ORIGINAL RESEARCH

Frailty and nutritional status predict postoperative complications in radical cystectomy patients

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ABSTRACT

INTRODUCTION: Radical cystectomy (RC) is associated with significant morbidity and mortality. While frailty and nutritional status have emerged as important predictors of surgical outcomes, their impact on RC complications remains incompletely characterized. We aimed to evaluate the relationship between frailty (using the Modified Frailty Index-5 [mFI-5], nutritional status (using the Nutritional Risk Index [NRI]), and postoperative outcomes in patients undergoing RC.

METHODS: We conducted a retrospective analysis of the American College of Surgeons National Surgical Quality Improvement Program database. Frailty was defined as mFI-5 score ≥2 and malnutrition as NRI ≤97.5. Hypoalbuminemia was defined as preoperative albumin ≤3.5. Outcomes included 30-day complications, length of stay, and mortality.

RESULTS: Among 8297 patients, 1793 (21.6%) were classified as frail. Frail patients experienced higher rates of infectious (sepsis: 10.2% vs. 6.72%, p<0.001), cardiopulmonary (myocardial infarction: 2.56% vs. 1.09%, p<0.001), and renal (renal insufficiency: 9.53% vs. 5.23%, p<0.001) complications. Mortality was twice as high in frail patients (2.45% vs. 1.17%, p<0.001). Among 8297 patients with nutritional data, 668 (8.05%) were malnourished, and 910 (15.2%) had hypoalbuminemia. Malnourished patients had higher rates of transfusion requirements (46.4% vs. 24.9%, p<0.001) and mortality (2.54% vs. 1.35%, p=0.032). Hypoalbuminemic patients demonstrated increased major complications (56.7% vs. 38.5%, p<0.001). The predictive accuracy of these indices varied by outcome, with area under the curve values ranging from 0.53–0.63.

CONCLUSIONS: Both frailty and poor nutritional status are associated with increased postoperative complications and mortality following RC; however, the modest predictive accuracy of these indices indicates they should be used as part of a broader risk assessment strategy.

INTRODUCTION

Radical cystectomy (RC) is a common surgical approach for patients with muscle-invasive bladder cancer (MIBC) and certain cases of non-muscle-invasive bladder cancer;[1] however, this procedure is associated with significant risks, with studies showing 90-day complication rates ranging from 36.5–80.5%, and a mortality rate of up to 5%.[2] As a result, bladder-sparing treatment options have been explored as alternatives to RC.[3]

In determining which patients are appropriate candidates for trimodal therapy instead of RC, oncologic factors like tumor size, multifocality, carcinoma in situ, hydronephrosis, and variant histologies have traditionally played a significant role;[4] however, recent evidence suggests that patient-specific factors, such as frailty and nutritional status, are also crucial predictors of surgical complications. Malnourished and frail patients tend to face more postoperative complications, longer hospital stays, and higher mortality rates. These findings highlight the importance of reliable tools to assess frailty and nutritional status to better identify which patients would benefit from RC and which might do better with alternative treatments.

Frailty is a clinical condition characterized by increased vulnerability, making patients more susceptible to both internal and external stressors. In surgical contexts, frailty status significantly impacts treatment decisions and outcomes.[5] The Modified Frailty Index-5 (mFI-5) is a scoring system commonly used to evaluate frailty in patients, and it has been shown to

KEY MESSAGES

- Frail patients had higher rates of sepsis, myocardial infarction, renal insufficiency, and doubled mortality.
- Malnourished patients had higher transfusion needs and mortality, while hypoalbuminemia increased major complications.
- Frailty and nutrition indices had modest predictive power and should be part of a broader risk assessment strategy.

predict both overall and major complications following bladder tumor resections.[6,7] Studies have found that higher mFI-5 scores correlate with worse prognosis in RC patients, including lower survival rates, even after adjusting for other factors (hazard ratio [HR] 1.79). Therefore, mFI-5 is an effective tool for assessing the suitability of RC for MIBC patients.[8]

Nutritional status is another key factor that can influence a patient's response to cancer treatment and surgery.[9,10] Malnutrition is a prevalent issue, affecting up to 70% of cancer patients, and can lead to complications such as longer hospital stays, increased risk of complications, and reduced survival rates.[11] Inadequate nutrition in cancer patients can lead to a range of adverse effects, mirroring those seen in frail individuals.[12] Researchers have developed various tools to assess nutritional risk, one of which is the Nutritional Risk Index (NRI). This index combines two factors — serum albumin levels and weight loss — to evaluate nutritional risk.[13,14] By standardizing the assessment, the NRI helps healthcare providers identify patients who may need nutritional intervention to improve their surgical outcomes.

In this retrospective study of the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database, we aimed to describe the impact of frailty and nutritional status on postoperative outcomes, as assessed through the mFI-5 index and NRI, and propose it as an effective tool for risk stratification for patients under consideration for RC.

