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Association of frailty with outcomes after elective colon resection for diverticular disease

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ABSTRACT

Background: Frailty has been associated with greater postoperative morbidity and mortality but its impact has not been investigated in patients with diverticulitis undergoing elective colon resection. Therefore, the present study examined the association of frailty with perioperative outcomes following elective colectomy for diverticular disease.
Methods: The 2017–2019 American College of Surgeons-National Surgical Quality Improvement Program data registry was queried to identify patients (aged ≥18 years) undergoing elective colon resection for diverticular disease. The 5-factor modified frailty index (mFI-5) was used to stratify patients into *non-frail* (mFI 0), *prefrail* (mFI 1), and *frail* (mFI ≥2) cohorts. Major adverse events, surgical site infection, and postoperative ileus as well as prolonged length of stay, nonhome discharge, and unplanned readmission were evaluated using multivariable logistic models.
Results: Of the 20,966 patients, 10.0% were frail. Compared to others, frail patients were generally older (*non-frail*: 55 years, [46–63], *prefrail*: 62, [54–70], *frail*: 64, [57–71]) and more commonly female (*non-frail*: 53.1%, *prefrail*: 58.6, *frail*: 64.4, $P < .001$). Frail patients more frequently underwent open colectomy and stoma creation compared with others. Frailty was associated with greater adjusted odds of major adverse event (adjusted odds ratio 1.25, 95% confidence interval 1.06–1.48), surgical site infection (adjusted odds ratio 1.28, 95% confidence interval 1.06–1.54), and postoperative ileus (adjusted odds ratio 1.59, 95% confidence interval 1.27–1.98). Similarly, frailty portended greater odds of prolonged length of stay, nonhome discharge, and unplanned readmission.
Conclusion: Frailty as defined by the mFI-5 was associated with greater morbidity and hospital resource use. Deployment of frailty instruments may augment traditional risk calculators and improve patient selection for elective colectomy.

Introduction

Colonic diverticulitis affects 10% to 25% of Americans over the age of 60 and accounts for an annual $2.2 billion in healthcare expenditure in the United States.[1,2] Given the high rates of complications and ostomy formation associated with urgent operative intervention for diverticulitis, delayed colectomy has garnered significant interest.[3] In fact, in 2006 a change in operative guidelines for diverticulitis published by the American Society of Colon and Rectal Surgeons (ASCRS) resulted in decreasing incidence of urgent/emergent colectomy and a concomitant increase in elective operations.[4] Elective operations may be preferred due to several advantages that include control of local infection, hemodynamic stability, and nutritional optimization.[5–7] Nonetheless, several patient factors including advanced age and comorbidities such as diabetes, hyperlipidemia, chronic renal disease, and smoking have been associated with the development of complications following colectomy.[8]

Traditional risk factors aside, frailty has emerged as an independent predictor of perioperative complications. Generally defined as a loss of physiologic reserve, frailty increases the patient's vulnerability to surgical stresses such as blood loss and infection.[9–11] Despite the lack of a universal definition, frailty has

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been quantified using several physical and cognitive instruments. However, none have achieved widespread adoption due to their resource-intensive nature and difficulty in pragmatic implementation.[12] More recently, administrative tools such as the modified frailty index (mFI) have been developed to facilitate the assessment of frailty. The mFI has been utilized to evaluate the impact of frailty on perioperative outcomes in a variety of operations in the American College of Surgeons ACS) surgical database.[13–15] Such coding-based strategies have facilitated the detection of frailty and improved the discriminatory power of risk models in several surgical subpopulations. In a study of pancreaticoduodenectomy operations, Mogal et al (2017) demonstrated how mFI significantly enhanced the prediction of 30-day mortality and complications.[16]

With a shift in operative management of diverticular disease, accurate risk models are of increasing value and essential to shared decision-making as well as choice of intervention. To date, examination of frailty on outcomes of elective colectomy for diverticulitis remains limited. Thus, we examined the association of frailty as measured by mFI with acute outcomes of elective colectomy in a national cohort of patients with diverticulitis. We hypothesized frailty to be associated with an increased risk of perioperative complications, prolonged length of stay (pLOS), and nonhome discharge as well as unplanned 30-day readmission.

