ORIGINAL RESEARCH

# COVID-19–Associated Outcomes of Critical Illness in Patients with Frailty: a Cohort Study

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## ABSTRACT

### Background

Pre-admission frailty has been associated with higher hospital mortality in patients with critical illness. We aimed to measure the prevalence of frailty and its associated outcomes in patients with COVID-19 critical illness.

### Methods

A historical cohort study of all adults admitted to ICU with a pneumonia diagnosis in Alberta, Canada between May 1, 2020, and October 31, 2020. At ICU admission patients were routinely assessed for frailty using the Clinical Frailty Scale (CFS). Frailty was defined as a CFS score ≥5. Primary outcomes were pre-admission frailty prevalence and hospital mortality.

### Results

The cohort (n=521) prevalence of frailty was 34.2% (n=178), mean (SD) age was 58.8 (14.9) years, APACHE II 22.8 (8.0), and 39.5% (n=206) were female. COVID-19 pneumonia was diagnosed in (19.0%; n=99) admissions; pre-admission frailty was present in 20.2% (n=20) vs. 79.8% (n=79) non-frail ($p$<.001). Among ICU patients admitted with COVID-19, hospital mortality in frail patients was 35.4% (n=63) vs. 14.0% (n=48) in non-frail ($p$<.001).

### Conclusion

Pre-admission frailty was present in 20.2% of COVID-19 ICU admissions and was associated with higher risk of hospital mortality. Frailty assessment may yield valuable prognostic information when considering COVID-19 ICU admission; however, further study is needed to identify effect on patient-centred outcomes in this heterogeneous population.

**Key words:** intensive care, COVID-19, frailty, ICU survivorship, pneumonia

## INTRODUCTION

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic and resulting coronavirus disease (COVID-19) resulted in elevated risk of critical illness and mortality in patients with greater number of comorbidities or older age.[1-3] In addition to these indicators, frailty is also an important measure of a patient's health status. An assessment of baseline functional status may reveal patients who were living with frailty prior to hospital admission.[4,5] Frailty can be measured in critical care settings using validated instruments, such as the Clinical Frailty Scale (CFS) and Edmonton Frail Scale (EFS).[6-9] However, there has been limited evaluation of frailty in critically ill COVID-19 patients.

A limited number of international reports of COVID-19–related ICU outcomes have described an elevated risk of mortality associated with pre-admission frailty.[1,10] Frailty has previously been shown to be superior to chronological age alone, adding incremental value for prognostication. Frailty can inform patient-centred care planning discussions that consider an individual's acute illness and potential need for invasive interventions, to confirm expectations for a clinical course of ICU treatment.[6,7,11] Although contentious, frailty has been integrated into pandemic hospital surge triage scoring and decision algorithms associated with pandemic surge in multiple countries.[12-15]

The concept of frailty should be at the forefront of acute and critical care assessment for its value in predicting outcomes among the older patient population at risk for ICU admission. Accordingly, we performed a population-based cohort study to evaluate the prognostic value of routinely captured pre-admission frailty scores on outcomes for patients with COVID-19 pneumonia admitted to ICU in Alberta, Canada. We hypothesized that critically ill COVID-19 patients with pre-admission frailty would have higher mortality and more frequent adverse outcomes than patients assessed as non-frail.

## METHODS

This study was approved by the Research Ethics Board at the University of Alberta (Pro00102891). The requirement for informed consent was waived for use of secondary administrative health data. Verbal consent was received from phone survey respondents. The reporting of this study follows recommendations outlined in the STROBE statement.[16]

### Design, Setting, Population

The study population was retrospectively identified from all patients admitted to 14 adult ( ≥18 years) mixed general medical/surgical ICUs. ICUs were in seven cities across Alberta, Canada: Edmonton (5 units); Calgary (4 units); Red Deer (1 unit); Lethbridge (1 unit); Grande Prairie (1 unit); Medicine Hat (1 unit); and Fort McMurray (1 unit). Among the ICUs, two were classified as academic, two tertiary, five community, and five regional, corresponding with hospital size. All ICUs were staffed by intensivists available 24-hours/day, along with residents or clinical associate coverage. All patients were admitted to ICU with a diagnosis that included pneumonia (i.e., bacterial, viral, aspiration, other) between May 1, 2020 and October 31, 2020, prior to COVID-19 vaccines becoming available. During this time, occupancy in Alberta ICUs ranged from 75-86% (mean 81.2%). Speciality ICUs (i.e., neurosciences and cardiovascular surgery) were excluded as admission diagnosis was less likely to be respiratory. Despite the differences in ICU locations, provincial guidelines were available to all ICUs to standardize care of COVID-19 patients.

