

Effect of Frailty on Postoperative Outcomes Following Major Abdominal Surgeries: A Prospective Observational Study

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ABSTRACT

Background: Frailty poses unique challenges for patients undergoing major cancer surgeries due to their extreme vulnerability to physiological stressors and can be an important factor in determining postoperative outcomes.

Aims and objective: The objective of the study was to determine the incidence of frailty in patients undergoing major abdominal cancer surgeries and identify the risk factors predicting poor outcomes.

Materials and methods: This was a prospective observational study conducted following institutional ethics approval and CTRI registration. We included 308 adult patients who underwent major abdominal cancer surgeries over two years. The preoperative frailty score was calculated using the 11-point modified frailty index score (mFI scale). Patients with a mFI score ≥ 3 points were considered frail. Clinical outcomes such as postoperative complications (Clavien–Dindo grades III and IV), surgical site infections, need for vasopressors, mechanical ventilation, acute kidney injury (AKI), length of ICU and hospital stay, and mortality at 30 days were recorded.

Results: The overall incidence of frailty according to the mFI scale was 8.1%. Age and higher American Society of Anesthesiology (ASA) status were significantly associated with frailty (OR –1.073, $p < 0.001$, and OR –10.220, $p < 0.001$) respectively. Frailty was an independent predictor of major postoperative complications (OR –8.147, 95% CI –2.524–26.292, $p < 0.001$). Frailty was also significantly associated with an increased duration of mechanical ventilation and length of stay ($p < 0.001$).

Conclusion: The modified frailty index (mFI) score remains a strong predictor of postoperative complications in patients undergoing major abdominal cancer surgeries and can help optimize risk factors to minimize complications.

Keywords: Frailty, Major abdominal cancer surgeries, Postoperative complications.

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HIGHLIGHTS

- Prevalence of frailty in oncology patients may be quite high due to the effect of cancer and its treatment.
- Aging and comorbidities may add to the risk of developing frailty.
- Frailty is strongly associated with increased postoperative complications, length of hospital stay, and mortality.

INTRODUCTION

A frail patient undergoing major cancer surgery presents unique challenges in the perioperative period due to extreme vulnerability to physiological stressors, impaired ability to maintain homeostasis, and potential changes caused by cancer and the treatment received.¹ All these influence the course and may lead to poor postoperative outcomes. Frailty may be a cause for increase in the postoperative complications, delirium, prolonged recovery requiring an increased length of hospital stay, and mortality. Patient selection is the most important factor, particularly in complex and morbid oncosurgeries. Frailty increases exponentially with age after 65 years.

Conventionally, patient selection for surgery has depended on subjective clinical assessment of the stage of the disease, comorbidities, and surgical risk factors. However, this may not allow reliable prediction of adverse outcomes.² Anesthesiologists commonly use American Society of Anesthesiology (ASA) physical status classification as a tool for risk stratification. There are other less commonly used outcome prediction tools, such as the Physiological and Operative Scoring System for Enumeration of Morbidity

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and Mortality (POSSUM), and American College of Surgeons' National Surgery Quality and Improvement Project (NSQIP). They have not been consistent in effectively predicting postoperative complications in patients undergoing major abdominal surgeries.^{3–5}

A standardized measurement of frailty and overall physiological reserve can provide valuable insights to clinicians

regarding patient's ability to withstand the surgical procedure. It can also serve as a more accurate predictor of postoperative complications and patient outcomes and thereby help the caring team to take preventive measures to avoid complications. The modified frailty index (mFI) score is a measure of frailty that reflects the likely compromise of organ function due to patients' comorbidities.⁵ It has been validated across various surgical specialties. It was developed by assessing 70 variables taken from the Canadian Study of Health and Aging Frailty Index with 11 comorbidities, along with variables from the NSQIP database. Although, ASA physical status classification is the commonest risk stratification tool used for all surgeries, the addition of a formal frailty assessment may be a useful adjunct for patients undergoing major abdominal oncosurgeries and these can help in improving postoperative outcomes. We, therefore, conducted this study looking at the mFI scale to determine the incidence of frailty in patients undergoing major abdominal oncosurgeries, as a primary outcome measure. We also evaluated the association of frailty to various short-term postoperative outcomes as secondary outcome measures.

