Original Article

Comparison of frailty indexes as predictors of clinical outcomes after major thoracic surgery

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Background: Despite greater appreciation for the importance of frailty in surgical patients, due to improved understanding that frailty is often linked to poor outcomes, the optimal method of assessment remains unknown. In this study, we sought to evaluate the prevalence of frailty in patients considered for elective thoracic surgery and to test the ability of several frailty measurements to predict postoperative outcomes.

Methods: Patients included were candidates for major elective thoracic surgery. Preoperative assessment of frailty included the Fried frailty phenotype, the Edmonton Frail Scale (EFS), the modified frailty index (mFI), the Clinical Frailty Scale (CFS), and additional components of frailty. Outcome data include days with chest drain, length of hospital stay, and postoperative adverse events.

Results: According to the Fried frailty phenotype, 53% of 94 patients included were prefrail or frail. A significant association between frailty and postoperative complications was found (odds ratio 7.65; P=0.001). No association between CFS, mFI, EFS, and complications was observed. The Frailty Phenotype seemed the most accurate in predicting postoperative complications, with an area under the curve (AUC) of 0.77. Twenty-seven percent of patients meet the criteria for depression according to the Geriatric Depression Scale and they showed a higher risk of postoperative complications (OR 2.47; P=0.03). A lower psoas muscle index was associated with a higher risk of complications (OR 3.40; P=0.04).

Conclusions: According to our results, the Fried frailty phenotype seems the most accurate tool to test frailty in patients undergoing thoracic resections. Surgeons should be aware that, although these aspects are not routinely tested, they are potential targets to improve clinical outcomes. Studies on additional interventions specifically targeting frail people in the setting of elective thoracic surgery are required.

Keywords: Frailty; frail patients; thoracic surgery; preoperative evaluation

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Introduction

In the preoperative setting, the ability to judge the appropriateness of surgery or its anticipated outcomes is an important skill for surgeons. Identifying vulnerabilities early in the preoperative pathway may allow the physician to assess the individual risk and optimize the preparation and surgical treatment. However, this evaluation has often been based on the presence of comorbidities and an overall impression formed during clinical encounters. The accuracy of this impression can be widely variable, as it depends on the physician's experience.

Population aging along with improvements in surgical outcomes, are leading to an increasing number of older people with multiple comorbidities undergoing thoracic surgery. One of the most problematic expressions of this demographic transition is frailty, a multidimensional condition characterized by diminished resistance to stressors and greater vulnerability to sudden health status changes triggered by apparently minor adverse events (1-3). Multiple tools have been developed to identify frailty in both clinical and research settings (4-6).

Despite greater appreciation for the importance of frailty in surgical patients, due to improved understanding that frailty is often linked to poor outcomes, the optimal method of assessment remains unknown (4,7). Several potential methods to test frailty, which are based on two models, have been described. The first is the "physical phenotype", which observes weight loss, exhaustion, grip strength, gait speed, and physical activity level (3). An alternative is the "cumulative deficit" model (8), which is based on the assumption that additive comorbidity effects produce an overall functional decline.

Based on these two models, currently available tests to assess frailty are described in the following paragraphs.

- Fried frailty phenotype: Fried frailty phenotype is also known as the Cardiovascular Health Study (CHS) frailty phenotype (3). According to this phenotype, a person is considered frail if at least three of the following criteria are present: unintentional weight loss (4.5 kg during the last year), self-reported exhaustion (two items from the modified Center for Epidemiological Studies-Depression scale), weakness (decreased grip strength), slow walking speed, and low physical activity (evaluated using the Minnesota Leisure Time Activity Questionnaire). Individuals with three or more of these variables are considered "frail", while those with one or two are "pre-frail". This phenotype uniquely assesses daily activities, slowness, strength and exhaustion. The downside is that the test has to be carried out, at least in part, with the assistance of a healthcare worker. The Fried frailty phenotype has been used to evaluate surgical outcomes in several studies, especially in general surgery (9).
- Edmonton Frail Scale (EFS): the EFS is a typical geriatric assessment of cognitive and physical function, which assesses nine domains: cognition, general health status, functional independence, social support, medication use, nutrition, mood, continence, functional performance. A patient is considered frail if the score is more than 5. It is user-friendly and requires less than 5 minutes to administer. It was found to be a valid measure of frailty compared to the clinical impression of geriatric specialists (10,11).
- Modified frailty index (mFI): the mFI is based on the deficit accumulation model, and it assesses comorbidities (12). It has been developed as a shorter derivative of a 70-item frailty index (Canadian Study of Health and Aging Frailty Index, CSHA-FI). It includes the following 11 items: non-independent functional status; no diabetes or diabetes controlled by diet, oral antihyperglycemic or insulin; chronic obstructive pulmonary disease exacerbation within 1 month; congestive heart failure exacerbation within 1 month; history of myocardial infarction within 6 months; history of angina within 30 days or any coronary intervention; hypertension; peripheral vascular disease; acutely impaired

Highlight box

Key findings

- Many thoracic surgery patients are frail or prefrail, and the Fried frailty phenotype seems the most accurate tool to assess it. Frailty is a risk factor predicting adverse postoperative events, along with sarcopenia and depression.

