Outcomes Related to Frailty in Older Patients Referred for Cardiac Surgery

by

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Abstract

Objective

A substantial proportion of patients admitted to intensive care units (ICU) are frail; however, its epidemiology at a population-level has not been explored. Following implementation of a validated frailty measure into a provincial ICU clinical information system, we sought to retrospectively describe the population-based prevalence, correlates and outcomes associated with frailty in patients admitted to ICU.

A second, prospective cohort study investigated patients referred for cardiac surgery in Alberta, all of whom are admitted to ICU after surgery. A provincial perspective was of interest, in order to establish a baseline description of the relationship between frailty and the clinical and cost outcomes associated with cardiac surgery.

Methods

Data were captured using multiple data sources. eCritical Alberta informed a retrospective cohort study of all Alberta adult ICU admissions January 2016 through June 2017, using the Clinical Frailty Scale (CFS) score assigned by admitting physicians to measure frailty (CFS ≥5).

A further prospective cohort study focussed on patients ≥50 years of age referred for non-emergent cardiac surgery in Alberta November 2011 through March 2014. Patients were assessed pre-operatively for frailty (CFS ≥5) and data were captured on socio-demographics, baseline functional status, comorbid disease and health-related quality-of-life (HRQL). Postoperatively, patients were followed to assess CFS, health services use, vital status and

HRQL (EuroQol-5-Dimension-3-Level) allowing for assessment of quality adjusted life years (QALYs). Public payer costs attributable to frailty were calculated in a propensity score matched difference-in-difference (DID) model comparing annual health services costs post-surgery to one-year pre-surgery. Exposure was defined as CFS score ≥5. Primary outcomes were hospital mortality; health services duration and intensity; attributable cost of frailty.

Results

In general ICU admissions across the province 15,238 (81%) patients were assigned a CFS score at ICU admission. Of these, 28% (95% CI, 27-28%) were frail. Compared to non-frail patients, frail patients were older (mean [SD] 63[15] vs. 56[17] years, p<0.001), more likely male (54% vs. 46%, p<0.001), had higher APACHE II scores (22[8] vs. 17[8], p<0.001), received less mechanical ventilation (62% vs. 68%, p<0.001) and vasoactive therapy (24% vs. 57%, p<0.001); but more non-invasive ventilation (22% vs. 9%, p<0.001). Frail patients had greater hospital mortality (23% vs. 9%; adjusted-OR, 1.80; 1.64-2.05), longer ICU (4[2-8] vs. 3[2-6] days, p<0.001) and hospital stay (16[8-36] vs. 10[5-20] days, p<0.001) compared to non-frail patients.

In the cardiac surgery cohort (n=529) mean (SD) age was 67 (9) years, 26% were female, and the prevalence of frailty was 10% (n=51; 95% CI, 7%-13%) with median (IQR) CFS 3 (3–4). Compared to nonfrail patients, those with frailty were older (73[9] vs. 67[9], p<0.001), more frequently female (51% vs. 23%, p<0.001), received valve surgery (76% vs. 57%, p=0.01), and had higher median (IQR) EuroSCORE (8[6–9] vs. 5[3–7], p<0.001). Pre-operatively, frail patients were more likely to require help walking (43% vs. 5%, p<0.001) and report recent falls (35% vs. 11%, p<0.001). Post-operatively frail patients had longer median (IQR) duration of stay

in ICU (3[1–5] vs. 1[1–3] days, p<0.001) and hospital (12[8-25] vs. 7[6-10] days, p<0.001). ICU mortality (4% vs. 0.4%; adjusted-OR, 4.89; 95% CI, 0.60-40.03) and hospital mortality (10% vs. 1%; adjusted-OR, 6.33; 95% CI, 1.15-34.71) were elevated in the frail group.

Among patient referred for cardiac surgery, median (IQR) health services costs for frail compared to non-frail patients were higher overall ($387,360 [$187,254-$613,684] vs. $178,860 [$136,779-$265,611]; p<0.001), in the first year post-surgery ($200,709 [$146,177-$486,852] vs. $147,730 [$100,674-$177,025]; p<0.001). Fewer QALYs were realized at one year for frail vs. non-frail patients (0.71 [0.57-0.77] vs. 0.82 [0.75-0.86]; p<0.001). The attributable cost of frailty in the first post-operative year was $57,836 (SE $44,104).

Conclusion

A validated measure of frailty implemented at the population-level revealed a 28% prevalence of frailty among adult ICU patients and 10% among patients referred for cardiac surgery. Frailty was associated with additional health services duration and intensity as well as greater risk of adverse events. Frailty, along with its associated health services costs and patient reported HRQL may have relevance for prognostic and recovery purposes, to optimally inform patients, caregivers and clinicians about risks associated with critical illness, while cost outcomes may be of specific interest to health services planners and decision makers.

Keywords: critical illness, cardiac surgery, frail, mortality, cost comparison, adult

Preface

This thesis is an original work by Carmel L. Montgomery. The research project, of which this thesis is a part, received research ethics approval from the University of Alberta Research Ethics Board, Project Name "Outcomes of Cardiac Surgery for older patients with frailty", No. Pro00074770, May 17, 2018 and Project Name "Measuring Frailty in Critical Illness: Province-Wide Implementation of the Clinical Frailty Scale (CFS) Score in a Population-Based Electronic Medical Record System (eCritical) in Alberta", No. Pro00056591, July 8, 2015.

The research conducted for this thesis forms part of a provincial research collaboration, led by Professor S.M. Bagshaw at the University of Alberta. Manuscript composition and data analysis in all chapters are my original work.

Chapter 2 of this thesis has been published as C.L. Montgomery, D.J. Zuege, D.B. Rolfson, D. Opgenorth, D. Hudson, H.T. Stelfox, and S.M. Bagshaw, "Implementation of Population-Level Screening for Frailty Among Patients Admitted to Adult Intensive Care in Alberta, Canada," in the Canadian Journal of Anesthesia, vol. 66, issue 11, 1310-1319. I was responsible for the data acquisition and analysis as well as the manuscript composition. D.J. Zuege, D.B. Rolfson, D. Opgenorth, D. Hudson, and H.T. Stelfox contributed to manuscript edits. S.M. Bagshaw was the supervisory author and was involved with concept formation, data acquisition, manuscript composition and edits.

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Chapter 1. Introduction

1.1 Background & Problem to be Addressed

The challenges associated with our ageing population have arrived as predicted.[1] Frailty has been identified as the most common condition leading to death among community-dwelling elderly persons.[2] It is described as an age-related multidimensional syndrome contributing to an accumulation of deficits and exaggerated vulnerability to adverse outcomes following stressful events.[1, 3] Rapid growth in the older demographic and concomitant increased prevalence of frailty have been linked to greater health services use, increased mortality, major morbidity, loss of independence and decline in overall quality of life.[4-6] Frailty is dynamic in nature and usually associated with a spiral of decline rather than improvement.[1] With such unfavorable outcomes, it is imperative to identify patients whose frailty puts them at risk of hospital admission, critical illness or complex and invasive procedures (e.g., cardiac surgery). Strategies to identify pre-existing frailty among patients considered for admission to the intensive care unit (ICU) are necessary to better inform patients, their families, clinicians and administrators about the risk of suboptimal outcomes, post-ICU care and rehabilitative needs to avoid further decline.

1.2 Defining Frailty

Frailty has been established as a predictor of survival in healthy individuals and correlated with treatment intensity, health resource utilization and mortality in critical illness, outperforming chronological age.[6-8] Although not an inevitable consequence of ageing, frailty is strongly correlated with age.[3] It can be considered simultaneously as a state and syndrome. Frailty as a state is described as an exaggerated vulnerability to stressors due to reduced reserve, associated with age-related accumulation of deficits. The lifetime accumulation of discrete deficits results in vulnerability and an inability to withstand stress, even if the individual deficits would not define the frail state. The syndrome of frailty remains latent in a dynamic, nonlinear system of worsening vulnerability until stressed.[1]

The observable result of deficit accumulation is the syndrome of frailty. Different models have been proposed with regard to formally identifying frailty. The biological vulnerability, or phenotype model describes physical characteristics thought to be biologically linked.[9] Multiple judgement-based models allow for individual assessment of frailty severity. In comparison, the mathematical cumulative deficit model highlights frailty where the number of non-specific deficits, rather than the nature of deficits, are considered at an individual level but allows for screening to occur at a population level.[10] Comparisons of models have demonstrated an overlap in frailty identification and statistical convergence, supporting the argument that state and syndrome are a unified construct.[1, 11]

1.2.1 Assessment of and Measurement of Frailty

The prevalence of frailty within closely aligned age strata, even in the very old, can be variable.[12] Since frailty was initially described,[9, 13, 14] a number of measurement instruments have been developed. The instruments are generally classified as rule-based, clinical judgement-based, performance or multidimensional.[15] Instruments have primarily been developed for use in the community or outpatient setting, demonstrating limited utility in acute care settings when tested. Many of these validated tools are challenging to apply in prospective routine use at the bedside, or in a pre-operative assessment setting due to being time-consuming, requiring specialized training or comprehensive data sets.[16]

Rule-Based Instruments

The original method of rule-based determination of phenotype frailty was developed from the Cardiovascular Health Study cohort of 5,317 participants aged 65 years or older.[9] Core elements associated with a standardized phenotype for frailty were described using results from lengthy assessment of physical and cognitive function in addition to laboratory blood results. The methodology was the first example of translational research to support the objective measure of a frailty syndrome with predictive validity. Frailty was defined by the presence of three or more of the following physical features: weight loss, weakness, exhaustion, low activity level and slow gait speed. The measures and methods in the study provided a foundation for future work in developing standardized scoring instruments for community-dwelling individuals at risk of frailty.[9]

Judgement-Based Instruments

The judgement based instrument most commonly used to screen for frailty is the Clinical Frailty Scale (CFS), validated using observations from 2,305 patients aged 65 years or older in the Canadian Study on Health and Aging (CSHA). The original 7-point CFS has since expanded to a scale of 1-9.[3] The CFS has advantages as a tool to grade the degree of frailty present in an individual. It is reliable, easy to understand and is simpler to apply compared with other available frailty assessment tools. While the CFS is judgment-based and has some subjectivity; it captures a spectrum of information that transcends several aspects of a patient's pre-morbid health state, including active disease symptoms, mobility, energy level, physical activity, cognitive function and degree of independence performing activities of daily living, providing an accurate global assessment of a patient's frailty.

Frailty Index

The frailty index (FI) approach measures the severity of frailty associated with the number of deficits accumulated by an individual over time. With age it is expected that recovery time slows and the average relative intensity of stresses increases, resulting in accumulation of deficits, and elevated risk for suboptimal health related outcomes.[17-20] Deficits may include disease states, symptoms, signs, disabilities, geriatric syndromes and laboratory abnormalities,[21] becoming significant in defining frailty if their number is sufficiently large as operationalized through the frailty index.[22] Candidate deficits must accumulate with age, confer a health risk, not saturate too early, and collectively represent the whole person. The quotient of actual divided by potential deficits drawn from a database represents the FI score.[21] On an individual level the number of deficits and recovery time may be unpredictable but on a population level it has been shown that deficits accumulate as people age and the recovery time increases with age.[19, 22] The FI provides a reliable method of measuring risk associated with the accumulation of deficits.

In previous studies assessing outcomes associated with frailty in patients with critical illness, the CFS was shown to add discriminatory value for predicting complications including delirium, prolonged hospitalization, mortality and discharge to a skilled nursing or long-term care facility.[23] Accordingly, the CFS was integrated into the admission data collected in all ICUs across the province of Alberta. An evaluation of the feasibility of CFS implementation was timely. A rigorous prospective study of the subgroup of patients referred for cardiac surgery, a known stressor with subsequent ICU admission, was also proposed. The results presented in this dissertation identify the clinical and cost outcomes of patients with frailty who are admitted to ICU in Alberta.

1.3 Critical Illness in Alberta

Critically ill adult patients from across Alberta (and some portions of neighboring provinces and territories) are cared for in one of Alberta's 17 adult intensive care units (ICUs), with approximately 13,000 admissions annually. Most ICUs in the province provide general ICU care for medical and surgical admissions. Approximately 29% of ICU admissions are to specialized cardiac surgery and neurosurgery units.[24] ICU beds are resource-intensive due to the needs of critically ill patients, including specialized staffing models, pharmaceuticals, medical devices and equipment. Compared to other provinces in Canada, Alberta has the fewest adult ICU beds (9.8) per 100,000 population. As demand for limited ICU capacity continues to grow, efficient use of costly ICU beds relies on sound decision-making on the part of patients, caregivers and clinicians. These important decisions can be better informed by evidence from the Alberta context which is inclusive of chronic conditions such as frailty.[25, 26]

Outcomes of Older Adults with Frailty After Critical Illness

Previous research on the prevalence and outcomes of patients admitted to ICU with frailty, as measured using the CFS, in Alberta demonstrated an elevated risk of in-hospital mortality, adverse events, re-admission, functional dependence, physical and cognitive disability and lower quality of life compared to non-frail patients, regardless of age.[6, 24, 27, 28] Compelling evidence that frailty is an important modifier of short and long-term adverse outcomes and considerable use of health services for patients with critical illness led to a project to implement routine capture of the CFS in all ICU admission documentation across the province.[24] The first paper in this dissertation is a follow-up feasibility and epidemiology study following successful implementation of the CFS into the ICU electronic health record (EHR).

1.4 Cardiac Surgery in Alberta

Alberta adult cardiac surgery programs in Edmonton and Calgary perform approximately 2,800 complex open heart surgeries annually.[29, 30] All patients are admitted to ICU following cardiac surgery. Previous publications indicate the mean age of patients was 65 years of age and 24% were women. Cardiac surgeries are generally grouped as isolated coronary artery bypass grafting (CABG, 49%); combined CABG/valvular replacement/repair (8%), and isolated valvular replacement/repair (10%). Of these procedures, 8% were classified as non-urgent and low risk; however, 48% were performed as urgent out-of-hospital referrals; 40% as urgent in-hospital transfers or referrals, and 4% were classified as emergency procedures. Patients undergoing cardiac surgery had estimated median lengths of stay in the ICU and hospital of 2 and 7 days, respectively and provincial risk-adjusted 30-day in-hospital mortality after isolated CABG was 1.4%.[31, 32]

Outcome Prediction After Cardiac Surgery

Prognostication in cardiac surgery has been well researched. Several pre-operative cardiac surgery-specific risk prediction scores, including the European System for Cardiac Operative Risk Evaluation [EuroSCORE] score;[33, 34] Parsonnet score;[35] Society of Thoracic Surgeons [STS] risk score[36] and postoperative illness severity scoring systems such as the Acute Physiology and Chronic Health Evaluation (APACHE) II,[37, 38] and Sequential Organ Failure Assessment (SOFA),[39] have been validated, are commonly used in cardiac surgery and have modeled clinical risk and illness severity to estimate the probability of survival. These scoring systems are largely dominated by preoperative cardiac risk factors, selected comorbid states, pre-operative critical illness and/or additional measures of physiology present prior to surgery. However, these scoring systems do not incorporate factors associated with frailty such as socio-demographic characteristics (e.g. social support, education, income) or measures of pre-hospital functional status, with the exception of the EuroSCORE which incorporates "limited mobility" (defined as severe impairment of mobility secondary to musculoskeletal or neurological dysfunction) as variables in the risk score.[33]

Outcomes of Older Adults with Frailty After Cardiac Surgery

When individuals with frailty are admitted to hospital with injury or illness their likelihood of developing new or worsening disability increases, hazard ratio (HR) 8.9 (95% CI, 7.05-11.22) and 168 (95% CI, 118-239) respectively.[40] A recent systematic review of outcomes of cardiac surgery for older adults concluded that frailty status may predict longer-term mortality postoperatively as well as functional decline after minimally invasive surgery. These outcomes are closely aligned with patient-reported values.[4] While cardiac surgical procedures are increasing along with the prevalence of cardiac disease in the growing population of older adults, a recent systematic review by Kim et al.[4] indicated that the heterogeneity of instruments used to identify frailty limits the quality of study findings and no studies in the systematic review examined functional status. The presence of a frail state prior to cardiac surgery may have added clinical relevance beyond current risk prediction, be independently predictive of both short-term and long-term clinical outcomes, and show important interaction with several factors including illness severity, co-morbid illness, and the social and structural environment.

Despite evidence to suggest that frailty may be an important determinant of clinical outcome for patients subjected to the significant stress of cardiac surgery with cardiopulmonary bypass and mechanical ventilation, to our knowledge, no cardiac surgery programs are routinely screening and addressing the risk associated with this vulnerability. This is an important knowledge-to-care gap for both prognostication and peri-operative support for a procedure as commonly performed as cardiac surgery. The measurement of frailty may represent a useful detail to highlight patients who could potentially benefit from further evaluation and intervention prior to surgery.

Distinguishing between those patients who have the potential for recovery from those who are approaching the end of their lives is crucial in determining who will benefit from invasive cardiac procedures and who will benefit from medical therapy and palliative care for their cardiac symptoms.[41] Cardiac surgery presents a stressor that challenges the level of resilience an individual can assemble. Studies of cardiac surgery patients with frailty have estimated the prevalence of frailty in this population at 4-50% with greater risk of post-operative morbidity and mortality, longer lengths of stay and institutionalization following surgery.[23, 42-45] These studies suggest the assessment of pre-operative frailty can refine risk estimates for post-operative complications and may guide more informed decision-making. Nevertheless, we need more accurate and robust methods for predicting quality-adjusted survival and optimizing the therapeutic recovery in all patients referred for cardiac surgery. The final two papers of this dissertation address the clinical, cost and quality of life outcomes associated with frailty in a cohort of cardiac surgery patients enrolled in Alberta.

This program of research was designed to describe the prevalence, correlates, clinical and cost outcomes associated with frailty in the province of Alberta. The findings are intended to inform patients, caregivers, clinicians and decision-makers about the risk associated with frailty in our ICU population, particularly patients admitted following cardiac surgery. Frailty case-finding may aid in the design of novel interventions such as care pathways that lead to better informed decision-making on the part of patients, caregivers and clinicians to optimize outcomes and minimizes unnecessary health care expenditures.

1.5 Aims and Hypotheses:

The research question was ‘what are the prevalence, correlates, clinical and cost outcomes associated with frailty in the general ICU and cardiac surgery ICU population in Alberta’? In a three-paper dissertation, the following specific hypotheses are addressed.

