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CLINICAL INVESTIGATION

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Treatment limitations and clinical outcomes in critically ill frail patients with and without COVID-19 pneumonitis

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Abstract

Background: The presence of treatment limitations in patients with frailty at intensive care unit (ICU) admission is unknown. We aimed to evaluate the presence and predictors of treatment limitations in patients with and without COVID-19 pneumonitis in those admitted to Australian and New Zealand ICUs.

Methods: This registry-based multicenter, retrospective cohort study included all frail adults (≥16 years) with documented clinical frailty scale (CFS) scores, admitted to ICUs with admission diagnostic codes for viral pneumonia or acute respiratory distress syndrome (ARDS) over 2 years between January 01, 2020 and December 31, 2021. Frail patients (CFS ≥5) coded as having viral pneumonitis or ARDS due to COVID-19 were compared to those with other causes of viral pneumonitis or ARDS for documented treatment limitations.

Results: 884 frail patients were included in the final analysis from 129 public and private ICUs. 369 patients (41.7%) had confirmed COVID-19. There were more male patients in COVID-19 (55.3% *vs* 47.0%; $p = 0.015$). There were no differences in age or APACHE-III scores between the two groups. Overall, 36.0% (318/884) had treatment limitations, but similar between the two groups (35.8% [132/369] *vs* 36.1% [186/515]; $p = 0.92$). After adjusting for confounders, increasing frailty (OR = 1.72; 95%-CI 1.39–2.14), age (OR = 1.05; 95%-CI 1.04–1.06), and presence of chronic respiratory condition (OR = 1.58; 95%-CI 1.10–2.27) increased the likelihood of instituting treatment limitations. However, the presence of COVID-19 by itself did not influence treatment limitations (odds ratio [OR] = 1.39; 95%-CI 0.98–1.96).

Conclusions: The proportion of treatment limitations was similar in patients with frailty with or without COVID-19 pneumonitis at ICU admission.

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KEYWORDS
COVID-19, intensive care, pandemic, treatment limitations, viral pneumonia

INTRODUCTION

Coronavirus disease 2019 (COVID-19) pandemic unfolded in unprecedented ways demanding radical measures including nationwide lockdowns and a declaration of a state of emergency, in response to save as many lives as possible in this public health crisis. Countries stricken by the overwhelmed COVID-19 infection surges have certainly strained their healthcare services enormously, in multiple ways, including scarce resource availability, understaffed medical workforce, and insufficient bed capacity.[1] The extreme pressure has necessitated a triage system, to not only tackle the healthcare demands of the pandemic but also to provide holistic care for the more vulnerable frail, and older patients.[2–5] Not surprisingly, frailty tools such as the clinical frailty scale (CFS) have been thrust into the spotlight as an age-based adjunct for critical care triage decisions. The National Institute for Health and Care Excellence and earlier work (NICE triage guidelines)[6] demonstrated greater treatment limitations in older, frail cohorts.[7] This has triggered healthcare professionals to openly talk about advanced care planning and end-of-life care with vulnerable patients and their families to tailor the care plan for individual patients.[8] The American Geriatric Society in their position statement recommended that the emergency resource allocation strategies during the era of COVID-19 and future pandemics must not disproportionately disfavor older adults and that healthcare providers should not be expected to make rationing decisions in isolation.[9,10] Frail older patients were generally not surviving an intensive care unit (ICU) episode receiving invasive mechanical ventilation.[11]

There is good evidence that the presence of treatment limitations independently predicts mortality among patients with COVID-19.[12–14] In 2020, while the COVID-19 pandemic remained a period of uncertainty, there was significant emphasis on advance care planning and treatment limitations in older patients.[2,3,15,16] Despite that, a recent study identified that timely goals of care documentation occurred less frequently in patients with frailty during the COVID-19 pandemic than in the pre-COVID-19 era.[17]

The geographic isolation and very strict public health measures ensured that the Australian and New Zealand healthcare system was not overwhelmed in 2020,[18] allowing improved access to ICU earlier for all patients. This was however not the case in 2021 when a higher volume of cases put significant strain on the healthcare system in parts of Australia.[19] Consequently, it is unclear if there were any differences in the proportion of treatment limitations in frail patients with and without COVID-19, admitted to ICU. We hypothesized that there would be no differences in rates of treatment limitations between frail patients with and without COVID-19 at ICU admission. We also aimed to investigate whether the clinically relevant outcomes differed between frail patients with and without COVID-19.