MATERIALS AND METHODS

This prospective observational study was conducted following institutional ethics committee approval, informed consent, and CTRI registration. We included 308 consecutive adult patients who underwent major elective upper abdominal surgeries such as pancreatectomies, gastrectomies, hepatic resections, and cholecystectomies under general anesthesia, over a period of 2 years. Pediatric patients, those undergoing elective colorectal and emergency abdominal surgeries, and those who refused consent, were excluded from the study.

We collected the demographic data, ASA physical status, and other comorbidities, along with a history of previous chemotherapy, radiotherapy, or previous surgeries. The history of endoscopic retrograde cholangiopancreatography (ERCP) and biliary stenting, if performed, were noted. A history of unintentional weight loss >4.5 kg prior to surgery and the Eastern Cooperative Oncology Group (ECOG) Performance Status were noted. The patient's preoperative frailty score was calculated using the 11-point mFI scale. This scale includes 11-points-functional status before surgery, history of diabetes mellitus, hypertension, myocardial infarction, peripheral vascular disease, congestive heart failure, chronic obstructive pulmonary disease or pneumonia, previous percutaneous coronary intervention, angina or cardiac surgery, history of impaired sensorium, cerebrovascular accident, transient ischemic attack or stroke. Each item is allocated 1 point for the calculation of the score. The department follows the protocol enhanced recovery after surgery (ERAS) diligently for all major elective upper abdominal surgery.

A patient with score 0 was defined as being non-frail, patients with a score 1–2 (0.09–0.18) as mildly frail, patients with a score 3–4 (0.27–0.36) as intermediate frail, and those with a mFI score >4 (0.36) as highly frail. Overall, all patients with a score ≥ 3 points (0.27) were considered frail in our study cohort. A preoperative Subjective Global Assessment (SGA) nutrition score, which classified the patients into SGA-A, B, and C, was performed and the results noted. The most recent laboratory values from the preoperative period were obtained from the hospital Electronic Medical Record. All patients were followed for 30 days for postoperative complications (Clavien–Dindo grade III and IV complications), other

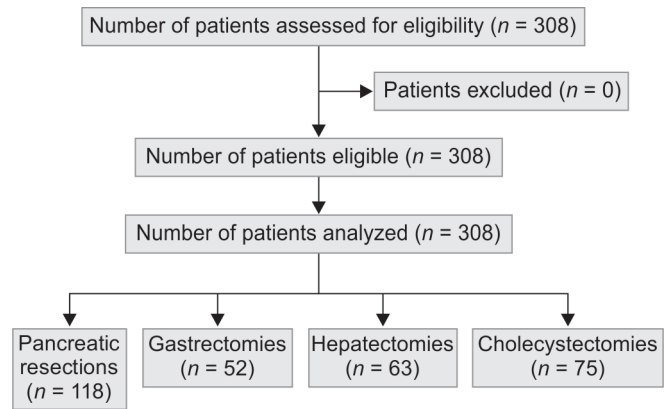


Fig. 1: CONSORT diagram

morbidity such as surgical site infection, need for vasopressors, need for invasive mechanical ventilation for > 24 hours, failure to wean from ventilator, acute kidney injury (AKI) and need for renal replacement therapy (RRT), length of ICU and hospital stay, need for ICU readmissions, and mortality.

Statistical Analysis

The categorical variables were expressed as frequencies (percentages) and the continuous variables were expressed as means (\pm standard deviation), and medians (with interquartile range) whichever was appropriate. Categorical variables were analyzed using the Chi-square test or the Fisher's exact test (for binary variables). Normality testing of continuous variables was done using Shapiro-Wilk test. The p -values less than 0.05 were considered statistically significant. Demographic characteristics between patients with a mFI ≥ 0.27 and those with a mFI < 0.27 were compared using Chi-square test for the categorical variables and two-sample t tests or the Mann-Whitney U test for continuous variables.

Sample Size Calculation

To estimate the incidence of frailty using the mFI scale in our patients, a sample size of 308 patients was deemed to be sufficient to produce a two-sided confidence interval of 95% with an actual width of 0.06388, assuming a sample proportion of 0.08. The lower and upper limits of the confidence interval were calculated to be 0.05226 and 0.11614, respectively.

RESULTS

We included 308 patients, who underwent elective major upper abdominal oncosurgeries over 24 months period (Fig. 1). The mean age was 53.7 years (± 11.7) and the mean BMI was 23.7 (± 4.1) kg/m². There were more males (62%) than females in our cohort, and 45.8, 49 and 5.2% had ASA I, II, and III physical status, respectively (Tables 1 and 2). Twenty-five patients (8.1%) were found to be frail according to the (mFI ≥ 0.27) (Table 3). The baseline investigations were within normal limits except the blood urea level, which was higher in the patients with frailty ($p = 0.035$) (Table 4).

