INTRODUCTION

Frailty, defined as a state of exaggerated vulnerability to adverse health outcomes due to the accumulation of age-related deficits, is increasingly recognized as an important factor associated with suboptimal outcomes for patients undergoing cardiac surgery.(1-4) Despite this association, there is no consistent screening strategy for frailty, limited incorporation of frailty-related functional measures into cardiac surgery risk scores, and no reliable care pathways to mitigate the peri-operative risk for vulnerable patients living with frailty.

As the Canadian population ages, the incidence of frailty and concomitant cardiovascular disease prompting consideration for complex interventions is expected to grow.(5-7) Advances in intensive care, anaesthetic and surgical techniques have improved outcomes, translating into older, more complex patients now routinely undergoing cardiac surgery.(5) Identifying patients with frailty prior to major cardiac surgery may have relevance for prognostic and recovery purposes, to optimally inform patients, caregivers and clinicians about pre-operative opportunity (e.g., pre-habilitation), peri-operative risk and post-operative care needs.

METHODS

This study was approved by the Research Ethics Board at the University of Alberta, Edmonton (ID Pro00074770). Participant consent was obtained at the time of enrollment. Reporting follows the recommendations in the STROBE statement.(8)

Design, Setting and Population

This was a prospective observational cohort study. Patients ≥50 years of age referred to the two adult (≥18 years) cardiac surgery programs for planned or urgent surgery in Alberta, Canada between November 2011 and March 2014 were eligible for enrolment. The two cardiac surgery centers are high-volume academic programs providing all cardiac surgical interventions for the province, in addition to complex cases referred from neighboring provinces/territories. Patients were excluded from the study if they were referred for emergent surgery, transcatheter aortic valve implantation or transplantation. (Figure 1)

Cardiac Surgery at Study Sites

The two adult cardiac surgery programs perform an average of 2,800 adult surgical procedures annually, 96% of which are planned or urgent.(9,10) The most common surgeries performed are isolated coronary artery bypass grafting (CABG) 49%; isolated valve procedures 10%; and combined CABG/valve procedures 8%.(11,12) After surgery, patients are admitted to dedicated, closed-model, cardiovascular surgical intensive care units (CVICU) staffed by board-certified intensivists available 24 hours per day. Patients are supported in a 24-bed CVICU with 10

cardiac surgeons in Edmonton and an 18-bed CVICU with 9 surgeons in Calgary.(9,10) The estimated median stay in CVICU and hospital are 2 and 7 days, respectively. Risk-adjusted 30-day in-hospital mortality after isolated CABG is 1.4%.(11,12)

Measure of Frailty

Frailty was assessed by application of the validated 9-point ordinal Clinical Frailty Scale (CFS) score.(13-16) Frailty was defined as a CFS score ≥5.(13,17) The CFS was further stratified as fit (CFS 1-3), vulnerable (CFS =4) and frail (CFS 5-9) to assess for gradient variations in outcome.(17)

Patients received a CFS score based on a review of their health records and by interview pre-operatively in pre-admission clinic or inpatient hospital settings. The abilities and condition of the patient two weeks prior to the index admission was considered in the assessment of the pre-operative CFS score. Frailty assessment was completed independently by research study coordinators trained on the use of the CFS.(17) Additional data were captured on socio-demographics (e.g., ethnicity, marital status, education, employment status, pre-hospital living arrangement), functional status (e.g., timed 'Up and Go' test (18)), pre-operative details (e.g., body mass index [BMI], home medications, comorbid disease) and health-related quality-of-life (HRQL), using the EuroQol 5-dimension 3-level (EQ-5D) health questionnaire with visual acuity scale (EQ-VAS).(19,20)

Data Sources

Health records were reviewed for post-operative course in CVICU and hospital, duration and intensity of organ support, the occurrence of complications and adverse events (e.g., acute kidney injury, atrial fibrillation, cardiopulmonary arrest, death).

At 6-months and 12-months after surgery patients were contacted to assess CFS score, HRQL and living arrangements (e.g., independent at home, at home with help, lodge or continuing care). The inpatient discharge abstract database and the provincial cardiac outcomes registry were queried to confirm vital status.(21,22) All data linkages were performed using facility medical record number and/or the Alberta nine-digit unique personal health number. Vital status was unavailable for 5 patients due to out-of-province residence (5/529; 0.9%).

Main Exposure and Outcome Measures

The primary exposure was pre-operative frailty. The primary outcome was all-cause hospital mortality. Secondary outcomes included intensity of organ support (i.e., receipt and duration of mechanical ventilation, vasoactive therapy, renal replacement therapy), death in CVICU, hospital discharge disposition (e.g., home, sub-acute rehabilitation, skilled nursing facility), health services use (i.e., duration of stay in CVICU and hospital), HRQL pre-surgery, at 6-months and 12-months, and mortality at 6-months, 12-months and 5 years following surgery.

Statistical Analysis

Descriptive statistics were tabulated by CFS score ≥5 (frail) compared to CFS score ≤4 (non-frail). Missing CFS scores (n=2) were imputed using mean of scores assigned by an expert panel of 5 clinicians after chart review. Univariate comparisons were performed to assess the impact of frailty on primary and secondary outcome measures. Normally distributed continuous data were reported as means with standard deviations (SD) and compared using Student's t-test. Non-normally distributed continuous data were reported as medians with interquartile ranges (IQR) and compared using Mann–Whitney U. Categorical variables were compared using Pearson's Chi-square test for independence where cells contained n>5 and Fisher's exact for comparisons where cell count was n≤5. Multivariate logistic regression was used to describe factors associated with hospital, 6-month and 12-month mortality. Cox proportional hazard regression was employed to determine hazard ratios for 6-month, 12-month and 5-year mortality. Covariates of significance were identified a priori for all regressions. Results were presented as odds ratios/hazard ratios with 95% confidence intervals (CI). A p-value <0.05 was considered significant for all statistical tests. Analyses were performed using Stata 14 (StataCorp, College Station, Texas).