What is known and what is new?

- Frailty is linked to poor postoperative outcomes, but the optimal method of assessment remains unknown.
- The Fried frailty phenotype seems to be the most accurate tool for assessing thoracic surgery patients' frailty.

What is the implication, and what should change now?

- Surgeons should be aware that frailty is a potential target for improving clinical outcomes. Studies on additional interventions specifically targeting frail people in the setting of elective thoracic surgery are required.

sensorium; cerebrovascular accident without deficits; cerebrovascular accident with deficits. This index has been developed for surgical studies, as it assesses comorbidities, it is objective and quick to administer. It can be used in retrospective studies as all the information required can be found in the patient's medical record.

- Clinical Frailty Scale (CFS): the CFS measures frailty based on clinical judgement. In using the CFS, the assessor makes a judgment about the degree of a person's frailty based on information from a formal clinical assessment that takes into account cognition, mobility, function, and comorbidities to assign a frailty level from 1 (very fit) to 9 (terminally ill, life expectancy <6 months) (8).

In this study, we sought to evaluate the prevalence of frailty in patients considered for elective thoracic surgery and to test the ability of several frailty measurements to predict postoperative outcomes. In addition to these scoring systems, we hypothesized that other measurements of single components of frailty [psoas muscle index (PMI), depression scales] may provide independent value to the existing frailty index. We present this article in accordance with the STARD reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-963/rc).

Methods

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Azienda Ospedaliero-Universitaria Maggiore della Carità Institutional Review Board on July 8, 2021 (approval No. CE168/21). Informed consent was taken from all individual participants.

Study design

A single-center, prospective observational cohort study was conducted between July and December 2021 in the Division of Thoracic Surgery at Azienda Ospedaliero-Universitaria Maggiore della Carità, in Novara, Italy.

Patients who were candidates for major thoracic surgery were recruited to participate in the screening for frailty during the preoperative clinic visit. Patients were enrolled if they met inclusion criteria, which were age 65 years or older, candidates for a major elective thoracic surgical procedure requiring hospital admission (lobectomies, segmentectomies), and willingness to participate in the study. Exclusion criteria included an inability to ambulate, poor manual dexterity or inability to grip, inability to understand the questionnaires, and candidates for minor or less common surgical procedures.

Preoperative assessment of frailty was determined in an outpatients' clinic by a physician (thoracic surgery resident) who was not involved in the decision to take the patient to surgery. The patient's attending surgeon was blinded of the frailty scores during the patient's evaluation, surgery, and recovery. This evaluation included several tests: the Fried frailty phenotype, the EFS, the mFI, and the CFS. Additional tests related to single components of frailty were performed as follows: sarcopenia was determined by cross-sectional psoas area at L3 normalized by the square of height in a preoperative computed tomography (CT) or positron emission tomography (PET) scan (if available), while other measurements were the traditional risk indices and patient-answered questions (Katz Activities of Daily Living and Instrumental Activities of Daily Living, Center for Epidemiologic Studies Depression Scale, Geriatric Depression Scale). Clinical and demographic variables were collected as reported in *Tables 1,2*. Short-term outcome data include days with chest drain, length of hospital stay, and complications. The type and severity of postoperative adverse events were recorded using the Clavien-Dindo classification. All the patient data were collected in a REDcap (13) database entry form.

The primary outcome measure was the prevalence of frailty according to different scores. The secondary were the complications within 30 days of surgery, the PMI, and the depression scores. The primary endpoint was the relationship between frailty and postoperative complications. The secondary endpoints were the relationship between the PMI and depression scores with postoperative complications.

Statistical analysis

Continuous data are reported as median (I, III quartiles); categorical data are reported as percentages and absolute frequencies. Numerical variables were compared by Wilcoxon-type tests. The Chi-square test or the Fischer exact test, whatever appropriate, compares categorical variables. In our analysis, each frailty score, depression score, and the PMI were tested individually.