Frailty was associated with increasing age ($p < 0.001$), ASA physical status II and higher ($p < 0.001$) (Table 5).

When we did a multivariate analysis of factors associated with frailty (mFI > 0.27), frailty was significantly associated with higher age (OR 1.073), unintentional weight loss greater ≥ 4.5 kg

Table 1: Demographics, ASA status and association with frailty (mFi \geq 0.27)

Variables	mFi < 0.27 (n = 283)	mFi \geq 0.27 (n = 25)	Total (n = 308)	p-value
Age (mean \pm SD)	52.8 (\pm 11.4)	64.1 (\pm 8.8)	53.7 (\pm 11.7)	<0.001*
BMI	23.6 (\pm 4)	24.4 (\pm 5.5)	23.7 (\pm 4.1)	0.246
Sex				
Male n, (%)	178 (62.9)	14 (56.0)	192 (62.3)	0.495
Female n, (%)	105 (37.1)	11 (44.0)	116 (37.7)	
Neoadjuvant chemotherapy n, (%)	80 (28.3)	7 (28.0)	87 (28.2)	0.977
Prior radiotherapy n, (%)	12 (4.2)	0 (0.0)	12 (3.9)	0.608
ASA status				
ASA I n, (%)	140 (49.5)	1 (4.0)	141 (45.8)	<0.001*
ASA II and higher n, (%)	143 (50.5)	24 (96)	167 (54.2)	
Obesity (BMI >30 kg/m ²) n, (%)	14 (4.9)	2 (8.0)	16 (5.2)	0.379
H/o unintentional weight loss >4.5 kg n, (%)	64 (22.6)	17 (68)	81 (26.3)	<0.001*
ECOG score n, (%)				
0	83 (29.3)	6 (24.0)	83 (28.7)	0.856
1	188 (66.4)	18 (72.0)	194 (67.1)	
2	12 (4.2)	1 (4.0)	12 (4.2)	

Data presented as mean (\pm SD) and n (%); *Significant difference. ASA, American Society of Anesthesiology

Table 2: Comorbidities and the components of modified Frailty Index

Variables	mFi < 0.27 (n = 283)	mFi \geq 0.27 (n = 25)	Total (n = 308)	Total (n = 308)
Bleeding disorders	2 (0.7)	0 (0.0)	2 (0.6)	1.000
H/o dyspnea	2 (0.7)	1 (4.0)	3 (1.0)	0.225
History of CKD**or need for dialysis or past h/o renal failure	3 (1.1)	0 (0.0)	3 (1.0)	1.000
Hepatic dysfunction	21 (7.4)	1 (4.0)	22 (7.1)	1.000
Preoperative ERCP/biliary stenting	53 (19.7)	4 (16.0)	57 (19.4)	0.796
SGA for nutrition				
SGA A	162 (57.2)	15 (60.0)	177 (57.5)	0.458
SGA B	113 (39.9)	8 (32.0)	116 (37.7)	
SGA C	8 (2.8)	2 (8.0)	10 (3.2)	

**CKD, chronic kidney disease; SGA, subjective global assessment; Data presented as mean (\pm SD) and n (%); *Significant difference

Table 3: Distribution of modified frailty index in our cohort

Variables	mFi < 0.27 (n = 283)	mFi \geq 0.27 (n = 25)	Total (n = 308)	p-value
Dependent functional status	2 (0.7)	2 (8.0)	4 (1.3)	0.034*
Diabetes mellitus	82 (29.0)	21 (84.0)	103 (33.4)	<0.001*
COPD or pneumonia	24 (8.5)	13 (54.2)	37 (12.1)	<0.001*
Congestive heart failure	1 (0.4)	1 (4.0)	2 (0.6)	0.156
Myocardial infarction	1 (0.4)	2 (8.0)	3 (1.0)	0.018*
History of PCI/cardiac surgery/angina	8 (2.8)	9 (36.0)	17 (5.5)	<0.001*
Hypertension requiring use of medications	63 (22.4)	23 (92.0)	86 (28.1)	<0.001*
Peripheral vascular disease or rest pain	4 (1.4)	1 (4.0)	5 (1.6)	0.347
Stroke either TIA OR cerebrovascular accident	4 (1.4)	3 (12.0)	7 (2.3)	0.013*
Neurological deficit history of cerebrovascular accident with neurological deficit	0 (0.0)	0 (0.0)	0 (0.0)	not applicable
Impaired sensorium	0 (0.0)	0 (0.0)	0 (0.0)	not applicable

