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## Validation of a frailty index in patients undergoing curative surgery for urologic malignancy and comparison to other risk stratification tools

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### Abstract

**Objective**—To retrospectively validate and compare a modified frailty index predicting adverse outcomes to other risk stratification tools among patients undergoing urologic oncological surgeries.

**Materials and Methods**—The American College of Surgeons National Surgical Quality Improvement Program was queried from 2005–2013 to identify patients undergoing cystectomy, prostatectomy, nephrectomy, and nephroureterectomy. Using the Canadian Study of Health & Aging Frailty Index, 11 variables were matched to the database; 4 were also added due to their relevance in oncology patients. The incidence of mortality, Clavien-Dindo IV complications, and adverse events were assessed with patients grouped according to their modified frailty index score.

**Results**—A total of 41,681 cases of patients were identified undergoing surgery for presumed urological malignancy. Patients with a high frailty index score of  $>0.20$  had a 3.70 odds of a Clavien-Dindo IV event (CI: 2.865–4.788,  $p<0.0005$ ) and a 5.95 odds of 30-day mortality (CI: 3.72–9.51,  $p<0.0005$ ) in comparison to non-frail patients after adjusting for race, gender, age, smoking history and procedure. Using C-statistics to compare the sensitivity and specificity of the predictive ability of different models per risk stratification tool and Akaike Information Criteria to assess for the fit of the models with the data, the modified frailty index was comparable or superior to the Charlson Comorbidity Index but inferior to the American Society of

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Anesthesiologists Risk Class in predicting 30-day mortality or Clavien-Dindo IV events. When the modified frailty index was augmented with the American Society of Anesthesiologists Risk Class, the new index was superior in all regards in comparison to risk stratification tools.

**Conclusion**—Existing risk stratification tools may be improved by incorporating variables in our 15 point modified frailty index as well as other factors such as walking speed, exhaustion, and sarcopenia to fully assess frailty. This is relevant in diseases like kidney and prostate cancer, where surveillance and other non-surgical interventions exist as alternatives to a potentially complicated surgery. In these scenarios, our modified frailty index augmented by the American Society of Anesthesiologists Risk Class may help inform which patients do not benefit from surgery although this index needs prospective validation.

### Keywords

Frail elderly; surgical outcomes; urologic oncology; pre-operative evaluation; patient survival

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### Introduction

Frailty is a growing issue for surgeons as frail patients have worse health outcomes with increased mortality rates, hospitalizations, and institutionalization rates [1]. Frailty is a medical syndrome with multiple contributors and characterized by diminished strength, endurance, and reduced physiologic function increasing an individual's vulnerability to dependency and death [2]. Frailty is associated with poor oncological outcomes like disease progression and diseasespecific mortality [3].

The Canadian Study of Health & Aging Frailty Index (CSHA-FI) is a clinically validated measure of frailty that includes the extent of comorbidities and quality of life variables in an accumulating deficit model of frailty [4]. Rockland, et al defined frailty as a function of the severity of a patient's comorbidities and declines in activities of daily living[4]. They validated their accumulating deficit model of frailty showing that it was equivalent to the phenotypic frailty model defined by the Fried Frailty Index, which takes into account factors like walking speed and weight loss[5]. Abbreviated versions of the CSHA-FI have been validated as preoperative risk stratification tools in prospective and retrospective fashion in general surgery, gynecological oncology, and orthopedic surgery [6–11]. An abbreviated version has been validated retrospectively using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) dataset among vascular surgery patients; patients undergoing colectomy; emergency and elective general surgery patients; and cardiothoracic patients undergoing lobectomies [11–15]. In all cases, frailty measured by increasing score in the frailty index was associated with adverse outcomes.

We used the variables from CSHA-FI mapped to the ACS-NSQIP dataset to create a modified 15-point frailty index (mFI) with additional variables pertinent to our patient population in a model of frailty that measures accumulating deficits [4, 5, 16]. We validated our modified FI in genitourinary patients to see how frailty and comorbidities impacts patients across the most common oncological surgeries in urology: prostatectomy, cystectomy, nephrectomy, and nephroureterectomy.

## Material and Methods

Under the data use agreement of the ACS, we reviewed the NSQIP participant use files from 2005–13. The NSQIP database is a national, validated, outcomes-based dataset managed by the ACS. The hospitals participating in the consortium are the source of the data used herein; they have not verified, and are not responsible, for the statistical validity of the data analysis or the conclusions we have derived.

We collected 11 variables from the CSHA-FI matched to preoperative variables in the NSQIP database of patients who were identified by the primary Current Procedure Terminology (CPT) as having undergone prostatectomy, cystectomy, nephrectomy, and nephroureterectomy. Non-oncological cases were excluded. Four additional variables were added to create our mFI: history of metastasis, chemotherapy/radiation exposure, weight loss, and renal failure (Table 1). History of metastasis and treatment with chemotherapy/radiation both denote the severity of a patient's cancer. Weight loss is a marker of frailty validated by the Fried Frailty Index [1]. Renal failure with creatinine > 3 mg/mL predisposes patients to adverse outcomes [17]. The mFI index score was calculated using the sum of risk factors per patients and divided by the amount of total risk factors. Variables in the frailty index with no mention of severity were dichotomized as absent (0) or present (1); other variables were trichotomized with 1 being most severe similar to Mitnitski, et al [5].

The following adverse events were recorded in binary fashion: 30-day mortality, septic shock (SS), failure to extubate (ventilator dependence), unplanned re-intubation, myocardial infarction (MI), acute renal failure (ARF), cardiac arrest requiring cardiopulmonary resuscitation (CA), surgical site infection or dehiscence, deep vein thrombosis (DVT), and pulmonary embolism (PE) as defined in the ACS-NSQIP participant user file. Complications were classified as Clavien-Dindo IV as Webb, et al. has done by including the following ACS-NSQIP variables: SS, MI, CA, PE, ARF, unplanned re-intubations, and ventilator dependence [18, 19].

Pearson's  $\chi^2$  test was used for categorical comparisons. Age, sex, race, smoking status, procedure, and the mFI were placed in a multivariate logistic regression model looking at mortality and Clavien-Dindo IV complications with the mFI included as an ordinal variable instead of continuous variable to improve the stability of the final model. Odds ratios (OR) with 95% confidence intervals (CI) were recorded. Two-tailed tests were used in all cases with significance defined as  $p < 0.05$ .