Methods

The 2017–2019 American College of Surgeons–National Surgical Quality Improvement Program (ACS-NSQIP) colectomy-targeted use files were queried to identify adults (aged ≥18 years) with diverticular disease who underwent elective colectomy. This multi-institutional data repository is maintained as part of the NSQIP and consists of over 150 variables including demographic, perioperative comorbidities, operative factors, and 30-day postoperative outcomes. To ensure the integrity of the collected data, each hospital has a designated NSQIP-trained reviewer for data collection and undergoes quality-control audits. The ACS-NSQIP and its participants are the source of the data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors.

Patients with a postoperative diagnosis for colonic diverticular disease without bleeding were identified utilizing the International Classification of Diseases, Tenth Revision (ICD-10) diagnosis codes (K57.20, K57.30, K57.32). Of those queried, those who underwent elective colon resection were identified using Current Procedural Terminology (CPT) codes and included for further study (Figure 1). We excluded patients who had emergent or outpatient operations, preoperative sepsis/septic shock, preoperative ventilator dependence or an American Society of Anesthesiologists (ASA) class V. Patients with missing key data including sex, race, and body mass index (BMI) as well as operative approach were also excluded (8.2%).

The previously validated 5-factor modified frailty index (mFI-5) was used to assess the extent of frailty among patients in our study cohort. In this scheme, subjects received 1 point for each of the following diagnoses available in NSQIP: preoperative dependent functional status, diabetes, hypertension, chronic obstructive pulmonary disease, and congestive heart failure.[17] As reported by Yagi et al. (2019), patients were then stratified into 3 groups (mFI-5 0: *non-frail*, 1: *prefrail*, ≥2: *frail*).[18]

Patient characteristics of interest included age, sex, and race as defined by the ACS-NSQIP Operations Manual. Patient BMI was calculated using the height and weight data fields. Patients were subsequently categorized as underweight (BMI <18.5 kg/m^2), normal (BMI 18.5–24.9 kg/m^2), overweight (BMI 25–29.9 kg/m^2), obese (BMI 30–39.9 kg/m^2) and morbidly obese (BMI ≥40 kg/m^2). The ASA classes were dichotomized into <III (healthy or mild burden from systemic illness) and ≥III (severe). Additional comorbidities including dyspnea, smoking status, and immunosuppressive therapy for management of a chronic condition were ascertained from ACS-NSQIP provided data fields. Preoperative bowel preparation along with operative characteristics were also in Table I. Concomitant procedures and ostomy types were incorporated into risk models and are shown in are shown in Supplementary Tables S1 and S2, respectively.

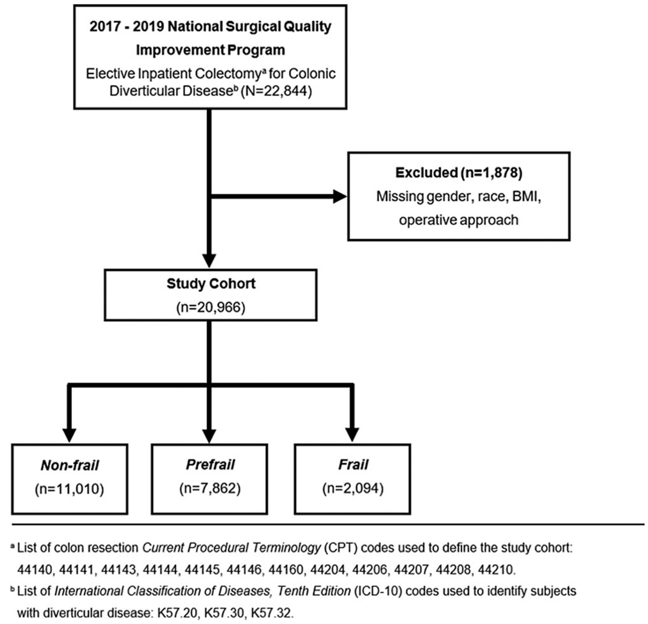

Figure 1. CONSORT diagram illustrating patient selection methodology.

