The impact of frailty on functional survival in patients 1 year after cardiac surgery

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ABSTRACT

Objective: This study determined whether frailty provides incremental value to the European System for Cardiac Operative Risk Evaluation II in identifying patients at risk of poor 1-year functional survival.

Methods: This prospective study in patients undergoing cardiac surgery defined frailty using 3 common definitions: (1) the Modified Fried Criteria; (2) the Short Physical Performance Battery; and (3) the Clinical Frailty Scale. The primary outcome was functional survival, defined as being alive at 1 year postsurgery with a health-related quality of life score greater than 60 on the EuroQol-Visual Analogue Scale.

Results: Of the 188 participants, 49.5%, 52.6%, and 31.9% were deemed frail according to the Modified Fried Criteria, Short Physical Performance Battery, and Clinical Frailty Scale, respectively. The median age of our cohort was 71.0 years (29.3% female). The probability of functional survival at 1 year for the entire cohort was 73.9%. After adjusting for the European System for Cardiac Operative Risk Evaluation II, patients deemed frail under the Modified Fried Criteria, Short Physical Performance Battery, and Clinical Frailty Scale had an increased odds ratio for poor functional survival of 3.44, 3.47, and 2.08, respectively. When compared with the European System for Cardiac Operative Risk Evaluation II alone, the Modified Fried Criteria, Short Physical Performance Battery, and Clinical Frailty Scale showed an absolute improvement in the discrimination slope of 6.7%, 6.5%, and 2.4% with a category-free classification improvement of 59.6%, 59.2%, and 35.1%, respectively.

Conclusions: Preoperative frailty was associated with a 2- to 3.5-fold higher risk of poor functional survival 1 year after cardiac surgery. The addition of frailty to the European System for Cardiac Operative Risk Evaluation II provides incremental value in identifying patients at risk of poor functional survival 1 year postsurgery, regardless of frailty definition. (J Thorac Cardiovasc Surg 2017;154:1990-9)

Frail patients are at a higher risk of poor functional survival after cardiac surgery.

Central Message

Adding frailty to the euroSCORE II provides incremental value in identifying patients at risk of poor functional survival 1 year after cardiac surgery.

Perspective

Functional survival, defined as being alive 1 year after cardiac surgery and having an adequate HRQoL, is a relevant patient-centered outcome. Identifying patients undergoing cardiac surgery at risk of poor functional survival would allow clinicians to improve the quality of patients' informed consent and allow healthcare teams to target modifiable risk factors perioperatively.

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As the global population ages, increasingly older and frail patients are presenting for cardiac surgery worldwide.¹ Recent analyses in this aging demographic of patients

have identified that in addition to survival, maintaining or improving health-related quality of life (HRQoL) after their surgical procedure is of equal if not greater importance.^{2,3} It

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Abbreviations and Acronyms

AUC	= area under the curve
CFS	= Clinical Frailty Scale
EQ-VAS	= EuroQol-Visual Analogue Scale
euroSCORE	= European System for Cardiac Operative Risk Evaluation
HRQoL	= health-related quality of life
IDI	= Integrated Improvement Index
MFC	= Modified Fried Criteria
NRI	= Net Reclassification Index
SPPB	= Short Physical Performance Battery

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to the article title page.

has been estimated that up to one half of older adults currently undergoing cardiac surgery can be considered frail.^{4,5} These patients are vulnerable to both in-hospital adverse outcomes and poor long-term HRQoL.⁶

Frailty can be defined as a biological syndrome of decreased physiologic reserve and resistance to stressors, resulting in increased vulnerability to adverse outcomes.⁶ Frail individuals have a significantly higher risk of falls, disability, hospitalizations, and death, particularly after major medical or surgical events.⁶⁻⁸ It is well established that cardiac surgery represents a major physiologic stressor, and patients who are frail are at an increased risk of major cardiac or cerebrovascular events, postoperative delirium, increased hospital length of stay, morbidity, and mortality.^{4,5,8-11}

The 2 most commonly used preoperative risk assessment tools in cardiac surgery, the Society of Thoracic Surgeons Predicted Risk of Mortality and Morbidity and the European System for Cardiac Operative Risk Evaluation (euroSCORE) II, do not include comprehensive measures of frailty. Furthermore, although these scores have been shown to provide adequate prediction of perioperative mortality and morbidity,^{12,13} there is a paucity of literature examining their ability to predict long-term “functional survival,” defined as being alive with a good HRQoL.¹⁴ Accurate prediction of functional survival can help guide treatment decisions for the patient, aid in informed consent, and improve patient selection for cardiac surgery.¹⁵

We conducted a prospective cohort study to determine the relative ability of 3 commonly used frailty measures to predict 1-year functional survival: (1) the Modified Fried Criteria (MFC),⁶ (2) the Short Physical Performance Battery (SPPB),¹⁶ and (3) the Clinical Frailty Scale (CFS).¹⁷ We

hypothesized that these preoperative measures of frailty, when added to current risk-assessment scores, would provide incremental value in identifying patients at risk of poor 1-year outcomes in patients undergoing cardiac surgery.

