



# Preoperative frailty based on laboratory data and postoperative health outcomes in patients undergoing coronary artery bypass graft surgery

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## ABSTRACT

**Background:** Frailty is associated with adverse surgical outcomes. Patients with cardiovascular diseases have many risk factors of frailty; thus, preoperative frailty evaluation is necessary to predict adverse outcomes after coronary artery bypass graft (CABG) surgery. Laboratory data based-frailty assessments are objective and not time-consuming, addressing the need for an accurate but simple frailty screening for patients awaiting CABG surgery.

**Objectives:** This retrospective study aimed to determine the association between laboratory based-frailty and patient health outcomes after CABG surgery.

**Methods:** We evaluated 896 patients who underwent on-pump or off-pump CABG surgery between August 1, 2015 and July 31, 2020 at a tertiary hospital. The frailty index-laboratory (FI-LAB), which comprises 32 laboratory parameters and vital signs, was used for frailty assessment.

**Results:** The patients were divided into three groups according to their preoperative FI-LAB level as low (FI-LAB <0.25, 23.0%), moderate (FI-LAB ≥0.25 to ≤0.4, 54.9%), and high (FI-LAB >0.4, 22.1%) frailty groups. In the confounder-adjusted analysis, the lengths of hospital stay and intensive care unit stay were longer by 2.20 days ( $p=0.023$ ) and by 0.89 days ( $p=0.009$ ), respectively, in the high frailty group than those in the low frailty group. The odds ratio for 30-day readmission was also 2.58 times higher in the high frailty group than that in the low frailty group.

**Conclusion:** A high preoperative FI-LAB score indicates increasing risks of adverse postoperative outcomes among CABG surgery patients. FI-LAB has potential strengths to capture the need for a more thorough frailty assessment for cardiac surgery patients.

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## Introduction

The increasing number of elderly surgery patients emphasizes the importance of the influence of preoperative frailty on postoperative care. Frailty is defined as a state of decreased physiological capacity to cope with stressors.<sup>1</sup> This is caused by multiple factors, including chronic inflammation and intermediate pathophysiological processes. In addition, potential risk factors, such as genetic/epigenetic factors or environmental/lifestyle stressors, might facilitate its pathophysiology.<sup>2</sup> Frailty is associated with adverse postoperative outcomes such as falls, delirium, disability, and higher mortality among surgery patients.<sup>3</sup> Therefore, preoperative frailty evaluation provides an opportunity to discuss surgery risks with patients, their families, and healthcare professionals.<sup>4</sup>

Patients with cardiovascular diseases (CVDs) have risk factors of frailty such as decreased physical activity and diabetes.<sup>5</sup> In addition,

common pathological mechanisms between frailty and CVD, such as chronic inflammation or insulin resistance, also accelerate frailty progression.<sup>5</sup> The prevalence of frailty is 10% to 60% among older adults with CVDs<sup>6</sup> and 50% among older patients undergoing elective surgery.<sup>7</sup> Hence, preoperative frailty evaluation is important for prediction of their risk of complications after cardiac surgery. Importantly, frailty is a multifactorial condition, and its mechanism is complicated; hence, the optimal modality for frailty assessment is yet to be established, with various approaches currently used.<sup>8,9</sup> The choice of a frailty assessment tool depends on the availability of information, the reason for the assessment, the time-limit or technique of the assessment, and the patients' condition.<sup>10</sup>

Previous studies on the effect of frailty on the health outcomes of patients undergoing cardiovascular surgery have used varying frailty assessment tools. Most studies evaluated frailty based on clinical symptoms or functional ability.<sup>11–14</sup> Frailty, regardless of definition, had a strong association with the increased risk of mortality, morbidity, and functional decline after cardiac surgery.<sup>13</sup> Although many studies have suggested the adverse effects of frailty on outcomes

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### Abbreviations and Acronyms

|                  |                                                         |
|------------------|---------------------------------------------------------|
| <i>APACHE</i>    | Acute Physiology and Chronic Health Evaluation II score |
| <i>BMI</i>       | body mass index                                         |
| <i>CABG</i>      | coronary artery bypass graft                            |
| <i>CVD</i>       | cardiovascular diseases                                 |
| <i>EuroSCORE</i> | European System for Cardiac Operative Risk Evaluation   |
| <i>FI-LAB</i>    | frailty index-laboratory                                |
| <i>ICU</i>       | intensive care unit                                     |
| <i>LVEF</i>      | left ventricular ejection fraction                      |
| <i>OPCAB</i>     | off-pump CABG                                           |
| <i>STS</i>       | Society of Thoracic Surgeons                            |
| <i>wCCI</i>      | weighted Charlson comorbidity index                     |

after cardiac surgery,<sup>12,15</sup> evaluating frailty of patients with acute coronary syndrome is sometimes challenging due to time constraints and understaffing.<sup>16</sup>

Generally, a comprehensive frailty assessment is regarded as the best approach to detect frail patients because frailty is related to multifactorial risk factors, including psychosocial factors. However, it may not be feasible to recognize patients' frailty levels and apply them to daily care if there is a limitation of time and resources to assess frailty levels. Recently, routine clinical data-based frailty assessments have been suggested as a pragmatic approach for screening frail patients in acute settings.<sup>17</sup> Among several tools used to assess frailty with routinely collected EHR data, the frailty index-laboratory (FI-LAB) has been useful in the acute setting.<sup>18,19</sup> The FI-LAB uses routine laboratory test results and vital signs; thus, it could be a more objective modality for assessing frailty as compared to a judgment-based evaluation.<sup>19</sup> Moreover, it would be a time-efficient intervention to detect clinically invisible frailty in busy clinical settings.<sup>20</sup>