Major adverse event (MAE) comprised of grade III/IV Clavien-Dindo complications as previously outlined (Supplementary Table S3).[19] Surgical site infection (SSI) was a binary variable and comprised of superficial and deep/organ-space infections. Postoperative ileus was defined as requiring nil per os (NPO) status or nasogastric tube use >3 days following colectomy. Prolonged length of stay (pLOS) was noted as a hospitalization >75th percentile of the overall cohort (≥5 days).[20]

Due to the low observed mortality rate in this cohort (0.2%), the primary outcome of interest was the development of MAE. Secondary endpoints included SSI, postoperative ileus, and pLOS as well as nonhome discharge and unplanned rehospitalization. A subgroup analysis was performed in order to evaluate the impact of operative approach, stoma formation as well as BMI on MAE and SSI in the frail cohort.

All statistical analyses were performed using Stata 16.0 software (StataCorp, College Station, TX). Categorical and continuous variables are reported as proportion (%) or median with interquartile range (median, [interquartile range (IQR)]), respectively. Statistical significance between cohort variables were assessed using Pearson's χ^2 and Kruskal-Wallis tests, as appropriate. We developed multivariable logistic models to identify the association of frailty with outcomes of interest. The least absolute shrinkage and selection operator (LASSO) regularization was used for variable selection and to optimize out-of-sample generalizability.[21] Models were chosen based on optimized area under the receiver operating characteristic (ROC) and Bayesian information criteria. Adjusted outcomes are reported as odds ratios with 95% confidence intervals (AOR, 95% CI). To account for the cohort size discrepancy along with significant intergroup differences among the *non-frail* and *frail*

Table I
Patient demographics, preoperative comorbidities and operative characteristics stratified by the 5-factor modified frailty index (mFI-5) defined groups

	Non-frail (n = 11,010)	*Prefrail* (n = 7,862)	*Frail* (n = 2,094)	*P* value
Patient demographics				
Female (%)	53.1	58.6	64.4	<.001
Age (years, median [IQR])	55 [46–63]	62 [54–70]	64 [57–71]	<.001
Race (%)				<.001
White	80.2	82.3	74.8	
Black	3.8	6.8	11.0	
Hispanic	9.5	6.4	9.5	
Other*	1.2	0.9	1.5	
Unknown	5.3	3.6	3.2	
Comorbidities (%)				
ASA class ≥3	23.9	49.4	76.2	<.001
Body mass index (kg/m^2)				<.001
Underweight	0.9	0.7	0.4	
Normal	24.3	17.2	11.8	
Overweight	36.6	34.7	26.8	
Obesity Class I	33.1	39.9	47.2	
Obesity Class ≥II	5.3	7.6	13.8	
Dyspnea	1.9	4.9	13.5	<.001
Smoker	18.8	15.9	18.7	<.001
Steroid use for chronic condition	2.8	4.7	7.9	<.001
Preoperative therapy (%)				
Bowel preparation	49.5	48.5	44.9	<.001
Oral antibiotics	45.7	44.4	42.7	.03
Operative factors (%)				
Complicated diverticular disease†	30.3	31.3	35.0	<.001
Operative approach				<.001
Open	13.1	16.4	21.7	
Laparoscopic	70.6	66.7	62.0	
Robotic	16.3	16.9	16.2	
Stoma creation	5.0	6.9	10.0	<.001
Unplanned conversion	1.5	1.5	2.3	.01
Splenic flexure mobilization	45.3	45.8	46.4	.55
Low pelvic anastomosis	57.4	56.9	55.7	.36

ASA Class ≥3 indicates severe systemic comorbidity.
IQR, interquartile range; *ASA*, American Society of Anesthesiologists' Physical Status Classification System.
* Other race includes Asian, Native Hawaiian, Pacific Islander, American Indian, and Alaskan Native.
† Complicated diverticular disease was defined as diverticular disease in the presence of perforation, or abscess (K57.20).

cohorts, a sensitivity analysis using 1:1 propensity score matching without replacement was performed. As reported by Caliendo & Kopeinig (2008), a standardized difference <5% was considered to reflect adequate balance of covariates among the matched groups.[22] Due to the de-identified nature of the database, this study was deemed exempt by the Institutional Review Board at the University of California, Los Angeles.