MATERIALS AND METHODS**Study Population**

The study was conducted at the St Boniface Hospital, a tertiary care center in Winnipeg, Canada, with a patient catchment of approximately 1.1 million people. The study was approved by the University of Manitoba Research Ethics Board and the St Boniface Hospital Research Review Committee before the initiation of the study. Patients aged more than 18 years and undergoing elective or urgent coronary artery bypass graft or valve procedures were eligible for enrollment in the study. Patients who gave informed consent within this investigation were initially enrolled as part of a previous study protocol.⁴ From this cohort, patients were subsequently approached for follow-up between 9 and 19 months after their index (ie, initial) operative procedure. Because of the nature of the initial study examining the impact of frailty on postoperative delirium,⁴ patients in whom postoperative delirium could not be reliably assessed were excluded (eg, patients with previous stroke, cerebral palsy, severe dementia, severe hearing disabilities, or the inability to understand English).

Measurements and Outcomes

Frailty assessment. The primary exposure variable was frailty, defined using 3 common definitions. Study participants underwent detailed frailty assessments, namely, (1) the MFC,⁶ (2) the SPPB,¹⁶ and (3) the CFS.¹⁷ Under the Modified Fried definition, a patient was deemed “frail” if he/she met 3 or more of the following 7 criteria: slowness (as determined by the 5-m gait speed measurement, average time on 2 trials >6 seconds),⁹ weakness (a handgrip strength measurement, <30 kg if male, <20 kg if female),⁶ weight loss (self-reported weight loss >4.5 kg or >5% body weight in past 12 months),⁶ exhaustion (the modified 2-item Center for Epidemiologic Studies Depression Scale; ≥1 of 2),¹⁸ depression (the 5-item Geriatric Depression Scale; ≥2 of 5),^{19,20} low physical activity (the Paffenbarger Physical Activity Index; <383 kcal per week if male, <270 kcal per week if female),²¹ and cognitive impairment (the Montreal Cognitive Assessment; <26 of 30).²² Under the SPPB definition, a patient was classified as “frail” if his/her composite score was 9 or less after the following 3 functional assessments, each scored from 0 to 4: a 5-m gait speed measurement,⁹ a side-by-side, semi-tandem, and tandem stand balance tests,²³ and the repeated chair stand test.²³ Under the CFS definition, a patient was deemed “frail” if his/her given score, which is based on a clinical judgment regarding a patient’s level of activity, comorbidities, and disabilities, was 4 or greater.¹⁹

All 7 constructs of the MFC were also analyzed individually as an indicator of frailty to determine whether any one in particular would be predictive of poor functional survival 1 year after cardiac surgery.

Health-related quality of life. The primary outcome variable was 1-year functional survival, defined as being alive at 1 year postsurgery and having a EuroQol-Visual Analogue Scale (EQ-VAS) score greater than 60. One-year postsurgery survival was determined by contacting the patient or patient’s family. The EQ-VAS is a part of the EQ-5D questionnaire and is widely considered a validated tool used to measure HRQoL.^{24,25} The EQ-VAS instrument is a scale from 0 (worst imaginable health state) to 100 (best imaginable health state) with which patients record their self-rated health. We administered the EQ-5D questionnaire in person at a clinic follow-up or over the telephone 1 year after a patient’s cardiac surgery. We chose an EQ-VAS less than 60 to represent poor HRQoL because it represented the median score for individuals with advanced heart failure, malignancy, and kidney failure, all of which are well-accepted states of poor HRQoL.^{26,27}

Secondary outcomes. The secondary outcome variable was in-hospital morbidity/mortality, defined as death, stroke, prolonged ventilation (>24 hours), sternal infection, renal failure (dialysis), or return

to the operating room. Hospital records were reviewed to collect data for this secondary outcome variable.

Statistical Analysis

Baseline characteristics between study patients and patients who were lost to follow-up were compared using the chi-square test or Fisher exact test for categorical variables and the *t* test or Mann-Whitney test for continuous variables. To evaluate the internal validity of the Modified Fried criteria, SPPB, and CFS models, discrimination and reclassification were computed.

Discrimination, which is the ability of a model to separate patients who experience an outcome of interest into a different risk group from those who do not experience the outcome, was assessed using the area under the curve (AUC). We also included several composite outcome scores, including the Charlson comorbidity index and the Functional Comorbidity Index, which predict 1-year mortality and physical function, respectively.

