Critical Care and Resuscitation 26 (2024) 161–168

Contents lists available at ScienceDirect

Critical Care and Resuscitation

journal homepage: www.elsevier.com/locate/ccrj

Original Article

Management of severe acute respiratory distress syndrome in Australia and New Zealand (SAGE-ANZ): An observational study

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ARTICLE INFORMATION

Article history:
Received 4 April 2024
Received in revised form
17 May 2024
Accepted 20 May 2024

Keywords:
Acute respiratory distress syndrome: adjunctive therapy
Lung protective ventilation
Mechanical ventilation
Prone positioning

ABSTRACT

Objective: Acute respiratory distress syndrome (ARDS) is associated with significant mortality, morbidity, and cost. We aimed to describe characteristics and management of adult patients admitted to intensive care units (ICUs) in Australia and New Zealand with moderate-severe ARDS, to better understand contemporary practice.
Design: Bi-national, prospective, observational, multi-centre study.
Setting: 19 ICUs in Australia and New Zealand.
Participants: Mechanically ventilated patients with moderate-severe ARDS.
Main outcome measures: Baseline demographic characteristics, ventilation characteristics, use of adjunctive support therapy and all-cause mortality to day 28. Data were summarised using descriptive statistics.
Results: 200 participants were enrolled, mean (±SD) age 55.5 (±15.9) years, 40% (n = 80) female. Around half (51.5%) had no baseline comorbidities and 45 (31%) tested positive for COVID-19. On day 1, mean SOFA score was 9 ± 3; median (IQR) PaO_2/FiO_2 ratio 119 (89, 142), median (IQR) FiO_2 70% (50%, 99%) and mean (±SD) positive end expiratory pressure (PEEP) 11 (±3) cmH_2O. On day one, 10.5% (n = 21) received lung protective ventilation (LPV) (tidal volume ≤6.5 mL/kg predicted body weight and plateau pressure or peak pressure ≤30 cm H_2O). Adjunctive therapies were received by 86% (n = 172) of patients at some stage from enrolment to day 28. Systemic steroids were most used (n = 127) followed by neuromuscular blockers (n = 122) and prone positioning (n = 27). Median ventilator-free days (IQR) to day 28 was 5 (0, 20). In-hospital mortality, censored at day 28, was 30.5% (n = 61).
Conclusions: In Australia and New Zealand, compliance with evidence-based practices including LPV and prone positioning was low in this cohort. Therapies with proven benefit in the treatment of patients

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https://doi.org/10.1016/j.ccrj.2024.05.001

with moderate-severe ARDS, such as lung protective ventilation and prone positioning, were not routinely employed.

1. Introduction

Acute respiratory distress syndrome (ARDS) is an acute inflammatory lung injury associated with significant morbidity, mortality, and associated costs.[1] ARDS is a heterogeneous disease and a common cause of admission to the intensive care unit (ICU). Treatment of moderate-severe ARDS is largely supportive and aimed at delivery of lung protective ventilation (LPV) to mitigate further lung injury and provision of adjunctive therapies such as neuromuscular blockade, inhaled pulmonary vasodilators, steroids, extracorporeal membrane oxygenation and prone positioning.[2] Several large epidemiological studies have provided insight and helped shape understanding of this syndrome,[1,3–8] however there remains limited information about the recognition, management, and outcomes of patients with moderate-severe ARDS in Australia and New Zealand (ANZ). Most recently a large multicentre, observational study described variation in early management of 2466 patients with moderate-severe ARDS in 25 ICUs across the United States of America (USA).[9] The SAGE-USA study[9] reported in-hospital mortality to day 28 was 40.7%; that there was significant variation between sites in the use of both evidence-based and non-evidence based therapies; and that adjunctive therapies were used commonly. Other reports have also highlighted regional variations in the management of patients with ARDS.[10,11] We aimed to describe the current management and outcomes of patients with moderate-severe ARDS in ANZ, to better understand practice across this region.