METHODS

Data for this study were obtained from the ACS-NSQIP database for the years 2019–2022. This multi-institutional dataset collects standardized perioperative data from almost 700 participating hospitals through trained clinical reviewers who follow strict protocols to ensure consistency and minimize observer bias. Our retrospective analysis used the participant user files (PUF) from this database.

This study used de-identified data from the ACS-NSQIP database. As per institutional review board (IRB) guidelines, studies using de-identified secondary data are classified as exempt from full IRB review. Since patient identifiers were not accessible, informed consent was not required and was waived in accordance with standard ethical protocols.

Patients were included in the study if they were 18 years of age or older, underwent RC (identified by CPT codes 51590, 51595, and 51596), and had a postoperative diagnosis of malignancy of the bladder at any site. Missing data were handled with median imputation in order to calculate NRI score when needed. No missing data points were encountered to calculate mFI-5 in our cohort. Patients were excluded from the study if they had any postoperative diagnosis other than bladder malignancy. Since these metrics rely on routinely collected clinical and laboratory data rather than subjective assessments, variability in measurement was minimized.

Patients were categorized by frailty and nutritional status. Frailty was assessed using mFI-5 and patients were classified as frail if they had at least two of the following: antihypertensive use, type 2 diabetes mellitus (T2DM), chronic obstructive pulmonary disease (COPD), conges-

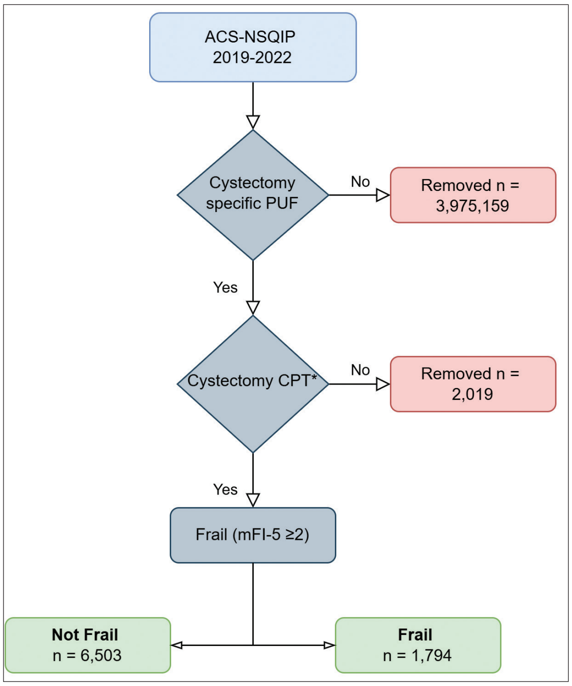

Figure 1. Patient inclusion flowchart.

Table 1. Patient baseline characteristics by frailty status

	Not frail n=6503	Frail n=1794	p
Female	1299 (20.0%)	309 (17.2%)	0.010
Age	68.7 (9.77)	71.0 (8.06)	<0.001
White race			0.052
White	4910 (93.0%)	1362 (90.9%)	
Black	244 (4.62%)	95 (6.34%)	
American Indian or Alaska native	8 (0.15%)	2 (0.13%)	
Other	20 (0.38%)	9 (0.60%)	
Asian	97 (1.84%)	31 (2.07%)	
Hispanic ethnicity	170 (3.18%)	64 (4.21%)	0.060
Diabetes	247 (3.80%)	1391 (77.5%)	0.000
BMI	28.0 (5.41)	30.2 (6.01)	<0.001
Smoker	1359 (20.9%)	366 (20.4%)	0.670
ASA >2	5010 (77.1%)	1666 (92.9%)	<0.001
Operative approach*			0.956
MIS	1829 (31.9%)	504 (32.0%)	
Open	3907 (68.1%)	1071 (68%)	
Hypoalbuminemia*	679 (10.4%)	231 (12.9%)	0.004
Malnourishment per NRI*	558 (8.58%)	110 (6.13%)	0.001

*Calculated based on the patients with available data after median imputation. ASA: American Society of Anesthesiologists; BMI: body mass index; MIS: minimally invasive surgery; NRI: nutritional risk index.

tive heart failure (CHF), or non-independent functional status. Nutritional status was determined using the NRI, with malnutrition defined as NRI ≤97.5. Devine's formula was used for ideal weight calculation. Hypoalbuminemia was defined as preoperative serum albumin ≤3.5.

Major complications included deep wound infection, reintubation, pneumonia, pulmonary embolism, failure to wean from a respirator, renal insufficiency, cerebrovascular accident, cardiac arrest, myocardial infarction, bleeding requiring transfusion, sepsis, or systemic shock. A subgroup analysis was performed for patients aged ≥65 years, as reported at the time of surgery, given the clinical relevance of this threshold in geriatric surgical risk assessment. While no additional adjustments were made specifically for age-related physiologic changes, all statistical models included covariates such as American Society of Anesthesiologists (ASA) classification, body mass index (BMI), and comorbidities to account for potential confounding factors.