### Measure of Frailty

Frailty was defined as a Clinical Frailty Scale (CFS) score ≥5.[5] The 9-point ordinal CFS score reflects the degree of frailty two weeks prior to the index admission, with a score of 1 being very fit and 8 being severely frail (9 indicates terminal illness). The CFS has been validated in hospital settings, including the ICU.[8,9,17] It has frequently been used as a dichotomous descriptor of frailty status in the ICU population.[6,9] Frailty was assessed and documented in the ICU electronic health record by the admitting ICU physician, a routine practice for all adult ICU admissions in Alberta.[7]

### Data Sources

Data were captured from the provincial ICU electronic health record database (i.e., TRACER/eCritical Alberta[7]) on all pneumonia admissions and related exposures (i.e., frailty, COVID-19 pneumonia), demographics (i.e., age, sex, comorbid illness, admission type, admission source, diagnostic category), health services use (i.e., duration of ICU and hospital stay, frequency of ICU readmission, illness severity, organ failure score, delirium score, vasoactive, sedation, neuromuscular block infusion, renal replacement therapy, prone positioning frequency/duration, ventilation assistance), and patient outcomes (i.e., survival at ICU and hospital discharge). No data on ethnicity are captured in this database. The diagnosis of COVID-19 was confirmed by nucleic acid-based testing, and positive results were verified by the provincial surveillance system of positive cases. Missing data were extracted manually from the health record by authors (CM and LM).

Outpatient outcome data were collected through telephone follow-up at ≥6 months post-hospital discharge from patients who responded to a letter mailed to their home address requesting their participation. Patients were asked to complete the EuroQol 5-dimension, 5-level (EQ-5D-5L) and visual analogue scale (EQ-VAS) quality-of-life instruments,[18] frailty assessments (i.e., CFS and the Edmonton Frail Scale (EFS)[5,19]), current weight, and living situation (i.e., at home independently or with support) to describe their overall functional status.

### Outcomes

The primary exposures were pre-admission frailty and COVID-19 pneumonia. The primary outcomes were prevalence of pre-admission frailty and all-cause hospital mortality. Secondary outcomes included ICU survival, measures of organ support (e.g., receipt and duration of invasive and non-invasive mechanical ventilation, vasoactive therapy, renal replacement therapy), health services use (e.g., ICU and hospital duration of stay), post-discharge health-related quality-of-life and frailty scores (i.e., CFS and EFS).

### Statistical Analysis

Descriptive characteristics were tabulated according to pre-admission frailty and COVID-19 status. This was also conducted for outcome data. Normally distributed continuous data were reported as means with standard deviations (SD). Non-normally distributed continuous data were reported as medians with interquartile ranges (IQR) or number with frequency (%). Continuous data were compared using *t*-test or Wilcoxon rank-sum test. Categorical variables were compared using Chi-square test for independence.

To describe the association of frailty to hospital mortality in COVID-19 pneumonia patients we performed multivariable logistic regression and multiple linear regression. Covariate inclusion in the model was limited to APACHE IV score at ICU admission, a decision driven by minimal missing scores and the low number of outcome events. A $p$ value <.05 was considered significant for all statistical tests. Analyses were performed using SAS 9.4 (SAS Institute Inc, Cary, NC) and Stata 16 (StataCorp, College Station, TX).

## RESULTS

### Overall Cohort Characteristics

In total, 521 patients were included in the study. The cohort mean (SD) age was 58.8 (14.9) years, APACHE II 22.8 (8.0), admission CFS 4.1 (1.6), 39.5% (n=206) were female. All patients had an ICU diagnosis of pneumonia; 44.0% (n=229) bacterial, 25.7% (n= 134) aspiration, 20.2% (n=105) viral, and 10.2% (n=53) other (i.e., fungal, parasitic). Overall, 19.0% (n=99) were diagnosed with COVID-19 (see Table 1).

Pre-admission frailty (CFS ≥5) was evident in 34.2% (n=178) of patients. The prevalence was greater in older patients, ranging from 27.8% (n=88) in patients <65 years of age to 58.3% (n=7) in those ≥85 years (Table 2). The mean (SD) age of patients with pre-admission frailty was older 62.3 (14.5) vs. 56.9 (14.8; p<.001), and acuity of illness was higher, as demonstrated by admission APACHE II scores 25.6 (7.8) vs. 21.3 (7.7; *p*<.001), compared with non-frail patients. Initial mean (SD) ratio of arterial oxygen partial pressure (PaO2 in mmHg) to fractional inspired oxygen (PF ratio) at ICU admission for frail patients was 138.3 (60.9) compared with 126.1 (53.1; *p*=.02), in non-frail, reflecting more severe hypoxemia among non-frail patients at ICU admission. (Appendix A, Table A1) Among all patients, 73.9% (n=385) received invasive mechanical ventilation, 76.4% (n=136) in the frail group vs. 72.6% (n=249; p=0.35), in the non-frail group. Non-invasive ventilation was provided to 18% (n=94) patients, 22.5% (n=40) in the frail group vs. 15.7% (n=54; p=0.06), in the non-frail group (Appendix A, Table A2).

In the overall cohort, hospital mortality was 21.3% (n=111) and in ICU 18.0% (n=94). Of the patients who died in hospital, most died in ICU (94/111, 84.7%). Frail patients had higher unadjusted hospital mortality 35.4% (n=63) vs. 14.0% (n=48; *p*<.001) compared with non-frail patients (OR 2.73, 95% CI 1.73 to 4.33). Mortality in ICU was 29.8% (n=53) in the frail group vs. 12.0% (n=41; *p*<.001) in the non-frail group (aOR 2.49, 95% CI 1.53 to 4.05) (Appendix A, Table A3). Overall, 4.1% (n=17) of patients were re-admitted to ICU during the index hospitalization, 5.2% (n=6) in the frail group vs. 3.7% (n=11; *p*=.50) in non-frail. The overall cohort mean (SD) duration of stay in ICU was 9.2 (12.2) days and 16.0 (25.7) days in hospital (Appendix A, Table A2).

