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# The Five-Factor Modified Frailty Index as a Predictor of Outcomes in Deep Brain Stimulation Surgery for Parkinson's Disease

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# **Abstract**

#### Introduction

Parkinson's disease (PD) is one of the most common neurodegenerative diseases worldwide. Though there are many pharmacological therapeutics approved today for PD, surgical interventions such as deep brain stimulation (DBS) have shown convincing symptom mitigation and minimal complication rates in aggregate. Recently, the concept of frailty - defined as reduced physiologic reserve and function affecting multiple systems throughout the patient - has gained traction as a predictor of short-term postoperative morbidity and mortality. As such, the Modified Frailty Index-5 (mFI-5) is a postoperative morbidity predictor based on five factors and has been used in neurosurgical subspecialties such as tumor, vascular, and spine. Yet, there is minimal literature assessing frailty in the field of functional neurosurgery. With the prevalence of DBS in PD, this study evaluated the mFI-5 as a predictor of postoperative complications in a selected patient population.

#### Methods

The American College of Surgeons National Surgical Quality Improvement Program 2010-2019 Database was queried for Current Procedural Terminology (CPT) codes, as well as the International Classification of Diseases (ICD)-9 and ICD-10 codes pertaining to DBS procedures in PD patients. Each patient was scored by the mFI-5 protocol and stratified into groups of No Frailty (mFI-5=0), Moderate Frailty (mFI-5=1), and Significant Frailty (mFI-5≥2). The No Frailty group was used as a reference in multivariate and univariate analyses of the groups.

## Results

A total of 1,645 subjects were included in the study and were subcategorized into groups of No Frailty (N=877), Moderate Frailty (N=561), and Significant Frailty (N=207) based on their frailty scores. The subjects' mean age was  $65.8\pm9.4$  years. Overall, 1,161 (70.6%) were male, while 484 (29.4%) were female. With reference to the No Frailty group in multivariate analysis, patients with moderate frailty experienced greater unplanned readmission (OR 2.613, 95% CI 1.143-5.973, p=0.023), while those with significant frailty experienced greater unplanned readmission (OR 3.723, 95% CI 1.376-10.073, p=0.010), any readmission (OR 2.396, 95% CI 1.098-5.230, p=0.028), non-home discharge (OR 4.317, 95% CI 1.765-10.562, p<0.001), and complications in aggregate (OR 2.211, 95% CI 1.285-3.806, p=0.004).

#### **Conclusions**

Until now, the available clinical tools were limited in providing accurate predictions with minimal information for postoperative outcomes in DBS for PD patients. Our data give clinicians insight into the relationship between frailty and surgical outcomes and will assist physicians in preparing for postoperative care by predicting outcomes of significantly frail PD patients receiving DBS therapy.

Categories: Neurosurgery

**Keywords:** post-operative outcomes, frailty, deep brain stimulation (dbs), movement disorders, modified frailty index-5 (mfi-5), parkinson's disease (pd)

#### Introduction

Parkinson's disease (PD) is a debilitating, neurodegenerative disorder that is characterized by motor system dysfunction and tremors. Although PD can be treated with a variety of pharmacological interventions, deep brain stimulation (DBS) has been shown to be a safe, non-pharmaceutical, intervention that can drastically augment a patient's quality of life. Pharmacological interventions are typically attempted in early stage PD, with DBS implantation being performed in refractory PD cases. Follow-up studies on patients after DBS have

found a significant improvement in motor system function [1] and survival [2].

Although widely regarded as a safe procedure, DBS is accompanied by a variety of risks that are being evaluated by using predictive models to improve the selectivity of appropriate surgical candidates [3-6]. Recently, frailty scores have been used as predictive models for surgical candidates with some success in a variety of neurosurgical subspecialties, but its value has yet to be adequately investigated in DBS specifically for PD patients [7-9]. These scores are applied to patients with various comorbidities that have been correlated with an increased risk of postoperative complications. Multiple studies evaluating the relationship between frailty and postoperative complications have found that an increased preoperative frailty score is associated with an increased length of stay (LOS), non-home discharge, and increased complication rates within 30 days following surgery [3-6,10,11].

The Canadian Study of Health and Aging Frailty Index (CSHA-FI) encompassed 70 criteria for calculating frailty scores, which was later shortened to the Modified Frailty Index-11 (mFI-11) and then the mFI-5 (Appendices) [12]. These shortened frailty indices have been shown to be appropriate and equivalent for predicting postoperative outcomes [12].