Data presented as mean (SD) and n (%); *, Significant difference

Table 4: Baseline investigations

Variables	mFI < 0.27 (n = 280)	mFI ≥ 0.27 (n = 25)	Total (n = 308)	p-value
Hb (gm/dL)	12.1 (±2.2)	11.7 (±1.5)	12.1 (±2.2)	0.149
WBC (/mCL)	7,909.8 (±4,859.1)	8,156.8 (±2,373)	7,929.9 (±4,704.1)	0.224
Platelet count (/mCL)	2,67,066 (115,626.6)	2,72,480 (125,504.7)	2,67,505.5 (116,251.3)	0.926
S.bilirubin (mg/dL)	1.2 (±2.1)	0.6 (±0.2)	1.1 (±2.1)	0.470
INR	1.1 (±1.4)	1 (±0.1)	1.1 (±1.3)	0.212
S. albumin (gm/dL)	3.9 (±0.5)	3.9 (±0.4)	3.9 (±0.5)	0.571
Blood urea (mg/dL)	23 (±8.4)	32.2 (±19.9)	23.8 (±10.1)	0.035*
S. creatinine (mg/dL)	0.7 (±0.2)	0.8 (±0.3)	0.7 (±0.2)	0.350

Data presented as mean (±SD) and n (%); *, Significant difference

Table 5: Surgery and anesthesia details

Variables	mFI < 0.27 (n = 283)	mFI ≥ 0.27 (n = 25)	Total (n = 308)	p-value
Surgery duration (mins)	338.2 (272.7)	322.6 (150.2)	337 (264.6)	0.763
Surgical access				
Open	269 (95.1)	24 (96.0)	293 (95.1)	1.000
Minimal access	14 (4.9)	1 (4.0)	15 (4.9)	
Procedures performed				
Radical cholecystectomy	72 (25.4)	3 (12.0)	75 (24.4)	0.440
Gastrectomy	48 (17.0)	4 (16.0)	52 (69.9)	
Hepatectomy	56 (19.8)	7 (28.0)	63 (20.5)	
Pancreatic surgeries	107 (37.8)	11 (44.0)	118 (38.3)	
Intraoperative blood loss				
≤950 mL	139 (49.3)	9 (36)	148 (48.4)	0.264
≥950 mL	144 (50.8)	16 (64)	160 (51.9)	
Anesthesia technique				
GA + Regional block	0 (0.0)	1 (4.0)	1 (0.3)	0.001*
GA + Epidural anesthesia	259 (91.5)	19 (76.0)	278 (90.3)	
General anesthesia	24 (8.5)	5 (20.0)	29 (9.4)	

Data presented as mean (±SD) and n (%); *Significant difference

(OR 4.929), preoperative increased urea (OR 1.043) and ASA II or higher status (OR 10.220) and led to increased Clavien–Dindo grade III and IV complications (OR 6.399), Clavien–Dindo Grade III and IV postoperative complications occurred in 114 patients. Frailty (mFI > 0.27) was associated with Clavien–Dindo complications grade III and IV (<0.001). As the mFI score increased, the rate of major complications also increased ($p < 0.001$)

Frailty was significantly associated with cardiac complications ($p = 0.001$), cerebrovascular complications ($p = 0.005$), sepsis and septic shock ($p < 0.001$), need for vasopressors ($p = 0.002$), invasive mechanical ventilation (MV) >24 hours and failure to wean from MV ($p < 0.001$), patients with frailty had increased ICU length of stay ($p < 0.001$), had longer duration of MV ($p < 0.001$), and also increased hospital length of stay ($p = 0.018$) (Tables 6 and 7).

Frailty (mFI ≥ 0.27) had the highest odds ratio (OR 8.147, 95% CI 2.524–26.292, $p < 0.001$) for predicting major complications. Endoscopic retrograde cholangiopancreatography and biliary stenting performed preoperative for pancreatic resections and hepatectomies was associated with an increased risk of complications (OR 2.835, 95% CI, 1.502–5.353, $p = 0.001$). History of unintentional weight loss >4.5 kg increased the odds of Clavien–Dindo 3 and 4 complications by 2.27 (95% CI-1.228–4.197, $p = 0.009$).