Preoperative frailty assessment for cardiac surgery patients should be quick, simple, highly accurate, and generalizable to these

patients.<sup>14</sup> Therefore, this study aimed to determine the association between routine laboratory-based frailty and postoperative outcomes (i.e., length of hospital stay, length of intensive care unit (ICU) stay, and readmission within 30 days) in patients undergoing coronary artery bypass graft (CABG) surgery.

### Methods

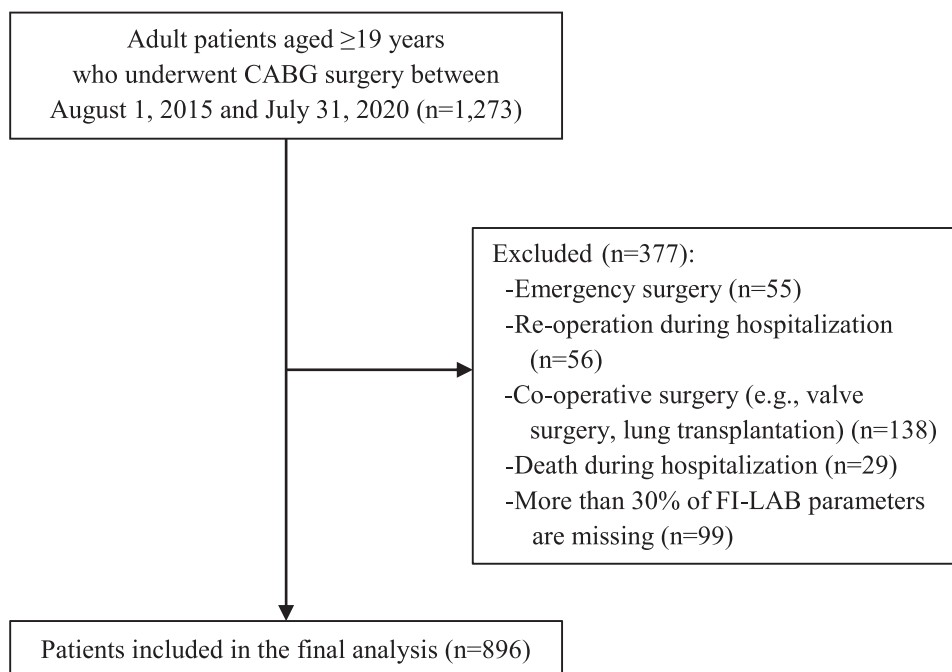
#### Study design and patients

This retrospective study was approved by the institutional review board of XX University Health System (reference no. Y-2020-0100). The investigation conformed with the principles outlined in the Declaration of Helsinki.<sup>21</sup> The need for informed consent was waived owing to the retrospective nature of the study and the use of anonymized data for the analysis.

The participants were patients aged >19 years who underwent CABG surgery between August 1, 2015 and July 31, 2020 at a tertiary hospital. Patients who underwent emergency surgery, co-operative surgery (e.g., valve surgery, lung transplantation), re-operation after CABG, or died during hospitalization were excluded. Patients with at least 30% of the FI-LAB items were missing were also excluded.<sup>22</sup> In total, 896 patients were included in the study (Fig. 1).

#### Frailty measurement

Frailty was assessed by the FI-LAB score suggested by Blodgett et al.<sup>20</sup> This version of FI-LAB has not been validated for CABG patients yet, but it was already reported to have predictive values for adverse outcomes after aortic valve replacement surgery.<sup>19</sup> The FI-LAB is comprised of 32 variables, 27 frailty-related laboratory parameters and five vital signs, and any value outside the reference range is considered a deficit. The frailty index was a continuous score ranging from 0 to 1 and calculated by the number of deficits divided by the total variable considered. For example, a patient with 10 abnormal and 27 total variables yielded 0.37 (10/27) for one's FI-LAB score. We used the most recent laboratory results before the surgery and the first measured vital signs at hospitalization for surgery. Thus, the



**Fig. 1.** Patient inclusion flowchart.

CABG: coronary artery bypass graft, FI-LAB: frailty index-laboratory.

frailty level was measured using data obtained before CABG surgery. Among the 32 variables, lactate dehydrogenase was not tested in all patients, and only serum folic acid value was available rather than folic acid in the red blood cells. Thus, we excluded these two variables from the analysis. We required at least 70% of items (23 out of 32 items) to measure a valid frailty index consistent with previous studies.<sup>18,22</sup>

FI-LAB determines the level of frailty as a continuum between robust and frail. Therefore, it was hard to divide our population into frail patients or non-frail patients dichotomously. As such, we classified the patients into the following three groups according to their FI-LAB scores, based on previous studies<sup>18,19</sup>: low frailty group, FI-LAB <0.25; moderate frailty group, FI-LAB  $\geq 0.25$  to  $\leq 0.4$ ; and high frailty group, FI-LAB >0.4.