2. Methods

2.1. Study design and setting

This prospective observational cohort study was conducted in 19 ICUs, nine in Australia and 10 in New Zealand with the first patient enrolled 22nd September 2019 and last patient enrolled 17th July 2021. The study was endorsed by the Australian and New Zealand Intensive Care Society Clinical Trials Group and registered (ANZCTR: ACTRN12619000403134). Ethics approval was gained from the Southern Health and Disability Ethics Committee, New Zealand (19/STH/54) and the Human Research Ethics Committee, ACT Health (2019/ETH/00054) and local approval or governance obtained from each location. The need for written informed consent was waived. Information regarding the study was displayed in each participating ICU to explain the study to relatives. See Supplemental Appendix 1 for a list of participating centres and research collaborators.

2.2. Participants

Adult patients (over 18 years of age) were screened daily by trained research staff for 5 days from the time of intubation to determine eligibility. To be eligible, participants had to be diagnosed with hypoxaemic respiratory failure, requiring invasive mechanical ventilation via an endotracheal tube or tracheostomy AND determined to have moderate to severe ARDS as defined by fulfilment of ALL the following in the previous 48 h: bilateral opacities in chest x-ray or CT, not fully explained by effusion, lung collapse or nodules; respiratory failure not fully explained by cardiac failure or fluid overload and PaO_2/FiO_2 ratio $\leq$150 with a minimum of 5 cmH_2O PEEP.

2.3. Data collection

Data were collected from medical records by trained research coordinators at each site for the first three days following study enrolment, and on days 7 and up to day 28 if the patient remained in the ICU. Prior to study initiation each site received education from the researchers regarding data collection and electronic submission, a data dictionary defined each data point with data entry and management overseen by a project manager. Data were collected and managed in a purpose-built Research Electronic Data Capture database, hosted on a secure server by the Medical Research Institute of New Zealand. See Supplemental Appendix 2 and 3 for the study protocol and full case report form.

2.4. Sample size

We estimated each site would enrol, on average, at least 1–2 participants per week. Assuming 25 sites participated in this study, an estimated 650–1300 participants would be enrolled over a 6-month period. However, recruitment of sites and participants was affected by the impact of the COVID-19 pandemic, which required a return of research staff to clinical work and curtailed study activities and recruitment.

2.5. Outcomes

Outcomes of interest included adherence to LPV; use of adjunctive support therapy (neuromuscular blockers, inhaled pulmonary vasodilators, prone positioning, high frequency oscillation, systemic steroids, ECMO); all-cause mortality to day 28 post enrolment; organ failure scores at day 7 post enrolment if still alive and in ICU; ICU and hospital length of stay; ventilator-free days to hospital discharge; hospital-free days to day 28 and destination upon discharge from hospital. See Supplemental Appendix for details on coding and measurements.

2.6. Statistical methods

Data on the frequency of practice and clinical characteristics were described using number and percentage for categorical variables and means and standard deviations (SD) or median and interquartile range (IQR), as appropriate, for continuous variables. We present descriptive data only; results are presented for both countries and all study sites combined in the main text, with an additional breakdown by country and other factors such as COVID-19 and extracorporeal membrane oxygenation (ECMO) status being displayed in the Supplemental Appendix. Missing data was described for all variables. Compliance with lung protective ventilation was defined as $V_T \leq 6.5$ mL/kg PBW and plateau pressure $\leq$30 cm H_2O. If plateau pressure was not available, peak pressure $\leq$30 cm H_2O was used.

3. Results

3.1. Baseline characteristics

In total 200 participants were enrolled from September 2019 to July 2021: 73 across 10 sites in New Zealand and 127 across 9 sites in Australia. Baseline characteristics are shown in Table 1 (Supplemental Table 1S) and did not differ by country.

Over half of enrolled participants (103/200) had no baseline comorbidities (Supplemental Tables 1S, 2S, 3S). The most common baseline ARDS risk factors included pneumonia (68%), sepsis (65%), and shock (32%) (Supplemental 4S and 5S).

3.2. Clinical characteristics

On day 1, 21/200 (10.5%) of participants received LPV ($V_T \leq 6.5$ mL/kg PBW and plateau [or peak] pressure ≤ 30 cmH_2O) (Fig. 1). Interestingly, plateau pressure was only measured in 5 participants. Clinical characteristics were broadly similar in ANZ (Table 2 and Supplemental Table 6S).