A modified Charlson Comorbidity Index (CCI) was calculated from variables in the ACS-NSQIP[20]. The American Society of Anesthesiologists Class Risk Group (ASA), functional status, work relative value unit (wRVU), and age were obtained from the ACS-NSQIP database. Different risk stratification tools were analyzed via an Area Under the Receiver Operator Characteristics Curve (ROC) comparing the area under the curve defined as the C-statistic between the different models. We compared our mFI to the previously cited 11-point CSHA-FI, CCI and ASA by assessing the Akaike Information Criterion (AIC)—a measure of the relative quality of a model with lower values being better—and C-statistic—a measure of assessing the optimization of sensitivity and specificity for a given

outcome—for each model while adjusting for age, surgical procedure and approach, smoking history, and gender for the outcomes of mortality and Clavien-Dindo IV complications. A further modified model combining ASA physical status with our 15 variable mFI with a weight of 0 for the lowest group of 0 and 5 points for those with > 4 physical status was also assessed. Statistical analyses were performed using SPSS version 20.0 or higher (IBM Corp, Armonk, NY).

## Results

The ACS-NSQIP database was queried for a total of 41,681 patients who met our selection criteria with the following clinical and demographic characteristics (Table 2). Cystectomy patients had the highest 30-day mortality rate (2.6%) and Clavien-Dindo IV complications (9.5%); prostatectomy patients had the lowest 30-day mortality (0.2%) and Clavien-Dindo IV complications (1.1%).

For prostatectomy patients, increasing mFI was associated with increased rates of Clavien-Dindo IV events, SS, ventilator dependence, unplanned re-intubations, ARF, CA, bleeding requiring blood transfusion, surgical site infections and dehiscence, re-operations and readmissions (Table 3.a,  $\chi^2$   $p < 0.01$  for all). For nephrectomies, increasing mFI was associated with 30 day mortality, Clavien-Dindo IV events, SS, ventilator dependence, unplanned re-intubations, MI, ARF, CA, DVT, bleeding requiring blood transfusion, and readmissions (Table 3.a  $\chi^2$   $p < 0.0005$  for all). For nephroureterectomies, increasing mFI was associated with increasing incidence of 30-day mortality, Clavien-Dindo IV complications, SS, ventilator dependence, re-intubations, MI, ARF, CA, DVT, bleeding requiring blood transfusion, and reoperations (Table 3.b,  $\chi^2$   $p < 0.05$ ). Finally, for cystectomy, increasing mFI was associated with increased incidence of 30-day mortality, Clavien-Dindo IV complications, ventilator dependence, re-intubations, ARF, and bleeding requiring blood transfusions (Table 3.b,  $\chi^2$   $p < 0.01$ ).

Our multivariate model (Hosmer and Lemeshow Test,  $p=0.358$ ) controlling for smoking history, gender, procedure and race showed that increasing mFI was associated with increased OR of Clavien-Dindo IV complications with an OR of 3.704 for the frailest patients ( $mFI > 0.20$ , CI: 2.865–4.788,  $p < 0.0005$ ) in comparison to the non-frail patients (Table 4). The mFI was significantly associated with mortality with the subgroup of patients with mFI of  $>0.20$  having an OR of 5.946 (CI: 3.718–9.509,  $p < 0.0005$ ) in comparison to the non-frail patients (Table 4).

The ROC curve showed that our mFI had fair sensitivity and specificity for predicting death in radical prostatectomy (C-statistic 0.760,  $p < 0.0005$ ) and nephroureterectomy (C-statistic 0.753,  $p < 0.0005$ ) (Figure 1). With regards to the ROC curve for Clavien-Dindo IV complications, the modified FI had poor sensitivity and specificity for all outcomes of interest (Figure 2). In both assessing mortality and Clavien-Dindo IV outcomes in all surgeries, the 15-point mFI was superior to the 11-point CSHA-FI used in the literature.

A multinomial logistic regression model was created using the multivariate model to assess the differences in AIC while also measuring the C-statistic for each model to compare our

15-point mFI with the 11-point CSHA-FI, ASA Class Risk, and CCI as well as a combined mFI + ASA index [21]. These each were compared as continuous variables. The mFI had fair sensitivity and specificity (C-statistic for mortality 0.66, for Clavien-Dindo IV Complications 0.72) while maintaining a low AIC (AIC for mortality= 2400.6, AIC for Clavien Dindo IV Complications=8371.6) although the ASA Class Risk groupings outperformed it in both outcomes with a higher sensitivity and specificity (C-statistic for mortality 0.67, for Clavien-Dindo IV Complications 0.72) and lower AIC (AIC mortality=2406.1, AIC Clavien-Dindo IV Complications =8345.1). The combined ASA and mFI was superior in all regards with the lowest AIC (Mortality=2372.7, Clavien Dindo IV Complications =8321.4) and the highest C-statistic (Mortality 0.71, Clavien Dindo IV Complications = 0.77) among models compared.

## Discussion

Compared to healthy patients, frail patients who are exposed to stressors such as surgical intervention may suffer disproportionate decompensation due to a lack of physiological reserve [22]. Therefore the risk-benefit ratio of surgery should include frailty and severity of comorbidities to capture the full risk of a surgical candidate undergoing a surgical oncological intervention.

In this retrospective study, using the ACS-NSQIP dataset, we validated a FI, modified it for patients undergoing surgery for a primary urologic malignancy, show the frailty indexes inferiority to the ASA Risk stratification tool and superiority to the CCI. Combining the prospectively collected ASA with the mFI, we created a superior risk stratification tool that predicts adverse events. The ASA Risk Stratification likely added elements not discernible from history alone at the day of surgery.

For cystectomy patients, the mFI was not as good of a predictor of 30-day mortality as other measures as it had a very poor sensitivity and specificity with a C-statistic < 0.6. This suggests that surgeries with high underlying risks like cystectomies may be harder to predict adverse events based on frailty or comorbidities alone. This may also be explained by the presentations of the different underlying diseases driving the need for surgery. Bladder cancer patients requiring surgery usually present with high-risk muscle invasive bladder cancer patients after failing local management. These patients tend to be at a higher tumor stage and underlying risk of death in comparison to patients undergoing partial nephrectomy or those with low and intermediate risk prostate cancer undergoing radical prostatectomy. For all surgeries, our mFI was superior or comparable to the CCI in predicting mortality or Clavien-Dindo IV outcomes but it was not superior to the ASA, which had a higher C-statistic and lower AIC. Hence, when the ASA was combined with our mFI, it was the best predictor of morbidity and mortality. Although this frailty index has been studied before, this study is the first to rigorously compare it to other risk indices used in clinical practice while creating a novel frailty index with potential clinical utility.