## COVID-19 Admissions Characteristics & Outcomes

The proportion of frail patients among all patients with COVID-19 was 20.2% (n=20) vs. 79.8% (n=79) non-frail (*p*=.001). In frail patients with COVID-19, the mean (SD) age was 66.2 (17.4) vs. 59.4 (14.7) years in non-frail patients (*p*=.07). In COVID-19 admissions, the mean (SD) APACHE II score at ICU admission in frail patients was 24.8 (5.1) vs. 19.2 (8.4) in non-frail patients (*p*=.001) (Table 1).

Among COVID-19 pneumonia patients, mean (SD) duration of stay in the ICU was 14.2 (9.9) days for frail patients vs. 13.3 (13.3; *p*=.23) days in non-frail patients. Duration of hospital stay for frail patients was 34.4 (66.7) vs. 14.1 (9.3; *p*=.03) days in non-frail patients. There was no significant difference in ICU interventions among frail and non-frail patients with COVID-19, including prone positioning in frail patients 25.0% (n=5) vs. 41.8% (n=33; *p*=.17) in non-frail, use

TABLE 1.
Characteristics of the cohort, stratified by COVID-19 status and by frailty status

| *Variable* | *Total (n=521)* | *COVID-19 (n=99)* | | *p* | *Non-COVID-19 (n=422)* | | *p* |
|---|---|---|---|---|---|---|---|
| | | *Frail (n=20)* | *Non-Frail (n=79)* | | *Frail (n=158)* | *Non-Frail (n=264)* | |
| Patient Characteristics | | | | | | | |
| Age (years), mean (SD) | 58.8 (14.9) | 66.2 (17.4) | 59.4 (14.7) | .07 | 61.8 (14.0) | 56.2 (14.8) | .0001 |
| Female, n (%) | 206 (39.5) | 6 (30.0) | 33 (41.8) | .34 | 65 (41.1) | 102 (38.6) | .61 |
| ICU Characteristics, n (%) | | | | | | | |
| Academic | 112 (21.5) | 4 (20.0) | 6 (7.6) | .32 | 37 (23.4) | 65 (24.6) | .67 |
| Tertiary | 158 (30.3) | 4 (20.0) | 23 (29.1) | | 47 (29.7) | 84 (31.8) | |
| Community | 151 (29.0) | 7 (35.0) | 23 (29.1) | | 44 (27.8) | 77 (29.2) | |
| Regional | 100 (19.2) | 5 (25.0) | 27 (34.2) | | 30 (19.0) | 38 (14.4) | |
| Unit Admitted From, n (%) | | | | | | | |
| Emergency | 162 (31.1) | 3 (15.0) | 22 (27.8) | .05 | 49 (31.0) | 88 (33.3) | .18 |
| ICU/CCU | 10 (1.9) | 0 (0.0) | 4 (5.1) | | 1 (0.6) | 5 (1.9) | |
| OR/Recovery | 7 (1.3) | 0 (0.0) | 0 (0.0) | | 2 (1.3) | 5 (1.9) | |
| Rural Hospital | 89 (17.1) | 8 (40.0) | 11 (13.9) | | 19 (12.0) | 51 (19.3) | |
| Ward | 185 (35.5) | 7 (35.0) | 39 (49.4) | | 61 (38.6) | 78 (29.5) | |
| Other | 68 (13.1) | 2 (10.0) | 3 (3.8) | | 26 (16.5) | 37 (14.0) | |
| Severity of Illness | | | | | | | |
| CFS at admit, Mean (SD) | 4.1 (1.6) | 5.9 (1.0) | 3.3 (0.9) | <.001 | 5.9 (0.6) | 2.5 (1.0) | <.001 |
| SOFA at admit, Mean (SD) | 8.1 (4.0) | 8.0 (3.1) | 6.3 (4.2) | .07 | 9.3 (3.8) | 8.0 (3.9) | .002 |
| APACHE II, Mean (SD) | 22.8 (8.0) | 24.8 (5.1) | 19.2 (8.4) | .001 | 25.7 (8.1) | 22.0 (7.4) | <.0001 |
| APACHE IV, Mean (SD) | 76.5 (29.0) | 84.5 (23.5) | 66.4 (32.1) | .004 | 85.3 (29.3) | 73.7 (26.7) | <.0001 |
| First PF Ratio, Mean (SD) | 130.3 (56.2) | 119.0 (62.7) | 116.3 (51.5) | .89 | 140.7 (60.5) | 129.0 (53.3) | .04 |
| Dialysis at admission, n (%) | 13 (2.5) | 1 (5.0) | 0 (0.0) | .05 | 8 (5.1) | 4 (1.5) | .034 |

ICU = intensive care unit; APACHE = Acute Physiology and Chronic Health Evaluation; CFS = clinical frailty scale score; OR = operating room; PF ratio = perfusion to fraction of inspired oxygen ratio; SOFA = Sequential Organ Failure Assessment.

of invasive mechanical ventilation 80.0% (n=16) vs. 65.8% (n=52; p=0.22), and non-invasive ventilation 20.0% (n=4) vs. 8.9% (n=7; *p*=.16) (Table 2).

