Impact of Modified Frailty Index on Readmissions Following Surgery for NSCLC

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Abstract

Background Analyzing the risk factors that predict readmissions can potentially lead to more individualized patient care. The 11-factor modified frailty index is a valuable tool for predicting postoperative outcomes following surgery. The objective of this study is to determine whether the frailty index can effectively predict readmissions within 90 days after lung resection surgery in cancer patients within a single health care institution.

Methods Patients who underwent elective pulmonary resection for nonsmall cell lung cancer (NSCLC) between January 2012 and December 2020 were selected from the hospital's database. Patients who were readmitted after surgery were compared to those who were not, based on their data. Propensity score matching was employed to enhance sample homogeneity, and further analyses were conducted on this newly balanced sample.

Results A total of 439 patients, with an age range of 68 to 77 and a mean age of 72, were identified. Among them, 55 patients (12.5%) experienced unplanned readmissions within 90 days, with an average hospital stay of 29.4 days. Respiratory failure, pneumonia, and cardiac issues accounted for approximately 67% of these readmissions. After propensity score matching, it was evident that frail patients had a significantly higher risk of readmission. Additionally, frail patients had a higher incidence of postoperative complications and exhibited poorer survival outcomes with statistical significance.

Conclusion The 11-item modified frailty index is a reliable predictor of readmissions following pulmonary resection in NSCLC patients. Furthermore, it is significantly associated with both survival and postoperative complications.

Keywords
- frailty
- thoracic surgery
- risk stratification
- surgical outcomes
- risk models

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Introduction

The competence of thoracic surgeons in effectively predicting and reducing operative risks has become increasingly challenging in light of recent advancements in multimodal treatment for pulmonary diseases. Consequently, the need for objective measures to assess functional reserve before surgery has become crucial for guiding patient selection and counseling. Frailty, a condition unrelated to biological age and characterized by reduced physiological function, strength, and endurance, renders patients more vulnerable to both internal and external stressors.[1] Frailty indices have been explored as tools to assist in surgical decision-making and predict postsurgical complications, utilizing a combination of variables such as performance status and medical comorbidities.[2] However, these measures of frailty have not been integrated into risk models due to a lack of consensus on the concept.

The literature reveals the existence of 20 different methods claiming to measure frailty,[3] with the majority incorporating a phenotypic description and/or a compilation of deficiencies definition.[4] The Canadian Study of Health and Aging developed the Frailty Index (FI) based on a patient's medical history and physical examination.[5] The 11-factor modified frailty index (mFI-11) is a deficit accumulation measure of frailty that has been validated in multiple studies,[6,7] accurately predicting surgical complications and offering improved guidance for preoperative care. However, limited data are available regarding the impact of frailty on unplanned readmissions.

Hospital readmission following lung resection surgery is not uncommon, with reported rates ranging from 7 to 23% within 90 days.[8,9] High readmission rates following surgery not only pose a significant financial burden on the health care system but also serve as an independent risk factor for both 30- and 90-day mortality.[10,11] The average cost of each readmission is estimated to exceed $43,000.[8] Therefore, the identification of potentially preventable readmissions is critical to alleviate the burden on patients and health care resources.[12] Most research on readmission after general thoracic surgical procedures has primarily relied on administrative datasets, such as the American College of Surgeons National Surgical Quality Improvement Program (NSQIP). Due to the nature of these databases, they have limitations in distinguishing between planned and unplanned readmissions and determining the precise reasons for readmissions.[13]

This study aims to assess whether the mFI-11 is associated with readmission rates following resection in patients with nonsmall cell lung cancer (NSCLC) using data from a single institutional cohort. We hypothesize that patient frailty is linked to an increased risk of readmission within 90 days after discharge.

Methods

Study Design

We retrospectively examined our institution registry to include in our study all patients undergoing elective thoracoscopic or open lung resection for primitive NSCLC between January 1, 2012, and December 31, 2020.

Data Collection

The following patient information was included: age, sex, body mass index (kg/m^2), length of stay in hospital, smoking habit. Comorbidities according to the Charlson Index were also collected[14] as well as Tumour, Node and Metastasis (TNM) scale (VIII edition), nodal size, neoadjuvant therapy, histologic subtypes, pulmonary function tests, blood analysis, type of resection, duration of the surgical procedure, Ottawa Thoracic morbidity and mortality classification system.[15]

Survival was assessed 30 days and 12 months after surgery. Additionally, data analysis took into account the emergence of disease recurrence after a year.

"Unplanned readmissions" were defined as an unscheduled readmission to any hospital within 30 or 90 days of discharge from hospital. This unexpected event, causes an increase in management costs both for patient and pathology, maybe also affecting outcome.