Results

Of the 20,966 patients who met study criteria, 10.0% were considered frail, 37.5% prefrail, and the remainder non-frail. Compared with *non-frail*, patients in the *prefrail* and *frail* cohorts were generally older (*non-frail*: 55 years, [46–63], *prefrail*: 62 years, [54–70], *frail*: 64 years, [57–71]) as well as more commonly female (*non-frail*: 53.1%, *prefrail*: 58.6, *frail*: 64.4, $P < .001$) and of Black race (*non-frail*: 3.8%, *prefrail*: 6.8, *frail*: 11, $P < .001$). Frail patients were more frequently of severe ASA class, morbidly obese, experienced dyspnea, and used steroids for a chronic condition compared to others (Table I).

Compared with the *non-frail* group, patients in the *prefrail* and *frail* cohorts less frequently received preoperative oral antibiotics or mechanical bowel preparation (Table I). Patients of the *frail* cohort had the greatest incidence of complicated diverticular disease of all groups (*non-frail*: 30.3%, *prefrail*: 31.3, *frail*: 35.0, $P < .001$). An open operative approach was more frequently deployed in the *prefrail* and *frail* cohorts (*non-frail*: 13.1%, *prefrail*: 16.4, *frail*: 21.7, $P < .001$). In addition, frail patients more commonly underwent stoma creation, concurrent operations, and unplanned conversion to open compared with others (Table I).

Although the overall incidence of mortality was low (0.2%), frail patients faced higher rates of postoperative complications. Specifically, MAE (*non-frail*: 7.5%, *prefrail*: 8.7, *frail*: 11.7, $P < .001$), SSI (*non-frail*: 5.9%, *prefrail*: 7.0, *frail*: 9.2, $P < .001$), and postoperative ileus (*non-frail*: 3.3%, *prefrail*: 4.3, *frail*: 6.6, $P < .001$) were significantly increased among the *frail* cohort. Similarly, compared to the *non-frail* group, patients in the *frail* cohort exhibited the highest observed rates of pLOS and unplanned 30-day readmission (Table II).

After adjustment of patient and operative factors, frailty portended a 26% increase in the relative odds of developing MAE (AOR 1.25, 95% CI 1.06–1.48) with non-frail as reference. Furthermore, frailty status was associated with a greater likelihood of SSI (AOR 1.28, 95% CI 1.06–1.54) and postoperative ileus (AOR 1.59, 95% CI 1.27–1.98). Frailty conferred greater odds of pLOS (AOR 1.38, 95% CI 1.18–1.54), nonhome discharge (AOR 2.29, 95% CI 1.74–3.03) and unplanned readmission (AOR 1.57, 95% CI 1.31–1.87). Prefrail status was not associated with an increase in odds for any of these evaluated complications (Figure 2). However, it did increase the odds of pLOS (AOR 1.11, 95% CI 1.01–1.22), nonhome discharge (AOR 1.34, 95% CI 1.06–1.70) as well as unplanned readmission (AOR 1.18, 95% CI 1.04–1.34) (Figure 3).