The mFI-5 scoring system includes five categorical variables: history of diabetes, chronic obstructive pulmonary disease (COPD), acute preoperative congestive heart failure (CHF), hypertension (HTN), and dependent functional status [8]. With these five variables, the mFI-5 is a useful tool for clinicians due to the ready availability of its components as part of a standard history and physical examination, and its corresponding ease of calculation. Though there are multiple studies using the mFI-5 to predict outcomes in general surgery [3,6] and neurosurgical specialties such as spine [1], tumor [5], and cerebrovascular [13], its application in predicting DBS postoperative outcomes in PD patients has only been minimally investigated. We hypothesize that increased mFI-5 scores will be associated with poor short-term postoperative outcomes in DBS surgical patients.

## **Materials And Methods**

#### Study design and population

This study is a retrospective cohort analysis of patient data from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database from 2010 to 2019. This database captures more than 150 clinical variables on individual patient cases, including demographic data, preoperative risk factors and lab values, intra-operative data, and significant events up to postoperative day 30. Given the deidentified nature of this dataset, the current study was cleared under a human subjects' exemption.

As per previously published inclusion criteria, the ACS-NSQIP 2010-2019 database was queried for Current Procedural Terminology (CPT) codes pertaining to DBS lead insertion (61863, 61864, 61867, 61868) and generator implantation procedures (61885 and 61886), as well as International Classification of Diseases (ICD)-9 (332.0) and ICD-10 (G20.0) diagnosis codes for PD [14]. Patients not diagnosed with PD, and those undergoing cortical lead implantation as well as revision or removal procedures were excluded, all in accordance with previous studies [14,15].

The mFI-5 scores were calculated for each patient as a sum of the number of conditions present and stratified into No Frailty (mFI-5 = 0), Moderate Frailty (mFI-5 = 1), and Significant Frailty (mFI-5  $\geq$  2) groups for analysis. This was done in accordance with previous studies using this index [16-18]. With these parameters, a total sample size of 1,645 subjects was identified (Figure 1).

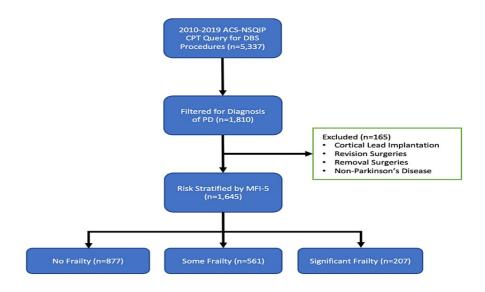


FIGURE 1: Patient selection.

#### **Outcome measures**

Our primary outcomes of interest were any major postoperative event, including systemic complications (such as urinary tract infection, sepsis, pneumonia, unplanned intubation, prolonged postoperative ventilator-assisted respiration >48 hours, cardiac arrest, myocardial infarction, acute kidney injury, deep vein thrombosis, pulmonary embolism, thrombophlebitis, sepsis, septic shock, and death), surgical site infections, and any event necessitating a return to the operating room. Secondary outcomes included readmission rates (any readmission and unplanned readmission, the latter defined by the ACS-NSQIP as a readmission likely due to a postoperative occurrence within 30 days of the principal procedure), rates of non-home discharge, and all complications in aggregate.

#### Statistical analysis

All calculations and statistics were performed using SPSS Version 26.0 (IBM Corp., Armonk, NY). Categorical variables are expressed with frequencies and proportions, while continuous variables are expressed with means and standard deviations. Univariable analyses were done on patient characteristics, comorbidities, and 30-day outcomes data using the chi-squared test or Fisher's exact test, as appropriate for categorical variables and the independent samples t-test for continuous variables. The populations compared in this study include No Frailty (mFI-5 score of 0), Moderate Frailty (mFI-5 score of 1), and Significant Frailty (mFI-5 score >2). The three groups were analyzed by using the No Frailty group as a reference. Thus, the statistics compare No Frailty versus Moderate Frailty and No Frailty versus Significant Frailty.

On multivariable analysis, characteristics and comorbidities that were significantly different at p<0.05, along with clinically important variables, were gathered for a binary logistic regression analysis to establish independent predictability of the mFI-5 on outcomes. Factors included in this analysis were mFI-5 score, age, sex, body mass index (BMI), smoking status, American Society of Anesthesiologists (ASA) Classification, bleeding disorders, dyspnea, and anemia. Diabetes, COPD, CHF, HTN, and functional status were not included as they are all accounted for by the mFI-5 index. Binary logistic regressions are reported with odds ratio (OR) and 95% confidence intervals (CI). Significance was assessed at p<0.05.