Key points

- This retrospective multicenter study in Australia and New Zealand found that a third of all frail patients and two-thirds of those aged ≥65 years had treatment limitations at ICU admission, with no difference in patients with or without COVID-19 pneumonitis.
- Increasing age, incremental increase in frailty scores, and presence of chronic respiratory disease were significant predictors for the presence of treatment limitations at ICU admission.
- Regardless of their treatment limitation status, frail patients with COVID-19 were more likely to die in hospital and have longer hospitalization, and are less likely to be discharged home.

Why does this paper matter?

Given that frail patients with COVID-19, regardless of their treatment limitation status, were more likely to die in hospital, and have longer hospitalization and are less likely to be discharged home, it is essential not only to establish early goal-concordant care in such patients but also to use that to guide critical care triaging decisions to rapidly assess patients for the severity of the presenting acute illness and the likelihood of medical interventions being successful.

METHODS

Ethics approval

The study was approved by the Alfred Hospital Ethics Committee (Project No: 176/21). Access to the Australian and New Zealand Intensive Care Society (ANZICS) Adult Patient Database (APD) was granted by the ANZICS Centre for Outcome and Resource Evaluation (CORE) Management Committee in accordance with standing protocols.

Study design and setting

This was a retrospective multicenter cohort study, analyzing the ANZICS-APD between January 1, 2020 to December 31, 2021.

Patient identification

All consecutive critically ill adult patients (age ≥16 years) with documented CFS score ≥5 and admitted to Australian and New Zealand ICUs with an Acute Physiology and Chronic Health Evaluation (APACHE) III-j admission diagnostic codes for viral pneumonia or acute respiratory distress syndrome (ARDS) were included. Patients with COVID-19 were identified using APACHE III-j diagnosis subcodes at ICU admission. Patients admitted for pneumonia or ARDS from other viral infections (henceforth defined as viral pneumonitis) were used for comparison between those with and without COVID-19 (Table S1). Non-frail patients (CFS scores ≤4) were excluded. Readmission episodes during the same hospitalization and admissions for palliative care or organ donation were also excluded. The CFS was assigned by trained data collectors working in the participating ICU, comprising of junior doctors, nurses, and administrative staff, and was based on the patient's level of physical function in the 2 months preceding ICU admission.[20]

ANZICS-APD

The ANZICS-APD contains routine quality assurance and benchmarking data collected by ANZICS CORE. This database includes 92% of all patients admitted to Australian ICUs and 67% of New Zealand ICUs, and prospectively collects de-identified patient data including admission diagnosis, chronic health status, and physiological and biochemical variables within the first 24 hours of admission. The definitions of each condition are described in the ANZICS-APD data dictionary.[20]

Definitions

Treatment limitation implied that medical treatment would be constrained by either patient wishes or medical futility but does not necessarily imply that the patient was expected to die during this ICU admission.

Study outcomes

The objective of the study was to investigate whether there were any differences in the prevalence of treatment limitations in frail patients with or without COVID-19 admitted to the ICU. The primary outcome was the presence of treatment limitations. Secondary outcomes were ICU and hospital mortality, ICU organ supports, ICU and hospital length of stays, and discharge destination.

Subgroup analysis

Subgroup analysis was performed on patients with treatment limitations based on their age (younger than 65 years, and those 65 years and older) and those receiving non-invasive ventilatory support.

Statistical analysis

Group comparisons were made using chi-square tests for proportions, student *t*-tests for normally distributed data and Mann–Whitney *U*-tests otherwise, with results presented as frequencies (%), means (standard deviations [SD]) or medians (interquartile range [IQR] 25%–75%) respectively. Multivariable logistic regression model adjusting for known covariates that were determined *apriori* (age, sex, APACHE III scores, and CFS) and any baseline comorbidity imbalance (chronic respiratory, cardiovascular, renal, liver, immunosuppressive conditions, diabetes mellitus, and metastatic cancer), with COVID-19 status being the principal exposure variable of interest. The results were reported as odds ratio (OR) and 95%-CI. To account for the competing risk of death, time to discharge was analyzed using competing risk regression with results reported as hazard ratios (95% CI). All analyses were performed using SPSS software (IBM, version 27), and a two-sided *p*-value of 0.05 was used to indicate statistical significance.