After obtaining adequate balance of covariates, the propensity matched sensitivity analysis yielded similar results as the regression models (Supplemental Table S4 and S5). However, the

Table II
Unadjusted comparison of outcomes following elective colonic resection for diverticular disease across the 3 study cohorts

(%)	*Non-frail* (*n* = 11,010)	*Prefrail* (*n* = 7,862)	*Frail* (*n* = 2,094)	*P* value
Surgical site infection*	5.9	7.0	9.2	*<0.001*
Major adverse event†	7.5	8.7	11.7	*<0.001*
Postoperative ileus‡	3.3	4.3	6.6	*<0.001*
Prolonged length of stay (≥5 days)	12.5	18.1	26.3	*<0.001*
Unplanned readmission	5.8	7.4	10.7	*<0.001*

* Composite of superficial, deep, and organ surgical site infection.
† Composite of grade III/IV Clavien-Dindo complication.
‡ Ileus requiring NPO status or nasogastric tube use >3 days postoperative.

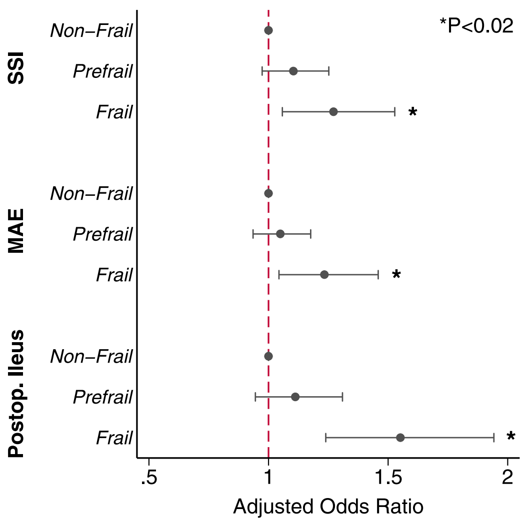

Figure 2. Adjusted odds of complications following elective colon resection for diverticular disease. With non-frail as reference, frailty status was associated greater odds for the 3 types of complications. *SSI*, surgical site infection; *MAE*, major adverse event; *Postop. Ileus*, postoperative ileus.

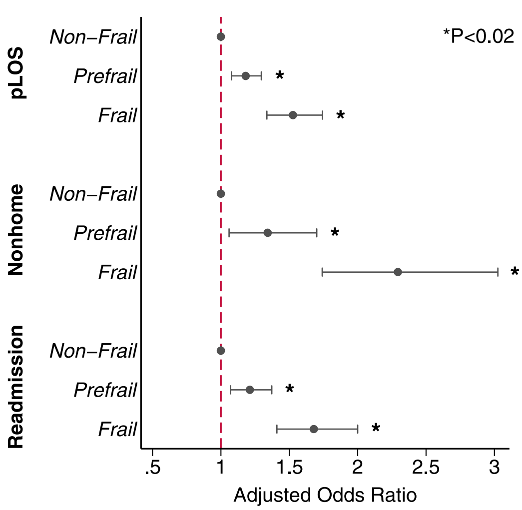

Figure 3. Adjusted odds of prolonged length of stay, nonhome discharge, and unplanned 30-day readmission. Compared with non-frail (ref.), both prefrail and frail were at increased odds of pLOS, nonhome discharge, and unplanned 30-day readmission. *pLOS*, prolonged length of stay (≥5 days); *Nonhome*, nonhome discharge; *Readmission*, unplanned 30-day readmission.

difference in SSI rates between the *non-frail* and *frail* groups was no longer significant.

Subgroup analysis of the *frail* cohort demonstrated laparoscopic and robot-assisted colectomy to be associated with lower odds of MAE and SSI in comparison with the open approach (Figure 4). In comparison to those who underwent primary anastomosis, stoma formation portended an increased likelihood of MAE but not SSI. Although patient BMI ≥25 kg/m^2 portended greater odds of SSI, only morbid obesity was associated with greater odds of both SSI and MAE.

Discussion

With the rapid growth of the older adult population in the US, surgeons are increasingly challenged to effectively manage patients of advanced age and their comorbidities. Age-associated factors such as frailty are now accepted to be better predictors of perioperative adverse outcomes compared to chronologic age alone. The present study utilized one of the largest, national surgical databases to assess the impact of frailty on outcomes following elective colectomy for diverticulitis. We employed the mFI-5, an accumulated deficits model of frailty, and identified ~10% of elective colectomy patients with diverticulitis as frail. Notably, frailty was associated with significantly increased odds of major adverse events as well as SSI and postoperative ileus. Similarly, frailty status portended greater odds of pLOS and readmission within 30 days. Several of our findings warrant further discussion.

