

## Original Investigation

# Modified Frailty Index and Body Mass Index as Predictors of Adverse Surgical Outcomes in Degenerative Spinal Disease

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**AIM:** To reveal the potential relationships and interactive effects between frailty and body weight and adverse surgical outcomes for degenerative spinal disease.

**MATERIAL and METHODS:** Patients who underwent open surgery for degenerative spinal disease in our hospital were included. Data on the patients and disease variables was obtained. The primary independent variables included body mass index (BMI) and modified Frailty Index (mFI). The primary outcome was the Clavien-Dindo complications classification. After univariate analyses, multinomial and ordinal regression analyses were applied with the Clavien-Dindo complications grade as the dependent variable and the potential risk factors for complications as independent variables, respectively, to determine the potential interactive relationship between the two primary risk factors and their impact on postoperative complications grading.

**RESULTS:** A total of 1970 patients were included in the study. The results showed that “underweight” could significantly increase the odds ratios of “prefrail” and “frail” at the same time; however, “obese” could only increase the odds ratio of “frail”. The “underweight”, “obese”, “prefrail” and “frail” subgroups could significantly increase the grading of postoperative complications, respectively. If mFI and BMI were combined as an interactive variable, the results showed that in the “underweight” and “normal weight” subgroups, both “prefrail” and “frail” could significantly increase the grading of postoperative complications; however, in the “overweight” and “obese” subgroups, only the “overweight/frail”, “obese/non-frail” and “obese/frail” subgroups displayed significantly increased grading of postoperative complications.

**CONCLUSION:** The present results serve to stratify susceptible patients with easily identified risk factors preoperatively.

**KEYWORDS:** Body mass index, Complication, Degenerative spinal disease, Modified frailty index

**INTRODUCTION**

There is a trend for an increase in the ageing population in China and worldwide, with a significant impact on the socioeconomic and daily life of this population. With this trend, co-morbidity in the elderly population has increased both in the normal population and in patients undergoing surgery, the latter of which are often associated with significantly higher incidences of postoperative complications or even mortality. Given the high incidence of potential complications in geriatric

populations, there is increased interest in determining the risks leading to adverse consequences in the surgical community.

Frailty represents a vulnerability to an external stressor event due to a decreased physiological reserve in older populations. Despite current discussions in this field, there is no defined, consistent, scientific consensus on how to score the grade of frailty. Until now, only two systems have been widely used to identify and evaluate the grade of frailty, including the phenotypic type and the frailty index (FI). The former



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definition includes five components: weight loss, self-reported exhaustion, muscle weakness, walking speed slowness, and reduced physical activity, all of which are subjective and self-reported by the patients (8). However, Sheehan et al. has contributed significant increase in body weight to the frailty index (23). The latter definition was named as the frailty index, which is based on cumulative physiological deficits, including 11 multisystem co-morbidities (15,22,30,31). Extensive studies in many fields have demonstrated that frailty has a significant influence on predicting various adverse outcomes in either general or orthopaedic spinal surgeries.

Recently, obesity has increasingly been considered a potential risk-factor for general postoperative and disease-specific complications in several research fields, including the population of spinal patients. However, the “obesity paradox” has been proposed as a protective factor in decreasing the mortality rate in chronic cardiovascular and neurologic diseases, which have been considered to be attributed to the overweight or even obese (29). Meanwhile, there is recently a “U” shaped correlation between obesity and frailty, suggesting that only underweight and obese subgroups are more susceptible to frailty complications (11).

Although a number of studies have analysed the effects of obesity on surgical outcomes in spinal patients, few have reported the interactive relationship between frailty and body weight and their effects on postoperative complications in the degenerative spinal patient population. The aim of this study was to reveal the potential effects and consequences of the self-contradictory relationship between frailty and body weight after degenerative spinal surgeries. Regarding various evaluation methods of postoperative complications, the Clavien-Dindo complications classification was incorporated in the present study to be considered as the endpoint of this series. The strength of this classification relied on an objective and reliable outcome evaluation to stratify the complications by severity and their respective therapy, which was previously used in cholecystectomy and liver transplantation surgeries. Recently, Grainger et al. evaluated the influence of complications by using the Clavien-Dindo complications classification on long-term outcomes for patients undergoing low back surgery (9).