#### Other variables

Other variables included the patient's age, sex, body mass index (BMI), history of smoking or alcohol consumption, number of current medications, left ventricular ejection fraction (LVEF), recent cardiovascular event (e.g., acute myocardial infarction, angina, atrial fibrillation), and type of surgery (e.g., on-pump or off-pump CABG). Activities of daily living based on the Korean version of Modified Barthel Index (MBI), which reflects patients' functional capacity,<sup>23</sup> and the Acute Physiology and Chronic Health Evaluation (APACHE) II score, which reflects postoperative condition at the immediate postoperative period,<sup>24</sup> were also collected. The weighted Charlson Comorbidity Index (wCCI), which is a comorbidity index weighted by the relative risk of 1-year mortality to reflect both the number and severity of comorbid diseases,<sup>25</sup> was calculated using diagnostic codes.

#### Statistical analysis

The patient characteristics were described as either a percentage of the total sample or as the mean  $\pm$  standard deviation. One-way analysis of variance and Pearson's chi-square test were used to examine patient characteristics and postoperative health outcomes according to the frailty level. We then checked normal distribution of the continuous variables, and particularly, the standard assumptions for linear regression analysis using residual plots and Q-Q plots. Multiple linear regression analysis was performed to examine the effect of frailty on the length of hospital stay and the length of ICU stay, while multiple logistic regression was used to explore the effect of frailty on readmission within 30 days. The covariates for the regression models were chosen based on the univariate findings, which yielded significant differences or correlations at least one outcome of this study. All statistical analyses were performed using R software (version 4.0.2 for Windows; The R Foundation; Vienna, Austria). A two-sided *p*-value of less than 0.05 was considered statistically significant.

#### Results

The mean patient age was  $66 \pm 9.0$  years, and 78% were men. The mean BMI was  $24.7 \text{ kg/m}^2$ , and 71.8% of the patients were overweight or obese. Hypertension was the most common comorbidity (68.9%), followed by diabetes (55.6%). Only 11% of the patients had heart failure, and the mean LVEF was  $54.4 \pm 15.0$ . Most patients (94.1%) underwent an off-pump rather than an on-pump CABG. The mean postoperative APACHE II score was  $23.1 \pm 5.7$ . The mean FI-LAB score was  $0.3 \pm 0.1$ . 23%, 54.9%, and 22.1% of the patients were categorized to the low, moderate, and high frailty groups, respectively. The patient characteristics are shown in Table 1.

Table 2 shows a descriptive comparison of FI-LAB variables among the three groups. Compared with the moderate and low frailty

**Table 1**

Clinical and demographic characteristics of the sample (*n* = 896).

| Variables                                 | Mean $\pm$ SD   | n (%)      |
|-------------------------------------------|-----------------|------------|
| Age (years)                               | 66.0 $\pm$ 9.0  |            |
| <40                                       |                 | 3 (0.3)    |
| 40–49                                     |                 | 29 (3.2)   |
| 50–59                                     |                 | 171 (19.1) |
| 60–69                                     |                 | 357 (39.8) |
| 70–79                                     |                 | 308 (34.4) |
| $\geq 80$                                 |                 | 28 (3.1)   |
| Sex                                       |                 |            |
| Female                                    |                 | 197 (22.0) |
| Male                                      |                 | 699 (78.0) |
| BMI ( $\text{kg/m}^2$ ) ( <i>n</i> = 874) | 24.7 $\pm$ 3.2  |            |
| Underweight (<18.5)                       |                 | 18 (2.1)   |
| Normal (18.5–22.9)                        |                 | 228 (26.1) |
| Overweight (23–24.9)                      |                 | 252 (28.8) |
| Obese ( $\geq 25$ )                       |                 | 376 (43.0) |
| Smoking status                            |                 |            |
| None                                      |                 | 455 (50.8) |
| Ex                                        |                 | 280 (31.2) |
| Current                                   |                 | 161 (18.0) |
| Drinking status                           |                 |            |
| None                                      |                 | 503 (56.1) |
| Ex                                        |                 | 143 (16.0) |
| Current                                   |                 | 250 (27.9) |
| FI-LAB                                    | 0.3 $\pm$ 0.1   |            |
| Low (<0.25)                               |                 | 206 (23.0) |
| Moderate ( $\geq 0.25$ – $\leq 0.4$ )     |                 | 492 (54.9) |
| High (>0.4)                               |                 | 198 (22.1) |
| wCCI                                      | 2.3 $\pm$ 1.9   |            |
| 0                                         |                 | 129 (14.4) |
| 1–2                                       |                 | 431 (48.1) |
| 3–4                                       |                 | 226 (25.2) |
| $\geq 5$                                  |                 | 110 (12.3) |
| Comorbidities (multiple responses)        |                 |            |
| Hypertension                              |                 | 617 (68.9) |
| Diabetes                                  |                 | 498 (55.6) |
| Myocardial infarction                     |                 | 314 (35.0) |
| Dyslipidemia                              |                 | 295 (32.9) |
| Heart failure                             |                 | 99 (11.0)  |
| Number of medications ( <i>n</i> = 837)   | 7.6 $\pm$ 3.6   |            |
| Modified Barthel Index                    | 98.4 $\pm$ 8.6  |            |
| Partially dependent                       |                 | 57 (6.4)   |
| Independent                               |                 | 839 (93.6) |
| LVEF (%) ( <i>n</i> = 868)                | 54.4 $\pm$ 15.0 |            |
| <40                                       |                 | 154 (17.7) |
| 40–49                                     |                 | 153 (17.6) |
| 50–59                                     |                 | 183 (21.1) |
| $\geq 60$                                 |                 | 378 (43.5) |
| Cardiovascular events ( <i>n</i> = 870)   |                 |            |
| Angina within 2 months                    |                 | 438 (50.3) |
| AMI within 3 weeks                        |                 | 218 (25.1) |
| A-fib during hospitalization              |                 | 18 (2.1)   |
| Surgery type                              |                 |            |
| CABG                                      |                 | 53 (5.9)   |
| OPCAB                                     |                 | 843 (94.1) |
| Number of grafts ( <i>n</i> = 883)        |                 |            |
| 1                                         |                 | 19 (2.2)   |
| 2                                         |                 | 69 (7.8)   |
| 3                                         |                 | 535 (60.6) |
| 4                                         |                 | 214 (24.2) |
| 5                                         |                 | 46 (5.2)   |
| APACHE II score                           | 23.1 $\pm$ 5.7  |            |