# **Results**

#### Patient comorbidities and characteristics

A total of 1,645 patients were identified. Baseline demographic and comorbidity data are summarized in Table  $\it 1$ . Mean age of subjects was 65.8 $\pm$ 9.4 years, with 1,161 (70.6%) males and 484 (29.4%) females. The most common demographics were 88.8% White, followed by 2.6% Asian and 1.9% African American. Mean BMI was 27.4 $\pm$ 6.1. The three most common mFI-5 criteria were HTN requiring medication (36.2%), followed by diabetes mellitus (11.4%) and dependent functional status (10.8%) (Table  $\it 2$ ).

Parameter	All Patients (N=1,645)	No Frailty (N=877)	Moderate Frailty (N=561)	P- value	Significant Frailty (N=207)	P- value

Mean age (years±SD)	65.8±9.4	64.1 ± 9.8	67.3±8.7	<0.001	69.1±7.8	<0.001
Sex				0.038		0.405
Male	1161 (70.6%)	600 (68.4%)	413 (73.6%)		148 (71.5%)	
Female	484 (29.4%)	277 (32.6%)	148 (26.4%)		59 (28.5%)	
Demographics				0.682		0.313
White	1460 (88.8%)	781 (89.1%)	489 (87.2%)		190 (91.8%)	
Black	31 (1.9%)	14 (1.6%)	13 (2.3%)		4 (1.9%)	
Asian	43 (2.6%)	26 (3.0%)	16 (2.9%)		1 (0.5%)	
Native Hawaiian/Pacific Islander	4 (0.2%)	3 (0.3%)	1 (0.2%)		0	
Native American	12 (0.7%)	4 (0.5%)	6 (1.1%)		2 (1.0%)	
Unknown	95 (5.8%)	49 (5.6%)	36 (6.4%)		10 (4.8%)	
Mean BMI (kg/m <sup>2</sup> ±SD)	27.4±6.1	26.4 ± 5.8	28.0 ± 5.9	<0.001	30.2 ± 6.6	<0.00
BMI (categorical obesity)				<0.001		<0.00
≥30	452 (27.5%)	182 (20.8%)	176 (31.4%)		94 (45.4%)	
<30	1193 (72.5%)	695 (79.2%)	385 (68.6%)		113 (54.6%)	
ASA classification				<0.001		<0.00
1	0	0	0		0	
2	485 (29.5%)	344 (39.2%)	115 (20.5%)		26 (12.6%)	
3	1136 (69.1%)	526 (60.0%)	440 (78.4%)		170 (82.1%)	
4	23 (1.4%)	7 (0.8%)	6 (1.1%)		10 (4.8%)	
Not assigned	1 (0.1%)	0	0		1 (0.5%)	
Smoking (past year)				0.898		0.180
No	1574 (95.7%)	836 (95.3%)	536 (95.5%)		202 (97.6%)	
Yes	71 (4.3%)	41 (4.7%)	25 (4.5%)		5 (2.4%)	
Dyspnea				0.023		<0.00
None	1585 (96.4%)	860 (1.8%)	537 (05.7%)		188 (90.8%)	
Moderate exertional	52 (3.2%)	15 (1.8%)	23 (4.1%)		13 (6.3%)	
At rest	8 (0.5%)	1 (0.1%)	1 (0.2%)		6 (2.9%)	
Bleeding disorders*	17 (1.0%)	3 (0.3%)	11 (2.0%)	0.003	3 (1.4%)	0.088
				0.004†		
Anemia**	271 (16.5%)	115	111	<0.001	45	0.002

## **TABLE 1: Patient characteristics.**

BMI, body mass index; ASA, American Society of Anesthesiologists

P-values are with reference to the No Frailty group

\*Bleeding disorders including chronic anticoagulation.

\*\*Anemia according to the WHO criteria of hematocrit <39.0% for males and hematocrit <36.0% for females [7]

†Fisher's exact test

Parameter	Patients (%) (N = 1,645)
Chronic obstructive pulmonary disease	29 (1.8%)
Congestive heart failure	1 (0.1%)
Diabetes mellitus	188 (11.4%)
Functionally dependent health status	177 (10.8%)
Hypertension	595 (36.2%)

TABLE 2: mFI-5 components with the frequency of affected patients.