To compare the improvement in discrimination of the frailty models relative to the euroSCORE II model, the Integrated Improvement Index (IDI)²⁸ was calculated. Changes in reclassification with the addition of the frailty constructs were assessed using the category-free Net Reclassification Index (NRI).²⁸ Category-free (continuous) NRI was chosen because of the lack of clinically accepted risk categories. The NRI describes the level of success with which a new model reclassifies a patient, that is, to a higher-risk group if he/she experienced the outcome of interest or to a lower-risk group if he/she did not experience the outcome. These statistics are being used more often in epidemiologic studies because of their higher sensitivity and intuitiveness in demonstrating predictive power than AUC statistics.⁹ *P* values for the IDI and NRI statistics were computed according to the methods described by Pencina and colleagues.²⁹ One-year functional survival and in-hospital mortality/morbidity outcomes were analyzed separately. All analyses were performed using Statistical Analysis System version 9.3 (SAS Institute Inc, Cary, NC).

RESULTS

Study Population

A total of 235 consecutively consenting patients undergoing an elective or urgent cardiac surgery procedure were enrolled in this study (Figure 1). Forty-seven patients were subsequently excluded; 10 patients did not undergo cardiac surgery, 9 patients chose to discontinue study participation, and 28 patients were lost to follow-up (after 3 separate contact attempts) 1 year after cardiac surgery. As such, a sample size of 188 patients was available for the final analyses. Although all 188 patients completed a SPPB and CFS assessment, only 186 in the cohort completed the full MFC. Fifty-five (29.3%) of the participants were women, and the median age was 71.0 years (interquartile range, 66.0-76.0) (Table 1). A total of 155 patients (82.4%) underwent elective surgeries, and 33 patients (17.6%) underwent urgent surgeries. The median euroSCORE II of the participants was 1.56 (interquartile range, 0.97-3.00).

Factors Associated With Frailty

Baseline frailty, defined using the Fried criteria, was associated with older age, a greater proportion of female patients, and a higher euroSCORE II when compared with the nonfrail cohort (Table 2). Postoperative hospital length of stay and incidence of delirium were higher among the frail cohort. The proportion of patients defined as being frail

FIGURE 1. Flowchart of study cohort recruitment. Description of how patients undergoing cardiac surgery were recruited for our study and included in the analyses.

varied depending on the frailty scale used. The Modified Fried, SPPB, and CFS scales were 49.5%, 52.6%, and 31.9%, respectively (Figure 2).

Association of Frailty With 1-Year Functional Survival

The probability of functional survival in the entire cohort was 73.9% (*n* = 139). After adjustment for the euroSCORE II, preoperative frailty was associated with a greater than 2- to approximately 3.5-fold higher odds of poor functional survival, depending on which frailty definition was used (Table 3). The addition of any frailty assessment score consistently resulted in an improvement in the prognostic value of the euroSCORE II in classifying functional survival, as evidenced by an absolute improvement in the discrimination slope (IDI) and a category-free NRI. For the Modified Fried, SPPB, and CFS, there was an absolute improvement in the discrimination slope of 6.7%, 6.5%, and 2.4% with a category-free classification improvement of 59.6%, 59.2%, and 35.1%, respectively (Table 4). There were no significant improvements in AUC with the addition of any frailty definition.

Individual Modified Fried frailty criteria of slow gait speed and cognitive impairment were associated with a similarly high rate of poor functional survival demonstrated by an adjusted odds ratio of 3.08 and 3.59, respectively (Table 5). Slow gait speed and cognitive impairment criteria also showed incremental value in identifying patients at risk of poor 1-year functional survival when compared with the euroSCORE II alone, as indicated by IDIs of 5.7% and 6.0%, and NRIs of 51.6% and 57.7%, respectively. The addition of individual Modified Fried frailty criteria did not significantly improve AUC values.

Association of Frailty With Secondary Outcomes

In this study, none of the frailty scales demonstrated that frailty results in a statistically significant improvement in

TABLE 1. Preoperative patient characteristics compared between study patients and patients who did not complete study

