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ORIGINAL RESEARCH

Postoperative Adverse Outcomes in Patients With Frailty Undergoing Urologic Surgery Among American Patients: A Propensity-Score Matched Retrospective Cohort Study

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Objective: Although the 5-item modified frailty index (mFI-5) has been found to be associated postoperative outcomes, there are limited studies examining its utility in urologic surgery. Our purpose is to evaluate the association between the mFI-5 and postoperative mortality and complications among patients undergoing urologic surgery.

Methods: This retrospective cohort study used the American College of Surgeons National Surgical Quality Improvement Program database from 2015 to 2020. All adult patients who underwent urologic procedures were included. The mFI-5 includes five items: hypertension, diabetes, congestive heart failure, chronic obstructive pulmonary disease, and physical function status. Each item is assigned one point, and an mFI-5 score of 2 or greater indicates frailty. The primary outcome was postoperative mortality, while secondary outcomes were postoperative complications. Propensity score analysis was employed to control for confounders.

Results: After propensity score matching, each group contained 55,322 surgical patients. The patients in the frailty group were at risks of in-hospital mortality (absolute risk increase [ARI] 0.29%) and higher postoperative complications, including acute myocardial infarction (ARI 0.25%), pneumonia (ARI 0.42%), sepsis (ARI 0.41%), and septic shock (0.2%). Compared to the non-frailty group, the length of hospital stay was higher in the frailty group.

Conclusion: Patients with an mFI-5 score of 2 or greater were associated with an increased risk of postoperative mortality and complications, including myocardial infarction, pneumonia, sepsis, and septic shock. The mFI-5 is a simple index that quickly identifies frail patients. This allows for the implementation of prehabilitation and nutritional strategies targeted at enhancing their physiological reserve and optimizing their surgical outcomes.

Keywords: frailty, surgery, mortality, complications

Introduction

Frailty is a clinical condition that often develops with age and is characterized by a decline in physiological capacity and dysfunction across multiple organ systems. The prevalence of frailty varies based on the definition used, with 15% of the non-nursing home population in the US experiencing frailty and 45% experiencing pre-frailty.[1] Frailty is more common

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in individuals with certain comorbidities, such as HIV infection, chronic obstructive pulmonary disease, and end-stage renal disease, and it is more prevalent with increasing age.[2]

A previous study have established a link between urologic issues and frailty.[3] Common geriatric ailments such as benign prostate hypertrophy, dementia, spinal disc herniation, and cerebral infarction are also associated with neurogenic bladder and other voiding difficulties.[4,5] However, even minimally invasive procedures may be risky due to the vulnerability of frail individuals. Prior studies have shown a strong correlation between frailty and the likelihood of postoperative mortality and morbidity. Patients classified as very frail have 30-day and 180-day mortality rates of approximately 10% and 40%, respectively, even following minor surgeries.[6]

A new tool for assessing frailty, the 5-item modified frailty index (mFI-5), has recently been developed using data from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database.[7] This simplified scale has demonstrated superior predictive ability compared to previously utilized tools. The mFI-5 has been studied across various surgical populations and has been found to be associated with unfavorable postoperative outcomes.[8,9] However, there are limited studies examining its utility in urologic surgery. Therefore, the purpose of this study is to investigate the association between the mFI-5 and postoperative mortality and complications among patients undergoing urologic surgery.

Methods

Source of Data

This retrospective cohort study utilized the ACS-NSQIP database from 2015 to 2020. The raw data contained demographic data, comorbidities, perioperative surgical data, surgical outcomes, and complications. The present study was reviewed and approved by the Joint Institutional Review Board of Taipei Medical University (TMU-JIRB-N202305003). In accordance with the regulations of the ethical committee and the Ministry of Health and Welfare, informed consent was waived as patient identities were anonymized and could not be traced. Our study ensured patient data confidentiality and adhered to the principles of the Declaration of Helsinki.

