challenges for the delivery of healthcare. Advancing age is associated with an increase in the incidence of cancer, with individuals over the age of 65 accounting for approximately 53% of newly diagnosed cases and 70% of all cancer deaths.^{1,2} Surgical resection of a malignancy is an established curative treatment option for a variety of cancer types, and has the capacity to prolong lifespan and improve quality of life in others.^{3,4} However, frailty is highly prevalent among the elderly, and is characterized by a loss of physiological reserve, decreased ability to maintain homeostasis, and increased vulnerability to morbidity and mortality following surgery.^{1,5–7} To assess preoperative risk, surgeons currently use tumor characteristics, patient comorbidities, and their clinical judgment. However, such assessments have resulted in the undertreatment of older patients with cancer, as well as significant debilitation among some treated with surgery.^{8,9}

A standardized, quantifiable measurement of frailty may inform clinicians of the patient's ability to tolerate surgical resection, and thus may improve patient outcomes. With the aim of identifying high-risk surgical candidates, several preoperative risk prediction models have been proposed, such as the Physiological and Operative Scoring System for enumeration of Morbidity and mortality (POSSUM), Estimation of Physiologic Ability, and Surgical Stress Score (E-PASS), NSQIP risk calculator, and comprehensive geriatric assessment (CGA).^{10–15} However, these models have several disadvantages, as they are complex, time-consuming, or inconsistent.^{16–21}

Recently, the Canadian Study of Health and Aging (CSHA) created a less complex, standardized frailty index (FI) that was based on the accumulation of physiological deficits.²² This CSHA-FI assessed 70 potential deficits that are easily identifiable during patient encounters, and was defined as the proportion of potential deficits that are present in an individual to the potential deficits that were evaluated. Subsequently, a modified frailty index (mFI) was derived by matching the CSHA-FI to 11 variables collected by the American College of Surgeons National Surgical Quality Improvement Program (NSQIP).²³ Since its creation, mFI has been found to be predictive of postoperative outcomes in several surgical populations, including those undergoing abdominal, vascular, and head and neck surgery.^{10,24–26} However, no studies have examined mFI in a large, national database in the context of high-risk elderly patients with gastrointestinal cancer. We hypothesized that a higher NSQIP mFI score is associated with adverse clinical outcomes after tumor resection in older, gastrointestinal cancer patients.

2 | METHODS

Patient data were collected from the NSQIP participant use files from 2005 to 2012, under the data use agreement of the American College of Surgeons and with Institutional Review Board approval. All patients (60–90 years old) who underwent surgical resection of the liver and bile duct, colon, and rectum, pancreas, esophagus, and stomach were identified by Current Procedural Terminology (CPT) and International Classification of Diseases, Ninth Revision (ICD-9) codes (Supplementary Appendix 1). Patients who were American Society

of Anesthesiology (ASA) 5, diagnosed with preoperative sepsis, undergoing emergency surgery, or missing at least one of the 11 variables used to determine mFI were excluded. Patient demographics, preoperative variables, intraoperative variables, and clinical outcomes were reviewed. Weight loss was defined as >10% of body weight loss in the past 6 months. Obesity was defined as ≥ 30 kg/m². Current smokers were defined as patients who smoked in the year prior to surgery.

mFI was defined by 11 preoperative variables within NSQIP, which were matched to the variables assessed by the CSHA-FI as previously described.²³ Patients were assigned one point for each of the following variables: functional status (not independent); diabetes; chronic obstructive pulmonary disease or pneumonia; congestive heart failure; history of myocardial infarction; either prior percutaneous coronary intervention, previous coronary surgery, or history of angina; hypertension requiring medication; impaired sensorium; peripheral vascular disease or rest pain; history of either transient ischemic attack or cerebrovascular accident; or history of cerebrovascular accident with neurologic deficit. The total number of points assigned to a patient was divided by 11, resulting in a mFI score between 0.0 and 1.0. On this scale, a higher mFI implied increased frailty. A patient with a mFI score of >0.27 was defined as frail. This cut-off of 0.27 has been used in previously published work to differentiate between those who were frail and non-frail.^{10,27–30}

Morbidity was defined by the Clavien-Dindo classification system, as previously described.³¹ Minor complications were defined as Clavien-Dindo class I/II, and included complications that did not require surgical, endoscopic, or radiological interventions. Major complications were defined as Clavien-Dindo class III/IV, and included complications that required surgical, endoscopic, or radiological interventions, and/or were life-threatening. Mortality was defined as death within 30 days of surgery.