Preoperative variables	Study patients (n = 188)	Patients who did not complete study (n = 37)	P value*	SD
Age, y	71.0 (66.0-76.0)	70.0 (67.0-76.0)	.75	0.06
Sex (female)	55 (29.3%)	7 (18.9%)	.20	0.24
BMI (kg/m ²)	28.4 (25.2-32.1)	27.8 (25.9-32.8)	.91	0.01
Procedure			.75	0.20
CABG	90 (47.9%)	16 (43.2%)		
Valve	56 (29.8%)	11 (29.7%)		
CABG + valve	33 (17.6%)	9 (24.3%)		
Other	9 (4.8%)	1 (2.7%)		
Urgency			.33	0.17
Elective	155 (82.4%)	28 (75.7%)		
Urgent	33 (17.6%)	9 (24.3%)		
Current smoker	9 (4.8%)	2 (5.4%)	1.00	0.17
Angina	126 (67.0%)	25 (67.6%)	.95	-0.01
Previous MI	64 (34.0%)	15 (40.5%)	.45	-0.13
Congestive heart failure	101 (53.7%)	19 (51.4%)	.74	0.06
Atrial fibrillation	39 (20.7%)	12 (32.4%)	.12	-0.27
Cardiogenic shock	3 (1.6%)	0 (0.0%)	1.00	0.18
Previous angioplasty/stent	37 (19.7%)	4 (10.8%)	.20	0.25
Previous cardiac surgery	15 (8.0%)	2 (5.4%)	.75	0.10
Diabetes	60 (31.9%)	15 (40.5%)	.31	-0.18
Hypertension	158 (84.0%)	33 (89.2%)	.42	-0.15
Dyslipidemia	137 (72.9%)	29 (78.4%)	.49	-0.13
Peripheral vascular disease	21 (11.2%)	7 (18.9%)	.18	-0.22
Cerebrovascular disease	23 (12.2%)	8 (21.6%)	.13	-0.25
Chronic renal failure	10 (5.3%)	1 (2.7%)	.70	0.13
Pulmonary hypertension	12 (6.4%)	2 (5.4%)	1.00	0.04
COPD	23 (12.5%)	4 (10.8%)	1.00	0.05
Arthritis	37 (19.7%)	3 (8.1%)	.09	0.34
Visual impairment	81 (43.1%)	11 (29.7%)	.13	0.28
Hearing impairment	16 (8.5%)	2 (5.4%)	.74	0.12
Depression	22 (11.7%)	4 (10.8%)	1.00	0.03
Falls in the past year	10 (5.3%)	1 (2.7%)	.70	0.13
Albumin (g/L)	37.5 (34.0-40.0)	38.0 (36.0-39.0)	.37	-0.18
Creatinine (μmol/L)	86.0 (73.0-104.5)	90.0 (76.0-104.0)	.48	0.03
Creatinine clearance	76.2 (59.1-97.5)	75.9 (31.0-96.7)	.71	-0.11
Hemoglobin (g/L)	136.0 (123.0-148.0)	134.0 (123.0-143.0)	.57	0.09
Hemoglobin A1C (%)	6.0 (5.7-6.7)	6.3 (5.8-7.1)	.23	0.06
STS PROM (%)	1.72 (0.84-2.96)	1.89 (0.80-2.97)	.63	0.09
STS PROMM (%)	13.3 (9.3-19.2)	15.12 (9.6-22.1)	.36	-0.04
euroSCORE II (%)	1.56 (0.97-3.00)	2.28 (1.50-3.31)	.13	0.08
Charlson Comorbidity Index	2.0 (1.0-3.0)	2.0 (1.0-3.0)	.56	0.11
Functional Comorbidity Index	4.0 (3.0-5.0)	4.0 (3.0-5.0)	.88	0.02

(Continued)

TABLE 1. Continued

Preoperative variables	Study patients (n = 188)	Patients who did not complete study (n = 37)	P value*	SD
Modified Fried frail (score ≥ 3)	92 (49.5%)	17 (46.0%)	.70	0.07
SPPB frail (SPPB <10)	97 (51.6%)	14 (37.8%)	.13	0.28
CFS ≥ 4	60 (31.9%)	12 (32.4%)	.95	−0.01

Continuous variables expressed as median (interquartile range) and categorical variables expressed as N (%). *SD*, Standard deviation; *BMI*, body mass index; *CABG*, coronary artery bypass grafting; *MI*, myocardial infarction; *COPD*, chronic obstructive pulmonary disease; *STS PROM*, Society of Thoracic Surgeons Predicted Risk of Mortality; *STS PROMM*, Society of Thoracic Surgeons Predicted Risk of Mortality and Morbidity; *euroSCORE II*, European System for Cardiac Operative Risk Evaluation II; *SPPB*, Short Physical Performance Battery; *CFS*, Clinical Frailty Scale. *Continuous variables were compared using the Mann–Whitney test, and categorical variables were compared using the chi-square or Fisher exact test.

prediction of in-hospital morbidity/mortality when compared with the euroSCORE II alone. For the Modified Fried, SPPB, and CFS, there was an absolute improvement in the discrimination slope of 0.1%, 1.2%, and 0.0% with a category-free classification improvement of 10.9%, 31.1%, and −3.0%, respectively, all with *P* values less than .05 (Table 4).

DISCUSSION

In this prospective cohort study of 188 adult patients undergoing cardiac surgery, the presence of preoperative frailty was associated with a 2- to 3.5-fold higher risk of poor functional survival 1 year after cardiac surgery. The addition of any comprehensive frailty assessment to the euroSCORE II resulted in a statistically significant improvement in the risk of poor 1-year functional survival when compared with the euroSCORE II alone. The magnitude of these improvements is consistent with well-known risk factors for morbidity and mortality in other prediction models, for example, cardiac markers such as troponin T improving the prediction of cardiovascular disease.^{30–32} The Modified Fried and SPPB frailty definitions generated consistent prevalence rates of frailty in our population (ie, Modified Fried: 49.5%, SPPB: 52.6%) and provided incremental value in identifying individuals at risk of poor 1-year functional survival. Both the SPPB and the MFC were superior in improving the predictive ability of the euroSCORE II compared with the CFS. Of note, frailty prevalence rates in the present study (ie, 31.9% to 52.6%) were similar to those in previous studies conducted in patients undergoing cardiac surgery; however, these rates remain significantly higher than the 14% of community-dwelling older adults who are considered frail.³³ As expected, frail patients were older, were more likely to be female, and had an increased burden of comorbidities (ie, diabetes mellitus, cerebrovascular disease, chronic obstructive pulmonary disease, arthritis, peripheral vascular disease, and hypertension). With respect to postoperative outcomes, frail patients experienced longer intensive care unit length of stay and hospital length of stay and were more likely to experience postoperative delirium, which is consistent with previous literature.^{4,9}