Study Design

The flowchart (Figure 1) illustrates the study design and the selection process of study subjects. All patients who underwent urologic procedures between 2015 and 2020 were recruited with the Current Procedural Terminology codes.[9] The included procedures were classified into two categories as follows: complex procedures, which included all urologic oncology surgeries as well as suburethral sling placement and laparoscopic pyeloplasty, and simple procedures, which included transurethral resection of the prostate, transurethral resection of the bladder tumor, ureteroscopy, hydrocelectomy, orchiectomy, spermatocelectomy, epididymectomy, and varicocelectomy. In this study, we determined the inclusion criteria as patients aged ≥ 20 years, receiving urologic surgery, and had no missing data in hypertension, diabetes, congestive heart failure, chronic obstructive lung disease, and physical function status.

Eligible patients were stratified into frailty and non-frailty groups using the mFI-5, a simplified index derived from a previous index with 11 items.[7,10] The mFI-5 contains five items, including hypertension, diabetes, congestive heart failure, chronic obstructive lung disease, and physical function status, with each item attributing 1 point. Patients with an mFI-5 score of 2 or greater were considered frail, while those with an mFI-5 score of 0 or 1 were considered non-frail. We excluded surgical patients who aged < 20 years, received non-urologic surgeries, and had missing data in age, types of surgery, hypertension, diabetes, congestive heart failure, chronic obstructive lung disease, and physical function status.

The primary outcome was postoperative mortality, and secondary outcomes included postoperative complications such as stroke, acute myocardial infarction, pneumonia, sepsis, septic shock, ventilator use >48 hours, reintubation, reoperation, and length of hospital stay. Propensity-score matching is considered a reliable technique for reducing the influence of covariates in non-randomized observational cohorts. Propensity-score matching was performed at a 1:1 ratio using the nearest-neighbor method with a caliper of 0.5. Potential confounders, including age, sex, American Society of Anesthesiologists Physical Status Classification (ASA class), race, body mass index (BMI), operation time, type of anesthesia, emergency, and medical conditions, were used to calculate PS. An absolute standardized difference