In the literature, frailty is associated with postoperative complications especially in older adults with comorbidities, across surgical specialties [11, 23]. However, little has been done to disentangle the relationship of the comorbidities measured by existing risk stratification

tools, and the different existing indexes for frailty. In a prospective study of patients below 65 years of age undergoing elective operations, Robinson et al. used walking speed as a surrogate for frailty. Decreased walking speed was associated with increased mortality at 1 year post-operation, but this test was not compared to other popular risk stratification tools [24]. Revenig, et al., in a prospective study assessing frailty by measuring shrinking, weakness, exhaustion, low activity, and slow walking speed showed that increasingly frail patients had increased complications, but it was not compared to other risk stratification tools [25]. Courtney-Brooks, et al., focused on patients undergoing surgery for gynecological malignancy. Their prospectively measured frailty index predicted 30-day post-op complication but did not detect deaths or readmissions [9]. Makary, et al. prospectively collected the Fried Frailty Index on patients undergoing elective general surgery while augmenting this index with the ASA Class Risk Groups, Lee's revised cardiac risk index, and the Eagle Score. This modified Fried Frailty index predicted worse outcomes and higher post-operative complications by increasing the sensitivity of other risk stratification tools, capturing more adverse outcomes [6]. No information was provided in comparing the performance of their modified Fried's Index with other validated risk stratification tools like the CCI.

There may be better ways to quantify frailty that do not depend on history and patient narratives. A novel method by Waits, et al. in Michigan used a surrogate for frailty called morphometric age, created from imaging characteristics of patients 90-days prior to undergoing surgery. Increasing morphometric age predicted an increased number of complications, and worse outcomes after liver transplantation [26]. Furthermore, a study by Psutka, et al. looked at patients with sarcopenia, determined by imaging, and who underwent cystectomy. They showed that patients with sarcopenia had worse survival and worse cancer specific outcomes [27].

Our study has several limitations including its retrospective nature. Patient cancer specific information, treatment history, and longitudinal follow-up after 30 days were not available. Those who received non-cytotoxic chemotherapeutic agents in the case of renal cell carcinoma were not recorded but given the decreased morbidity of these treatments in comparison to cytotoxic chemotherapeutic agents we believe these can be included in our mFI with a lower penalty. Another limitation is that we do not have information about institutions or surgeons performing the procedures in order to understand in which situations warrant the use of a frailty index calculation before surgery. This is important especially in prostate cancer where alternate non-surgical curative treatments exist such as radiation. Moreover, the 15 variables in our frailty index may only constitute a portion of the frailty syndrome with more variables needed to capture the spectrum of frailty. However, much of the literature has already used this modified 11 variable frailty index with similar results to our study although few have compared it to existing risk stratification tools as we have and our 15 variable modified frailty index was superior in predicting patients at higher risk of mortality (11 point CSHA-FI AUC= 0.659 vs. 15 point FI AUC= 0.716,  $p < 0.0005$  for both) and Clavien-Dindo IV complications (11 point CSHA-FI AUC= 0.645 versus 15 point FI AUC= 0.665,  $p < 0.0005$  for both). When combined with ASA Risk Stratification, its predictive ability was even more pronounced. Finally, 2.8% of patients were considered vulnerable with mFI > 0.20 and modifying Rockland's, et al definition of vulnerable in their

frailty index spectrum [4]. This implies that surgeons may prospectively identify extremely frail patients who are not surgical candidates, refusing to operate them. This may explain the low amount of adverse events observed although it is in line with the literature.

## Conclusion

There has been a growing need for a structured, evidence based preoperative evaluation for frail patients undergoing oncological genitourinary surgery [28, 29]. Our modified FI was associated with worse outcomes comparable to existing risk stratification tools when looking at 30-day mortality and Clavien-Dindo IV outcomes. When our mFI was combined with the ASA Class risk stratification, it was superior to all existing risk stratification tools indicating potential clinical application. We plan to apply this mFI to our active surveillance population in both renal cell carcinoma and prostate cancer to see whether it can predict who fails active surveillance or expires from competing causes of mortality.