3.3. Adjunctive therapies

From enrolment to day 28, 172/200 (86%) participants received adjunctive therapies at some stage (Supplemental Tables 7S and 8S). Systemic steroids were used in 127/200 (63.5%), neuromuscular blockers (NMB) in 122/200 (61%) and prone positioning in 47/200 (23.5%). Results were similar when analysed by country and COVID-19 status. Most therapies commenced study day 1, although some were not commenced until after study day 7 (Supplemental Tables 7S and 8S).

3.4. ECMO usage

In total 25/200 participants (12.5%) received ECMO; 12 in Australia and 13 in New Zealand. Patients who received ECMO were younger (44.7 ± 13.3 vs 57 ± 15.8) and lighter (76.7 ± 15.4 vs 87.1 ± 23.5) (Table 3). Baseline comorbidities and ARDS risk factors according to ECMO status are displayed in the e-Appendix (Supplemental Tables 9S and 10S and Table 11S). Of those receiving ECMO, 24 received veno-venous ECMO with 60% (15/25) initiated outside the study hospital. The mean ± SD length of time on ECMO was 16.1 ± 10.7 days with range 2–46 days. Further ECMO characteristics are displayed in Supplemental Table 11S and daily ECMO data regarding ECMO delivery and ventilation settings in Table 12S.

3.5. Participant outcomes

Median (IQR) ventilator-free days to day 28 was 5 days (0, 20) while the median (IQR) duration of mechanical ventilation was 10 days (5, 18) (Table 4). Median (IQR) ICU stay was 14 days (8, 24) and over half the participants had no hospital-free days to day 28 (Fig. 2). In-hospital mortality to 28 days was 30.5% while 56% were alive and receiving unassisted breathing at day 28. Forty-one

Table 1
Baseline characteristics.

Variable	Total (N = 200)	Australia (N = 127)	New Zealand (N = 73)
Age, years	55.5 ± 15.9	57.2 ± 15.5	52.6 ± 16.4
Sex, Female	80 (40)	52 (40.9)	28 (38.4)
Weight, kg	85.8 ± 22.9	86.8 ± 22.7	84.1 ± 23.2
BMI, kg/m^2	29.7 ± 7.6	30.1 ± 7.5	28.9 ± 7.8
Ethnicity			
European	82 (55.8)	35 (47.3)	47 (64.4)
Māori	8 (5.4)	0 (0)	8 (11)
Pacific	7 (4.8)	1 (1.4)	6 (8.2)
Asian	26 (17.7)	14 (18.9)	12 (16.4)
MELAA	16 (10.9)	16 (21.6)	0 (0)
Aboriginal or Torres Strait Islander	4 (5.4)	4 (5.4)	0 (0)
Other	4 (5.4)	4 (5.4)	0 (0)
Ethnicity not recorded	53 (26.5)	53 (41.7)	0 (0)
Comorbidity[a]			
No other conditions	103 (51.5)	60 (47.2)	43 (58.9)
Diabetes Mellitus	40 (20)	35 (27.6)	5 (6.8)
Immunosuppression	29 (14.5)	17 (13.4)	12 (16.4)
Chronic lung disease	11 (5.5)	8 (6.3)	3 (4.1)
Baseline ARDS risk factors			
Pneumonia	136 (68)	100 (78.7)	36 (49.3)
Sepsis	130 (65)	87 (68.5)	43 (58.9)
Shock	64 (32)	50 (39.4)	14 (19.2)
Aspiration	37 (18.5)	20 (15.7)	17 (23.3)
Blood product transfusion	12 (6)	9 (7.1)	3 (4.1)
Other	38 (19)	26 (20.4)	12 (16.4)
Transferred from another hospital			
Yes	55 (27.5)	33 (26.0)	22 (30.1)
COVID-19 or influenza testing			
Not tested	51 (25.5)	19 (15)	32 (43.8)
Tested	147 (73.5)	107 (84.3)	40 (54.8)
Unknown	2 (1.0)	1 (0.8)	1 (1.4)
Test result	*(N = 147)*	*(N = 107)*	*(N = 40)*
COVID positive	45 (30.6)	41 (38.3)	4 (10.0)
COVID negative	99 (67.3)	65 (60.7)	34 (85)
Influenza positive	2 (1.4)	0 (0)	2 (5.0)
Result unknown	1 (0.7)	1 (0.9)	0 (0)