Blood loss of >950 mL was associated with increased complications, with an odds ratio of 2.689 [95% CI-1.55–4.666 ($p < 0.001$)] (Table 8).

DISCUSSION

In our cohort of patients undergoing elective major abdominal surgeries, the incidence of frailty (mFI ≥ 0.27) was 8.1% ($n = 25$). The lower overall incidence of frailty in our study could be due to selection of relatively healthier patients for these major oncosurgeries as well as due to implementation of the ERAS program. Briefly, the ERAS program in our institute ensures that the patients receive nutritional and physiotherapy consultation on their first preoperative visit, followed by continuous follow-up visits, until they are deemed fit to undergo surgery. A recent publication found more than 84% compliance with most elements of ERAS in patients undergoing pancreatic resections. The same trend is present across all GI surgeries in our institute.⁶

Frail patients in our study were older, some of them had a prior history of unintentional weight loss >4.5 kg prior to surgery, an ASA physical status of II or higher, and had higher preoperative blood urea. Frailty was significantly associated with increased

Table 6: Frailty and postoperative outcomes

Variables	mFI < 0.27 (n = 283)	mFI ≥ 0.27 (n = 25)	Total (n = 308)	p-value
Clavien–Dindo complications ≥ grade 3	93 (32.9)	21 (84.0)	114 (37.0)	<0.001*
Cardiac events	27 (9.5)	9 (36.0)	36 (11.7)	0.001*
Cerebrovascular events	6 (2.1)	4 (16.0)	10 (3.3)	0.005*
Respiratory events	21 (7.4)	4 (16.0)	25 (8.1)	0.132
AKI requiring ICU admission or dialysis	4 (1.4)	1 (4.0)	5 (1.6)	0.347
Deep venous thrombosis	3 (1.1)	0 (0.0)	3 (1.0)	1.000
Need for blood transfusion	7 (2.5)	2 (8.0)	9 (2.9)	0.160
Length of hospital stay (days)	11.2 (7.7)	14.8 (8.5)	11.5 (7.8)	0.018*
Liver dysfunction	16 (5.7)	2 (8.0)	18 (5.8)	0.648
Need for invasive ventilation > 24 hours	36 (12.8)	11 (44.0)	47 (15.3)	<0.001*
Sepsis or septic shock	33 (11.7)	11 (44.0)	44 (14.3)	<0.001*
Use of vasopressors	21 (7.4)	7 (28)	28 (9.1)	0.002*
Need for reintubation	8 (2.8)	0 (0.0)	8 (2.6)	1.000
ICU LOS (h)	31.7 (45.4)	40.8 (18.3)	32.5 (43.9)	<0.001*
Surgical site infection	8 (2.8)	3 (12.0)	11 (3.6)	0.051
ICU readmission	6 (2.1)	0 (0.0)	6 (2.0)	1.000
Mortality within 30 days	3 (1.1)	0 (0.0)	3 (1.0)	1.000
Hospital readmission	23 (8.1)	3 (12.0)	26 (8.4)	0.455

Data presented as mean (±SD) and n (%); *, Significant difference. LOS, Length of stay

Table 7: Factors associated with frailty (mFI ≥ 0.27)

Variable	Odds ratio	Confidence interval		p-value
		Lower	Upper	
Age	1.073	1.016	1.135	0.012
Clavien–Dindo complications ≥ grade III	6.399	1.951	20.986	0.002
Unintentional wt loss >4.5 kg	4.929	1.730	14.046	0.003
Preoperative blood urea	1.043	1.001	1.087	0.044
ASA II and higher	10.220	1.258	83.052	0.030

Table 8: Factors predicting Clavien–Dindo grade III and IV complications

Variable	Odds ratio	Confidence interval		p-value
		Lower	Upper	
Frailty (mFI ≥ 0.27)	8.147	2.524	26.292	<0.001
Preoperative biliary stenting	2.835	1.502	5.353	0.001
Unintentional preoperative weight loss ≥ 4.5 kg	2.27	1.228	4.197	0.009
Blood loss ≥ 950 mL	2.689	1.55	4.666	<0.001

risk of Clavien–Dindo grade III and IV complications, as well as cardiac, and cerebrovascular complications postoperatively. Frailty was also associated with septic shock, increased ICU stay, need for vasopressors, need for invasive mechanical ventilation > 24 hours, and failure to wean from the ventilator, and increased ICU and hospital LOS. Clavien–Dindo grade III and IV complications were strongly associated with frailty (odds ratio-8.147), history of

preoperative biliary stenting (OR-2.835), unintentional weight loss >4.5kg (OR-2.27) and blood loss >950 mL (OR-2.689). Sandini et al., in their meta-analysis reported an incidence of frailty of 0.5–67.2%.⁷ The overall incidence of frailty in our study was 8.1% which is slightly lower than previous studies.