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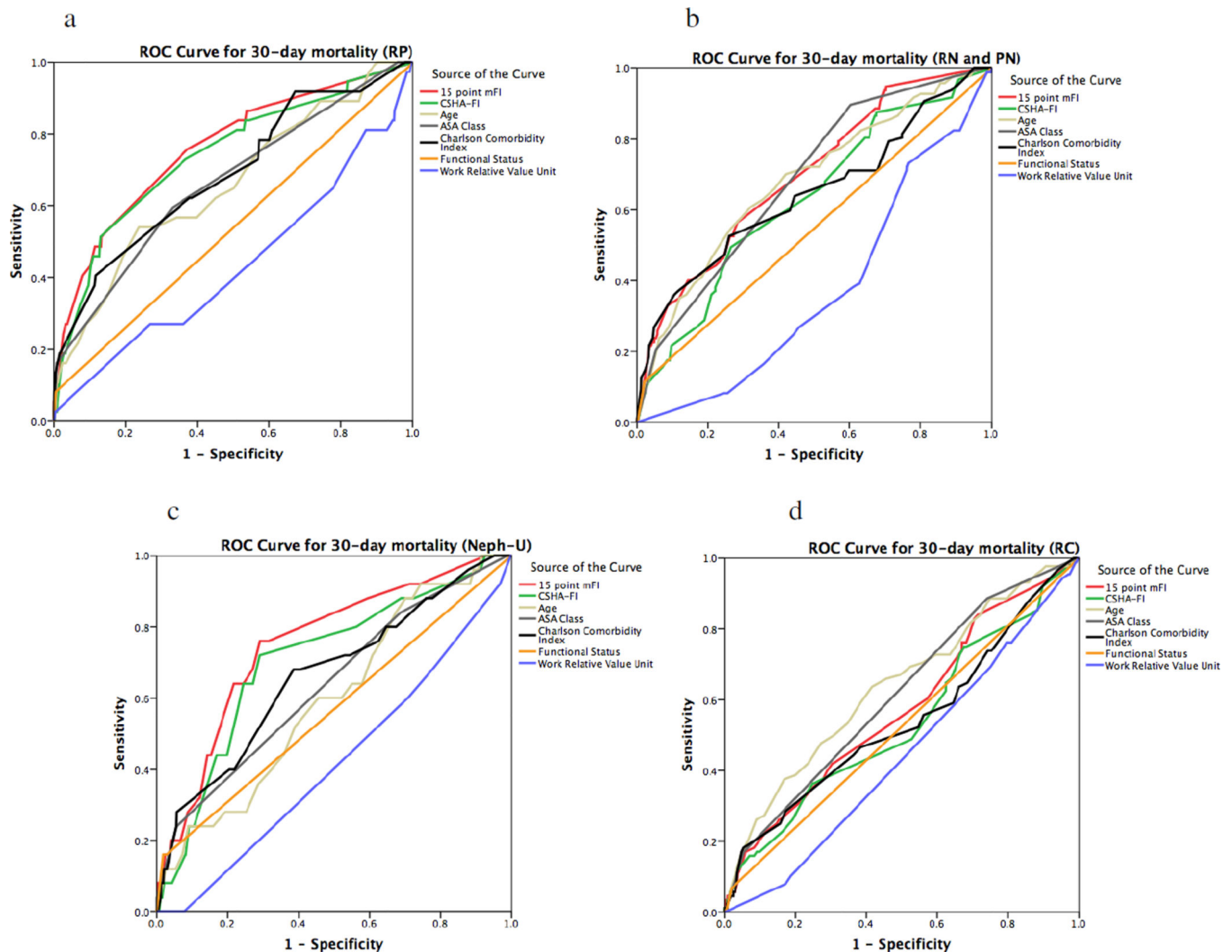
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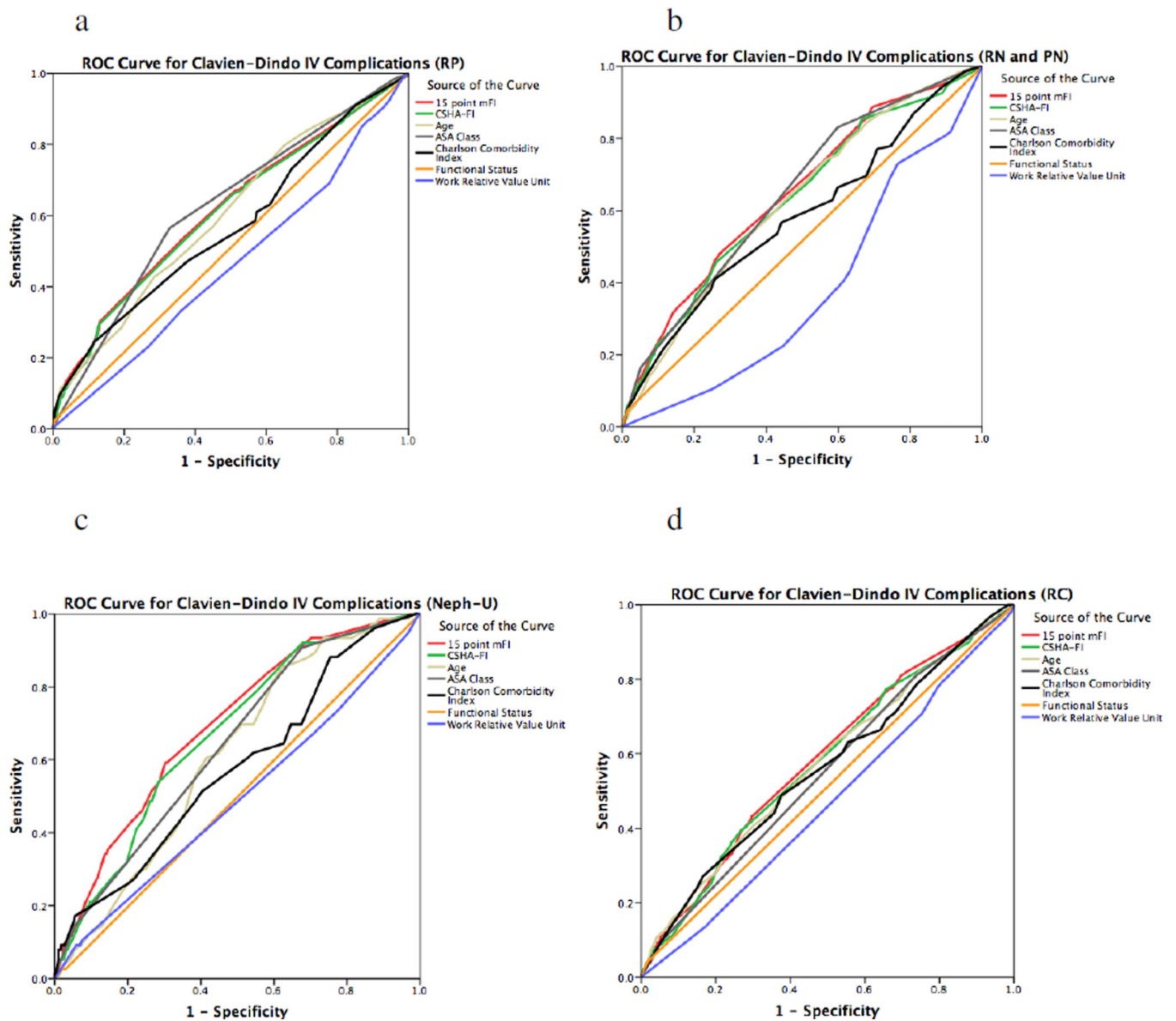


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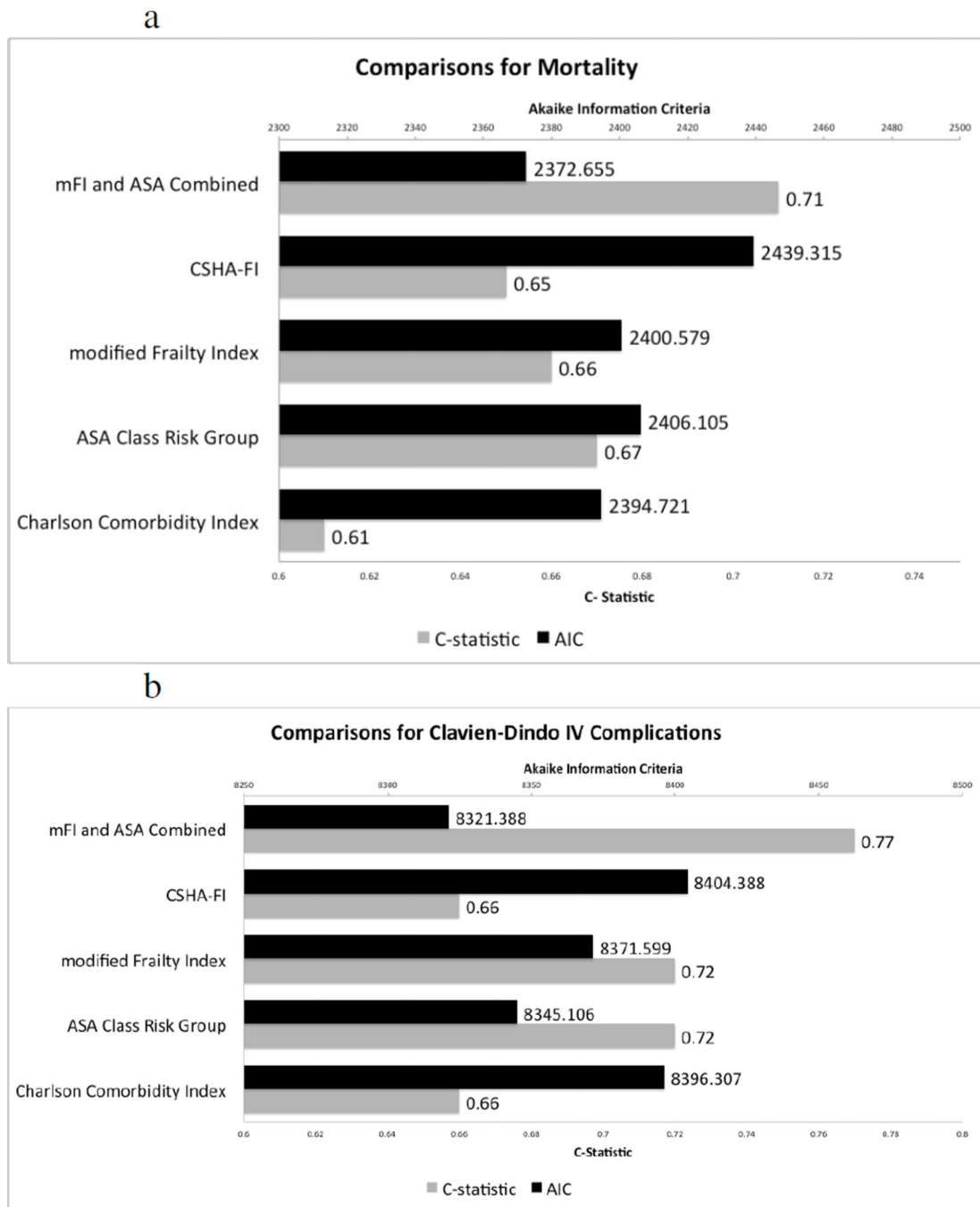