Among COVID-19 admissions, ICU mortality was 40.0% (n=8) in frail patients compared with 13.9% (n=11; *p*=.01) in non-frail admissions. In patients admitted with non-COVID pneumonia, ICU mortality was 28.5% (n=45) in frail patients vs. 11.4% (n=30; *p*<.001) in non-frail patients. Hospital mortality among COVID-19 frail patients was 40.0% (n=8) vs. 15.2% (n=12; *p*=.01) in non-frail patients. Hospital mortality in non-COVID pneumonia admissions with frailty was 34.8% (n=55) vs. 13.6% (n=36; *p*<.001) in non-frail (Table 3).

## COVID-19 Admissions—Regression Models

Using a multivariable regression model, we identified the impact of frailty and APACHE IV score on the odds of hospital mortality in patients admitted to ICU with COVID-19. Frailty status as a dichotomous variable was nonsignificant (aOR 2.80, 95% CI 0.87 to 8.96); however, as a continuous variable the frailty score alone (aOR 1.48, 95% CI 1.04 to 2.09, per incremental increase in the CFS score) and with APACHE IV score at ICU admission added to the model (aOR 1.03, 95% CI 1.01 to 1.05) showed significant prediction of hospital mortality (Table 4).

TABLE 2.
Health services use stratified by COVID-19 status and by frailty status

| *Variable* | *Total (n=521)* | *COVID-19* | | | *Non-COVID-19* | | |
|---|---|---|---|---|---|---|---|
| | | *Frail (n=20)* | *Non-Frail (n=79)* | *p* | *Frail (n=158)* | *Non-Frail (n=264)* | *p* |
| Duration of Stay | | | | | | | |
| ICU days, mean (SD) | 9.2 (12.2) | 14.2 (9.9) | 13.3 (13.3) | .23 | 8.9 (16.2) | 7.7 (8.4) | .79 |
| Hospital days, mean (SD) | 16.0 (25.7) | 34.4 (66.7) | 14.1 (9.3) | .03 | 17.0 (20.9) | 14.5 (25.9) | .004 |
| Readmitted to ICU, n (%) | 17 (4.1) | 2 (16.7) | 4 (6.0) | .20 | 4 (3.9) | 7 (3.1) | .70 |
| Readmission | | | | | | | |
| Readmitted pre 72 hours, n (%) | 7 (1.7) | 0 (0.0) | 3 (4.5) | .45 | 1 (1.0) | 3 (1.3) | .79 |
| Readmitted post 72 hours, n (%) | 10 (2.4) | 2 (16.7) | 1 (1.5) | .01 | 3 (2.9) | 4 (1.8) | .50 |
| ICU Discharge to readmit, days, mean (SD) | 10.6 (15.1) | 14.9 (12.0) | 14.9 (28.1) | .35 | 13.8 (14.1) | 5.2 (5.1) | 0.57 |
| ICU Therapies | | | | | | | |
| IMV, n (%) | 385 (73.9) | 16 (80.0) | 52 (65.8) | .22 | 120 (75.9) | 197 (74.6) | .76 |
| IMV days, mean (SD) | 7.4 (12.2) | 12.9 (7.7) | 14.8 (12.6) | .84 | 6.5 (16.5) | 5.5 (7.7) | .62 |
| NIV, n (%) | 94 (18.0) | 4 (20.0) | 7 (8.9) | .16 | 36 (22.8) | 47 (17.8) | .21 |
| NIV days, mean (SD) | 1.1 (1.5) | 1.4 (1.5) | 0.7 (0.5) | .26 | 1.2 (1.9) | 1.0 (1.2) | .94 |
| HFNC, n (%) | 128 (24.6) | 10 (50.0) | 24 (30.4) | .10 | 33 (20.9) | 61 (23.1) | .60 |
| HFNC days, mean (SD) | 2.6 (4.5) | 1.8 (1.9) | 1.9 (1.7) | .73 | 3.7 (7.5) | 2.3 (3.0) | .68 |
| Prone events, n (%) | 69 (13.2) | 5 (25.0) | 33 (41.8) | .17 | 8 (5.1) | 23 (8.7) | .16 |
| Prone Frequency, mean (SD) | 0.3 (1.1) | 0.6 (1.3) | 1.5 (2.2) | .12 | 0.1 (0.2) | 0.1 (0.7) | .15 |
| Prone days, mean (SD) | 1.8 (1.7) | 2.1 (0.9) | 2.5 (1.9) | .95 | 0.6 (0.4) | 1.2 (1.2) | .32 |
| Prone days average, mean (SD) | 0.8 (0.8) | 1.0 (0.6) | 0.9 (1.1) | .48 | 0.6 (0.4) | 0.7 (0.5) | .86 |
| Tracheostomy, n (%) | 42 (8.1) | 1 (5.0) | 11 (13.9) | .27 | 13 (8.2) | 17 (6.4) | .49 |
| Tracheostomy days[a], mean (SD) | 21.2 (25.5) | 19.8 (9.4) | 15.1 (11.0) | .47 | 32.6 (41.9) | 16.4 (10.9) | .52 |
| CRRT, n (%) | 38 (7.3) | 2 (10.0) | 8 (10.1) | .99 | 12 (7.6) | 16 (6.1) | .54 |
| CRRT days, mean (SD) | 4.2 (5.3) | 3.4 (0.1) | 3.4 (3.2) | .60 | 2.8 (2.4) | 5.8 (7.4) | .23 |
| IHD, n (%) | 20 (3.8) | 0 (0.0) | 3 (3.8) | .38 | 7 (4.4) | 10 (3.8) | .75 |
| IHD days, mean (SD) | 0.4 (0.6) | 0 (0.0) | 0.2 (0.1) | .0000 | 0.4 (0.4) | 0.4 (0.8) | .84 |
| Transfer Delay, days, mean (SD) | 0.6 (1.1) | 0.4 (0.8) | 0.4 (0.7) | .29 | 0.6 (1.2) | 0.7 (1.2) | .01 |
| Sedation, n (%) | 362 (69.5) | 17 (85.0) | 51 (64.6) | .08 | 109 (69.0) | 185 (70.1) | .81 |
| Sedation days, mean (SD) | 7.2 (10.3) | 10.8 (9.4) | 19.2 (17.2) | .07 | 3.5 (4.6) | 5.7 (7.5) | .0005 |
| Vasopressor, n (%) | 359 (68.9) | 15 (75.0) | 48 (60.8) | .24 | 120 (75.9) | 176 (66.7) | .04 |
| Vasopressor days, mean (SD) | 2.5 (4.3) | 2.8 (3.3) | 3.4 (5.0) | .61 | 2.4 (3.9) | 2.3 (4.4) | .12 |
| Inotrope, n (%) | 45 (8.6) | 3 (15.0) | 7 (8.9) | .42 | 12 (7.6) | 23 (8.7) | .69 |
| Inotrope days, mean (SD) | 2.4 (2.4) | 3.6 (2.8) | 2.7 (3.8) | .43 | 1.9 (1.9) | 2.4 (2.1) | .53 |
| Neuromuscular block, n (%) | 54 (10.4) | 2 (10.0) | 19 (24.1) | .17 | 7 (4.4) | 26 (9.8) | .05 |
| Neuromuscular block days, mean (SD) | 3.0 (3.1) | 3.5 (1.6) | 5.3 (3.8) | .81 | 0.8 (0.9) | 1.9 (1.8) | .06 |
| IMV & NIV, n (%) | 62 (11.9) | 2 (10.0) | 4 (5.1) | .41 | 19 (12.0) | 37 (14.0) | .56 |
| IMV & NIV, days, mean (SD) | 10.1 (21.1) | 17.0 (5.0) | 16.6 (14.9) | 1.00 | 15.5 (36.5) | 6.3 (5.9) | .18 |

