Six-month outcomes following venovenous ECMO for severe COVID-19 and viral pneumonitis: 2019–2020 Australian experience

Aidan JC Burrell, Ary Serpa Neto, Andrew Udy, Vincent Pellegrino and Carol Hodgson

Pandemic viral respiratory tract infections can lead to severe viral pneumonitis which is refractory to conventional intensive care unit (ICU) treatments, necessitating venovenous extracorporeal membrane oxygenation (VV-ECMO). Over the past 3 years, Australia has experienced two major viral outbreaks, including a non-coronavirus disease 2019 (COVID-19) (predominantly influenza) outbreak in 2019–2020 and the COVID-19 pandemic in 2020.¹ Few studies have directly compared the patient characteristics, disease course, or long term impact and resource use of these different viral diseases in VV-ECMO patients.

We performed a multicentre, observational study using the Australian national ECMO registry (NCT03793257). We compared patients with severe COVID-19 pneumonitis who were supported by VV-ECMO with patients with non-COVID-19 (predominantly influenza) viral pneumonitis. Six-month survival, as well as disability (World Health Organization Disability Assessment Schedule [WHODAS]) and quality of life (Five-level EuroQol five dimensions questionnaire [EQ-5D-5L]) were assessed by trained, central assessors.

From 30 March 2019 to 31 December 2020, 13 patients were initiated on VV-ECMO for COVID-19 and 23 were initiated for non-COVID-19 viral pneumonitis in seven centres (Table 1). In comparison to non-COVID-19 viral pneumonitis, COVID-19 patients were older (median age, 58 [interquartile range (IQR), 56–66] v 44 [IQR, 33–54] years), but illness severity, arterial partial pressure of oxygen to fraction of inspired oxygen ($\text{PaO}_2:\text{FiO}_2$) ratio, and driving pressure at the time of ECMO initiation were similar (Table 1). Median time from intubation to ECMO initiation was longer in patients with COVID-19 (7.4 [IQR, 3.3–14.0] v 0.7 [IQR, 0.2–4.6] days). Patients with COVID-19 also had increased duration of mechanical ventilation (30.4 v 16.7 days), ICU length of stay (45.6 v 23.8 days) and hospital length of stay (55.7 v 30.7 days) compared with viral pneumonitis patients. At 6 months, the mortality was numerically lower in the COVID-19 group (25% v 38.1%; $P = 0.70$) and the incidence of complications were similar. Functional outcomes at 6 months were available in 6/9 and 11/13 of the survivors respectively. Disability and health-related

ABSTRACT

Objective: To compare the characteristics, treatments and 6-month functional outcomes of patients with coronavirus disease 2019 (COVID-19) versus non-COVID-19 viral pneumonitis supported by venovenous extracorporeal membrane oxygenation (VV-ECMO).

Design: Prospective, observational cohort study in seven intensive care units (ICUs) across Australia.

Participants: Patients admitted to participating ICUs with laboratory-confirmed COVID-19 or viral pneumonitis requiring VV-ECMO.

Results: From 30 March 2019 to 31 December 2020, 13 patients were initiated on VV-ECMO for COVID-19 and 23 were initiated for non-COVID-19 viral pneumonitis. Patients with COVID-19 were older and had a longer duration from intubation to ECMO initiation, but had similar illness severity and APACHE IV scores at the time of initiation. Overall disability, health-related quality of life, and mortality were similar, but ICU and hospital length of stay were significantly longer in patients with COVID-19.

Conclusions: Six-month functional outcomes and mortality were similar between COVID-19 and viral pneumonitis patients treated with VV-ECMO. However, length of stay was longer in COVID-19 patients, which may have resource implications.

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quality of life were similar. No patients from either group underwent lung transplantation.

This nationwide study highlights important demographic and long term outcome differences in VV-ECMO patients with different types of viral pneumonitis. Although the patients had similar illness severity at baseline, COVID-19 patients were initiated on ECMO much later following

Table 1. Baseline characteristics of patients with coronavirus disease 2019 (COVID-19) or other viral pneumonitis receiving extracorporeal membrane oxygenation (ECMO)