Statistical analysis

R software (version 4.4.1; R Core Team, 2024) was employed alongside the packages "nsqipr," "compareGroups," and "dplyr" for data analysis and manipulation. Normality was assessed using the Kolmogorov-Smirnov test. Categorical variables were presented as frequencies and percentages and analyzed using Pearson's Chi-squared test or Fisher's exact test in counts <5, as appropriate. Continuous variables were summarized with means and standard deviations and tested using either the Student t-test or Mann-Whitney U test, based on the distribution and assumptions of the data from the Kolmogorov-Smirnov test. When a normal distribution was calculated, t-test was used. On the contrary, Mann-Whitney U test was used when normality assumption was not seen. A binomial logistic regression model was employed to evaluate the associations between selected variables.

The model's fit was assessed using the Omnibus test of model coefficients and Hosmer-Lemeshow test. Results were expressed as odds ratios (OR) with 95% confidence intervals (CI). A significance level of 0.05 was set for all statistical analyses.

The models' performance was assessed by determining the area under the receiver operating characteristic (ROC) curve, which was approximated using the trapezoidal rule.

RESULTS

Frailty status

A total of 8297 patients were included and categorized based on their frailty status, with 6503 patients classified as not frail, and 1793 patients categorized as frail. Figure 1 summarizes the patient inclusion flowchart. Frail patients were significantly older compared to the non-frail group (71.0±8.06 vs. 68.7±9.77 years, p<0.001) and had a higher BMI (30.2±6.01 vs. 28.0±5.41 kg/m^2, p<0.001). Moreover, the frail group had a higher prevalence of diabetes and ASA scores >2. Table 1 provides an overview of the baseline characteristics of both frail and non-frail patients.

Analysis of perioperative outcomes between frail and non-frail patients revealed that despite no differences in operative time and unplanned conversion to open surgery (OR 1.74, p=0.075), the length of stay was significantly prolonged in the frail group (8.17 days vs. 7.28 days, p<0.001). The risk of infection was significantly higher in the frail group when compared to the non-frail patients, as they developed higher rates of superficial wound infection (6.47% vs. 3.63%; OR

1.84, p<0.001), pneumonia (4.74% vs. 2.03%; OR 2.40, p<0.001), and sepsis (10.02% vs. 6.72%; OR 1.58, p<0.001).

Regarding cardiopulmonary complications, individuals with an mFI-5 score of ≥2 exhibited higher likelihoods of reintubation (2.62% vs. 1.40%; OR 1.90, p = 0.001), failure to wean from respiratory support (1.78% vs. 0.77%; OR 2.35, p<0.001), and myocardial infarction (2.56% vs. 1.09%; OR 2.39, p<0.001). Finally, the mortality rate was twice as high in frail patients (2.45% vs. 1.17%; OR 2.13, p<0.001). Table 2 presents a detailed summary of all the findings.

In a subgroup analysis of patients over the age of 65, we found that although there were no significant differences in operative time (325 min vs. 322 min, p=0.356) and unplanned conversions to open surgery (2.77% vs. 1.51 %; OR 1.86, p=0.070), the frail group had a significantly longer length of stay (8.41 days vs. 7.44 days, p<0.001). The frail group also exhibited increased rates of superficial wound infection (6.23% vs. 3.61%; OR 1.78, p<0.001), pneumonia (5.12% vs. 2.44%; OR 2.16, p<0.001), and sepsis (10.2% vs. 6.65%; OR 1.60, p<0.001) compared to their non-frail counterparts.

Cardiopulmonary complications were more common among frail patients, who were more likely to require reintubation (2.56% vs. 1.66%; OR 1.56, p=0.034) and had a higher likelihood of failing to wean from respiratory support (1.66% vs. 0.86 %; OR 1.94, p=0.014). Table 3 provides a detailed overview of these outcomes for patients aged over 65.