RESULTS

529 patients were enrolled, with a mean (SD) age of 67 (9) years, 26% (n=137) were female, 79% (n=418) lived with a spouse, 54% (n=284) were unemployed/retired, 55% (n=288) reported receiving help at home. Isolated valve procedures (41%; n=219), followed by isolated coronary artery bypass grafting (CABG) surgery (38%; n=202), and combined CABG and valve surgery (17%; n=91) were most common. The median (IQR) EuroSCORE was 5 (3-7) and 6% (n=32) of patients had prior cardiac surgery. (Table 1; Figure 2; Figure 3)

The prevalence of frailty was 10% (n=51, 95% CI, 7-13%), ranging from 2% in those <55 years to 33% in those ≥85 years. (Table 1; Figure 4) The median (IQR) duration of stay was 1 (1-3) day and 7 (6-11) days in CVICU and in hospital, respectively. Mortality in CVICU was 1% (n=4; 95% CI, 0.3-2%), in hospital was 2% (n=10; 95% CI, 1-4%) and at 5-years post-surgery was 12% (n=66; 95% CI, 10-16%). (Figure 5) Twenty-one patients (4%, 95% CI, 3-6%) were re-admitted to the CVICU during their index hospitalization.

Patient Characteristics Stratified by Frailty Status

Frail patients were older than non-frail patients (median [IQR] 75 [65-80] v. 67 [60-73] years, p<0.001), on more prescribed medications (6 [4-10] v. 5 [3-7], p<0.001), had higher EuroSCORE (mean [SD] 8 [3] v. 5 [3], p<0.001), longer timed 'Up and Go' measures (18 [11-27] v. 9 [8-12] seconds, p<0.001), received more combined valve and CABG surgery (29% v. 16%, p=0.02) and less isolated CABG (22% v. 40%, p=0.01). Frail patients had more comorbid

diseases, and were more likely to have reported a recent history of falls (35% v. 11%, p<0.001) than non-frail patients. (Table 1)

Complications of Cardiac Surgery by Frailty Status

Post-operative complications were more common in frail compared to non-frail patients. Frail patients were more likely to suffer post-operative bleeding (16% v. 5%, p=0.002) and acute kidney injury (14% v. 5%, p=0.007). Frail patients received more interventions and required greater escalation of intensity of treatment, including return to the operating theatre (10% v. 3%, p=0.02), receipt of blood products (53% v. 20%, p<0.001), re-intubation (12% v. 5%, p=0.03), enteral nutrition by feeding tube (20% v. 5%, p<0.001) and renal replacement therapy (12% v. 1%, p<0.001) compared to those who were non-frail. (Table 2)

Patient Outcomes

Hospital (10% v. 1%, adjusted-OR 6.33, 95% CI, 1.2-34.7) and CVICU (4% v. 0.4%, adjusted-OR 4.89, 95% CI, 0.6-40.0) mortality was greater in frail patients. The adjusted-hazard ratio [a-HR] at 6-months (10% v. 2%; a-HR 6.02, 95% CI, 1.7-20.2), at 12-months post-surgery (12% v. 3%; a-HR 4.34, 95% CI, 1.5-12.2) and 5-years (25% v. 11%; a-HR 2.12, 95% CI, 1.1-4.1) was greater for the frail compared to non-frail patients. Cox proportional hazard analysis using 3-level CFS score strata showed gradient increases in mortality at 1-year with greater frailty scores. (Table 3; Table 4; Supplementary Table 1)

Health Services Use

All measures of health services use were greater in frail compared to non-frail patients. Median (IQR) duration of mechanical ventilation (1 [0.5-1] v. 0.5 [0.4-1] days, p<0.001) and vasoactive medication administration were longer (1 [0.3-3] v. 0.5 [0.0-1] days, p<0.001) in frail patients. The proportion of patients receiving prolonged mechanical ventilation (>48 hours) was greater in frail patients compared to non-frail (9 [18%] v. 15 [3%], p<0.001). Median (IQR) duration of stay in CVICU (3 [1-5] v. 1 [1-3] day, p<0.001) and subsequent hospital stay following CVICU (9 [6-17] v. 5 [4-7] days, p<0.001) were longer for frail patients. Unplanned re-admissions to CVICU during the index hospital stay were also more common in frail patients (10% v. 3%, p=0.04). (Table 5)

Discharge Disposition

At the time of discharge from hospital, frail patients were more likely to go to a sub-acute/rehabilitation centre (20% v. 4%, p<0.001), were newly admitted to a lodge/facility (6% v. 1%, p=0.04), and were less likely to go home directly (65% v. 94%, p<0.001) compared to non-frail patients. (Table 3)

Health Related Quality of Life

Frail patients reported lower mean (SD) EQ-VAS at baseline (46 [19] v. 60 [20], p<0.001) and 12-months (60 [22] v. 76 [15], p<0.001) compared to their non-frail counterparts; however, the

mean difference (MD) was similar (MD=1, 95% CI, -5-8, p=0.68) between frail and non-frail survivors. (Table 3)

INTERPRETATION

In this prospective cohort study of patients ≥50 years of age referred for cardiac surgery, frailty was present in 10% and was associated with longer recovery and less favorable outcomes. A remarkable finding of this study was the gradient increase in mortality, as demonstrated by the hazard ratio incorporating 3-level measures of frailty compared to 2-level at 6-months and 12-months after surgery.