The mFI-11 was calculated using variables from NSQIP as defined by Velanovich et al.[5] The mFI-11 includes 11 patient history items which are described in ►**Table 1**.

Outcomes

Primary outcome data included in the analysis of the association of mFI-11 with 90-day readmissions. Secondary outcomes were the association between mFI-11 with postoperative complications and overall survival.

Statistical Analysis

The descriptive information about the data has been conveyed by presenting the median and interquartile range for quantitative variables, and absolute as well as relative frequencies for qualitative ones. To analyze differences between groups, the Wilcoxon test has been utilized for numerical features, while

Table 1 Eleven components of modified frailty index

1	Chronic obstructive pulmonary disease or recent pneumonia
2	Diabetes mellitus
3	Previous percutaneous coronary intervention or angina
4	History of cerebrovascular accident
5	New diagnosis of congestive heart failure (CHF) or an exacerbation of chronic CHF within 30 days of surgery
6	Hypertension requiring medication
7	Functional status of 2 or higher
8	Residual neurologic deficits following cerebrovascular accident
9	Impaired sensorium/dementia
10	Peripheral vascular disease or ischemic pain in limbs at rest
11	History of myocardial infarction

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the chi-square test or, if suitable, the Fisher's exact test has been used for categorical features. A data-driven approach has been considered to determine an optimal cutoff value for the mFI-11, a continuous variable, in the context of predicting readmission following postoperative thoracic surgery. A resampling (bootstrap) procedure has been considered with 1,000 bootstrapped samples to assess the stability and uncertainty of the determined cutoff value. The odds ratio (OR) method has been used as a criterion indicating that the cutoff is chosen to maximize the OR for readmission outcome.[16] A propensity score analysis has been carried out to reduce potential bias caused by baseline covariates. The Covariate Balance Propensity Score[17] method has been calculated, we ensured the covariate balance through graphical assessments of a standardized mean difference lower than 0.1 and applied inverse probability of treatment weights in our analysis.[18] The Fifth Penalization Logistic regression model[19] is utilized to assess associations between frailty score categories and readmission risk, providing robust estimates even in cases of separation and infinite estimates. Secondary endpoints, including postoperative complications and grading, are also examined using logistic regression. Survival analysis has been also carried by reporting Kaplan–Meier survival curves, log rank tests, and Cox proportional hazards regression models. Multiple testing adjustments, such as the Benjamini–Hochberg method, are applied to account for multiple testing. The analyses have been carried out in R 3.4.2.[20]

Results

Patient Demographics

A total of 439 patients were identified with a mean age of 72 (68–77) years, 35.5% of whom were female. Among this group, 55 patients (12.5%) were readmitted to the hospital in 30 or 90 days. The majority of the study population underwent lobectomy (74.3%). Video-assisted thoracic surgery (VATS) was performed in 283 cases (64.6%) with a conversion rate of 7.14%. The 30-day mortality was 1.4% (6 patients). Nonfrail patients with an mFI-11 of 0 to 1 were 91 (20.7%), while 348 (79.3%) had an mFI-11 $\geq$1. Then, we divided all patients into two groups (readmitted and not readmitted) to compare each other.

Postoperative Outcomes

Fifty-five (12.5%) patients were readmitted at least once within 90 days. Median time between discharge and readmission was 29.4 days. Respiratory insufficiency, pneumonia, and cardiac complications were the most common reason for unexpected readmission, affecting 67% of patients. The average duration of stay for readmission was 10.4 days.

The two groups had no statistically significant differences, including sex, Charlson Comorbidity Index, and operative time. When we investigated several preoperative factors, we found that age, a history of COPD, the surgical approach used, and the length of stay in the hospital following surgery were significant predictors of unexpected readmission ($p < 0.05$). Additionally, a statistically significant correlation was found between the Ottawa scale's postoperative problems and a frailty score (mFI-11) of greater than 1.

Univariate analysis is summarized in ►**Table 2**. After adjusted propensity score exposure, mFI-11 $\geq$1 was found to be the only factor significantly associated with readmissions (►**Fig. 1**). Survival analysis demonstrated that patients with mFI-11 $\geq$1 had a poorer survival compared with patients with mFI-11 <1 (►**Fig. 2**).

Association between FI and complications is shown in ►**Table 3**. An association between mFI-11 $\geq$1 and the occurrence of postoperative complications (0.0016) and complication grade II and IV according to the Ottawa scale ($p = 0.0001$). Furthermore, frailty score was associated with survival ($p = 0.0079$) while Charlson Index did not show this correlation ($p = 0.570$).