Table 2. Postoperative outcomes by frailty status

	Not frail n=6503	Frail n=1794	OR	pOR	p overall
Length of stay (days)	7.28 (4.22)	8.17 (5.10)	*	*	<0.001
Operative time (min.)	337 (115)	332 (110)	*	*	0.085
Unplanned conversion to open	35 (1.47%)	17 (2.53%)	1.74 [0.94; 3.09]	0.075	0.090
Deep wound infection	41 (0.63%)	18 (1.00%)	1.61 [0.90; 2.76]	0.109	0.132
Superficial wound infection	236 (3.63%)	116 (6.47%)	1.84 [1.46; 2.30]	<0.001	<0.001
Wound dehiscence	119 (1.83%)	36 (2.01%)	1.10 [0.75; 1.59]	0.617	0.696
Pneumonia	132 (2.03%)	85 (4.74%)	2.40 [1.81; 3.16]	<0.001	<0.001
Reintubation	91 (1.40%)	47 (2.62%)	1.90 [1.32; 2.70]	0.001	0.001
Pulmonary embolism	79 (1.21%)	22 (1.23%)	1.01 [0.62; 1.60]	0.951	1.000
Failure to wean from respirator	50 (0.77%)	32 (1.78%)	2.35 [1.49; 3.66]	<0.001	<0.001
Bleeding needing transfusion	1653 (25.4%)	554 (30.9%)	1.31 [1.17; 1.47]	<0.001	<0.001
Deep vein thrombosis	137 (2.11%)	40 (2.23%)	1.06 [0.73; 1.50]	0.740	0.821
Renal insufficiency	340 (5.23%)	171 (9.53%)	1.91 [1.57; 2.31]	<0.001	<0.001
Urinary infection	400 (6.15%)	128 (7.13%)	1.17 [0.95; 1.44]	0.134	0.145
Systemic shock	143 (2.20%)	58 (3.23%)	1.49 [1.08; 2.02]	0.015	0.015
Sepsis	437 (6.72%)	183 (10.2%)	1.58 [1.31; 1.89]	<0.001	<0.001
Return to operating room	311 (4.78%)	88 (4.91%)	1.03 [0.80; 1.30]	0.822	0.878
Major complication	2448 (37.6%)	909 (50.7%)	1.70 [1.53; 1.89]	0.000	<0.001
Still in hospital at 30 days	94 (1.45%)	52 (2.90%)	2.04 [1.44; 2.86]	<0.001	<0.001
Cerebrovascular accident	21 (0.32%)	11 (0.61%)	1.92 [0.88; 3.93]	0.097	0.123
Cardiac arrest	36 (0.55%)	20 (1.11%)	2.03 [1.15; 3.49]	0.016	0.016
Myocardial infarction	71 (1.09%)	46 (2.56%)	2.39 [1.63; 3.46]	<0.001	<0.001
Anastomotic leak	176 (2.71%)	59 (3.29%)	1.22 [0.90; 1.64]	0.193	0.217
Ureteral obstruction	260 (4.00%)	95 (5.30%)	1.34 [1.05; 1.70]	0.019	0.019
Ureteral fistula	238 (3.66%)	91 (5.07%)	1.41 [1.09; 1.80]	0.008	0.008
Rectal injury	86 (1.32%)	27 (1.51%)	Ref.	Ref.	0.634
Death	76 (1.17%)	44 (2.45%)	2.13 [1.45; 3.09]	<0.001	<0.001

OR not calculated for continuous variables. OR: odds ratio.

Nutritional status

When analyzing postoperative outcomes stratified by nutritional status, 8297 patients were included, of whom 7629 (91.9%) had normal nutritional status and 668 (8.05%) were classified as malnourished. Malnourished patients were significantly older compared to those with a normal nutritional status (70.2 ± 9.90 vs. 69.1± 9.43 years, p=0.006). No differences were found according to gender. Table 4 provides an overview of the baseline characteristics of both nourished and malnourished patients.

Malnourished patients experienced longer hospital stays compared to those with normal nutritional status (8.95±5.95 days vs. 7.35±4.25 days, p<0.001). Malnourished patients had higher rates of both superficial wound infections. Superficial wound infections were observed in 5.99% of malnourished patients vs. 4.09% of those with normal nutritional status (OR 1.50 [1.05–2.08], p=0.026). The most striking difference was observed in the rate of bleeding requiring transfusion, which occurred in 46.4% of malnourished patients compared to 24.9% of patients with normal nutritional status (OR 2.62 [2.23–3.07], p<0.001). Overall, malnourished patients had a significantly higher major complications (OR 2.02 [1.729–2.37], p<0.001). Moreover, the mortality was higher in the malnourished group (OR 1.92 [1.10–3.15], p=0.023). These findings are summarized in Table 5.

Table 3. Postoperative outcomes by frailty status in patients aged above 65 years old

