Predicting Short-term Outcomes After Radical Cystectomy Based on Frailty

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OBJECTIVE To evaluate the impact of frailty on adverse perioperative outcomes in patients treated with radical cystectomy for bladder cancer.

MATERIAL AND METHODS We identified 9459 adults (age ≥18) in the Nationwide Readmission Database who underwent radical cystectomy in 2014 for bladder cancer. We defined patients' frailty status using Johns Hopkins Adjusted Clinical Groups frailty-defining diagnosis indicator and compared in-hospital mortality, ICU-level complications, 30-day readmissions, nonhome discharge, length of hospitalization, and hospital-related costs between frail and nonfrail patients using χ^2 tests. We used multivariate logistic regression to identify predictors of the primary outcomes of interest.

RESULTS Of 9459 patients undergoing radical cystectomy, 7.1% ($n = 673$) met criteria. Frail patients were more likely than nonfrail patients to have comorbid conditions (68.2% vs 59.7%; $P = .005$), in-hospital mortality (4.2% vs 1.5%; $P = .04$), ICU-level complications (52.9% vs 18.6%; $P < .001$), nonhome discharge (33.9% vs 11.6%; $P < .001$), longer length of stay (median 15 vs 7 days; $P < .001$), and higher median cost of the index admission ($39,665 vs $27,307). Frailty was the strongest independent predictor of ICU-level complications, nonhome discharge, increased length of stay, and hospital-related costs of any covariate.

CONCLUSION Frail patients receiving radical cystectomy were more likely than nonfrail patients to have adverse perioperative outcomes and higher odds of in-hospital mortality, ICU-level complications, nonhome discharge, increased length of stay, and hospital-related costs. Preoperative consideration of frailty may be useful in clinical guidance and shared decision-making. UROLOGY 133: 25−33, 2019.

Bladder cancer represents nearly 5% of all new cancer diagnoses annually in the United States.[1] Radical cystectomy is the gold standard treatment for patients with nonmetastatic, muscle-invasive and select cases of high-grade, nonmuscle-invasive bladder cancer.[2] Although radical cystectomy is often curative, large cohort studies show post-operative complication rates of up to 78% and mortality rates as high as 15% within 90 days of discharge.[3,4] Clinicians may use risk assessment tools, such as the modified Charlson Comorbidity Index, Cardiac Risk Index (Lee Criteria), and the American Society of Anesthesiologists Physicians Status Classification to counsel bladder cancer patients and guide selection of surgical candidates.[5] However, these tools focus primarily on medical comorbidities, excluding broader measures of physiological fitness. Furthermore, they emphasize mortality as a target outcome and provide little information on the association between patient risk factors and outcomes related to morbidity and health care resource utilization.[5,6] As our healthcare moves from fee-for-service to value-based compensation, better risk assessment is becoming critical.[7]

Frailty assessment is potentially a more accurate and practical method to evaluate an aging patient's surgical risk.[8] Broadly, frailty is the loss of physiological reserve and increased vulnerability to stressors as a result of the accumulation of age, comorbidities, and disability. Regardless of the specific definition, frailty appears to be associated with increased risk for surgical complications, morbidity, and mortality.[8] While numerous definitions of frailty exist, one widely accepted definition describes frailty as a phenotype represented by 5 physical components: involuntary weight loss, level of exhaustion, activity level, gait speed, and handgrip strength. Surgical risk increases linearly with the

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number of frailty components met.[8] A more comprehensive definition comes from the Canadian Study of Health and Aging, which assessed frailty across 70 possible clinical deficits, ranging from comorbidity and disability to neurocognitive health status.[9] The Johns Hopkins Adjusted Clinical Groups (ACG) frailty-defining diagnosis indicator adapted these definitions to create a claims-based instrument for identifying frailty which researchers can apply to a wider range of secondary datasets.[10]

We sought to evaluate the impact of frailty on perioperative outcomes, hospital readmissions, and cost of care in patients treated with radical cystectomy for bladder cancer using a nationally-representative, population-based cohort. We hypothesized that frailty status would independently correlate with higher rates of adverse perioperative outcomes, hospital readmissions, and higher costs of care.