\*A-fib: atrial fibrillation; AMI: acute myocardial infarction; APACHE: Acute Physiology and Chronic Health Evaluation; BMI: body mass index; CABG: coronary artery bypass graft; FI-LAB: frailty index-laboratory; LVEF: left ventricular ejection fraction; OPCAB: off-pump coronary artery bypass; SD: standard deviation; wCCI: weighted Charlson comorbidity index.

groups, the high frailty group showed higher wCCI, number of medications, and APACHE II score and lower BMI, MBI score, and LVEF. Recent angina, acute myocardial infarction, and atrial fibrillation were associated with being frail. Readmission within 30 days was also associated with frailty level. Moreover, the postoperative length

**Table 2**  
FI-LAB parameters by level of frailty (*n* = 896).

| Variables (Unit)                  | Low frailty ( <i>n</i> = 206) | Moderate frailty ( <i>n</i> = 492) | High frailty ( <i>n</i> = 198) |
|-----------------------------------|-------------------------------|------------------------------------|--------------------------------|
| Albumin (g/dL)                    | 4.2 ± 0.3                     | 4.1 ± 0.4                          | 3.6 ± 0.5                      |
| Alkaline phosphatase (U/L)        | 69.4 ± 20.9                   | 68.7 ± 21.1                        | 82.3 ± 64.5                    |
| Bicarbonate (mmol/L)              | 22.8 ± 2.0                    | 22.0 ± 2.3                         | 21.8 ± 3.2                     |
| Bilirubin, total (mg/dL)          | 0.6 ± 0.2                     | 0.6 ± 0.3                          | 0.5 ± 0.3                      |
| Blood pressure- diastolic (mmHg)  | 75.1 ± 8.2                    | 76.1 ± 11.7                        | 80.2 ± 16.6                    |
| Blood pressure- systolic (mmHg)   | 127.5 ± 11.5                  | 134.1 ± 19.3                       | 147.2 ± 28.3                   |
| Blood urea nitrogen (mg/dL)       | 15.9 ± 4.1                    | 17.5 ± 6.6                         | 24.8 ± 14.6                    |
| C-reactive protein (mg/L)         | 2.4 ± 3.9                     | 5.0 ± 12.0                         | 12.6 ± 20.9                    |
| Creatinine (mg/dL)                | 0.8 ± 0.2                     | 1.0 ± 0.8                          | 2.6 ± 2.8                      |
| Direct HDL-cholesterol (mg/dL)    | 42.8 ± 9.2                    | 42.1 ± 10.3                        | 38.7 ± 9.9                     |
| Folate, RBC (ng/mL)               | *                             | *                                  | *                              |
| Glucose (mg/dL)                   | 133.5 ± 63.8                  | 148.4 ± 59.0                       | 157.9 ± 72.5                   |
| Glycohemoglobin levels (%)        | 7.1 ± 1.7                     | 7.3 ± 1.5                          | 7.2 ± 1.6                      |
| Hemoglobin (g/dL)                 | 14.0 ± 1.3                    | 13.0 ± 1.8                         | 11.1 ± 1.8                     |
| Iron, refrigerated (μg/dL)        | 90.7 ± 27.5                   | 82.6 ± 33.7                        | 70.5 ± 48.2                    |
| Lactate dehydrogenase (U/L)       | *                             | *                                  | *                              |
| Mean arterial pressure (mmHg)     | 92.6 ± 8.3                    | 95.4 ± 12.9                        | 102.5 ± 18.9                   |
| Mean cell volume (fL)             | 91.9 ± 3.7                    | 91.8 ± 4.6                         | 91.9 ± 5.9                     |
| Phosphorus (mmol/L)               | 3.6 ± 0.4                     | 3.6 ± 0.6                          | 3.7 ± 1.0                      |
| Platelet count (1000 cells/μL)    | 224.1 ± 57.0                  | 220.6 ± 63.2                       | 213.0 ± 76.2                   |
| Protein, total (g/dL)             | 6.9 ± 0.4                     | 6.7 ± 0.6                          | 6.2 ± 0.7                      |
| Pulse (beats/min)                 | 72.9 ± 10.5                   | 74.6 ± 14.5                        | 81.6 ± 17.9                    |
| Pulse pressure (mmHg)             | 52.4 ± 9.5                    | 58.1 ± 14.8                        | 67.0 ± 20.7                    |
| Red cell distribution width (%)   | 12.8 ± 0.6                    | 13.1 ± 0.9                         | 14.2 ± 1.8                     |
| Segmented neutrophils percent (%) | 58.0 ± 8.3                    | 59.5 ± 9.1                         | 63.5 ± 10.1                    |
| Sodium (mmol/L)                   | 140.4 ± 1.8                   | 140.0 ± 2.7                        | 138.8 ± 3.7                    |
| Total calcium (mg/dL)             | 9.2 ± 0.4                     | 9.0 ± 0.5                          | 8.6 ± 0.7                      |
| Total cholesterol (mmol/L)        | 181.0 ± 0.0                   | 212.4 ± 50.9                       | 184.0 ± 97.6                   |
| Triglyceride (mg/dL)              | 167.2 ± 211.7                 | 139.2 ± 81.7                       | 120.2 ± 61.7                   |
| Uric acid (mg/dL)                 | 5.4 ± 1.5                     | 5.5 ± 1.5                          | 5.3 ± 1.9                      |
| Vitamin B12 (pg/mL)               | 814.2 ± 269.8                 | 645.9 ± 378.7                      | 673.2 ± 349.6                  |
| Vitamin D (ng/mL)                 | 24.8 ± 0.0                    | 19.8 ± 11.6                        | 21.1 ± 7.5                     |