[a]Tracheostomy days reflect procedure on patients receiving IMV.
ICU = intensive care unit; IMV = invasive mechanical ventilation; NIV = non-invasive ventilation; HFNC = high-flow nasal cannula; CRRT = continuous renal replacement therapy; IHD = intermittent hemodialysis.

### Outpatient Follow-up Characteristics

In response to the mailed invitation to participate, 3.8% of the cohort (n=20 patients) provided verbal consent to collection of telephone follow-up assessment of their outpatient functional status and health-related quality-of-life. The mean (SD) age of respondents was 62.1 (11.9) years, pre-admission CFS 3.9 (1.6), APACHE II 22.5 (5.6), 20% (n=4) had COVID-19 pneumonia, 20% (n=5) pre-admission CFS ≥5, and 25.0% (n=5) were female. Their mean (SD) duration of ICU stay was 5.4 (4.3) days and hospital stay 10.4 (5.9) days. The location of ICU admission was 55.0% (n=11) in Edmonton, 30.0% (n=6) in Calgary, and 15.0% (n=3) in regional centres. Patients were contacted by phone at 8.7 (1.4) months following hospital discharge.

During their ICU stay, 75.0% (n=14) of respondents received vasopressors (n=3 with pre-admission frailty) and 65% (n=13) received a combination of continuous sedation, invasive mechanical ventilation, and enteral feeding (n=2 with pre-admission frailty).

Following discharge, 20% (n=2) respondents reported CFS ≥5, 40% (n=8) respondents scored ≥8, indicating frailty on the EFS. On average, respondents reported 5.8 kg weight loss, with 35% (n=7; n=2 with pre-admission frailty) reporting >10% weight loss compared to their ICU admission weight. No patients were readmitted to ICU during the hospital stay.

The reported EQ-5D mean (SD) quality of life index was 0.648 (0.19) with median (IQR) VAS 57.5 (45.0-73.8) (Table 5).

## DISCUSSION

In this study describing the impact of frailty on COVID-19 survival outcomes among adults admitted to ICU, the prevalence of frailty among adult COVID-19 ICU admissions was 20.2% and in-hospital mortality was 40.0%. Previous studies have found that severity of baseline frailty influences outcomes of patients with COVID-19 admitted to ICU, reporting greater mortality among patients with incrementally more severe frailty, reaching as much as 40.1% has been reported.[20-23] Disparities among results may be explained by regional variations in ICU patient selection and routine pre-admission frailty assessment.