Data are presented as N (%) or mean ± SD. BMI = body mass index; ECMO = extracorporeal membrane oxygenation; MELAA = Middle Eastern, Latin American, African
[a] Comorbidities are representative only. Full details of all comorbidities reported are in Supplemental Appendix Table 2S.

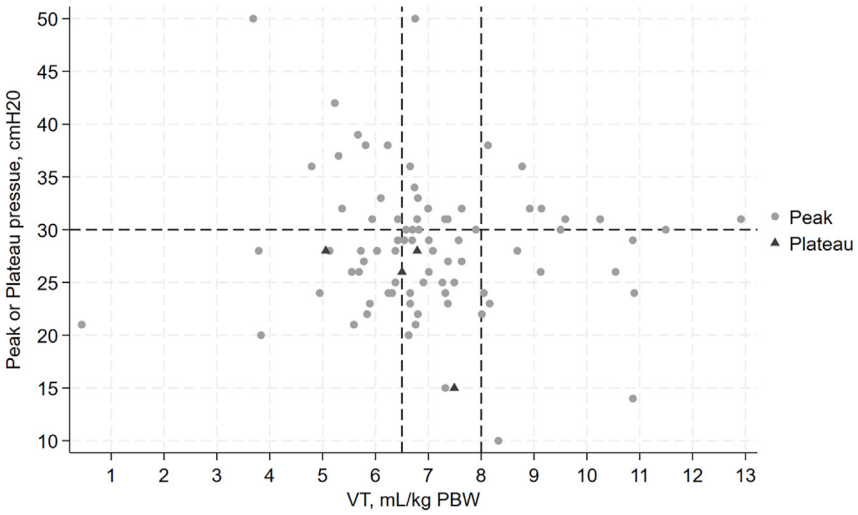

Fig. 1. Distribution of tidal volume vs peak or plateau pressure on day 1.

participants received a tracheostomy. Five of the 25 participants who received ECMO died by day-28 (Table 13S e-Appendix). Of all participants discharged alive from hospital, most were discharged home. Others were discharged to hospital wards, transferred to other ICUs, hospice, and rehabilitation centres. Fourteen participants were still receiving mechanical ventilation on discharge from the study ICU however they were all transferred to other ICUs. Life-sustaining therapies were permanently withdrawn or withheld in 52 participants for reported multiorgan failure, poor prognosis on maximum therapy, and a change to palliative care from active treatment. All but one subsequently died in ICU.

4. Discussion

This observational study reports contemporary management practices of moderate-severe ARDS patients in ANZ. We found low adherence to LPV and prone positioning, relatively low mortality and common use of adjunctive therapies. This study echoes previous studies questioning why therapies with proven benefit in the treatment of patients with moderate-severe ARDS are not routinely employed.[3,12,13]

Lung protective ventilation remains a cornerstone of ventilatory management in ARDS, ventilation strategies that adopt a lower plateau pressure and lower tidal volume can reduce mortality rates and increase ventilator-free days.[14–16] We found LPV was not routinely provided to this cohort with 64.8% of participants receiving V_T 6.6–8 mL/kg PBW and 24% V_T > 8 mL/kg PBW. The finding of non-adherent LPV is not new and aligns with previous work.[3,8,9] A mean Day 1 V_T of 7 mL/kg PBW was reported in Canada, the USA, Ireland, and Saudi Arabia,[1,8,9] despite clear recommendations in guidelines.[17,18]

In a recently updated systematic review, higher levels of PEEP were associated with improved oxygenation, and decreased use of adjunctive therapies, but do not appear to increase the number of ventilator-free days or reduce in-hospital mortality.[19] We found higher average PEEP was applied in ANZ (11 ± 3 cmH_2O) when compared to 9 ± 4 cmH_2O in the USA,[9] but similar to that reported in Canada (10.5 ± 3.7 cmH_2O).[8]

Table 2
Clinical characteristics on day 1.