Many studies examining the influence of frailty on postoperative outcomes in patients undergoing cardiac surgery focus primarily on perioperative and in-hospital events.^{4,5,8,9} Although these outcomes are essential, understanding the risk factors of poor long-term functional outcomes after cardiac surgery is equally important. Likewise, previous studies linking frailty to long-term outcomes of cardiac surgery have primarily sought to understand its impact on mortality.⁸ These studies have consistently demonstrated that frailty assessments, defined using multiple criteria, are effective at predicting 1-year all-cause mortality. To our knowledge, this is the first study to examine the predictive ability of multiple frailty constructs in determining a composite of survival and HRQoL 1 year after cardiac surgery. Indeed, previous literature has confirmed that preoperative frailty status is associated with poor postoperative HRQoL in minimally invasive cardiac procedures; however, our study is the first to examine this association in patients undergoing major cardiac intervention.³⁴

In undertaking the analysis of the 3 frailty assessment methods used in this study, the prevalence of frailty was similar between the MFC, which includes 3 domains of objective assessment (ie, physical ability, mood, and cognition), and the SPPB, which objectively assesses physical ability alone. According to the MFC and SPPB, a frail patient was approximately 3.5 times as likely to have a poor functional survival at 1 year compared with a nonfrail patient after adjustment for the euroSCORE II. The CFS is perhaps the most immediately “implementable” of these frailty evaluations and more semiquantitatively in nature provided incremental value in identifying patients at risk of poor 1-year outcomes, but at a lower degree when compared with the MFC and SPPB. However, the advantage of the CFS is that it is a more rapid tool requiring less training and resource allocation than the other frailty definitions used in this study.¹⁷ A more thorough and objective assessment of frailty (ie, the Modified Fried or the SPPB) appears to result in a greater proportion of patients defined as frail and has greater predictive capability of poor 1-year functional survival. This suggests that a more brief and subjective frailty assessment may not be comprehensive

TABLE 2. Characteristics of “frail” versus “nonfrail” according to the modified Fried criteria

Characteristic	Fried frail (N = 92)	Not Fried frail (N = 94)	P value	SD
Preoperative characteristics				
Age, y	73.0 (67.0-79.5)	70.0 (66.0-73.0)	<.01	0.48
Sex (female)	33 (35.9%)	21 (22.3%)	.04	0.30
BMI (kg/m ²)	28.4 (25.1-31.3)	28.3 (25.3-33.1)	.34	−0.19
Diabetes mellitus	36 (39.1%)	23 (24.5%)	.03	0.32
Hemoglobin A1c (%)	6.1 (5.8-7.1)	6.0 (5.7-6.5)	.27	0.22
Cerebrovascular disease	17 (18.5%)	6 (6.4%)	.01	0.37
COPD	17 (18.9%)	6 (6.5%)	.01	0.38
Clinical depression	15 (16.3%)	7 (7.5%)	.06	0.28
Arthritis	25 (27.2%)	12 (12.8%)	.01	0.37
Angina	63 (68.5%)	61 (64.9%)	.60	0.08
Smoking history	56 (61.5%)	60 (63.8%)	.75	−0.05
Current smoker	5 (5.5%)	4 (4.3%)	.70	0.06
Albumin (g/L)	37 (34-39)	38 (35-40)	.03	−0.23
Chronic renal failure	8 (8.7%)	2 (2.1%)	.06	0.29
Creatinine (μmol/L)	86 (70-116)	86 (76-99)	.90	0.25
Peripheral vascular disease	15 (16.3%)	6 (6.4%)	.03	0.32
Dyslipidemia	68 (73.9%)	67 (71.3%)	.69	0.06
Hypertension	83 (90.2%)	73 (77.7%)	.02	0.35
CHF	53 (58.2%)	48 (51.6%)	.37	0.13
MI	34 (37.0%)	29 (30.9%)	.38	0.13
Atrial fibrillation	22 (23.9%)	16 (17.0%)	.24	0.17
Previous angioplasty/stent	23 (25.0%)	14 (14.9%)	.08	0.25
Previous cardiac surgery	6 (6.5%)	9 (9.6%)	.44	−0.11
euroSCORE II (%)	2.06 (1.26-3.71)	1.30 (0.85-2.03)	<.01	0.20
STS PROM (%)	1.85 (1.08-3.55)	1.30 (0.75-2.23)	<.01	0.34
STS PROMM (%)	15.20 (11.03-22.60)	11.40 (8.39-16.87)	<.01	0.43
Frailty characteristics				
Modified Fried Frailty Score	4 (3-5)	1 (1-2)	<.01	3.10
Gait speed	48 (52.8%)	8 (8.5%)	<.01	1.09
Grip strength	45 (49.5%)	5 (5.4%)	<.01	1.14
Physical inactivity	80 (87.0%)	36 (38.3%)	<.01	1.16
Weight loss	23 (25.0%)	5 (5.3%)	<.01	0.57
Exhaustion	60 (65.2%)	17 (18.1%)	<.01	1.09
Cognitive impairment	75 (81.5%)	35 (37.6%)	<.01	1.00
Depression	46 (50.0%)	5 (5.3%)	<.01	1.15
Intraoperative characteristics				
Procedure type			.79	0.15
Isolated CABG	47 (51.1%)	41 (43.6%)		
Isolated valve	26 (28.3%)	30 (31.9%)		
CABG + valve	15 (16.3%)	18 (19.2%)		
Other	4 (4.4%)	5 (5.3%)		
CPB time	92 (73-122)	97 (79-138)	.28	−0.14
Postoperative outcomes				
ICU LOS (d)	2 (1-4)	1 (1-2)	.05	−0.03
Hospital LOS (d)	9 (6-14)	6 (5-11)	<.01	0.22
ICU LOS >72 h	33 (36.3%)	23 (24.5%)	.08	0.26
Hospital LOS >7 d	65 (71.4%)	42 (44.7%)	<.01	0.56
Major adverse event (30 d)	4 (4.4%)	1 (1.1%)	.21	0.13
Postoperative delirium	30 (33.0%)	14 (14.5%)	<.01	0.43
In-hospital mortality	3 (3.3%)	1 (1.1%)	.37	0.15
1-y follow-up outcomes				
EuroQol-VAS score	74 (50-83)	80 (70-87)	<.01	−0.54