The contrast in proportion of frail patients compared to non-frail among COVID-19 admissions, particularly in

TABLE 3.
Outcomes of ICU admission for pneumonia stratified by COVID-19 status and frailty status

| *Variable* | *Total (n=521)* | *COVID-19* | | *p* | *Non-COVID-19* | | *p* |
|---|---|---|---|---|---|---|---|
| | | *Frail (n=20)* | *Non-Frail (n=79)* | | *Frail (n=158)* | *Non-Frail (n=264)* | |
| Mortality, n (%) | | | | | | | |
| ICU death | 94 (18.0) | 8 (40.0) | 11 (13.9) | .01 | 45 (28.5) | 30 (11.4) | <.0001 |
| Hospital death | 111 (21.3) | 8 (40.0) | 12 (15.2) | .01 | 55 (34.8) | 36 (13.6) | <.0001 |
| ICU death within 3 days | 28 (5.4) | 1 (5.0) | 2 (2.5) | .57 | 18 (11.4) | 7 (2.7) | .0002 |
| ICU Discharge Disposition, n (%) | | | | | | | |
| Died | 94 (18.0) | 8 (40.0) | 11 (13.9) | .02 | 45 (28.5) | 30 (11.4) | .003 |
| Ward | 301 (57.8) | 9 (45.0) | 56 (70.9) | | 78 (49.4) | 158 (59.8) | |
| ICU/CCU | 27 (5.2) | 1 (5.0) | 4 (5.1) | | 6 (3.8) | 16 (6.1) | |
| Rural Hospital | 14 (2.7) | 1 (5.0) | 0 (0.0) | | 4 (2.5) | 9 (3.4) | |
| Home | 7 (1.3) | 0 (0.0) | 1 (0.0) | | 2 (1.3) | 5 (1.9) | |
| Rehabilitation Facility | 1 (0.2) | 0 (0.0) | 0 (0.0) | | 0 (0.0) | 1 (0.4) | |
| Not documented | 77 (14.8) | 1 (5.0) | 9 (11.4) | | 23 (14.6) | 45 (17.0) | |

TABLE 4.
Impact of frailty on hospital mortality for patients admitted to ICU with COVID-19 pneumonia, logistic regression model

| *Model* | *Variable(s)*[a] | *Odds Ratio* | *95% CI* |
|---|---|---|---|
| Unadjusted | Frailty (Yes vs No) | 3.72 | 1.25 to 11.01 |
| Adjusted | Frailty (Yes vs No) | 2.80 | 0.87 to 8.96 |
| | APACHE IV Score (continuous) | 1.03 | 1.01 to 1.05 |
| Unadjusted | Frailty (continuous) | 1.62 | 1.18 to 2.22 |
| Adjusted | Frailty (continuous) | 1.48 | 1.04 to 2.09 |
| | APACHE IV Score (continuous) | 1.03 | 1.01 to 1.05 |

[a]Frailty was defined as Clinical Frailty Scale score ≥5; the CFS ordinal scale 1-9 was also assessed as a continuous variable; the number of covariates in model was limited by COVID-19 hospital mortality events (n=20).

TABLE 5.
EQ-5D-5L frequencies and proportions reported by dimension and level

| | *Mobility n (%)* | *Self-care n (%)* | *Usual Activities n (%)* | *Pain/Discomfort n (%)* | *Anxiety/Depression n (%)* |
|---|---|---|---|---|---|
| Level 1 (no problems) | 8 (40) | 15 (75) | 4 (20) | 3 (15) | 10 (50) |
| Level 2 (slight problems) | 6 (30) | 0 (0) | 8 (40) | 6 (30) | 5 (25) |
| Level 3 (moderate problems) | 2 (10) | 2 (10) | 3 (15) | 7 (35) | 3 (15) |
| Level 4 (severe problems) | 2 (10) | 1 (5) | 3 (15) | 4 (20) | 1 (5) |
| Level 5 (severe problems) | 2 (10) | 2 (10) | 2 (10) | 0 (0) | 1 (5) |
| *Total* | 20 (100) | 20 (100) | 20 (100) | 20 (100) | 20 (100) |

academic centres, raises the question of whether there was non-formal triage of patients, with pre-admission frailty influencing admission decisions. Comparable results were seen in patients with pre-admission chronic kidney disease where the proportion of COVID-19 patients was less than half that of non-COVID admissions. These findings may be linked to effects of bed availability on goals of care discussions during times of limited ICU bed availability, a trend previously documented in Alberta.[24] Other contributing factors may have been selection bias (i.e., older patients with frailty not being referred to ICU) and COVID-19 mortality among frail patients prior to ICU referral, although we do not have supporting data.

In both frail and non-frail patients, the initial measured PF ratio was lower in the COVID-19 pneumonia patients than non-COVID pneumonia admissions. This may reflect the nature of COVID-19 pneumonia being a primarily isolated respiratory disease without other organ dysfunction necessitating ICU admission. During the time frame of this study, larger sites (academic, tertiary, and community hospitals) developed dedicated COVID-19 wards where patients could be managed with higher oxygen demand than is usual practice. Patients transferred to ICU had exhausted the respiratory support available outside of the ICU setting. Non-COVID patients would not have had the same dedicated support in general ward environments. These findings suggest we may have room for improvement in the assessment and support of ward patients prior to ICU admission to ensure equitable care.