Variable	Total (N = 200)
PaO_2:FiO_2 ratio	119 (89, 142)
Missing	*1*
FiO_2, %	70 (50, 99)
SOFA total score	9 ± 3
Vasopressors (infusion lasting >1 h)	170 (85.0%)
Missing	*30*
PEEP, cmH_2O	11 ± 3
Missing	*3*
Plateau pressure, cmH_2O	28 (26, 28)
Plateau pressure > 30 cmH_2O	1 (20.0%)
Missing	*195*
Peak pressure, cmH_2O	28 (24, 31)
Peak pressure > 30 cmH_2O	46 (32.2%)
Missing	*57*
V_T, mL/kg PBW	7 ± 2
V_T > 6.5 mL/kg PBW	81 (64.8%)
V_T > 8 mL/kg PBW	30 (24.0%)
Missing	*75*
LPV compliant[a]	21 (10.5%)
LPV non-compliant	112 (56.0%)
Data not available	*67 (33.5%)*

Data presented using median (IQR), mean ± SD or N (%), as appropriate. FiO_2 = fraction of inspired oxygen; LPV = lung protective ventilation; PaO_2 = partial pressure of arterial oxygen; PBW = predicted body weight; PEEP = positive end expiratory pressure; SOFA = sequential organ failure assessment; V_T = tidal volume.
[a] Defined as $V_T \leq 6.5$ mL/kg PBW and plateau pressure ≤30 cm H_2O. If plateau pressure was missing, peak pressure was used.

Table 3
Baseline characteristics by ECMO status.

Variable	No ECMO (N = 175)	ECMO (N = 25)
Age, years	57 ± 15.8	44.7 ± 13.3
Sex, Female	68 (38.9)	12 (48)
Weight, kg	87.1 ± 23.5	76.7 ± 15.4
BMI, kg/m^2	30.2 ± 7.8	26.1 ± 4.6
Ethnicity		
European	70 (54.3)	12 (66.7)
Māori	8 (6.2)	0 (0)
Pacific	6 (4.7)	1 (5.6)
Asian	22 (17.1)	4 (22.2)
MELAA	15 (11.6)	1 (5.6)
Aboriginal or Torres Strait Islander	4 (3.1)	0 (0)
Other	4 (3.1)	0 (0)
Ethnicity not recorded	46 (26.3)	7 (28.0)
Transferred from outside hospital	38 (21.7)	17 (68.0)

Data are presented as N (%) or mean ± SD. BMI = body mass index; ECMO = extracorporeal membrane oxygenation; MELAA = Middle Eastern, Latin American, African.

Table 4
Outcomes.

Variable	Total (N = 200)	Australia (N = 127)	New Zealand (N = 73)	COVID Negative (N = 99)	COVID Positive (N = 45)	Unknown COVID (N = 54)
Ventilator-free days to day 28	5 (0, 20)	14 (0, 22)	0 (0, 15)	10 (0, 21)	3 (0, 20)	0 (0, 20)
Missing[a]	*5*	*5*	*0*	*0*	*5*	*0*
Mechanical ventilation duration, days	10 (5, 18)	9 (6, 17)	10 (5, 20)	8 (4, 11)	11 (6, 19)	7 (5, 12)
Missing[a]	*16*	*10*	*6*	*2*	*9*	*3*
Duration of initial ICU stay, days	14 (8, 24)	13 (8, 22)	15 (8, 28)	10 (7, 17)	12 (8, 21)	12 (6, 17)
Missing	*3*	*1*	*2*	19	17	19
Alive day 7	157 (79.3)	97 (77.6)	60 (82.2)	77 (78.6)	38 (86.4)	40 (74.1)
Missing	*2*	*2*	*0*	1	1	0
SOFA total score day 7	8 ± 5	7 ± 4	9 ± 5	8 ± 5	6 ± 4	8 ± 5
Alive and with UAB day 28	108 (56.0)	77 (64.2)	31 (42.5)	57 (58.8)	24 (60.0)	26 (48.1)
Missing	*7*	*7*	*0*	22	7	13
Hospital-free days to day 28	0 (0, 11)	0 (0, 13)	0 (0, 2)	0 (0, 12)	0 (0, 12)	0 (0, 3)
Missing	*1*	*0*	*1*	2	5	0
Hospital length of stay, days	19 (10, 28)	19 (11, 28)	19 (9, 28)	17 (10, 28)	20 (12, 28)	19 (9, 28)
Missing	*1*	*0*	*1*	1	0	0
28-day in-hospital mortality	61 (30.5)	31 (24.4)	30 (41.1)	31 (31.3)	9 (20.0)	21 (38.9)