1. Hypothesis: Frailty in patients presenting with critical illness will be associated with greater morbidity, mortality and utilization of health services. The feasibility of

implementing a province-wide frailty screening instrument and description of population-based prevalence and outcomes of frailty in patients admitted to adult ICUs across Alberta will be explored.

2. Hypothesis: Pre-operative frailty in cardiac surgery patients will be associated with greater morbidity, mortality and utilization of health services. An epidemiological description of pre-operative frailty, its prevalence and associated outcomes will provide evidence of this relationship in patients referred for cardiac surgery in Alberta.

3. Hypothesis: Pre-operative frailty in cardiac surgery patients will be associated with higher costs in the year prior to surgery and subsequent years following surgery. Pre-operative frailty will have greater impact on quality-adjusted life year (QALY) gained. A cost comparison demonstrating the impact of frailty on costs and measures of quality of life will provide support for developing and implementing interventions aimed at improving outcomes for patients with frailty referred for cardiac surgery.

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Chapter 2. Implementation of Population-Level Screening for Frailty Among Patients Admitted to Adult Intensive Care in Alberta, Canada

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Abstract

Purpose

A substantial proportion of patients admitted to intensive care units (ICU) are frail; however, its epidemiology at a population-level has not been explored. Following implementation of a validated frailty measure into a provincial ICU clinical information system, we describe the population-based prevalence and outcomes of frailty in patients admitted to ICU.

Methods

Retrospective cohort study of adult admissions to 17 ICUs. Data were captured using eCritical Alberta. A Clinical Frailty Scale (CFS) score assigned at ICU admission was used to define the exposure (CFS score ≥5). Primary outcome was hospital mortality. Secondary outcomes were ICU and hospital stay; and receipt of organ support.

Results

15,238 (81%) were assigned a CFS score at ICU admission. Of these, 28% (95%CI, 27-28%) were frail. Prevalence was 9-43% across ICUs. Frail patients were older (mean [SD] 63[15] vs. 56[17] years, p<0.001), more likely male (54% vs. 46% female, p<0.001), had higher APACHE II scores (22[8] vs. 17[8], p<0.001) compared to non-frail. Frail patients received less mechanical ventilation (62% vs. 68%, p<0.001) and vasoactive therapy (24% vs. 57%, p<0.001); but more non-invasive ventilation (22% vs. 9%, p<0.001). Frail patients had greater hospital mortality (23% vs. 9%; adjusted-OR, 1.80; 1.64-2.05), along with greater ICU (4[2-8] vs. 3[2-6] days, p<0.001) and hospital stay (16[8-36] vs. 10[5-20] days, p<0.001) compared to non-frail.

Conclusion

A validated measure of frailty can be implemented at the population-level in ICU. Frailty is common in ICU patients and has implications for health services use and clinical outcomes.

2.1 Background and Introduction

The general health status and functional trajectory of patients prior to an episode of critical illness and intensive care unit (ICU) admission are increasingly recognized as important determinants of the complexity and duration of organ support and outcome[1-4]. Observational studies have estimated one-third of critically ill patients are frail[5-7]. The prevalence of frailty appears greatest among older patients[8, 9]; however, is not insignificant among younger patients[10].

Frailty has shown consistently heightened risk for worse short and long-term patient outcomes and greater use of health services[5-7, 11]. As such, an understanding of baseline frailty status during critical illness provides additional context on survivorship expectations for patients, families, and healthcare professionals, especially when making decisions on the intensity and/or duration of support provided in ICU settings[12].

The Canadian healthcare system is confronted with a growing burden of persons living with frailty. There have been widespread recommendations to integrate measurements of frailty into day-to-day clinical practice and across the healthcare spectrum, including in ICU settings[13]. Recently, we implemented the routine capture of a validated clinical frailty measure into a provincial ICU-specific bedside electronic health record [EHR][14]. Herein we describe the population-level epidemiology of frailty among critically ill patients across all adult ICUs in the province of Alberta.

2.2 Methods

This study was approved by the Research Ethics Board at the University of Alberta, Edmonton (File # Pro00056591) and the University of Calgary Conjoint Health Research Ethics Board, University of Calgary, Calgary (File # REB15-1728). The need for written informed consent was waived. This study follows the recommended reporting outlined in the STROBE statement[15].

2.2.1 Design, Setting, and Population

This was a retrospective multi-centre population-based cohort study. All adult patients (aged ≥18 years) admitted to all 17 ICUs in Alberta between January 1, 2016 and June 30, 2017 were eligible. These ICUs included 14 mixed medical/surgical units; two cardiovascular surgical ICUs and one neurosciences ICU. Study ICUs are in seven cities: Edmonton (7 units); Calgary (5 units); Red Deer (1 unit); Lethbridge (1 unit); Grand Prairie (1 unit); Medicine Hat (1 unit) and Fort McMurray (1 unit). Of these, five are classified as academic, two as tertiary, and 10 as community/regional ICUs (Supplementary Table 2-1). All ICUs were staffed by board-certified intensivists, generally had in-house coverage by clinical associates or resident trainees and had availability of after-hour intensivist coverage.

2.2.2 Data Sources

The primary data source was eCritical Alberta, which includes a bedside clinical information system (*eCritical MetaVision*^{TM}, iMDsoft, Boston) and a data warehouse and clinical analytics system (*eCritical TRACER*). eCritical has been implemented in all ICUs across Alberta since 2012 and serves as a key tool to foster and support best practice in critical care medicine (Alberta Health Services, 2012, eCritical Alberta)[14]. eCritical provides for full electronic interdisciplinary clinical documentation and collation of demographic, diagnostic/case-mix (i.e., comorbid disease, diagnostic classification, surgical status), illness severity (i.e., Acute Physiology and Chronic Health Evaluation [APACHE] II and IV scores, Sequential Organ Failure Assessment [SOFA] scores), laboratory and intervention data (i.e., use of invasive/non-invasive ventilation, vasoactive therapy and renal replacement therapy [RRT]) utilizing standardized documentation and data definitions for all admissions. Data are directly entered into *eCritical MetaVision*^{TM}, using forms with discreet data elements and decision support to guide proper documentation and directly downloaded from medical devices. The *eCritical* Program includes a comprehensive quality assurance process to track and remediate completion of important data elements (i.e., physician admission form; diagnostic/case-mix; Clinical Frailty Scale [CFS] score). Data from *eCritical MetaVision*^{TM} are imported unaltered into *eCritical TRACER* using an extract-transform-load tool (Informatica, Redwood City, California). *eCritical TRACER* provides a reporting and data-extraction capability that supports research, education, planning and decision-making by providing data and reports from a comprehensive repository of patient-specific ICU clinical information[14]. The *eCritical/TRACER* repository is housed within Alberta Health Services (AHS) and is governed by a provincial executive group that oversees its rigorous data quality assurance and audit[14]. *eCritical/TRACER* has previously been used to support health services and outcomes research[16-19].

2.2.3 Provincial Implementation of the CFS into eCritical

Prior to the implementation, ICU professionals across adult Alberta ICUs, particularly physicians, were prepared with a multi-faceted education strategy that focused on providing rationale for CFS implementation, an overview of current evidence on frailty in ICU settings, a summary of the implementation process and a demonstration on how to assign CFS scores in *eCritical MetaVision*^{TM}. This included: 1) grand rounds in both major academic sites with video-conference to all zonal and regional ICU sites; 2) online webinars; 3) development of a dedicated CFS implementation website; and 4) provision of a project newsletter.

eCritical engineers built and configured the CFS into *eCritical MetaVision*^{TM} documentation, followed by creation of mock-ups of the CFS documentation in eCritical development and test systems to allow for improvement cycles, and functional and technical testing prior to being placed in production. The 9-point CFS score appears as a drop-down list coupled with a visual analogue guide and scoring definitions embedded directly into the *Physician Admission Form* (Supplementary Figure 2-1).

The *Physician Admission Form* is mandatorily completed by the admitting intensivist within the first 24 hours for every new patient admitted to ICU. Additional data captured on this form demographics, diagnostic, comorbid disease, case-mix and acuity of illness data. Once documented by the admitting intensivist in *eCritical MetaVision*^{TM}, the CFS score is further integrated and displayed across inter-professional charting, including nursing, physiotherapy, occupational therapy, dietician, and social work.

The CFS was implemented in *eCritical MetaVision*^{TM} as a permanent addition to the *Physician Admission Form* in December 2015 in all adult ICUs in Alberta. During the initial implementation phase, documentation of the CFS score was made a non-mandatory field on the form in order to audit the compliance with documentation and allow for user feedback on usability. A threshold of ≥80% completion of CFS scores was targeted. Compliance data were audited and ICU-level feedback reports were provided quarterly. The CFS scores were also exported into the *eCritical/TRACER* data repository to enable reporting of aggregate "frailty" reports (Supplementary Figure 2-2). In response to user feedback, the CFS documentation was modified to include the additional choice of "*Not sure despite review of available information*"; with the intent to transition CFS score documentation to a mandatory data element.

2.2.4 Exposures and Outcomes

The primary exposure was the CFS score at the time of ICU admission[5, 20]. Frailty was defined as a CFS score ≥5. The primary outcome was all-cause hospital mortality. Secondary outcomes included ICU mortality, hospital discharge disposition (i.e., home, skilled nursing facility, hospital transfer), measures of organ support (i.e., receipt mechanical ventilation, vasoactive therapy, and RRT) and health services use (i.e., ICU stay, hospital stay).

2.2.5 Statistical analysis

Descriptive statistics were stratified according to CFS score ≤4 compared to CFS score ≥5. Nonparametric univariate comparisons were performed to assess the impact of frailty on primary and secondary outcome measures. Normally (and near 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 Likelihood Ratio and Pearson’s Chi-squared tests for independence. Independent risk factors for hospital mortality and selected organ supports were identified by multivariate logistic regression using CFS score at ICU admission, age, sex, diagnostic category, pre-ICU duration of hospitalization and APACHE II score as covariates. Results were presented as odds ratios with 95% confidence intervals. All comparisons were considered statistically significant with a p-value <0.05. Analyses were performed using Stata 14 (StataCorp, College Station, Texas).

2.3 Results

There were 19,556 patients admitted to Alberta ICUs during the study period (Figure 2-1). After excluding patients with missing CFS scores (n=3,669; 19%)(Supplementary Tables 2-2 and 2-3) and those who died within 24 hours following admission (n=649; 3%), a total of 15,238 (81%) patients were included. At the time of data extraction, 122 (0.8%) patients remained alive and still in hospital 90 days after ICU discharge. Overall compliance with CFS score completion was 81% and showed improvement over time (Supplementary Table 2-4).

Overall, the mean age (SD) was 58 years (17), 39% (n=5,984) were female, mean (SD) APACHE II score was 19 (8) and 38% (n=5,750) were admitted following surgery. ICU and hospital mortality were 9% (n=1,295) and 13% (n=2,019), respectively.

2.3.1 Prevalence of frailty in ICU

The median (IQR) CFS score was 3 (2-5). In total, 28% (n=4,199) had a CFS score ≥5. There were significant differences across ICUs in the proportions of patients with a CFS score ≥5 (range 9% to 43%; p<0.001)(Table 2-1; Figure 2-2).

2.3.2 Patient characteristics stratified by CFS score

CFS scores were greater for older patients (Figure 2-3; Table 2-2). Patients with CFS score ≥5 were significantly older compared to those with CFS score ≤4 (mean [SD] 63 years [15] vs. 56 [17] years; p<0.001). Females had greater CFS scores compared with males (4 [2-5] vs. 3 [2-4], p<0.001); and the proportion of females with a CFS score ≥5 was higher than males (32% for females vs. 25% for males, p<0.001).

CFS scores were lower for patients admitted for surgical compared with medical diagnoses (3 [3-4] vs. 4 [2-5], p<0.001). Patients with a CFS score ≥5 were more likely non-operative (medical) compared to those with a CFS score ≤4 (69% vs. 57%, p<0.001). APACHE II scores at admission were correlated with CFS score (Figure 2-4). Patients with CFS score ≥5 had greater mean (SD) APACHE II scores (22 [8] vs. 17 [8], p<0.001) and admission SOFA scores (7 [4] vs. 6 [4], p<0.001) compared to those with a CFS score ≤4 (Table 2-2).

2.3.3 Patient outcomes and health services use

In multivariable analysis, ICU death was not statistically different for patients with CFS scores ≥5 compared to those CFS scores ≤4 (12% vs. 7%; adjusted-odds ratio [OR], 1.09; 95% CI, 0.95-1.25, p=0.21). Hospital death was greater for patients with CFS scores ≥5 compared to CFS scores ≤4 (23% vs. 9%; adjusted-OR, 1.83; 95% CI, 1.64-2.05, p<0.001)(Table 2-3). In analysis using the CFS score as a continuous variable, a higher CFS score was associated with greater hospital mortality (adjusted-OR 1.19; 95% CI, 1.15-1.23; p<0.001), and showed further gradient increases for CFS scores >5 (Supplementary Table 2-5).

Patients with a CFS scores ≥5 were less likely to receive invasive mechanical ventilation (62% vs. 68%; adjusted-OR 0.56; 95% CI, 0.51-0.61, p<0.001) but more likely to receive non-invasive ventilation (22% v. 9%, adjusted-OR 2.07; 95% CI, 1.86-2.31, p<0.001) compared with patients with CFS scores ≤4 (Table 2-2). Patients with a CFS scores ≥5 were also less likely to receive vasoactive support (24% vs. 57%; adjusted-OR 0.73; 95% CI, 0.67-0.80, p<0.001); though use of RRT was similar (7% vs. 5%; adjusted-OR 0.95; 95% CI, 0.80-1.13; p=0.60) compared to those with CFS scores ≤4. Among patients receiving any form of organ support, those with CFS scores ≥5 received it for longer durations that those patients with CFS scores ≤4 (Table 2-2).

Patients with CFS score ≥5 had longer median [IQR] ICU stay (4 [2.1-8.0] vs. 3 [1.5-5.9] days, p<0.001) and total hospital stay (16 [7.6-36.0] vs. 10 [5.2-20.3] days, p<0.001) compared to those with a CFS score ≤4. The patients with CFS score ≥5 also had longer median [IQR] hospital stay prior to ICU admission (0.4 [0.02-4.7] vs. 0.2 [0.01-1.3] days, p<0.001) and after ICU discharge (7 [0.7-19.0] vs. 4 [0.9-10.7] days, p<0.001)(Table 2-3).

2.3.4 Discharge disposition

The majority (79%) of patients were discharged from ICU to an acute care unit or another acute care facility, with the next most common disposition being discharge home (9%) or deceased in ICU (9%). Patients with CFS score ≤4 were more likely to be discharged directly home compared to than those with a CFS score ≥5 (11% v. 6%, $p<0.001$)(Table 2-4).

2.4 Discussion

National guidelines have recommended population-level screening for frailty[13, 21]. Aligned with this recommendation, we have successfully implemented a validated frailty measure, the Clinical Frailty Scale score, into our provincial ICU-specific EHR, which is routinely completed by attending ICU physicians for all adult ICU admissions in Alberta. We have shown population-level screening for frailty in ICU settings is feasible.

2.4.1 Context with Prior Work

In this first population-level description of frailty screening in ICU settings, we confirmed prior data showing frailty, captured by the CFS score, was common, occurring in 1 in 4 admissions[5-7]. We also found considerable variation in reported frailty prevalence across adult ICUs in Alberta. Frailty prevalence was modified by several factors, particularly age, sex, case-mix, surgical status and illness acuity. Prior work is limited by describing frailty in older ICU cohorts (i.e., ≥65, ≥80 years); however, our study adds new knowledge by evaluating frailty at a population-level across an adult age continuum[8, 22-24]. The average age of frail patients in our cohort was only 63 years, suggesting a significant number of younger persons living with frailty may be at substantial risk for critical illness and associated adverse outcomes[10]. Baseline frailty status was found to confer greater risk of hospital death, as well as longer duration of post-ICU and total hospitalization. These data further support prior work establishing the predictive validity of the CFS and patient outcomes[5, 6, 23]. Frailty status was also associated with differences in health services use and advanced organ support. Fewer frail patients were treated with invasive mechanical ventilation and vasoactive support; while more received non-invasive ventilation when compared to non-frail patients[8].

2.4.2 Implications for Clinicians, Policy and Research

Provincial-level screening for frailty upon ICU admission provides novel information on its prevalence and evolving burden[13, 21]. Variations in reported prevalence across ICUs can provide insights into where enhanced evaluation and/or support structures can be targeted. Routine frailty evaluation, as demonstrated in our study, also provides opportunity for healthcare decision-makers to better strategically plan for future health services demand. A growing prevalence of patients living with frailty and developing critical illness with organ support in ICU settings should factor into resource and capacity planning for ICU services, particularly recognizing their greater complexity, their longer recovery and their greater health services use[5, 6].

Identifying vulnerable and frail patients upon ICU admission presents unique opportunities for the design and implementation of health services innovations aimed at improving the quality and transitions in care those surviving their acute episode of critical illness[25]. Such interventions could include inter-disciplinary ICU care pathways, to personalize recovery and transitions of care. Including the CFS in ICU care pathways could trigger confirmatory evaluation and detailed interrogation of frailty domains (i.e., multidimensional frailty measures or a comprehensive geriatric assessment), as well as timely referral to clinicians with expertise in frailty-specific interventions (e.g., geriatric medicine, dietetics, rehabilitative medicine, palliative care). Interventions and focused care pathways targeting prevention or mitigation of disability onset or worsening severity in ICU could align with frailty case-finding to better risk identify patients most likely to benefit and improve functional outcomes post-ICU[6, 22].

The relationship between baseline frailty status prior to critical illness and new or worsening functional and cognitive disability among survivors is well established[12, 26, 27]; however, future work should further aim to unravel whether there is an association between baseline frailty, the development of chronic or persistent critical illness, and trajectories in survivorship amenable to care innovative to improve outcomes of ICU stay as well as subsequent hospital stay[16]. This may also include opportunities for frail survivors of critical illness to re-visit goals-of-care discussions with family and healthcare professionals. There is also little data focused on how clinicians may use information about frailty status in their discussions with patients and families or to guide decision-making prior to admission or during their course in

ICU. In the VIP study, older frail patients were significantly more likely to have support withheld and withdrawn in the ICU compared with those not frail[8].