## ■ MATERIAL and METHODS

### Design and Inclusion Criteria

This was a retrospective study approved by the local Ethics and Institutional Review Committees. Patients who underwent open surgery for degenerative spine disease between 2005-2015 were included in this study.

Patients who were admitted with a primary diagnosis of osteoporotic vertebral compression fractures, vertebral metastases, haemangioma, myeloma, and idiopathic scoliosis, or who underwent minimally invasive surgery or did not receive a general anaesthetic were excluded from the study.

### Data Collection and Patient Variables

Data on the patients and diseases variables was obtained

from the electrical medical records system. Patient variables included age, sex, smoking, alcohol abuse, body mass index (BMI, kg/m<sup>2</sup>), and hospital length of stay (LOS). Diseases variables included spinal level, co-morbidities, and complications within 30 days postoperatively.

### Predictor Variables and Outcomes

The primary independent variables of interest included BMI and a modified Frailty Index (mFI). According to the BMI classification determined by World Health Organization, a BMI of less than 18.5 is categorized as underweight, 18.5 to 25 as normal weight, 25.0 to 29.9 as overweight, and more than 30.0 as obese (32).

The mFI was previously proposed by Saxton and Velanovich and incorporates 11 variables from the 70 variables in the Canadian Study of Health and Ageing Frailty Index (CSHA-FI), based on the theory of “accumulating deficits”. As an assessment tool, this modified version has been studied and validated to predict postoperative morbidity and mortality in the spinal patient population. The mFI score is calculated by dividing the number of preoperative deficits or co-morbidities by 11, with a range between 0 and 1. The 11 deficits or co-morbidities include non-independent functional status, a history of diabetes mellitus, chronic obstructive pulmonary disease or pneumonia, congestive heart failure, myocardial infarction, percutaneous coronary intervention (PCI), stenting, angina, hypertension requiring medication, peripheral vascular disease or rest pain, impaired sensorium, transient ischaemic attack, or cerebrovascular accident with a neurological deficit. According to the number of deficits of each individual, patients were categorized as non-frail (no deficit, mFI of 0), prefrail (one or two deficits, mFI of 0.09-0.18), and frail (three or more deficits, mFI  $\geq$  0.21) (21).

The primary outcome of this study was the Clavien-Dindo complications classification (5), which includes Grade I, any deviation from the normal postoperative course; Grade II, requiring pharmacological treatment, blood transfusions or total parenteral nutrition; Grade III, requiring radiological, endoscopic, or surgical interventions; Grade IV, life-threatening complications requiring ICU management; Grade V, death. This complications classification was updated and modified based on the classification of complications of surgery proposed by Clavien et al. (3), which was designed to categorize the postoperative complications by their degree of severity and has been validated in clinical research in general and in urological surgery (2,34). Recently, Grainger et al. explored the ability of the Clavien-Dindo complications classification in evaluating the influence of perioperative complications on the long-term postoperative outcomes for patients after lumbar spinal surgery (9). In the present study, we aimed to expand the application of the Clavien-Dindo complications classification to the entire range of spinal surgeries.

### Statistical Analysis

After proving normal distribution and homogeneity of variance of the measurement data by the Kolmogorov-Smirnov and Levene tests, respectively, the measurement data were analysed by an independent samples t-test. Categorical

variables were analysed by the Pearson's Chi square and Fisher's exact tests. Correlations between categorical variables were analysed by the Spearman rank correlation test. After the abovementioned univariate analyses, an ordinal regression analysis was applied with the Clavien-Dindo complications grade as the dependent variable and the potential risk factors for complications as the independent variables. The validity of the regression model was verified by the Hosmer-Lemeshow test for goodness of fit. A p value less than 0.05 was considered statistically significant. All statistical analyses were conducted with SPSS 20 software (SPSS Inc., Chicago, IL, USA).

**RESULTS**

Overall, a total of 1970 patients with a mean age of 58.1 years were included in this study, including 1045 males and 925 females. Table I presents the comparisons of the clinical characteristics between genders. There were no significant differences in the LOS, spinal level, mFI, BMI category and the Clavien-Dindo complications grade between the two gender groups. However, there was a significant difference in the ages and the proportions of those that were current smokers and alcohol drinkers between males and females.