Discussion

Although there is no specific definition for frailty, it is characterized by a reduced ability to withstand the increased metabolic and physical demands of surgery and its associated risks. With the aging population, a thorough preoperative evaluation becomes critical in improving risk assessment, aiding decision-making, and minimizing postoperative morbidity and mortality. Numerous studies have explored methods for predicting mortality and other outcomes in patients based on their existing comorbidities and characteristics like age and functional status. This line of research has led to the development of frailty indices, which link a patient's cumulative impairments and comorbidities to the risks of short- and long-term complications and mortality. It is believed that frailty's pathophysiology is associated with a combination of persistent systemic inflammation and limited reserve.[21] This lack of physiological reserve in frail individuals makes them less capable of responding adequately to even minor disturbances, and when subjected to major physical trauma, such as lung resection, it can result in a wide range of postoperative problems.

Traditional frailty models mentioned in the literature include the Fried criteria,[22] which are based on physical phenotype, and the Rockwood frailty index,[23] which relies on deficit accumulation. While these models are well-established and reliable, they have not been widely adopted in surgical patients due to the time and effort required to compute the 70 components in the Rockwood model and the need for training and equipment to assess Fried frailty. Consequently, more contemporary frailty assessment models have been developed.

Among the various frailty screening tools,[24–26] the mFI-11 was created by matching the 70 factors from the Canadian Study of Health and Aging Frailty Index[27] with 11 comorbidity and deficit indicators from the American College of Surgeons' NSQIP.[28–32] The 11-item modified frailty index, which accounts for 11 comorbidities, has been shown to be the most accurate predictor of frailty in women with gynecologic cancer in a comprehensive analysis.[33] Additionally to the mFI-11, other risk stratification models have been employed in the past to anticipate complications following surgery. For instance, the Charlson Comorbidity Index, which categorizes patients based on their age and 14 distinct medical

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Table 2 Patients' characteristics and univariate analysis on differences between readmitted and nonreadmitted cases

Variable	Overall $N = 439$	No readmission $N = 384$	Readmission $N = 55$	OR	*p*-Value
Age (mean, years)	72.0 [68.0; 76.0]	72.0 [68.0; 76.0]	74.0 [71.0; 77.5]	1.30 [1.02; 1.65]	0.032
Gender					
Female	156 (35.5%)	142 (37.0%)	14 (25.5%)	Ref.	Ref.
Male	283 (64.5%)	242 (63.0%)	41 (74.5%)	1.70 [0.92; 3.36]	0.094
Charlson Comorbidity Index	5.00 [4.75; 7.00]	5.00 [4.00; 6.50]	6.00 [5.00; 7.00]	1.09 [0.91; 1.30]	0.363
COPD (yes)	75 (17.1%)	59 (15.4%)	16 (29.1%)	2.26 [1.16; 4.27]	0.018
Hospital stay (mean, days)	6.00 [4.00; 8.00]	6.00 [4.00; 8.00]	7.00 [5.75; 12.2]	1.09 [1.03; 1.16]	0.004
Grading					
G1	29 (9.83%)	25 (9.88%)	4 (9.52%)	Ref.	Ref.
G2	161 (54.6%)	139 (54.9%)	22 (52.4%)	0.96 [0.33; 3.61]	0.950
G3	105 (35.6%)	89 (35.2%)	16 (38.1%)	1.10 [0.36; 4.22]	0.881
FEV1	2.19 [1.77; 2.66]	2.18 [1.77; 2.68]	2.20 [1.80; 2.52]	0.74 [0.48; 1.14]	0.174
VATS	283 (64.6%)	251 (65.5%)	32 (58.2%)	0.73 [0.41; 1.32]	0.292
Conversion to open	31 (7.14%)	25 (6.58%)	6 (11.1%)	1.80 [0.63; 4.39]	0.248
Extent of resection					
Sublobar resection	151 (34.4%)	133 (34.6%)	18 (32.7%)	0.92 [0.49; 1.67]	0.791
Sleeve resection	10 (2.28%)	6 (1.56%)	4 (7.27%)	4.97 [1.19; 18.5]	0.030
Lobectomy	326 (74.3%)	290 (75.5%)	36 (65.5%)	0.61 [0.34; 1.14]	0.121
Bilobectomy	10 (2.28%)	8 (2.08%)	2 (3.64%)	1.87 [0.25; 7.90]	0.481
Pneumonectomy	15 (3.42%)	12 (3.12%)	3 (5.45%)	1.85 [0.39; 6.16]	0.392
Operative time (minutes, mean)	180 [127; 210]	180 [125; 210]	170 [134; 205]	1.00 [0.99; 1.00]	0.459
Postoperative complications (According to Ottawa)	160 (42.8%)	127 (38.8%)	33 (70.2%)	3.68 [1.92; 7.38]	<0.001
Complications According To Ottawa Thoracic Morbidity and Mortality Classification	160 (42.8%)	127 (38.8%)	33 (70.2%)	3.68 [1.92; 7.38]	<0.001
0	212 (58.9%)	199 (63.2%)	13 (28.9%)	Ref.	Ref.
1	14 (3.89%)	10 (3.17%)	4 (8.89%)	6.13 [1.47; 21.8]	0.016
2	99 (27.5%)	80 (25.4%)	19 (42.2%)	3.61 [1.70; 7.86]	0.001
3	22 (6.11%)	16 (5.08%)	6 (13.3%)	5.72 [1.77; 16.9]	0.005
4	13 (3.61%)	10 (3.17%)	3 (6.67%)	4.67 [0.91; 18.0]	0.063
Frailty index					
<1	91 (20.7%)	86 (22.4%)	5 (9.09%)	Ref.	Ref.
≥1	348 (79.3%)	298 (77.6%)	50 (90.9%)	2.80 [1.18; 8.39]	0.017
frailty_index	1.00 [1.00; 2.00]	1.00 [1.00; 2.00]	2.00 [1.00; 3.00]	1.22 [0.99; 1.50]	0.066