TABLE 1 Patients with and without COVID-19 with an admission diagnosis of viral pneumonitis

Variable	Frail patients with COVID-19 ($n = 369$)	Frail patients without COVID-19 ($n = 515$)	p-value*
Jurisdiction			
New South Wales	192 (52.0%)	165 (32.0%)	**<0.001**
Victoria	163 (44.2%)	134 (26.0%)	
Queensland	3 (0.8%)	80 (15.5%)	
Western Australia	3 (0.8%)	36 (7.0%)	
Australian Capital Territory	7 (1.9%)	26 (5.0%)	
South Australia	0 (0)	26 (5.0%)	
Northern Territory	0 (0)	12 (2.3%)	
Tasmania	0 (0)	5 (1.0%)	
New Zealand	1 (0.3%)	31 (6.0%)	
Indigenous, *n* (%)	5 (1.4%)	35 (7.0%)	**<0.001**
Male sex, *n* (%)	204 (55.3%)	242 (47.0%)	**0.015**
Age (years), median (Q1, Q3)	71.3 (61.9, 79.1)	71.8 (61.1, 80.2)	0.56
Age category, *n* (%)			
Age <65 years	119 (32.2%)	170 (33.0%)	0.81
Age ≥65 years	250 (67.8%)	345 (67.0%)	
CFS score, median (Q1, Q3)	6 (5, 6)	6 (5, 6)	0.38
Hospital admission source, *n* (%)			
Home	283 (76.7%)	401 (77.9%)	0.05
Other acute hospital (not ICU)	45 (12.2%)	77 (14.9%)	
Nursing home or chronic care	13 (3.5%)	18 (3.5%)	
Other hospital ICU	26 (7.0%)	13 (2.5%)	
Other (rehabilitation, MH)	1 (0.3%)	4 (0.8%)	
Missing	1 (0.3%)	2 (0.4%)	
ICU admission source, *n* (%)			
Emergency department	147 (39.8%)	217 (42.1%)	**<0.001**
Ward	176 (47.7%)	245 (47.6%)	
Another acute hospital	17 (4.6%)	38 (7.4%)	
Other hospital ICU	27 (7.3%)	9 (1.8%)	
From operating theater	0 (0)	1 (0.2%)	
Direct admission	2 (0.5%)	5 (1.0%)	
Comorbidities, *n* (%)			
Chronic respiratory condition	80 (21.7%)	163 (31.7%)	**0.001**
Chronic cardiovascular condition	69 (18.7%)	93 (18.1%)	0.81
Chronic renal failure	30 (8.1%)	78 (15.1%)	**0.002**
Chronic liver disease	10 (2.7%)	20 (3.9%)	0.34
Diabetes mellitus	155 (43.2%)	182 (37.0%)	0.07
Immune suppressive disease	40 (10.8%)	65 (12.6%)	0.42
Lymphoma	5 (1.4%)	10 (1.9%)	0.51
Leukemia	11 (3.0%)	19 (3.7%)	0.57
Metastatic cancer	12 (3.3%)	36 (7.0%)	**0.016**
Obesity (BMI ≥30 $kg.m^{-2}$)	189 (77.5%)	299 (68.6%)	**0.014**

TABLE 1 (Continued)

Variable	Frail patients with COVID-19 ($n = 369$)	Frail patients without COVID-19 ($n = 515$)	p-value*
ICU admission post MET call, n (%)	140 (38.1%)	215 (41.8%)	0.27
Cardiac arrest, n (%)	2 (0.6%)	4 (0.8%)	0.73
Pre-ICU (hours), median (Q1, Q3)	3.0 (1.3, 22.9)	3.6 (1.6, 22.9)	0.97
Organ failure scores			
APACHE III, mean (SD)	62.7 (21.2)	64.8 (21.5)	0.15
ANZROD (%), mean (SD)	20.0 (18.9)	22.7 (21.3)	**<0.001**

Abbreviations: ANZROD, Australia New Zealand risk of death; APACHE, Acute Physiology and Chronic Health Evaluation; ARDS, acute respiratory distress syndrome; BMI, body mass index; CFS, clinical frailty scale; ED, emergency department; ICU, intensive care unit; MET, medical emergency team; MH, mental health; Q, quartile; SD, standard deviation.
*Numbers in bold imply statistical significance.