Of the 1,645 subjects, 877 (53.3%) had no frailty, 561 (34.1%) had moderate frailty, and 207 (12.5%) had significant frailty. Compared to the No Frailty group, subjects in both Moderate Frailty and Significant Frailty groups were older (No Frailty:  $64.1\pm9.8$  years; Moderate Frailty:  $67.3\pm8.7$  years, p<0.001; Significant Frailty:  $69.1\pm7.8$  years, p<0.001), more likely to be obese (No Frailty: 20.8%; Moderate Frailty: 31.4%, p<0.001; Significant Frailty 45.4%, p<0.001), more likely to have a higher ASA classification (p<0.001 and p<0.001), and more likely to have a history of dyspnea (p=0.023 and p<0.001) and anemia (p<0.001 and p=0.002) (defined according to the WHO criteria of hematocrit <39.0% for males and hematocrit <36.0% for females). Those with moderate, but not significant frailty, were more likely to be male (73.6% versus 68.4%, p=0.038) and to have a history of bleeding disorders (2.0% versus 0.3%, p=0.003).

#### Univariable analysis

The results of univariable analysis are included in Table 3. Using the No Frailty group as a reference, the Moderate Frailty and Significant Frailty groups had higher rates of both unplanned readmission (3.8% and 4.7% versus 1.4%; p=0.005 and p=0.004) and any readmission (4.6% and 5.8% versus 2.6%; p=0.040 and p=0.020), non-home discharge destination (2.6% and 6.9% versus 1.2%; p=0.050 and p<0.001), and complications in aggregate (8.6% and 13.0% versus 5.8%; p=0.045 and p<0.001). Otherwise, major postoperative complications, individualized systemic complications, wound infection, and reoperation rates had relatively low instances and were not found to be significantly different based on this risk stratification.

Parameter	All Patients (N=1,645)	No Frailty (N=877)	Moderate Frailty (N=561)	P- value	Significant Frailty (N=207)	P- value
Any complication	126 (7.7%)	51 (5.8%)	48 (8.6%)	0.045	27 (13.0%)	<0.001
Any readmission	61 (3.7%)	23 (2.6%)	26 (4.6%)	0.04	12 (5.8%)	0.02
Unplanned readmission	39 (2.4%)	11 (1.4%)	19 (3.8%)	0.005	9 (4.7%)	0.004
Non-home DC	38 (2.3%)	10 (1.2%)	14 (2.6%)	0.05	14 (6.9%)	<0.001
Major postoperative complications (systemic insults, reoperation, wound infection)	51 (3.1%)	24 (2.7%)	23 (4.1%)	0.156	4 (1.9%)	0.512
Myocardial infarction	0	0	0	-	0	-
Urinary tract infection	6 (0.4%)	2 (0.2%)	2 (0.4%)	0.652	2 (1.0%)	0.115
Total LOS (days)	0.61±2.37	0.63±2.41	0.51±1.94	0.232	0.77±3.14	0.071
Superficial SSI	11 (0.7%)	7 (0.8%)	3 (0.5%)	0.558	1 (0.5%)	0.634
Deep SSI	0	0	0	-	0	-
Organ space SSI	2 (0.1%)	0	2 (0.4%)	0.077	0	-
Wound dehiscence	0	0	0	-	0	-
Acute renal failure*	0	0	0	-	0	-

Progressive renal insufficiency**	0	0	0	-	0	-
Transfusion	0	0	0	-	0	-
Cardiac arrest	0	0	0	-	0	-
Clostridium diff colitis	0	0	0	-	0	-
Deep vein thrombosis	4 (0.2%)	2 (0.2%)	1 (0.2%)	0.84	1 (0.5%)	0.53
Pneumonia	0	0	0	-	0	-
Pulmonary embolism	3 (0.2%)	0	2 (0.4%)	0.077	1 (0.5%)	0.039
Tullionary embolism	3 (0.270)	O	2 (0.470)	0.011	1 (0.570)	0.191†
Sepsis	3 (0.2%)	1 (0.1%)	2 (0.4%)	0.326	0	0.627
Septic shock	0	0	0	-	0	-
Inplanned reintubation	1 (0.1%)	0	0		1 (0.5%)	0.039
onplanned formabation	1 (0.170)	O .	Ü		1 (0.070)	0.191†
Prolonged intubation***	0	0	0	-	0	-
Unplanned reoperation	18 (1.1%)	10 (1.1%)	8 (1.4%)	0.634	0	0.123
Any reoperation	20 (1.2%)	10 (1.1%)	10 (1.8%)	0.31	0	0.123
LOS ≥ 3 days	71 (4.3%)	37 (4.2%)	22 (3.9%)	0.782	12 (5.8%)	0.326
Still in hospital >30 days	1 (0.1%)	1 (0.1%)	0	0.426	0	0.621
Death	2 (0.1%)	2	0	0.258	0	0.492