The greater rate of MAEs among frail patients in the present work may, in part, be ascribed to maladaptive physiologic processes contributing to poor wound healing, altered immune response, and overall reduction in resilience to surgical stress. Such deficits often exceed what is expected with advanced age.[23–26] Our findings are concordant with prior studies demonstrating greater rates of infectious, respiratory, and grade III/IV C-D complications following elective and emergent operations among the frail.[12,14,27–29] Inspired by frailty and geriatric studies, several organizations along with the ACS have spearheaded research to identify geriatric-specific risk factors and are formulating clinical pathways to improve outcomes among older adults. In a study of 214 patients (aged ≥70 years) receiving oncologic operations, incorporation of geriatric experts in multidisciplinary teams along with frailty assessments were associated with a reduction in grade II–IV complications among older adults.[30] Furthermore, frail patients who complied with prehabilitation exercise programs demonstrated a reduction in surgical complication risk compared with the frail who did not undergo prehabilitation.[31] These efforts are aligned with evidence-based practices to address the specific needs of older adults and minimize the risk of undertreatment based on their chronological age.

We also found frailty to be associated with a 59% relative increase in odds of postoperative ileus following elective colon resection for diverticulitis when compared with non-frail. This dreaded but common complication following colorectal surgery has been associated with protracted hospitalization and readmission.[32] Advanced age, open operative approach, and ostomy formation are other

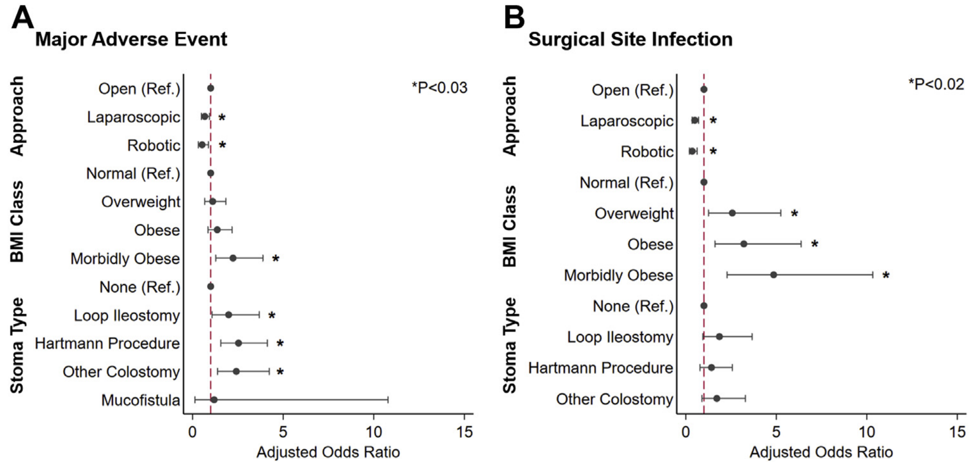

Figure 4. Subgroup analysis of *frail* cohort evaluating operative and patient factors associated with (A) MAE and (B) SSI. Compared with the open approach, minimally-invasive approach (laparoscopic and robot-assisted) portended lower odds of MAE and SSI. Stoma formation was found to be associated with greater odds of MAE but not SSI. *MAE,* major adverse event; *SS,* surgical site infection; *BMI Class,* body mass index classification 25–29.9 kg/m^2 (overweight), 30–39.9 (obese), ≥40 (morbidly obese); *Stoma type,* categorical variable comprised of stoma types if created.

reported factors associated with postoperative ileus all of which characterize patients in our *frail* cohort.[33,34] Effective analgesic stewardship, early feeding, and ambulation, as well as avoidance of prophylactic nasogastric tube placement have all been shown to stimulate bowel function after surgery.[35–37] While various forms of these measures have been adopted as part of enhanced recovery pathways (ERP) for younger patients, their feasibility and safety in the frail and older adults have not been thoroughly investigated. Moreover, concerns of aspiration due to nausea/vomiting along with the greater prevalence of dysphagia may dissuade surgeons from employing some of these measures in the frail.[38,39] Nonetheless, several studies have reported lower rates of postoperative complications and shorter lengths of stay in the older adult population undergoing colorectal operations at ERP centers compared with non-ERP.[40] Further investigation is paramount to establish the safety and efficacy of ERP in the frail and the older adult population.