RESULTS

During the study period, a total of 884 frail patients from 129 ICUs across Australia and New Zealand were included in the final analysis. A flow diagram describing the proportion of patients with frailty included in the final analysis is illustrated in Figure S1. Of these, 369 patients (41.7%) had COVID-19. Most of the patients with COVID-19 were from the Australian states of New South Wales and Victoria (52.0% and 44.2%, respectively; Figure S2). The median age [IQR] was no different between the patients with and without COVID-19 (71.3 [61.9–79.1] *vs* 71.8 [61.1, 80.2]; $p = 0.56$), with more than 65% of the patients 65 years and older in both groups. There were more male patients with COVID-19 (55.3% *vs* 47.0%; $p = 0.015$). The CFS and APACHE-III scores were similar for patients with and without COVID-19. The patients with COVID-19 had lower chronic respiratory conditions, chronic renal failure and metastatic disease when compared to those without COVID-19, however, a higher proportion of patients with COVID-19 had a BMI $\geq$30 kg.m^{-2} than patients without COVID-19. The baseline characteristics are presented in Table 1.

Primary outcome

Overall, 36.0% (318/884) of the patients admitted to ICUs with or without COVID-19 had treatment limitations. There were no differences in the proportion of treatment limitations between patients with and without COVID-19 (35.8% [132/369] *vs* 36.1% [186/515]; $p = 0.92$; Table 2). There was no difference in treatment limitations between the two groups at equivalent frailty levels (Figure 1). Furthermore, despite the patients with treatment limitations being older, there were no differences between the two groups at equivalent frailty levels (Figure S3). Multivariable regression analysis showed each incremental increase in the CFS (OR = 1.72; 95%-CI 1.39–2.14; $p < 0.001$), age (OR = 1.05; 95%-CI 1.04–1.06; $p < 0.001$) and those with chronic respiratory condition (OR = 1.58; 95%-CI 1.10–2.27; $p = 0.014$) had a higher likelihood of having treatment limitations in place. Male sex, APACHE-III score, COVID-19 status, and other comorbidities did not influence treatment limitations (Table 3).

Secondary outcomes

The raw secondary outcomes for all patients are presented in Table 2, while the univariable and adjusted (for age, sex, CFS, APACHE-III, and treatment limitation status) logistic regression for COVID-19 status are presented in Table S2. The patients with COVID-19 were more likely to die in ICU (raw: 22.1% *vs* 16.0%; $p = 0.021$; adjusted analysis: OR = 1.71; 95%-CI: 1.18–2.47; $p = 0.005$) than patients without COVID-19 pneumonitis. Similarly, the patients with COVID-19 were more likely to die in hospital (raw: 31.9% *vs* 24.3%; $p = 0.013$; adjusted analysis: OR = 1.69; 95%-CI: 1.22–2.35; $p = 0.002$). The patients with COVID-19 were more than twice as likely to receive mechanical ventilation (33.9% *vs* 15.3%; $p < 0.001$), with the risk increasing further after multivariable adjustment (OR = 4.07; 95%-CI: 2.79–5.96; $p < 0.001$). Patients with COVID-19 also spent a longer duration on mechanical ventilation than patients without COVID-19 (median [IQR] 166.5 h [48.8–302.0 h] *vs* 87.0 h [49.0–152.5 h]; $p < 0.001$). Multivariable analysis, following adjustment to covariates, demonstrated that a lower proportion of patients with COVID-19 were likely to receive non-invasive ventilation (OR = 0.76; 95%-CI: 0.58–0.99; $p = 0.045$). Multivariable analysis demonstrated that patients with COVID-19 were more likely to receive vasopressor support (OR = 1.51; 95%-CI: 1.09–