The mFI showed a significant positive correlation with complications grading and a significant negative correlation with BMI (Tables II, III). However, the Spearman correlation coefficient was very low, especially the negative correlation between mFI and BMI, with a r of -0.0427, which might be of no significant clinical influence.

To reveal the potential influence of BMI on the mFI, we performed a multinomial logistic regression analysis, with BMI and mFI as independent and dependent variables, respectively. The results are shown in Table IV. It can be seen that "underweight" significantly increases the odds ratios of both "prefrail" and "frail" at the same time; however, "obese" only increases the odds ratio of "frail".

To analyse the potential influence of the BMI and frailty on postoperative complications in an independent or interactive manner, and after balancing all the potential risk factors, we established ordinal logistic regression models for the complications grade with mFI and BMI as individual independent variables or interactive variables. Table V shows that when mFI and BMI were set as individual independent variables, only the "underweight" and "obese" subgroups significantly increased the grading of postoperative complications; however, both "prefrail" and "frail" significantly increased the grading of postoperative complications. If mFI and BMI were combined

**Table I:** The Characteristics of Patients and Diseases

Factors		Male (n=925)	Female (n=1045)	p	Total (n=1970)
Age (years, Mean ± SD)		57.41 ± 7.4	59.15 ± 8.67	<0.001	58.1 ± 5.91
Hospital LOS (days, Mean ± SD)		12.35 ± 5.15	14.65 ± 7.42	0.93	13.1 ± 5.28
Current smoker		261	115	<0.001	376
Alcohol drinking		293	174	<0.001	467
Level (N)	Cervical	307	355	0.658	662
	Thoracic	21	18		
	Lumbar	597	672		
Modified Frailty Index (N)	0	380	455	0.46	835
	0.09-0.18	514	561		
	≥ 0.27	31	29		
BMI Category (N)	Underweight	75	95	0.452	170
	Normal	511	545		
	Overweight	244	302		
	Obese	95	103		
Clavien Complications Grade (N)	I	213	216	0.467	660
	II	331	395		
	III	45	66		
	IV	19	21		
	V	2	2		

as interactive variables, the analysis results were as shown in Table VI. When “normal weight/non-frail” was considered as the reference subgroup, the results showed that in the “underweight” and “normal weight” subgroups, both “prefrail” and “frail” could significantly increase the grading of postoperative complications; however, in the “overweight” and “obese” subgroups, only the “overweight/frail”, “obese/non-frail” and “obese/frail” subgroups displayed a significantly increased grading of postoperative complications.

**DISCUSSION**

To our knowledge, this is the first study to explore the interactive effect and influence of frailty and body weight on postoperative complications in the spinal patient population.

Like previous studies in other fields, we also concluded that there exists the phenomenon of an “obesity paradox”; however, this effect played a role only when combined with the specific frailty status. As stated in the results section, the adverse impact of frailty on the short-term postoperative outcomes was offset by an elevated body weight to a certain extent.

For a long time, the respective effects of frailty and body weight on both long-term and short-term postoperative complications have been analysed and established in different studies but with inconsistent results. Srinivasan et al. and Singh et al. both found that elevated BMI showed no significant associations with early major complications after cervical surgeries (26,28). However, Wilson et al. reported that obese

**Table II:** Correlation Analysis between BMI and Frailty

BMI	Frailty Subgroups		
	Nonfrail	Prefrail	Frail
Underweight	29	66	7
Normal	532	683	36
Overweight	250	285	14
Obese	24	42	2

Spearman  $r = -0.0427, p < 0.001$ .

**Table III:** Correlation Analysis between Complications Grading and Frailty

Complications	Frailty Subgroups		
	Nonfrail	Prefrail	Frail
I	167	255	7
II	297	412	17
III	35	55	21
IV	9	23	8
V	0	1	3

Spearman  $r = 0.1407, p < 0.001$ .