A multitude of factors may be responsible for the greater rates of prolonged length of stay and readmission among the *frail* cohort. Aside from the increased risk of postoperative complications, frail patients underwent open colectomy with concurrent ostomy formation more frequently than others. In our study, the proportion of frail patients requiring diverting loop ileostomy and Hartmann's procedure was approximately 4% and 5%, respectively. Despite the known risk of protracted hospitalization and readmission, formation of stoma at the time of colectomy for diverticulitis could be indicated due to greater severity of illness and concerns of anastomotic leak in frail patients.[41] Although reasons for the type of approach are not discernable from our database, one could surmise that case complexity, surgeon preference, and concerns of physiologic alterations seen with pneumoperitoneum could have contributed to greater use of the open approach among the frail. In the present study, we have shown minimally-invasive approach to confer lower odds of MAE and SSI among the frail. The potential benefits of minimally-invasive colectomy have been consistently demonstrated over the past 3 decades.[42,43] In fact, the latest guidelines from ASCRS support minimally-invasive surgery for diverticulitis as a strong recommendation with highest level of evidence.[44] With an emphasis on patient-centered care, frail patients should be informed of their anticipated postoperative course given that they may require an open operation with the possibility of ostomy formation. Additionally, use of minimally-invasive approach in geriatric patients should be strongly considered to minimize suboptimal outcomes seen in this surgical cohort.

Aside from physiologic impairment, frail and older patients often lack the social support and resources needed for postoperative care. This may translate into greater rates of nonhome discharge particularly among older adults. We also demonstrated frailty to portend more than a two-fold increase in odds of nonhome discharge. In an analysis of the University Health System Consortium database, Damle et al. (2014) found nonhome discharge to be strongly associated with readmissions following oncologic colorectal operations.[45] Interestingly, Pattakos et al. (2012) have suggested that preoperative identification of high-risk patients for nonhome discharge could help reduce length of stay and resource use following cardiac surgery.[46] Early coordination of discharge to acute care or other nursing facilities by case management and social workers could reduce the number of postoperative hospital days. Thus, preoperative assessment of both clinical and social aspects of frailty is necessary to determine if home health or higher level of care are required. Anticipation of such needs and early coordination of care may reduce hospital stay and resource use.

The present study has several important limitations. We could not account for surgical complexity nor the selection bias in operative approach used by the performing surgeon. We could not adjust for hospital factors such as utilization of the Enhanced Recovery after Surgery protocol which has proven to reduce overall complications and length of hospital stay at these centers.[47,48] Lastly, given that the patient data in our study was acquired from ACS-accredited centers, our findings may not be nationally representative. Nonetheless, we used the largest, surgery-focused database to evaluate the impact of frailty on outcomes following colectomy for diverticular disease.

In conclusion, the present study found frailty to be associated with increased perioperative complications, prolonged length of stay, nonhome discharge, and unplanned readmission following elective colon resection for diverticulitis. Our findings encourage preoperative assessment of frailty as defined by the mFI-5 as an effective risk stratification tool. The adoption of such instruments has the potential to better inform operative candidacy among patients with diverticular disease. More importantly, the diagnosis of frailty could better inform shared decision-making and postoperative expectations. Lastly, evidence-based enhanced recovery pathways for the older adult and frail population should be further explored to achieve better outcomes in this population.

Conflict of interest/Disclosure

None of the authors have any conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.surg.2022.03.025.

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