Statistical analysis was performed using the SAS version 9.4 (SAS Institute, Cary, NC). Descriptive statistics were used to summarize the data for the study cohort. Continuous variables were summarized by the mean and standard deviation, while categorical variables were summarized by count and proportions, based on frailty score (mFI >0.27 vs mFI ≤ 0.27). Univariate analysis was used to evaluate the association between clinical variables and outcomes, which were reported with odds ratios and confidence intervals. Multivariate logical regression analysis was adjusted for age, gender, BMI, ASA, and albumin <3 , and was reported as odds ratios and 95% confidence intervals. Statistical significance was defined by a *P*-value of <0.05 .

3 | RESULTS

41 455 patients met the eligibility criteria. The study cohort included 10.2% of patients with hepatic or biliary cancer ($n = 4234$), 13.1% of patients with pancreatic cancer ($n = 5440$), 69.3% of patients with colorectal cancer ($n = 28\,708$), 2.3% of patients with esophageal cancer ($n = 953$), and 5.1% of patients with gastric cancer ($n = 2120$) (Table 1). The study population had a mean age of 72.4 (SD: 7.9) years and BMI of 27.6 (SD: 6.1) kg/m², and was 47.4% female (Table 2).

The mean mFI for the study population was 0.11. The mFI score with the highest proportion of patients was 0.09, which represented 41.5% of the study population ($n = 17\,193$) (Fig. 1). Patients with high mFI (>0.27) accounted for 2.8% of the study population ($n = 1164$). Patients with high mFI were more likely to be male, obese, and ASA Class 3–4 (all $P < 0.05$). Patients with high mFI also were more likely to have bleeding disorders, dyspnea at rest, or with moderate exertion, and each of the preoperative variables used in the calculation of mFI (all $P < 0.0001$). In addition, patients with high mFI were less likely to have undergone chemotherapy within the 30-days prior to surgery ($P < 0.0001$).

In terms of the postoperative course, patients with high mFI were more likely to have increased length of stay (11.7 vs 9.0 days, $P < 0.0001$). Also, as mFI increased, the rate of any complications, major complications, and 30-day mortality increased (all $P < 0.0001$). In total, complications of all severities occurred in 26.2% of patients ($n = 10,844$), major complications occurred in 19.0% of patients ($n = 7891$), and mortality within 30 days of surgery occurred in 2.8% of patients ($n = 1150$). Of those patients with a mFI score >0.27 , 36.8% developed a complication ($n = 1548$), 29.1% developed a major complication ($n = 1223$), and 5.6% died within 30-days of surgery ($n = 235$). Patients with mFI ≤ 0.27 were less likely to develop complications, as their rates of any complications, major complications, and 30-day mortality was 25.0% ($n = 9296$), 17.9% ($n = 6668$), and 2.5% ($n = 915$), respectively (all $P < 0.0001$).

Univariate analysis revealed that mFI was associated with major complications (OR 1.882, CI 1.752–2.022, $P < 0.0001$) and 30-day mortality (OR 2.352, CI 2.030–2.724, $P < 0.0001$), (Table 3). In addition, a 10-year increase in age, being male, race, obesity, weight loss, ASA of 3–4, smoking, functional status, transfer from a facility other than one's home, operative time, and length of stay were associated with the development of a major complication ($P < 0.05$). A 10-year increase in age, being male, BMI, obesity, weight loss, ASA of 3–4, smoking, functional status, transfer from a facility other than one's home, operative time, and length of stay were also associated with 30-day mortality ($P < 0.05$).

After adjusting for age, gender, BMI, ASA, and albumin level, multivariate analysis revealed that mFI was an independent predictor of major complications (OR 1.516, CI 1.393–1.649, $P < 0.0001$) and 30-day mortality (OR 1.477, CI 1.244–1.753, $P < 0.0001$), (Table 4). Additionally, a 10-year increase in age, being male, ASA of 3–4, and albumin >3 g/dL were independent predictors of the development of a major complication and 30-day mortality. An ASA of 3–4 was the most predictive of major complications (OR 1.680, CI 1.567–1.800, $P < 0.0001$) and of 30-day mortality (OR 2.870, CI 2.320–3.550, $P < 0.0001$). mFI was the second most predictive variable of major complications and 30-day mortality.