Implications for Clinicians and Policy-makers

Pre-operative Opportunities to Modify the Impact of Frailty

Frailty screening prior to surgery presents an opportunity to understand and address the contributors and potentially modify the impact of frailty on adverse events, duration of stay and discharge disposition.(23) Innovative care pathways could ensure vulnerable patients have the best opportunity for recovery by applying interventions tested pre-operatively on patients across a wide spectrum of community and acute care settings.(24,25) Although frailty-friendly pathways already exist for many non-cardiac surgical interventions (e.g., colorectal procedures(26), hip and knee arthroplasty(27)) cardiac surgical services have largely focused on post-operative targets (e.g., early extubation, mobilization)(28) to reduce duration of ICU and subsequent acute hospital stay. A recent study describes a comprehensive (pre-surgery, intraoperative and post-surgery) enhanced recovery after cardiac surgery pathway targeting all non-emergency adult patients; however, this study did not specifically address frailty.(24) Further potential exists for comprehensive care pathway development that includes identification of frailty as a key factor in the pre-surgery phase, triggering involvement of specialist services to

enhance recovery for patients living with frailty. Oversight by specialists in geriatric medicine, exercise physiology, nutrition, physical therapy and occupational therapy could yield meaningful pre-surgical care plans focused on the domains driving frailty.(24,29-35)

Consent for surgery should acknowledge how frailty modifies the risk of adverse events and can translate into longer than expected recovery, to better inform and empower patients and caregivers in the decision-making process to ensure autonomy is respected and realistic expectations are clear.(2,36-39) In light of the elevated risks associated with frailty, pre-operative discussions should include frailty-related risk of adverse events following surgery, mortality, and potential loss of functional autonomy and independence. These details should be reconciled with individual symptoms and with what risk or trade-offs are acceptable to the patient.

Post-operative Opportunities to Modify the Impact of Frailty

In addition to routine cardiac rehabilitation, post-ICU hospital stays should address physical and cognitive disabilities associated with surviving critical illness.(40,41) Cardiac surgery patients who accumulate further deficits during their hospitalization need devoted attention to mitigate the long-term effects of new deficits contributing to worsening frailty (i.e., geriatric medicine referral). One reassuring finding in our study aligns with findings of recent studies where patients with frailty prior to cardiac surgery have seen improvements in their quality-of-life.(42,43) Sustaining gains requires communication at transitions in care to ensure continued follow-up of significant deficits after discharge from acute care.

Future Research Potential

The findings of this study support prior work describing the substantial effect of frailty on cardiac surgery outcomes, and potential for value in adding a frailty indicator to prospective risk stratification.(23,44,45) Although mobility (EuroSCORE) and gait speed (Society of Thoracic Surgeons) have been acknowledged in recent updates, the addition of a comprehensive frailty indicator to existing cardiac surgery risk scoring instruments is urgently needed.(23,31,44)

For health system planners, frailty as a meaningful and measurable confounder could inform the adjusted estimates required to adequately plan for every phase of cardiac surgery care. The addition of frailty to administrative databases and registries, as a routinely calculated or clinically assessed risk factor is a topic that requires more investigation.

Limitations of the Study

This study is noteworthy for its comprehensive collection of prospective pre-operative validated frailty measures, risk factors, peri-operative clinical course, post-operative complications and long-term objective outcomes for patients living with frailty on a provincial scale.

The study does have several limitations. The CFS instrument was derived and validated in the Canadian ambulatory population ≥65 years of age and has not been evaluated against a

comprehensive geriatric assessment in the cardiac surgery setting. Although previous studies have tested the reliability of trained research staff determining CFS scores,(17,18) we did not measure the inter-rater reliability in this study. Our study may be predisposed to selection bias due to no available information on the frailty status of patients who may have been referred for cardiac surgery but declined or were counselled not to undergo surgery. Generalizability of these results may be limited due to the acuity within cardiac surgical programs in the study sites in comparison to other regions with differing program capabilities and population demographics.

Conclusion

Frailty was observed in 10% of the adults ≥50 years old referred for cardiac surgery. The presence of pre-operative frailty was associated with a higher risk of morbidity, mortality and health services use. These findings suggest that routine frailty screening could provide an opportunity to better inform patients, families, caregivers, health professionals and health system administrators about outcomes after cardiac surgery and reengineer care pathways to better plan for complex care after surgery.

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Supplementary Data

Table 1. Baseline characteristics of cohort, stratified by Clinical Frailty Scale (CFS) score.

