Frailty as a predictor of complications after radical cystectomy: A prospective study of various preoperative assessments

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Abstract

Purpose: Frailty has been correlated with worse postoperative outcomes. Prospective studies examining frailty and bladder cancer are lacking. We aimed to determine whether a prospective frailty assessment or traditional risk indices can identify patients undergoing radical cystectomy (RC) at risk for complications.

Materials and methods: Patients ≥ 65 years undergoing RC were preoperatively assessed using Fried Frailty Criteria (FFC; grip strength, gait speed, exhaustion, physical activity, shrinking), Charlson Comorbidity Index, American Society of Anesthesiologists score, Katz Index of Independence in Activities of Daily Living, Karnofsky Performance Scale, Eastern Cooperative Oncology Group performance status, and Center for Epidemiological Studies Depression scale. Thirty-day and 90-day postoperative complications were recorded. Univariate and multivariate analyses were performed.

Results: One hundred and twenty three patients were assessed with median age of 74 years. Fifty-nine patients (48.0%) had ≥ 1 complication within 30 days and 72 (58.5%) within 90 days. Center for Epidemiological Studies Depression scale (odds ratio [OR] 1.08, 95% confidence interval [CI] 1.01−1.17, $P = 0.027$) and shrinking (OR 3.79, 95% CI 1.64−9.26, $P = 0.0024$) were significant for any 30-day complication, while physical activity was protective (OR 0.84, 95% CI 0.69−1.00, $P = 0.072$) for any 90-day complication. Being intermediately frail or frail was associated with high-grade 30-day (OR 4.87, 95% CI 1.39−22.77, $P = 0.022$) and 90-day complications (OR 3.01, 95% CI 1.05−9.37, $P = 0.045$), along with Eastern Cooperative Oncology Group score ≥ 3 (OR 45.00, 95% CI 6.92−437.69, $P = 0.0010$ and OR 17.85, 95% CI 3.21−143.26, $P = 0.0079$, respectively).

Conclusions: Fried Frailty Criteria were predictive of high-grade complications, while individual components were predictive of having any complication. Elderly patients should be routinely assessed prior to RC to guide postoperative care. © 2018 Elsevier Inc. All rights reserved.

Keywords: Frailty; Radical cystectomy; Bladder cancer; Elderly; Complications

1. Introduction

In the United States in 2018, it is estimated 81,190 patients will be diagnosed with bladder cancer, and 17,240 patients will die due to the disease [1]. Both men and women are usually diagnosed at an advanced age, with an average age of 69 years for men and 71 years for women [2]. The 5-year cause-specific survival rate for those 60 to 65 years old is 84% and decreases to 60% in those 85 years and older [3]. While radical cystectomy is the gold standard treatment for muscle-invasive bladder cancer, this procedure carries significant morbidity, with reported 30-day complication rates ranging from 31.5% to 58% [4−9] and 90-day complication rates from 47% to 78% [10]. As the percentage of individuals aged 65 years and older in the population

continues to rise [11], the incidence of bladder cancer is expected to increase. Thus, a preoperative risk stratification tool for prospective radical cystectomy candidates that can be easily implemented in the clinic is needed. Although grading systems based on patient comorbidities have been used to classify patients at increased risk for complications [12−15], recent research has explored frailty as a better metric for predicting postoperative outcomes [16−18].

Frailty has been defined as a syndrome of physiological decline with increased vulnerability to adverse health outcomes [19]. Frailty can be characterized using either phenotypic frailty or a frailty index. Phenotypic frailty asserts that physiologic changes which come with aging create a phenotype that can be measured using 5 criteria: weight loss (known as shrinking), grip strength, gait speed, activity level, and feelings of exhaustion. These 5 criteria have been established as the Fried Frailty Criteria (FFC) and assign patients an overall frailty score based on their results in each domain (also known as Hopkins Frailty Score, Table 1) [20]. The frailty index is based on a deficit accumulation model, which proposes that patients become frail as they accumulate certain medical, functional, and social deficits over time [21]. These comprehensive deficits are categorized into a frailty index, which creates a frailty score based on number of deficits present. The modified Frailty Index (mFI) is used most often by surgeons [17,22−24], which is a shorter 11-item version of the original 70-item Canadian Study of Health and Aging Frailty Index [25].