Data presented using median (IQR), mean ± SD or N (%), as appropriate. ICU = intensive care unit; SOFA = sequential organ failure assessment; UAB = unassisted breathing.
[a] Note this includes n = 4 participants who had a repeat intubation but no information on repeat extubation dates, therefore ventilation time could not be calculated.

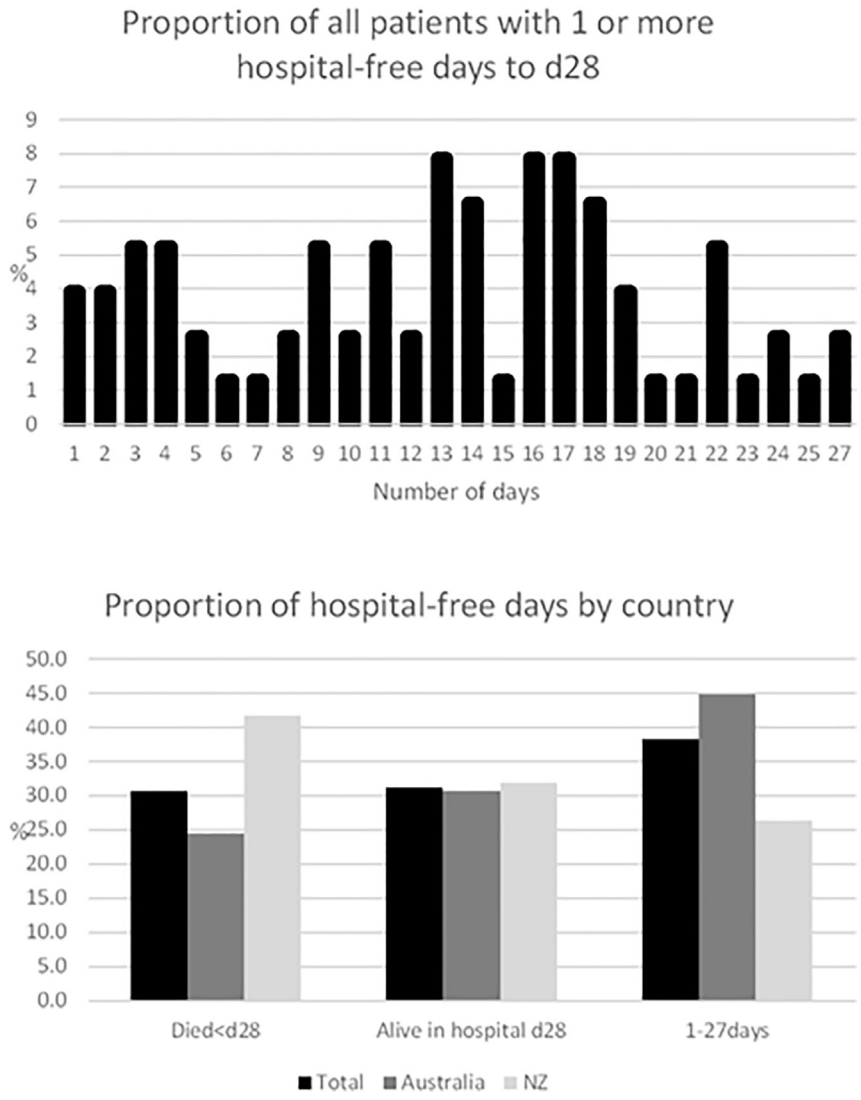

Fig. 2. Hospital-free days.