Characteristic	**Overall (n=529)**	**CFS ≥5 (n= 51,10%)**	**CFS ≤4 (n= 478, 90%)**	**p-value**
CFS pre- surgery (median,IQR)	3 (3-4)	5 (5-6)	3 (5-6)	<0.001
Sex, female	137 (26)	26 (51)	111 (23)	<0.001
Age (median; IQR)	67 (60-74)	75 (65-80)	67 (60-73)	<0.001
Age <60	124 (23)	7 (14)	117 (24)	0.08
Age 60-69	198 (37)	10 (20)	188 (39)	0.01
Age 70-79	154 (29)	19 (37)	135 (28)	0.18
Age 80-89	53 (10)	15 (29)	38 (8)	<0.001
Employed or Volunteer	242 (46)	9 (18)	233 (49)	<0.001
Independent living	240 (46)	17 (33)	223 (47)	0.07
Education Post-Secondary	290 (56)	35 (71)	255 (54)	0.02
Married	417 (79)	38 (75)	380 (80)	0.39
EuroSCORE (mean,SD)	5 (3)	8 (3)	5 (3)	<0.001
Parsonnet Score (mean,SD)	14 (8)	22 (10)	13 (8)	<0.001
Charlson Comorbidity Index (median; IQR)	1 (0-3)	2 (0-4)	1 (0-3)	0.04
Timed 'Up & Go' (median; IQR), seconds	10 (8-12)	18 (11-27)	9 (8-12)	<0.001
Timed 'Up & Go' ≤19 seconds	469 (91)	24 (56)	445 (95)	<0.001
Surgery Type				
CABG only	202 (38)	11 (22)	191 (40)	0.01
Valve only	219 (41)	24 (47)	195 (41)	0.39
Combined CABG & Valve	91 (17)	15 (29)	76 (16)	0.02
Myomectomy/ASD/Myxoma	9 (2)	0 (0)	9 (2)	-
Aorta only	8 (2)	1 (2)	7 (1)	0.78
Pre-surgical Conditions				
Cardiac				
CHF	80 (15)	17 (33)	63 (13)	<0.001
PVD	58 (11)	10 (20)	48 (10)	0.04
Pacemaker or AICD	18 (3)	6 (12)	12 (3)	0.001
Aortic valve stenosis	227 (43)	31 (61)	196 (41)	0.01
Previous cardiac surgery	32 (6)	3 (6)	29 (6)	0.96
Pulmonary arterial hypertension	47 (9)	11 (22)	36 (8)	0.001
Non-cardiac				
PUD	30 (6)	5 (10)	25 (5)	0.20
Malignancy	68 (13)	13 (26)	55 (12)	0.01
Rheumatoid arthritis	81 (15)	19 (37)	62 (13)	<0.001
Neurologic dysfunction*	85 (16)	16 (31)	69 (14)	0.002
Creatinine, Pre-Surgery (mean,SD)	91 (47)	97 (39)	91 (48)	0.20
Chronic kidney disease†	6 (1)	2 (4)	4 (1)	0.11
BMI (Mean, SD)	30 (6)	31 (6)	30 (6)	0.45
BMI Abnormal‡	232 (44)	25 (49)	207 (43)	0.43
History of Falls	69 (13)	17 (35)	52 (11)	<0.001
Memory Loss	146 (28)	20 (39)	126 (26)	0.05

Previous 12-month Hospitalizations	128 (25)	22 (45)	106 (23)	0.001
Prescribed medications Median (IQR)	5 (3-7)	6 (4-10)	5 (3-7)	<0.001
On ≤5 prescribed medications	292 (55)	36 (71)	256 (54)	0.02
Peri-operative Course				
Aorta cross-clamp (median,IQR), minutes	86 (62-114)	89 (71-118)	86 (60-113)	0.35
Cardio-pulmonary bypass (median,IQR), minutes	109 (83-144)	111 (90-162)	109 (82-143)	0.35

Note. Data are presented as n (%) unless otherwise indicated.
* Neurologic dysfunction: Disease severely affecting ambulation or day-to-day functioning.
† Creatinine >200 pre-surgery.
ǂ BMI abnormal if <19 or >29.
Abbreviations: CABG coronary artery bypass graft; ASD atrial septal defect; CHF congestive heart failure; PVD peripheral vascular disease; AICD automated implanted cardioverter/ defibrillator; PUD peptic ulcer disease; BMI body mass index.

Table 2. Post-operative complications, stratified by Clinical Frailty Scale (CFS) score.

Post-op Complications	**Overall (n= 529)**	**CFS ≥5 (n= 51,10%)**	**CFS ≤4 (n= 478, 90%)**	**p-value**
Atrial fibrillation	133 (25)	15 (29)	118 (25)	0.46
Bleeding	31 (6)	8 (16)	23 (5)	0.002
Atrioventricular Block	11 (2)	0 (0)	11 (2)	-
Delirium	41 (8)	7 (14)	34 (7)	0.09
Acute kidney injury*	29 (5)	7 (14)	22 (5)	0.01
Acute myocardial infarction	1 (0.2)	0 (0)	1 (0.2)	-
Post-op Interventions	**Overall (n= 529)**	**CFS ≥5 (n= 51,10%)**	**CFS ≤4 (n= 478, 90%)**	**p-value**
Transfusion	121 (23)	27 (53)	94 (20)	<0.001
Left ventricular assist device	1 (0.2)	1 (2)	0 (0)	-
Cardiac catheterization	3 (1)	2 (4)	1 (0.2)	0.03
Pulmonary arterial catheter	1 (0.2)	1 (2)	0 (0)	-
Cardiac tamponade	4 (1)	1 (2)	3 (1)	0.33
Epicardial pacing	117 (22)	9 (18)	108 (23)	0.48
Pacer wire insertion	114 (22)	12 (24)	102 (21)	0.71
Intra-aortic balloon pump	3 (1)	1 (2)	2 (0.4)	0.16
Defibrillation	16 (3)	2 (4)	14 (3)	0.66
Cardioversion	27 (5)	5 (10)	22 (5)	0.17
Cardiopulmonary resuscitation	2 (0.4)	1 (2)	1 (0.2)	0.18
Re-exploration in operating theatre	20 (4)	5 (10)	15 (3)	0.02
Extracorporeal membrane oxygenation	0	0	0	-
Re-intubate	28 (5)	6 (12)	22 (5)	0.03
Tracheostomy	7 (1)	1 (2)	6 (1)	0.51
Total parenteral nutrition	6 (1)	2 (4)	4 (1)	0.11
Tube feeds	36 (7)	10 (20)	26 (5)	<0.001
Endoscopy	3 (1)	2 (4)	1 (0.2)	0.03
Gastro-intestinal surgery	0	0	0	-

Renal replacement therapy	9 (2)	6 (12)	3 (1)	<0.001
Note: Data are presented as n (%) unless otherwise indicated. All comparisons Chi-square tests of independence. * Creatinine >200 pre-surgery.				

Table 3. Outcomes of cardiac surgery, stratified by Clinical Frailty Scale (CFS) score.