Although urologists have studied frailty and its impact on postoperative outcomes, these studies have nearly all been retrospective analyses of the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database using the mFI, with few examining only radical cystectomy. The majority of these studies have found frailty to be a predictor of worse postoperative outcomes after radical cystectomy [17,22,23], while one study examining specific adverse events did not find frailty to be predictive [26]. Two prospective studies have found frailty to be associated with worse postoperative outcomes, however, both included patients undergoing different procedures with < 15% of patients undergoing radical cystectomy [16,27]. Thus, no study to date has prospectively examined frailty in a cohort of patients all undergoing radical cystectomy, which is often considered one of the most complex urologic surgeries carrying the highest complication rates. The goal of this study is to determine if a validated preoperative frailty assessment or traditional surgical risk indices are able to predict which patients undergoing radical cystectomy are at increased risk for 30-day and/or 90-day postoperative complications, after adjusting for patient and surgical covariables limited in most retrospective analyses.

2. Materials and methods

The Institutional Review Board approved this project. Patients were consented for a prospectively maintained cystectomy database. Patients planning for radical cystectomy were identified at a preoperative surgical clearance clinic within 1 month before surgery from February 2014 to October 2017. Inclusion criterion was any patient 65 years or older undergoing open or robotic radical cystectomy for bladder cancer. This age cutoff was chosen to better assess possible nuances that may be determinants of frailty. Eight surgeons were involved, who all perform > 10 radical cystectomies per year at a tertiary-care referral center.

Patients were assessed in clinic using grip strength, gait speed, shrinking (≥ 10 pounds of unintentional weight loss in the past year), feelings of exhaustion (questions #1 and #2), and physical activity level. Full assessment details reported in Table 1. Patients were also scored using the Center for Epidemiological Studies Depression (CES-D) scale, Charlson Comorbidity Index , Katz Index of Independence in Activities of Daily Living, Karnofsky Performance Scale (KPS), and Eastern Cooperative Oncology Group (ECOG) performance status. Laboratory values recorded include preoperative hemoglobin, albumin, and creatinine levels. Additional patient variables reported in Table 3. Thirty-day and 90-day postoperative complications were recorded per the Clavien-Dindo classification system [28]. The majority of patients return to our institution for follow-up visits throughout the 90-day period, and for those who do not, a database manager actively solicits patients' referring urologist, primary care provider, and patients directly to further capture complications.

Pearson's chi-square, Fisher's exact test, and multivariable logistic regression analyses were performed using SAS, Version 9.4 (SAS Institute Inc., Cary, NC). Stepwise selection was used to choose statistically significant variables in the multivariable setting. The final model included statistically significant variables and important clinical variables for control purposes. All P values reported are 2-sided; $P < 0.05$ is considered statistically significant. Preoperative assessment variables were analyzed as continuous and, if applicable, dichotomous variable for association with occurrence of 30-day and 90-day complications (overall and Grade $\geq$ IIIa) and readmissions. For the FFC, each variable was categorized as "frail" or "not frail," and patients were assigned 1 point per frailty criteria present which comprised an overall score, categorizing them as "not frail" (0−1 point), "intermediately frail" (2−3 points), or "frail" (4−5 points) [16,20].

3. Results

A total of 134 patients undergoing radical cystectomy were assessed preoperatively by various research staff. After exclusion of patients with delayed surgeries or final pathology other than primary bladder cancer, 123 patients were included. The final cohort had a median age of 74 years, majority were male (82.9%) and undergoing open radical cystectomy (66.7%), 57 patients (46.3%) received an orthotopic urinary diversion, and 45 patients (36.6%) received neoadjuvant chemotherapy, which were