(Continued)

TABLE 2. Continued

Characteristic	Fried frail (N = 92)	Not Fried frail (N = 94)	P value	SD
EuroQol-VAS ≤ 60	26 (28.3%)	9 (9.6%)	<.01	0.55
1-y mortality	9 (9.8%)	5 (5.3%)	.25	0.17
1-y poor functional	35 (38.0%)	14 (14.9%)	<.01	0.54

Continuous variables are expressed as median (interquartile range), and categoric variables are expressed as N (%). Continuous variables were compared using the Mann-Whitney test, and categoric variables were compared using the chi square or Fisher exact test. *SD*, Standard deviation; *BMI*, body mass index; *COPD*, chronic obstructive pulmonary disease; *CHF*, congestive heart failure; *MI*, myocardial infarction; *euroSCORE II*, European System for Cardiac Operative Risk Evaluation II; *STS PROM*, Society of Thoracic Surgeons Predicted Risk of Mortality; *STS PROMM*, Society of Thoracic Surgeons Predicted Risk of Mortality and Morbidity; *CABG*, coronary artery bypass graft; *CPB*, cardiopulmonary bypass; *ICU*, intensive care unit; *LOS*, length of stay; *VAS*, Visual Analogue Scale.

enough to discover all patients who are at increased risk, and thus may not adequately estimate level of risk.

In our analysis, we further sought to determine which specific components within the MFC were most strongly associated with poor functional survival 1 year after cardiac surgery. Previous literature from Afilalo and colleagues^{5,9} has demonstrated a strong association between slow gait speed and an increased risk of in-hospital morbidity and mortality after cardiac surgery. In the present study, slow gait speed and cognitive impairment were associated with a similarly strong association poor functional survival at 1 year as the MFC and SPPB. These specific criteria may represent frailty assessment tools that are less resource intensive to implement when compared with the more thorough testing required for the definitions based on MFC and SPPB.

Clinical Importance

We propose that identifying patients at risk for poor functional survival would allow clinicians to improve the quality of patients' informed consent.¹⁵ Recognizing this vulnerable cohort of patients also allows the healthcare team to target modifiable risk factors in this vulnerable group both preoperatively and postoperatively. Specifically, previous investigators have proposed physical frailty to be highly

related to sarcopenia or the loss of muscle tissue due to aging.^{35,36} A recent systematic review has demonstrated that exercise interventions, especially resistance training, may have a role in reversing sarcopenia in older adults, and thus possibly reversing frailty.³⁷ Therefore, one could envision that if a reduction in frailty in the preoperative and postoperative setting patient was possible, improvements in functional survival 1 year after cardiac surgery may be achievable.³⁸