**Figure 1.**

Receiver operator characteristics (ROC) curve for mortality using our mFI in comparison to the existing parameters of predicting adverse outcomes. Our mFI had very poor sensitivity and specificity for predicting death in radical cystectomy (RC, Fig. 1.d C-statistic 0.574,  $p < 0.0005$ ), fair sensitivity and specificity for predicting death in radical prostatectomy (RP, Fig. 1.a, C-statistic 0.760,  $p < 0.0005$ ), fair sensitivity and specificity for predicting death in nephroureterectomy (Neph-U, Fig. 1.c, C-statistic 0.753,  $p < 0.0005$ ), and poor sensitivity and specificity for predicting death in partial and radical nephrectomy (PN and RN, Fig. 1.b, C-statistic 0.698,  $p < 0.0005$ ). In all cases except RC, our 15-point mFI performed better than the ASA Risk Class Stratification System and the Charlson Comorbidity Index. For RC, the ASA Class outperformed the mFI with a C-statistic of 0.612 ( $p < 0.0005$ ) in comparison to the 15-point mFI that had a C-statistic of 0.574 ( $p < 0.0005$ ). Our 15-point mFI was superior to the 11-point CSHA-FI in all cases.



**Figure 2.** Receiver operator characteristics (ROC) curve for Clavien-Dindo IV outcomes using the mFI in comparison to the existing parameters of frailty. The mFI had poor sensitivity and specificity in radical prostatectomy (RP, Fig. 1.a, C-statistic 0.615,  $p < 0.0005$ ), very poor sensitivity and specificity in radical cystectomy (RC, Fig. 1.d, C-statistic 0.585,  $p < 0.0005$ ), poor sensitivity and specificity in nephroureterectomy (Neph-U, Fig. 1.c, C-statistic 0.691,  $p < 0.0005$ ), and poor sensitivity and specificity in radical and partial nephrectomy (RN and PN, Fig. 1.b, C-statistic 0.646,  $p < 0.0005$ ). However, the mFI equaled or surpassed the Charlson Comorbidity Index or ASA Class Risk stratification in RN, PN and Neph-U. In RP, the ASA Class outcompeted the mFI with a higher C-statistic of 0.623 in comparison to 0.615. In RC, the ASA Class also outcompeted the mFI with a higher C-statistic of 0.612 in comparison to 0.585. The 15-point mFI was superior to the 11-point CSHA-FI in all the comparisons.



**Figure 3.**

A comparison of different risk stratification tools with the modified frailty index in our multivariate model. The parameters measured to assess the different models were Akaike information criteria (AIC) and the C-Statistic. A low AIC indicates better goodness of fit while a higher C-statistic value indicates an optimized model with both good sensitivity and specificity for a given outcome. The outcomes assessed were mortality (Figure 3.a) and Clavien-Dindo IV complications (Figure 3.b). The modified frailty index had fair sensitivity and specificity (C-statistic for mortality 0.66, for Clavien Dindo IV Complications 0.72)

while maintaining a low AIC (AIC for mortality= 2400.6, AIC for Clavien Dindo IV Complications=8371.6) although the ASA Class Risk groupings outperformed it in both outcomes with an equal or higher sensitivity and specificity (C-statistic for mortality 0.67, for Clavien Dindo IV Complications 0.72) and lower AIC (AIC mortality=2406.1, AIC Clavien Dindo IV Complications =8345.1). However, when the ASA Class Risk Group and the mFI were combined, it was superior in all regards with lowest AIC (Mortality=2372.7, Clavien Dindo IV Complications =8321.4) and the highest C-statistic (Mortality 0.71, Clavien Dindo IV Complications = 0.77).

**Table 1**

Eleven ACS-NSQIP variables were similar to 11 variables in the CSHA-FI. Four ACS-NSQIP variables related to oncology patients were added to make the FI consisting of 15 variables in total. The number of positive factors in the FI was recorded for each patient and divided by 15 to create a frailty index value.

ACS-NSQIP Variables	CSHA-FI Variables
1.Diabetes mellitus	History of Diabetes Mellitus
2.Functional Status	Impaired mobility, problems dressing oneself
3.History of severe COPD	Lung Problems
4.CHF exacerbation in 30 days before surgery	Congestive Heart Failure
5.History of MI 6 months prior to surgery	MI
6.Previous PCI, cardiac surgery, or history of angina	Cardiac Problems
7.Hypertension requiring medication	Arterial Hypertension
8.Peripheral vascular disease or rest pain	Peripheral Pulses
9.Impaired sensorium	Clouding/Delirium/Changes in mental function
10.History of TIA or CVA without neurologic deficit	Cerebrovascular Problems
11.History of CVA with neurologic deficit	History of stroke
12.Weight loss within last 6 months greater than 10%	
13.Chemotherapy or radiation prior to surgery	
14.History of Metastasis	
15. Severe Renal Failure or currently on dialysis	

Demographic and clinical characteristics for the different patients undergoing urologic surgeries for malignancy. Elderly patients were concentrated in the groups undergoing nephroureterectomy and radical cystectomy. The patients undergoing radical prostatectomy were a lower risk group overall with a larger proportion being ASA Class II or less in comparison to the groups undergoing other surgeries. Mortality after surgery was highest in those undergoing radical cystectomy (2.6%) while it was lowest for those undergoing radical prostatectomy (0.2%).