\*Missing variables.

†Data are presented as the mean ± SD.

‡FI-LAB: frailty index-laboratory, HDL: high-density lipoproteins, RBC: red blood cell.

of hospital stay and length of ICU stay were longer in the high frailty group than in the low frailty group (Table 3).

In the covariate-adjusted analysis, the length of hospital stay and the length of ICU stay were longer by 2.20 days ( $p=.023$ ) and 0.89 ( $p=.009$ ), respectively, in the high frailty group than in the low frailty group. With respect to readmission within 30 days, the odds ratio of the high frailty group was 2.58 (95% CI = 1.15–5.80) times higher than that of the low frailty group (Table 4).

## Discussion

This retrospective EHR analysis found that preoperative frailty assessed by routine laboratory data was associated with adverse postoperative outcomes of prolonged length of hospital and ICU stays and readmission within 30 days. Particularly, patients with a high level of frailty were likely to have a longer length of both hospital and ICU stays and also had a higher odds ratio for hospital readmission within 30 days. With respect to the characteristics of the study population, about 94% of patients underwent off-pump CABG (OPCAB), which is higher than the 70% off-pump rate of CABG in Korean tertiary hospitals.<sup>26</sup> The reason might be that the institution where we conducted the study specializes in OPCAB and we only included isolated CABG patients; thus, patients who concurrently underwent CABG with other surgeries where cardiopulmonary bypass is needed were excluded.

In this study, we focused on the frailty effects on length of stay and readmission rather than mortality because we aimed to assess how frailty affects the treatment journey of CABG patients. Mortality, which is usually the final result of diseases, cannot illustrate the mechanism by which frailty affects postoperative hospital experience in the short term. Initial ICU care is key to a successful recovery after CABG surgery. Prolonged ICU stays can cause complications such as

pneumonia, sepsis, and stroke due to various reasons.<sup>27</sup> Moreover, inactivity in the ICU could diminish patient mobility and functional capacity. Collectively, these imply that preoperative frailty is associated with postoperative maladaptation and the increased need for care. A previous study showed that the cost of cardiac surgery is higher in frail patients than in non-frail patients, with the nursing cost being the most increased.<sup>28</sup> This means that frailty significantly increases the level of postoperative care. Therefore, considering the patient's frailty level in postoperative care is required to improve the quality of care and patient experiences during hospitalization.

Our result that frailty is associated with adverse surgery outcomes is consistent with those of previous studies.<sup>11,29</sup> However, our research is valuable because it shows that laboratory-based frailty level is associated with increased length of stay and readmission in patients undergoing CABG surgery. Patients who undergo cardiac surgery are usually evaluated preoperatively to determine their ability to endure the surgery. From this perspective, checking laboratory test results and vital signs is essential for preoperative preparation. Therefore, using routine laboratory data to evaluate preoperative frailty is a feasible and convenient strategy for both patients and healthcare professionals. A previous study showed that physical alterations represented by abnormal laboratory test results are associated with frailty.<sup>30</sup> Furthermore, using clinical data can help detect molecular or cellular defects at an earlier period before clinical symptoms appear.<sup>31</sup> However, previous studies using FI-LAB mostly evaluated the association between frailty and the risk of death rather than the length of stay or readmission.<sup>19,22</sup> Therefore, our primary outcomes present the possibility of expanding the application of FI-LAB in the clinical setting.