2.4.3 Strengths & Limitations

Our study is notable for provincial population-level ascertainment of all ICU admissions; having the CFS score routinely documented by the most responsible physician (i.e., attending ICU physician); and having robust and comprehensive clinical, outcome and health services data to associate with measures of frailty. We also showed improved compliance with CFS completion over the duration of the study; implying greater adoption by ICU physicians. However, our study has important limitations. First, a significant proportion of CFS scores were missing. This was attributed to completion of the CFS score in the *Physician Admission Form* not being a mandated field. We have shown with education, audit and feedback and reminders that compliance with completion of the CFS significantly improved during the study. Second, due to CFS scores being obtained after ICU admission, we are unable to comment whether frailty was an important determinant for decisions not to admit patients (i.e., patients who declined or were not offered ICU admission). Both of these may contribute to selection and information bias, inherent in all observational studies. Third, we recognize the CFS was initially validated in ambulatory care settings to screen for frailty and, while also showing predictive validity in ICU settings; we did not confirm frailty status with a more comprehensive evaluation (i.e., multi-dimensional or comprehensive geriatric assessment). Similarly, we were also not able to evaluate the inter-rater reliability of CFS score assignment. Fourth, we did not have data on patient goals-of-care status at ICU admission, whether this changed during ICU admission, or other decisions related to the intensity or duration of ICU support. Fifth, we did not have data on long-term outcomes beyond index hospitalization; though prior data have shown frailty to be associated with greater mortality, institutionalization and impaired quality-of-life[6, 22, 27]. Finally, while this is a provincial population-level study, it is limited to a single Canadian province and may not be generalizable to other health jurisdictions.

2.5 Conclusion

A validated measure of frailty was feasible to implement at the population-level into a provincial ICU-specific EHR. Frailty was common, occurring in 1 in 4 adults admitted to ICU and was associated with disproportionate risk of hospital death. Frail patients showed important differences in organ support and health services use that may have prognostic and health planning implications. The value of this novel method of frailty screening can meaningfully support appropriate frailty-specific ICU interventions and future healthcare resource planning.

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Table 2-1. Distribution of CFS scores across 17 adult ICUs in Alberta.

ICU	Total (n=15,238)	CFS ≤4 (Not Frail) (n=11,039; 72%)	CFS ≥5 (Frail) (n=4,199; 28%)	p
1	699	436 (62%)	263 (38%)	<0.001
2	1,645	1,504 (91%)	141 (9%)	<0.001
3	1,541	1,212 (79%)	329 (21%)	<0.001
4	641	507 (79%)	134 (21%)	<0.001
5	1,528	983 (64%)	545 (36%)	<0.001
6	422	326 (77%)	96 (23%)	<0.05
7	602	360 (60%)	242 (40%)	<0.001
8	274	240 (88%)	34 (12%)	<0.001
9	927	663 (72%)	264 (28%)	=0.52
10	448	358 (80%)	90 (20%)	<0.001
11	1,569	1,097 (70%)	472 (30%)	<0.05
12	591	405 (69%)	186 (31%)	<0.05
13	582	421 (72%)	161 (28%)	=0.95
14	500	284 (57%)	216 (43%)	<0.001

15	461	314 (68%)	147 (32%)	<0.05
16	1,917	1,202 (63%)	715 (37%)	<0.001
17	891	727 (82%)	164 (18%)	<0.001

Table 2-2. Summary of patient characteristics stratified by CFS score.

Feature	Total (n=15,238)	CFS ≤4 (Not Frail) (n=11,039; 72%)	CFS ≥5 (Frail) (n=4,199; 28%)	p
Age (mean [SD]), yr	58 (17)	56 (17)	63 (15)	<0.001
Sex, female (n;%)	5,984 (39%)	4,067 (37%)	1,917 (46%)	<0.001
Admission category, (n;%)				<0.001
Medical/non-operative	9,184 (60%)	6,274 (57%)	2,910 (69%)	
Elective Surgical	3,447 (23%)	2,821 (26%)	626 (15%)	
Emergency Surgical	2,524 (17%)	1,896 (17%)	628 (15%)	
No Admission Category Assigned	83 (0.5%)	48 (0.4%)	35 (0.8%)	
Admission Classification, (n;%)				<0.001
Medical	7,506 (49%)	4,968 (45%)	2,538 (60%)	
Neurology	1,188 (8%)	956 (9%)	232 (6%)	
Surgical	5,750 (38%)	4,440 (40%)	1,310 (31%)	
Trauma	700 (5%)	620 (6%)	80 (2%)	
No Admission Classification Assigned	94 (0.6%)	55 (0.5%)	39 (0.9%)	
Diagnostic Category, (n;%)				<0.001

Cardiovascular	4,768 (31%)	3,602 (33%)	1,166 (28%)	
Respiratory	2,165 (20%)	1,322 (31%)	3,487 (23%)	
Gastrointestinal/hepatic	1,757 (12%)	1,197 (11%)	560 (13%)	
Endocrine/metabolic	434 (3%)	363 (3%)	71 (2%)	
Neurologic	2,536 (17%)	2,036 (18%)	500 (12%)	
Hematologic/oncologic	39 (0.3%)	24 (0.2%)	15 (0.4%)	
Musculoskeletal	442 (3%)	295 (3%)	147 (4%)	
Urological/kidney	432 (3%)	301 (3%)	131 (3%)	
Trauma	886 (6%)	769 (7%)	117 (3%)	
Transplant	218 (1%)	106 (1%)	112 (3%)	
No Diagnostic Category Assigned	239 (2%)	181 (2%)	58 (1%)	
APACHE II score, (mean [SD])	19 (8)	17(8)	22(8)	<0.001
Admission SOFA score, (mean [SD])	6 (4)	6 (4)	7 (4)	<0.001
Invasive Mechanical Ventilation, (n;%) Duration, (median [IQR]), days	10,124 (66%) 1 (0.4-3.9)	7,527 (68%) 1 (0.3-3.5)	2,597 (62%) 2 (0.7-5.2)	<0.001 <0.001
Non-invasive ventilation, (n;%) Duration, (median [IQR]), days	1,894 (12%) 0.9 (0.3-2.3)	957 (9%) 0.7 (0.3-1.9)	937 (22%) 1 (0.3-2.5)	<0.001 <0.001
Vasoactive medications, (n;%) Duration, (median [IQR]), days	7,743 (51%) 1 (0.3-3.2)	5,494 (57%) 1 (0.3-2.8)	2,249 (24 %) 2 (0.5-4.1)	<0.001 <0.001

Renal replacement therapy, (n;%) Duration, (median [IQR]), days	803 (5%) 3 (1.6-6.8)	496 (5%) 3 (1.5-6.8)	307 (7%) 4 (1.7-7.1)	<0.001 =0.308

Table 2-3. Summary of patient outcomes stratified by CFS score.

Feature	Total (n=15,238)	CFS ≤4 (Not Frail) (n=11,039; 72%)	CFS ≥5 (Frail) (n=4,199; 28%)	p
ICU death, (n;%)	1,295 (9%)	772 (7%)	523 (12%)	<0.001
Hospital death, (n;%)	2,019 (13%)	1,037 (9%)	982 (23%)	<0.001
ICU LOS (median [IQR]), days	3 (2-6)	3 (1.5-5.9)	4 (2-8)	<0.001
Hospital LOS, (median [IQR]), days	11 (6-24)	10 (5-20)	16 (8-36)	<0.001
Hospital Stay Prior to ICU Admit (median [IQR]), days	0.3 (0.01-2)	0.2 (0.01-1.3)	0.4 (0.02-5)	<0.001
Hospital LOS following ICU Discharge (median [IQR]), days	5 (1-13)	4 (1-11)	7 (1-19)	<0.001

Table 2-4. Summary of ICU discharge destination stratified by CFS score.

ICU Discharge Destination	Total (n=15,238)	CFS ≤4 (Not Frail) (n=11,039; 72%)	CFS ≥5 (Frail) (n=4,199; 28%)	p
Acute ward or hospital	12,060 (79%)	8,777 (80%)	3,283 (78%)	0.07
Deceased	1,295 (9%)	772 (7%)	523 (12%)	<0.001
Home	1,392 (9%)	1,160 (11%)	232 (6%)	<0.001
Transfer to alterative ICU/CCU	200 (1%)	135 (1%)	65 (2%)	0.12
Long Term Care	27 (0.2%)	4 (0.04%)	23 (0.6%)	<0.001
Hospice	4 (0.03%)	1 (0.01%)	3 (0.07%)	<0.05
Detox	3 (0.02%)	2 (0.02%)	1 (0.02%)	0.82
Sub-acute or rehabilitation	2 (0.01%)	2 (0.02%)	0 (0%)	0.38
Not Documented	255 (2%)	186 (2%)	69 (2%)	0.86

Supplementary Table 2-1. List of participating ICUs

ICU name	Location	ICU type	Hospital type	Hospital classification (CIHI)*	eCritical implementation date
Foothills Medical Center Multi-Systems ICU	Calgary	Mixed (medical, surgical, neurosurgical, trauma)	Academic	Teaching	July 2012
Foothills Medical Centre CVICU	Calgary	Cardiovascular surgical	Academic	Teaching	August 2012
University of Alberta Hospital General Systems ICU	Edmonton	Mixed (medical, surgical, trauma, transplant)	Academic	Teaching	April 2013
University of Alberta Neuro ICU	Edmonton	Neurosciences	Academic	Teaching	June 2013
Mazankowski Alberta Heart Institute CVICU	Edmonton	Cardiovascular surgical	Academic	Teaching	October 2013
Peter Lougheed Hospital ICU	Calgary	Mixed (medical, surgical, vascular)	Tertiary	Teaching	August 2012
Royal Alexandra Hospital ICU	Edmonton	Mixed (medical, surgical, trauma)	Tertiary	Teaching	July 2013

Rockyview General Hospital ICU	Calgary	Mixed (medical, surgical)	Community	Teaching	June 2012
South Health Campus ICU	Calgary	Mixed (medical, surgical)	Community	Community large	February 2013
Sturgeon Community Hospital ICU	St. Albert	Mixed (medical, surgical)	Community	Community large	January 2014
Grey Nuns Community Hospital ICU	Edmonton	Mixed (medical, surgical, vascular)	Community	Teaching	February 2014
Misericordia Community Hospital	Edmonton	Mixed (medical, surgical)	Community	Teaching	March 2014
Medicine Hat Regional Hospital ICU	Medicine Hat	Mixed (medical, surgical)	Regional	Community large	June 2015
Northern Lights Health Centre ICU	Fort McMurray	Mixed (medical, surgical)	Regional	Community median	November 2015
Chinook Regional Hospital ICU	Lethbridge	Mixed (medical, surgical)	Regional	Community large	December 2015
Grande Prairie QEII Regional Hospital	Grande Prairie	Mixed (medical, surgical)	Regional	Community large	February 2016
Red Deer Regional Hospital ICU	Red Deer	Mixed (medical, surgical)	Regional	Community large	March 2016

Abbreviations: ICU = intensive care unit; CIHI = Canadian Institute for Health Information.

*Hospitals were categorized by Canadian Institute of Health Information by hospital type as follows: teaching (full membership in the Association of Canadian Academic Healthcare Organizations; any size), large (≥200 beds), medium (50-199 beds), and small (1-49 beds) community hospitals

Supplementary Table 2-2. Summary of CFS scores, including missing CFS scores, by ICU site.

ICU	Total (n=15,238)	CFS ≤4 (Not Frail) (n=11,039; 72%)	CFS ≥5 (Frail) (n=4,199; 28%)	Missing CFS Score (n=3,669; 19%)
1.	1,008	436 (43.3%)	263 (26.1%)	309 (30.7%)
2.	1,979	1,504 (76%)	141 (7.1%)	334 (16.9%)
3.	1,702	1,212 (71.2%)	329 (19.3%)	161 (9.5%)
4.	648	507 (78.2%)	134 (20.7%)	7 (1.1%)
5.	2,415	983 (40.7%)	545 (22.6%)	887 (36.7%)
6.	660	326 (49.4%)	96 (14.6%)	238 (36.1%)
7.	616	360 (58.4%)	242 (39.3%)	14 (2.3%)
8.	493	240 (48.7%)	34 (6.9%)	219 (44.4%)
9.	1,033	663 (64.2%)	264 (25.6%)	106 (10.3%)
10.	472	358 (75.9%)	90 (19.1%)	24 (5.1%)
11.	1,973	1,097 (55.6%)	472 (23.9%)	404 (20.5%)
12.	752	405 (53.9%)	186 (24.7%)	161 (21.4%)
13.	653	421 (64.5%)	161 (24.7%)	71 (10.9%)
14.	517	284 (54.9%)	216 (41.8%)	17 (3.3%)
15.	520	314 (60.4%)	147 (28.3%)	59 (11.4%)
16.	2,348	1,202 (51.2%)	715 (30.5%)	431 (18.4%)

17.	1,118	727 (65%)	164 (14.7%)	227 (20.3%)

Supplementary Table 2-3. Summary of patient characteristics stratified by CFS scores, including missing CFS scores.

Feature	Total (n=18,907)	CFS ≤4 (Not Frail) (n=11,039; 58%)	CFS ≥5 (Frail) (n=4,199; 22%)	Missing CFS Score (n=3,669; 19%)
Age (mean [SD]), yr	58 (17)	56 (17)	63 (15)	59 (16)
Sex, female (n;%)	7,304 (39%)	4,067 (37%)	1,917 (46%)	1,320 (36%)
Admission category, (n;%)				
Medical/non-operative	10,600 (56%)	6,274 (57%)	2,910 (69%)	1,416 (39%)
Elective Surgical	4,766 (25%)	2,821 (26%)	626 (15%)	1,319 (36%)
Emergency Surgical	2,896 (15%)	1,896 (17%)	628 (15%)	372 (10%)
No Admission Category Assigned	645 (3%)	48 (0.4%)	35 (0.8%)	562 (15%)
Admission Classification, (n(%)	n=18,907	n=11,039	n=4,199	n=3,669
Medical	8,663 (46%)	4,968 (45%)	2,538 (60%)	1,127 (31%)
Surgical	7,402 (39%)	4,440 (40%)	1,310 (31%)	1,652 (45%)
Neuro	1,369 (7%)	956 (9%)	232 (6%)	181 (5%)
Trauma	829 (4%)	620 (6%)	80 (2%)	129 (4%)
No Admit Classification Assigned	674 (4%)	55 (1%)	39 (1%)	580 (16%)

Diagnostic Category, (n;%)	**n=18,907**	**n=11,039**	**n=4,199**	**n=3,669**
Cardiovascular	6,133 (32%)	3,602 (32%)	1,166 (28%)	1,365 (37%)
Respiratory	3,973 (21%)	2,165 (20%)	1,322 (32%)	486 (13%)
Gastrointestinal	2,062 (11%)	1,197 (11%)	560 (13%)	305 (8%)
Neurologic	3,012 (16%)	2,036 (18%)	500 (12%)	476 (13%)
Trauma	1,055 (6%)	769 (7%)	117 (3%)	169 (5%)
Urological/kidney	501 (3%)	301 (3%)	131 (3%)	69 (2%)
Hematology	48 (0.3%)	24 (0.2%)	15 (0.4%)	9 (0.3%)
Metabolic / Endocrine	500 (3%)	363 (3%)	71 (2%)	66 (2%)
MSK / Skin	505 (3%)	295 (3%)	147 (4%)	63 (2%)
Transplant	276 (1%)	106 (1%)	112 (3%)	58 (2%)
No Category Assigned	842 (5%)	181 (2%)	58 (1%)	603 (16%)
APACHE II score, (mean [SD])	18 (8)	17 (8)	22 (8)	17 (8)
Admission SOFA score, (mean [SD])	6 (4)	6 (4)	7 (4)	6 (4)
Noninvasive Ventilation, (n;%) Duration, (med [IQR]), days	2,188 (12%) 0.8 (0.3-2.2)	957 (9%) 0.8 (0.3-1.9)	937 (22%) 1 (0.3-2.5)	294 (8%) 0.7 (0.2-1.9)

Mechanical Ventilation, (n;%) Duration, (med [IQR]), days	12,514 (66%) 1.1 (0.4-3.7)	7,527 (68%) 1.0 (0.4-3.5)	2,597 (62%) 2.0 (0.7-5.2)	2,390 (65%) 0.7 (0.2-2.5)
Vasoactive therapy, (n;%) Duration, (med [IQR]), days	9.564 (51%) 1.1 (0.3-3.1)	5,494 (57%) 1.0 (0.3-2.8)	2,249 (24%) 1.6 (0.5-4.1)	1,821 (19%) 0.9 (0.2-2.7)
RRT, (n;%) Duration, (med [IQR]), days	930 (5%) 3 (1.5-6.6)	496 (5%) 3.0 (1.5-6.8)	307 (7%) 3.5 (1.7-7.1)	127 (3%) 3.0 (1.2-5.7)
ICU death, (n;%)	1,532 (8%)	772 (7%)	523 (12%)	237 (6%)
Hospital death, (n;%)	2,388 (13%)	1,037 (9%)	982 (23%)	369 (10%)
ICU LOS (med [IQR]), days	3 (1.6-6.1)	2.9 (1.5-5.9)	4.1 (2.1-8.0)	2.6 (1.2-5.0)
Hospital LOS, (med [IQR]), days	11 (5.5-22.4)	9.8 (5.2-20.3)	16.46 (7.6-36.0)	8.8 (5.2-17.0)

Supplementary Table 2.4. Summary of missing CFS score frequency by quarter.

Time Quarter	CFS Missing at ICU Admission	CFS Entered at ICU Admission	Total ICU Admissions
2016Q1	777 (24%)	2408 (76%)	3185
2016Q2	769 (24%)	2390 (76%)	3159
2016Q3	642 (21%)	2486 (79%)	3128
2016Q4	536 (17%)	2561 (83%)	3097
2017Q1	483 (15%)	2713 (85%)	3196
2017Q2	462 (15%)	2680 (85%)	3142

Supplementary Table2-5. Summary of multi-variable logistic regression analysis for hospital mortality using the CFS score as a continuous variable (ordinal score from 1-9) adjusted for age, sex, APACHE II score, hospital stay prior to ICU admission.