4 | DISCUSSION

There is an urgent gap in knowledge regarding how oncologists should assess an older patient's risk for adverse outcomes following aggressive therapies.^{32–34} Frailty is increasingly being described in both the geriatric and oncologic literature, as a clinical syndrome that may provide insight into risk stratification.^{32–35} It has been estimated that frailty exists in approximately 11% of patients aged 65 or older, and in 43% of those aged 85

years or older.^{36,37} Among cancer patients, frailty has been found to be more prevalent. In a systematic review, Handforth et al reported that the median rate of frailty in cancer patients with a mean age of 72 or older was approximately 43%.³⁸ Differentiating between those who are frail and non-frail in the older cancer patient population is critical, as aggressive cancer therapies can inflict significant stresses and result in poor outcomes.⁵⁻⁷ A frailty index that can predict postoperative outcomes may both reduce the undertreatment of the non-frail and the overtreatment of the frail, while improving clinical outcomes.^{8,9}

To reduce the undertreatment of older cancer patients, surgeons, and medical oncologists should collaborate more frequently and use objective measurements in their evaluations of patients for surgery and medical therapies. Choti et al recently reported that medical oncologists are significantly less likely to refer patients with colorectal liver metastases for surgical consultation if the oncologist believed that the lesion was resectable only after chemotherapy or never resectable.³⁹ However, medical oncologists often significantly underestimate the resectability of colorectal liver metastases and were found to agree with the surgeon's assessment in only 37.7% of cases.³⁹ These findings suggest that more collaboration between multi-disciplinary teams is necessary to reduce the undertreatment of older cancer patients. Additionally, in evaluating older patients for cancer therapy, the effects of comorbidities on postoperative outcomes are often overestimated. After adjusting for comorbidities, Schrag et al found that age was the strongest predictor of whether a patient received adjuvant chemotherapy after surgery for stage III colon cancer.⁴⁰ Similarly, Quipourt et al reported that colorectal cancer patients who were 75 years and older were significantly less likely to receive resection for cure and adjuvant chemotherapy than younger patients, even if they had few or no comorbidities.⁴¹ To reduce subjectivity in patient evaluations, a frailty index may assist multi-disciplinary teams in risk stratification.

In assessing preoperative risk, the comprehensive geriatric assessment (CGA) has been hailed as the "gold standard" in the identification of frailty in older patients, in the literature.^{32,42} However, the time required for its implementation has limited its use in busy clinics.^{32,42} In contrast, mFI can be quickly calculated from information gathered from a standard history and physical examination, and has been found to be predictive of postoperative outcomes, including after major abdominal surgery.^{10,24,25,43} Specifically, Louwers et al reported that increased mFI was associated with a significant increase in Clavien Class 4 complications and mortality in patients undergoing hepatectomy,²⁴ while Obeid et al found that increased mFI scores were associated with Clavien Class 4 and 5 complications in patients undergoing colectomy.²⁵ However, less data has been presented on the association between mFI and postoperative outcomes in cancer patients. Chappidi et al and Uppal et al recently reported that increased mFI scores were an independent predictor of Clavien Class 4 or 5 complications in cancer patients undergoing radical cystectomy and gynecological surgery, respectively.^{44,45} As the global population continues to age, a frailty index that can predict postoperative outcomes in older cancer patients is becoming increasingly urgent.

To our knowledge, the present study is the first to evaluate mFI in elderly surgical patients with gastrointestinal cancer in a large, national database. This study found that patients with high mFI were more likely to be male (61.7% vs 51.6%), obese (38.1% vs 27.5%), and ASA Class 3-4 (94.2% vs 63.4%). They also were more likely to have bleeding disorders (11.6%

vs 3.5%), and each of the preoperative variables included in the calculation of mFI. The differences between groups for these characteristics were large, and may be useful in assessing patients for frailty. Given our large sample size, we were also aware of the risk of identifying patient characteristics and outcomes that were statistically significant, but not clinically significant.^{46,47} For example, we found small differences in age (mean difference: 2.7 years), preoperative serum albumin (mean difference: -0.2 g/dL), smoking status (14.1% vs 12.4%), and operative time (mean difference: -18.0 mins) between the frail and non-frail groups. While these characteristics were found to be statistically significant, these differences were too small to be clinically meaningful.