The generalized linear models, ordinary least square for continuous endpoint and logistic regression for categorical

Table 1 Preoperative characteristics

Variable	Results
Age (n=94), years	72 [67–75]
Gender (n=94), female	44 (47)
ECOG scale (n=94)	
0	9 (10)
1	64 (68)
2	21 (22)
WBC count (n=91), /mm^3	6,990 [5,400–8,380]
Hemoglobin (n=91), g/dL	13.7 [12.6–15.1]
Body mass index (n=94), kg/m^2	25.0 [22.5–27.5]
Serum creatinine (n=91), mg/dL	0.79 [0.64–1.07]
eGFR (n=90), mL/min/1.73 m^2	81.5 [59.5–94]
C-reactive protein (n=86), mg/L	0.15 [0.06–0.7]
Albumin (n=84), g/dL	4.6 [4.4–4.7]
Prealbumin (n=75), g/dL	27.5 [23.7–30.1]
Transferrin (n=76), mg/dL	240 [219–268]
Corticosteroid use (n=94)	4 (4)
Tobacco use (n=93)	
Current	21 (23)
Former	46 (49)
Never smoker	26 (28)
Age-adjusted Charlson Comorbidity Index (n=94)	5 [4–6]
History of myocardial infarction	11 (12)
Peripheral vascular disease	9 (10)
Cerebrovascular disease	14 (15)
Dementia	0 (0)
Chronic pulmonary disease	13 (14)
Connective tissue disease	3 (3)
Mild liver disease	1 (1)
Diabetes without complications	15 (16)
Diabetes with end-organ damage	1 (1)
Moderate or severe renal disease	4 (4)
Solid tumor (non-metastatic)	66 (70)
Lymphoma or multiple myeloma	2 (2)
Moderate or severe liver disease	1 (1)
Metastatic solid tumor	10 (11)
FEV1% (n=93)	87 [74–100]
DLCO% (n=92)	69 [53.5–83]
FEV1/FVC% (n=93)	75 [70–79.5]

Table 1 (*continued*)

Table 1 (*continued*)

Results are n (%) or median [interquartile range]. ECOG, Eastern Collaborative Oncology Group; WBC, white blood cell; eGFR, estimated glomerular filtration rate; FEV1, forced expiratory volume in the first second; DLCO, diffusing capacity of the lungs for carbon monoxide; FVC, forced vital capacity.

Table 2 Surgical characteristics and pathology report

Variable	Result
Surgical approach (n=94)	
Thoracotomy	18 (19)
VATS	61 (65)
RATS	15 (16)
Surgical procedure (n=94)	
Lobectomy	58 (62)
Segmentectomy	35 (37)
Histology subtype (lung) (n=94)	
Squamous	10 (11)
Adenocarcinoma	49 (52)
Carcinoid	8 (8)
Metastasis	11 (12)
Other (benign)	16 (17)
Lung cancer staging (TNM 8th ed.) (n=67)	
IA	37 (55)
IB	10 (15)
IIA	4 (6)
IIB	5 (8)
IIIA	9 (13)
IIIB	2 (3)

Results are n (%). VATS, video-assisted thoracoscopic surgery; RATS, robot-assisted thoracoscopic surgery; TNM, tumour, node, metastasis.

Table 3 Postoperative complications

Variable	Total, n (%)
Postoperative complications (n=94)	
Death	3 (3%)
Acute bleeding	4 (4%)
Prolonged air leak	4 (4%)
Pneumonia	2 (2%)
Respiratory failure	1 (1%)
Atrial fibrillation	3 (3%)
Myocardial infarction	1 (1%)
Pulmonary embolism	1 (1%)
Atelectasis	1 (1%)
Acute kidney failure	1 (1%)
Nerve damage	1 (1%)
Other	3 (3%)
Clavien-Dindo grading (n=94)	
0	72 (77%)
I	6 (6%)
II	9 (10%)
IIIA	1 (1%)
IIIB	4 (4%)
IVA–B	0 (0%)
V	2 (2%)
30-day mortality (n=94)	3 (3%)

ones, were constructed to account for potential confounders by using the Inverse Probability Weight Estimation Propensity Score. The propensity was estimated using the Covariate Balance Propensity on the frailty score, by adjusting for age, American Society of Anesthesiologists (ASA) class, Eastern Cooperative Oncology Group (ECOG) Performance Status Scale, Charlson Comorbidity Index, type of surgery and we accounted for their effect on the relationship of frailty and outcomes. Odds ratios are reported for categorical endpoints, and model estimates (β) for continuous endpoints. The final model for complications was adjusted using a propensity score weighting for the following covariates: age, gender, ASA class, ECOG scale, white blood cell count, hemoglobin, transferrin, prealbumin, albumin, creatinine, estimated glomerular filtration rate (eGFR), C-reactive protein (CRP), age-adjusted Charlson Comorbidity Index, FEV1%, DLCO/VA%, FEV1/FVC%, surgical approach, procedure.