CFS Score	Adjusted-OR	95% CI	p-value
1	-	-	-
2	0.97	0.76 - 1.24	0.82
3	0.77	0.61 - 0.98	0.03
4	0.85	0.66 - 1.08	0.18
5	1.19	0.92 - 1.53	0.19
6	1.61	1.26 - 2.08	<0.001
7	2.03	1.54 - 2.68	<0.001
8	2.68	1.61 - 4.47	<0.001
9	8.78	4.40 - 17.50	<0.001
CFS score (per 1-point increase)	1.19	1.15-1.23	<0.001

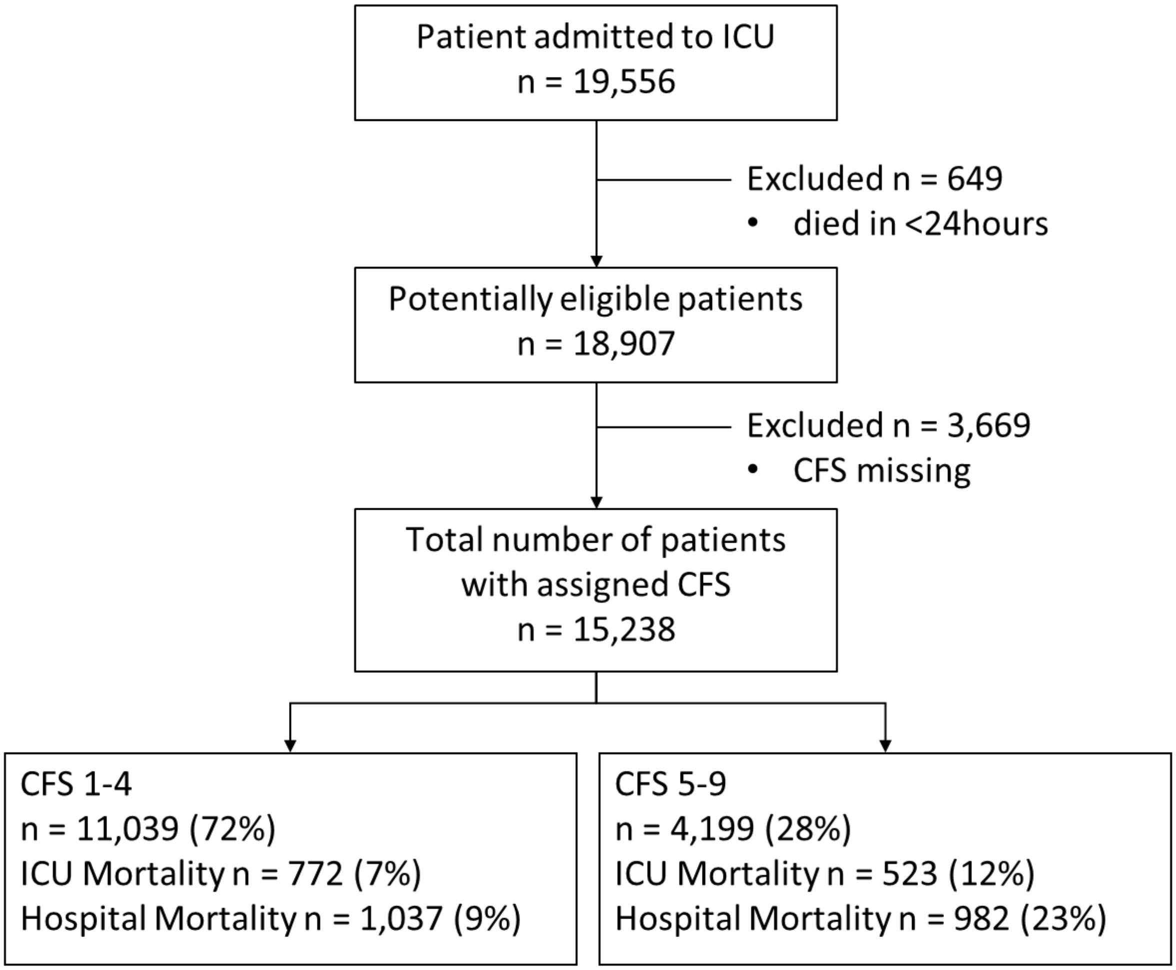


Figure 2-1. Selection of Alberta ICU patients for the study cohort.

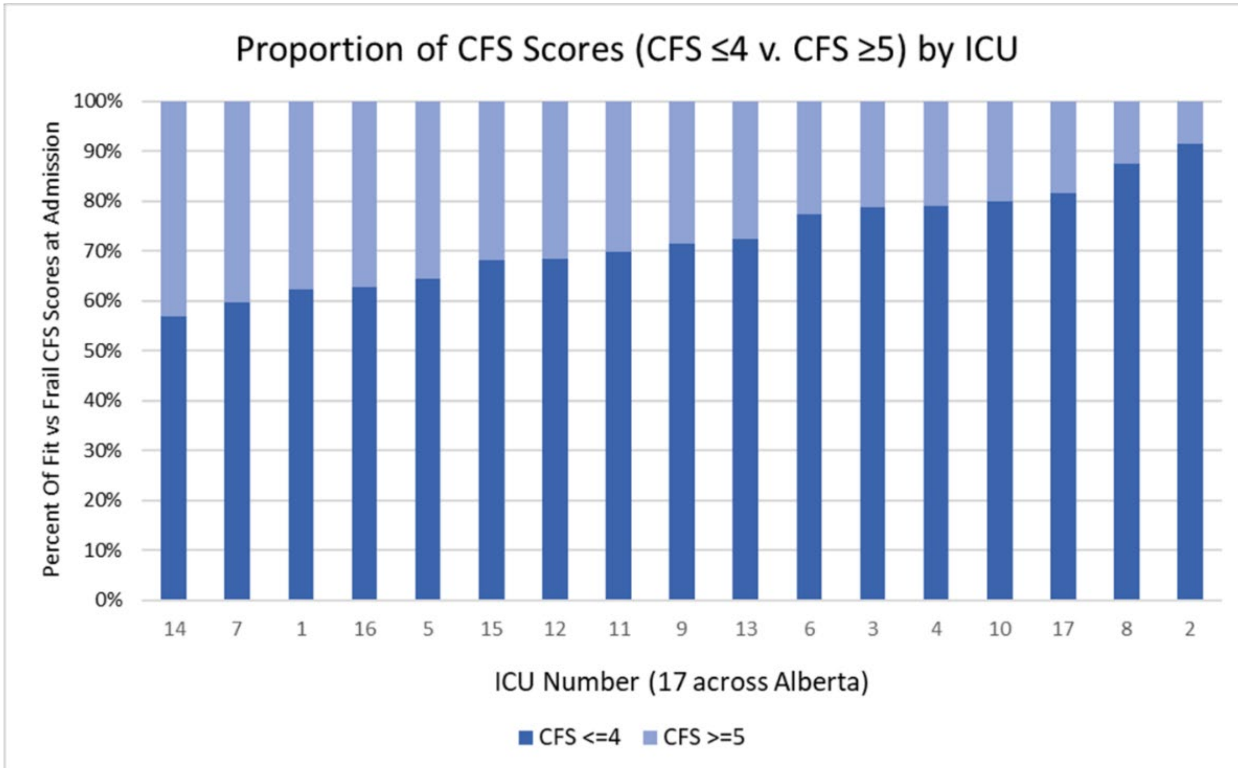


Figure 2-2. Distribution of Clinical Frailty Scale scores among 17 adult ICUs in Alberta.

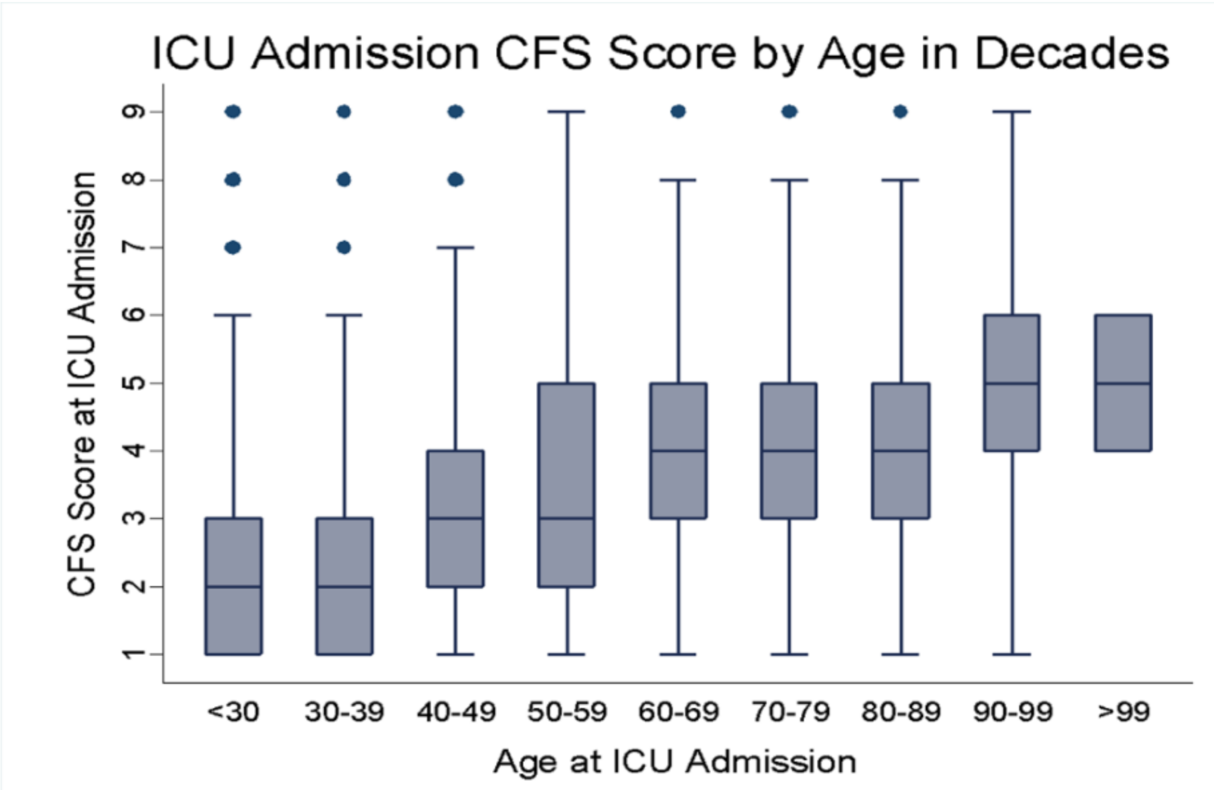


Figure 2-3. Distribution of Clinical Frailty Scale scores by age group in Alberta adults admitted to ICU.

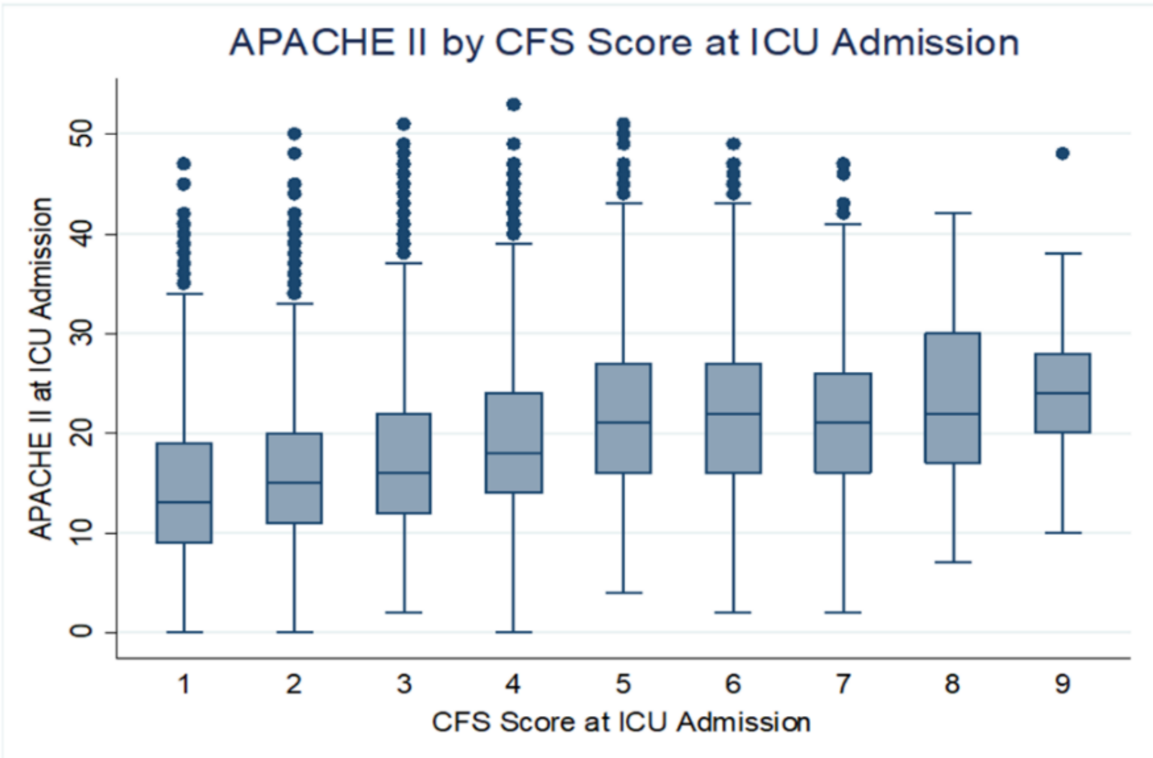
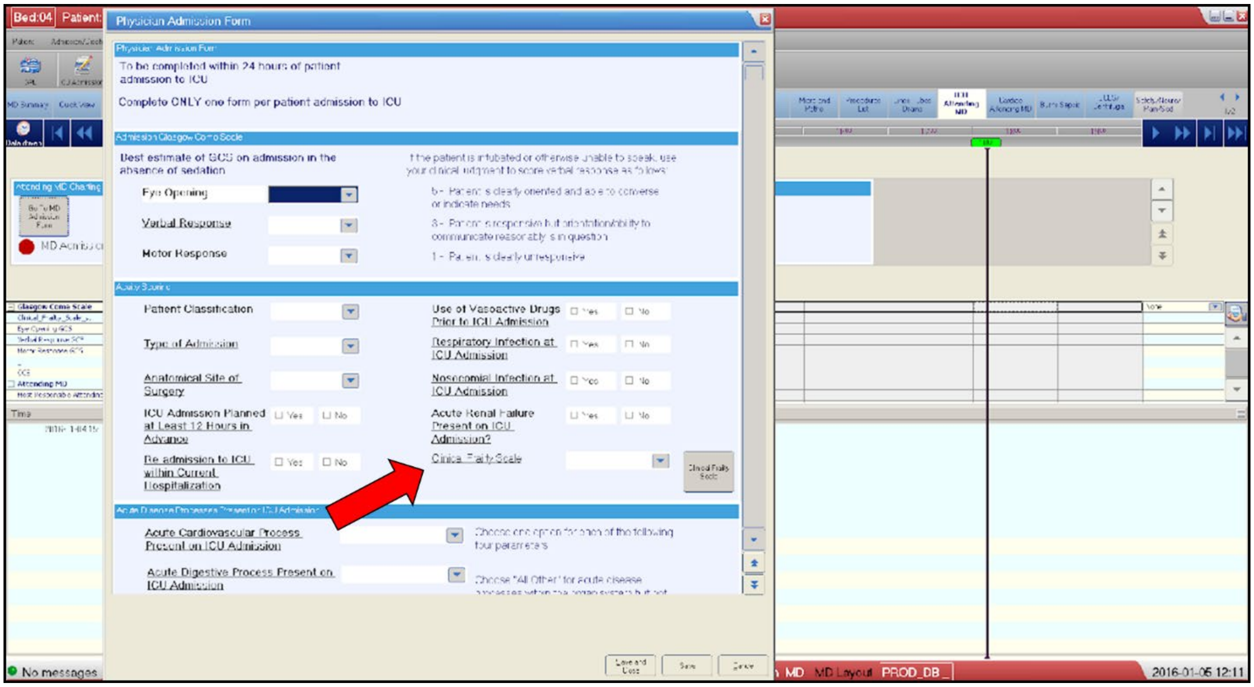


Figure2-4. Distribution of APACHE II admission scores across Clinical Frailty Scale (CFS) scores in patients admitted to adult ICU in Alberta.



Supplementary Figure 2-1. Demonstration of integration of the Clinical Frailty Scale into the Physician Admission Form of eCritical MetaVision charting.