METHODS

Data Source

We performed a retrospective cohort study using data from the Nationwide Readmissions Database (NRD) from January to November 2014. This is a database of all-payer hospital inpatient stays sponsored by the Agency for Healthcare Research and Quality as part of the Healthcare Cost and Utilization Project.[11] Data are constructed from individual State Inpatient Databases, which in 2014 included 22 states accounting for more than 50% of all US hospitalizations. Sample weights provided by the database allow investigators to produce estimates representative of 100% of discharges nationally. An advantage of the NRD over other nationally representative databases such as the Nationwide Inpatient Sample is that the NRD also contains verified patient-linkage numbers that can track patients across hospitals to facilitate readmission analysis. The patient-linkage numbers do not track patients across states or across years. Further information on the NRD is available through Healthcare Cost and Utilization Project.[11] Because the database uses publicly available information with no personal identifiers, this study was exempt from full review by the University of California-Los Angeles Institutional Review Board.

Study Population and Variables

We used ICD-9 codes to identify all hospital discharges for adult (age ≥18) patients with bladder cancer (188.x, 233.7) undergoing radical cystectomy (57.71, 57.79). Patient characteristics, including age, sex, primary payer, household income quartile, frailty, and comorbidity, were tabulated. We categorized patients as frail using the Johns Hopkins Adjusted Clinical Groups frailty-defining diagnoses indicator.[12] This validated, binary measure of frailty was developed specifically for use on health administrative data, and assesses frailty using 10 clusters of frailty-defining diagnoses (Fig. 1), whereby patients with one or more of these diagnoses are defined as frail. Comorbidity was graded using the Charlson index as implemented by Deyo et al.[13] Procedure and hospital characteristics included surgical approach (open vs minimally invasive), hospital bed number, and teaching status.

Outcome Measures

In-hospital mortality, ICU-level complications, readmission within 30 days of discharge, nonhome discharge (ie, to a nursing facility or short-term hospital), length of hospitalization, and hospital-related costs were analyzed as dependent variables. ICU-level complications were classified as Clavien-Dindo Grade IV (CDIV) morbidity, based on ICD-9 codes previously described for major urological procedures.[14]

When analyzing 30-day readmissions, we excluded patients who died during the index admission (n = 163). We excluded patients discharged in December (n = 667) because the NRD does not capture readmission that occur in a separate calendar year from the index discharge date and patients with out-of-state residence (n = 1,294) to avoid potential loss of follow-up.

Statistical Analysis

Data are presented as the mean (standard deviation) or median (interquartile range). We compared the baseline characteristics of frail and nonfrail patients using Student's t test for continuous variables or χ^2 tests for categorical variables. We generated national estimates using survey weights from the NRD. Inpatient costs were converted from NRD charges using the hospital-specific cost-to-charge ratios provided by the NRD, and adjusted for inflation to 2014 dollars using the medical component of the consumer price index.[15] We used multivariate logistic regression to evaluate the relationship between the independent variables and the primary outcomes of interest. We also present absolute risk differences with their 95% confidence intervals (CI). Length of stay and cost are distributed with high positive skew, compromising the interpretation of measures of central tendency commonly used in regression analysis.[16] To account for this, length of stay and cost were analyzed using generalized linear regression modeling with a log link. Statistical tests were 2-sided and statistical significance was indicated by P<.05. Statistical analyses were performed using Stata 14 (StataCorp, College Station, TX).

RESULTS

Baseline Characteristics

Table 1 describes baseline characteristics of the 9459 patients undergoing radical cystectomy who met inclusion criteria and list factors associated with frailty. The median age of our cohort was 70 (IQR 63-76) years and the majority (84%) were male. Approximately 7.1% of patients met criteria for frailty, most commonly due to malnutrition (74%), weight loss (14%), and presence of decubitus ulcers (11%). Comorbid conditions were significantly more common in frail than nonfrail patients (68.2% vs 59.7%, +Δ8.6%; 95% CI, 0.3%-14.5%, P= .005). Multivariable logistic regression demonstrates an independent association between age ≥75 years and frailty, medical comorbidity burden was not an independent predictor of frailty status. After controlling for other covariates, frailty was significantly associated with advanced age, but not with increasing comorbidity burden.