Table 1
Preoperative frailty assessment

Assessment	Description	Patients assessed	Frequency and/or median
Fried Frailty Criteria	Based on the 5 criteria listed below, patients are given 1 point per criteria qualifying as frail. The overall frailty score (Hopkins Frailty Score) then categorizes patients as not frail (0−1 points), intermediately frail (2−3 points), or frail (4−5 points).	109	NF: 60 (55.1%) IF: 43 (39.5%) F: 6 (5.5%)
Grip strength, kg	Measured 3× in each hand using a JAMAR hydraulic hand dynamometer. Patient squeezed device while seated with entire forearm resting on arm of chair. Highest grip strength of either hand recorded. Patients qualified as frail per thresholds based on gender and BMI. Men were frail if BMI and grip strength were ≤ 24 and ≤ 29 kg, 24.1−28 and ≤ 30 kg, and > 28 and ≤ 32 kg. respectively. Women were frail if BMI and grip strength were ≤ 23 and ≤ 17 kg, 23.1−26 and ≤ 17.3 kg, 26.1−29 and ≤ 18 kg, and > 29 and ≤ 21 kg, respectively.	122	28 (21−35) 60 patients frail (49.2%)
Gait speed, s	Measured as time to walk 15 feet at normal pace. The average of 3 measurements was recorded. Patients qualified as frail per thresholds based on gender and height. Men were frail if height and gait speed were ≤ 173 cm and ≥ 7 s or > 173 cm and ≥ 6 s, respectively. Women were frail if height and gait speed were ≤ 159 cm and ≥ 7 s or > 159 cm and ≥ 6 s, respectively.	112	5.08 (4.15−5.69) 16 patients frail (14.3%)
Physical activity, kcals	Patients were asked "Do you do any exercise on a regular basis?" and if not, then, "How many hours per day do you spend walking and/or standing?" Although the Minnesota Time and Leisure Activities Questionnaire has been used by prior studies, this question was substituted due to necessity for a quick assessment in clinic. Hours spent per activity were converted to kilocalories (kcals) of energy spent. Men were frail if they spent < 383 kcals and women < 270 kcals of energy per week on activities.	119	749 (258−1635) 40 patients frail (33.6%)
Shrinking	Defined as ≥ 10 lbs. of unintentional weight loss in the past year. A positive answer qualified a patient as frail.	122	37 patients frail (30.3%)
Exhaustion	Patients were asked how often in the last week they felt "everything I did was an effort" (#1) and "I could not get going" (#2). For each statement, patients rated how often they felt this way as 0 (rarely or none), 1 (some or a little of the time), 2 (moderate amount of time), or 3 (most of the time). A rating of ≥ 2 on either question qualified a patient as frail. Although patients answered these questions on the CES-D, they were directly asked these 2 questions again for the assessment.	122	18 patients frail (14.8%)

Other risk indices and performance status assessments

Charlson Comorbidity Index (CCI)	A cumulative scoring index based on type and severity of specific comorbidities. Patients' primary bladder tumor (2 points) was not included in the score to better demonstrate true burden of comorbidities, and score was not age-adjusted.	123	1 (0−2)
American Society of Anesthesiologists Score (ASA)	Patients assigned a score of 1, 2, 3, or 4 based on patient comorbidities with 1 being least comorbidities.	123	1: 0 (0%) 2: 16 (13.0%) 3: 101 (82.1%) 4: 6 (4.9%)
Eastern Cooperative Oncology Group (ECOG) performance status	Developed specifically for oncology patients to determine how their functional status has changed since their diagnosis. Patients assigned a score of 0 (completely symptom free) to 5 (dead).	122	0: 57 (46.7%) 1: 51 (41.8%) 2: 7 (5.7%) 3: 7 (5.7%) 4: 0 (0%)
Katz Index of Independence in Activities of Daily Living (Katz ADL)	Scores patients based on need for assistance in bathing, dressing, toileting, transferring, continence, or feeding. Patients receive 1 point for activity they are independent in, with a score of 6 representing complete independence in aforementioned ADL's.	122	≤ 4: 1 (0.8%) 5: 10 (8.2%) 6: 111 (91.0%)
Karnofsky Performance Status Scale (KPS)	Scores patients from 50 to 100 in intervals of 10 based on symptoms of disease affecting functional status, with 100 being completely symptom free.	120	50: 3 (2.5%) 60: 7 (5.8%) 70: 16 (13.3%) 80: 23 (19.2%) 90: 49 (40.8%) 100: 22 (18.3%)

Table 1 (**Continued**)