In terms of postoperative outcomes, patients with high mFI were more likely to have increased length of stay, complications, and mortality. Moreover, patients with incrementally higher frailty scores had increasing rates of postoperative complications and 30-day mortality. Additionally, after adjusting for age, gender, BMI, ASA, and albumin level, frailty was found to be an independent predictor of major complications and 30-day mortality. In this study, other variables were also found to be independent predictors of the development of a major complication and 30-day mortality, including a 10-year increase in age, being male, ASA of 3–4, and albumin >3 g/dL. Only ASA was found to be more predictive of major complications and 30-day mortality than frailty. The strength of ASA as a predictor of these outcomes may be due to the significant overlap of ASA Class 3–4 and high frailty. Specifically, there was a very low frequency of patients with high frailty score and ASA 1–2 ($n = 244$). Overall, the findings suggest that mFI may be a valuable tool, in combination with other “traditional” risk factors, in preoperative risk stratification in gastrointestinal cancer patients.

The current study has implications for gastrointestinal cancer patients. First, mFI provides an objective measurement of frailty that can be easily calculated from a standard history and physical examination. Unlike the CGA, this makes the integration of mFI feasible for preoperative risk stratification.^{32,42} Additionally, the identification of frail patients does not preclude them from receiving potentially lifesaving therapies. Rather, it provides an opportunity to improve a patient’s physiological reserve before undergoing an aggressive treatment. In fact, frailty and related factors, such as sarcopenia, malnutrition, and poor performance status, are potentially modifiable. Preoperative exercise and nutritional therapies may have the capacity to augment frailty, as such therapies have been found to increase functional walking capacity, improve postoperative recovery, or decrease length of stay in patients undergoing surgery for gastrointestinal malignancies.^{48–51} For these reasons, the incorporation of mFI into clinical decision-making may improve patient outcomes.

The present study also has several limitations. First, it was a retrospective study, and the utility of using mFI in clinical encounters would require that it be used as a prospective tool. Secondly, this study encompassed a wide range of procedures and included both open and laparoscopic approaches. Some procedures carry significantly more postoperative risks than others, which may have confounded the results. Additionally, clinical judgment may have created selection bias, as those perceived as having significant risk factors for adverse outcomes likely did not undergo surgery and thus were not included in this study. A third limitation is that this study could only evaluate the variables included in the NSQIP

database. For this reason, all 70 of the variables used in the CSHA could not be studied. Finally, given our large sample size, small differences in patient characteristics were identified as statistically significant even though they were not clinically meaningful. Despite these limitations, we believe that mFI has the potential to provide valuable information on the postoperative course in clinical settings.

5 | CONCLUSIONS

There is an urgent need for a frailty index that can be used for preoperative risk stratification in older cancer patients. This study demonstrated that high mFI scores were strongly associated with increased length of stay, postoperative complications, and 30-day mortality in surgical patients with gastrointestinal cancer. Moreover, mFI score was found to be an independent predictor of major complications and 30-day mortality. Future studies should focus on the prospective application of mFI and its use in decision-making in surgical oncology. mFI should also be studied as a potential tool for the identification of patients who may benefit from prehabilitation therapy prior to surgery. Such therapy may modify the frailty status of surgical candidates with gastrointestinal cancer and lead to improved postoperative outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

REFERENCES

1. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci*. 2001;56:M146–M156. [PubMed: 11253156]
2. Howlader N, Noone A, Krapcho M, et al. SEER Cancer Statistics Review, 1975–2012, National Cancer Institute Bethesda, MD, http://seer.cancer.gov/csr/1975_2012/, based on November 2014 SEER data submission, posted to the SEER web site, 4 2015.
3. Faber W, Stockmann M, Schirmer C, et al. Significant impact of patient age on outcome after liver resection for HCC in cirrhosis. *Eur J Surg Oncol*. 2014;40:208–213. [PubMed: 24275202]
4. Richards CH, Platt JJ, Anderson JH, et al. The impact of perioperative risk, tumor pathology and surgical complications on disease recurrence following potentially curative resection of colorectal cancer. *Ann Surg*. 2011;254:83–89. [PubMed: 21572320]
5. Makary MA, Segev DL, Pronovost PJ, et al. Frailty as a predictor of surgical outcomes in older patients. *J Am Coll Surg*. 2010;210: 901–908. [PubMed: 20510798]
6. Saxton A, Velanovich V. Preoperative frailty and quality of life as predictors of postoperative complications. *Ann Surg*. 2011;253:1223–1229. [PubMed: 21412145]
7. 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. [PubMed: 25403592]
8. Berger NA, Savvides P, Koroukian SM, et al. Cancer in the elderly. *Trans Am Clin Climatol Assoc*. 2006;117:147–55-6.
9. Bouleuc C, Poinot R, Vedrine L, et al. Does a geriatric oncology consultation modify the cancer treatment plan for elderly patients? *J Gerontol A Biol Sci Med Sci*. 2008;63:724–730. [PubMed: 18693227]
10. Karam J, Tsiouris A, Shepard A, et al. Simplified frailty index to predict adverse outcomes and mortality in vascular surgery patients. *Ann Vasc Surg*. 2013;27:904–908. [PubMed: 23711971]