	Not frail n=4514	Frail n=1444	OR	p OR	p overall
Length of stay (days)	7.44 (4.30)	8.41 (5.21)	*	*	<0.001
Operative time (min.)	322 (108)	325 (108)	*	*	0.356
Unplanned conversion to open	25 (1.51%)	15 (2.77%)	1.86 [0.95; 3.53]	0.070	0.086
Deep wound infection	31 (0.69%)	15 (1.04%)	1.53 [0.80; 2.80]	0.195	0.247
Superficial wound infection	163 (3.61%)	90 (6.23%)	1.78 [1.36; 2.31]	<0.001	<0.001
Wound dehiscence	83 (1.84%)	25 (1.73%)	0.94 [0.59; 1.46]	0.805	0.878
Pneumonia	110 (2.44%)	74 (5.12%)	2.16 [1.60; 2.92]	<0.001	<0.001
Reintubation	75 (1.66%)	37 (2.56%)	1.56 [1.04; 2.31]	0.034	0.037
Pulmonary embolism	57 (1.26%)	19 (1.32%)	1.05 [0.60; 1.74]	0.860	0.983
Failure to wean from respirator	39 (0.86%)	24 (1.66%)	1.94 [1.15; 3.23]	0.014	0.015
Bleeding needing transfusion	1155 (25.6%)	462 (32.0%)	1.37 [1.20; 1.56]	<0.001	<0.001
Deep vein thrombosis	104 (2.30%)	33 (2.29%)	1.00 [0.66; 1.46]	0.980	1.000
Renal insufficiency	237 (5.25%)	146 (10.1%)	2.03 [1.63; 2.52]	<0.001	<0.001
Urinary infection	259 (5.74%)	103 (7.13%)	1.26 [0.99; 1.59]	0.057	0.062
Systemic shock	112 (2.48%)	50 (3.46%)	1.41 [1.00; 1.97]	0.051	0.057
Sepsis	300 (6.65%)	148 (10.2%)	1.60 [1.30; 1.97]	<0.001	<0.001
Return to operating room	221 (4.90%)	71 (4.92%)	1.01 [0.76; 1.32]	0.966	1.000
Major complication	1713 (37.9%)	749 (51.9%)	1.76 [1.56; 1.99]	0.000	<0.001
Still in hospital at 30 days	76 (1.68%)	44 (3.05%)	1.84 [1.25; 2.67]	0.002	0.002
Cerebrovascular accident	17 (0.38%)	10 (0.69%)	1.86 [0.81; 4.02]	0.138	0.183
Cardiac arrest	33 (0.73%)	13 (0.90%)	1.24 [0.63; 2.32]	0.518	0.641
Myocardial infarction	64 (1.42%)	39 (2.70%)	1.93 [1.28; 2.88]	0.002	0.002
Anastomotic leak	105 (2.33%)	49 (3.39%)	1.48 [1.04; 2.07]	0.030	0.033
Ureteral obstruction	179 (3.97%)	77 (5.33%)	1.37 [1.03; 1.79]	0.029	0.031
Ureteral fistula	145 (3.21%)	72 (4.99%)	1.58 [1.18; 2.11]	0.002	0.002
Death	68 (1.51%)	36 (2.49%)	1.68 [1.10; 2.51]	0.016	0.017

*OR not calculated for continuous variables. OR: odds ratio.

Hypoalbuminemia

When stratifying malnourished patients by albumin levels, a total of 8297 patients were included, of whom 7387 (89.03%) had normal albumin levels and 910 (10.9%) were classified as having hypoalbuminemia. Patients with hypoalbuminemia experienced longer hospital stays compared to those with normal albumin levels (8.98±6.09 days vs. 7.29±4.15 days, p<0.001). Deep wound infections occurred in 1.54% of hypoalbuminemic patients compared to 0.61% of patients with normal albumin levels (OR 2.57 [135–4.59], p=0.003). Wound dehiscence was also more common in the hypoalbuminemic group (2.97% vs. 1.73%, OR 1.74 [1.12–2.61], p=0.015).

The most striking difference was observed in the rate of bleeding requiring transfusion, which occurred in 45.8% of hypoalbuminemic patients compared to 24.2% of patients with normal albumin levels (OR 2.64 [2.30–3.04], p<0.001). Hypoalbuminemic patients also were more likely to still be hospitalized at 30 days postoperative (2.75% vs. 1.64%, OR 1.70 [1.08–2.59], p=0.023).

Overall, hypoalbuminemic patients had a significantly higher rate of major complications (56.7% vs. 38.5%, OR 2.10 [1.82–2.41], p<0.001). Interestingly, mortality rates were not significantly different between the two groups (1.65% vs. 1.42%, OR 1.17 [0.65–1.96], p=0.0.575). Table 6 summarizes these findings.

Three statistical models were developed to predict perioperative complications using NRI status, mFI-5 score, and preoperative albumin. For predicting bleeding requiring transfusion, preoperative albumin had the highest area under the curve (AUC) at 0.68, followed by mFI-5 at 0.58 and NRI at 0.47. Preoperative albumin was also the best predictor for major complications.

Table 4. Patient baseline characteristics by nutritional status

	Normal n=7629	Malnourished n=668	p
Female	1489 (19.5%)	119 (17.8%)	0.309
Age	69.1 (9.43)	70.2 (9.90)	0.006
White race			<0.001
White	5783 (93.0%)	489 (87.2%)	
Black	292 (4.70%)	47 (8.38%)	
American Indian or Alaska native	7 (0.11%)	3 (0.53%)	
Other	26 (0.42%)	3 (0.53%)	
Asian	109 (1.75%)	19 (3.39%)	
Hispanic ethnicity	214 (3.39%)	20 (3.57%)	0.917
Diabetes	1552 (20.3%)	86 (12.9%)	<0.001
BMI	29.0 (5.43)	22.0 (3.41)	<0.001
Smoker	1495 (19.6%)	230 (34.4%)	<0.001
ASA >2	6110 (80.2%)	566 (84.7%)	0.005

ASA: American Society of Anesthesiologists; BMI: body mass index.