Clinical Outcomes

Frail patients were more likely to experience in-hospital mortality (4.2% vs 1.5%, +Δ2.6%; 95% CI, 0.1%-5.2%, P= .04), ICU-level complications (52.9% vs 18.6%, +Δ34.3%; 95% CI, 30.0%-40.6%, P <.001) and nonhome discharge (33.9% vs 11.6%, +Δ22.2%; 95% CI, 16.2%-14.5%, P<.001). Medical cost of index admission was considerably higher among frail patients (median $39,665, IQR $28,196-$56,397) compared with nonfrail patients (median $27,307, IQR $21,145-$36,049). Similarly, the median length of stay of the index admission was significantly longer among frail patients compared with nonfrail patients, 15 (IQR 9-21) and 7 IQR 6-10) days, respectively.

Procedures/Diagnoses		ICD-9 Codes
Bladder cancer		188.x, 233.7
Radical cystectomy		57.71, 57.79
Frailty-Defining Diagnoses in Johns Hopkins ACG Frailty Indicator		
Malnutrition	Nutritional marasmus	261, 262, 263.8, 263.9, V77.2
	Other severe protein-calorie malnutrition	
Dementia	Senile dementia with delusional or depressive features	290.20, 290.21, 290.3
	Senile dementia with delirium	
Severe vision impairment	Profound impairment, both eyes	369.0, 369.00, 369.01, 369.03, 369.04, 369.06, 369.07, 369.08
	Moderate or severe impairment, better eye/lesser eye: profound	
Decubitus ulcer	Decubitus ulcer	707.0, 707.00, 707.01, 707.02, 707.03, 707.04, 707.05, 707.06, 707.07, 707.09, 707.20, 707.21, 707.22, 707.23, 707.24, 707.25
Incontinence of urine	Incontinence without sensory awareness	788.34, 788.37
	Continuous leakage	
Loss of weight	Abnormal loss of weight and underweight	783.2, 783.21, 783.22, 783.3
	Feeding difficulties and mismanagement	
Fecal incontinence	Incontinence of feces	787.6
Social support needs	Lack of housing	V60.0, V60.1, V60.2
	Inadequate housing	
	Inadequate material resources	
Difficulty in walking	Difficulty in walking	719.7, 781.2
	Abnormality of gait	
Fall	Fall on stairs or steps	E880, E880.0, E880.1, E880.9, E884.3
	Fall from wheelchair	

Figure 1. ICD-9 procedure and diagnosis codes. ACG, adjusted clinical groups.

Of the 7312 patients eligible for readmission analysis, 2159 (29.5%) were readmitted within 30 days of discharge. Thirty-day readmission rate was similar between frail and nonfrail patients (31.8% vs 29.3%, +Δ2.5%; 95% CI, −4.2% to 9.2%). However, when readmitted, frail patients had significantly higher median costs ($35,732, IQR $26,638-56,440) of readmission compared with nonfrail patients ($29,319, IQR $22,314-$39,513). The median length of stay for the readmission was similar among frail and nonfrail patients, 6 (IQR 3-11) vs 5 (IQR 3-8) days, respectively (P= .12).

Table 1. Baseline characteristics of patients undergoing radical cystectomy by frailty status