Outcome	**Overall (n= 529)**	**CFS ≥5 (n= 51,10%)**	**CFS ≤4 (n= 478, 90%)**	**OR (95% CI)**
Mortality				
CVICU mortality	4 (1)	2 (4)	2 (0.4)	4.89 (0.60-40.03)
Hospital mortality	10 (2)	5 (10)	5 (1)	6.33 (1.15-34.71)
6-month mortality	12 (2)	5 (10)	7 (1)	4.03 (0.85-18.96)
1-year mortality	18 (3)	6 (12)	12 (3)	2.86 (0.77-10.69)
5-year mortality	66 (12)	13 (25)	53 (11)	1.68 (0.74-3.84)
Death at any time during follow-up (≤7 years)	92 (17)	15 (29)	77 (16)	1.22 (0.56-2.69)
Hospital Discharge Disposition				**p-value**
Home independent	54 (10)	1 (2)	53 (11)	0.04
Home with help	428 (81)	32 (63)	396 (83)	<0.001
Home (independent or with help)	482 (91)	33 (65)	449 (94)	<0.001
Subacute care	28 (5)	10 (20)	18 (4)	<0.001
Lodge or facility	9 (5)	3 (6)	6 (1)	0.04
Health Related Quality of Life				**p-value**
EQ VAS at baseline (mean,SD)	58 (21)	46 (19)	60 (20)	<0.001
EQ VAS 6-month (mean,SD)	72 (17)	62 (15)	73 (16)	<0.001
EQ VAS 12-month (mean,SD)	75 (17)	60 (22)	76 (15)	<0.001
Note. Data are presented as n (%) unless otherwise indicated.				

Table 4. Adjusted hazard ratio for death within one year after cardiac surgery, stratified by Clinical Frailty Scale (CFS) score.

Cox proportional hazards model	**Pre-Surgery CFS Score**	**Hazard Ratio**	**95% Confidence Interval**
CFS 2-level, Age, Sex	CFS 1-4 CFS 5-9	1.00 (ref) 4.59	 1.58-13.28
CFS 2-level, Age, Sex, EuroSCORE log	CFS 1-4 CFS 5-9	1.00 (ref) 4.34	 1.54-12.19
CFS 3-level, Age, Sex	1-3 4 5-9	1.00 (ref) 2.25 7.11	 0.70-7.21 1.97-25.71
CFS 3-level, Age, Sex, EuroSCORE log	1-3 4 5-9	1.00 (ref) 1.86 6.06	 0.56-6.21 1.71-21.51
CFS 4-level, Age, Sex	CFS 1-3 CFS 4 CFS 5 CFS 6-9	1.00 (ref) 2.24 5.94 11.85	 0.70-7.18 1.46-24.13 2.11-66.69
CFS 4-level, Age, Sex, EuroSCORE log	CFS 1-3 CFS 4 CFS 5 CFS 6-9	1.00 (ref) 1.81 4.80 12.86	 0.54-6.09 1.20-19.16 2.30-72.05

Table 5. Health services use, stratified by Clinical Frailty Scale (CFS) score.

Outcome	Overall (n= 529)	CFS ≥5 (n= 51,10%)	CFS ≤4 (n= 478, 90%)	p-value
Duration of Stay				
CVICU stay (median,IQR), days	1 (1-3)	3 (1-5)	1 (1-3)	<0.001
Post-CVICU hospital stay (median,IQR), days	5 (4-8)	9 (6-17)	5 (4-7)	<0.001
Pre-operative hospital stay (mean,SD), days	1 (6)	2 (5)	1 (6)	0.01
Post-operative hospital stay (median,IQR), days	7 (6-11)	12 (8-25)	7 (6-10)	<0.001
Readmission to ICU	21 (4)	5 (10)	16 (3)	0.04
Health Services Use				
Mechanical ventilation (MV) (median,IQR), days	1 (0.4-1)	1 (0.4-1)	0.5 (0.4-1)	<0.001
MV ≤48 hours	505 (95)	42 (82)	463 (97)	<0.001
MV 49-72 hours	11 (2)	3 (6)	8 (2)	0.05
MV 73-120 hours	6 (1)	3 (6)	3 (0.6)	<0.001
MV >120 hours	7 (1)	3 (6)	4 (0.8)	0.003
Vasoactive medication duration (median,IQR), days	455 (86) 1 (0.2-1)	45 (88) 1 (0.3-3)	410 (86) 1 (0-1)	0.63 <0.001
Note. Data are presented as n (%) unless otherwise indicated.				

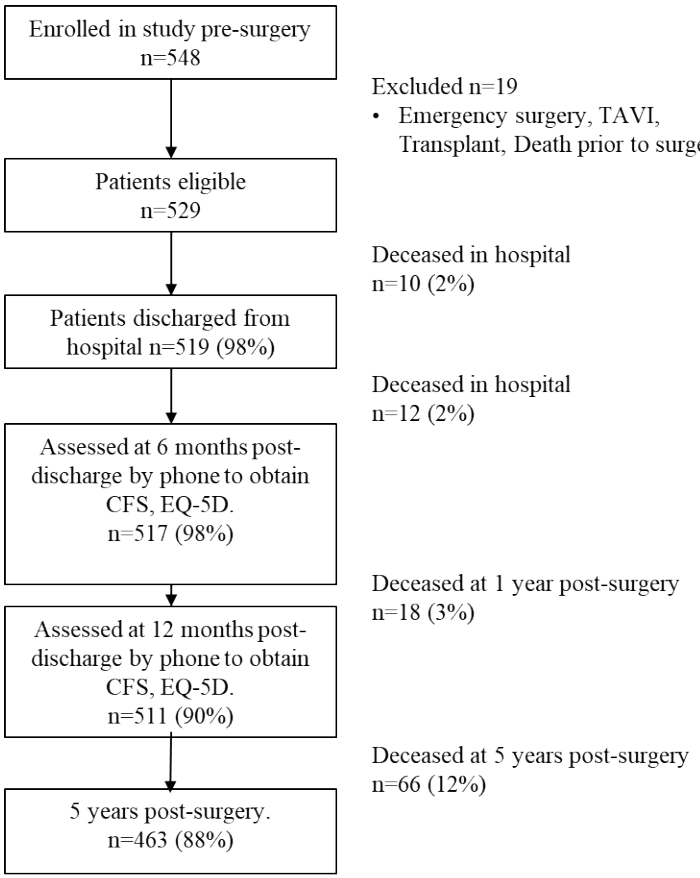

Figure 1. Patient selection for cardiovascular surgery study cohort.