We observed that frailty was associated with increasing age ($p < 0.0001$). Although ageing is not synonymous with frailty, it is the aggregate risk due to old age or disease related physiologic deficits.^{8,9}

The ASA physical status scale is widely used worldwide to determine a patient's physical status. Frailty was found to be associated with a higher ASA status (<0.001). Frailty was also associated with unintentional weight loss >4.5 kgs and significant postoperative Clavien–Dindo complications grade III and IV (odds ratio-2.27, $p = 0.009$).

Although, history of weight loss was significantly associated with frailty and increased postoperative complications, malnutrition, as measured by the SGA score was not significant for frailty.

Frail patients in whom ERCP and biliary stenting were done in pancreatic and liver resections had an increased risk of postoperative major complications (OR -2.835, $p = 0.001$). Among the type of surgeries, pancreatic resections performed in frail patients had an increased risk of postoperative complications (OR: 3.08, 95% CI 1.608–5.904; $p = 0.001$).

Blood loss ≥ 950 mL was a significant predictor of postoperative complications, (odds ratio of 2.69, $p < 0.001$), thus indicating that higher blood loss during surgery was associated with increased complications.

Frailty was associated with poor 30-day postoperative outcomes. An increasing frailty score was associated with an increased risk of major complications ($p < 0.001$). This is in agreement with Vermilion et al., who concluded that a higher mFI score was associated with an

increased incidence of postoperative complications and mortality.¹⁰ In this study, frail patients were more likely to have increased hospital length of stay (11.7 vs 9.0 days), major postoperative complications (29.1% vs 17.9%), and 30-day mortality (5.6% vs 2.5%), ($p < 0.001$). Kalaiselvan et al. studied frailty in ICU patients and reported that frailty was associated with an increasing length of stay and mortality.¹¹ In our study, frailty was significantly associated with major postoperative complications (84% vs 32.9%), cardiac complications (36% vs 9.5%), cerebrovascular complications (16% vs 2.1%), sepsis or septic shock (44% vs 11.7%), increased ICU stay (40.8 vs 31.7 hours), need for vasopressors (7.4% vs 28%), need for invasive mechanical ventilation > 24 hours, (44% vs 12.8%) and increased hospital stay (14.8 days vs 11.2) days.

Mogal et al. in 9986 patients who underwent pancreatoduodenectomies reported higher postoperative morbidity ($p < 0.001$) and 30-day mortality ($p < 0.001$).⁵ Sandini et al. in their meta-analysis of 35 studies, found that frailty was associated with increased risk of major postoperative morbidity (OR-2.56, 95% CI-2.08–3.16), short-term (OR- 5.77, 95% CI-4.41–7.55,) and long-term mortality (HR 2.71, 95% CI- 1.63–4.49).⁷ Clavien–Dindo grade III and IV major complications were strongly associated with frailty (OR-8.147, $p < 0.001$) in our study.

A multidisciplinary collaborative team approach to optimizing the frail patient's preoperatively can help mitigate the risks associated with specific risk factors.⁵

Our study had some limitations. The eleven variables that are included in the mFI scale may not completely represent the entire spectrum of frailty parameters in our population. Some surgeries may carry significantly more postoperative risks than others. Frail patients undergoing pancreatic resections were more likely to have major complications. We had a significant number of patients undergoing pancreatic surgeries, who, by the very nature of the surgery and disease being treated, had a higher complication rate. This may have led to an increased number of complications in our study.

CONCLUSION

The mFI score seems to be a good predictor of postoperative complications for patients undergoing major abdominal surgeries. In a preoperative setting, this score can help to risk-stratify patients, identify subgroups at increased risk of developing adverse events, and subsequently institute rehabilitation measures to potentially optimize modifiable factors and minimize complications. Future work should examine the elements of the mFI to determine whether they can be modified preoperatively to improve postoperative outcomes.

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