The significant time and resources allocated to conducting comprehensive frailty assessments in routine clinical practice must be taken into consideration. For example, it may not be practical for physicians and other health care providers to complete a Modified Fried assessment (ie, 15-25 minutes) in every patient. On the basis of the data presented in the present study, the SPPB (ie, 5-10 minutes to complete) is shorter and as effective in predicting functional survival postoperatively when compared with the MFC. Even so, the SPPB may be impractical to implement in clinical settings. The CFS was developed to be a quick and subjective tool for assessing frailty; however, the data from this study would suggest it might lack sensitivity to predict an increased risk of poor functional survival in patients undergoing cardiac surgery. Our study also demonstrated that the 5-m gait speed assessment might be just as effective as the MFC and SPPB composite scores, while taking approximately 1 minute to administer. Although the 5-m gait speed assessment is an important indicator of sarcopenia, at this time, it is difficult to recommend the utility of using one test over another to stratify risk among surgical patients.

Study Limitations

There are several important limitations when interpreting the results of our study. First, the majority of patients enrolled in this study were undergoing elective procedures (ie, 82.4%). As such, this may limit the generalizability of the study findings in patients requiring an urgent or emergency cardiac procedure. However, it is unlikely that a frail older adult patient undergoing a more urgent procedure would have superior 1-year functional survival than a patient requiring an elective procedure. Second, several patients who were screened refused to participate in the study. Therefore, it is likely to be an element of selection

FIGURE 2. The prevalence of frailty. Depiction of the proportions of patients undergoing cardiac surgery deemed frail preoperatively using 3 different frailty definitions.

TABLE 3. Association between preoperative frailty and 1-year poor functional survival

Frailty definition	Frail	Not frail	P value	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*
Modified Fried frail (score ≥ 3)	38.0% (35)	14.9% (14)	<.01	3.51 (1.73-7.11)	3.44 (1.69-7.00)
SPPB frail (SPPB ≤ 9)	37.1% (36)	14.3% (13)	<.01	3.54 (1.73-7.25)	3.47 (1.69-7.12)
CFS frail (CFS ≥ 4)	36.7% (22)	21.1% (27)	.02	2.17 (1.10-4.25)	2.08 (1.05-4.12)

OR, Odds ratio; CI, confidence interval; SPPB, Short Physical Performance Battery; CFS, Clinical Frailty Scale. *Adjusted for the euroSCORE II. Categorical variables expressed as % (N).

bias, wherein robust patients were more agreeable to enroll in the study. We speculate that patients with more severe frailty may have been less likely to enroll in the study because of the time commitment required for baseline and follow-up testing. Thus, the study population may not accurately represent a true elective patient population, which would include both robust and severely frail patients. In future studies, we are seeking to develop and implement a more concise assessment methodology to identify an appropriate level of information required for risk prediction, while not being a burden to the patient. Third, this study lost 20% of patients to follow-up. We speculate that participants became unable to communicate with the research team because of changes in telephone number, changes in residence, or worsening health condition. Furthermore, because of the unique geographic context of the study site, it is possible that travel from remote rural locations of the province presented a barrier to participating in the follow-up protocol for some study participants. Even so, the percentage of patients lost to follow-up is similar to other studies in cardiac surgery, with some studies losing greater than 45% of patients to follow up.¹⁰ We also aimed to conduct follow-up assessments within 2 to 3 months of the desired 1-year follow-up period; however, because of patient availability and scheduling, follow-up assessments ranged from 9 to 19 months after cardiac surgery. We acknowledge that there may be differences in outcomes, specifically with respect to HRQoL due to the range of follow-up appointments. However, the majority (52%) of

the appointments were scheduled within 3 months of the target 1-year follow-up date. We also acknowledge that poor HRQoL at 1 year may reflect impaired HRQoL at baseline before surgical intervention. However, the EQ-VAS was not administered during the preoperative period. In future studies, we endeavor to investigate changes in HRQoL throughout the perioperative period.

Frailty has been associated with several short-term outcomes after cardiac surgery, including postoperative major morbidity, mortality, adverse cardiac and cerebrovascular events, secondary in-hospital outcomes, and postoperative delirium.^{4,5,8-11} This present study did not show statistical significance of frailty improving prediction of in-hospital mortality/morbidity when compared with the euroSCORE II alone. A reason for this lack of significance may have been due to our cohort population consisting of mostly (82.4%) elective procedures, which generally have more favorable outcomes than urgent and emergency procedures. Another possible reason for this lack of significance could have been our relatively small sample size, which in turn had a small incidence of in-hospital mortality. As such, our analysis was not powered to include a large number of covariates in the multivariable models; therefore, we decided to include the euroSCORE II because it provides a clinically validated surgical risk score that includes a large number of covariates. The low postoperative mortality rate at this study's cardiac surgery center relative to reported outcomes from other Canadian cardiac surgery centers may at least partially explain the lack of incremental value

TABLE 4. Improvements in prediction of 1-year functional survival and in-hospital mortality/morbidity by the addition of frailty* (compared with European System for Cardiac Operative Risk Evaluation II)