## TABLE 3: Univariable analysis of outcomes data.

DC, discharge; LOS, length of stay; SSI, surgical site infection; ACS-NSQIP, American College of Surgeons National Surgical Quality Improvement Program

P-values are with reference to the No Frailty group

\*Acute renal failure defined as requiring dialysis by ACS-NSQIP

\*\*Progressive renal insufficiency defined as >2 rise in creatinine during stay without dialysis

\*\*\*Prolonged intubation defined as mechanical ventilation >48 hours

†Fisher's exact test

## Multivariable analysis

The results of multivariable analysis are included in Table 4 and Figures 2, 3. Compared to no frailty as reference, moderate frailty was an independent predictor of unplanned readmission only (OR 2.613, 95% CI 1.143-5.973, p=0.023), while significant frailty remained a significant predictor for all outcomes including unplanned readmission (OR 3.723, 95% CI 1.376-10.073, p=0.01), any readmission (OR 2.396, 95% CI 1.098-5.230, p=0.028), non-home discharge (OR 4.317, 95% CI 1.765-10.562, p<0.001), and complications in aggregate (OR 2.211, 95% CI 1.285-3.806, p=0.004).

Outcome	No Frailty	Moderate frailty OR (95% CI)	P-value	Significant Frailty OR (95% CI)	P-value
Any complication	Ref	1.344 (0.866-2.085)	0.187	2.211 (1.285-3.806)	0.004
Any readmission	Ref	1.672 (0.903-3.099)	0.102	2.396 (1.098-5.230)	0.028
Unplanned readmission	Ref	2.613 (1.143-5.973)	0.023	3.723 (1.376-10.073)	0.01
Non-home DC	Ref	1.627 (0.699-3.790)	0.259	4.317 (1.765-10.562)	<0.001

## **TABLE 4: Multivariable analysis of outcomes.**

OR, odds ratio; CI, confidence interval; DC, discharge; BMI, body mass index; ASA, American Society of Anesthesiologists

Controlled for age, BMI, sex, ASA class (1-2 vs. >3), bleeding disorders, dyspnea, anemia, and smoking status.

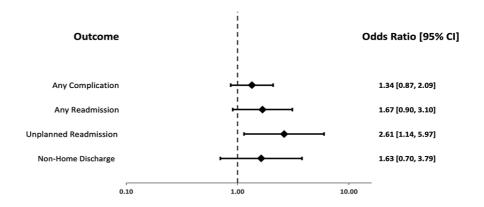


FIGURE 2: Forest plot of odds ratios from binary logistic regression. Moderate Frailty versus No Frailty as a reference group.

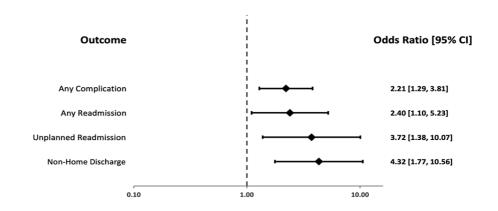


FIGURE 3: Forest plot of odds ratios from binary logistic regression. Significant Frailty versus No Frailty as a reference group.

## **Discussion**

This study is an early evaluation of the mFI-5's role as a predictor of outcomes for PD patients undergoing DBS treatment and to show its potential application to patient selection for DBS in the future. The limited number of complication events increased the difficulty of achieving significant correlations when

attempting to assess the predictive power of the mFI-5 for postoperative issues. Despite this, the mFI-5 still independently predicted multiple outcomes including aggregated complications, readmission rates, and non-home discharge. Given the limitations of what is reported by the ACS-NSQIP database, a direction of future research may include accessing outcome measures that are specific to PD, such as changes in sleep, speech, tremors, balance, and ability to work [14]. Additionally, given the chronicity and progressiveness of PD, future studies should include analysis of postoperative outcomes in follow-up lengths extending to months or even years.