**Table 2**

	Prostatectomy	Partial Nephrectomy	Radical Nephrectomy	Nephroureterectomy	Cystectomy
Total number of cases	23350	5709	7791	1443	3388
Mean Age, y (SD)	62(7)	59 (12)	62 (13)	62 (12)	59 (12)
Males	100%	60.8%	61.1%	61.3%	80.4%
	23350/23350	3466/5709	4760/7791	883/1443	2722/3388
Nonwhite race or Hispanic	24.1%	21.1%	24.0%	17.8%	7.6%
	5421/23350	1155/5709	1778/7791	247/1443	228/3388
Diabetes Mellitus	11.3%	19.4%	20.2%	19.9%	19.6%
	2644/23350	1107/5709	1576/7791	287/1443	665/3388
Current Smoker	12.5%	21.0%	19.4%	24.3%	24.7%
	2926/23350	1198/5709	1514/7791	351/1443	836/3388
Hypertension	50.4%	60.9%	64.7%	68.0%	60.8%
	11784/23350	3479/5709	5044/7791	981/1443	2061/3388
End stage renal disease	0.3%	0.4%	1.0%	2.4%	1.0%
	66/23350	24/5709	396/7791	34/1443	34/3388
Charlson Comorbidity Index					
0	8 (<0.1%)	94 (1.6%)	78 (1.0%)	3 (0.2%)	5 (0.1%)
1	522 (2.2%)	238 (4.2%)	230 (3.0%)	11 (0.8%)	43 (1.3%)
2	2916 (12.5%)	351 (6.2%)	507 (6.5%)	54 (3.7%)	154 (4.5%)
3	4206 (18.0%)	434 (7.6%)	600 (7.7%)	106 (7.3%)	289 (8.5%)
4	1481 (6.3%)	560 (9.8%)	827 (10.6%)	173 (11.9%)	381 (11.2%)
5	851(3.6%)	709 (12.4%)	781 (10.1%)	161 (11.2%)	280 (8.3%)
6	4372 (18.7%)	972 (17.1%)	1100 (14.1%)	149 (10.3%)	336 (10.0%)
7	6288(27.0%)	1170 (20.5%)	1318 (17.0%)	198 (13.7%)	592 (17.5%)
8	2309 (9.9%)	798 (14.0%)	1135 (14.6%)	268 (18.6%)	719 (21.3%)
>9	406 (1.7%)	380 (6.7%)	1212 (15.6%)	320 (22.2%)	589 (17.4%)
ASA Class					
I	964 (4.1%)	135 (2.4%)	164 (2.1%)	16 (1.1%)	20 (0.6%)

	Prostatectomy	Partial Nephrectomy	Radical Nephrectomy	Nephro-ureterectomy	Cystectomy
2	14654 (62.8%)	2432 (42.7%)	2584 (33.2%)	430 (29.8%)	844 (24.9%)
3	7521 (32.2%)	2981 (52.3%)	4448 (57.1%)	908 (63.0%)	2325 (68.7%)
4	186 (0.8%)	153 (2.7%)	588 (7.5%)	87 (6.1%)	195 (5.8%)
Frailty Score out of 15					
0-0.05	11312 (48.4%)	2101 (36.8%)	2289 (29.4%)	410 (28.4%)	1108 (32.7%)
0.05-0.10	9526 (40.8%)	2377 (41.6%)	3169 (40.7%)	634 (43.9%)	1330 (39.3%)
0.10-0.15	1656 (7.1%)	701 (12.3%)	833 (10.7%)	181 (12.5%)	423 (12.2%)
0.15-0.20	637 (2.7%)	407 (7.1%)	942 (12.1%)	130 (9.0%)	351 (10.4%)
> 0.20	219 (0.9%)	123 (2.2%)	558 (7.2%)	88 (6.1%)	176 (5.2%)
Functional Status					
Independent	23241 (99.5%)	5633 (98.7%)	7583 (97.3%)	1400 (97.0%)	3314 (97.8%)
Limited Dependence	50 (0.2%)	50 (0.9%)	160 (2.1%)	30 (2.1%)	48 (1.4%)
Totally Dependent	5 (<0.1%)	0 (0%)	15 (0.2%)	0 (0%)	22 (0.6%)
Unknown	62 (0.3%)	26 (0.5%)	33 (0.4%)	13 (0.9%)	4 (0.1%)
Procedure subtypes					
Open	5333 (22.8%)	2284 (40.0%)	3128 (40.1%)	434 (30.1%)	3388 (100%)
Minimally Invasive	18026 (77.2%)	3425 (60.0%)	4663 (59.9%)	1009 (69.9%)	-
30-Day Mortality	0.2%	0.4%	1.0%	1.7%	2.6%
	37/23350	20/5709	79/7791	25/1443	88/3388
Clavien-Dindo IV Complications	1.1%	2.3%	3.9%	5.3%	9.5%
	246/23350	129/5709	306/7791	76/1443	322/3388
Septic Shock or Sepsis	0.8%	1.2%	1.6%	3.0%	12.5%
	191/23350	67/5709	127/7791	43/1443	422/3388
Ventilator Dependence	0.1%	0.4%	1.2%	1.3%	2.6%
	34/23350	21/5709	93/7791	19/1443	89/3388
Unplanned re-intubation	0.2%	0.8%	1.5%	1.7%	3.3%
	54/23350	44/5709	116/7791	25/1443	112/3388
Myocardial Infarction	0.2%	0.5%	0.5%	1.0%	1.7%
	41/23350	26/5709	40/7791	15/1443	58/3388
Renal Failure	0.4%	1.4%	1.8%	3.0%	3.5%
	98/23350	79/5709	142/7791	43/1443	120/3388
Cardiac arrest	0.1%	0.4%	0.4%	0.6%	1.0%
	23/23350	21/5709	35/7791	8/1443	33/3388
Pulmonary Embolism	0.5%	0.4%	0.6%	0.5%	2.6%
	113/23350	23/5709	47/7791	7/1443	87/3388



	<b>Prostatectomy</b>	<b>Partial Nephrectomy</b>	<b>Radical Nephrectomy</b>	<b>Nephro-ureterectomy</b>	<b>Cystectomy</b>
Deep Venous thrombosis	0.7% 171/23350	0.5% 27/5709	0.8% 61/7791	1.4% 20/1443	3.4% 116/3388
Surgical site infection or dehiscence	1.4% 334/23350	1.7% 96/5709	2.4% 190/7791	2.8% 40/1443	14.4% 487/3388
Bleeding requiring blood transfusion	4.1% 952/23350	7.4% 423/5709	14.7% 1147/7791	13.2% 191/1443	39.1% 1326/3388
Readmission	4.2% 272/6534	5.6% 146/2625	6.5% 210/3223	8.3% 46/553	17.6% 469/2659
Re-operation	0.9% 62/6534	1.8% 48/2625	2.0% 64/3223	3.8% 21/553	5.8% 155/2694

**Table 3**

Outcomes grouped by type of surgery and their modified frailty index score.