Frail patients in the COVID-19 group received more frequent NIV for longer duration than non-frail patients, and shorter duration IMV, suggesting possible limitations on duration and intensity of ICU therapies. This may also be an indicator of pre-determined limitations of intensity of care discussions with these patients. Despite admission sequential organ failure assessment (SOFA) scores being similar in the frail and non-frail COVID-19 patients, the proportion of ICU and hospital deaths were higher among frail patients. These results may imply worsening condition in the frail patients with subsequent limitation of continued ICU therapies, consistent with findings from other studies.[25] There was a higher proportion of frail patients transferred from community hospitals to academic centres, which is congruent with their increased severity of illness but also suggests that frail patients require increased resource utilization compared to non-frail patients. Although not available to this study, routine documentation of discussions encompassing goals of care and limited trials of ICU therapies would be valuable to capture in the ICU electronic health record to help describe planning of patient care.

At outpatient follow-up of the patients, it was noted that patients reported lower CFS scores on follow-up than was assessed at ICU admission, potentially reflecting bias caused by the effects of acute illness on their apparent functioning as observed by the admitting ICU physician. An observational study examining CFS of patients at three-month follow-up found that approximately 27% of the included patients had increased frailty from their baseline.[26] Overall these findings suggest that frailty exists on a dynamic spectrum and can be changed. Further exploration of the modifiable aspects of frailty may identify patients who would benefit from aggressive interventions, such as multidisciplinary rehabilitation and social supports prior to discharge, to improve outpatient outcomes.[27,28]

Respondents reported a mean utility score of 0.648 in the context of ICU survivorship, suggesting limitations in the five dimensions assessed by the EQ-5D seemingly driven by reported problems with usual activities and pain/discomfort. The median EQ-VAS score (57.5) is context-dependent, but implies that respondents were experiencing health problems and limitations that were impacting their quality of life at eight-to-nine months following hospital discharge. Although we have no baseline scores to compare with, these reported scores are lower than other COVID-19 and ARDS follow-up studies.[29,30] This may be related to the small sample size combined with selection bias of respondents.

## Strengths and Limitations

Our study is noteworthy for access to provincial ICU population-level clinical data with routine capture of pre-admission frailty status and clinical details in the electronic health record. Due to the paucity of evidence-based therapies for COVID-19 at the outset of the pandemic, when data from our study was collected, our results demonstrate the most potent effect

of frailty on COVID-19 patients. Once specific therapies were used, it is possible that the effect of frailty may have been modulated.

However, our study also has important limitations. First, frailty was assessed by physicians at ICU admission and could be susceptible to misclassification bias, although previous studies have compared intensivist frailty assessment to geriatric medical assessment and concluded the assessment is feasible and valid.[8,31]

Second, no data were available to describe patients who were referred to ICU but declined admission. We are therefore unable to comment on the frailty status of those patients and its influence on ICU admission decisions. In the scenario of COVID-19 pneumonia and its media attention related to suboptimal outcomes in older patients, patients may have been hesitant to move to ICU for what they interpreted as non-beneficial therapies. Similarly, decisions by ICU physicians may have been influenced by early publications highlighting poor ICU outcomes among older and frail patients with COVID-19. Goals of care status at the time of admission and throughout the ICU duration of stay were not available.

Third, long-term condition and survival outcomes of COVID-19 infection and frailty were not available for the cohort. Follow-up data reported in the paper are subject to response bias and were incomplete in some instances. Fourth, although this study included all pneumonia admissions during the study time frame, results from a single Canadian province may not be generalizable to other regions. Finally, these data were collected prior to vaccine availability and reflect the initial six months of a pandemic that has since progressed through multiple waves of significant morbidity across the world.

## CONCLUSION

Frailty was observed in 20.2% of adult patients admitted to ICU with COVID-19 pneumonia. Pre-admission frailty was associated with an incremental increased risk of hospital mortality and health services use. Our findings suggest that frailty screening may be an important prognostic tool for ICU discussions about admission for COVID-19 and associated outcomes; however, it must be used as part of a holistic approach to the heterogeneous ICU patient population.

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None to declare.

## CONFLICT OF INTEREST DISCLOSURES

We have read and understood the *Canadian Geriatrics Journal*'s policy on conflicts of interest disclosure and declare the following: Dr. Bagshaw is supported by a Canada Research Chair in Critical Care Outcomes and Systems Evaluation. No other authors report competing interests with this work.