Results with $P<0.05$ were considered significant. To estimate the overall accuracy of these scores in predicting postoperative complications, receiver operating characteristic curves (ROC) were produced for each tested score. An area under the curve (AUC) of 0.5 suggested no discrimination, 0.7 to 0.8 was considered acceptable, 0.8 to 0.9 excellent, and more than 0.9 outstanding. Analyses have been performed with R 3.4.2.

Results

Of the 127 eligible patients, 101 consented, 11 declined, and 15 were not approached. Seven were excluded because their final surgery was pneumonectomy or thymectomy. The median age of the participants was 72 years [interquartile range (IQR): 67–75]. All patients were Caucasian. Regarding the patients' general conditions, most (64%) were classified as ASA 2. The majority of patients were independent in performing at least 5 of 6 activities of daily living (94%) and 6 of 8 instrumental activities of daily living (85%). Complete preoperative characteristics are presented in *Table 1*. Characteristics regarding the surgical approach, procedure, and postoperative pathological staging are described in *Table 2*. Among patients diagnosed with lung cancer, most had stage I (49%). No patient received preoperative chemotherapy, immunotherapy or radiation treatment. The most common surgical procedures were lobectomies (57.4%) performed via video-assisted thoracoscopic surgery (62%). Twenty-four complications were recorded. The median number of days with chest drain was 2 (IQR 2–4), while the median length of hospital stay was 4 days (IQR 3–6) Complications and their severity according to the Clavien-Dindo Grading are listed in *Table 3*. There were three deaths, of which two occurred during postoperative hospital stay (one due to intestinal infarction and one to myocardial infarction), whereas one was caused by pneumonia within 30 days after discharge. The results of each frailty test and of the indicators of sarcopenia and depression are shown in *Table 4*.

The adjusted log odds of complications as a function of each frailty test were calculated (*Tables 5-9*) and curves as a function of Fried frailty phenotype are shown in *Figures 1,2*. Median adjusted hospital length of stay (*Figure 2*) as a function of Fried frailty phenotype is shown. Multivariable logistic regression showing the relationship of frailty and

Table 4 Indicators of frailty, sarcopenia and depression

Indicator (cut-off values)	Result
Clinical Frailty Scale (n=94)	3 [2–3]
Non frail [<4]	91 (97)
Mildly/moderately frail [4–5]	3 (3)
Severely frail	0 (0)
Modified frailty index (n=94)	0.09 [0.09–0.18]
Non frail [0]	19 (20)
Low frail [0.09]	42 (44)
Intermediate frail [0.18]	25 (26)
Frail [≥0.27]	8 (8)
Fried frailty phenotype (n=94)	1 [0–2]
Non frail [0]	44 (47)
Prefrail [1–2]	41 (44)
Frail [≥3]	9 (9)
Edmonton Frail Scale (n=94)	3 [2–4]
Non frail [0–5]	83 (88)
Vulnerable [6–7]	7 (7)
Mildly frail [8–9]	4 (4)
Moderately frail [10–11]	0 (0)
Severely frail [12–17]	0 (0)
Geriatric Depression Scale (n=94)	3 [1–6]
Normal [0–4]	72 (77)
Mild depression [5–8]	18 (19)
Moderate depression [9–11]	2 (2)
Severe depression [12–15]	2 (2)
Center for Epidemiological Studies-Depression Scale (n=94)	9.5 [5.5–17.3]
Not depressed [0–15]	67 (71)
Depressed [≥16]	27 (29)
Psoas muscle index (n=89) (cm^2/m^2)	4.91 [3.46–6.20]

Results are n (%) or median [interquartile range].

Table 5 Multivariable logistic regression showing the relationship between the scores and the presence of postoperative complications

Indicator	Presence of postoperative complications		
	OR	95% CI	P value
Clinical Frailty Scale	1.43	0.69–2.95	0.33
Modified frailty index	0.96	0.44–2.09	0.92
Fried frailty phenotype	7.65	2.18–26.82	0.001
Edmonton Frail Scale	1.09	0.68–1.76	0.71
Geriatric Depression Scale	2.47	1.51–4.98	0.03
Center for Epidemiological Studies-Depression Scale	1.76	0.86–3.61	0.12
Psoas muscle index	3.40	1.29–15.99	0.04

OR, odds ratio; CI, confidence interval.