Variable	Total Patients (*n* = 9,459) No. (%)	Patients Without Frailty (*n* = 8,785) No. (%)	Patients With Frailty (*n* = 673) No. (%)	*P* Value
Age (y)				
<75	6568 (69.4)	6196 (70.5)	371 (55.1)	<.001
≥75	2890 (30.6)	2588 (29.5)	302 (44.9)	
Male	7968 (84.2)	7404 (84.3)	564 (83.8)	.82
Payer				
Private	2646 (28.0)	2516 (28.7)	129 (19.3)	.006
Medicare	6039 (64.0)	5549 (63.3)	489 (72.8)	
Medicaid	476 (5.0)	439 (5.0)	36 (5.5)	
Other	272 (2.9)	255 (2.9)	16 (2.4)	
Median household income quartile for zip code				
76th-100th percentile	1826 (19.7)	1664 (19.3)	161 (24.5)	.11
51st-75th percentile	2651 (28.6)	2461 (28.5)	189 (28.8)	
26th-50th percentile	2521 (27.2)	2378 (27.6)	143 (21.7)	
≤25th percentile	2284 (24.6)	2119 (24.6)	164 (25.0)	
Comorbidity score				
0	3,754 (39.7)	3,540 (40.3)	213 (31.7)	.03
1	2,683 (28.4)	2,487 (28.3)	195 (29.0)	
2	1,513 (16.0)	1,382 (15.7)	131 (19.5)	
≥3	1,507 (15.9)	1,374 (15.6)	133 (19.8)	
Index admission from ED	284 (3.0)	221 (2.5)	62 (9.3)	<.001
Hospital bedsize				
Small	890 (9.4)	824 (9.4)	66 (9.8)	.97
Medium	1930 (20.4)	1795 (20.4)	135 (20.0)	
Large	6638 (70.2)	6165 (70.2)	472 (70.2)	
Hospital teaching status				
Nonteaching hospital	986 (10.4)	886 (10.1)	99 (14.8)	.01
Teaching hospital	8473 (89.6)	7898 (89.9)	574 (85.2)	
Surgical technique				
Nonrobotic	7236 (76.5)	6684 (76.1)	552 (82.0)	0.03
Robotic	2222 (23.5)	2101 (23.9)	121 (18.0)	

ED, emergency department.

Multivariable Models

We report the result of the multivariable logistic regression analysis of factors associated with in-hospital mortality, ICU-level complications, nonhome discharge, and 30-day readmission in Table 2. After adjusting for all covariates, frailty, comorbidity score of 2, age ≥75 years, lower household income, and larger hospital size are independent predictors of in-hospital mortality. Independent predictors of ICU-level complications include frailty, advanced comorbidity (Charlson score ≥ 3), age ≥75 years, Medicare or Medicaid insurance, and second lowest household income quartile. The odds of nonhome discharge were significantly higher in patients with frailty, advanced comorbidity, age ≥75 years, female gender, Medicare or Medicaid insurance, and open surgical approach. Advanced comorbidity was significantly associated with increased odds of 30-day readmission. Notably, frailty was not independently associated with 30-day readmission. Compared with advanced comorbidity or age ≥75 years, frailty was a stronger predictor of both ICU-level complications and nonhome discharge, whereas age ≥75 years was a stronger predictor of in-hospital mortality.

Table 3 describes the multivariable generalized linear regression analysis of factors associated with length of hospitalization and hospital-related costs. Frailty, advanced comorbidity, age ≥75 years, female gender, lower household income, larger hospital size, nonteaching hospital status, and open surgical approach were associated with significantly greater length of hospitalization. Independent predictors of increased hospital-related costs included frailty, advanced comorbidity, age ≥75 years, and minimally invasive approach. Frailty was a stronger predictor of ICU-level complications, nonhome discharge, increased length of stay, and hospital-related costs than any other covariate analyzed.

DISCUSSION

In this large population-based study, we found that frail patients were significantly more likely to experience ICU-level complications, nonhome discharge, increased length of stay, higher hospital-related costs, and greater mortality than nonfrail patients after radical cystectomy for bladder cancer.

Frailty and comorbidity have both been linked to increased mortality and adverse outcomes across surgical specialties, however they are distinct concepts.[17] While frailty describes the aggregate loss of physiological reserve leading to susceptibility to acute stressors, comorbidity may be defined as the accumulation of more than 2 diseases based on disease-specific criteria.[9] One of the first studies to illustrate this distinction showed that frail adults had higher levels of inflammatory markers, increased coagulation factors, and altered metabolism compared with nonfrail adults. However, these frail patients did not have

Table 2. Multivariate logistic regression analysis of factors significantly associated with mortality, ICU-level complications, nonhome discharge, and 30-day readmission