Assessment	Description	Patients assessed	Frequency and/or median
Center for Epidemiological Studies Depression (CES-D) scale	A 20-question survey in which patients respond to each question with a response of 0 (rarely or none), 1 (some or a little of the time), 2 (moderate amount of time), or 3 (most of the time). Patients are assigned points per question rated ≥ 1, with scores of ≥ 16 usually representing depression.	115	2.5 (0−7)

BMI = body mass index; F = frail; IF = intermediately frail; NF = not frail.

not associated with 30-day or 90-day complications ($P >$ 0.05, Table 3). Per the FFC, 109 patients (88.6%) had a full assessment. Sixty patients (55.1%) were not frail (NF), 43 (39.5%) were intermediately frail (IF), and 6 (5.5%) were frail (F). Remaining results for preoperative assessments reported in Table 1 and patient demographics and surgical details in Tables 2 and 3.

3.1. Thirty-day complications

Fifty-nine patients (48.0%) had ≥ 1 postoperative complication within 30 days, and 16 patients (13.0%) had a high-grade complication. When assessing each preoperative variable on univariate analysis, shrinking ($P = 0.0054$), decreased physical activity ($P = 0.044$), low KPS score ($P = 0.030$), positive answer to feelings of exhaustion (question #1, $P = 0.031$), high CES-D score ($P = 0.0036$), and low preoperative hemoglobin ($P = 0.0048$) were associated with having at least one 30-day complication. Examining Grade ≥ IIIa 30-day complications, physical activity ($P = 0.0085$), and KPS score ($P = 0.0004$) remained significant, while decreased grip strength ($P = 0.013$), Charlson Comorbidity Index score ≥ 1 ($P = 0.049$), higher ECOG score ($P = 0.0004$), and frail gait speed ($P = 0.02$) were also significant. Stratified by the FFC, patients who were IF or F (IF/F) were more likely to have a high-grade complication ($P = 0.018$), although frailty status was not predictive for having any 30-day complication ($P = 0.1$). Remaining preoperative assessment variables and associated P values reported in Table 4.

On multivariable logistic regression analysis, shrinking (odds ratio [OR] 3.79, 95% confidence interval [CI] 1.64 −9.26, $P = 0.0024$) and high CES-D score (OR 1.08, 95%

CI 1.01−1.17, $P = 0.027$) remained significant for having any 30-day complication after adjusting for patient age, pathologic stage, and urinary diversion. For high-grade complications, physical activity (OR 0.36, 95% CI 0.12 −0.78, $P = 0.041$), ECOG score ≥ 3 (OR 45.00, 95% CI 6.92−437.69, $P = 0.0010$), and frailty status IF/F (OR 4.87, 95% CI 1.39−22.77, $P = 0.022$) remained significant; however, no covariables were included due to limited number of complications (Table 5).

3.2. Ninety-day complications

Seventy-two patients (58.5%) had a complication within 90 days, and 23 patients (18.7%) had a high-grade complication. For any 90-day complication, decreased gait speed ($P = 0.042$) and decreased physical activity ($P = 0.042$) were significantly associated with having at least 1 complication. For Grade ≥ IIIa 90-day complications, gait speed ($P = 0.028$) and physical activity ($P = 0.029$) remained significant, while feelings of exhaustion (question #2, $P = 0.0043$), low KPS score ($P = 0.011$), high ECOG score ($P = 0.0046$), and frail gait speed ($P = 0.038$) were also significant (Table 4).

On multivariable logistic regression analysis, only physical activity remained protective (OR 0.84, 95% CI 0.69 −1.00, $P = 0.027$) for having any 90-day complication, after adjusting for patient age, pathologic stage, and urinary diversion. For high-grade complications, significant preoperative assessment variables included gait speed (OR 1.70, 95% CI 1.05−2.89, $P = 0.038$), frailty status IF/F (OR 3.01, 95% CI 1.05−9.37, $P = 0.045$), and ECOG score 3 (OR 17.85, 95% CI 3.21−143.26, $P = 0.0079$). Covariables and remaining assessment variables reported in Table 5.