Alberta Health Services

Clinical Frailty Score

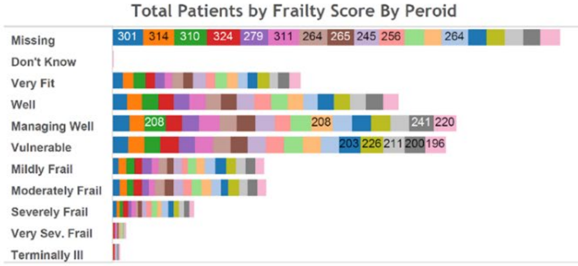
eCritical ALBERTA

Type All | Zone All | Site All

01-Jan-16 to 30-Jun-17

Site / Clinical Frailty Score	Grand Total	Missing	Don't Know	Very Fit	Well	Managing Well	Vulnerable	Mildly Frail	Moderately Frail	Severely Frail	Very Sev. Frail	Terminally Il
Chinook Regional Hospital ICU	1,063	381 35.8%	0 0.0%	68 6.4%	106 10.0%	139 13.1%	129 12.1%	70 6.6%	100 9.4%	60 5.6%	8 0.8%	2 0.2%
Foothills Medical Center CVICU	1,992	380 19.1%	0 0.0%	117 5.9%	284 14.3%	677 34.0%	402 20.2%	76 3.8%	38 1.9%	10 0.5%	2 0.1%	6 0.3%
Foothills Medical Center ICU	1,841	214 11.6%	0 0.0%	231 12.5%	366 19.9%	367 19.9%	336 18.3%	122 6.6%	128 7.0%	67 3.6%	8 0.4%	2 0.1%
Grande Prairie QEII Regional ..	486	27 5.6%	0 0.0%	71 14.6%	85 17.5%	126 25.9%	83 17.1%	42 8.6%	43 8.8%	8 1.6%	1 0.2%	
Grey Nuns Hospital ICU	693	8 1.2%	0 0.0%	93 13.4%	150 21.6%	141 20.3%	160 23.1%	52 7.5%	58 8.4%	31 4.5%		
Mazankowski Alberta Heart In..	2,435	999 41.0%	0 0.0%	48 2.0%	130 5.3%	317 13.0%	469 19.3%	186 7.6%	194 8.0%	54 2.2%	30 1.2%	8 0.3%
Medicine Hat Regional Hospita..	681	276 40.5%	0 0.0%	62 9.1%	72 10.6%	86 12.6%	93 13.7%	41 6.0%	32 4.7%	13 1.9%	1 0.1%	5 0.7%
Misericordia Community Hosp..	645	22 3.4%	0 0.0%	35 5.4%	78 12.1%	119 18.4%	151 23.4%	69 10.7%	84 13.0%	73 11.3%	12 1.9%	2 0.3%
Northern Lights Health Centre ..	500	257 51.4%	0 0.0%	96 19.2%	42 8.4%	37 7.4%	46 9.2%	4 0.8%	10 2.0%	4 0.8%	2 0.4%	2 0.4%
Peter Lougheed Centre ICU	1,087	130 12.0%	0 0.0%	146 13.4%	177 16.3%	173 15.9%	190 17.5%	110 10.1%	104 9.6%	48 4.4%	7 0.6%	2 0.2%
Red Deer Regional Hospital ICU	782	184 23.5%	0 0.0%	64 8.2%	110 14.1%	102 13.0%	145 18.5%	82 10.5%	58 7.4%	27 3.5%	5 0.6%	5 0.6%
Rockyview General Hospital I..	696	88 12.6%	0 0.0%	45 6.5%	117 16.8%	141 20.3%	131 18.8%	74 10.6%	64 9.2%	28 4.0%	7 1.0%	1 0.1%
Royal Alexandra Hospital ICU	2,066	484 23.4%	0 0.0%	197 9.5%	321 15.5%	280 13.6%	335 16.2%	183 8.9%	146 7.1%	98 4.7%	13 0.6%	9 0.4%
South Health Campus ICU	552	69 12.5%	0 0.0%	48 8.7%	89 16.1%	95 17.2%	98 17.8%	52 9.4%	59 10.7%	30 5.4%	7 1.3%	5 0.9%
Sturgeon Community Hospital..	540	21 3.9%	0 0.0%	28 5.2%	104 19.3%	82 15.2%	79 14.6%	71 13.1%	105 19.4%	43 8.0%	6 1.1%	1 0.2%
University of Alberta GS/BUR..	2,447	559 22.8%	0 0.0%	274 11.2%	293 12.0%	345 14.1%	330 13.5%	221 9.0%	235 9.6%	160 6.5%	24 1.0%	6 0.2%
University of Alberta NEURO I..	1,158	287 24.8%	0 0.0%	220 19.0%	282 24.4%	145 12.5%	88 7.6%	28 2.4%	50 4.3%	52 4.5%	2 0.2%	4 0.3%

Total Patients by Frailty Score By Peroid



January 2016 | February 2016 | March 2016 | April 2016 | May 2016 | June 2016 | July 2016 | August 2016 | September 20.. | October 2016 | November 2(

CFS Score Demographics (Averages)

CFS Score	Total Pts	Age	APACHE II	APACHE III	LOS (days)	ICUMortality
0	0	0.0	0.0	0.0	0.0	0.0%
1	1,561	41.8	15.0	53.1	5.4	9.9%
2	2,384	52.4	16.4	57.6	4.8	11.2%
3	2,858	61.0	17.8	61.9	4.7	9.3%
4	2,726	62.3	20.4	68.9	5.4	14.4%
5	1,190	65.2	22.3	75.1	6.7	20.3%
6	1,219	66.2	22.7	75.2	6.1	22.9%
7	635	60.9	22.2	73.6	7.4	24.3%
8	99	64.7	24.1	80.2	7.6	41.4%
9	54	62.0	27.3	95.4	4.6	57.4%

Supplementary Figure 2-2. Summary of AHS eCritical Alberta Clinical Frailty Scale dashboard and TRACER web report.

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Chapter 3. Association Between Pre-Operative Frailty and Outcomes Among Adults Undergoing Cardiac Surgery: A Prospective Cohort Study

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Abstract

Introduction

Few studies have prospectively applied validated measures of frailty case-finding prior in cardiac surgery. The identification of frailty prior to complex and invasive procedures may have relevance for prognostic and recovery purposes, to optimally inform patients, caregivers and clinicians about peri-operative risk and post-operative care needs.

Methods

A prospective cohort study enrolled patients ≥50 years of age referred for planned or urgent cardiac surgery in the two adult cardiac surgery centres in Alberta, Canada between 2011-2014. Patients were screened pre-operatively, in pre-admission clinic or while awaiting surgery on inpatient hospital care units, for frailty using the Clinical Frailty Scale (CFS) and data were captured on socio-demographics, baseline functional status and comorbid disease. Postoperatively, patients were contacted at 6-months and 12-months to assess CFS, health-related quality-of-life (HRQL) and health services use. Vital status was assessed for 5 complete years post-surgery.

Results

The cohort (n=529) mean age (SD) was 67 (9) years, 26% were female, and the prevalence of frailty was 10% (n = 51; 95% CI 7%-13%; CFS ≥5) with median (IQR) CFS 3 (3 – 4). Compared to nonfrail patients, those with frailty were older (73 [9] vs. 67 [9], p<0.001), more frequently female (51% vs. 23%, p<0.001), received valve surgery with or without coronary artery bypass (76% vs. 57%, p<0.05), and had higher median (IQR) EuroSCORE (8 [6 – 9] vs. 5 [3 – 7], p<0.001). Pre-operatively, frail patients were more likely to require help walking (43% vs. 5%, p<0.001) and report a history of falls (35% vs. 11%, p<0.001). Post-operatively frail patients had longer median (IQR) duration of stay in ICU (3 [1 – 5] vs. 1 [1 – 3] days, p<0.001) and hospital (12 [8 – 25] vs. 7 [6 – 10] days, p<0.001). ICU mortality (4% vs. 0.4%; adjusted-OR, 4.89; 95% CI 0.60 – 40.03) and hospital mortality (10% vs. 1%; adjusted-OR, 6.33; 95% CI 1.15 – 34.71) were elevated in the frail group.

Discussion

Pre-operative frailty has important implications for post-operative clinical course, outcomes and resource utilization for cardiac surgery patients. In this prospective cohort study of patients ≥50 years of age referred for cardiac surgery frailty was present in 10% of patients and identified a group of patients with longer duration of hospital stay, greater risk of adverse events, more complex and intense treatment and who were less likely to be discharged home following surgery. Frailty case-finding identifies patients who may benefit from a personalized care pathway that incorporates interventions focused on frailty.

3.1 Background and 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.

3.2 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)

3.2.1 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 3-1)

3.2.2 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)

3.2.3 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)

3.2.4 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%).

3.2.5 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.

3.2.6 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).

3.3 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 3-1; Figure 3-2; Figure 3-3)

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 3-1; Figure 3-4) 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 3-5) Twenty-one patients (4%, 95% CI, 3-6%) were re-admitted to the CVICU during their index hospitalization.

3.3.1 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 3-1)

3.3.2 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 3-2)

3.3.3 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 3-3; Table 3-4; Supplementary Table 3-1)

3.3.4 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 3-5)

3.3.5 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 3-3)

3.3.6 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 3-3)

3.4 Discussion

3.4.1 Statement of principal findings

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.

3.4.2 Strengths and 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.

3.4.3 Implications for clinicians and policy-makers

3.4.3.1 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.

3.4.3.2 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.

3.4.4 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.

3.5 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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Table 3-1. 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) Chronic kidney disease†	91 (47) 6 (1)	97 (39) 2 (4)	91 (48) 4 (1)	0.20 0.11
BMI (Mean, SD) BMI Abnormal‡	30 (6) 232 (44)	31 (6) 25 (49)	30 (6) 207 (43)	0.45 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.

‡ 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 3-2. 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
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)	0.007
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**
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 3-3. 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**
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**

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 3-4. 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	1-4	1.00 (ref)	
	5-9	4.59	1.58-13.28
CFS 2-level, Age, Sex, EuroSCORE log	1-4	1.00 (ref)	
	5-9	4.34	1.54-12.19
CFS 3-level, Age, Sex	1-3	1.00 (ref)	
	4	2.25	0.70-7.21
	5-9	7.11	1.97-25.71
CFS 3-level, Age, Sex, EuroSCORE log	1-3	1.00 (ref)	
	4	1.86	0.56-6.21
	5-9	6.06	1.71-21.51
CFS 4-level, Age, Sex	1-3	1.00 (ref)	
	4	2.24	0.70-7.18
	5	5.94	1.46-24.13
	6-9	11.85	2.11-66.69
CFS 4-level, Age, Sex, EuroSCORE log	1-3	1.00 (ref)	
	4	1.81	0.54-6.09
	5	4.80	1.20-19.16
	6-9	12.86	2.30-72.05

Table 3-5. 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
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.				

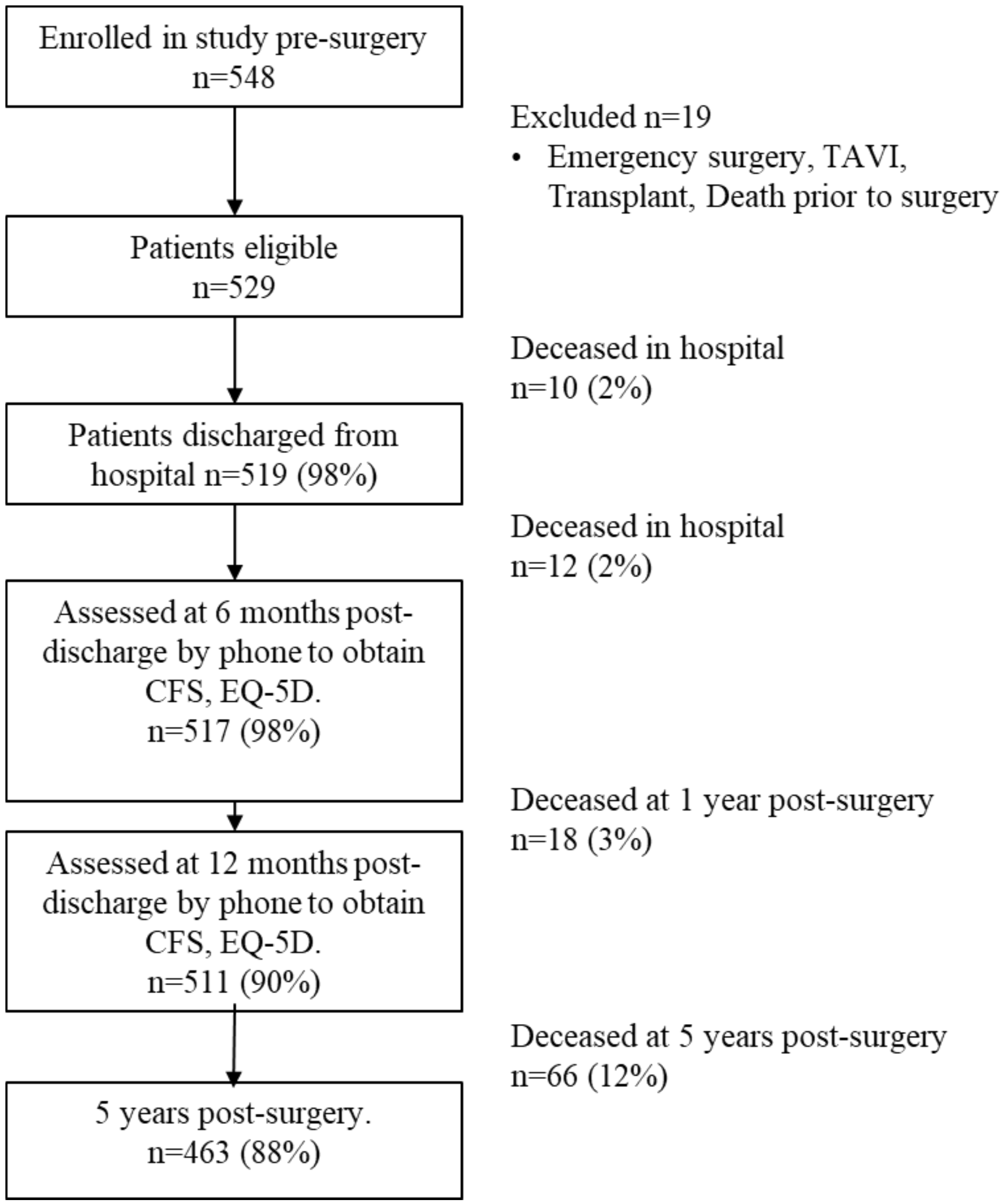

Figure 3-1. Patient selection for cardiovascular surgery study cohort.

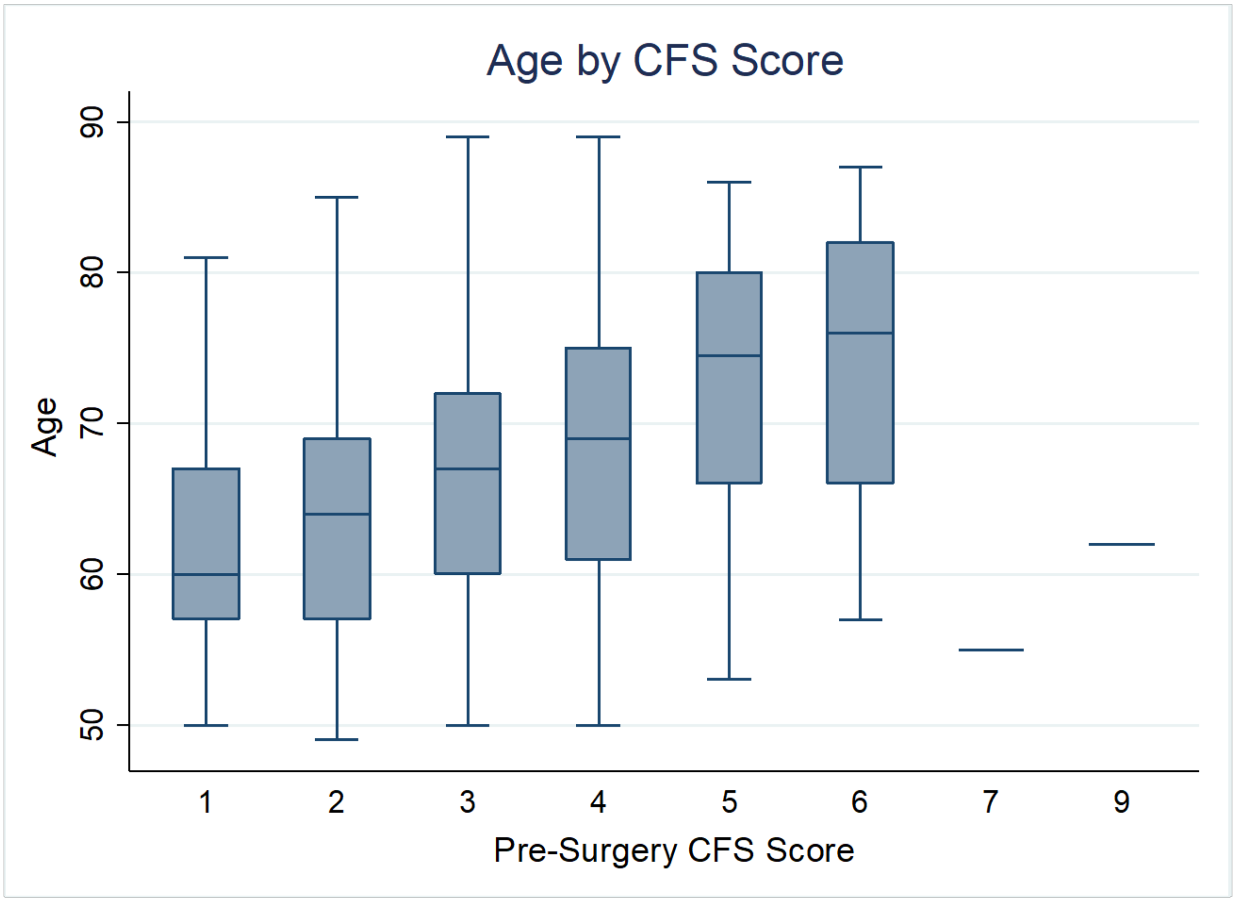

Figure 3-2. Distribution of age across pre-surgery CFS scores.

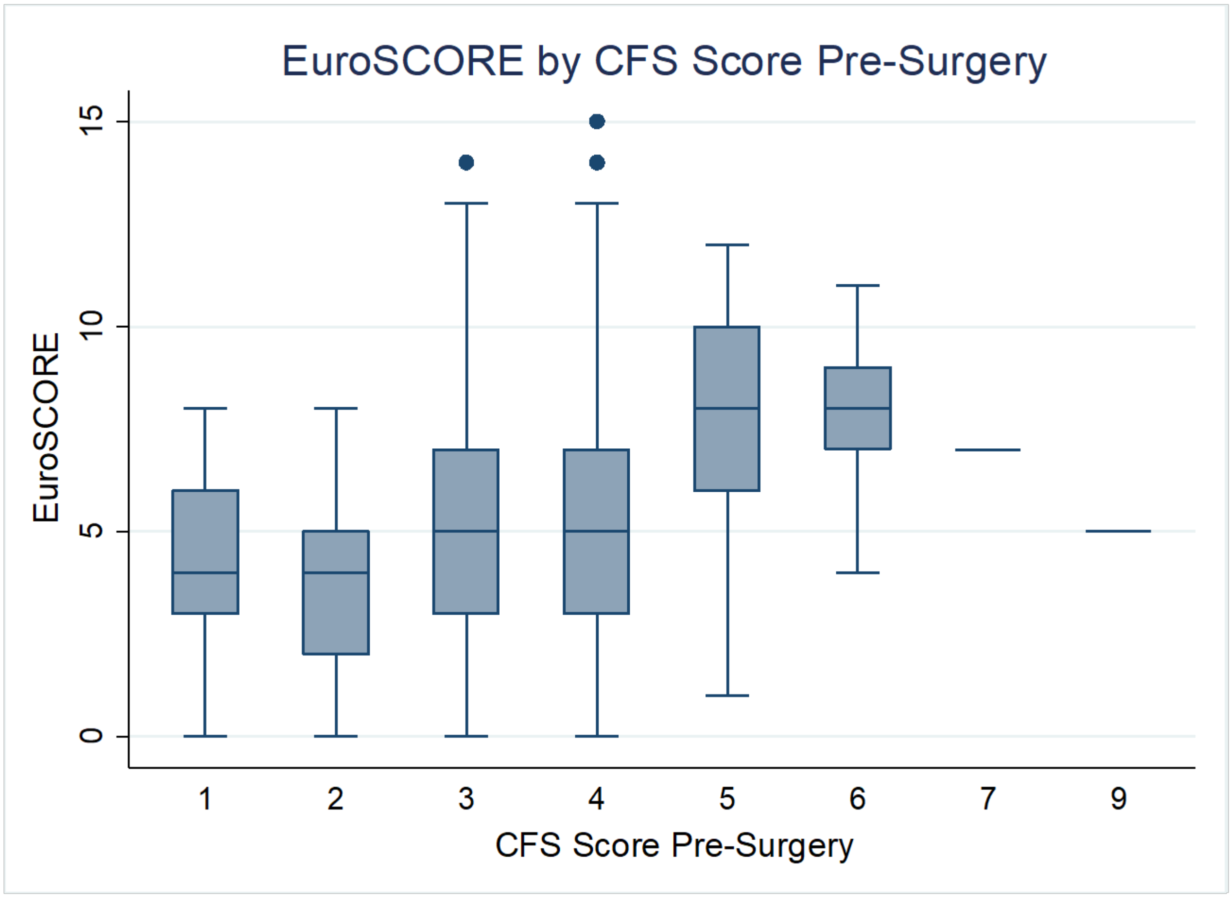

Figure 3-3. Distribution of EuroSCORE (standard) across pre-surgery Clinical Frailty Scale (CFS) scores.