Table 6 Multivariable logistic regression showing the relationship between the scores and Clavien-Dindo grading for complications

Indicator	Clavien-Dindo grading		
	OR	95% CI	P value
Clinical Frailty Scale	1.51	0.76–2.89	0.25
Modified frailty index	0.89	0.47–1.7	0.74
Fried frailty phenotype	1.90	0.75–4.83	0.18
Edmonton Frail Scale	1.52	1.10–1.71	0.05
Geriatric Depression Scale	2.10	1.11–4.31	0.04
Center for Epidemiological Studies-Depression Scale	1.13	0.58–2.17	0.72
Psoas muscle index	2.69	1.38–7.25	0.02

OR, odds ratio; CI, confidence interval.

outcomes is reported in *Tables 5-9*.

CFS

As shown in *Table 4*, the CFS was analyzed as a categorical variable, and only three patients fell into the "vulnerable" or "mildly frail" categories. No significant association between higher scores and the presence of postoperative complications was found (OR 1.43; 95% CI: 0.69–2.95; P=0.33), nor any significant association between higher scores and higher grades of complications (OR 1.51; 95% CI: 0.76–2.89; P=0.25), or longer length of hospital stay [β 0.55; standard error (S.E.) =0.90; P=0.54], or 30-day mortality (OR 1.58; 95% CI: 0.44–5.74; P=0.48).

mFI

According to the mFI, low (45%) or intermediate frailty (27%) was common, whereas frailty was not (8%). The mFI showed no significant association between higher scores and

Table 7 Multivariable logistic regression showing the relationship between the scores and 30-day mortality

Indicator	30-day mortality		
	OR	95% CI	P value
Clinical Frailty Scale	1.58	0.44–5.74	0.48
Modified frailty index	1.34	0.24–7.41	0.74
Fried frailty phenotype	2.54	0.34–18.82	0.36
Edmonton Frail Scale	1.38	0.40–4.80	0.61
Geriatric Depression Scale	6.58	3.92–12.45	0.04
Center for Epidemiological Studies-Depression Scale	3.97	1.07–14.76	0.04
Psoas muscle index	2.65	0.91–9.15	0.05

OR, odds ratio; CI, confidence interval.

postoperative complications (OR 0.96; 95% CI: 0.44–2.09; P=0.92), nor any significant association between scores and Clavien-Dindo complications (OR 0.89; 95% CI: 0.47–1.70; P=0.74); or longer length of hospital stay (β 0.75; S.E. =0.62; P=0.23) or 30-day mortality (OR 1.34; 95% CI: 0.24–7.41; P=0.74).

Fried frailty phenotype

According to the Fried frailty phenotype, 44% of patients were prefrail, and 9% were frail. A significant association between higher frailty scores and higher prevalence of postoperative complications was found (OR 7.65; 95% CI: 2.18–26.82; P=0.001) (*Figure 1*), whereas the association between higher frailty scores and higher Clavien-Dindo

Table 8 Multivariable logistic regression showing the relationship between the scores and the outcomes (days with air leak)

Indicator	Days with air leak			
	Estimate, β	Standard error	95% CI	P value
Clinical Frailty Scale	0.67	0.60	−0.51 to 1.86	0.27
Modified frailty index	0.31	0.35	−0.38 to 1.00	0.38
Fried frailty phenotype	1.06	0.76	−0.45 to 2.57	0.16
Edmonton Frail Scale	−0.04	0.74	−1.51 to 1.42	0.95
Geriatric Depression Scale	−0.36	0.61	−1.58 to 0.86	0.56
Center for Epidemiological Studies-Depression Scale	−1.30	0.79	−2.87 to 0.26	0.10
Psoas muscle index	0.43	0.41	−0.29 to 9.49	0.33

CI, confidence interval.

Table 9 Multivariable logistic regression showing the relationship between the scores and the outcomes (length of hospital stay)

Indicator	Length of hospital stay			
	Estimate, β	Standard error	95% CI	P value
Clinical Frailty Scale	0.55	0.90	−1.24 to 2.3	0.54
modified frailty index	0.75	0.62	−0.48 to 1.98	0.23
fried frailty phenotype	3.33	1.02	1.31 to 5.36	0.001
Edmonton Frail Scale	−0.04	0.74	−1.51 to 1.42	0.95
Geriatric Depression Scale	0.22	1.00	−1.77 to 2.21	0.83
Center for Epidemiological Studies-Depression Scale	−0.85	0.99	−2.83 to 1.12	0.39
Psoas muscle index	−0.98	0.86	−2.68 to 0.73	0.26

CI, confidence interval.