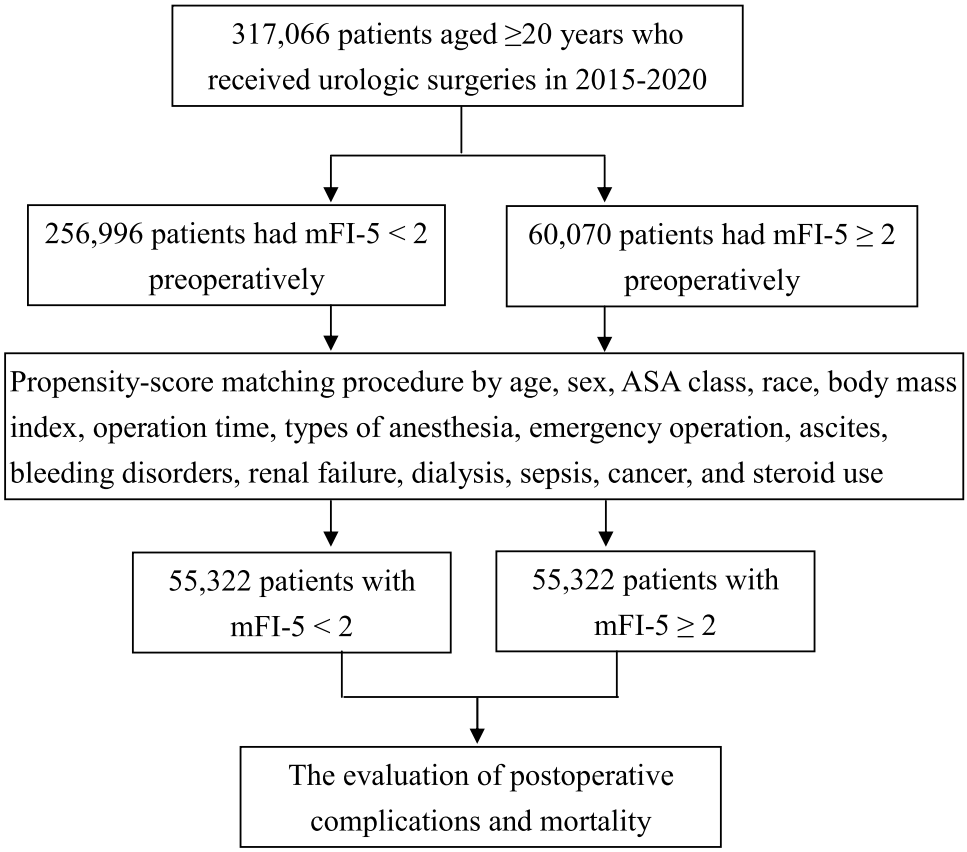

Figure 1 The flowchart for the study design and the selection process of study subjects.

was used to evaluate the quality of matching. An absolute standardized difference value of <0.1 indicates balance between each group and good quality matching.[10] Because of propensity-score matching, there were 206395 patients (201647 patients in mFI-5 <2 group and 4748 patients in mFI-5 ≥2 group) who were not included in the final analysis and this may lead to selection bias. We calculate the sample size should be 19078 under the alpha level of 0.05, power=0.8, and the postoperative mortality were 0.7% and 0.4% in frailty groups and in non-frailty group, respectively.

Statistical Analysis

Continuous variables such as BMI (<18.5, 18.5–24.9, 25–29.9, 30–34.9, 35–39.9, and ≥40 kg/m^2) and operation time (< 2, 2–4, and > 4 hours) were categorized. The baseline characteristics were compared between patients with and without frailty (mFI-5 ≥2). We used chi-squared test and *t*-test to analyzed categorical data and continuous variables (included body mass index, operation time, and length of hospital stay), respectively. After the normality check by Kolmogorov–Smirnov test (Table S1), we used Wilcoxon rank-sum test, to analyzed continuous variables.

Multivariate logistic regression models were used to evaluate the adjusted odds ratio (OR) and 95% confidence interval (CI) of complications and mortality associated with frailty (mFI-5 ≥2). For the interpretation of odds ratio, the rare disease assumption is necessary in this study. We considered the odds ratio closely approximates the risk ratio when the disease is rare and the controls accurately represent the general population in terms of exposure.[11] In this study, we considered OR as an estimate of relative risk and we also calculated absolute risk increase (ARI) for postoperative complications and mortality. The urologic surgeries were classified into simple procedures and complex procedures for subgroup analysis. All analyses and tests were performed by using SAS (version 9.4; SAS Institute Inc, Cary, North Carolina) software.

Results

A total of 317,076 surgical cases were enrolled in the ACS-NSQIP database from 2015 to 2020. The non-frailty group contained 256,996 patients, and the frailty group had 60,070 patients. The characteristic variables were different between the two groups. The frailty group had an overall higher proportion of patients in ASA class III, higher BMI distributions, and higher rates of preoperative comorbidities (Table 1).

The demographic data after PS matching are summarized in Table 2. Each group contained 55,322 surgical patients. The ASD was zero in all variables, indicating balanced matching and good quality of comparability. Among these patients, 81% were male and 83.6% were over 60 years old. Most of these patients (74.3%) were classified as ASA class III, and half of the patients were obese.