A longitudinal study showed that frailty is associated with increasing age, particularly biological rather than chronological age.<sup>20</sup> Therefore, to reflect the biological age of clinically ill patients,

**Table 3**  
Clinical and demographic characteristics of the sample by FI-LAB frailty group (n = 896).

| Variables                      | Total (n = 896) | Low frailty (n = 206) | Moderate frailty (n = 492) | High frailty (n = 198) | F or $\chi^2$ (p)                  |
|--------------------------------|-----------------|-----------------------|----------------------------|------------------------|------------------------------------|
| Age (years)                    | 66.0 ± 9.0      | 63.5 ± 9.3            | 66.6 ± 8.8                 | 67.1 ± 8.9             | 10.39 (<0.001) a<b, c <sup>†</sup> |
| ≥65                            | 522 (58.3)      | 96 (46.6)             | 307 (62.4)                 | 119 (60.1)             | 12.25 (<0.001)                     |
| <65                            | 374 (41.7)      | 110 (53.4)            | 185 (37.6)                 | 79 (39.9)              |                                    |
| Sex                            |                 |                       |                            |                        |                                    |
| Female                         | 197 (22.0)      | 47 (22.8)             | 106 (21.5)                 | 44 (22.2)              | 0.145 (0.930)                      |
| Male                           | 699 (78.0)      | 159 (77.2)            | 386 (78.5)                 | 154 (77.8)             |                                    |
| BMI (kg/m <sup>2</sup> )       | 24.7 ± 3.2      | 25.1 ± 3.0            | 24.7 ± 3.2                 | 24.3 ± 3.2             | 3.30 (0.037) a>c <sup>†</sup>      |
| Underweight                    | 18 (2.1)        | 2 (1.0)               | 11 (2.3)                   | 5 (2.7)                | 8.91(0.174)*                       |
| Normal                         | 228 (26.1)      | 46 (22.5)             | 120 (24.8)                 | 62 (33.2)              |                                    |
| Overweight                     | 252 (28.8)      | 59 (28.9)             | 144 (29.8)                 | 49 (26.2)              |                                    |
| Obese                          | 376 (43.0)      | 97 (47.5)             | 208 (43.1)                 | 71 (38.0)              |                                    |
| Smoking status                 |                 |                       |                            |                        |                                    |
| None                           | 455 (50.8)      | 110 (53.4)            | 243 (49.4)                 | 102 (51.5)             | 3.66 (0.455)                       |
| Ex                             | 280 (31.2)      | 66 (32.0)             | 159 (32.3)                 | 55 (27.8)              |                                    |
| Current                        | 161 (18.0)      | 30 (14.6)             | 90 (18.3)                  | 41 (20.7)              |                                    |
| Drinking status                |                 |                       |                            |                        |                                    |
| None                           | 503 (56.1)      | 121 (58.7)            | 270 (54.9)                 | 112 (56.6)             | 10.47 (0.033)                      |
| Ex                             | 143 (16.0)      | 24 (11.7)             | 76 (15.4)                  | 43 (21.7)              |                                    |
| Current                        | 250 (27.9)      | 61 (29.6)             | 146 (29.7)                 | 43 (21.7)              |                                    |
| wCCI                           | 2.3 ± 1.9       | 1.3 ± 1.2             | 2.1 ± 1.7                  | 3.8 ± 2.2              | 112.10 (<0.001) a<b<c <sup>†</sup> |
| 0                              | 129 (14.4)      | 56 (27.2)             | 67 (13.6)                  | 6 (3.0)                | 178.72 (<0.001)                    |
| 1–2                            | 431 (48.1)      | 125 (60.7)            | 256 (52.0)                 | 50 (25.3)              |                                    |
| 3–4                            | 226 (25.2)      | 22 (10.7)             | 119 (24.2)                 | 85 (42.9)              |                                    |
| ≥5                             | 110 (12.3)      | 3 (1.5)               | 50 (10.2)                  | 57 (28.8)              |                                    |
| Number of medications          | 7.6 ± 3.6       | 7.0 ± 3.4             | 7.5 ± 3.5                  | 8.8 ± 3.9              | 12.48 (<0.001) a, b<c <sup>†</sup> |
| ADLs                           |                 |                       |                            |                        |                                    |
| Dependent                      | 57 (6.4)        | 6 (2.9)               | 27 (5.5)                   | 24 (12.1)              | 15.77 (<0.001)                     |
| Independent                    | 839 (93.6)      | 200 (97.1)            | 465 (94.5)                 | 174 (87.9)             |                                    |
| LVEF (%)                       | 54.4 ± 15.0     | 58.4 ± 13.4           | 54.8 ± 15.0                | 49.1 ± 15.0            | 20.02 (<0.001) a>b>c <sup>†</sup>  |
| ≥55                            | 468 (53.9)      | 132 (66.0)            | 260 (54.5)                 | 76 (39.8)              | 27.27 (<0.001)                     |
| <55                            | 400 (46.1)      | 68 (34.0)             | 217 (45.5)                 | 115 (60.2)             |                                    |
| Angina within 2 months         |                 |                       |                            |                        |                                    |
| Y                              | 438 (50.3)      | 90 (45.0)             | 227 (47.4)                 | 121 (63.4)             | 17.202 (0.002)                     |
| N                              | 432 (49.7)      | 110 (55.0)            | 252 (52.6)                 | 70 (36.6)              |                                    |
| AMI within 3 weeks             |                 |                       |                            |                        |                                    |
| Y                              | 218 (25.1)      | 26 (13.0)             | 108 (22.5)                 | 84 (44.0)              | 53.671 (<0.001)                    |
| N                              | 652 (74.9)      | 174 (87.0)            | 371 (77.5)                 | 107 (56.0)             |                                    |
| A-fib during hospitalization   |                 |                       |                            |                        |                                    |
| Y                              | 18 (2.1)        | 1 (0.5)               | 7 (1.5)                    | 10 (5.2)               | 11.01 (0.021)*                     |
| N                              | 852 (97.9)      | 199 (99.5)            | 472 (98.5)                 | 181 (94.8)             |                                    |
| Surgery type                   |                 |                       |                            |                        |                                    |
| CABG                           | 53 (5.9)        | 12 (5.8)              | 27 (5.5)                   | 14 (7.1)               | 0.64 (0.726)                       |
| OPCAB                          | 843 (94.1)      | 194 (94.2)            | 465 (94.5)                 | 184 (92.9)             |                                    |
| APACHE II score                | 23.1 ± 5.7      | 22.0 ± 5.1            | 22.6 ± 5.6                 | 25.6 ± 6.0             | 23.79 (<0.001) a, b<c <sup>†</sup> |
| Length of hospital stay (days) | 11.3 ± 9.3      | 9.3 ± 4.8             | 10.4 ± 7.8                 | 14.7 ± 13.5            | 21.7 (<0.001) a, b<c <sup>†</sup>  |
| Length of ICU stay (days)      | 3.3 ± 3.7       | 2.4 ± 1.3             | 2.8 ± 2.1                  | 4.3 ± 5.0              | 24.2 (<0.001) a, b<c <sup>†</sup>  |
| Readmission within 30 days     | 86 (9.6)        | 12 (5.8)              | 47 (9.6)                   | 27 (13.6)              | 7.1 (0.029)                        |