**Table IV:** Multinomial Logistic Regression for Frailty by BMI

BMI	Prefrail		Frail	
	Odds Ratio (95% CI)	p	Odds Ratio (95% CI)	p
Underweight	1.645 (1.11-2.439)	<b>0.013</b>	1.396 (1.111-1.755)	<b>0.004</b>
Normal	1		1	
Overweight	1.44 (.925-2.24)	0.106	.578 (.227-1.47)	0.249
Obese	.927 (.361-2.385)	0.876	3.304 (2.083-5.564)	<b>0.001</b>

**Table V:** Ordinal Logistic Regression for Complication Grade by Frailty and BMI

Factors	Grade	$\beta$	95% CI for $\beta$	p
BMI	Underweight	4.153	1.035 - 7.257	<b>0.006</b>
	Normal	0		
	Overweight	0.708	-0.051 - 1.214	0.071
	Obese	3.195	0.442 - 6.525	<b>0.021</b>
mFI	Nonfrail	0		
	Prefrail	1.710	0.107 - 3.037	<b>0.018</b>
	Frail	3.132	1.515 - 4.917	<b>&lt; 0.001</b>

<sup>1</sup>Hosmer-Lemeshow test,  $p = 0.217$ ;  $\beta$ : regression coefficient; CI: confidential interval.

**Table VI:** Ordinal Logistic Regression for Complications Grade

Factors		$\beta$	95% CI for $\beta$	p
BMI	mFI			
Underweight	Nonfrail	0.218	-0.123 - 1.071	0.064
	Prefrail	2.135	0.753 - 3.532	<b>0.007</b>
	Frail	1.697	0.431 - 3.02	<b>&lt; 0.001</b>
Normal	Nonfrail	0		
	Prefrail	2.145	1.073 - 4.135	<b>&lt; 0.001</b>
	Frail	1.89	0.37 - 3.55	<b>&lt; 0.001</b>
Overweight	Nonfrail	0.418	-0.14 -0.973	0.071
	Prefrail	0.107	-1.04 - 1.46	0.31
	Frail	1.335	1.057 - 5.593	<b>&lt; 0.001</b>
Obese	Nonfrail	3.305	1.085 - 6.775	<b>&lt; 0.001</b>
	Prefrail	0.302	-1.07 - 1.135	0.703
	Frail	2.071	0.824 - 4.35	<b>&lt; 0.001</b>

<sup>1</sup>Hosmer-Lemeshow test,  $p=0.431$ ;  $\beta$ : regression coefficient; CI: confidential interval.

patients had worse patient-reported outcomes, such as neck disability and physical health status, at 1-year post surgery (33). With regard to lumbar spinal surgery, Puvanesarajah et al. concluded that obesity and morbidly obese patients were at significantly increased risk of short-term major medical or minor complications, such as wound problems and urinary tract infection, postoperatively (18,19). Higgins et al.'s study presented similar conclusions after surgeries for entire degenerative spine disease (10). Meanwhile, Sing et al. found similar results in patients after revision spine surgery (25). De la Garza-Ramos et al. found that after lumbar fusion surgeries, the obese patients subgroup had higher complication rates and lower functional assessment results at either short- or long-term follow-up than the non-obese subgroup (4). Some authors reported different outcomes after lumbar fusion obese patients showed similar clinical improvements when compared with non-obese patients (6).

Unfortunately, the current research data do not reveal how obesity impacts patients' outcomes after degenerative spine surgery. Puvanesarajah et al. mentioned the potential effect and relationship of elderly age with obesity on postoperative outcomes (19). Although some studies also viewed increasing age as a potential risk factor and an important predictor for poor postoperative outcome (17), other authors proposed that the chronologic age did not necessarily account for a weakened physiologic reserve or an increased vulnerability for an external stressor event independent of existing comorbidity and deficit accumulation. Previous studies also have shown that 75% of patients over 85 years old are physiologically robust (16,27).