Conversely, the mFI-5 score proved more effective in predicting prolonged hospital stays (AUC 0.61) and postoperative death (AUC 0.53) compared to NRI and preoperative albumin. These findings are summarized in Figure 2.

DISCUSSION

In this ACS-NSQIP retrospective study, we examined the impact of frailty, nutritional status, and preoperative albumin on postoperative complications in RC for MIBC. Frail patients had higher rates of infectious, cardiopulmonary and renal complications, longer hospital stays, and increased mortality, findings consistent in those over 65. Malnourished patients had longer stays, higher wound infection rates, and nearly doubled transfusion needs (47.4% vs. 26.4%), with increased mortality (2.35% vs. 1.23%). Hypoalbuminemic patients had more wound complications, respiratory failure, and bleeding, with major complications significantly elevated (56.7% vs. 39.3%) compared to those with normal albumin. These results reinforce the growing evidence that frailty and poor nutrition worsen surgical outcomes in RC patients.

Surgical decisions are often based on age-related criteria. While the link between aging and physiologic decline is undeniable, it is crucial to recognize that other aspects beyond chronologic age significantly influence these outcomes.[15] Previous literature has established a correlation between frailty and malnutrition, evaluated using various assessment tools, and adverse postoperative outcomes across diverse surgical contexts.[6,16-20]

An interdisciplinary approach involving geriatricians for a thorough assessment is regarded as the gold standard for evaluating and approaching frailty and malnutrition; however, this method presents significant challenges.[15,21] The process is often time-consuming and may not be feasible in many clinical settings due to limited resources and practical constraints.

For patients undergoing RC, the mFI-5 and NRI have been recognized as valuable predictors of surgical complications and may be more efficient risk-stratification tools. Sathianathen et al demonstrated that the mFI-5 outperformed other commonly used methods, establishing it as a more practical tool compared to other measures like the 11-item Modified Frailty Index.[22] Similarly, the NRI's use of simple objective (serum albumin and % usual body weight) rather than subjective parameters easily quantifies nutritional risk and can be used for various patient populations,[13] providing increased utility for clinicians.

RC is a complex surgical procedure and is accompanied by a high incidence of postoperative challenges.[23] Research indicates that nearly half of patients experience issues within the initial 30 days after surgery.[24] Among these, infections and cardiopulmonary complications are the most prevalent and significantly contribute to mortality rates at both 30 and 90 days postoperative. For instance, a study by Sobhani et al highlighted infectious (25%), pulmonary (19%), and cardiac (12%) complications as the primary causes of 90-day mortality, with aspiration pneumonia and myocardial infarction being common specific concerns.[25]

In a study by Chappidi et al of 2679 patients undergoing RC, the mFI-5 was identified as an independent predictor of major complications, defined as Clavien-Dindo grades 4 and 5, with its predictive power being strongest for these higher-grade complications.

Table 5. Postoperative outcomes by nutritional status

	Normal n=7629	Malnourished n=6687	OR	p OR	p overall
Length of stay (days)	7.35 (4.25)	8.95 (5.95)	*	*	<0.001
Operative time (min.)	338 (114)	313 (106)	*	*	<0.001
Deep wound infection	50 (0.66%)	9 (1.35%)	2.10 [0.96;4.09]	0.063	0.052
Superficial wound infection	312 (4.09%)	40 (5.99%)	1.50 [1.05;2.08]	0.026	0.025
Wound dehiscence	141 (1.85%)	14 (2.10%)	1.15 [0.63;1.93]	0.632	0.761
Pneumonia	195 (2.56%)	22 (3.29%)	1.31 [0.81;2.00]	0.259	0.308
Reintubation	123 (1.61%)	15 (2.25%)	1.41 [0.79;2.36]	0.231	0.285
Pulmonary embolism	97 (1.27%)	4 (0.60%)	0.49 [0.15;1.16]	0.115	0.181
Failure to wean from respirator	71 (0.93%)	11 (1.65%)	1.80 [0.90;3.28]	0.094	0.112
Bleeding needing transfusion	1897 (24.9%)	310 (46.4%)	2.62 [2.23;3.07]	0.000	<0.001
Deep vein thrombosis	162 (2.12%)	15 (2.25%)	1.07 [0.60;1.77]	0.809	0.944
Renal insufficiency	473 (6.20%)	38 (5.69%)	0.92 [0.64;1.27]	0.610	0.658
Urinary infection	496 (6.50%)	32 (4.79%)	0.73 [0.49;1.03]	0.076	0.098
Systemic shock	184 (2.41%)	17 (2.54%)	1.07 [0.62;1.71]	0.806	0.934
Sepsis	568 (7.45%)	52 (7.78%)	1.05 [0.77;1.40]	0.738	0.808
Return to operating room	363 (4.76%)	36 (5.39%)	1.14 [0.79;1.61]	0.460	0.524
Major complication	2980 (39.1%)	377 (56.4%)	2.02 [1.72;2.37]	0.000	<0.001
Still in hospital at 30 days	129 (1.69%)	17 (2.54%)	1.53 [0.88;2.48]	0.123	0.145
Cerebrovascular accident	30 (0.39%)	2 (0.30%)	0.82 [0.12;2.71]	0.777	1.000
Cardiac arrest	51 (0.67%)	5 (0.75%)	1.15 [0.39;2.64]	0.768	0.803
Myocardial infarction	110 (1.44%)	7 (1.05%)	0.74 [0.31;1.48]	0.423	0.511
Death	103 (1.35%)	17 (2.54%)	1.92 [1.10;3.15]	0.023	0.021

*OR not calculated for continuous variables. OR: odds ratio.