\* Fisher's exact test.

† Bonferroni post-hoc test; A-fib: atrial fibrillation; AMI: acute myocardial infarction; APACHE: Acute Physiology and Chronic Health Evaluation; BMI: body mass index; CABG: coronary artery bypass graft; FI-LAB: frailty index-laboratory; ICU: intensive care unit; LVEF: left ventricular ejection fraction; MBI: modified Barthel index; OPCAB: off-pump coronary artery bypass; wCCI: weighted Charlson comorbidity index.

we decided to include all adult patients instead of older patients who are usually considered at a high risk of frailty. Similarly, in a systematic review of studies on frailty assessment in the critically ill, many studies did not limit their participants to older patients.<sup>32</sup> Moreover, the FI-LAB was significantly associated with the increasing risk of mortality in the age 40–65-year group as well as 65 years and older group.<sup>20</sup> These findings indicate that the need for frailty assessment is possibly gradually expanding to various age groups in acute care settings. However, this increasing burden for measuring frailty could be reduced by laboratory-based frailty assessment, which can detect patients who need comprehensive evaluation for frailty. Moreover, according to the conceptualization of frailty by Chen et al.,<sup>2</sup> frailty is associated with chronic inflammation and various intermediary systems, including cardiovascular, endocrine, and musculoskeletal systems; therefore, it could be reasonable to measure frailty by using laboratory data that reflect the status of various physiological systems.

With respect to current risk scores, the European System for Cardiac Operative Risk Evaluation (EuroSCORE) II calculates the risk of

death,<sup>33</sup> while the Society of Thoracic Surgeons (STS) score yields the risk score for various outcomes (e.g., including length of stay and prolonged ventilation, and mortality) after cardiac surgery.<sup>34</sup> However, these tools need additional efforts to evaluate the risk score because the scores are calculated by using a level of mobility, cardiac status, and surgery-related factors.<sup>33,34</sup> This process might prevent routine evaluation for the risk of the surgery unless the data were extracted from electronic health records automatically. Moreover, a study reported that the FI-LAB showed better performance for predictions of survival after aortic valve replacement surgery than the EuroSCORE and the STS score.<sup>19</sup> The prediction power increased when the FI-LAB and the EuroSCORE were integrated.<sup>19</sup> Therefore, the FI-LAB could be considered for supporting the decision-making process.

The possible concern for decision-making based on frailty levels is that risk stratification for surgery might exclude some patients from appropriate treatments. A study noted that older cancer patients were more likely to be excluded from active cancer treatment because of the concern that they are too frail to withstand the cancer treatment.<sup>35</sup> However, adverse health outcomes are more likely to