11. Partridge JSL, Harari D, Martin FC, Dhesi JK. The impact of preoperative comprehensive geriatric assessment on postoperative outcomes in older patients undergoing scheduled surgery: a systematic review. *Anaesthesia*. 2014;69:8–16. [PubMed: 24303856]
12. Bilimoria KY, Liu Y, Paruch JL, et al. Development and evaluation of the universal ACS NSQIP surgical risk calculator: a decision aid and informed consent tool for patients and surgeons. *J Am Coll Surg*. 2013;217:833–843. [PubMed: 24055383]
13. Mogal HD, Fino N, Clark C, Shen P. Comparison of observed to predicted outcomes using the ACS NSQIP risk calculator in patients undergoing pancreaticoduodenectomy. *J Surg Oncol*. 2016;114: 157–162. [PubMed: 27436166]
14. Copeland GP, Jones D, Walters M. POSSUM: a scoring system for surgical audit. *Br J Surg*. 1991;78:355–360. [PubMed: 2021856]
15. Haga Y, Ikei S, Ogawa M. Estimation of physiologic ability and surgical stress (E-PASS) as a new prediction scoring system for postoperative morbidity and mortality following elective gastrointestinal surgery. *Surg Today*. 1999;29:219–225. [PubMed: 10192731]
16. Deyle S, Banz Martine V, Wagner M, et al. Estimation of physiologic ability and surgical stress score does not predict immediate outcome after pancreatic surgery. *Pancreas*. 2011;40:723. [PubMed: 21654545]
17. Hashimoto D, Takamori H, Sakamoto Y, et al. Can the physiologic ability and surgical stress (E-PASS) scoring system predict operative morbidity after distal pancreatectomy? *Surg Today*. 2010;40:632–637. [PubMed: 20582514]
18. Hashimoto D, Takamori H, Sakamoto Y, et al. Is an estimation of physiologic ability and surgical stress able to predict operative morbidity after pancreaticoduodenectomy? *J Hepatobiliary Pancreat Sci*. 2010;17:132–138. [PubMed: 19430714]
19. Khan AW, Shah SR, Agarwal AK, Davidson BR. Evaluation of the POSSUM scoring system for comparative audit in pancreatic surgery. *Dig Surg*. 2003;20:539–545. [PubMed: 14534377]
20. Wagner D, DeMarco MM, Amini N, et al. Role of frailty and sarcopenia in predicting outcomes among patients undergoing gastrointestinal surgery. *World J Gastrointest Surg*. 2016;8:27–40. [PubMed: 26843911]
21. Feng MA, McMillan DT, Crowell K, et al. Geriatric assessment in surgical oncology: a systematic review. *J Surg Res*. 2015;193:265–272. [PubMed: 25091339]
22. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. *Sci World J*. 2001;1:323–336.
23. Velanovich V, Antoine H, Swartz A, et al. Accumulating deficits model of frailty and postoperative mortality and morbidity: its application to a national database. *J Surg Res*. 2013;183:104–110. [PubMed: 23415494]
24. Louwers L, Schnickel G, Rubinfeld I. Use of a simplified frailty index to predict Clavien 4 complications and mortality after hepatectomy: analysis of the National Surgical Quality Improvement Project database. *Am J Surg*. 2015;211:1071–1076. [PubMed: 26800866]
25. Obeid NM, Azuh O, Reddy S, et al. Predictors of critical care-related complications in colectomy patients using the National Surgical Quality Improvement Program: exploring frailty and aggressive laparoscopic approaches. *J Trauma Acute Care Surg*. 2012;72:878–883. [PubMed: 22491599]
26. Adams P, Tamer G, Stachler R, et al. Frailty as a predictor of morbidity and mortality in inpatient head and neck surgery. *JAMA Otolaryngol Head Neck Surg*. 2016;139:783–789.
27. Ali R, Schwalb JM, Nerenz DR, et al. Use of the modified frailty index to predict 30-day morbidity and mortality from spine surgery. *J Neurosurg Spine*. 2016;25:537–541. [PubMed: 27153143]
28. Tsiouris A, Hammoud ZT, Velanovich V, et al. A modified frailty index to assess morbidity and mortality after lobectomy. *J Surg Res*. 2013;183:40–46. [PubMed: 23273884]
29. Farhat JS, Velanovich V, Falvo AJ, et al. Are the frail destined to fail? Frailty index as predictor of surgical morbidity and mortality in the elderly. *J Trauma Acute Care Surg*. 2012;72:1526–1531. [PubMed: 22695416]
30. Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. *J Gerontol A Biol Sci Med Sci*. 2007;62:738–743. [PubMed: 17634321]