Moreover, this study reaffirms the consensus that DBS procedures are safe with low complication rates. In this study, a mere 7.7% experienced any complication, 3.7% experienced any readmission, and 2.3% experienced non-home discharge. This agrees with a similar study using ACS-NSQIP data for 650 PD patients undergoing DBS procedures, which found that 32 (4.92%) patients experienced major postoperative complications [19]. Of the 650 PD patients, 481 (74%) had thorough discharge information, and of these 481 patients, 3.7% were discharged to a facility and 3.3% had an unplanned readmission. Furthermore, the patients in this comparable study recorded low event rates of pulmonary embolism (0.15%), stroke/cerebrovascular episodes (0.31%), deep venous thrombosis (0.46%), and urinary tract infection (0.77%) [19], while our study recorded these events 0.2%, 0.5%, 0.2%, and 0.4% of the time, respectively.

A recent similar study by Owodunni et al. compared the utility of the risk analysis index (RAI) to the mFI-5 for predicting Clavien-Dindo complications in DBS procedures with data sourced from the ACS-NSQIP database [20]. Their study concluded that RAI was a more robust scale to use for predicting postoperative outcomes in patients undergoing DBS. However, the length of this scale must be acknowledged, considering it requires 14 variables, while the mFI-5 only uses five variables. Of note, their retrospective study investigated DBS implantation in patients with no specific diagnosis, while our study selected DBS implantation in patients with PD. Additionally, their study's investigation of the mFI-5 only found significant correlations (p<0.001) with frail patients being discharged to non-home facilities (skilled nursing or rehabilitation) [20], while our study found significant correlations (p<0.05) with overall complications, readmission rates, and non-home discharge in severely frail patients. The combined results of these two studies further support the potential utility of the mFI-5 in clinical risk assessment, though limitations are present and supplementary refinement of the scale may be indicated.

#### Limitations

Conducting a retrospective cohort study using an external database does have its advantages and limitations. The ACS-NSQIP contains a large sample size of DBS patients with adequate data spanning a decade (2010-2019, for our study) on short-term complications after surgery. It is a national dataset compiling information from numerous hospitals, which limits the risk of regional or local confounders and selection biases. These factors allow robust comparisons of outcomes among subgroups of interest for any given procedure recorded by the database.

The ACS-NSQIP's limitations and disadvantages, however, cannot go unmentioned. Firstly, past medical and surgical histories are insufficiently characterized by the database. Common elements of the medical history, such as hypertension and diabetes, are recorded in a binary fashion, limiting the potential for evaluation of condition severity. Additionally, patients' list of medications is limited to items impacting bleeding risk, coagulopathy, and wound healing, but tells us nothing about neurological therapeutics. Previous DBS device implantation and the presence of other devices are not recorded. Complete DBS device implantation is commonly performed in two separate procedures, but these data are also not recorded in the database, which obscures the postoperative short-term complication timeline.

Secondly, outcomes of this database, as intended, focus on general surgical outcomes rather than procedure-specific outcomes. The lack of specific neurosurgical measures relating to PD symptoms limits our ability to analyze the practicality of the mFI-5 in predicting short-term outcomes in DBS patients. Lastly, socioeconomic and insurance status are considerable metrics to evaluate concerning discharge destination and readmission [14,19], but these data are not collected. Though there are many limitations present, the ACS-NSQIP provides a consolidated and nationally recognized dataset for statistical evaluation of surgical procedures and has been used previously to report DBS outcomes [14].

Finally, while mFI-5 may be a quick and easy tool, it is arguably reductive and perhaps loses the overall picture of frailty that the CSHA-FI intended. For example, by mFI-5 assessment, a patient who has well-controlled hypertension and well-controlled diabetes would be considered frailer than a patient with completely dependent functional status and no other elements of mFI-5. Indeed, this may raise uncertainty as to who truly has less physiological reserve according to this index. This is not to invalidate the mFI-5 as to where it currently stands but rather to suggest that a more robust version of this index ought to also weigh conditions in terms of severity. This would still allow for simplicity of the index, given that there would still be just a handful of items that could be entered by clinicians into a calculator such as MDcalc [21] or automatically calculated by an electronic medical record software, as is already done with other weighted risk scores such as the atherosclerotic cardiovascular risk score [22].

# **Conclusions**

Increased frailty was positively associated with independent predictability of the mFI-5 for postoperative outcomes, including major postoperative complications, any readmission, unplanned readmission, and non-home discharge. By exploring the relationship between a patient's frailty status and postoperative outcomes, surgeons can better predict the postoperative care required for each individual patient. Our paper provided evidence of the potential for the mFI-5 to be utilized as a quick, streamlined tool for physicians to assess and stratify a PD patient's risk of short-term postoperative complications from DBS, especially in severely frail patients. However, the limitations of the binary data collection methods must be considered and may suggest that a more refined scale is necessary for clinical use. Future studies with long-term follow-up and PD-specific outcomes will assist physicians in predicting necessary clinical care for significantly frail patients who wish to undergo DBS treatment.