Table 1 Characteristics of Study Population With and Without Frailty (mFI-5 ≥2)

	mFI-5 <2 (n=256996)		mFI-5 ≥2 (n=60070)		ASD
	n	%	n	%	
Sex					0.023
Female	58601	22.80	12038	20.04	
Male	198395	77.20	48032	79.96	
Age, years					0.253
20–29	4972	1.93	61	0.10	
30–39	9891	3.85	313	0.53	
40–49	20803	8.90	1780	2.96	
50–59	50083	19.49	7827	13.03	
60–69	84641	32.93	20056	33.39	
70–79	69164	23.41	20471	34.08	
≥80	26,442	10.29	9562	15.92	
ASA class					0.622
I	12401	4.83	80	0.13	
II	125449	48.81	10861	18.08	
III	112255	43.68	43218	71.95	
IV	6864	2.67	5894	9.81	
V	27	0.01	17	0.03	
Race					0.113
Asian	7235	2.82	1936	3.22	
Black	19866	7.73	6687	11.13	
Other/unknown	55041	21.42	11,753	19.57	
White	174854	68.04	39,694	66.08	
BMI. kg/m^2					0.234
<18.5	2701	1.05	488	0.81	
18.5–24.9	63818	24.83	9349	15.56	
25–29.9	101773	39.60	19349	32.21	
30–34.9	57792	22.49	16795	27.96	
35–39.9	20731	8.07	8648	14.40	
≥40	10181	3.96	5441	9.06	
Median (IQR)	28.1 (6.7)		30.5 (8.2)		0.396
Operation time, hours					0.116
< 2 hours	141708	55.14	35937	59.83	
2–4 hours	79789	31.05	15772	26.62	
> 4 hours	35499	13.81%	8361	13.92	
Median (IQR), hours	1.63 (2.43)		1.3 (2.42)		0.077

(*Continued*)

Table 1 (Continued).

	mFI-5 <2 (n=256996)		mFI-5 ≥2 (n=60070)		ASD
	n	%	n	%	
Type of anesthesia					0.108
General anesthesia	239898	93.35	54404	90.57	
Other/unknown	17098	6.65	5666	9.43	
Emergency	1961	0.76	655	1.09	0.016
Medical conditions					
Ascites	116	0.05	40	0.07	0.012
Bleeding disorders	4959	1.93	2722	4.53	0.166
Steroid use	6558	2.55	2411	4.01	0.091
Preoperative renal failure	578	0.22	368	0.61	0.068
Dialysis	2284	0.89	1162	1.93	0.108
Sepsis	1945	0.76	913	1.52	0.092
Cancer	6017	2.34	1689	2.81	0.021

Abbreviations: mFI-5, the 5-item modified frailty index; ASA class, American Society of Anesthesiologists Physical Status Classification; BMI, body mass index; IQR, interquartile range.

Table 2 Characteristics of Study Population After Propensity Score Matching

	mFI-5 <2 (n=55322)		mFI-5 ≥2 (n=55322)		ASD
	n	%	n	%	
Sex					0.00
Female	10514	19.01	10514	19.01	
Male	44808	80.99	44808	80.99	
Age, years					0.00
20–29	40	0.07	40	0.07	
30–39	254	0.46	254	0.46	
40–49	1580	2.86	1580	2.86	
50–59	7214	13.04	7214	13.04	
60–69	18681	33.77	18681	33.77	
70–79	18867	34.10	18867	34.10	
≥80	8686	15.70	8686	15.70	
ASA class					0.00
I	56	0.10	56	0.10	
II	10580	19.12	10,580	19.12	
III	41078	74.25	41078	74.25	
IV	3608	6.52	3608	6.52	
Race					0.00
Asian	1595	2.88	1595	2.88	
Black	5709	10.32	5709	10.32	
Other/unknown	10760	19.45	10760	19.45	
White	37258	67.35	37258	67.35	
BMI, kg/m^2					0.00
<18.5	331	0.60	331	0.60	
18.5–24.9	8706	15.74	8706	15.74	
25–29.9	18396	33.25	18396	33.25	
30–34.9	15676	28.34	15676	28.34	
35–39.9	7701	13.92	7701	13.92	
≥40	4512	8.16	4512	8.16	
Median (IQR)	30.3 (8.1)		30.3 (7.9)		0.00

(*Continued*)

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Table 2 (Continued).