31. Dindo D, Demartines N, Clavien P. Classification of surgical complications. *Ann Surg*. 2004;240:205–213. [PubMed: 15273542]
32. Ruiz M, Cefalu C, Reske T, Estrada J. Management of elderly and frail elderly cancer patients: the importance of comprehensive geriatrics assessment and the need for guidelines. *Am J Med Sci*. 2013;346:66–69. [PubMed: 23154654]
33. Audisio RA, van Leeuwen B. When reporting on older patients with cancer, frailty information is needed. *Ann Surg Oncol*. 2011; 18:4–5. [PubMed: 20859696]
34. Audisio RA, van Leeuwen BL. Beyond “Age”: frailty assessment strategies improve care of older patients with cancer. *Ann Surg Oncol*. 2015;22:3774–3775. [PubMed: 26242368]
35. Huisman MG, Kok M, de Bock GH, van Leeuwen BL. Delivering tailored surgery to older cancer patients: preoperative geriatric assessment domains and screening tools—A systematic review of systematic reviews. *Eur J Surg Oncol*. 2017;43:1–14. [PubMed: 27406973]
36. Collard RM, Boter H, Schoevers RA, Oude Voshaar RC. Prevalence of frailty in community-dwelling older persons: a systematic review. *J Am Geriatr Soc*. 2012;60:1487–1492. [PubMed: 22881367]
37. Song X, Mitnitski A, Rockwood K. Prevalence and 10-Year outcomes of frailty in older adults in relation to deficit accumulation. *J Am Geriatr Soc*. 2010;58:681–687. [PubMed: 20345864]
38. 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. [PubMed: 25403592]
39. Choti MA, Thomas M, Wong SL, et al. Surgical resection preferences and perceptions among medical oncologists treating liver metastases from colorectal cancer. *Ann Surg Oncol*. 2016;23:375–381. [PubMed: 26561404]
40. Schrag D, Cramer LD, Bach PB, Begg CB. Age and adjuvant chemotherapy use after surgery for stage III colon cancer. *J Natl Cancer Inst*. 2001;93:850–857. [PubMed: 11390534]
41. Quipourt V, Jooste V, Cottet V, et al. Comorbidities alone do not explain the undertreatment of colorectal cancer in older adults: a french population-based study. *J Am Geriatr Soc*. 2011;59:694–698. [PubMed: 21438864]
42. Huisingh-Scheetz M, Walston J. How should older adults with cancer be evaluated for frailty? *J Geriatr Oncol*. 2016;16:S1879–S4068.
43. Cloney M, D’Amico R, Lebovic J, et al. Frailty in geriatric glioblastoma patients: a predictor of operative morbidity and outcome. *World Neurosurg*. 2016;89:362–367. [PubMed: 26775233]
44. Chappidi MR, Kates M, Patel HD, et al. Frailty as a marker of adverse outcomes in patients with bladder cancer undergoing radical cystectomy. *Urol Oncol*. 2016;34:256.e1–6.
45. Uppal S, Igwe E, Rice LW, et al. Frailty index predicts severe complications in gynecologic oncology patients. *Gynecol Oncol*. 2015;137:98–101. [PubMed: 25602715]
46. Bhardwaj SS, Camacho F, Derrow A, et al. Statistical significance and clinical relevance: the importance of power in clinical trials in dermatology. *Arch Dermatol*. 2004;140:1520–1523. [PubMed: 15611433]
47. Tingey R, Lambert M, Burlingame G, Hansen N. Assessing clinical significance: proposed extensions to method. *Psychother Res*. 1996;6:109–123. [PubMed: 22242565]
48. Carli F, Charlebois P, Stein B, et al. Randomized clinical trial of prehabilitation in colorectal surgery. *Br J Surg*. 2010;97:1187–1197. [PubMed: 20602503]
49. Cho H, Yoshikawa T, Oba MS, et al. Matched pair analysis to examine the effects of a planned preoperative exercise program in early gastric cancer patients with metabolic syndrome to reduce operative risk: the Adjuvant Exercise for General Elective Surgery (AEGES) study group. *Ann Surg Oncol*. 2014;21:2044–2050. [PubMed: 24671637]
50. 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. [PubMed: 25076007]
51. Li C, Carli F, Lee L, et al. Impact of a trimodal prehabilitation program on functional recovery after colorectal cancer surgery: a pilot study. *Surg Endosc*. 2013;27:1072–1082. [PubMed: 23052535]