3.3. Additional surgical variables

Thirty-day and 90-day complications were associated with length of hospital stay ($P < 0.0001$ and $P = 0.0006$, respectively), days in the intensive care unit ($P = 0.0060$ and $P = 0.081$, respectively), and having received ≥ 1 blood transfusion ($P < 0.0001$ and $P = 0.0046$, respectively). However, these variables are surrogate markers of complications themselves, as patients who have complications usually have prolonged hospital stays and/or are transferred to the intensive care unit, while any postoperative blood transfusion is considered a Grade II complication [28]. Remaining surgical variables and associated P values reported in Table 3.

Table 2
Patient and surgical demographics

Total patients enrolled	123
Age, y (median)	74 (69−80)
Male	102 (82.9%)
Body mass index (median)	26.2 (24−28.5)
Neoadjuvant chemotherapy	45 (36.6%)
Robotic radical cystectomy	41 (33.3%)
Any 30-d complication	59 (48.0%)
Clavien-Dindo Grade ≥ IIIa 30-d complication	16 (13.0%)
Any 90-d complication	72 (58.5%)
Clavien-Dindo Grade ≥ IIIa 90-d complication	23 (18.7%)
Any 30-d readmission	19 (15.4%)
Any 90-d readmission	42 (34.1%)

Table 3
Univariate analysis of patient demographic and surgical variables and 30-day and 90-day complications

Variable	Median or frequency	30-d complications P value	30-d Grade ≥ 3 P value	90-d complications P value	90-d Grade ≥ 3 P value
Age, y	74 (69−80)	0.7	0.3	0.7	0.9
Male	102 (82.9%)	1.0	1.0	1.0	0.4
BMI	26.2 (24−28.5)	0.9	0.7	0.3	0.3
Preop Hgb, mg/dl	11.9 (9.8−13.6)	**0.005**	0.6	0.2	0.9
Preop albumin, mg/dl	4.1 (3.9−4.4)	0.4	0.8	0.6	0.8
Preop creatinine, mg/dl	1.1 (0.9−1.3)	0.3	1.0	0.6	0.6
Neoadjuvant chemotherapy	45 (36.6%)	0.3	1.0	0.9	0.6
Robotic RC	41 (33.3%)	0.4	0.8	0.6	0.6
Operative time, h	5.6 (4.7−6.7)	0.8	0.4	0.9	0.2
EBL, ml	400 (250−700)	0.6	0.7	0.6	0.3
Length of hospital stay, d	5 (4−6)	**< 0.0001**	**0.013**	**< 0.001**	0.1
D in ICU	0 (0−0)	**0.006**	**< 0.0001**	0.0807	**< 0.001**
Pathologic stage	OC: 65 (52.9%)	0.0760	0.3	0.4	0.4
	EV: 26 (21.1%)				
	LN+: 32 (26.0%)				
Urinary diversion	Orthotopic: 57 (46.3%)	0.5	0.6	0.7	0.8
	Nonorthotopic: 66 (53.7%)				
≥ 1 blood transfusion[a]	48 (39.0%)	**< 0.0001**	**0.054**	**0.005**	**0.031**
# prior TURBT	2 (1−3)	0.9	0.5	0.7	0.3

BMI = body mass index; EBL = estimated blood loss; EV = extravesical disease; Hgb = hemoglobin; ICU = intensive care unit; LN+ = lymph node positive disease; OC = organ confined disease; Preop = preoperative; RC = radical cystectomy TURBT = transurethral resection of bladder tumor.

[a] Includes any intraoperative or postoperative blood transfusions received.

P values < 0.05 bolded for convenience.

Table 4
Univariate analysis of preoperative assessment variables and 30-day and 90-day complications