Variable	OR	95% CI	*P* Value
In-hospital mortality			
Frailty	2.30	1.08-4.92	.03
Comorbidity score of 2	2.28	1.03-5.02	.04
Age ≥75	3.04	1.44-6.45	.004
Median household income, ≤25th percentile	2.93	1.14-7.54	.03
Median household income, 26th-50th percentile	2.57	1.22-5.38	.01
Hospital bed size, medium	11.3	1.44-89.3	.02
Hospital bed size, large	8.52	1.16-62.5	.04
ICU-level complication			
Frailty	4.74	3.60-6.25	<.001
Comorbidity score of 1	1.30	1.03-1.63	.027
Comorbidity score of 2	1.85	1.42-2.41	<.001
Comorbidity score ≥3	2.09	1.62-2.70	<.001
Age ≥75	1.37	1.12-1.68	.002
Medicare insurance status	1.36	108-1.71	.008
Medicaid insurance status	1.63	1.02-2.60	.04
Median household income, 26th-50th percentile	1.31	1.03-1.66	.03
Nonhome discharge			
Female	2.09	1.59-2.75	<.001
Frail	3.43	2.50-4.69	<.001
comorbidity score 2	1.44	1.05-1.97	.02
Comorbidity score ≥3	1.92	1.42-2.58	<.001
Age ≥75	2.96	2.36-3.72	<.001
Medicare insurance status	2.46	1.76-3.43	<.001
Medicaid insurance status	2.27	1.16-4.46	.02
30-Day Readmission			
Comorbidity score ≥3	1.84	1.44-2.36	<.001

CI, confidence interval; OR, odds ratio.

Table 3. Generalized linear regression analysis of length of stay and hospital costs

Variable	OR	95% CI	*P* Value
Length of stay			
Female	0.07	0.01-0.13	.04
Frailty	0.58	0.50-0.66	<.001
Comorbidity score 2	0.07	0.005-0.14	.03
Comorbidity score ≥3	0.01	0.05-0.18	.001
Age ≥75	0.14	0.09-0.20	<.001
Medicaid insurance status	0.17	0.04-0.29	.007
Median household income, ≤25th percentile	0.09	0.02-0.16	.02
Median household income, 51st-75th percentile	0.06	0.008-0.12	.03
Hospital bed size, medium	0.09	0.01-0.16	.023
Hospital bed size, large	0.06	0.004-0.12	.036
Hospital costs (2014 USD)			
Frail	0.42	0.34-0.49	<.001
Comorbidity score 2	0.06	0.006-0.12	.03
Comorbidity score ≥3	0.14	0.08-0.19	<.001
Age ≥75	0.05	0.003-0.09	.03
Surgical technique, Robotic	0.10	0.06-0.14	<.001

CI, confidence interval; ED, emergency department; OR, odds ratio.

higher rates of comorbidities.[18] Similarly, in our study frailty was not significantly associated with comorbidity burden. Furthermore, frailty was a stronger predictor of adverse events than either comorbidity or increased age in our study. Understanding the differences between comorbidity and frailty is important because they can co-occur and, in a subset of patients, comorbidity may contribute to the development of worsening of frailty.[8,17]

Our study found that frail patients were significantly more likely to experience ICU-level complications and mortality compared with nonfrail patients after radical cystectomy. Chappidi et al found a similar trend using the modified Frailty Index to measure frailty in a National Surgical Quality Improvement Program cohort of patients who underwent radical cystectomy.[19] Furthermore, Suskind et al and Loscano et al analyzed a wider scope of 21 different urologic procedures and also found that a high modified Frailty Index score was associated with increased risk of complications compared with patients with a lower modified Frailty Index score.[20,21] In contrast, Meng et al recently reported frailty to be a weaker predictor of poor short-term perioperative outcomes than either the modified Charlson Comorbidity Index or American Society of Anesthesiologists score.[22] Observed discrepancies between studies may be related to the varying measures of frailty used as well as their relatively small sample sizes ($n \leq$,516) compared with our study. Additionally, we found that medium and large hospitals had higher rates of mortality relative to small hospitals. Although the impact of hospital bed number on surgical outcomes has not been thoroughly addressed in the urology literature, few existing studies have suggested larger hospitals tend to have superior outcomes.[23] We suspect the potentially contradictory findings in our analysis are explained by the relatively small portion of patients treated at small bed number hospitals (9%). Given the inherent complexity of radical cystectomy, patients treated at small hospitals may have been relatively healthier or had more minimal disease for which referral to a larger center was not performed, leading to a correlation between small bed number and reduced mortality. This finding merit further investigation in future studies. While direct comparison with our study is limited given the use of different frailty metrics, our results further support the predictive value of frailty in major urologic surgery.