TABLE 2 Raw secondary outcomes for all patients

Outcomes	Frail patients with COVID-19	Frail patients without COVID-19	*p*-value*
Primary outcome			
Treatment limitations, *n* (%)	132/369 (35.8%)	186/515 (36.1%)	0.92
Secondary outcomes			
ICU mortality, *n* (%)	81/366 (22.1%)	82/513 (16.0%)	**0.021**
Hospital mortality, *n* (%)	115/360 (31.9%)	125/514 (24.3%)	**0.013**
ICU LOS, median (Q1, Q3)	4.4 (1.8, 10.1)	2.9 (1.5, 5.3)	**<0.001**
Hospital LOS, median (Q1, Q3)	13.9 (7.0, 23.8)	10.8 (5.5, 19.1)	**0.007**
Mechanical ventilation (MV), *n* (%)	125/369 (33.9%)	79/515 (15.3%)	**<0.001**
MV duration, (hours) median (Q1, Q3)	166.5 (48.8, 302.0)	87.0 (49.0, 152.5)	**<0.001**
Non-invasive ventilation (NIV), *n* (%)	171/369 (46.3%)	281/515 (54.6%)	**0.016**
NIV duration, (hours) median (Q1, Q3)	18.0 (5.0, 69.0)	12.0 (3.0, 33.3)	**0.004**
Inotropes, *n* (%)	124/348 (35.6%)	134/464 (28.9%)	**0.041**
Extracorporeal membrane oxygenation, *n* (%)	2/359 (0.6%)	3/501 (0.6%)	0.94
Renal replacement therapy, *n* (%)	18/355 (5.1%)	49/507 (9.7%)	**0.013**
Tracheostomy, *n* (%)	14/369 (3.8%)	8/515 (1.6%)	**0.035**
Nursing home discharge, *n* (%)	10/369 (2.7%)	18/515 (3.5%)	0.51
Home discharge, *n* (%)	158/369 (42.8%)	278/515 (54.0%)	**0.001**

Abbreviations: COVID-19, Coronavirus disease 2019; ICU, intensive care unit; LOS, length of stay; MV, mechanical ventilation; NIV, non-invasive ventilation; Q, quartile.
*Numbers in bold imply statistical significance.

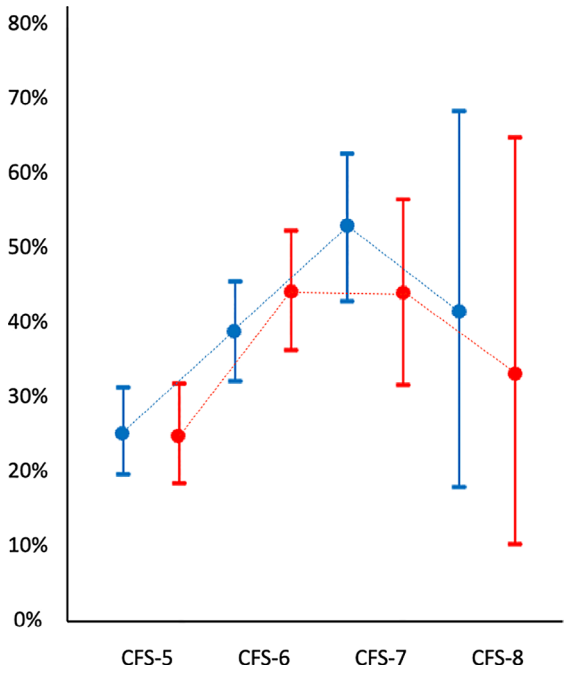

FIGURE 1 Proportion of patients (and 95% confidence intervals) with treatment limitations based on individual CFS scores

2.09; $p = 0.014$). On the contrary, patients with COVID-19 were less likely to receive renal replacement therapy (OR = 0.52; 95%-CI: 0.28–0.95; $p = 0.033$). Patients with COVID-19 were less likely to be discharged home (OR = 0.56; 95%-CI: 0.42–0.75; $p < 0.001$), however, having COVID-19 did not influence nursing home discharge. Compared to patients without COVID-19, the patients with COVID-19 were less likely to be discharged alive from the hospital (HR = 0.72; 95%-CI: 0.61–0.85; $p < 0.001$; Figure 2).

Subgroup analysis

Patients ≤65 years of age. 289 patients (32.7%) younger than 65 years were admitted to ICUs, however, there was no difference in the proportion of treatment limitations between patients with and without COVID-19 (32.2% *vs* 33.0%; $p = 0.81$; Table S3). There were no differences in the proportion of treatment limitations between patients with and without COVID-19 (17.6% *vs* 21.8%; $p = 0.39$).

Patients ≥65 years of age. Most patients (67.3%, $n = 595$) were aged 65 years and older, but there was no difference in the proportion of treatment limitations between patients with and without COVID-19 (67.8% *vs* 67.0%; $p = 0.81$). Despite 43.7% ($n = 260$) having treatment limitations at ICU admission, there were no differences in the proportion of treatment limitations between the 2 groups (44.4% *vs* 43.2%; $p = 0.77$).