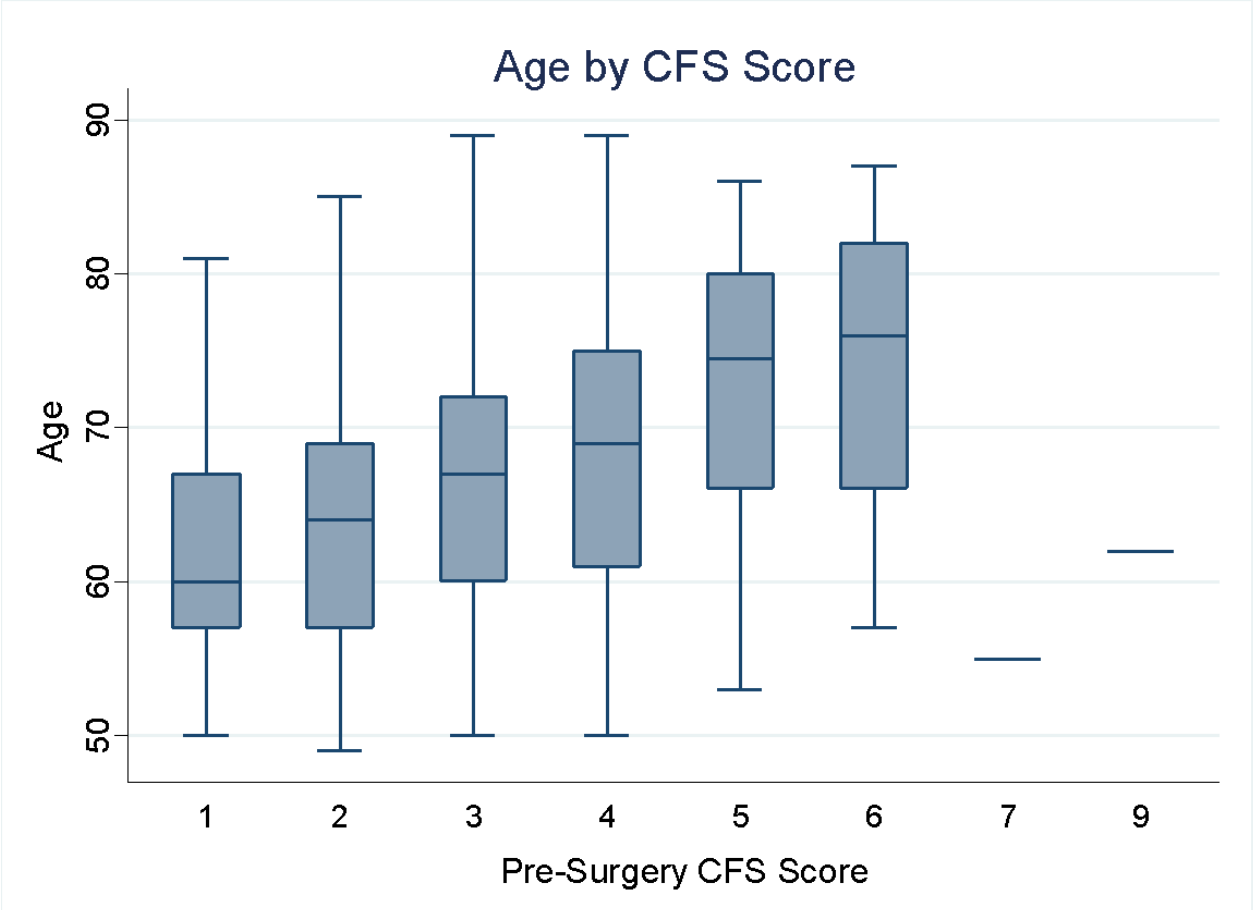

Figure 2. Distribution of age across pre-surgery Clinical Frailty Scale (CFS) scores.