Although there was a low level of adherence to LPV found in this study, we found a lower 28-day in-hospital mortality rate (30.5%) than reported previously. A recent cross-sectional analysis of 25,170 adults admitted with ARDS in the USA reported an index admission mortality rate of 37.5% (95% confidence interval 36.2–38.8),[20] while the LUNGSAFE study reported 28-day mortality of 35.2% (95%CI 32.4–38.1) for moderate ARDS and 40.9% (95%CI 36.8–45.1) for severe ARDS.[3]

Recently, the call is to consider a more targeted, patient-centred approach to the treatment of ARDS with the application of personalised or precision medicine based on baseline characteristics, imaging, biomarkers, metabolomics and identification of subphenotypes and ventilatory parameters.[21–25] It is possible that the lower observed mortality in this study and decreased adherence to recommended LPV targets reflects greater individualisation of care in ANZ.

The lower mortality rate in our study should be interpreted cautiously as reasons are likely multifactorial and may be a result of the patients selected to be admitted into the participating ICUs, not necessarily because of the care provided. A previous report of ARDS in 21 Australian ICUs also found a lower 28-day mortality rate (34%) when compared to other countries.[4] Additionally, in our study, death occurred mainly due to multi-organ failure rather than primary respiratory failure which again is consistent with previous studies.[4,26] Finally, a reduction has been seen in ARDS mortality rates over time,[27] as demonstrated in a comparative systematic review.[28]

4.1. Use of adjunctive therapies

Our findings agree with those of Qadir et al.[9] that specific therapies targeted to ARDS patients and known to improve survival are underutilised and unproven therapies utilised extensively. In this study we found 86% of participants received one or more adjunctive therapies.

The use of NMBs is far higher in our study (61%) than reported in SAGE-USA (27.4%)[9] and LUNGSAFE (36%)[3] and is difficult to explain. The recent large Revaluation of Systemic Early Neuromuscular Blockade trial (ROSE) demonstrated limited benefit of NMBs in this cohort,[29] with the investigators proposing several reasons for this including lighter sedation targets used, and the use of prone positioning.[29] The use of NMBs prevents spontaneous breathing activity in ARDS patients, which has been shown to be potentially beneficial in early ARDS.[30] Interestingly the use of prone positioning in SAGE-ANZ was greater again (23.5% SAGE-ANZ vs 15.8% in ROSE[29] vs 7.9% LUNGSAFE[3] vs 5.8% SAGE-USA) suggesting a correlation between the use of prone positioning and requirement for NMBs in mechanically ventilated patients. A possible explanation is the higher use of ECMO in SAGE-ANZ coupled with early experience of treating COVID-19 patients in ANZ, both of which may have been associated with higher NMB use. The recently released European Society of Intensive Care Medicine (ESICM) guidelines on ARDS recommend against routine use of continuous infusions of NMBs in patients with moderate-severe ARDS without COVID-19.[31]

The benefits of prone positioning in severe ARDS have been demonstrated,[32–34] however not routinely enacted due to reported difficulties and perceptions of risk and adverse events. Prone positioning in patients with moderate-severe ARDS, holds a strong recommendation in guidelines from the American Thoracic Society, ESICM, Society of Critical Care Medicine and the Faculty of Intensive Care Medicine.[17,18,31] The use of prone positioning in our study was almost twice as common in participants who were COVID-19 positive than in those who were not. This may reflect translation of both anecdotal and then accruing evidence from centres in Europe and North America early in the pandemic. However, a recent systematic review and meta-analysis reported insufficient evidence to support the beneficial effects of prone positioning in intubated patients with COVID-19.[35] It should be recognised though that implementation of prone positioning requires exposure to the procedure, comfort with instituting it through sustained experience, protocolised care, and adequate resources to facilitate greater use.[36] As management of COVID-19 associated ARDS evolves and matures, reports suggest a reduction in the use of prone positioning for COVID-19 ARDS.[37] A multicentre, prospective registry of prone positioning in COVID-19 patients may help us understand outcomes in this group.[38]