Hospital length of stay and direct costs were more than twice as long and 1.5 times as high, respectively, for frail patients compared with the nonfrail. Our results are comparable to other large-scale studies across surgical specialties that found increased length of hospital stay and medical costs among frail patients.[17,18] This significant increase in length of stay may relate to frail patients' greater supportive needs during the recovery process or increased susceptibility to postoperative complications and exacerbation of underlying comorbidities. Moreover, frail patients were significantly more likely to require further specialized care after discharge. Besides a delay in recovery, a prior study suggested that nonhome discharge is associated with additional costs of care and worse reported quality of life.[24] Discussion of recovery, overall health expectations, and the potential associated financial burden should be included during the preoperative visit with frail patients. Additionally, female gender was an independent predictor of greater length of stay and nonhome discharge. This is in concordance with previous studies which have shown that women are more likely to have locally advanced tumors at presentation, higher perioperative adverse outcomes including cancer recurrence and mortality, and experience significant delay in urological referrals.[25] Preoperative recognition of high-risk frail patients and their increased resource utilization may allow hospitals to take early steps to streamline the care and eventual discharge of patients, such as securing a bed at a skilled nursing facility, to avoid unnecessarily prolonged hospital stays. Taken together, these results underscore the importance of incorporating frailty assessment into the preoperative urology visit.

Despite the apparent potential for frailty assessment to improve surgical risk prediction, defining the optimal frailty assessment tool has been limited by lack of consensus as to which criteria are the most important to assess. Several validated tools have been developed to measure frailty. The modified Frailty Index, derivative of a 70-item list created from the Canadian Study of Health and Aging database, is the most studied and used by surgeons.[9] Although the modified Frailty Index is an 11-item scale, some studies suggest that this number may be reduced by only including items that provide comprehensive information about the body's function and have the highest predictive potential.[26] Thus, a more practical alternative is the 5-item Fried Frailty Criteria which measures grip, strength, gait speed, exhaustion, physical activity, and shrinking ($\geq$10 pounds of unintentional weight loss in the past year). Even more practical, the Timed Up and Go Test is a quick way to test frailty by recording the time it takes a patient to get up from a sitting position. In recent years, 2 retrospective studies evaluated the Fried Frailty Criteria and the Timed Up and Go Test in patients undergoing urologic surgery. The authors found that these tools were predictive of adverse postoperative outcomes, required minimal assessment time, and were relatively inexpensive.[27,28] However, considering the increasing technology-driven medical management, use of electronic medical records for frailty assessment may be the most practical option. In a recent study, a chart-derived frailty score model using routine preoperative data predicted adverse surgical outcomes in geriatric patients comparable to other frailty tools.[29] Similarly, our study showed that a claims-based frailty assessment instrument can predict several negative postoperative outcomes in patients undergoing radical cystectomy. Using the frailty tool propose in our study may have several clinical advantages. First, our work further supports the idea that this type of claims-based frailty assessment may be a more practical, less burdensome method for risk-stratifying patients prior to radical cystectomy. Second, the potential for clinical integration into the electronic medical record may facilitate wider clinical adoption. Third, this tool may serve as a reference to coordinate care for frail patients, discuss treatment option, and initiate share decision-making. However, future randomized control trials are needed to evaluate the effectiveness of these tools. Lastly, incorporation of a frailty risk-assessment may facilitate management of frailty related issues such as nutritional status. Although nutritional status has not been extensively study in frail patients, previous research has shown improved perioperative outcomes in those nutritionally optimized prior to surgery.[30]

There are several limitations to our analysis. These include potential limitations related to coding inaccuracy of the NRD, lack of more granulated data about patient's disease burden, and absence of information regarding previous treatment. Our analysis was limited to outcomes from the initial hospital admission and any readmission within 30 days of discharge. Thus, we could not evaluate long-term sequelae from intraoperative intervention. Furthermore, although the Johns Hopkins frailty indicator is one of several validated measure of frailty that has been reported. Because the variables included in other frailty measures, such as the modified Frailty Index, are not included in the NRD, we were unable to directly compare the predictive value of different frailty metrics. Additionally, this database does not provide pathology findings, tumor characteristics, or information on prior surgery, chemotherapy, or radiation which affects our assessment of the extent of disease, clinical outcomes, and likelihood of complications. Given the lack of granularity and potential for coding errors or omissions in our data sample, we may have underestimated the burden of frailty due to undercoding of frailty-diagnosis ICD-9 entries by hospital personnel. Furthermore, binary coding used to tabulate frailty did not allow for evaluation of different degrees of frailty and further subcohort stratification.