Frailty Index	Radical Prostatectomy					p-value	Frailty Index	Radical and Partial Nephrectomy					p-value
	0-0.05	0.05-0.10	0.10-0.15	0.15-0.20	>0.20			0-0.05	0.05-0.10	0.10-0.15	0.15-0.20	>0.20	
30-day Mortality*	0.1% 6/11312	0.1% 14/9526	0.4% 7/1656	1.1% 7/637	1.4% 3/219	<0.005	30-day Mortality*	0.3% 12/4390	0.6% 36/5546	0.8% 12/1534	1.2% 16/1349	3.4% 23/681	<0.0005
Clavien-Dindo IV*	0.7% 81/11312	1.1% 109/9526	1.4% 24/1656	3.0% 19/637	5.9% 13/219	<0.0005	Clavien-Dindo IV*	1.5% 66/4390	3.0% 169/5546	4.0% 61/1534	6.1% 82/1349	8.4% 57/681	<0.0005
Septic Shock/Sepsis*	0.5% 61/11312	0.9% 82/9526	1.4% 24/1656	2.2% 14/637	4.6% 10/219	<0.0005	Septic Shock/Sepsis*	0.9% 39/4390	1.5% 83/5546	0.8% 12/1534	1.5% 36/1349	3.5% 24/681	<0.0005
Ventilator Dependent*	<0.1% 5/11312	0.2% 17/9526	0.3% 5/1656	0.5% 3/637	1.8% 4/219	<0.0005	Ventilator Dependent*	0.3% 13/4390	0.7% 38/5546	1.3% 20/1534	1.7% 23/1349	2.9% 20/681	<0.0005
Re-Intubated*	0.1% 10/11312	0.3% 27/9526	0.3% 5/1656	1.1% 7/637	2.3% 5/219	<0.0005	Re-Intubated*	0.5% 21/4390	1.0% 55/5546	1.5% 23/1534	2.7% 36/1349	3.7% 25/681	<0.0005
Myocardial Infarction*	0.1% 10/11312	0.2% 19/9526	0.2% 4/1656	0.6% 4/637	1.8% 4/219	<0.0005	Myocardial Infarction*	0.2% 7/4390	0.5% 27/5546	0.5% 8/1534	1.0% 13/1349	1.6% 11/681	<0.0005
Acute Renal Failure*	0.1% 15/11312	0.6% 53/9526	0.7% 11/1656	1.7% 11/637	3.7% 8/219	<0.0005	Acute Renal Failure*	0.6% 28/4390	1.4% 80/5546	2.7% 42/1534	3.4% 46/1349	3.7% 25/681	<0.0005
Cardiac Arrest*	<0.1% 5/11312	0.1% 10/9526	0.3% 5/1656	0.3% 2/637	0.5% 1/219	<0.0005	Cardiac Arrest*	0.2% 9/4390	0.4% 23/5546	0.3% 4/1534	1.0% 13/1349	1.0% 7/681	<0.0005
Pulmonary embolism	0.5% 56/11312	0.5% 43/9526	0.5% 9/1656	0.3% 2/637	1.4% 3/219	0.365	Pulmonary embolism	0.4% 16/4390	0.6% 31/5546	0.8% 12/1534	0.4% 6/1349	0.7% 5/681	0.285
Deep venous thrombosis	0.7% 77/11312	0.8% 73/9526	0.8% 14/1656	0.8% 5/637	0.9% 2/219	0.913	Deep venous thrombosis*	0.3% 15/4390	0.7% 41/5546	0.8% 12/1534	1.1% 15/1349	0.7% 5/681	0.017
Surgical Site Infection or dehiscence*	1.1% 125/11312	1.6% 150/9526	1.8% 30/1656	2.8% 18/637	5.0% 11/219	<0.0005	Surgical Site Infection or dehiscence	1.9% 83/4390	2.1% 114/5546	2.3% 36/1534	2.4% 32/1349	3.1% 21/681	0.280
Bleeding requiring blood transfusion*	3.7% 417/11312	4.2% 392/9526	4.2% 69/1656	8.0% 51/637	10.5% 23/219	<0.0005	Bleeding requiring blood transfusion*	7.2% 315/4390	11.1% 617/5546	13.0% 200/1534	20.9% 282/1349	22.9% 156/681	<0.0005
Readmission (2011-2013)*	3.4% 108/3201	4.5% 116/2596	5.4% 29/542	9.0% 16/178	17.6% 3/17	<0.0005	Readmission (2011-2013)*	4.0% 80/2021	5.9% 137/2304	6.8% 50/736	10.3% 60/583	14.2% 29/204	<0.0005
Re-operation (2011-2013)*	0.6% 19/3201	1.2% 32/2596	1.1% 6/542	2.8% 5/178	0% 0/17	0.010	Re-operation (2011-2013)*	1.5% 30/2021	1.9% 14/2304	1.9% 14/736	2.7% 16/583	3.9% 8/204	0.075