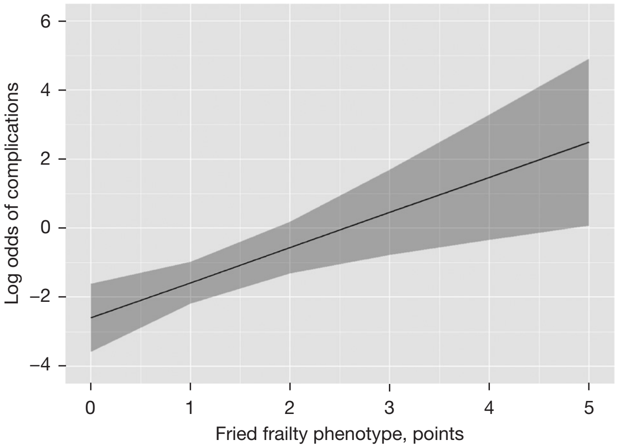

Figure 1 Relationship between Fried frailty phenotype and log odds of complications. The grey bands represent a 95% confidence interval.

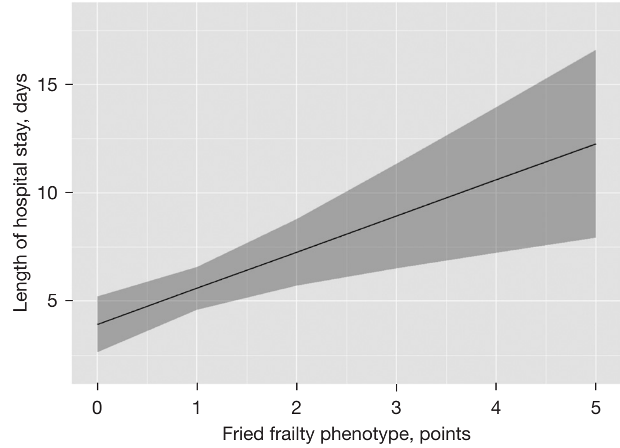

Figure 2 Relationship between Fried frailty phenotype and length of hospital stay. The grey bands represent a 95% confidence interval.

grading did not reach statistical significance (OR 1.90; 95% CI: 0.75–4.83; P=0.18) as well as 30-days mortality (OR 2.54; 95% CI: 0.34–18.82; P=0.36). Higher frailty scores were strongly associated with a longer length of stay (β 3.33; S.E. =1.02; P=0.001) but not with prolonged air leak (β 1.06; S.E. =0.76; P=0.16) (*Figure 2*).

EFS

According to the EFS, twelve percent of patients were deemed vulnerable or mildly frail. No significant relationship between the presence of vulnerability/mild frailty and postoperative complications was found (OR 1.09; 95% CI: 0.68–1.76; P=0.71). These patients seemed to have a higher risk of worse postoperative complications (OR 1.52; 95% CI: 1.10–1.71; P=0.05) but not an increasing length of hospital stay (β −0.04; S.E. =0.74; P=0.95) or 30-day mortality rate (OR 1.38; 95% CI: 0.40–4.80; P=0.61).

Geriatric Depression Scale-Short Form (GDS-S)

According to the GDS-S, 19% of our patients meet the criteria for mild, 2% for moderate, and 3% for severe depression. When comparing patients whose scores indicate at least mild depression to normal patients, the former showed a higher risk of postoperative complications (OR 2.47; 95% CI: 1.51–4.98; P=0.03) and a higher Clavien-Dindo grading (OR 2.10; 95% CI: 1.11–4.31; P=0.04). Also 30-day mortality seems to be influenced by the presence of depression (OR 6.58; 95% CI: 3.92–12.45; P=0.04).

Center for Epidemiological Studies-Depression Scale (CES-D)

Thirty percent of patients met the criteria for depression according to the CES-D. In our sample, these patients do not have a higher risk of postoperative complications or increased length of stay. However, they showed higher 30-day mortality (OR 3.97; 95% CI: 1.07–14.76; P=0.04).

PMI

Patients with a PMI below the first quartile were considered sarcopenic. These patients showed a higher risk of postoperative complications (OR 3.40; 95% CI: 1.29–15.99; P=0.04) and more severe complications (OR 2.69; 95% CI: 1.38–7.25; P=0.02), whereas there was no relationship with prolonged air leak (β −0.98; S.E. =0.86; P=0.26) or length of hospital stay. Thirty-day mortality significantly associated with a lower PMI (OR 2.65; 95% CI: 0.91–9.15; P=0.05).