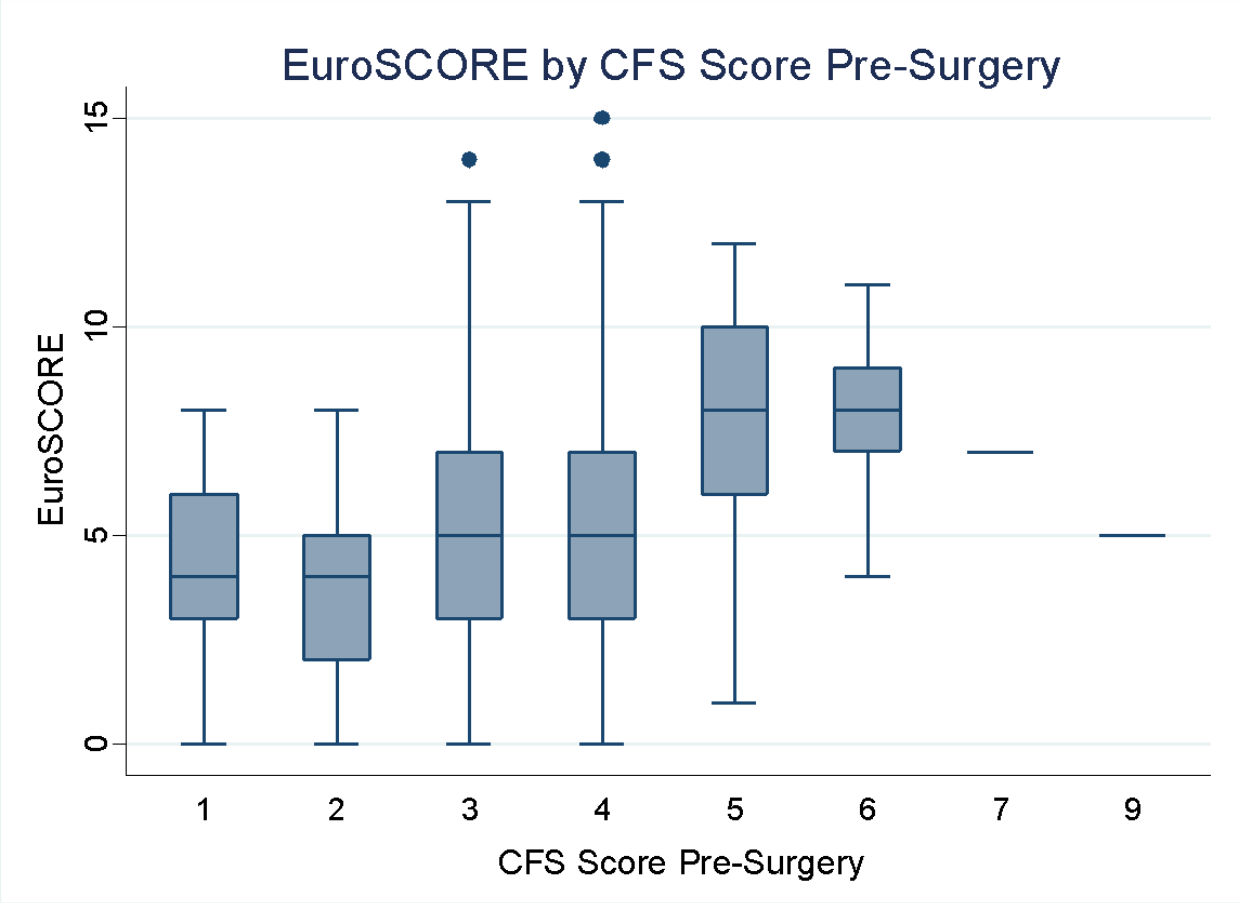

Figure 3. Distribution of EuroSCORE (standard) across pre-surgery Clinical Frailty Scale (CFS) scores.

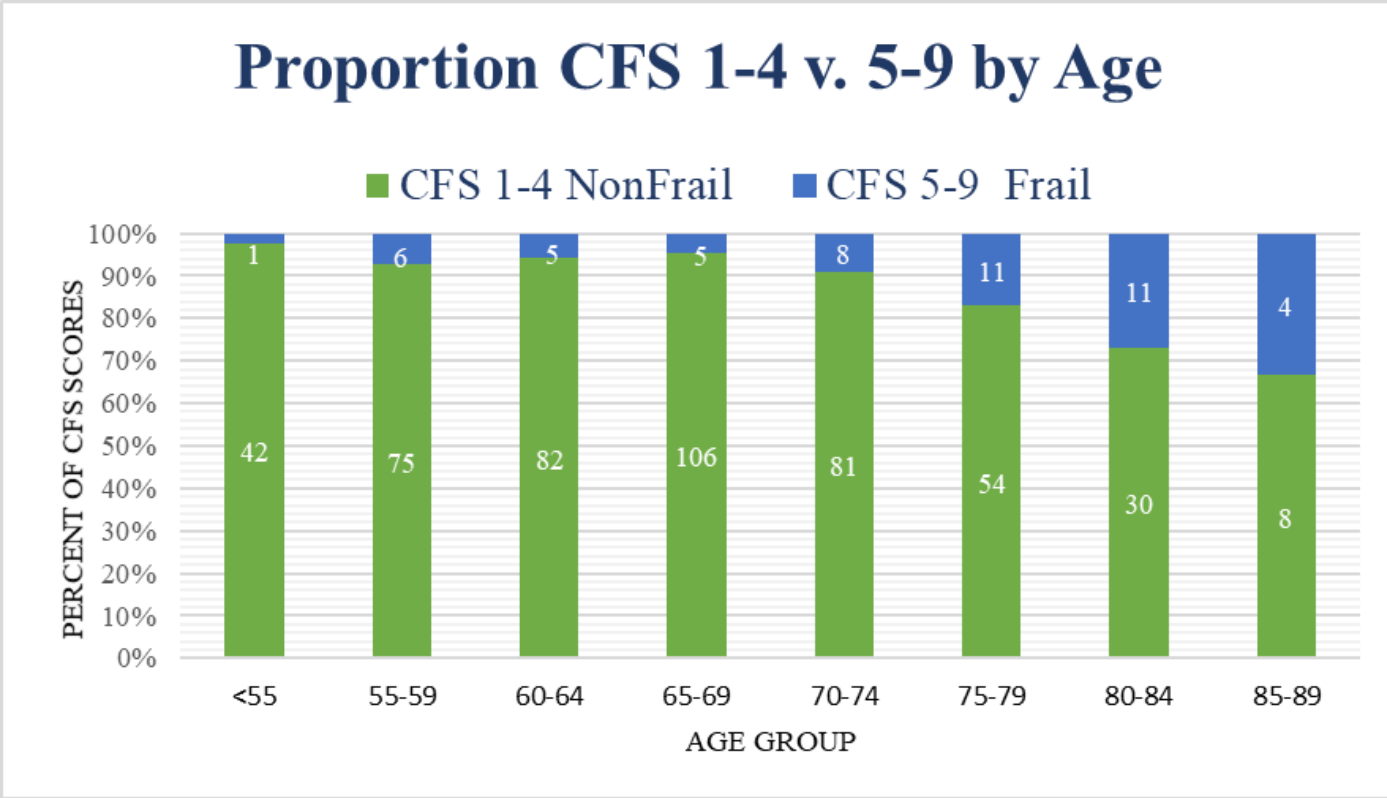

Figure 4. Prevalence of pre-surgery frailty (CFS 5-9) across age groups.