**Table 3.b**

Frailty Index	Nephroureterectomy					Radical Cystectomy					p-value	
	0-0.05	0.05-0.10	0.10-0.15	0.15-0.20	>0.20	0-0.05	0.05-0.10	0.10-0.15	0.15-0.20	>0.20		
30-day Mortality*	0.5% 2/410	0.9% 6/634	3.3% 6/181	4.6% 6/130	5.7% 5/88	<0.0005	2.1% 21/1008	2.6% 34/1330	2.4% 10/423	3.1% 11/351	6.8% 12/176	0.005
Clavien-Dindo IV*	1.2% 5/410	5.0% 32/634	7.2% 13/181	11.5% 15/130	12.5% 11/88	<0.0005	6.6% 73/1108	9.2% 122/1330	14.2% 60/423	10.5% 37/351	17.0% 30/176	<0.0005
Septic Shock/Sepsis*	1.2% 5/410	2.5% 16/634	7.2% 13/181	8.5% 11/130	4.5% 4/88	0.001	10.6% 117/1108	13.5% 179/1330	14.7% 62/423	11.7% 41/351	13.1% 23/176	0.135
Ventilator Dependent*	0.2% 1/410	0.8% 5/634	3.9% 7/181	2.3% 3/130	5.7% 5/88	<0.0005	1.4% 15/1108	2.4% 32/1330	4.7% 20/423	3.4% 12/351	5.7% 10/176	<0.0005
Re-Intubated*	1.0% 4/410	0.9% 6/634	2.8% 5/181	4.6% 6/130	6.8% 6/88	<0.0005	2.1% 23/1108	2.9% 39/1330	5.4% 23/423	4.3% 15/351	6.8% 12/176	0.001
Myocardial Infarction*	0% 0/410	1.1% 7/634	1.7% 3/181	1.5% 2/130	1.1% 1/88	0.043	1.1% 12/1108	1.7% 22/1330	2.4% 10/423	2.8% 10/351	2.3% 4/176	0.113
Acute Renal Failure*	1.0% 4/410	3.3% 21/634	2.8% 5/181	6.2% 8/130	4.5% 4/88	0.024	1.6% 18/1108	3.5% 46/1330	4.7% 20/423	6.6% 23/351	7.4% 13/176	<0.0005
Cardiac Arrest*	0.2% 1/410	0.2% 1/634	3.3% 6/181	2.3% 3/130	2.8% 2/88	0.006	0.8% 9/1108	1.1% 15/1330	0.7% 3/423	1.1% 4/351	1.1% 2/176	0.870
Pulmonary embolism	0% 0/410	0.6% 4/634	0.6% 1/181	0.8% 1/130	1.1% 1/88	0.511	2.6% 29/1108	2.6% 35/1330	2.8% 12/423	2.0% 7/351	2.3% 4/176	0.969
Deep venous thrombosis*	0.7% 3/410	0.8% 5/634	3.9% 7/181	1.5% 2/130	3.4% 3/88	0.008	3.0% 33/1108	3.8% 51/1330	4.0% 17/423	2.6% 9/351	3.4% 6/176	0.628
Surgical Site Infection or dehiscence	2.2% 9/410	2.8% 18/634	2.2% 4/181	3.8% 5/130	4.5% 4/88	0.679	12.5% 139/1108	15.0% 200/1330	16.8% 71/423	13.4% 47/351	17.0% 30/176	0.148
Bleeding requiring Blood transfusion*	7.1% 29/410	12.5% 79/634	17.1% 31/181	23.1% 30/130	25.0% 22/88	<0.0005	34.6% 383/1108	39.9% 531/1330	44.2% 187/423	42.5% 149/351	43.2% 76/176	0.002
Readmission (2011-2013)	8.2% 15/182	6.3% 14/221	7.3% 6/82	14.3% 7/49	21.1% 4/19	0.108	15.9% 138/866	17.4% 182/1046	21.1% 75/355	18.5% 50/270	19.7% 24/122	0.264
Re-operation (2011-2013)*	2.7% 5/182	2.7% 6/221	2.4% 2/82	8.2% 4/49	21.1% 4/19	0.001	4.4% 39/882	6.6% 70/1057	7.5% 27/358	5.2% 14/271	4.0% 5/126	0.116

There are differences between the subgroups for the given adverse outcome (noted with an \*). 30-day mortality and Clavien Dindo IV complications were significantly associated with increasing frailty index score for all surgeries. Readmission was significant with increasing frailty index score for all surgeries except radical cystectomy (p=0.264) and nephroureterectomy (p=0.108). Re-operation was significant with increasing frailty index score for all except radical cystectomy (p=0.116).

**Table 4**

A multivariate logistic regression model with the outcomes of mortality or Clavien IV outcomes for all surgeries was done with the results as shown after selection from univariate analysis. The model adjusts for age, gender, race, smoking status, and procedure and was a good fit for the data (Hosmer and Lemeshow Test,  $p=0.358$ ). All variables were included as categorical variables with the exception of age, which was a continuous variable. There were increased odds of a Clavien-Dindo IV outcome for all the risk groups ranging from 1.553 in those with a mFI of 0.05–0.10 to 3.704 for those with a mFI > 0.20 in comparison to the reference group of mFI 0–0.05 ( $p<0.0005$ ). There were increased odds of death for those with a mFI greater than 0.10–0.15 for Clavien-Dindo IV outcomes ( $p<0.0005$ ) but not mortality when compared to the reference group of mFI 0–0.05 ( $p=0.066$ ).

Characteristic	Clavien-Dindo IV Complications		95% Confidence Interval		P-value	30-Day Mortality	95% Confidence Interval		P-value
	Odds Ratio	Lower Bound	Upper Bound	Lower Bound			Upper Bound		
Age (years)	1.034	1.027	1.041	<0.0005	1.060	1.044	1.076	<0.0005	
Gender									
Male	Ref.	-	-	-	Ref.	-	-	-	
Female	1.228	1.038	1.453	0.017	0.892	0.651	1.223	0.479	
Modified FI									
0–0.05	Ref.	-	-	-	-	-	-	-	
0.05–0.10	1.553	1.305	1.848	<0.0005	1.452	0.975	2.162	0.066	
0.10–0.15	2.076	1.660	2.597	<0.0005	1.939	1.183	3.176	0.009	
0.15–0.20	2.761	2.199	3.466	<0.0005	3.397	2.133	5.409	<0.0005	
>0.20	3.704	2.865	4.788	<0.0005	5.946	3.718	9.509	<0.0005	
Race and Ethnicity									
White	Ref.	-	-	-	Ref.	-	-	-	
Non-White or Hispanic	1.150	0.978	1.352	0.091	1.192	0.848	1.676	0.312	
Smoking Status									
Non-Smoker	Ref.	-	-	-	Ref.	-	-	-	
Smoker	1.314	1.116	1.547	0.001	1.411	1.007	1.979	0.046	
Procedure									
MIS prostatectomy	Ref.	-	-	-	Ref.	-	-	-	
Open prostatectomy	1.485	1.119	1.969	0.006	1.758	0.872	3.545	0.115	
MIS radical nephrectomy	1.756	1.344	2.295	<0.0005	2.337	1.285	4.252	0.005	
Open radical nephrectomy	5.759	4.595	7.216	<0.0005	6.792	3.984	11.580	<0.0005	

Characteristic	Clavien-Dindo IV Complications		95% Confidence Interval		P-value	30-Day Mortality	95% Confidence Interval		P-value
	Odds Ratio	Lower Bound	Upper Bound	Lower Bound			Upper Bound		
MIS partial nephrectomy	1.482	1.059	2.073	0.022	1.535	0.676	3.484	0.306	
Open partial nephrectomy	3.677	2.781	4.862	<0.0005	2.606	1.219	5.573	0.013	
MIS nephroureterectomy	3.402	2.402	4.817	<0.0005	5.667	2.907	11.048	<0.0005	
Open nephroureterectomy	4.734	3.071	7.298	<0.0005	6.236	2.684	14.493	<0.0005	
Radical Cystectomy	7.420	6.013	9.155	<0.0005	9.550	5.794	15.743	<0.0005	

MIS: Minimally Invasive