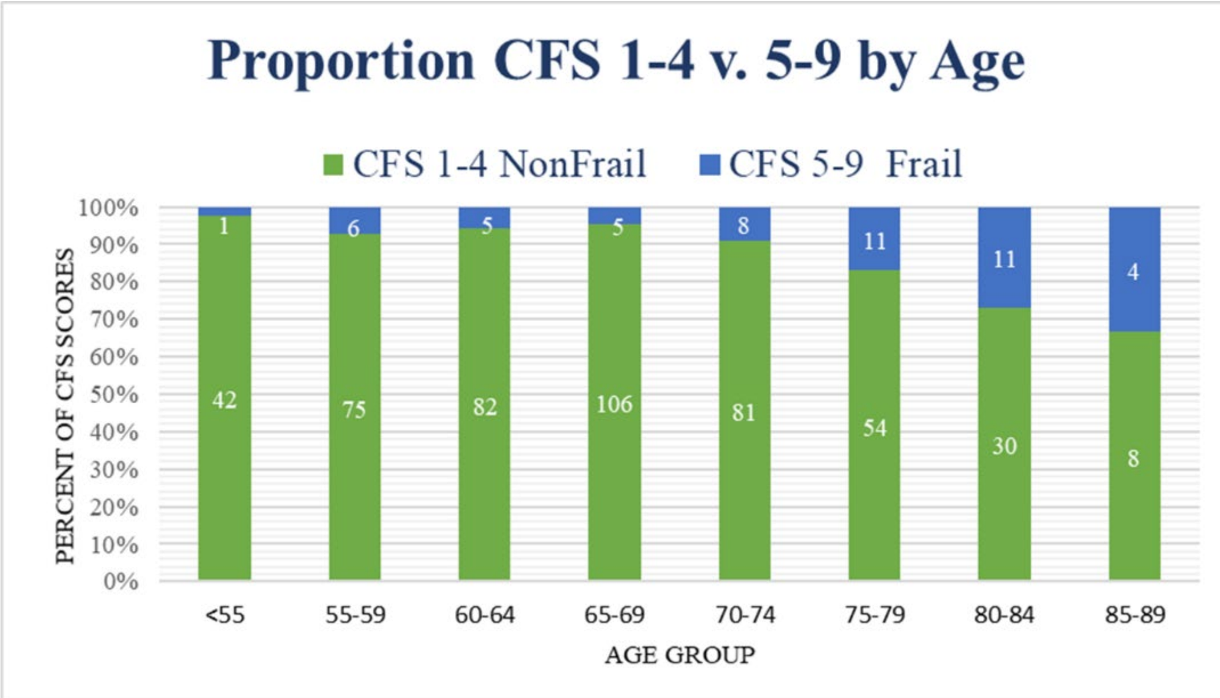

Figure 3-4. Prevalence of frailty (CFS 5-9) across age groups.

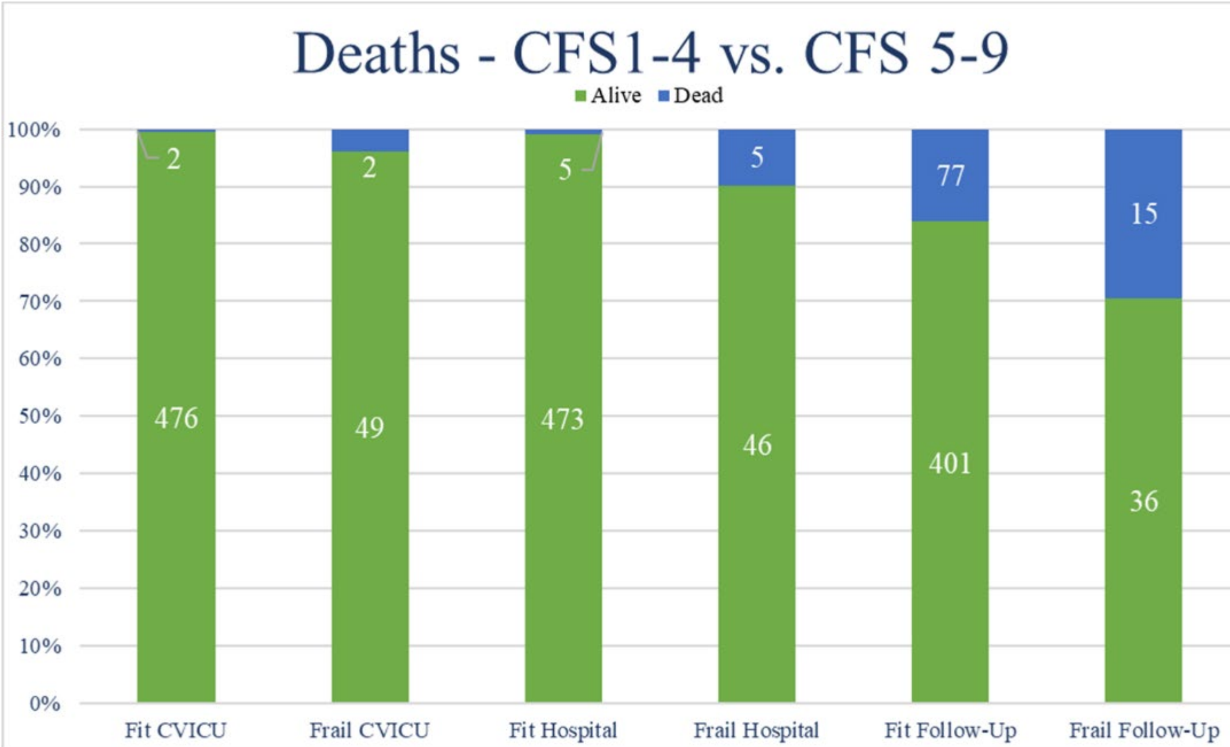

Figure 3-5. Number of deaths in cohort during ≤7-year follow-up, stratified by Clinical Frailty Scale (CFS) score non-frail (CFS 1-4) vs. frail (CFS 5-9).

Supplementary Table 3-1. 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	1-4	1.00 (ref)	
	5-9	5.96	1.72-20.64
CFS 2-level, Age, Sex, EuroSCORE log	1-4	1.00 (ref)	
	5-9	6.02	1.79-20.23
CFS 3-level, Age, Sex	1-3	1.00 (ref)	
	4	2.00	0.44-9.13
	5-9	8.63	1.84-40.50
CFS 3-level, Age, Sex, EuroSCORE log	1-3	1.00 (ref)	
	4	1.51	0.30-7.48
	5-9	7.50	1.64-34.35

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Chapter 4. The Impact of Pre-Operative Frailty on the Clinical and Cost Outcomes of Adult Cardiac Surgery in Alberta, Canada: A Prospective Cohort Study

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Abstract

Background

There is limited evaluation of the impact of frailty on healthcare costs in cardiac surgery. This study aimed to determine quality-adjusted life-years (QALYs) and costs associated with pre-operative frailty in patients referred for cardiac surgery.

Methods and Results

A prospective cohort study of patients ≥50 years of age, referred for non-emergent cardiac surgery from 2011-2014 in Alberta, were screened pre-operatively for frailty using the Clinical Frailty Scale (CFS). Vital status, health services use, costs and EuroQol-5-D (to calculate QALYs) were assessed post-operatively. Public payer costs attributable to frailty were calculated in a difference-in-difference (DID) model.

The cohort (n=529) mean age (SD) was 67 (9) years, EuroSCORE was 5 (3), 26% were female and prevalence of frailty (CFS ≥5) was 10% (n=51; 95% CI 7%-12%). Valve surgery with/without coronary artery bypass was more frequent (76% vs. 57%, p=0.01), post-surgery median (IQR) duration of stay was longer in ICU (3 [1-5] vs. 1 [1-3] day; p<0.001) and in hospital (12 [8-25] vs. 7 [6-10] days; p<0.001) for frail vs. non-frail patients. QALYs gained were similar (0.02 [-0.02-0.05] vs. 0.02 [0.00-0.04], p=0.58, median difference 0.003 [95% CI -0.01-0.02]) at 1-year for frail and non-frail patients. Median (IQR) costs for frail patients were higher in the first year post-surgery ($200,709 [$146,177-$486,852] vs. $147,730 [$100,674-$177,025]; p<0.001); DID attributable cost of frailty was $57,836 (SE $44,104).

Conclusions

Frailty was present in 10% of patients referred for non-emergent cardiac surgery and identified a population with impaired quality-of-life and greater healthcare costs at baseline and following surgery. These findings should inform decisions on health system planning for cardiac surgical services in an ageing population with growing prevalence of frailty.

4.1 Background and Introduction

Frailty is the most common condition leading to death among community-dwelling elderly persons.[1] It is described as a multidimensional syndrome resulting from the accumulation of deficits over time, and characterized by exaggerated vulnerability to adverse outcomes, especially following conditions of stress.[2,3] Rapid growth in the older demographic and concomitant increased prevalence of cardiovascular disease and frailty have been linked to prolonged duration of hospital stay, major morbidity, loss of independence, decline in overall quality-of-life and higher costs related to health services use near the end of life.[4-7] Despite frailty adding discriminative value to explain the observed variance in costly adverse events, it is rarely identified prior to cardiac surgery.[8] With the population over 65 years of age expected to increase to 23-39% across Organization for Economic Co-operation and Development (OECD) countries,[9] the number of people living with chronic conditions (e.g., diabetes mellitus, hypertension, coronary artery disease) and frailty are anticipated to rise, as will demand for cardiac surgery.

Previous studies have focused on the ability of established pre-operative risk stratification models, age,[10] and postoperative complications (e.g., infection,[11] bleeding,[12] atrial fibrillation,[13] acute kidney injury[14]) to predict costs associated with cardiac surgery. While non-cardiac surgical procedures have been the focus of cost prediction in the presence of pre-operative frailty, only one small single-center study has focused on cardiac surgery.[8]

In a publicly-funded health care system, it is essential to measure the relative benefits and costs of invasive and complex procedures that may use a substantial proportion of health spending relative to alternatives, including foregoing procedures.[15] From the national perspective, cardiac surgery (i.e., coronary artery bypass graft and valve replacement) is the most frequent surgical procedure among patients admitted to ICU, responsible for at least 21,000 ICU admissions per year. Moreover, ICU care has been identified as one of the most resource-intensive and costly services in acute care hospitals.[16-18] In the province of Alberta, cardiac surgery is provided to relatively few people, with approximately 2,700 surgeries performed annually amongst a provincial population of 4 million.[19-21] Pre-operative screening for frailty can provide an opportunity to potentially intervene to better manage costs and improve clinical outcomes in this population. Accordingly, we aimed to describe the outcomes, health services use and costs associated with patients living with frailty undergoing cardiac surgery. Our hypothesis was pre-operative frailty in cardiac surgery patients would be associated with greater morbidity, utilization of health services and higher costs in the year prior to surgery and subsequent years following surgery.

4.2 Methods

Health research ethics approval was obtained from the University of Alberta Research Ethics Board (File #Pro00074770). Each patient or legally authorized representative provided written informed consent prior to participation.

4.2.1 Study Design and Setting

We conducted a comparative cost analysis of frailty within a prospective observational cohort of patients ≥50 years of age referred for planned or urgent surgery at the two cardiac surgical centers in Alberta, Canada 2011-2014. The cohort was assessed for frailty (i.e., exposure) using the validated Clinical Frailty Scale (CFS)[3,22-24] and health related quality of life (HRQL) using the EuroQol (EQ-5D-3L)[25] prior to surgery, at 6-months and at 12-months post-surgery. Surgical details, comorbidities and adverse events were obtained from health records. The CFS is an instrument widely available, intuitive to use and easy to apply to patients in any setting and has been used in regression models to predict patient-centered outcomes in community, acute care and critical care environments.[3,26,27] For the purpose of identifying patients with frailty for this study, patients were categorized according to their CFS score as frail (CFS ≥5) or non-frail (CFS≤4).[3,26]

4.2.2 Perspective and Time Horizon

This comparative cost analysis was completed from a public payer perspective to account for costs to the Alberta health care system, over a time horizon one year prior and extending to 5 complete years following the index surgery.

4.2.3 Data Sources and Costing Methods

The health care system in Alberta is publicly funded and administered whereby all residents of the province receive universal access to essential hospital and medical services. Data are captured for all encounters with publicly funded health services in the province. For this study, costing data were obtained from Alberta Health Services (AHS) and Alberta Health (AH). Cost components were captured reflecting inpatient services, outpatient visits, emergency department visits, practitioner/physician service claims and community care services (i.e., long-term facility-based care [LTC], designated supportive living [DSL] and home living [HL]). Alberta cost data is rigorously validated in accordance with provincial and national guidelines, ensuring they are of high quality.[28,29] Data linkages were performed using facility medical record numbers and/or the provincial 9-digit unique personal health number. An inflation rate referencing the Canadian consumer price index, was used to adjust all costs to 2018 Canadian dollar equivalent.[30] All costs were summed at the patient level annually.

Cost of individual hospitalization was estimated by adjusting the cost per standard hospital stay (CSHS) by the resource intensity weight (RIW). The RIW is assigned on discharge, reflecting the amount of resources consumed by an individual patient relative to what is expected for the case mix group (CMG), age, discharge status and comorbidities.[31,32] In Alberta, the inpatient discharge abstract database (DAD) captures demographic, administrative and clinical data for inpatient interventions to determine the RIW. The CSHS includes inpatient nursing services, surgical, ICU, general ward, medical imaging, clinical laboratory and pharmacy for the duration of hospital stay, and is estimated using a Canadian Institute for Health Information (CIHI) micro-costing approach to inpatient DAD elements for each CMG.[31] CSHS was obtained from the AH Interactive Health Data Application (IHDA).[33]

We obtained average cost adjusted for inflation from the IHDA for each individual emergency department visit, outpatient clinic visit and day procedure. Visits were grouped by the CIHI Comprehensive Ambulatory Care Classification System grouping methodology.[34]

Practitioner claims were captured for each fee-for-service claim in line with the provincial schedule of medical benefits, and the assessed amount for each alternative relationship plan

(ARP) claim in the provincial practitioner claims database.[35] Duration of stay in LTC and DSL were captured in the Alberta Continuing Care Information Systems (ACCIS), a transaction processing system that supports the delivery of LTC, DSL and HL. Continuing Care costs depend on assessed resource needs and authorized services. The mean daily costs in LTC and DSL sites for the cohort were provided by AH for this study and applied to actual patient days in care.[36] Costs associated with HL services were excluded.

Outpatient prescription drugs costs were excluded due to inconsistent patient insurance coverage in the 50-65-year-old group, recognizing that patients in this age group would be eligible for coverage from multiple private insurance payers.

4.2.4 Measured Outcomes

The primary outcome was the difference-in-difference (DID) cost between propensity score matched frail and non-frail patients prior to and following surgery, considered to be the cost attributable to frailty. Secondary outcomes included: quality-adjusted life years (QALYs) realized in the year following the index surgery; the QALYs gained attributable to frailty at one year following surgery; health services use; and mortality.

4.2.5 Statistical Methods

In alignment with recommendations from the Canadian Agency for Drugs and Technologies in Health (CADTH),[37] a DID approach presented a simple model to describe the attributable cost of frailty among patients referred for cardiac surgery. A propensity score-matched analysis was performed to account for differences in socio-demographic, comorbidity and clinical factors among the cohort, and the likelihood of confounding variables predicting frailty at the time of surgery. Propensity scores were calculated by logistic regression with pre-operative frailty as the dependent variable. All pre-operative variables were included in the initial logistical model, with subsequent step-wise removal of covariates that predicted the treatment perfectly, were non-significant ($p>0.25$) or where observations were missing.[38] (Supplementary Table 4-1)

Subsequent DID analyses of cost differences between frail and non-frail patients during the pre-surgery year compared to each year post surgery were performed. Patients were excluded from each annual comparison if a full year of costs were unavailable (i.e., death or lost-to-follow-up). (Figure 4-1) Baseline characteristics between groups were compared before and after propensity score adjustment to assess balance and bias reduction. (Supplementary Table 4-2) We conducted the DID using kernel-based matching on estimated propensity scores, matching each frail patient with one or more non-frail patients. Results were compared using local linear matching, followed by bootstrapping to estimate the standard error.[39]

HRQL was measured using EQ-5D-3L survey results, combined with the Canadian valuation of health states to determine equivalent health utilities.[40] The average of baseline and 6-month, and 6-month and 12-month health utilities were summarized to calculate QALYs. Further, DID was used to compare frail to non-frail QALYs gained at 1-year following surgery, to demonstrate the differential effect of frailty on QALYs gained.

Descriptive statistics were tabulated by CFS score ≥5 (frail) compared to CFS score ≤4 (non-frail). Normal (and near-normal) distributed data were reported as means with standard deviations (SD) and compared using Student's t-test. Non-normal distributed continuous data were reported as medians with interquartile ranges (IQR) and compared using Mann–Whitney U or Hodges-Lehmann generalized median differences with 95% confidence intervals (CI). Categorical variables were compared using Pearson's Chi-square test for independence (cell $n>5$) and Fisher's exact (cell $n\leq5$). All tests of significance were two-sided with $p<0.05$ considered statistically significant. Statistical analyses were performed using Stata 14 (College Station, Texas).