Abbreviation: FEV1, Forced Expiratory Volume in the first second; OR, odds ratio; VATS, video-assisted thoracic surgery.

comorbidities, has been found to be a highly accurate predictor of postoperative problems.[14] However, the assessment of numerous comorbidities in this model may result in a time-consuming and expensive preoperative evaluation.

Lastly, the patient's American Society of Anesthesiologists (ASA) class, which assesses a patient's overall physical health condition before surgery based on the extent of systemic illness, is utilized. Nevertheless, the ASA class may carry some bias. For example, a study questioned anesthesia physicians about 10 different patient scenarios and found no interrater reliability in any of the scenarios, indicating that the ASA score primarily reflects anesthesia professionals' opinions regarding a patient's anesthetic risk rather than surgical risk.[34]

The objective of the present study was to assess the independent relationship between the mFI-11 and postoperative outcomes in patients who underwent elective lung resection for lung cancer. Our findings indicate that patients classified as frail are more likely to experience unfavorable postoperative outcomes. Our primary focus was on readmissions, as they serve as

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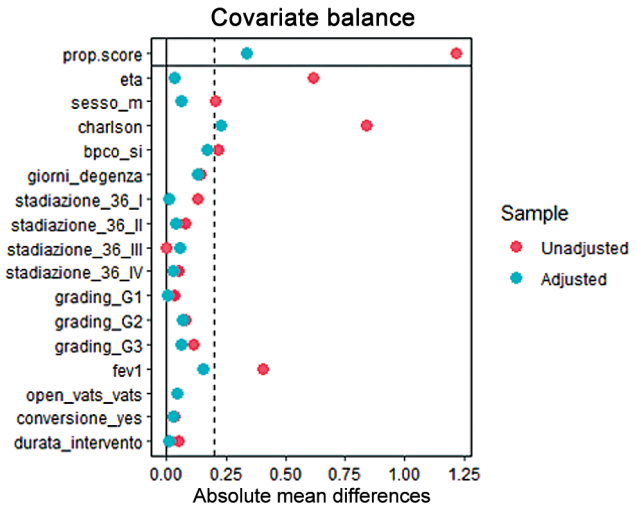

Fig. 1 Adjusted propensity score.

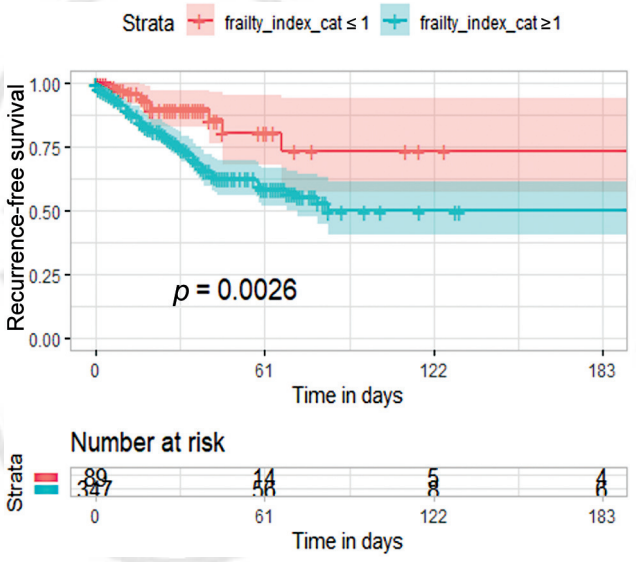

Fig. 2 Survival analysis.