Table 6. Postoperative outcomes by albumin levels

	Normal n=7387	Hypoalbuminemia n=910	OR	p OR	p overall
Length of stay (days)	7.29 (4.15)	8.98 (6.09)	*	*	<0.001
Operative time (min.)	337 (114)	326 (112)	*	*	0.010
Deep wound infection	45 (0.61%)	14 (1.54%)	2.57 [1.35; 4.59]	0.005	0.003
Superficial wound infection	299 (4.05%)	53 (5.82%)	1.47 [1.08; 1.97]	0.016	0.015
Wound dehiscence	128 (1.73%)	27 (2.97%)	1.74 [1.12; 2.61]	0.015	0.014
Pneumonia	190 (2.57%)	27 (2.97%)	1.16 [0.76; 1.72]	0.475	0.552
Reintubation	120 (1.62%)	18 (1.98%)	1.23 [0.72; 1.98]	0.428	0.516
Pulmonary embolism	87 (1.18%)	14 (1.54%)	1.32 [0.72; 2.26]	0.351	0.438
Failure to wean from respirator	68 (0.92%)	14 (1.54%)	1.70 [0.91; 2.94]	0.093	0.109
Bleeding needing transfusion	1790 (24.2%)	417 (45.8%)	2.64 [2.30; 3.04]	0.000	<0.001
Deep vein thrombosis	145 (1.96%)	32 (3.52%)	1.83 [1.22; 2.66]	0.004	0.003
Renal insufficiency	443 (6.00%)	68 (7.47%)	1.27 [0.97; 1.64]	0.087	0.094
Urinary infection	479 (6.48%)	49 (5.38%)	0.82 [0.60; 1.10]	0.197	0.226
Systemic shock	179 (2.42%)	22 (2.42%)	1.00 [0.62; 1.54]	0.986	1.000
Sepsis	546 (7.39%)	74 (8.13%)	1.11 [0.86; 1.42]	0.421	0.462
Return to operating room	350 (4.74%)	49 (5.38%)	1.15 [0.83; 1.54]	0.388	0.437
Major complication	2841 (38.5%)	516 (56.7%)	2.10 [1.82; 2.41]	0.000	<0.001
Still in hospital at 30 days	121 (1.64%)	25 (2.75%)	1.70 [1.08; 2.59]	0.024	0.023
Cerebrovascular accident	31 (0.42%)	1 (0.11%)	0.30 [0.01; 1.37]	0.144	0.251
Cardiac arrest	51 (0.69%)	5 (0.55%)	0.82 [0.28; 1.87]	0.662	0.783
Myocardial infarction	106 (1.43%)	11 (1.21%)	0.85 [0.43; 1.52]	0.608	0.691
Death	105 (1.42%)	15 (1.65%)	1.17 [0.65; 1.96]	0.575	0.694

*OR not calculated for continuous variables. OR: odds ratio.

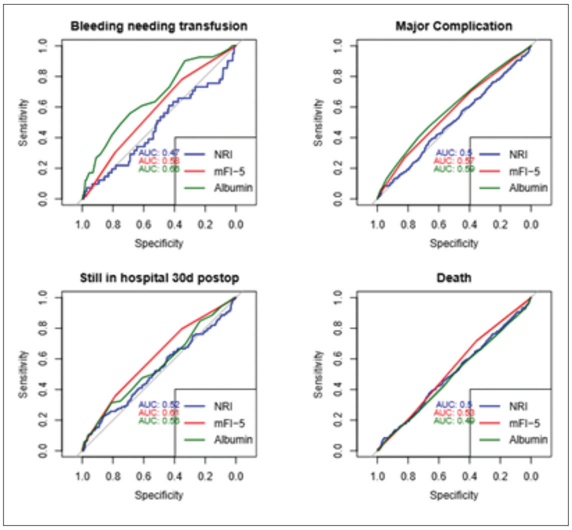

Figure 2. Response operator curves for the area under the curve analysis for key Modified Frailty Index-5 (mFI-5), Nutritional Risk Index (NRI), and albumin level's performance on predicting key outcomes.