4.3 Results

4.3.1 Demographic and clinical characteristics

Of 529 patients enrolled in the study, 10% (n=51) were considered frail (CFS ≥5) pre-operatively. The median (IQR) age was 67 (60-74) years, 26% were female, mean (SD) EuroSCORE was 5 (3), 41% (n=219) underwent isolated valve surgery, 38% (n=202) isolated CABG surgery, and 17% (n=91) received combined CABG/valve surgery. The median (IQR) CVICU stay following surgery was 1 (1-3) day, and post-operative hospital stay was 7 (6-11) days. Mortality was 1% in CVICU (n=4), 3% (n=18) at 1-year post-surgery, and 12% (n=66) at 5 years following surgery. (Table 4-1; Supplementary Tables 4-3 & 4-4)

4.3.2 Healthcare costs and resource utilization

The overall costs associated with comprehensive health services for the cohort during one year prior to surgery up to 7 years following surgery was $149 million. Patients with frailty had higher median (IQR) overall costs compared to non-frail patients ($387,360 [$187,254-$613,684] vs. $178,860 [$136,779-$265,611], p<0.001), a median cost difference $145,166 (95% CI $67,519-$265,909). The costs of all services in the year prior to surgery were higher for patients with frailty compared to non-frail patients ($12,708 [$7,775-$18,852] vs. $7,642 [$5,802-$11,513], p<0.001), median difference $3,994 (95% CI $1,906-$6,611). Health services cost in the year following surgery for patients with frailty were $200,709 ($146,177-$486,852) compared to $147,730 ($100,674-$177,025) in the non-frail group (p<0.001), median difference $70,171 (95% CI % $34,137-$140,797). (Table 4-2; Figure 4-2)

In propensity-matched DID analysis, the mean (SE) cost attributable to frailty in the first year following surgery was $57,863 ($44,104). In the second year following surgery that cost fell to $10,098 ($9,912). Subsequent years' results indicated, conditional on patients surviving three years post-surgery, that the costs attributable to patients with frailty approached that of the non-frail patients. Although small numbers of patients in the frail group resulted in non-significant statistical results, the direction of effect favors diminishing costs for frail patients over time. Similar results were found using local linear matching with standard error calculation by bootstrapping. (Table 4-3)

4.3.3 Health-related quality of life

HRQL was more impaired for patients with frailty compared to non-frail patients at baseline, at 6-months and at 12-months following surgery. Complete EQ-5D results were obtained for 88% (n=464) of patients at all 3 measurement points (frail n=47, 92%; non-frail n=417, 87%). Median (IQR) estimated QALYs in the year following surgery was 0.81 (0.74-0.86). Between the pre-operative and 12-month measures, patients with frailty had fewer QALYs realized compared to non-frail patients (0.71 (0.57-0.77) vs. 0.82 (0.75-0.86), $p<0.001$). QALYs gained were similar for frail and non-frail patients (median [IQR] 0.016 [-0.02-0.05] vs. 0.018 [0.00-0.04], $p=0.58$), median difference 0.003 [95% CI -0.01-0.02]). (Table 4-4) Results from the DID model were similar, demonstrating a mean QALY gain in the year following surgery of 0.006 attributable to frailty ($p=0.61$).

4.4 Discussion

4.4.1 Key Findings

In this prospective cohort study of patients ≥50 years of age referred for cardiac surgery, we found 10% of patients were identified as frail prior to surgery. As expected, patients with frailty were older, had lower baseline HRQL, higher EuroSCOREs and underwent more complex surgical interventions. We found that patients with frailty had longer durations of stay in CVICU and in hospital, had similar QALYs gained at 1-year after surgery and had greater health care costs one year prior to and following surgery.

4.4.2 Context with prior research

While these findings are consistent with those from studies performed in non-cardiac surgery populations,[41,42] the cost implications of frailty have not been rigorously explored in cardiac surgical settings. Prior work has focused on the proximate acute care costs associated with older patients undergoing cardiac surgery.[10,43] Only one single centre study has previously described the hospitalization-related costs among patients with frailty after cardiac surgery. In this study of 235 older patients referred for cardiac surgery, those found to be frail (defined as a Fried score >3 or a Short Performance Battery Score <5)[44,45] not only incurred greater risk of complications following surgery, but also greater median (IQR) costs during hospitalization compared to non-frail patients ($32,742 [$23,221-$49,627] vs. $23,370 [$19,977-$29,705]).[8] Our findings are largely consistent with these observations; however, our study adds new knowledge on the mortality-adjusted costs and long-term survival for patients with frailty undergoing cardiac surgery. Not surprisingly, our results also showed HRQL in frail patients was more impaired at baseline and at one year after surgery, compared to non-frail patients. Furthermore, we were able to show patients with and without frailty have similar incremental gains in QALYs through one-year.

Importantly, we also showed that by 3 years, costs attributable to frailty among survivors were similar between patients who were frail compared to non-frail, a finding potentially related to survival bias. Functional and HRQL recovery improved over time for frail patients and may take longer than 1 year to be realized. These results were similar to findings from a study of 534 cardiac surgery patients ≥75 years of age over 5 years post-surgery.[46] Although the cohort was older than our study, the overall HRQL improved from baseline to six months post-operatively, and remained stable up to five years after surgery.

4.4.3 Implications for policy, clinicians and research

Patients with frailty undergoing cardiac surgery are at greater risk of complications, prolonged hospitalization, death and higher proximate healthcare costs, along with greater burden of downstream impairment in HRQL, health services use, and long-term healthcare costs, as confirmed in our study. Accordingly, a standardized assessment for frailty may offer numerous opportunities for improving patient outcomes and optimizing health resource use.

Frailty case-finding prior to surgery can provide clinicians and patients (and their caregivers) better information about the risk of adverse events associated with frailty and cardiac surgery. Knowledge of pre-operative frailty status may afford opportunity to delay surgery and improve relative fitness (i.e., prehabilitation)[47-49] or target innovative care pathways designed to rapidly restore cognitive and functional status following surgery (i.e., analogous to enhanced recovery after surgery [ERAS] pathways).[50] The impact of these strategies in cardiac surgery should be evaluated in clinical trials.

4.4.5 Strengths and limitations

Our study has a number of strengths including being prospective, using a validated instrument to determine frailty, including HRQL measures, comprehensive baseline and long-term outcome and costing data capture. Our study also has limitations. First, while the CFS was developed in an older ambulatory population and has been validated in ICU settings; it has not been explicitly described in cardiac surgery. Second, the CFS score was not obtained by geriatric medicine clinicians; rather it was obtained by experienced research personnel trained to reliably capture the CFS score; as previously described.[24,26] Third, we only obtained HRQL data to one-year following surgery; limiting our ability to project cost per QALY gained for a longer duration. Fourth, we had no comparison group without surgical intervention to determine the net benefit of surgery in frail patients. Finally, our study was performed in a single-payer health system in a single Canadian province with two cardiac surgery referral centers. As such, our study may have limited generalizability to other health care jurisdictions with differences in socio-demographic factors, surgical case mix and health systems funding models.

4.5 Conclusion

Frailty was present in 10% of patients referred for non-emergent cardiac surgery and identified a population with impaired quality-of-life and greater healthcare costs. Costs attributable to frailty in the year following surgery were $57,863, representing opportunity costs that should be considered in future cardiac surgical services planning in the context of our ageing population with growing prevalence of frailty.

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Disclosures

The manuscript was read and approved by all authors. All authors confirm their responsibility for its present form. All authors have completed the ICMJE uniform disclosure form (available on request from the corresponding author) and declare: all authors are independent of the study funding agency; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Table 4-1. Characteristics of the cohort, comparisons before and after propensity score matching.

Characteristic	Before Matching (n=529)			After Matching§ (n=482)		
	Frail CFS ≥5 (n= 51)	**Non-frail CFS ≤4 (n= 478)**	**p**	**Frail CFS ≥5 (n=41)**	**Non-frail CFS ≤4 (n=441)**	**p**
CFS prior to surgery (median,IQR)	5 (5-6)	3 (5-6)	<0.001	5 (5-5)	3 (3-4)	<0.001
Sex, female	26 (51)	111 (23)	<0.001	21 (51)	107 (24)	<0.001
Age (median; IQR)	75 (65-80)	67 (60-73)	<0.001	74 (63-80)	67 (60-73)	0.001
EuroSCORE (mean,SD)	8 (3)	5 (3)	<0.001	8 (3)	5 (3)	<0.001
Charlson comorbidity index (median; IQR)	2 (0-4)	1 (0-3)	0.04	1 (0-3)	1 (0-3)	0.26
Employed or volunteer	9 (18)	233 (49)	<0.001	9 (22)	214 (49)	0.001
Education post-secondary	35 (71)	255 (54)	0.02	27 (69)	236 (54)	0.07
Married	38 (75)	380 (80)	0.39	33 (80)	349 (79)	0.86
Race non-Caucasian	8 (16)	50 (11)	0.25	8 (20)	45 (10)	0.06
Support at home	34 (67)	254 (53)	0.07	28 (68)	231 (53)	0.05
Previous 12-month hospitalizations	22 (45)	106 (23)	0.001	17 (44)	101 (23)	0.005
Pre-surgical conditions						

Cardiac						
CHF	17 (33)	63 (13)	<0.001	14 (34)	59 (13)	<0.001
PVD	10 (20)	48 (10)	0.04	7 (17)	44 (10)	0.16
Pacemaker or AICD	6 (12)	12 (3)	0.001	3 (7)	11 (2)	0.11
Aortic valve stenosis	31 (61)	196 (41)	0.01	23 (56)	181 (41)	0.06
Previous cardiac surgery	3 (6)	29 (6)	0.96	2 (5)	24 (5)	1.00
PAH	11 (22)	36 (8)	0.001	10 (24)	29 (7)	<0.001
HTN	41 (80)	360 (75)	0.42	32 (78)	334 (76)	0.74
Dyslipidemia	37 (73)	335 (70)	0.71	30 (73)	313 (71)	0.77
Smoker current	4 (8)	60 (13)	0.50	4 (10)	55 (13)	0.80
Smoker previous	22 (43)	218 (46)	0.74	19(46)	203 (46)	0.97
EF <40	2 (4)	42 (9)	0.30	2 (5)	36 (8)	0.76
Past MI	10 (20)	97 (20)	0.91	10 (24)	87 (20)	0.48
Recent MI	1 (2)	13 (3)	1.00	1 (2)	13 (3)	1.00
Previous CVICU	5 (10)	24 (5)	0.17	3 (8)	20 (5)	0.42
Non-cardiac						
Coagulopathy	6 (12)	12 (3)	0.001	5 (12)	12 (3)	0.01
Liver	1 (2)	13 (3)	1.00	1 (2)	11 (3)	1.00
Creatinine, pre-surgery (mean,SD)	97 (39)	91 (48)	0.20	91 (36)	90 (40)	0.86

Chronic kidney disease*	2 (4)	4 (1)	0.11	1 (2)	3 (1)	0.30
Renal	13 (25)	50 (10)	0.002	9 (22)	45 (10)	0.02
COPD	18 (35)	91 (19)	0.006	14 (34)	84 (19)	0.02
Hypothyroid	15 (7)	52 (11)	<0.001	10 (24)	49 (11)	0.01
Weight loss	10 (20)	64 (14)	0.22	9 (22)	60 (14)	0.14
NIDDM	14 (28)	120 (25)	0.71	9 (22)	110 (25)	0.67
IDDM	2 (4)	33 (7)	0.56	1 (2)	32 (7)	0.34
PUD	5 (10)	25 (5)	0.20	3 (7)	23 (5)	0.48
Malignancy	13 (26)	55 (12)	0.01	9 (22)	51 (12)	0.05
Rheumatoid arthritis	19 (37)	62 (13)	<0.001	14 (34)	56 (13)	<0.001
BMI (mean, SD) BMI abnormal†	31 (6) 25 (49)	30 (6) 207 (43)	0.45 0.43	31 (7) 18 (44)	30 (6) 194 (44)	0.44 0.99
History of falls	17 (35)	52 (11)	<0.001	12 (29)	50 (11)	0.001
Memory loss	20 (39)	126 (26)	0.05	16 (39)	114 (26)	0.07
Cognitive loss	8 (16)	256 (54)	0.01	7 (17)	20 (5)	0.001
General mental	7 (14)	26 (5)	0.01	5(12)	16 (4)	0.03
Neurologic dysfunction‡	16 (31)	21 (4)	0.002	13 (32)	64 (15)	0.004
Paralysis	2 (4)	69 (14)	0.29	2 (5)	8 (2)	0.21
Cerebral vascular disease	5 (10)	9 (2)	0.85	4 (10)	48 (11)	1.00

Prescribed medications (median,IQR)	6 (4-10)	5 (3-7)	<0.001	6 (4-10)	5 (3-7)	0.005
Surgery Type						
CABG only	11 (22)	191 (40)	0.01	10 (24)	178 (40)	0.05
Valve only	24 (47)	195 (41)	0.39	19 (46)	183 (42)	0.55
Combined CABG & Valve	15 (29)	76 (16)	0.02	11 (27)	66 (15)	0.05
Myomectomy/ ASD/ Myxoma	0 (0)	9 (2)	0.32	0 (0)	9 (2)	-
Aorta only	1 (2)	7 (1)	0.78	1 (2)	7 (1)	0.68

Note. Data are presented as n (%) unless otherwise indicated.

* Creatinine >200 pre-surgery.

† BMI abnormal if <19 or >29.

‡Neurologic dysfunction: Disease severely affecting ambulation or day-to-day functioning.

§ Kernel common matching using logit of propensity score from age group, sex, employment status, cognitive loss, congestive heart failure, aortic valve stenosis, pulmonary arterial hypertension, chronic obstructive pulmonary disease, hypothyroidism, malignancy, rheumatoid arthritis, neurologic dysfunction and falls.

Abbreviations: CHF congestive heart failure; PVD peripheral vascular disease; AICD automated implanted cardioverter/defibrillator; HTN hypertension; EF ejection fraction; MI myocardial infarction; CVICU cardiovascular intensive care unit; NIDDM non-insulin dependent diabetes mellitus; PUD peptic ulcer disease; BMI body mass index; CABG coronary artery bypass graft; ASD atrial septal defect.

Table 4-2. Health services costs for cohort.

Health Services Costs	Overall cohort (n=529)	Frail CFS ≥5 (n= 51)	Non-frail CFS ≤4 (n= 478)	p
1-year pre-surgery (median, IQR)	$7,753 ($5,914 - $12,393)	$12,708 ($7,775 - $18,852)	$7,642 ($5,802 - $11,513)	<0.001
1-year post-surgery (median, IQR)	$149,532 ($103,124 - $193,470)	$200,709 ($146,177 - $486,852)	$147,730 ($100,674 - $177,025)	<0.001
Cumulative costs - 1-year pre-surgery to ≤7 years post-surgery (median, IQR)	$184,243 ($141,224 - $281,776)	$387,360 ($187,254 - $613,684)	$178,860 ($136,779 - $265,611)	<0.001
Health services costs = hospital, ambulatory care, claims, supportive living and long term care costs.				

Table 4-3. Difference-in-difference, frail vs. non-frail by year following surgery compared to year prior to surgery for patients with a full year of costs available.

Year Post-Surgery to Year Pre-Surgery	Cohort	Frail Mean Cost ($)	Non-frail Mean Cost ($)	Difference-in-difference ($)	Standard Error	T-stat	p
1st Year	Unmatched	$ 251,921	$ 159,553	**$ 92,369**	$ 23,673	3.90	<0.001
	Matched (ATT)	$ 261,692	$ 203,856	**$ 57,836**	$ 44,104	1.31	0.19
Total matched	n = 482	n = 37	n = 441				
2nd Year	Unmatched	$- 3496	$-5,774	**$2,278**	$6,208	0.37	0.71
	Matched (ATT)	$ 2,079	$-8,019	**$10,098**	$9,912	1.02	0.31
Total matched	n = 462	n = 37	n = 425				
3rd Year	Unmatched	$- 8,996	$-688	**$-8,308**	$8,418	-0.99	0.32
	Matched (ATT)	$- 8,115	$2,998	**$-11,113**	$11,554	-0.96	0.34
Total matched	n = 443	n = 35	n = 408				

Matched (ATT) = Cost 'Attributed to Treatment', where frailty is the 'treatment' variable, matched on propensity score. Kernel common matching method.
Unmatched = comparison of annual cost prior to matching.
Difference in difference = Cost attributable to frailty.

Table 4-4. Quality-adjusted life years (QALYs) pre-surgery to one-year following cardiac surgery.

QALY Related Measure	Overall completed EQ-5D (n=464)	Frail (n=47)	Non-frail (n=417)	p
Cost per QALY realized (median, IQR)	$183,777 ($129,566 - $260,686)	$328,514 ($199,334 - $908,639)	$178,450 ($125,276 - $236,429)	<0.001
1-year QALYs realized (mean, SD)	0.77 (0.14)	0.63 (0.21)	0.79 (0.12)	<0.001
1-year QALYs gained (mean, SD)	0.02 (0.05)	0.01 (0.07)	0.02 (0.05)	0.17
QALY = Quality Adjusted Life Year QALYs calculated by multiplying the health utility score by the time midpoint between surveys.				

Supplementary Table 4-1. Logistic model to predict frailty in cardiac surgery cohort. Variables chosen to include in propensity score model.

Frailty (dependent)	**Odds Ratio**	**SE**	**z**	**p-value**	**95% CI**
Age group	1.23	0.15	1.74	0.08	0.97 - 1.56
Sex	0.49	0.18	-1.92	0.05	0.23 - 1.01
Employed	2.19	1.10	1.57	0.18	0.82 - 5.85
Cognitive Loss	3.68	2.17	2.21	0.03	1.16 – 11.70
CHF	2.31	0.95	2.03	0.04	1.03 – 5.19
AV Stenosis	2.19	0.83	2.08	0.04	1.04 – 4.60
PAH	2.36	1.18	1.72	0.09	0.89 – 6.31
COPD	1.62	0.66	1.19	0.24	0.73 – 3.58
Hypothyroid	2.20	0.98	1.77	0.08	0.92 – 5.29
Malignancy	2.38	1.04	1.98	0.05	1.01 – 5.61
Rheumatoid Arthritis	3.26	1.26	3.06	0.002	1.53 – 6.94
Neurologic Disease	2.39	0.95	2.18	0.03	1.09 – 5.21
Falls	2.56	1.12	2.15	0.03	1.08 - 6.04
_cons	0.01	0.004	-7.83	0.000	0.002 – 0.02

*$R^2 = 0.2788$, $p<0.001$

Supplementary Table 4-2. Balance test of propensity score matched variables.