Frailty, defined as weakened physiologic reserves and multi-system co-morbidity, is a more objective index as compared

with increasing age alone. The frailty concept was first introduced in geriatric medicine and has been used to evaluate the potential risks of patients in several surgical specialties. The FI was developed by the Canadian Study of Health and Aging (CSHA), which is a standardized evaluation tool, as it incorporates over 70 objective parameters (13,14). Compared with other predicting tools, such as American Society of Anesthesiologists (ASA) classification and even the frailty phenotype, there are some practical advantages of the FI. The variables of the FI can be retrieved by medical history or bedside physical examination, which is an objective process and can easily be calculated and recorded perioperatively, while the rating of the frailty phenotypic type and ASA classification are subjective processes and patient- or physician-reported. Therefore, the FI has been extensively described in most surgical specialties. Meanwhile, Rockwood et al. found that a combination of any 10 or 15 items from the original 70 items showed a similar predicting ability (20). The mFI, which is a subset of the original variables of the CSHA-FI (including 15 or less variables), has been studied by several authors and shown to be an independent risk factor for adverse postoperative events in multiple surgical specialties. The present mFI version included 11 variables and has been analysed and verified in limited spine studies (15,22,30,31).

Ali et al. first demonstrated the predicting value of the mFI in the spine population and showed that a score  $\geq 0.27$  can independently predict morbidity and mortality postoperatively (1). Flexman et al.'s study also showed that the mFI could independently predict major postoperative complications, prolonged LOS, and 30-day mortality in patients who underwent degenerative spine surgeries (7). Leven et al. first analysed the applicability of mFI in adult spinal deformity

patients undergoing multiple level spinal fusion surgery and reported a mFI score of 0.09 or 0.18 was an independent risk factor for predicting postoperative complications; mean while, the mortality increased in a stepwise manner as the mFI score increased beyond 0.27 (12). Phan et al. investigated individuals undergoing anterior lumbar interbody fusion and determined that the cut off mFI value of 0.27 was significantly associated with postoperative morbidity (17). Furthermore, Shin et al. reported that a mFI  $\geq$  0.36 was the only independent risk factor for predicting the Clavien–Dindo grading IV complications (24).

The relationship and interaction between body weight and frailty has been investigated by several authors. The so called “obesity paradox” has been shown to reveal the potential protective effect of overweight or even obesity on mortality and morbidity in regard to chronic disease in the geriatric population. However, the studies reporting this phenomenon mainly conceptualized frailty using the phenotypic model, which consisted of weight loss as one of the frailty syndromes. To minimize this contradictory definition and effect between elevated body weight and the frail phenotypic model, we incorporated mFI to evaluate the combined effect of body weight and frailty on surgical adverse outcome. According to the above mentioned analyses and the reported protocol defining frailty as three or more co-morbidities (21), the included patients were categorized into three subgroups in the present study, including non-frail with a mFI of 0, prefrail with a mFI of 0.09 or 0.18, and frail with a mFI equal to or greater than 0.21.

With regard to postoperative complications, previous studies mainly incorporated each single complication as the study outcome, such as pulmonary, renal, cardiac, central nervous system complications, deep vein thrombosis/pulmonary embolism, urinary tract infections, and wound complications. In this situation, the severity grades of these postoperative complications and their impact on the patients’ prognosis cannot be fully determined with an association with preoperative risk factors. Similar to the objective ratings of frailty using the FI, the Clavien–Dindo complications classification is considered as the primary endpoint of our study. This therapy-oriented, 5-level severity grading index places the complications at the same level together into the same classification. Thus, even several complications at the same division only needed therapy and intervention at the same level without resulting in a more deteriorating situation.

Our results showed that either deviation from normal BMI, including underweight and obese or frailty, could lead to up-graded postoperative complications, but could not completely repeat the classic “obesity paradox” phenomenon reported by previous studies. The increased BMI is to some extent protective in the overweight subgroup; however, in the obesity subgroup, this neutralization was further strengthened with a protective effect only existing in the prefrail subgroup. The strength of our study was that both the primary dependent and independent variables of our analysis model were objective parameters, which minimized the inter-rater variability accompanying patient- or physician-reported evaluation rating methods. The limitation of this study is the retrospective

nature, which may have limited the ability of other risk factors included in the analysis model to reveal their potential impact and interaction with the co-existing factors in a prospective manner. Thus, long-term follow-up data cannot be collected and analysed in our study.

## ■ CONCLUSION

The present results serve to stratify susceptible patients with easily identified risk factors preoperatively.

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