Patients receiving non-invasive ventilation. More than half the patients with frailty (51.1%, $n = 452$)

TABLE 3 Univariable and multivariable analysis for the presence of treatment limitations in frail ICU admissions with pneumonitis

	Univariable analysis		Multivariable analysis	
Covariates	**OR (95%-CI)**	***p*-value**	**OR (95%-CI)**	***p*-value***
CFS	1.60 (1.34–1.90)	**<0.001**	1.72 (1.39–2.14)	**<0.001**
Age	1.06 (1.04–1.07)	**<0.001**	1.05 (1.04–1.06)	**<0.001**
Male sex	0.80 (0.61–1.05)	0.11	0.84 (0.60–1.17)	0.84
APACHE III score	1.01 (1.00–1.01)	**0.047**	1.00 (0.99–1.01)	0.53
COVID-19 status	0.99 (0.75–1.30)	0.92	1.39 (0.98–1.96)	0.06
Chronic respiratory condition	1.29 (0.27–6.21)	0.75	1.58 (1.10–2.27)	**0.014**
Chronic renal disease	1.26 (0.82–1.93)	0.30	1.35 (0.82–2.22)	0.24
Metastatic disease	1.84 (1.03–3.30)	**0.040**	1.49 (0.75–2.95)	0.25
Obesity (BMI ≥30 kg.m^{-2})	1.10 (0.78–1.54)	0.60	1.03 (0.71–1.50)	0.88

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; BMI, body mass index; CFS, clinical frailty scale; CI, confidence interval; COVID-19, Coronavirus disease 2019; OR, odds ratio.
*Numbers in bold imply statistical significance.

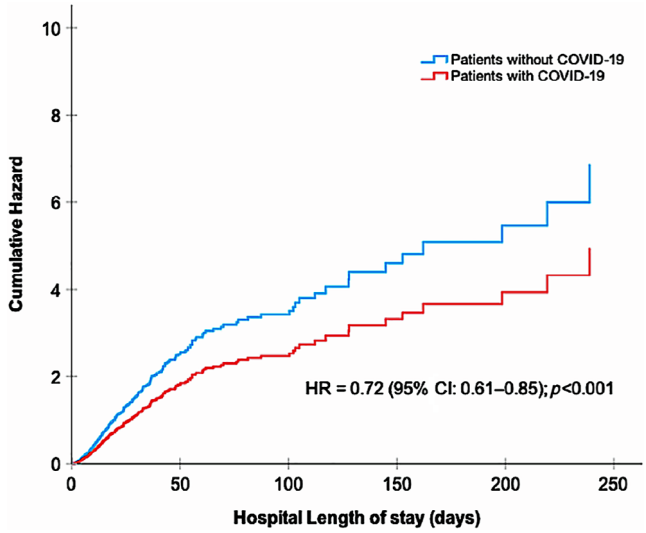

FIGURE 2 Cumulative incidence curves displaying time to hospital discharge with COVID-19 frail patients less likely to be discharged

received non-invasive ventilatory support, a lower proportion among patients with COVID-19, when compared with patients without COVID-19 (46.3% *vs* 54.6%; $p = 0.016$). There were no differences in the proportion of treatment limitations between the two groups (42.1% *vs* 40.2%; $p = 0.69$).

DISCUSSION

Key findings

This multicenter retrospective observational study that compared the treatment limitations among 369 frail patients with COVID-19 and 515 frail patients without COVID-19 admitted to ICU in Australia and New Zealand revealed a few important findings. Firstly, more than a third of the overall patients with frailty had treatment limitations at ICU admission. However, the multivariable model predicting treatment limitations indicated that increasing age, incremental increase in frailty scores, and presence of chronic respiratory disease were significant predictors for the presence of treatment limitations at ICU admission. Secondly, there were no differences in the proportion of treatment limitations between patients with frailty with or without COVID-19. Thirdly, more than two-thirds of frail patients aged ≥65 years had treatment limitations at ICU admission, but the proportion was no different between those with and without COVID-19. Fourthly, more than half the patients with frailty who needed non-invasive ventilatory support had treatment limitations at ICU admission, but the proportion was no different between those with and without COVID-19. Finally, the frail patients with COVID-19 were more likely to have higher ICU and hospital mortalities required more mechanical ventilatory, and vasopressor support and were less likely to be discharged home.