Variable		Mean Frail (treated)	Mean Non-frail (controls)	% Bias	% Bias Reduction	p-value
Age in 5-year increments	Unmatched	4.15	2.90	68		<0.001
	Matched	3.95	3.93	1	98	0.95
Sex	Unmatched	0.49	0.77	-60		<0.001
	Matched	0.49	0.46	5	91	0.83
Employed or Volunteer	Unmatched	0.82	0.51	70		<0.001
	Matched	0.78	0.78	0	100	1.00
Cognitive Loss	Unmatched	0.16	0.05	34		0.005
	Matched	0.17	0.15	8	76	0.77
CHF	Unmatched	0.33	0.13	49		<0.001
	Matched	0.34	0.34	0	100	1.00
AV Stenosis	Unmatched	0.61	0.41	40		0.007
	Matched	0.56	0.66	-20	51	0.37
PAH	Unmatched	0.22	0.08	40		0.001
	Matched	0.24	0.20	14	65	0.60
COPD	Unmatched	0.35	0.19	37		0.006
	Matched	0.34	0.32	6	85	0.82
Hypothyroidism	Unmatched	0.29	0.11	47		<0.001
	Matched	0.24	0.27	-6	87	0.80
Malignancy	Unmatched	0.25	0.12	36		0.005
	Matched	0.22	0.27	-13	65	0.61
Rheumatoid Arthritis	Unmatched	0.37	0.13	58		<0.001
	Matched	0.34	0.29	12	80	0.64
Neurologic Dysfunction	Unmatched	0.31	0.14	41		0.002
	Matched	0.32	0.29	6	86	0.81
Falls history	Unmatched	0.35	0.11	59		<0.001
	Matched	0.29	0.24	12	80	0.62

*R^2 Unmatched 0.279 p<0.001 Matched 0.021 p=0.999

Supplementary Table 4-3. Patient health services use associated with index cardiac surgery.

Duration of Stay	**Overall (n=529)**	**Frail CFS ≥5 (n= 51)**	**Non-frail CFS ≤4 (n= 478)**	**p**
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 CVICU (n;%)	21 (4%)	5 (10%)	16 (3%)	0.04

Supplementary Table 4-4. Patient mortality following index cardiac surgery.

Post-operative mortality	Overall (n=529)	Frail CFS ≥5 (n= 51)	Non-frail CFS ≤4 (n= 478)	p
CVICU	4 (1%)	2 (4%)	2 (0.4%)	0.05
Hospital	10 (2%)	5 (10%)	5 (1%)	<0.001
30-day	7 (1%)	2 (4%)	5 (1%)	0.14
6-month	12 (2%)	5 (10%)	7 (1%)	<0.001
1-year	18 (3%)	6 (12%)	12 (3%)	0.001
5-year	66 (12%)	13 (25%)	53 (11%)	0.003
Death at any time during follow-up (≤7 years)	92 (17%)	15 (29%)	77 (16%)	0.02
*Mortality statistics obtained from discharge abstract database (inpatient deaths captured) and Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease.				

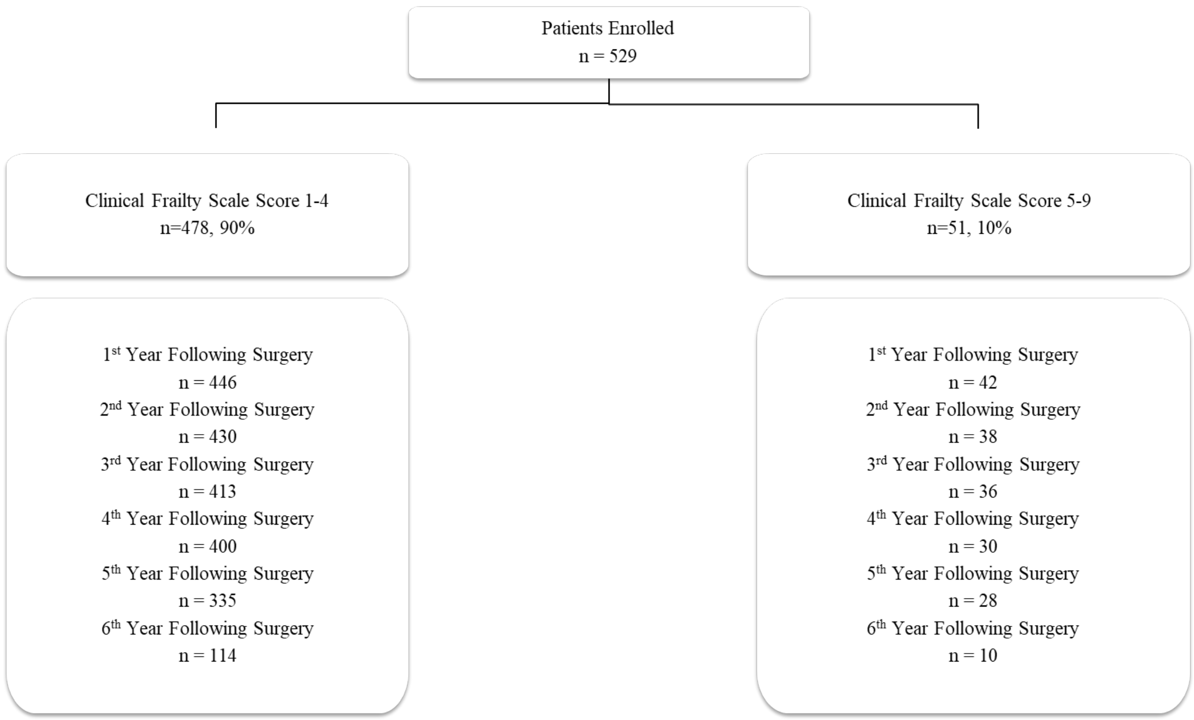

Figure 4-1. Costs accumulated frail v. nonfrail, 1-year prior and post-surgery.

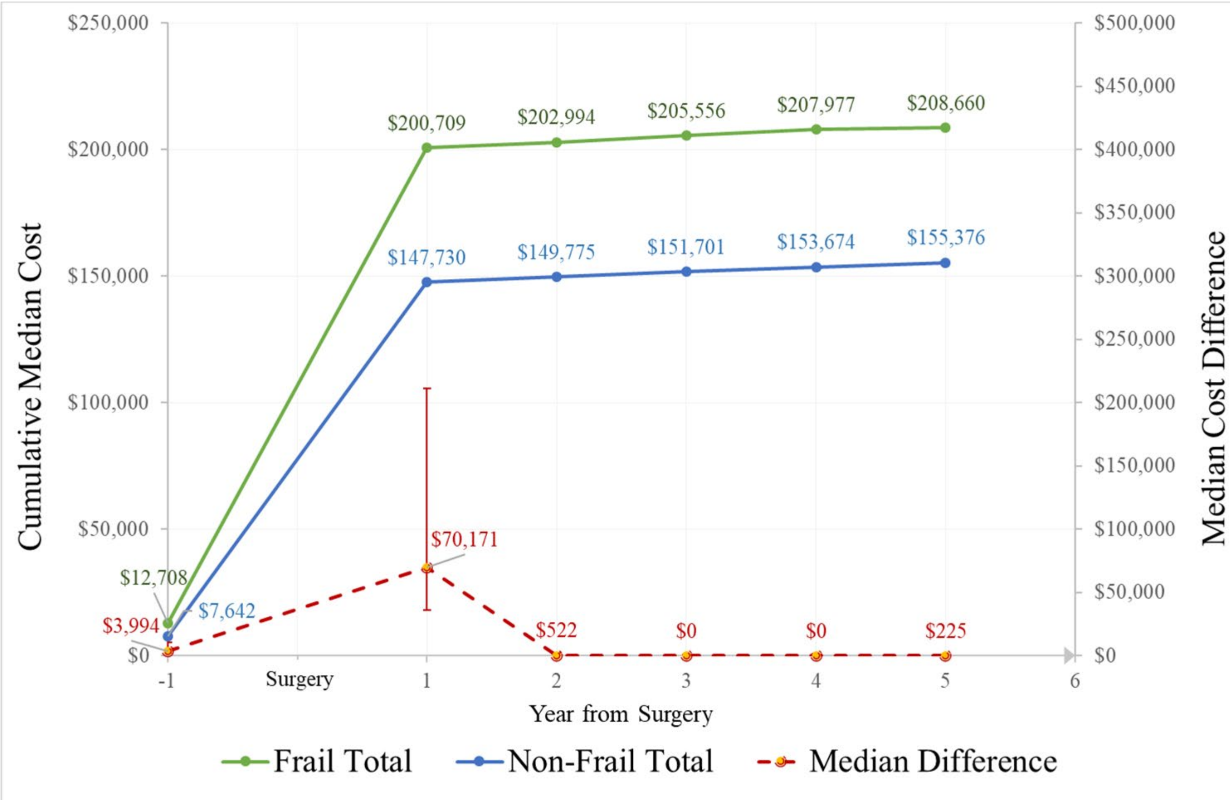

Figure 4-2: Cumulative median cost of frail v. non-frail patients one-year pre-surgery to five years post-surgery.

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Chapter 5. Summary

5.1 Overview of the Research

As the Canadian population ages we can anticipate more patients living with advanced, chronic and complex diseases presenting for treatment in hospital. In Alberta, we have successfully implemented the validated Clinical Frailty Scale (CFS) score into the provincial electronic health record (EHR) for all adult ICU admissions, demonstrating population-level screening for frailty in ICU settings is feasible.[1, 2]

Frailty, in the context of critical illness, informs the risk for worse short and long term outcomes and greater overall use of health services. This program of research describing the epidemiology of frailty and its associated costs contributes a comprehensive assessment of the baseline prevalence of frailty, its correlates, and its associated outcomes in the broader ICU population as well as the cardiac surgery subgroup from a provincial perspective. The routine capture of frailty measures in the provincial ICU EHR provides a viable platform to re-evaluate frailty and its associated clinical and cost outcomes when targeted interventions are implemented.

5.2 Objectives

The objectives associated with the three stated hypotheses were achieved. First, the population-based epidemiology of frailty across all admissions to adult ICUs in Alberta was described. The results of this study establishes a baseline prevalence of frailty for all residents of Alberta with critical illness admitted to ICU. Using results from a cohort study of cardiac surgery patients, the epidemiology of frailty amongst patients referred for cardiac surgery in the province was described. Further to these general descriptions, the comparison of costs between frail and non-frail patients offered a baseline description of the costs and quality-adjusted life years (QALYs) attributable to frailty. To our knowledge this is the first time population measures of frailty and related costs incurred over an extended number of years have been reported.

5.3 Summary of the Findings

Findings from the provincial implementation of the CFS into the ICU EHR highlighted the feasibility of incorporating a valid frailty score into routine collection of patient information at admission. The prevalence of frailty in this population-level study was similar to previous studies, confirming prior data showing that frailty was common, observed in the approximately 1 in 4 admissions to ICU. This finding is in the context of all admissions to ICU in Alberta, rather than previous cohort studies limited to patients 50 years of age or older in a limited number of ICUs. Baseline frailty status was associated with longer duration of stay in ICU and post-ICU hospitalization, substantial health services use and advanced organ support.[1]

In a prospective cohort study of patients referred for cardiac surgery we found 1 in 10 patients were frail. The frail patients were older, had higher EuroSCORE, received more complex surgical interventions, and spent longer in CVICU and hospital, accumulating higher health care costs compared to their non-frail counterparts. Similar to previous published findings, the survivors in this study reported improvements in their health-related quality of life (HRQL) over the year post-surgery. This study is the first to describe the cost and QALYs attributable to frailty. Importantly, we showed that if patients survived the first year after surgery, the costs they incurred annually started to resemble those of their non-frail counterparts. These findings support the need for the application of frailty case-finding in the pre-operative clinical setting to optimize pre-surgical planning, peri-operative care, post-operative rehabilitation and minimize overall costs.

5.4 Implications

5.4.1 Clinical Application

Routine frailty evaluation provides an opportunity for patients, caregivers, clinicians and decision-makers to plan improved interactions between patients living with frailty and the healthcare system. Innovations in care processes and transitions between settings could be customized, specific to frail patients' needs and trajectories, if clinicians were familiar with case-finding tools and available frailty-appropriate interventions. The development of frailty-inclusive care pathways would appear justified and timely as ageing, and subsequent frailty of our population continues to grow.

For healthcare decision-makers, future strategies to address the health services demand of frailty is essential. Resource planning for future ICU service capacity must consider the growth of the older ICU patient population presenting with frailty and their greater complexity, slower recovery and subsequent health services use and accumulated cost. Further planning should incorporate the expected needs of survivors of acute critical illness throughout their recovery and subsequent transitions in care.[3]

Potential interventions include interdisciplinary care pathways to ensure personalized frailty-inclusive care prior to ICU admission, within the ICU and following transition to the hospital ward and community. Recognizing frailty prior to ICU admission may inform discussion about the likely duration of stay, challenges during recovery and risk of subsequent loss of independence following admission. Within the ICU, care pathways could trigger timely investigations of frailty domains to inform care plans and referral to experts in interventional frailty care (e.g., geriatric medicine, dietetics, rehabilitative medicine, palliative care). Focused care pathways targeting frailty case-finding could better identify patients most likely to benefit and improve functional outcomes post-ICU, while mitigating the onset or worsening severity of disability for all patients with frailty.[4, 5]

5.4.2 Future Research

While baseline frailty status prior to critical illness and its substantial relationship to mortality, ICU and hospital duration of stay, new or worsening functional and/or cognitive disability among survivors has been explored, knowledge about the interaction between frailty and critical illness is limited and presents a number of future research opportunities.[6] Future research should aim to evaluate the association between baseline frailty and the longer term susceptibility to adverse events or complications while in ICU and following transition out of the ICU. At present we can only speculate on the interaction of baseline frailty and the mechanisms contributing to persistent critical illness and prolonged ICU stay (e.g., nosocomial infections, delirium, sarcopenia). Frailty is a complex, multidimensional construct at baseline and its fluctuating severity during and after critical illness is not yet understood.

Identifying frailty using valid and reliable methods across populations is an opportunity provided by the electronic frailty index (eFI).[7] In the current context of expanding EHR use, the eFI may be an option deployed across a broader population to aide in focusing on areas of high prevalence and potential interventions. A scenario where frailty is known prior to acute illness may provide useful context to discussions about treatment choices, decisions and expectations. Further updates to an eFI reflecting acute changes in health status require exploration and validation in the Canadian context. Assessment of frailty following critical illness is in early stages, with recent studies showing frail survivors endure high levels of symptom burden, indicating this is an area in need of further study.[8] Survivorship issues have been evaluated for ICU patients admitted for a variety of specific diagoses[9] but are in the early stages for frailty.[6] The identification of patient-specific frailty domains amenable to focused care planning may be possible within the EHR.

Models of care delivery should be investigated to determine the best fit for the growing population of older adults living with frailty. Patients admitted to ICU with varying severities of frailty are unlikely to gain optimal benefit from a routine approach to ICU care and treatment focused only on the primary reason for admission. Tailoring ICU care and treatments to the severity of frailty and primary drivers may improve outcomes. Targeted investigations to understand the drivers of frailty and direct attention to the vulnerabilities in survivors may optimize patient-centred outcomes (e.g., adverse events, duration of stay, disability, HRQL) and protect against future episodes of acute illness.

Potential interventions that need further evidence to determine their benefit for pre-surgery patients who are routinely admitted to ICU (i.e., cardiovascular) include pre-habilitation models where physical, cognitive, nutritional, pharmacological and comorbid disease management could be optimized prior to planned procedures. Limited results are available on such frailty-specific programs.[10-14]

Further research on the real-world application of informed decision-making considering the severity of frailty prior to admission, and prior to discharge from ICU, is an area in need of focus. There are sparse published data focused on how clinicians use information about frailty status in their discussions with patients and families, to guide decision-making prior to admission or during their course in ICU. It is possible that patients would choose limited intensity and duration of advanced life support in the context of advanced pre-morbid frailty, if informed about the risk of suboptimal outcomes (e.g., extended stay in ICU and hospital, impaired HRQL, further hospital admissions, dependent living)[15, 16] for survivors of critical illness. There may also be opportunities for frail survivors of critical illness to re-visit goals-of-care discussions with family and healthcare professionals.[17]

Another area that warrants investigation is determining the severity of frailty associated with a terminal trajectory. The opportunity to consider and provide palliative care in situations where overwhelming symptom burden is not amenable to ICU interventions has yet to be explored. We do know that withholding or withdrawing ICU support is common in studies where limitations of therapy were documented, as high as 43% in patients identified as frail.[18] Details around decision to limit therapy in ICU are yet to be examined.[19]

Finally, expanding research to better understand the cost of frailty is essential to providing context to the future impact of our ageing population with greater numbers of patients with frailty at risk for critical illness. Decision-makers faced with future service planning should have frailty adjusted results to inform their work.

5.5 Limitations

Despite the overall strengths of this research, including the provincial perspective, consistent frailty measurement, comprehensive co-morbidity, clinical, outcome and robust health services data availability, the program of research had several important limitations.

The CFS score in the provincial ICU electronic health record was completed by the attending physician and was not a mandated field, thus the score was frequently missing (19%), although data suggested improvement over the past 2 years. We are confident that audit and feedback will continue to improve compliance. Our reported prevalence of frailty in the study was similar to previous studies in Alberta ICUs but we do not have any data showing how ICU physicians compared to their specialist geriatric colleagues as gold standard in the assignment of CFS scores. In the cardiac surgery study, the CFS was assigned by a research coordinator. Although previous studies have shown reliable results we do not have any information on inter-rater reliability for this study. Across studies, CFS scores were assigned at ICU admission, at pre-admission clinic or during acute hospitalization awaiting surgery. Although the CFS was initially validated in Canadian ambulatory care settings, previous studies have shown its predictive validity in ICU settings. Frailty may have played a role in decisions not to admit patients to the ICU (i.e., patients who declined or were not offered ICU admission). It could also have played a part in selecting patients referred for cardiac surgery. This unknown selection and/or information bias is inherent in all observational studies. Finally, the research presented was limited to a single Canadian province and may not be generalizable to other health jurisdictions.

5.6 Conclusions

The three papers presented clearly show the association of frailty with higher risk of morbidity, mortality and health services use. There is a convincing argument for the routine case-finding of frailty across all ICU admissions, but planned invasive procedures such as cardiac surgery allows for earlier recognition and potential intervention. Knowledge of risk associated with frailty and critical illness could help inform patients, caregivers, clinicians and administrative decision-makers about specific needs for this vulnerable patient population.

5.7 References

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