# **Appendices**

CSHA-FI	mFI-11	mFI-5
Changes in everyday activities	Chronic obstructive pulmonary disease	Chronic obstructive pulmonary disease
Mood problems	Congestive heart failure	Congestive heart failure
Seizures, partial complex	Diabetes mellitus	Diabetes mellitus
Head and neck problems	Functionally dependent health status	Functionally dependent health status
Feeling sad, blue, depressed	Hypertension	Hypertension
Seizures, generalized	History of angina	
Poor muscle tone in the neck	Impaired sensorium	
History of depressed mood	Peripheral vascular disease	
Syncope or blackouts	Prior myocardial infarction	
Bradykinesia, facial tiredness all the time	Stroke with neurologic deficit	
Headache	Stroke with no residual deficit	
Problems getting dressed		
Depression (clinical impression)		
Cerebrovascular problems		
Problems with bathing		
Sleep changes		
History of stroke		
Problems carrying out personal grooming		
Restlessness		
History of diabetes mellitus		
Urinary incontinence		
Memory changes		
Arterial hypertension		
Toileting problems		
Short-term memory impairment		
Peripheral pulses		
Bulk difficulties		
Long-term memory impairment		
Cardiac problems		
Rectal problems		

Changes in general mental functioning	
Myocardial infarction	
Gastrointestinal problems	
Onset of cognitive symptoms	
Arrhythmia	
Problems cooking	
Clouding or delirium	
Congestive heart failure	
Sucking problems	
Paranoid features	
Lung problems	
Problems going out alone	
History relevant to cognitive impairment	
Respiratory problems	
Impaired mobility	
History of thyroid disease	
Musculoskeletal problems	
Family history relevant to cognitive impairment	
Thyroid problems	
Bradykinesia of the limbs	
Skin problems	
Impaired vibration	
Poor muscle tone in limbs	
Malignant disease	
Tremor at rest	
Poor limb coordination	
Breast problems	
Postural tremor	
Poor coordination, trunk	
Abdominal problems	
Intention tremor	
Poor standing posture	
Presence of snout reflex	
History of Parkinson's disease	
Irregular gait pattern	
Presence of palmomental reflex	
Falls	
Family history of degenerative disease	
Other medical history	

#### TABLE 5: Historical elements of frailty indices, such as CSHA-FI, mFI-11, and mFI-5.

CSHA-FI, Canadian Study of Health and Aging Frailty Index; mFI-5, 5-item modified frailty index; mFI-11, 11-item modified frailty index

## **Additional Information**

#### **Author Contributions**

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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#### **Disclosures**