ROC curves

According to the ROC curves, among the tested scores, the Fried frailty phenotype seemed the most accurate in predicting postoperative complications, with an AUC of 0.77, as shown in *Figure 3*. The GDS-S also shows an acceptable AUC of 0.66 (*Figure 4*), while the AUC of the PMI was only 0.6. The age-adjusted Charlson Comorbidity Index was also tested to estimate its accuracy in predicting adverse events (*Figure 5*). It showed an AUC of 0.57,

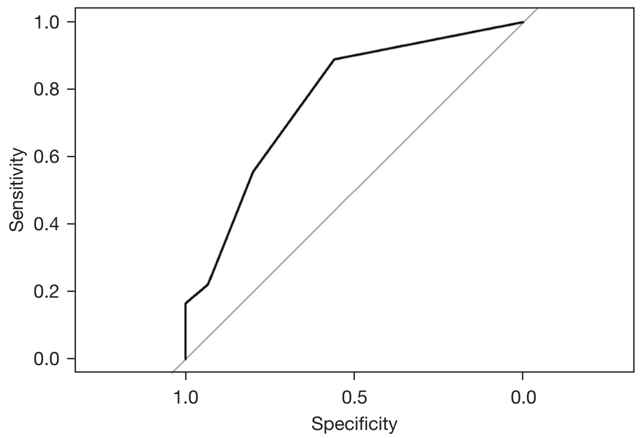

Figure 3 Fried frailty phenotype ROC curve, displaying the trade-off between sensitivity and specificity in predicting postoperative complications. The Fried frailty phenotype seemed the most accurate in predicting postoperative complications, with an AUC of 0.77. ROC, receiver operating characteristic; AUC, area under the curve.

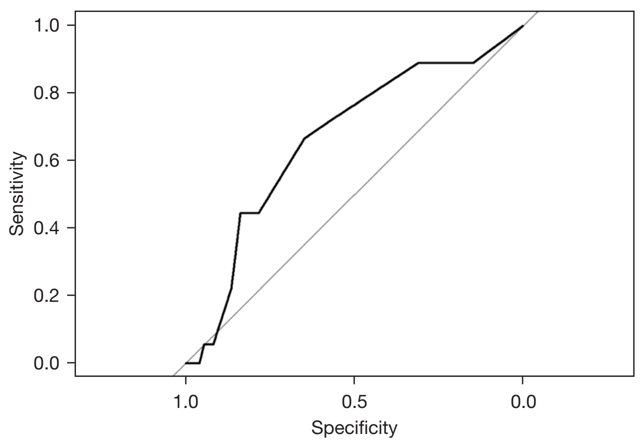

Figure 4 GDS-S ROC curve, displaying the trade-off between sensitivity and specificity in predicting postoperative complications. The GDS-S shows an acceptable AUC of 0.66. GDS-S, Geriatric Depression Scale-Short Form; ROC, receiver operating characteristic; AUC, area under the curve.

demonstrating its inefficacy in predicting adverse outcomes.

Discussion

In our sample, more than half of patients were frail or prefrail according to the Fried frailty phenotype, which seemed the most accurate tool in predicting postoperative adverse events, as it resulted as an independent predictor

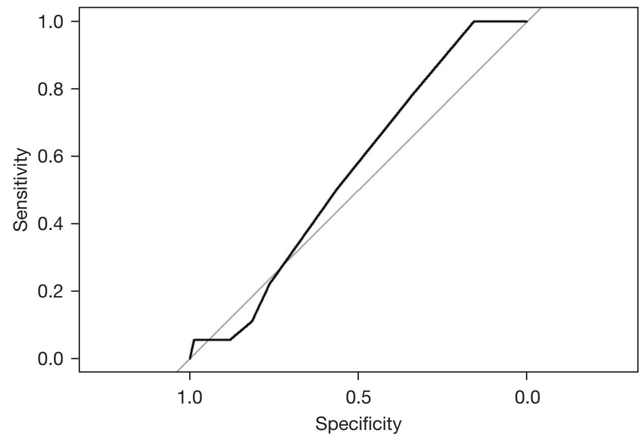

Figure 5 Charlson Comorbidity Index ROC curve, displaying the trade-off between sensitivity and specificity in predicting postoperative complications. The age-adjusted Charlson Comorbidity Index was tested to estimate its accuracy in predicting adverse events, showing an AUC of 0.57, demonstrating its inefficacy in predicting adverse outcomes. ROC, receiver operating characteristic; AUC, area under the curve.

of both postoperative complications and length of hospital stay. This tool was developed in a landmark study by Fried *et al.* (3) and includes unintentional weight loss, exhaustion, weakness, slow walking speed, and low physical activity. This phenotype provides an interesting, multidimensional assessment, but it requires the assistance of a healthcare worker. The Fried frailty phenotype has been used in several studies on surgical outcomes, and the results were similar to our findings, as frail patients were more likely to experience postoperative complications (9,14,15). In thoracic surgery, a prevalence study has been conducted by Beckert *et al.* (15), who found that 68.8% of patients were prefrail or frail, while in our study the prevalence of frailty was slightly less. According to our results, the Fried frailty phenotype is the most interesting and valuable tool to implement in clinical practices.