Variable	30-d complications P value	30-d Grade ≥ IIIa P value	90-d complications P value	90-d Grade ≥ IIIa P value
Grip strength	0.2	**0.013**	0.3	0.4
Gait speed	0.4	0.1	**0.042**	**0.028**
Physical activity	**0.044**	**0.009**	**0.042**	**0.029**
Exhaustion #1	**0.031**	0.1	0.2	0.1
Exhaustion #2	0.2	0.061	0.4	**0.004**
CCI	0.081	0.2	0.2	0.2
CCI (0, 1+)	0.1	**0.049**	0.6	0.053
ASA	0.5	0.3	0.8	0.6
ASA (3−4, 1−2)	0.4	1.0	0.6	1.0
KPS	**0.030**	**< 0.001**	0.055	**0.011**
ECOG	0.3	**< 0.001**	0.6	**0.005**
Katz ADL	0.2	0.2	0.4	0.5
CES-D	**0.004**	0.3	0.2	0.3
CES-D (≤ 15, 16−25, ≥ 26)	0.2	0.4	0.8	0.7
Fried Frailty Criteria (frail, not frail)				
Grip strength	0.5	0.056	0.3	0.4
Gait speed	1.0	**0.020**	0.8	**0.038**
Shrinking	**0.005**	0.6	0.1	1.0
Physical activity	0.7	0.2	1.0	0.3
Exhaustion	0.6	0.061	0.6	0.1
Hopkins Frailty Score (intermediately frail/frail, not frail)	0.1	**0.018**	0.2	0.052

ASA = American Society of Anesthesiologists Score; CCI = Charlson Comorbidity Index; CES-D = Center for Epidemiological Studies Depression Scale; ECOG = Eastern Cooperative Oncology Group Performance Status; Katz ADL = Katz Index of Independence in Activities of Daily Living; KPS = Karnofsky Performance Status Scale.

P values < 0.05 bolded for convenience.

Table 5
Multivariable logistic regression of preoperative assessment variables and 30-day and 90-day complications

Variable	OR (95% CI)	*P* value
Any 30-d complication[a]		
CES-D	1.08 (1.01−1.17)	0.027
Shrinking	3.79 (1.64−9.26)	0.002
30-d Grade ≥ IIIa complication[b]		
Physical activity	0.36 (0.12−0.78)	0.041
ECOG, 3 vs. 0	45.00 (6.92−437.69)	0.001
Frailty score, IF/F vs. NF	4.87 (1.39−22.77)	0.022
Any 90-d complication[a]		
Physical activity	0.84 (0.69−1.00)[†]	0.027[c]
90-d Grade ≥ IIIa complication		
Gait speed[d]	1.70 (1.05-2.89)	0.038
Exhaustion (Quest. #2), 3 vs. 0[b]	20.00 (2.74−405.17)	0.012
ECOG, 3 vs. 0[b]	17.85 (3.21−143.26)	0.008
Frailty score, IF/F vs. NF[e]	3.01 (1.05−9.37)	0.045

CES-D = Center for Epidemiological Studies Depression scale; CI = confidence interval; ECOG = Eastern Cooperative Oncology Group Performance Status; OR = odds ratio.

Each assessment variable was used alone in the statistical model, with covariables as denoted below.

[a] Adjusted for age, pathologic stage, urinary diversion.
[b] No other covariables able to be used in model.
[c] Likelihood ratio test *P* value reported.
[d] Adjusted for age and urinary diversion.
[e] Adjusted for urinary diversion.

Examining readmission rates, no preoperative assessment variables were significant for 30-day readmissions. For 90-day readmissions, decreased gait speed (*P* = 0.015) was significantly associated with being readmitted.

4. Discussion

Our study, to the best of our knowledge, is the first to examine frailty using a prospective frailty assessment among a cohort of patients all undergoing radical cystectomy, compared to all prior studies using a frailty index, while also comparing the prospective frailty assessment to traditional surgical risk indices. Given the complexity and associated morbidity of this procedure for a predominately elderly patient population, preoperative risk stratification tools evaluated specifically for radical cystectomy are likely to perform better than those studied in cohorts undergoing different urologic procedures, especially nononcologic interventions. Overall, preoperative assessment components that remained significant on multivariable logistic regression analysis were more objective (FFC, gait speed, shrinking, and physical activity) or focused on patient reported symptoms (ECOG, CES-D, and feelings of exhaustion), while more subjective assessments (American Society of Anesthesiologists score, Katz Index of Independence in Activities of Daily Living) had no association whatsoever.