Relationship to previous studies

Treatment limitation is the cornerstone in guiding clinicians on patient management. Quite often a more conservative treatment approach is adopted for the frail and older patients, as 25% of the patients who are admitted to Australian and New Zealand ICUs have severe pre-existing illnesses that are serious enough to be life-limiting.[21] As a result, providing potentially non-beneficial therapies to these patients may be distressing to patients, families, and staff.[22,23] Moreover, such therapies cost the Australian

healthcare system 153 million AUD each year.[24] Furthermore, patients with frailty generally have poorer outcomes including mortality, longer hospitalization, functional dependence, disability, and quality of life.[25,26]

A study based in the United Kingdom observed that COVID-19 had prompted earlier and widespread Do Not Attempt Cardiopulmonary Resuscitation (DNACPR) decisions.[27] Another study reported a significant increase in DNACPR documentation during the COVID-19 pandemic, when compared to the pre-COVID-19 era, from 13.3% (pre-COVID-19) to 50% (during COVID-19).[28,29] A recent European study that included patients ≥80 years from the COVIP (for patients with COVID-19) and VIP-2 (for non-COVID-19 patients) and found that patients with COVID-19 had treatment limitations instituted more frequently compared to similar old non-COVID patients.[30] In contrast, our overall rates of treatment limitations in patients with frailty were comparable, but importantly, no different in patients with and without COVID-19. Our study findings were comparable to a pre-COVID-19 Australian registry-based study that found a third of the adult ICU patients ≥65 years admitted with pneumonia were frail.[31] 38.3% of these patients with frailty had documented treatment limitations at ICU admission.[31] This finding is particularly important as the Australian healthcare system experienced COVID-19-related stress with higher daily ICU Activity Index and mortality recorded by all ICUs reporting to the Critical Health Information System (CHRIS) between August and November 2021.[32,33]

Also, our study's findings suggest that illness severity, increasing age, and incremental increase in frailty scores played a significant role in decisions regarding treatment limitations, rather than the presence of COVID-19 infection. A recent systematic review pre-pandemic reported older age and higher APACHE and Sepsis Related Organ Failure Assessment score have been associated with an increased likelihood of limitations.[34] In the COVID-19 era, the relationship between treatment limitation in frailty and adverse health implications is undeniably an ongoing phenomenon. We demonstrated a clear trend that a higher prevalence of treatment limitations was associated with increasing frailty. Consequently, goals of care decisions for the frail and older patients are a significant risk factor for death and adverse outcomes, especially in the face of the current pandemic.[2,17,35]

Our study found that frail patients with COVID-19, regardless of their treatment limitation status, were likely to die in hospital, had longer hospitalization and were less likely to be discharged home. A recent individual patient data meta-analysis found that triaging patients just based on their frailty status was not justified.[36] Although Australia and New Zealand have evaded the magnitude of the pandemic that has overwhelmed healthcare systems in many parts of the world, our study has demonstrated that intensive care teams have been selective in admitting frail patients with COVID-19 into their ICUs. Close and colleagues reported on some reluctance and lack of transparency from governments to develop and/or release standardized triaging guidelines before another pandemic crisis wave.[37]

A recent study, although not specific to patients with COVID-19, reported on many frailty-specific integrated care models to support the care of frail older people in hospitals and the community in their horizon-scanning review.[38] Such integrated models could potentially reduce the number of frail older people requiring ICU and may improve outcomes also for those who eventually are admitted to and discharged from ICU.

The emergence of the newer SARS-CoV-2 variants has significantly strained the healthcare system in many Australian states.[39] Despite vaccinations and public health measures to mitigate this pandemic, COVID-19 may continue to severely impact frail older and vulnerable patients. Further improvements in the outcomes in these patients are likely with increased uptake of vaccinations. As the ethical approach in managing critically ill patients is to facilitate early goals of care conversations,[1–3,12] it is essential that we ensure that frail and older patients receive timely goal-concordant care, which may avoid burdensome treatment, and may facilitate the provision of goal-concordant care.[2,17,40]