	mFI-5 <2 (n=55322)		mFI-5 ≥2 (n=55322)		ASD
	n	%	n	%	
Operation time, hours					0.00
< 2 hours	32948	59.56	32948	59.56	
2–4 hours	14684	26.54	14684	26.54	
> 4 hours	7690	13.90	7690	13.90	
Median(IQR), hours	1.40 (2.38)		1.31 (2.42)		0.00
Type of anesthesia					0.00
General anesthesia	50580	91.43	50580	91.43	
Other/unknown	4742	8.57	4742	8.57	
Emergency	246	0.76	246	0.76	
Medical conditions					
Ascites	5	0.01	5	0.01	0.00
Bleeding disorders	1782	3.22	1782	3.22	0.00
Steroid use	1628	2.94	1628	2.94	0.00
Renal failure	47	0.08	47	0.08	0.00
Dialysis	499	0.90	499	0.90	0.00
Sepsis	289	0.52	289	0.52	0.00
Cancer	1115	2.02	1115	2.02	0.00

Abbreviations: mFI-5, the 5-item modified frailty index; ASD, absolute standardized difference; ASA class, American Society of Anesthesiologists Physical Status Classification; BMI, body mass index; IQR, interquartile range.

Table 3 shows the results of the multivariate logistic regression analysis. The patients in the frailty group were associated with a higher in-hospital mortality rate (OR 1.69; ARI 0.29%). In addition, there was a higher risk of postoperative complications in the frailty group, including acute myocardial infarction (OR 1.75; ARI 0.25%), pneumonia (OR 1.76; ARI 0.42%), sepsis (OR 1.38; ARI 0.41%), and septic shock (OR 1.77; 0.2%). The frail group was associated with increased risk for ventilator use >48 hours (OR 1.74; ARI 0.14%) and reintubation (OR 1.68; ARI 0.25%) compared with the non-frailty group. Compared to the non-frailty group, the length of hospital stay was higher in the frailty group.

Table 3 Risk of Postoperative Mortality and Complications in Frail Patients

Postoperative Outcome	mFI-5 <2		mFI-5 ≥2		Outcome Risk	
	Events	%	Events	%	OR	(95% CI)
In-hospital mortality	241	0.44	402	0.73	1.69	(1.44–1.99)
Stroke	99	0.18	123	0.22	1.24	(0.95–1.62)
AMI	191	0.35	332	0.6	1.75	(1.46–2.09)
Pneumonia	319	0.58	555	1	1.76	(1.53–2.02)
Sepsis	612	1.11	839	1.52	1.38	(1.24–1.54)
Septic shock	148	0.27	260	0.47	1.77	(1.44–2.17)
Ventilator >48 hours	107	0.19	185	0.33	1.74	(1.37–2.21)
Reintubation	204	0.37	341	0.62	1.68	(1.41–2.00)
Reoperation	1239	2.24	1314	2.38	1.06	(0.98–1.15)
Length of hospital stay, days*	2.2±3.9		2.5±4.5			
Length of hospital stay, days†	1.0 (2.0)		1.0 (3.0)			

Notes: *Mean ± standard deviation was calculated by *t*-test. †Median and interquartile range was calculated by Wilcoxon rank-sum test.

Abbreviations: mFI-5, the 5-item modified frailty index; AMI, acute myocardial infarction; CI, confidence interval; OR, odds ratio.

Table 4 Risk of Postoperative Mortality and Complications in Complex and Simple Procedures