Revenig et al. have conducted the only prior study using the FFC to prospectively assess frailty in a urological cohort [18]. They found the FFC and shrinking to be most predictive of any grade 30-day complication, although this cohort only included 27 patients (14.3%) undergoing radical cystectomy [16]. Although we did not find the FFC to be predictive of having any 30-day complication, shrinking was significantly associated with having at least one 30-day complication. We also found physical activity to be protective for any 90-day complication, which together corroborate prior research associating sarcopenia with worse postoperative outcomes after radical cystectomy [29].

Additionally, we found CES-D score associated with 30-day complications when assessed as a continuous variable. However, Revenig et al. nor our study found any association using the standard CES-D cutoffs as a categorical variable, with scores > 15 indicating depression [16]. Although psychosocial factors are already known to impact recovery after radical cystectomy [18], our findings show that patients do not need to be severely symptomatic to be at risk for complications. Our findings of shrinking, physical activity, and CES-D score also indicate potential areas to implement prehabilitation, which are preoperative interventions to optimize patients [30]. While studies have examined the impact of preoperative nutrition and begun investigating the use of preoperative physical therapy, psychosocial interventions may be a new approach for decreasing radical cystectomy complication rates [30].

In contrast to the study by Revenig et al., we found the FFC to be predictive of Grade ≥ IIIa 30-day and 90-day complications on multivariable logistic regression analysis, along with ECOG score 3. This difference is likely attributable to the high overall complication rate of radical cystectomy. However, screening tools which predict those at risk for high-grade complications may be preferred for guiding treatment. Patients determined to be at increased risk may be better candidates for prehabilitation or for alternative treatment modalities altogether, such as chemoradiation. Phenotypic frailty also provides a metric for determining whether prehabilitation had any effect due to its modifiable definition of frailty, which is not possible with risk indices (i.e., mFI). Additionally, these preoperative risk stratification tools may contribute to shared decision-making by helping patients make more informed decisions about whether to have surgery. Although feelings of exhaustion and gait speed were also predictive of high-grade 90-day complications on multivariable analysis, the FFC and ECOG were the only assessments both predictive of high-grade 30-day and 90-day complications, making these tools most useful in clinical practice. Of note, frailty status and ECOG score 3 did not directly correlate. Thirty-three percent of F patients had ECOG score 2, and 42.9% of ECOG score 3 patients were IF. Thus, multiple frailty assessments may be needed in order to identify all patients at increased risk of complications.

Additionally, our findings that frailty is a predictor of high-grade 30-day complications contradict those of Meng et al., who did not find frailty to be a predictor of specific adverse events [26]. However, this study used the mFI on

the NSQIP database, compared to our study which used the FFC to assess frailty on an institutional cohort. The discrepancy in findings between our study and that by Meng et al. is likely due to this difference in method of frailty assessment and limitations inherent in the NSQIP database, including limited information on patient disease status and comprehensiveness of complications captured.

Although the phenotypic frailty assessment appears time and labor intensive, it can easily be performed in 5 to 7 minutes in clinic by ancillary staff. We realize some urologists may not have the resources to perform an entire frailty assessment. However, individual components found to be significant can be easily done in clinic, such as asking about shrinking, measuring gait speed, or assessing ECOG performance status. Even for urologists who may not have the resources to implement preoperative interventions, simply knowing that a patient is at increased risk for complications can help the physician and patient anticipate a potentially more challenging recovery and initiate an earlier discussion on postoperative care, such as discharge disposition. Regardless of case volume or hospital level of care, all elderly patients undergoing radical cystectomy should be assessed preoperatively for physical and psychosocial deficits.

Being a high-volume tertiary-care center, limitations of our study include routine use of multidisciplinary care and enhanced recovery after surgery protocols for all patients undergoing radical cystectomy, which may lower our complication rates. Although we did not directly assess sarcopenia, we did assess muscle strength by measuring grip strength and gait speed, which are known to be surrogate markers of sarcopenia. Our sample size may be smaller than retrospective analyses, which may limit the strength of the multivariate analysis, especially for 30-day high-grade complications. However, given that it was a prospective study lends credence to the validity of our results.

5. Conclusion

Our study demonstrates the FFC, ECOG performance status, and CES-D score may predict which patients are at increased risk for 30-day and 90-day complications after radical cystectomy. Additionally, these assessments may indicate areas to further develop and implement prehabilitation interventions.

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