FIGURE 1. mFI Distribution and Outcomes. The distribution of mFI in the study population is shown. As the mFI score increased, the proportion of patients experiencing any complications, major complications, and 30-day mortality increased (all $P > 0.0001$)

TABLE 1

Preoperative diagnoses

Preoperative diagnosis	N (% of study population)
Liver or biliary cancer	4234 (10.2)
Pancreatic cancer	5440 (13.1)
Colorectal cancer	28,708 (69.3)
Esophageal cancer	953 (2.3)
Gastric cancer	2120 (5.1)

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

TABLE 2

Patient characteristics

	Frailty index 0.27 (N = 37 252)	Frailty index >0.27 (N = 4203)	Overall (N = 41 455)	P-value
Age, years	72.1 (7.9)	74.8 (7.6)	72.4 (7.9)	<0.0001
Female, no. (%)	18 005 (48.4)	1610 (38.3)	19 615 (47.4)	<0.0001
Race, no. (%)				<0.0001
White	20 431 (73.7)	2307 (78.0)	22 738 (74.2)	
Black	2469 (8.9)	288 (9.7)	2757 (9.0)	
Other	4804 (17.3)	362 (12.2)	5166 (16.8)	
BMI, mean (SD) (kg/m ²)	27.5 (6.0)	29.0 (6.6)	27.6 (6.1)	<0.0001
Obesity, no. (%)	10 127 (27.5)	1578 (38.1)	11 705 (28.6)	<0.0001
Weight loss, no. (%)	3151 (8.5)	383 (9.1)	3534 (8.5)	0.1501
ASA class				<0.0001
ASA 1–2, no. (%)	13 621 (36.6)	244 (5.8)	13 865 (33.5)	
ASA3 or ASA 4, no. (%)	23 596 (63.4)	3953 (94.2)	27 549 (66.5)	
Preoperative Serum Albumin (g/dL), no. (%)	3.8 (0.6)	3.6 (0.6)	3.8 (0.6)	<0.0001
Current smoker, no. (%)	4609 (12.4)	592 (14.1)	5201 (12.6)	0.0015
Bleeding disorders, no. (%)	1288 (3.5)	487 (11.6)	1775 (4.3)	<0.0001
Chemotherapy 30 days before surgery, no. (%)	1755 (4.7)	99 (2.4)	1854 (4.5)	<0.0001
Dyspnea				<0.0001
At rest, no. (%)	241 (0.7)	160 (3.8)	401 (1.0)	
Moderate exertion, no. (%)	4071 (10.9)	1118 (26.6)	5189 (12.5)	
Preoperative variables included in mFI				
Functional status (totally or partially dependent), no. (%)	889 (2.4)	1062 (25.3)	1951 (4.7)	<0.0001
Diabetes, no. (%)	4305 (11.6)	2548 (60.6)	6853 (16.5)	<0.0001
COPD or pneumonia, no. (%)	1651 (4.4)	1184 (28.2)	2835 (6.8)	<0.0001
CHF in 30 days before surgery, no. (%)	109 (0.3)	285 (6.8)	394 (1.0)	<0.0001
MI 6 months prior to surgery, no. (%)	58 (0.2)	239 (5.7)	297 (0.7)	<0.0001
Previous PCI, previous cardiac surgery, or history of angina, no. (%)	3523 (9.5)	2699 (64.2)	6222 (15.0)	<0.0001
Hypertension, no. (%)	23,011 (61.8)	4077 (97.0)	27 088 (65.3)	<0.0001
Impaired sensorium, no. (%)	34 (0.1)	50 (1.2)	84 (0.2)	<0.0001
History of PVD, no. (%)	227 (0.6)	521 (12.4)	748 (1.8)	<0.0001