	mFI-5 <2		mFI-5 ≥2		Outcome Risk	
	Events	%	Events	%	OR	(95% CI)
Complex procedures						
In-hospital mortality	133	0.47	213	0.78	1.67	(1.34–2.07)
Stroke	54	0.19	71	0.26	1.35	(0.95–1.92)
AMI	127	0.45	210	0.77	1.71	(1.37–2.14)
Pneumonia	238	0.84	409	1.49	1.78	(1.52–2.10)
Sepsis	453	1.6	571	2.09	1.29	(1.13–1.46)
Septic shock	111	0.39	190	0.69	1.76	(1.39–2.22)
Length of hospital stay, days*	3.3±4.1		3.7±4.7			
Length of hospital stay, days†	2.0 (3.0)		2.0 (3.0)			
Simple procedures						
In-hospital mortality	108	0.4	189	0.68	1.74	(1.36–2.21)
Stroke	45	0.17	52	0.19	1.11	(0.75–1.66)
AMI	64	0.24	122	0.44	1.85	(1.37–2.51)
Pneumonia	81	0.3	146	0.52	1.76	(1.34–2.31)
Sepsis	159	0.59	268	0.96	1.64	(1.34–1.99)
Septic shock	37	0.14	70	0.25	1.84	(1.23–2.74)
Length of hospital stay, days*	1.3±3.5		1.6±4.2			
Length of hospital stay, days†	0.0 (1.0)		0.0 (1.0)			

Notes: *Mean ± standard deviation was calculated by *t*-test. †Median and interquartile range was calculated by Wilcoxon rank-sum test.

Abbreviations: mFI-5, the 5-item modified frailty index; AMI, acute myocardial infarction; CI, confidence interval; OR, odds ratio.

The results of the subgroup analysis are presented in Table 4. For patients who received complex procedures, there was a association of frailty and in-hospital mortality (OR 1.67; ARI 0.31%) with postoperative complications. Among those who received simple procedures, there was also a similar pattern of mortality (OR 1.74; 0.28%) and morbidity in frail patients.

Discussion

This study demonstrated the association between frailty and postoperative mortality and complications in patients who underwent urologic procedures. Patients with frailty had a statistically higher in-hospital mortality rate than non-frailty patients. There were also more postoperative complications in the frailty group, including myocardial infarction, pneumonia, sepsis, and septic shock. The length of stay was also prolonged in the frailty group. After stratification, the results were consistent in both the complex and simple procedures.

In this study, the in-hospital mortality rate of patients with frailty was 0.73%, which was approximately 1.7 times higher than that of patients with non-frailty, agreeing with previous results.[12] Patients with underlying malignancies have a heavy burden on their physiological status. Cancer itself and its treatment are strong stressors that challenge the reserves and lead to vulnerability.[13] A previous study found that the median prevalence of frailty across all studies is 42% among cancer patients, and the 5-year all-cause mortality rate in the frailty group is 1.87 times higher than that in the non-frailty group.[14]

In this study, there was an increase in mortality among frail patients who underwent complex procedures. Similar patterns were also found in frail patients who underwent simple procedures. With a decreased reserve, even minor stress can be harmful and result in higher mortality. In a previous retrospective study, patients who are frail and very frail who underwent low-stress procedures had mortality rates exceeding those typically reported for the highest-risk surgical procedures.[15] This study identified a 1.7-fold increase in in-hospital death among those receiving minor surgery. These results suggest that low-stress procedures are not low risk for patients who are frail.

This study found an association between frailty and a higher rate of acute myocardial infarction, which was consistent with previous studies. Cardiovascular disease shares similar features and risks with frailty, such as being influenced by lifestyle or medical risk factors, including smoking, lack of exercise, poor diet, diabetes, and proinflammatory status.[16,17] Reduced physical activity is often the first indication of frailty and is strongly linked with cardiovascular disease. Importantly, every item in the mFI-5 is related to the risk of myocardial infarction, which makes the present findings reasonable and solid.[18,19]

A previous prospective cohort study on pulmonary complications following major abdominal surgery reported that patients with frailty have an increased risk of postoperative pneumonia.[20] A retrospective study using the ACS-NSQIP database for patients undergoing minimally invasive partial nephrectomy also revealed that the risk of postoperative pneumonia is higher for patients with a higher mFI-5 score.[21] This study supported these findings and further demonstrated that the risk of postoperative pneumonia is also increased in the category of minor urologic surgery.