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# References

- Krack P, Batir A, Van Blercom N, et al.: Five-year follow-up of bilateral stimulation of the subthalamic nucleus in advanced Parkinson's disease. N Engl J Med. 2003, 349:1925-34. 10.1056/NEJMoa035275
- Bang Henriksen M, Johnsen EL, Sunde N, Vase A, Gjelstrup MC, Østergaard K: Surviving 10 years with deep brain stimulation for Parkinson's disease--a follow-up of 79 patients. Eur J Neurol. 2016, 23:53-61. 10.1111/ene.12614
- Al-Khamis A, Warner C, Park J, et al.: Modified frailty index predicts early outcomes after colorectal surgery: an ACS-NSQIP study. Colorectal Dis. 2019, 21:1192-205. 10.1111/codi.14725
- Flexman AM, Charest-Morin R, Stobart L, Street J, Ryerson CJ: Frailty and postoperative outcomes in patients undergoing surgery for degenerative spine disease. Spine J. 2016, 16:1315-23. 10.1016/j.spinee.2016.06.017
- Nguyen S, Kim RB, Cox P, Gamboa NT, Karsy M, Couldwell WT, Menacho ST: Impact of modified Frailty Index-11 (mFI-11) on postoperative complications in patients undergoing transsphenoidal resection of pituitary tumors: analysis of 2006-2014 ACS-NSQIP database. J Clin Neurosci. 2021, 92:22-6. 10.1016/j.jocn.2021.07.046
- Ravivarapu KT, Garden EB, Al-Alao O, Small AC, Palese MA: Adrenalectomy outcomes predicted by a 5-item frailty index (5-iFI) in the ACS-NSQIP database. Am J Surg. 2022, 223:1120-5. 10.1016/j.amjsurg.2021.11.020
- de Divitiis E, Laws ER, Giani U, Iuliano SL, de Divitiis O, Apuzzo ML: The current status of endoscopy in transsphenoidal surgery: an international survey. World Neurosurg. 2015, 83:447-54.
   10.1016/j.wneu.2014.12.029
- Huq S, Khalafallah AM, Jimenez AE, et al.: Predicting postoperative outcomes in brain tumor patients with a 5-factor modified frailty index. Neurosurgery. 2020, 88:147-54. 10.1093/neuros/nyaa335
- Lee H, Tan C, Tran V, et al.: The utility of the Modified Frailty Index in outcome prediction for elderly
  patients with acute traumatic subdural hematoma. J Neurotrauma. 2020, 37:2499-506.
  10.1089/neu.2019.6943
- Chimukangara M, Helm MC, Frelich MJ, Bosler ME, Rein LE, Szabo A, Gould JC: A 5-item frailty index based on NSQIP data correlates with outcomes following paraesophageal hernia repair. Surg Endosc. 2017, 31:2509-19. 10.1007/s00464-016-5253-7
- Tomlinson SB, Piper K, Kimmell KT, Vates GE: Preoperative frailty score for 30-day morbidity and mortality after cranial neurosurgery. World Neurosurg. 2017, 107:959-65. 10.1016/j.wneu.2017.07.081
- Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, Mitnitski A: A global clinical measure of fitness and frailty in elderly people. CMAJ. 2005, 173:489-95. 10.1503/cmaj.050051
- 13. Araújo-Andrade L, Rocha-Neves JP, Duarte-Gamas L, et al.: Prognostic effect of the new 5-factor modified

- frailty index in patients undergoing carotid endarterectomy with regional anesthesia a prospective cohort study. Int J Surg. 2020, 80:27-34. 10.1016/j.ijsu.2020.05.074
- Hu K, Moses ZB, Hutter MM, Williams Z: Short-term adverse outcomes after deep brain stimulation treatment in patients with Parkinson disease. World Neurosurg. 2017, 98:365-74.
   10.1016/j.wneu.2016.10.138
- Rolston JD, Englot DJ, Starr PA, Larson PS: An unexpectedly high rate of revisions and removals in deep brain stimulation surgery: analysis of multiple databases. Parkinsonism Relat Disord. 2016, 33:72-7. 10.1016/j.parkreldis.2016.09.014
- Sastry RA, Pertsch NJ, Tang O, Shao B, Toms SA, Weil RJ: Frailty and outcomes after craniotomy for brain tumor. J Clin Neurosci. 2020, 81:95-100. 10.1016/j.jocn.2020.09.002
- Wilson JM, Holzgrefe RE, Staley CA, Schenker ML, Meals CG: Use of a 5-item Modified Frailty Index for risk stratification in patients undergoing surgical management of distal radius fractures. J Hand Surg Am. 2018, 43:701-9. 10.1016/j.jhsa.2018.05.029
- Yagi M, Michikawa T, Hosogane N, et al.: The 5-Item Modified Frailty Index is predictive of severe adverse events in patients undergoing surgery for adult spinal deformity. Spine (Phila Pa 1976). 2019, 44:E1083-91. 10.1097/BRS.0000000000003063
- Lindenauer PK, Lagu T, Rothberg MB, Avrunin J, Pekow PS, Wang Y, Krumholz HM: Income inequality and 30 day outcomes after acute myocardial infarction, heart failure, and pneumonia: retrospective cohort study. BMJ. 2013, 346:f521. 10.1136/bmj.f521
- Owodunni OP, Roster K, Varela S, et al.: Preoperative frailty risk in deep brain stimulation patients: risk analysis index predicts Clavien-Dindo IV complications. Clin Neurol Neurosurg. 2023, 226:107616. 10.1016/j.clineuro.2023.107616
- 21. MDCalc Medical calculators, equations, scores, and guidelines. (2022). Accessed: September 11, 2023: https://www.mdcalc.com/.
- Garg N, Muduli SK, Kapoor A, Tewari S, Kumar S, Khanna R, Goel PK: Comparison of different cardiovascular risk score calculators for cardiovascular risk prediction and guideline recommended statin uses. Indian Heart J. 2017, 69:458-63. 10.1016/j.ihj.2017.01.015