	Frailty index	0.27 (N = 37 252)	Frailty index >0.27 (N = 4203)	Overall (N = 41 455)	P-value
History of TIA, no. (%)	802 (2.2)		721 (17.2)	1523 (3.7)	<0.0001
CVA, no. (%)	464 (1.2)		706 (16.8)	1170 (2.8)	<0.0001
Operative time (mins)	207.1 (121.6)		189.1 (115.1)	205.3 (121.0)	<0.0001
Length of stay (days)	9.0 (9.4)		11.7 (10.6)	9.4 (9.6)	<0.0001
Any complications, no. (%)	9296 (25.0)		1548 (36.8)	10 844 (26.2)	<0.0001
Minor complications, no. (%)	4047 (10.9)		589 (14.0)	4636 (11.2)	<0.0001
Major complications, no. (%)	6668 (17.9)		1223 (29.1)	7891 (19.0)	<0.0001
30-day mortality, no. (%)	915 (2.5)		235 (5.6)	1150 (2.8)	<0.0001

ASA, American Society of Anesthesiologists; BMI, Body Mass Index; CHF, congestive heart failure; CI, Confidence Interval; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; mFI, modified Frailty Index; MI, myocardial infarction; OR, Odds ratio; PCI, percutaneous cardiac intervention; PVD, peripheral vascular disease; TIA, transient ischemic attack.

TABLE 3

Univariate model of major complications and 30-day mortality

Outcome	Major complication			30-day mortality		
	OR	CI	P-value	OR	CI	P-value
Age (10 yr increase)	1.103	1.070–1.138	<0.0001	1.647	1.529–1.774	<0.0001
Gender (male vs female)	1.362	1.296–1.432	<0.0001	1.294	1.149–1.458	<0.0001
Race			0.0001			0.8127
Black vs White	1.146	1.039–1.264	0.0065	0.936	0.731–1.199	0.6023
Other vs White	0.892	0.824–0.967	0.0053	0.958	0.795–1.155	0.6559
Obesity	1.080	1.023–1.140	0.0054	0.822	0.717–0.942	0.0049
Weight loss	1.530	1.413–1.657	<0.0001	2.547	2.186–2.967	<0.0001
ASA (3–4 vs 1–2)	1.914	1.808–2.027	<0.0001	4.398	3.639–5.316	<0.0001
Albumin >3 g/dL	0.470	0.433–0.509	<0.0001	0.242	0.210–0.279	0.1001
Smoking	1.312	1.223–1.407	<0.0001	1.190	1.008–1.406	0.0404
mFI (mFI >0.27 vs 0.27)	1.882	1.752–2.022	<0.0001	2.352	2.030–2.724	<0.0001
Functional status			<0.0001			<0.0001
Partially dependent vs independent	2.108	1.901–2.337	<0.0001	3.696	3.092–4.418	<0.0001
Totally dependent vs independent	2.980	2.222–3.996	<0.0001	5.542	3.566–8.612	<0.0001
Transferred from other facility vs home	2.167	1.909–2.461	<0.0001	3.415	2.741–4.255	<0.0001
Operative time (10 min increase)	1.029	1.027–1.031	<0.0001	1.014	1.009–1.018	<0.0001
Length of stay	1.133	1.128–1.137	<0.0001	1.020	1.014–1.026	<0.0001

ASA, American Society of Anesthesiologists; BMI, Body Mass Index; CI, Confidence Interval; mFI, modified Frailty Index; OR, Odds ratio.

TABLE 4

Multivariate model of major complications and 30-day mortality

Outcome	Major complication			30-day mortality		
	OR	CI	P-value	OR	CI	P-value
Age (10 yr increase)	1.049	1.011–1.089	0.0110	1.425	1.306–1.554	<0.0001
Gender (male vs female)	1.345	1.269–1.426	<0.0001	1.358	1.185–1.557	<0.0001
Obesity	1.068	1.002–1.138	0.0444	0.890	0.760–1.042	0.1481
ASA (3–4 vs 1–2)	1.680	1.567–1.800	<0.0001	2.870	2.320–3.550	<0.0001
Albumin >3 g/dL	0.514	0.473–0.558	<0.0001	0.298	0.257–0.346	<0.0001
mFI (mFI >0.27 vs 0.27)	1.516	1.393–1.649	<0.0001	1.477	1.244–1.753	<0.0001

ASA, American Society of Anesthesiologists; BMI, Body Mass Index; CI, Confidence Interval; mFI, modified Frailty Index; OR, odds ratio.