a key indicator of the effectiveness of patient care, making their analysis of utmost importance. The early and accurate prediction of readmissions would be beneficial for patients, payors, and health care systems, as it presents a targeted opportunity to reduce the significant associated mortality and financial burden on the health care system. It is worth noting that most studies analyzing 90-day readmissions after lung resection have reported readmission rates exceeding 18%.[7]

While several factors have been associated with readmission after lung resection, the influence of frailty has been inadequately explored.[35] Our study revealed that the FI is a reliable predictor of unplanned hospital readmissions. In fact, an mFI-11 score of ≥1 was the only factor significantly associated with readmissions. Although we could not assess costs directly, we believe that patients requiring readmission will demand more resources over time, as previously reported. Overall, even well-powered studies with detailed perioperative patient-level data find it challenging to predict postoperative readmissions. An important clinical implication of our findings is that FI could optimize discharge planning for hospitalized frail patients by creating dedicated pathway for these cases. A deeper understanding of the associations between patients' characteristics, risk of readmission, settings, processes, and outcomes should lead to a more appropriate intervention design and improved outcomes for frail persons and their families.

The introduction of the mFI-11 can provide a slight improvement in our overall predictive capability and independence. In addition to its correlation with readmissions, our study demonstrated that the mFI-11 is associated with postoperative complications and survival. Importantly, frailty's adverse impact on postoperative outcomes was not influenced by factors such as age or the extent of the resection. Other studies[36,37] have also shown an association between frailty and postoperative complications. Tsiouris and colleagues,[30] for instance, evaluated cases undergoing open lobectomy using a modified FI score. In our study, 65% of cases underwent minimally invasive surgery, which is currently the preferred approach for lung resections. Thus, we believe our research more accurately represents the current surgical strategy for lung cancer. Nevertheless, our data support the notion that frailty influences postoperative outcomes regardless of the surgical method used.

Although the differential weighting of mFI-11 factors might result in a more accurate measure, our study did not explore factor weighting, as the primary goal was to assess the utility of the mFI as initially constructed for measuring frailty and its association with risk. Frailty is an evolving concept increasingly employed as a preoperative evaluation tool for patients undergoing pulmonary operations. Our findings align with previous studies that have used various indices to investigate the role of frailty in postoperative outcomes following lung resection. Notably, a significant proportion of patients in our study underwent surgery using minimally invasive techniques, which was a novel aspect. Furthermore, we examined the relationship between frailty and survival. The Receiver Operating Characteristic (ROC) curve presented in ►**Fig. 2** indicates that patients with a higher FI have significantly lower survival at 6 and 12 months. These patients also happen to be the group most at risk of readmission, so it can be concluded that a higher FI is

Table 3 Association between postoperative complications and modified frailty index scores

Variable	mFI ≥1	Lower 95	Upper 95	*p*-Value	OR
Complications	n 32	1.25	2.477	0.0016	1.756
Ottawa complication grade III–IV	n 9	1.831	4.004	0.0000007975	2.689

Abbreviation: mFI, modified frailty index; OR, odds ratio.

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associated with a higher risk of readmission and, as a result, lower 12-month survival when compared to our control group. As our understanding of the significance of frailty continues to grow, a deeper exploration of clinical and biochemical contributing factors will enable us to better define an effective predictive index that can be applied in real-time at the point of care. One potential future implication of our study is the implementation of preoperative interventions for frail patients, such as exercise programs, respiratory prehabilitation, or nutrition supplementation. This assumption has been supported by preliminary investigations in patients undergoing nonpulmonary surgeries.[37,38] Additionally, the FI can serve as a valuable tool for postdischarge recommendations based on frailty status.

Our study has limitations, including its retrospective database and short-term follow-up. Furthermore, any risk classification method that aggregates comorbidities runs the risk of treating all factors equally and failing to account for the severity of each condition.

Conclusion

According to our findings, mFI-11 is a quick and simple strategy for designating a cohort of patients who are at high risk of readmission after elective lung resection for cancer. Patients with a high mFI-11 score had a considerably increased incidence of readmission, complications, and death. As a result, the mFI-11 can be used as a fast tool to detect frailty in patients receiving lung resection for NSCLC, aid in family discussions, and predict outcomes.

Conflict of Interest

None declared.

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