Outcome	Frailty definition	Improvement in C-statistic	P value	IDI	P value	NRI	P value
In-hospital mortality/morbidity*	Modified Fried frail (score ≥ 3)	−0.039	.23	0.1%	.68	10.9%	.59
	SPPB frail (SPPB ≤ 9)	−0.02	.57	1.2%	.15	31.1%	.13
	CFS frail (CFS ≥ 4)	0.015	.14	0.0%	.84	−3.0%	.88
1-y functional survival†	Modified Fried frail (score ≥ 3)	0.041	.18	6.7%	<.01	59.6%	<.01
	SPPB frail (SPPB ≤ 9)	0.032	.30	6.5%	<.01	59.2%	<.01
	CFS frail (≥ 4)	−0.014	.57	2.4%	.04	35.1%	.03

IDI, Integrated Improvement Index; NRI, Net Reclassification Index; SPPB, Short Physical Performance Battery; CFS, Clinical Frailty Scale. *In-hospital morbidity/mortality defined as death, stroke, prolonged ventilation (>24 h), sternal infection, renal failure (dialysis), or return to the operating room. †One-year functional survival defined as being alive at 1 year or having EuroQoL-VAS score greater than 60.

TABLE 5. Association between preoperative modified Fried criteria and 1-year poor functional survival

Frailty definition	Frail	Nonfrail	P value	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*	C-Statistic	P value	IDI	P value	NRI†	P value
Modified Fried Frail (score ≥ 3)	38.0% (35)	14.9% (14)	<.01	3.51 (1.73-7.11)	3.44 (1.69-7.00)	0.712	.18	6.7%	<.01	59.6%	<.01
Gait speed	42.9% (24)	19.1% (25)	<.01	3.18 (1.60-6.31)	3.08 (1.54-6.18)	0.692	.43	5.7%	<.01	51.6%	<.01
Grip strength	40.0% (20)	21.3% (29)	.01	2.46 (1.22-4.95)	2.40 (1.19-4.84)	0.672	.98	3.3%	.02	37.8%	.02
Physical inactivity	29.1% (34)	21.1% (15)	.23	1.53 (0.76-3.07)	1.53 (0.76-3.07)	0.642	.44	0.8%	.20	19.4%	.24
Weight loss	39.3% (11)	23.8% (38)	.08	2.08 (0.90-4.82)	2.06 (0.89-4.79)	0.668	.90	1.6%	.13	20.4%	.22
Exhaustion	35.1% (27)	18.9% (21)	.02	2.18 (1.13-4.23)	2.14 (1.10-4.16)	0.674	.94	2.7%	.03	38.3%	.02
Cognitive impairment	35.5% (39)	13.0% (10)	<.01	3.68 (1.70-7.95)	3.59 (1.65-7.78)	0.717	.22	6.0%	<.01	57.7%	<.01
Depression	35.3% (18)	22.6% (31)	.08	1.86 (0.93-3.76)	1.82 (0.90-3.67)	0.651	.56	1.5%	.11	26.0%	.12

Categoric variables expressed as % (N). OR, Odds ratio; CI, confidence interval; IDI, Integrated Improvement Index; NRI, Net Reclassification Index. *Adjusted for the euroSCORE II. †Improvement in prediction of 1-year poor functional survival compared with the euroSCORE II alone.

for in-hospital outcomes. (Canadian Institute for Health Information 2011-2014 data not shown). In our initial analysis, we demonstrated a 1.1% operative mortality rate in the nonfrail cohort and a 3.3% operative mortality rate in the frail cohort. If this trend continued, a sample size of 690 patients in each group would be required to detect these differences with a 2-tailed alpha of 0.05 and a power of 80%. Although a standard definition of functional survival does not currently exist in the literature, we chose the EQ-VAS cutoff score of 60 as a measure of adequate HRQoL and to identify a relevant patient-centered health outcome.

Future Directions

This study needs to be replicated in other centers to determine whether the frailty measurement tools, along with their individual criteria, show similar ability to predict long-term functional survival as was shown in this study. Investigation into which frailty assessment is most effective at improving this prediction needs to occur and investigation into which is the most practical in terms of cost, time, and resources required to implement. Our research team is currently investigating the role of preoperative exercise interventions in frail patients undergoing cardiac surgery with the hypothesis that improving domains of frailty (“prehabilitation”) will correlate with improvements in mortality and functional survival.³⁸

CONCLUSIONS

Preoperative frailty was associated with poor functional survival 1 year after cardiac surgery. The addition of any quantitative or semiquantitative frailty measure to the euroSCORE II provided incremental value in identifying patients at risk of poor 1-year functional survival. Future research should investigate the feasibility of incorporating frailty assessment tools to assist with patient selection, promote shared-decision making, and identify

potentially vulnerable patients requiring perioperative risk optimization.

Conflict of Interest Statement

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Key Words: frailty, cardiac surgery, long-term outcomes, survival, HRQoL

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