According to our results, the EFS was inaccurate in predicting postoperative complications. However, a higher score was associated with more severe complications. Among our patients, the prevalence of frailty, according to this tool, was very low, as only 12% could be considered vulnerable or mildly frail. This scale is a geriatric assessment of cognitive and physical function: cognition, general health status, functional independence, social support, medication use, nutrition, mood, continence, and functional performance (10,11). In a multidisciplinary surgical study (16), increasing frailty according to the EFS was associated with increased postoperative complications, length of hospitalization, and inability to be discharged home.

The mFI was widely used in surgical studies, as it does not require patient participation and can be applied retrospectively (17,18). Based on the deficit accumulation model (8), it explores functional status, diabetes, chronic obstructive pulmonary disease, congestive heart failure, coronary artery disease, hypertension, peripheral vascular disease, impaired sensorium, and cerebrovascular disease. Using the mFI, Velanovich *et al.* (12) observed that frailty increases postoperative morbidity and mortality in several surgeries, including thoracic. In thoracic surgery, a higher mFI is associated with higher postoperative morbidity and mortality (18,19). However, despite its success in other multidisciplinary studies, it did not prove accurate in our sample. One of the reasons may be that, in our study, the regression model to test the index was adjusted for comorbidities, which are a large part of what is assessed by the mFI.

In our population, similarly to available literature, patients with a low PMI experienced more severe complications, with an association between lower PMI and thirty-day mortality. Sarcopenia may be seen as one-dimensional, while the general condition of the frail elderly individual is determined by a complex interplay of factors (2,20). However, the overlap between frailty and sarcopenia is evident in the physical aspects of the frailty phenotype: low grip strength, gait speed, and muscle mass. In thoracic surgery, the low psoas area seems to be associated with worse outcomes and survival (21-23). Despite our work not analyzing long-term outcomes, our results seem to confirm these previous findings on postoperative prognosis.

Recent studies have suggested that 16–35% of frail individuals experience coexisting depression (24), which is prevalent before major surgery and may be a predictor of adverse clinical outcomes (25). Among several tools available to guide clinical decision-making in the perioperative period, none include an evaluation of depressive conditions (26). In our series of patients, approximately a quarter could be considered depressed, according to the GDS-S (27). These patients showed an increased risk of postoperative complications and mortality. Similarly, 30-day mortality was higher in patients with a CES-D score above 15 (28). Our results suggest that a patient's emotional health may influence postoperative recovery, and there may be a place for preoperative psychological screening to enable targeted support.

Future directions should explore preoperative optimization of frail patients. Preoperative recommendations in thoracic Enhanced Recovery After Surgery programs include smoking cessation and nutritional and anemia management, whereas prehabilitation is limited to patients with poor pulmonary reserve (28). Most trials demonstrate that prehabilitation enhances postoperative outcomes in high-risk patients, but they rarely target frail thoracic surgery patients. Specifically, several studies showed an improvement in exercise capacity in patients with resectable lung cancer and impaired pulmonary function, while the benefit in the postoperative complications and mortality has not been clarified (29). However, few more recent studies support the evidence that it may improve outcomes also in frail surgical patients (30). These interventions should include multimodal prehabilitation based on physical exercise (home-based, rehabilitation unit, or outpatient physiotherapy), nutritional optimization, and psychological support. Protocols to standardize prehabilitation programs are being evaluated (31). Randomized clinical trials targeting frailty are required to test these interventions' efficacy in elective thoracic surgery.

Limitations

This study is limited by the single-center setting, which reduces generalizability to broader clinical practice, and by the small number of patients included; therefore, it is subject to confounding. Moreover, despite the majority of patients underwent a minimally invasive approach, some of these patients were treated by and open procedure (thoracotomy). The extent of resection was also variable (lobar versus sublobar resection).

Conclusions

According to our results, the Fried frailty phenotype seems the most accurate tool to test frailty in patients undergoing major thoracic resections. More than half of patients selected for elective thoracic surgery are frail or prefrail, which is a risk factor predicting adverse postoperative events, along with the PMI and depression tools. This tool may be implemented in clinical practice. Thoracic surgeons should be aware that even if these aspects are not routinely tested, they may have a role in clinical decisions and may be targeted in preoperative settings to improve clinical outcomes. Trials on additional interventions specifically targeting frail people in the setting of elective thoracic surgery are required.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-963/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-963/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Azienda Ospedaliero-Universitaria Maggiore della Carità Institutional Review Board on July 8, 2021 (approval No. CE168/21), and informed consent was taken from all individual participants.

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