Significant differences were found in the rate of postoperative complications between patients with a score <2 compared to those with a score ≥2, with the latter group exhibiting a higher incidence of respiratory, renal, and cardiovascular complications. Their analysis also demonstrated small but significant differences between groups in operation time (352.1 vs. 353.6 min, p<0.01) and length of stay (10.0 vs. 11.0 days; p<0.01).[26]

Our findings parallel these results. We observed higher rates of myocardial infarction (1.09% vs. 2.56%), renal insufficiency (5.23% vs. 9.53%), and pulmonary complications among frail individuals. Similarly, we found a modest but significant difference in length of stay (7.28 vs. 8.17 days) between frail and non-frail patients. The rates of unplanned conversion to an open approach and operative time were comparable between groups in our cohort.

The impact of nutritional status on surgical outcomes extends beyond frailty considerations in patients undergoing RC. Our analysis revealed that malnourished patients experienced significantly higher rates of wound complications and nearly doubled rates of transfusion requirements (47.4% vs. 26.4%) compared to well-nourished patients. These findings align with broader surgical literature examining the relationship between nutrition and postoperative outcomes.

For instance, in a large, multi-institutional study of colorectal cancer patients, hypoalbuminemia was found to be an independent predictor of both mortality (HR 3.0) and overall complications, with the strongest association with increased length of hospital stay.[27] Similarly, our data demonstrated that hypoalbuminemic patients had markedly elevated rates of major complications (56.7% vs. 39.3%) and prolonged hospitalizations (8.98 vs. 7.18 days). The consistency of these findings across surgical populations suggests that poor nutritional status, whether measured by NRI or albumin levels, represents a potentially modifiable risk factor that warrants attention in the preoperative period. This underscores the importance of early nutritional screening and intervention as part of comprehensive preoperative optimization for patients considering RC.

While multiple analyses of the ACS-NSQIP database have demonstrated this relationship between frailty and postoperative complications, studies from other cohorts have shown mixed results.[22,28,29] For instance, in a multicenter study of an eastern group by Yamashita et al, no statistically significant results were found regarding any grade of postoperative complications (p=0.87) and length of hospitalization (p=0.09) among frail and non-frail patients using a similar mFI-5 cutoff as in this study; however, when examining long-term outcomes, they found that a high mFI-5 score was an independent predictor of overall survival in one of their two models.[8] These contrasting findings highlight the importance of validating frailty indices across different patient populations and healthcare systems.

Our findings underscore the clinical relevance of the mFI-5 and NRI as preoperative assessment tools for risk stratification in patients undergoing RC. By assessing physiologic reserves and identifying increased vulnerability, these tools have the potential to optimize surgical decision-making. Clear delineation of frailty and nutritional status allows us to select suitable candidates for surgery and identify those for whom cystectomy may not be ideal, prompting consideration of alternative management strategies.[26]

While this study demonstrates that frailty is associated with some worse outcomes in RC patients, it is important to note that the predictive power of this tool as a screening method is limited. The AUC values for various outcomes are relatively low. For instance, the mFI-5 score showed an AUC of only 0.53 for predicting bleeding requiring transfusion and 0.63 for predicting pneumonia. Even for predicting postoperative death, the AUC was just 0.53. These values, being close to 0.5, indicate that the mFI-5's discriminatory ability is only slightly better than chance. Therefore, while frailty assessment using the mFI-5 can provide valuable insights into potential risks, its use as a standalone screening tool for specific complications or outcomes is limited due to its low predictive accuracy. This underscores the need for comprehensive preoperative assessments that consider multiple factors beyond frailty alone.

Limitations

This study has several limitations that need to be considered. It is primarily a retrospective cohort study, inherently introducing biases. Also, our analysis relies on data from the ACS-NSQIP database, which may not be fully generalize to populations beyond the Western world and, like all database studies, is subject to potential errors in ICD-10 and CPT coding that could influence the results.

In addition, the variables analyzed are limited to observations within 30 days due to the database's reporting constraints, focusing solely on short-term outcomes. Furthermore, data on socioeconomic status, which might play a significant role in frailty, was not available for assessment. Other factors related to frailty, such as preoperative physical activity levels, are also not captured in this database.

Finally, while the mFI-5 and NRI are validated tools for assessing frailty and nutritional status, they have inherent limitations. The mFI-5 captures only five clinical variables and may not fully encompass the multifaceted nature of frailty, which includes other physiologic and functional components. Additionally, the NRI is based on albumin levels and weight, which do not account for other nutritional deficiencies, body composition changes, or muscle mass loss, all of which may impact surgical outcomes. These limitations should be considered when interpreting our findings.

Despite these limitations, our sample size provides substantial data for informing urologists about expected perioperative outcomes for RC in frail and malnourished patients with bladder cancer.

CONCLUSIONS

Frailty and nutritional status significantly impact postoperative complications and mortality following RC. These findings suggest that such patients should be considered for non-surgical management options, such as bladder-preservation protocols, as RC may not be optimal for all; however, the modest predictive accuracy of these indices indicates they should be used as part of a broader risk-assessment strategy.

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