Despite these limitations, our study suggests a claims-based method for identifying frailty may effectively risk stratify patients with bladder cancer considering radical cystectomy.

CONCLUSION

Radical cystectomy in frail patients is associated with higher odds of in-hospital mortality, ICU-level complications, nonhome discharge, increased length of stay, and hospital-related costs. Frailty assessment during preoperative evaluation may be useful in risk stratification, clinical assessment, and shared decision-making about surgical candidacy. Although our results are significant in a 30-day period, future studies should evaluate intervals of 60 or 90 days to fully understand the extent of the impact of frailty on perioperative outcomes.

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EDITORIAL COMMENT

Radical cystectomy (RC) is the standard of care for muscle-invasive and highest risk nonmuscle-invasive bladder cancer although is often burdened by a high rate of perioperative complications and a non-negligible mortality rate.[1,2] In this study, the authors aimed to evaluate the impact of frailty, assessed through a claims-based frailty index extracting data from the US NRD, on perioperative outcomes of RC. More than 7% of patients were considered frail at time of surgery and frailty status was the strongest predictor of ICU-level complications as well as it was associated with a more than 2-fold increase of in-hospital mortality. Frailty was the main determinant of nonhome discharge and increased hospital costs, while, notably, medical comorbidity burden was not an independent predictor of frailty status. Therefore, frailty assessment is pivotal for an adequate risk stratification and preoperative counseling since comorbidity index, age and American Society of Anesthesiologists physical status classification alone seem not to be adequate.[3]

In this context, robot-assisted RC (RARC) has been introduced to minimize the complication burden of open RC (ORC) and its oncologic noninferiority has been adequately reported.[4,5] However, although RARC is associated with more favorable perioperative features compared to ORC such as reduced estimated blood loss and hospital length of stay, a clear advantage of RARC over ORC still has to be proven. These results can be partly explained by the fact that RC is a procedure inherently affected by a notable risk of complications. In this scenario, frail patients, that express higher levels of inflammatory markers, hyperactivation of the coagulation system and altered metabolism compared with nonfrail counterparts,[6] are those most likely to benefit from a robotic approach due to its intrinsic minimal invasiveness, reduced surgical stress, tissue trauma, and systemic inflammation.[7,8] Conversely, RARC is often underused in frail patients as confirmed by the results of the present study.

In conclusion, frailty assessment before RC is crucial to better stratify and forecast patients' surgical risk and to provide a tailored preoperative counseling. The impact of frailty on perioperative and oncologic outcomes of RC deserves a critical appraisal in large prospective trials. Moreover, the benefit of interventions to prevent or reduce the level of frailty in patients with bladder cancer undergoing RC should be investigated.[9] Indeed, prospective trials comparing ORC and RARC should consider the impact of frailty on surgical outcomes and the benefit of minimally-invasive approach in this specific cohort of patients.

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AUTHOR REPLY

We thank you for the positive editorial comments. We agree with the assertion that perioperative frailty assessment should be considered for patients undergoing a radical cystectomy. Our work focuses on a claims-based frailty assessment tool that may be practical in urologist's office visits. For example, a frailty score is calculated from prepopulated chart-data and further information about the patient's clinical assessment is added to determine their overall perioperative risk during the same office visit. Implementation of such assessment tools may also yield identification and management of frailty related issues before undergoing surgical intervention. However, we also observed that there are numerous frailty tools being used, but few studies have focus on delineating the "best" tool. Although we do not tackle this problem head on, our work adds further evidence that frailty assessment is critical and may be implemented into electronic medical record system.

Furthermore, we concur with the editor's comments that future prospective studies should consider stratifying patients by frailty status. Ideally patients should be stratify using various frailty assessment tools for comparison. Frailty can be a significant confounding factor hindering a true assessment of postoperative outcomes as we have reported. In this context, comparative surgical outcomes studies in patients undergoing open vs robotic-assisted radical cystectomy for bladder cancer should consider the impact of frailty.

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