The precise mechanisms underlying postoperative pneumonia and frailty remain unclear. Frailty is associated with a decline in immune function, increased oxidative stress, mitochondrial dysfunction, and cellular senescence.[22,23]

Moreover, dysregulation of the inflammatory response has also been observed in frail patients.[23,24] Inappropriate responses include increased blood levels of proinflammatory mediators in the absence of an initial inflammatory stimulus and a reduced ability to produce a functional inflammatory response when sufficient stimulation is present.[22] In addition, respiratory impairment may also play a role in the risk of postoperative pneumonia. A cross-sectional and longitudinal study reported a strong association between frailty and respiratory impairment (airflow limitation and restrictive pattern) in frail elderly patients.[25] A cross-sectional study from Japan revealed that frailty affects the vulnerability and severity of pneumonia in elderly individuals.[26] These factors may contribute to the increased risk of postoperative pneumonia in frailty.

In this study, the sepsis and septic shock rates were higher in the frailty group compared to the non-frailty group. As mentioned above, frailty is associated with multidimensional systemic dysregulation composed of proinflammatory status as well as endocrine and micronutrient deficiencies.[17,23] Elevated biomarkers, such as high-sensitivity C-reactive protein and interleukin-6, are both associated with frailty and infection.[27] In one large longitudinal cohort study with over 30,000 participants, sepsis incidence was higher in the frailty group as lung and urinary tract infections were the most common sources of infection; low physical activity and weakness were independently associated with sepsis, and high-sensitivity C-reactive protein levels were statistically higher in the frailty group.[28] Worse outcomes, including higher mortality rates and delayed discharge, have been found in patients with preexisting frailty and simultaneous sepsis.[28,29] A orthopedic research suggested that the cost and time-effective markers and their cut-offs effectively quantify the surgical inflammatory response in frail patients, identifying the extent of surgical intervention along with procedure duration and blood loss.[30]

This study had several limitations. First, this was a retrospective cohort study using the ACS-NSQIP database. Because the database only reports 30-day outcomes, mortality and morbidity beyond 30 days are unknown. Second, to minimize potential bias, PS matching was performed to adjust for known confounding factors. In PS matching analysis, however, only known and measured variables can be adjusted for. Although we matched many covariates, some residual confounding factors may not have been considered. Finally, the definition of frailty in this study relied on the mFI-5, which gives equal weight to each variable and does not evaluate the severity of diseases or their duration. In practice, well-controlled hypertension and diabetes carry different postoperative risks than severe COPD or heart failure with reduced ejection fraction.

Conclusion

In conclusion, patients with an mFI-5 score of 2 or greater who undergo urologic surgery are associated with an increased risk of postoperative mortality and complications, including myocardial infarction, pneumonia, sepsis, and septic shock. Additionally, the frailty group experiences a prolonged hospital stay. The mFI-5 serves as a simple index for promptly identifying frail patients. This allows for the implementation of prehabilitation and nutritional strategies targeted at enhancing their physiological reserve and optimizing their surgical outcomes.

Abbreviations

ACS-NSQIP, American College of Surgeons National Surgical Quality Improvement Program; ASA class, Anesthesiologists Physical Status Classification; ASD, absolute standardized difference; BMI, body mass index; CI, confidence interval; COPD, chronic obstructive lung disease; mFI-5, 5-item modified frailty index; OR, odds ratio; PS, Propensity score.

Data Sharing Statement

The data underlying this study is from the Health and Welfare Data Science Center. Interested researchers can obtain the data through formal application to the Health and Welfare Data Science Center, Department of Statistics, Ministry of Health and Welfare, Taiwan (http://dep.mohw.gov.tw/DOS/np-2497-113.html) and contact the agency with email (stpeicih@mohw.gov.tw). Under the regulations from the Health and Welfare Data Science Center, we have made the formal application (included application documents, study proposals, and ethics approval of the institutional review board) of the current insurance data from in 2019. The authors of the present study had no special access privileges in accessing the data which other interested researchers would not have.

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Author Contributions

All authors made contributions to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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