Duggal et al.[11] suggest the need to consider patient, clinician and systems-level factors associated with the use of adjunctive therapies as well as geographical disparities. This may explain some of the variance seen between the SAGE-USA and SAGE-ANZ studies where marked differences exist between the healthcare systems including nurse: patient ratios and the make-up of the treating clinical team. Nurse:patient daytime ratios are higher in both New Zealand and Australia when compared to the USA (median [IQR] 0.9 [0.8–1.1] vs 1.2 [1.0–1.3] vs 0.7 [0.5–0.8] respectively)[10] where medical and nursing clinicians manage patient management including ventilation rather than respiratory therapists and respiratory physicians. ICUs in ANZ are also predominantly closed, general ICUs with trained intensivists and transfer of patients to tertiary centres to access a higher level of care is not uncommon.

When comparing SAGE-USA and SAGE-NZ, several factors need to be taken into account. The regions have very different healthcare systems which may affect therapies available and employed and therefore possibly outcomes. Data collection in the SAGE-USA study occurred before the COVID-19 pandemic and there was a five-year gap between the two studies during which time there may have been changes in practice that perhaps limits interpretation of direct comparisons between the two datasets.

There is a new global definition of ARDS,[39] so it would be interesting to revisit this study in light of recommendations to allow a new global definition of ARDS to include patients who are not-intubated but receiving high flow nasal oxygen therapy and to analyse outcomes and management in that group.

4.2. Strengths and limitations

Apart from one previous study in three states of Australia,[4] this is the first to look solely at practice and outcomes across ANZ. This adds valuable data for the generation of future research hypotheses and interventions that could be tested.

The impacts of delayed recruitment and COVID-19 on this study mean the sample size was not achieved, and we could not undertake centre-to-centre comparisons to understand variation in practice. Due to the small sample enrolled, conclusions from this study should be interpreted cautiously.

There could have been several factors that influenced our findings, including the unexpected nature of the pandemic and the resulting changes in clinical practice as evidence accrued. Of note, most participants in New Zealand were recruited prior to widespread community transmission of COVID-19. It would appear that plateau pressures are not routinely measured in Australia and New Zealand and alternative measures such as peak inspiratory pressure was only recorded in two-thirds of participants. This would be of importance for future trials of mechanical ventilation in this region.

5. Conclusions

In this cohort study across Australia and New Zealand, we found a large proportion of participants received ventilation strategies that were not adherent to the principles of LPV; however, the use of

adjunctive therapies was common. Despite this observed mortality was less than previously reported in other countries and regions.

Funding

This study received funding in the form of a Faculty Research Development Fund New Staff grant, The University of Auckland (Project number 3719322) and from the College of Health and Medicine, Australian National University (crisis research seed funding). Funders had no input into study design, analysis, or reporting.

Conflict of interest

RLP, SM and KC and EG work in the Cardiothoracic and Vascular ICU, Te Toka Tumai Auckland. Research in the CVICU is supported in part by way of an unrestricted grant from Fisher and Paykel Healthcare, New Zealand Ltd.

All other authors declare no conflicts.

CRediT authorship contribution statement

This study was designed by RP, SM, KC, AC, SB, SB, AC, EG, CH, EL, CM, CN, AP, JT, SW and FvH.

RLP, KC and AC had full access to the raw data. AC, RP and SM analysed and interpreted the data.

The initial manuscript was drafted by RLP, SM, and FvH. All authors provided input into, critically revised, and approved the final version of the manuscript.

We would like to sincerely thank the SAGE-USA investigators Dr Nida Qadir, Dr Raquel Bartz, Dr Michelle Ng Gong and Dr Pauline Park for their collaboration and encouragement and for sharing their protocol and case report form with us.

Acknowledgments

We sincerely thank the SAGE-ANZ site investigators and research coordinators who collected the data for this study (Supplemental Appendix 1).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ccrj.2024.05.001.

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