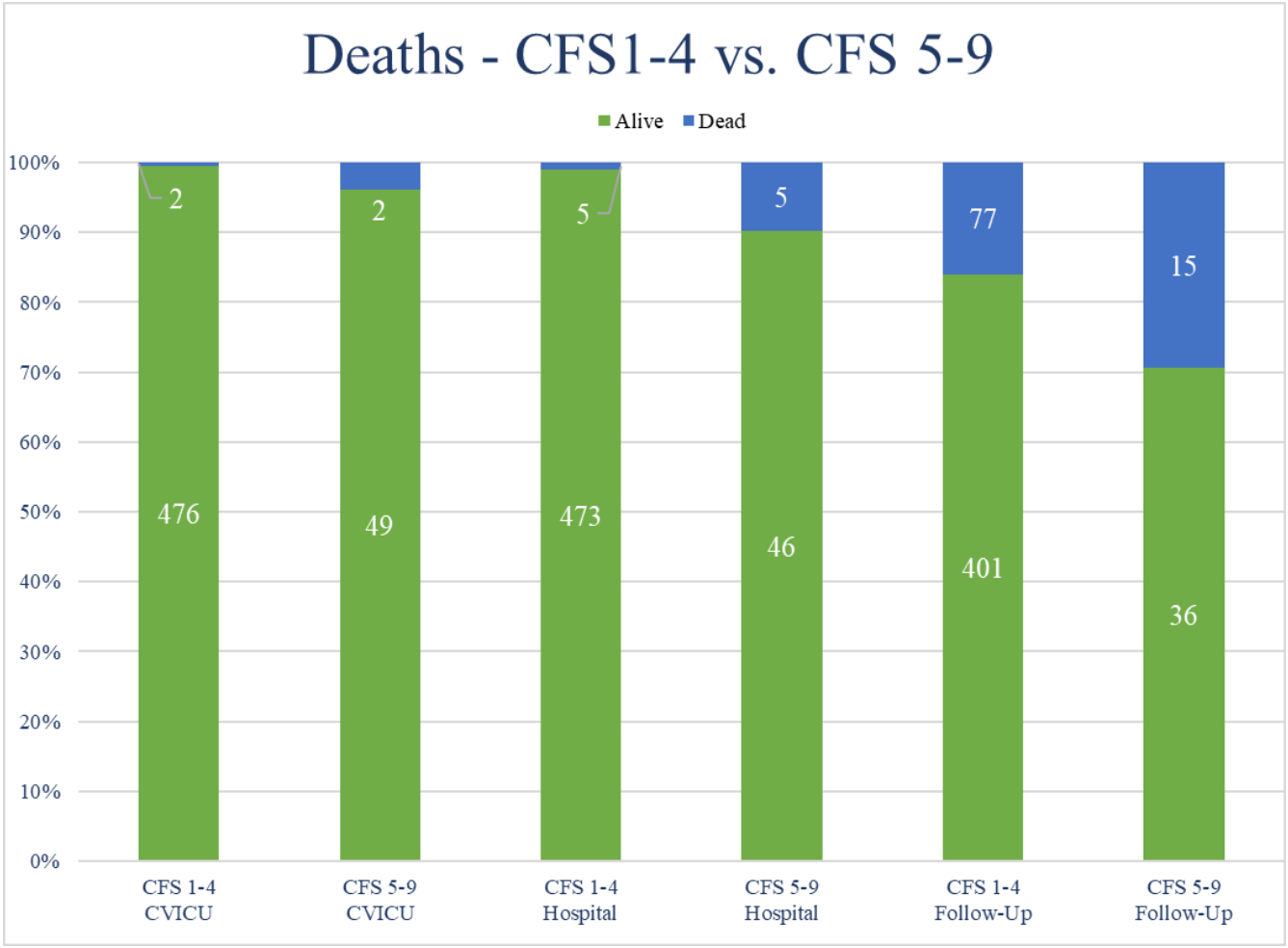

Figure 5. Number of deaths in cohort during ≤7-year follow-up, stratified by Clinical Frailty Scale (CFS) score non-frail (CFS 1-4) vs. frail (CFS 5-9).

Supplementary Table 1. Adjusted hazard ratio for death within six months after cardiac surgery, stratified by Clinical Frailty Scale (CFS) score.

Cox proportional hazards ratio model	**CFS Score**	**Hazard Ratio**	**95% Confidence Interval**
CFS 2-level, Age, Sex	CFS 1-4 CFS 5-9	1.00 (ref) 5.96	 1.72-20.64
CFS 2-level, Age, Sex, EuroSCORE log	CFS 1-4 CFS 5-9	1.00 (ref) 6.02	 1.79-20.23
CFS 3-level, Age, Sex	1-3 4 5-9	1.00 (ref) 2.00 8.63	 0.44-9.13 1.84-40.50
CFS 3-level, Age, Sex, EuroSCORE log	1-3 4 5-9	1.00 (ref) 1.51 7.50	 0.30-7.48 1.64-34.35