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# APPENDIX A

TABLE A1.
Baseline characteristics of patients admitted to ICU, stratified by frailty status

| *Variable* | *Total (N=521)* | *Frail (N=178)* | *Non-Frail (N=343)* | *p* |
|---|---|---|---|---|
| Patient Characteristics | | | | |
| Covid-19, n (%) | 89 (17.1) | 16 (9.0) | 73 (21.3) | .0004 |
| Age, years, mean (SD) | 58.8 (14.9) | 62.3 (14.5) | 56.9 (14.8) | <.0001 |
| Sex, n (% female) | 206 (39.5) | 71 (39.9) | 135 (39.4) | .91 |
| ICU Characteristics | | | | |
| Academic, n (%) | 112 (21.5) | 41 (23.0) | 71 (20.7) | .90 |
| Tertiary, n (%) | 158 (30.3) | 51 (28.7) | 107 (31.2) | |
| Community, n (%) | 151 (29.0) | 51 (28.7) | 100 (29.2) | |
| Regional, n (%) | 100 (19.2) | 35 (19.7) | 65 (19.0) | |
| Source of transfer to ICU, n (%) | | | | |
| Emergency Department | 162 (31.1) | 52 (29.2) | 110 (32.1) | .35 |
| ICU/CCU | 10 (1.9) | 1 (0.6) | 9 (2.6) | |
| OR/Recovery | 7 (1.3) | 2 (1.1) | 5 (1.5) | |
| Rural Hospital | 89 (17.1) | 27 (15.2) | 62 (18.1) | |
| Ward | 185 (35.5) | 68 (38.2) | 117 (34.1) | |
| Other | 68 (13.1) | 28 (15.7) | 40 (11.7) | |
| Severity of Illness | | | | |
| SOFA at admit, mean (SD) | 8.1 (4.0) | 9.1 (3.8) | 7.6 (4.0) | <0.001 |
| APACHE II, mean (SD) | 22.8 (8.0) | 25.6 (7.8) | 21.3 (7.7) | <.0001 |
| APACHE IV, mean (SD) | 76.5 (29.0) | 85.2 (28.7) | 72.0 (28.1) | <.0001 |
| CFS at admit, mean (SD) | 4.1 (1.6) | 5.9 (0.9) | 3.1 (1.0) | <.0001 |
| Initial PF Ratio, mean (SD) | 130.3 (56.2) | 138.3 (60.9) | 126.1 (53.1) | .02 |
| Dialysis at admission, n (%) | 13 (2.5) | 9 (5.1) | 4 (1.2) | .01 |

ICU = intensive care unit; APACHE = Acute Physiology and Chronic Health Evaluation; CFS = clinical frailty scale score; OR = operating room; PF ratio = perfusion to fraction of inspired oxygen ratio; SOFA = Sequential Organ Failure Assessment.

TABLE A2.
Health services use and treatment intensity of pneumonia ICU admission, stratified by frailty status

| *Variable* | *Total (n=521)* | *Frail (n=178)* | *Non-Frail (n=343)* | *p* |
|---|---|---|---|---|
| ICU Healthcare Utilization, n (%) | | | | |
| IMV | 385 (73.9) | 136 (76.4) | 249 (72.6) | .35 |
| NIV | 94 (18.0) | 40 (22.5) | 54 (15.7) | .06 |
| HFNC | 128 (24.6) | 43 (24.2) | 85 (24.8) | .88 |
| Prone positioning events | 69 (13.2) | 13 (7.3) | 56 (16.3) | .004 |
| Tracheostomy[a] | 42 (10.9) | 14 (3.6) | 28 (7.2) | .53 |
| CRRT | 38 (7.3) | 14 (7.9) | 24 (7.0) | .72 |
| IHD | 20 (3.8) | 7 (3.9) | 13 (3.8) | .94 |
| Duration of Stay | | | | |
| ICU days, mean (SD) | 9.2 (12.2) | 9.5 (15.7) | 9.0 (10.0) | .78 |
| Hospital days, mean (SD) | 16.0 (25.7) | 18.9 (29.9) | 13.4 (23.1) | .002 |
| Readmitted | 17 (4.1) | 6 (5.2) | 11 (3.7) | .50 |

[a]Tracheostomy reflects procedure on patients receiving IMV (n=385).
ICU = intensive care unit; IMV = invasive mechanical ventilation; NIV = non-invasive ventilation; HFNC = high-flow nasal cannula; CRRT = continuous renal replacement therapy; IHD = intermittent hemodialysis.

TABLE A3.
Outcomes of ICU admission for pneumonia stratified by frailty status

| *Variable* | *Total (n=521)* | *Frail (n=178)* | *Non-Frail (n=343)* | *p* |
|---|---|---|---|---|
| Mortality | | | | |
| ICU death, n (%) | 94 (18.0) | 53 (29.8) | 41 (12.0) | <.0001 |
| Hospital death, n (%) | 111 (21.3) | 63 (35.4) | 48 (14.0) | <.0001 |
| ICU Discharge disposition, n (%) | | | | |
| Died, n (%) | 94 (18.0) | 18 (29.8) | 76 (12.0) | .003 |
| Ward, n (%) | 301 (57.8) | 87 (48.9) | 244 (62.4) | |
| ICU/CCU, n (%) | 27 (5.2) | 7 (3.9) | 20 (5.8) | |
| Rural hospital, n (%) | 14 (2.7) | 5 (2.8) | 9 (2.6) | |
| Home, n (%) | 7 (1.3) | 2 (1.1) | 5 (1.5) | |
| Rehabilitation facility, n (%) | 1 (0.2) | 0 (0) | 1 (0.3) | |
| Not documented, n (%) | 77 (14.8) | 24 (13.5) | 53 (15.4) | |