Implications of study findings

Our study found that a third of all frail patients and two-thirds of all those aged ≥65 years had treatment limitations at admission to ICU, however, there was no difference in treatment limitations between those with and without COVID-19. This has potential implications. Firstly, Australia and New Zealand's healthcare system was not as overwhelmed as other parts of the world. Secondly, Australia and New Zealand have a good baseline health infrastructure, resources, and economic might to ensure strict public health measures such as prolonged and protracted lockdowns till most of their citizens were vaccinated. Thirdly, more importantly, the lack of difference could suggest the decision to admit them to ICU was irrespective of their COVID-19-illness. Increasing age, incremental increase in frailty scores, and presence of chronic respiratory disease were significant predictors for the presence of treatment limitations at ICU admission. We also found that, regardless of their treatment limitation status, frail patients with COVID-19 were more likely to die in hospital and have longer hospitalization,

and are less likely to be discharged home. This implies that it is essential not only to establish early goal-concordant care in patients with frailty but also to use that to guide critical care triaging decisions to rapidly assess patients for the severity of the presenting acute illness and the likelihood of medical interventions being successful.[36,41]

Strengths and limitations

The strengths of our study include its multicenter design, which incorporated high-quality data, as well as a larger sample size than many other studies. We also adjusted for appropriate confounders. To our knowledge, ours is the only study to compare treatment limitations between frail patients with and without COVID-19. However, there are a few limitations to this study. Firstly, the retrospective study design meant that data collection was reliant on existing datasets and medical records. Secondly, despite the ANZICS-APD being recognized as a high-quality clinical registry dataset, the effect of data coding inaccuracy on the study findings could not be assessed. Thirdly, COVID-19 patients that did not have an admission diagnosis of pneumonitis would not have been included. Fourthly, we only assessed the patients admitted to ICU. There is good evidence that pre-existing goals of care documentation strongly influence ICU physicians' decisions in admitting patients older than 80 years.[42] Fifthly, we did not have the data on the number of patients where all their active treatments were formally withdrawn. Sixthly, there may be large variabilities in the treatment limitation practices among the ICUs across Australia and New Zealand, which needs to be acknowledged.[34] Seventhly, we did not have any information about the proportion of patients being treated with antiviral agents and the duration of antiviral treatment pre-ICU. Furthermore, although the new treatment options, such as anti-viral agents (Molnupiravir[43]), JAK inhibitors (Baricitinib[44]), etc., have improved outcomes, this information was not available in ANZICS-APD. Eighthly, we were unable to determine inter-rater reliability for CFS in our study. However previous studies showed that the inter-rater reliability was strong for CFS.[45–47] Finally, the Australia and New Zealand healthcare system had been very fortunate with the magnitude of COVID-19 infections and stringent public health measures, therefore the results may not be generalizable in resource-constrained healthcare systems.

CONCLUSION

This retrospective multicenter study in Australia and New Zealand found that a third of the patients with frailty had treatment limitations at ICU admission, it was not different among patients with or without COVID-19 pneumonitis. Increasing age, incremental increase in frailty scores, and presence of chronic respiratory disease were significant predictors for the presence of treatment limitations at ICU admission.

AUTHOR CONTRIBUTIONS

Ashwin Subramaniam: This author conceived the project idea, conducted the literature review, performed the data analysis, wrote the initial drafts of the manuscript, created tables and figures, and finalized the manuscript. **Ravindranath Tiruvoipati**: This author contributed to the concept and project design, edited, critically evaluated, and finalized the manuscript. **David Pilcher**: This author contributed to the concept and project design, edited, critically evaluated, and finalized the manuscript. **Michael Bailey**: This author contributed to the concept and project design, assisted with the statistical analysis, created figures, edited, critically evaluated, and finalized the manuscript. All authors critically reviewed the manuscript and approved the final version before submission.

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All authors declare no support from any organization for the submitted work, and no competing interests with regards to the submitted work: (1) We declare that we have no proprietary, financial, professional, or other personal interest of any nature or kind in any product, service, and/or company that could be construed as influencing the position presented in the submitted manuscript. (2) This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

Table S1. Diagnostic codes and subcodes for patients included in the study between January 2020 and December 2021.
Table S2. The odds ratio (OR) for COVID-19 status is presented as unadjusted and adjusted (for age, sex, CFS, APACHE-III, and treatment limitation status) logistic regression analysis for outcomes in frail patients.
Table S3. Raw outcomes in patients categorized based on age and those requiring non-invasive ventilatory support.
Figure S1. Flow diagram demonstrating patient inclusion.
Figure S2. Patients with COVID-19 pneumonitis were predominantly from NSW and VIC.
Figure S3. Age comparison categorized by CFS compared with and without COVID-19 pneumonitis: all patients (top panel), patients without (middle panel) and with (bottom panel) treatment limitations.

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