**Table 4**  
Effect of frailty on postoperative health outcomes.

|                       | Length of hospital stay <sup>†</sup> |                | Length of ICU stay <sup>†</sup> |                | Readmission within 30 days <sup>‡</sup> |
|-----------------------|--------------------------------------|----------------|---------------------------------|----------------|-----------------------------------------|
|                       | $\beta$                              | p value (> t ) | $\beta$                         | p value (> t ) | OR (95% CI)                             |
| FI-LAB                |                                      |                |                                 |                |                                         |
| Low (Reference)       |                                      |                |                                 |                |                                         |
| Moderate              | −0.34                                | .638           | −0.01                           | .975           | 1.51 (0.76–2.99)                        |
| High                  | 2.20                                 | .023           | 0.89                            | .009           | 2.58 (1.15–5.80)                        |
| wCCI                  |                                      |                |                                 |                |                                         |
| 0 (Reference)         |                                      |                |                                 |                |                                         |
| 1–2                   | 0.20                                 | .818           | 0.01                            | .978           | 1.23 (0.56–2.68)                        |
| 3–4                   | 1.70                                 | .098           | 0.68                            | .057           | 0.77 (0.31–1.92)                        |
| ≥5                    | 6.42                                 | <0.001         | 1.53                            | <0.001         | 1.70 (0.64–4.52)                        |
| MBI                   |                                      |                |                                 |                |                                         |
| Dependent (Reference) |                                      |                |                                 |                |                                         |
| Independent           | −1.20                                | .319           | −0.20                           | .630           | 0.53 (0.24–1.17)                        |
| LVEF                  |                                      |                |                                 |                |                                         |
| <55% (Reference)      |                                      |                |                                 |                |                                         |
| ≥55%                  | −0.42                                | .507           | −0.26                           | .245           | 0.79 (0.47–1.32)                        |
| AMI                   |                                      |                |                                 |                |                                         |
| No (Reference)        |                                      |                |                                 |                |                                         |
| Yes                   | 0.19                                 | .797           | 0.26                            | .305           | 0.55 (0.30–1.04)                        |
| Surgery type          |                                      |                |                                 |                |                                         |
| CABG (Reference)      |                                      |                |                                 |                |                                         |
| OPCAB                 | −8.29                                | <0.001         | −1.83                           | <0.001         | 0.87 (0.33–2.32)                        |
| APACHE II             | 0.13                                 | .020           | 0.05                            | .006           | 0.98 (0.94–1.02)                        |

\*Adjusted for age and sex.

§AMI: acute myocardial infarction; APACHE: Acute Physiology and Chronic Health Evaluation; CABG: coronary artery bypass graft; CI: confidence interval; FI-LAB: frailty index-laboratory; ICU: intensive care unit; LVEF: left ventricular ejection fraction; MBI: modified Barthel index; OPCAB: off-pump coronary artery bypass; OR: odds ratio; wCCI: weighted Charlson Comorbidity Index.

<sup>†</sup> Multiple linear regression.

<sup>‡</sup> Multiple logistic regression.

occur in frail patients, not older patients, because they are more related to biological age, not chronological age.<sup>36</sup> It implies that assessing frailty at an appropriate time using the appropriate tools can adequately stratify high-risk patients and prevent the exclusion of robust older patients from active treatment. Moreover, our findings highlight that risk stratification using frailty does not necessarily lead to excluding frail patients from treatment due to its reversible characteristic.

Unlike disability, frailty is reversible, and thus, preoperative interventions are possible to improve frailty levels, leading to the prevention of adverse postoperative outcomes. Waite et al.<sup>37</sup> suggested that preoperative home-based rehabilitation for patients awaiting cardiac surgery might improve physical frailty and lead to a reduction in the length of hospital stay after the surgery. Based on the literature, various types of interventions are combined to improve patients' frailty levels, such as exercise, nutrition, and cognitive training.<sup>38,39</sup> However, a recent narrative review article regarding the preoperative evaluation of the frail patient mentioned the lack of robust randomized control trials for intervention to reduce frail levels at this time; thus, the authors suggested studies on the efficacy of preoperative interventions targeting frail patients.<sup>40</sup> Moreover, patients awaiting elective cardiac surgery may have different characteristics from patients with other diseases, including activity intolerance related to cardiac symptoms. For this reason, further studies are necessary to establish an effective perioperative intervention for patients with CVDs and identify the intervention's effect on preventing or alleviating postoperative adverse outcomes. Linking the home-based intervention to the perioperative period and discharge plan should also be discussed.

This study had some limitations. First, this was a single-center study, and only those who underwent CABG surgery were included. The potential selection bias could limit the generalization of our findings. Second, we only used laboratory test results and vital signs to assess frailty level. Therefore, this approach might not evaluate frailty comprehensively. Third, all laboratory results and vital signs were

not collected on the same day, and we included patients with more than 70% of the variables. For example, we did not use lactate dehydrogenase and folate in red blood cells for calculating frailty because they were unavailable in our dataset. These things might affect the accuracy of the frailty index and be a potential source of bias in the current study. Lastly, we could not compare the association of the EuroSCORE or the STS score and postoperative health outcomes with our findings because they were not available from the EHR. Further research is needed to compare the predictive effects of these tools on adverse postoperative outcomes.

Despite these limitations, this study is valuable as it evaluated the effect of frailty on postoperative outcomes using routinely collected data that did not involve a time-consuming assessment. Compared to the conventional method of frailty evaluation, a frailty index based on abnormal laboratory data and vital signs might be more efficient for admitted patients awaiting surgery. Therefore, laboratory-based frailty assessment has the potential to capture the need for a more thorough frailty assessment for cardiac surgery patients. In addition to this study's findings, further research is necessary to identify laboratory-based frailty's effect on other CABG outcomes, such as postoperative mortality or complications.

## Conclusions

Preoperative frailty assessments can help identify high-risk patients of CABG surgery. If healthcare professionals could easily assess patients' frailty levels using laboratory data in the EHR to identify high-risk patients, individualized perioperative care according to the patient's frailty level would contribute to improving postoperative health outcomes.

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## Declaration of Competing Interest

The authors declare that there is no conflict of interest.

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