	Overall	COVID-19	Viral pneumonitis	P
Total number of patients	36	13	23	
Age, years, median (IQR)	50 (37–60)	58 (56–66)	44 (33–54)	0.005
Sex, female	10 (27.8%)	5 (38.5%)	5 (21.7%)	0.440
APACHE IV, median (IQR)	47 (33–84)	40 (15–64)	48 (36–86)	0.277
SOFA, median (IQR)				
Total	9 (6–12)	7 (5–10)	9 (8–12)	0.393
Respiratory	4 (4–4)	3 (3–4)	4 (4–4)	0.001
Coagulation	0 (0–1)	0 (0–0)	0 (0–1)	0.524
Liver	0 (0–0)	0 (0–0)	0 (0–1)	0.568
Cardiovascular	3 (1–4)	2 (1–4)	3 (2–4)	0.350
Renal	1 (0–2)	0 (0–1)	1 (0–2)	0.135
Days between ICU admission and ECMO start, median (IQR)	5.2 (0.9–11.5)	13.6 (7.4–16.8)	1.8 (0.3–6.1)	0.001
Days between intubation and ECMO start, median (IQR)	3.3 (0.4–7.3)	7.4 (3.3–14.0)	0.7 (0.2–4.6)	0.006
Type of support				0.361
VA-ECMO	1 (2.8%)	1 (7.7%)	0 (0.0%)	
VV-ECMO	35 (97.2%)	12 (92.3%)	23 (100.0%)	
Body mass index, kg/m ² , median (IQR)	29.9 (25.7–34.3)	27.5 (23.9–32.7)	30.4 (26.2–35.6)	0.246
Charlson Comorbidity Score, median (IQR)	1 (0–2)	2 (2–3)	0 (0–1)	0.002
Comorbidities				
Heart failure	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
Chronic obstructive pulmonary disease	1 (2.8%)	0 (0.0%)	1 (4.3%)	0.999
Diabetes	5 (13.9%)	4 (30.8%)	1 (4.3%)	0.047
Chronic kidney disease	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
Cancer	1 (2.8%)	1 (7.7%)	0 (0.0%)	0.361
Metastatic cancer	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
Leukaemia	1 (2.8%)	1 (7.7%)	0 (0.0%)	0.361
Lymphoma	1 (2.8%)	0 (0.0%)	1 (4.3%)	0.999
Clinical frailty score, median (IQR)	3 (2–3)	3 (3–3)	2 (2–3)	0.057
Support before ECMO				
Invasive ventilation	36 (100.0%)	13 (100.0%)	23 (100.0%)	–
Prone positioning	8 (22.2%)	1 (7.7%)	7 (30.4%)	0.213
Recruitment manoeuvre	5 (16.7%)	1 (11.1%)	4 (19.0%)	0.999
Neuromuscular blocking agents	17 (48.6%)	5 (41.7%)	12 (52.2%)	0.725
Norepinephrine	27 (77.1%)	10 (83.3%)	17 (73.9%)	0.685
Renal replacement therapy	6 (17.1%)	2 (16.7%)	4 (17.4%)	0.999
Vital signs before ECMO, median (IQR)				
Temperature, °C	36.9 (36.4–37.6)	36.8 (36.3–37.4)	37.0 (36.4–37.6)	0.495
Heart rate, beats/min	96.0 (87.0–110.5)	95.5 (89.5–106.5)	100.0 (85.0–116.5)	0.626
Mean arterial pressure, mmHg	76.0 (69.0–82.5)	81.0 (77.5–85.8)	73.0 (68.0–81.5)	0.081
SpO ₂ , %	91.5 (87.2–95.8)	91.0 (87.5–95.2)	92.0 (87.2–95.8)	0.610
Ventilatory variables before ECMO, median (IQR)				
Tidal volume, mL/kg PBW	5.3 (4.0–6.5)	5.1 (4.6–5.9)	5.6 (3.8–6.5)	0.958
Peak pressure, cmH ₂ O	29.0 (24.0–35.0)	27.5 (23.5–31.0)	31.0 (25.0–36.0)	0.209
PEEP, cmH ₂ O	12.0 (10.0–15.0)	12.0 (10.0–15.0)	12.0 (10.0–15.0)	0.880
Total respiratory rate, breaths/min	22.0 (16.5–26.0)	26.0 (23.0–30.0)	20.0 (12.0–23.0)	0.004
Driving pressure, cmH ₂ O	16.0 (10.0–24.0)	15.0 (11.0–19.5)	19.0 (10.0–24.0)	0.274
FiO ₂ , %	100.0 (80.0–100.0)	100.0 (80.0–100.0)	100.0 (85.0–100.0)	0.970

(Continues)

Table 1. Baseline characteristics of patients with coronavirus disease 2019 (COVID-19) or other viral pneumonitis receiving extracorporeal membrane oxygenation (ECMO) (continued)

	Overall	COVID-19	Viral pneumonitis	P
Laboratory tests before ECMO, median (IQR)				
pH	7.24 (7.13–7.34)	7.28 (7.20–7.34)	7.20 (7.12–7.34)	0.358
PaO ₂ :FiO ₂	83.0 (67.0–115.0)	87.9 (67.0–108.3)	83.0 (67.0–118.0)	0.808
PaCO ₂ , mmHg	67.0 (52.0–76.0)	70.5 (55.7–76.0)	66.0 (52.0–75.0)	0.640
Lactate, mmol/L	1.3 (0.9–1.7)	1.6 (1.2–1.7)	1.2 (0.9–1.7)	0.301
Hospital outcomes				
Complications during ECMO				
▶ Renal replacement therapy	23 (65.7%)	8 (61.5%)	15 (68.2%)	0.726
▶ Pneumothorax	3 (8.3%)	2 (15.4%)	1 (4.3%)	0.539
▶ Cardiac arrest	3 (8.3%)	0 (0.0%)	3 (13.0%)	0.288
▶ Major bleeding	8 (22.2%)	5 (38.5%)	3 (13.0%)	0.107
▶ Pulmonary embolism	1 (2.8%)	1 (7.7%)	0 (0.0%)	0.361
▶ CNS diffuse ischaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
▶ CNS bleeding	2 (5.6%)	0 (0.0%)	2 (8.7%)	0.525
▶ Lung infection	17 (47.2%)	5 (38.5%)	12 (52.2%)	0.502
▶ Thrombosis of ECMO circuit	1 (2.8%)	0 (0.0%)	1 (4.3%)	0.999
▶ Thrombosis of ECMO filter	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
Duration of ECMO, days, median (IQR)	9.8 (6.7–15.8)	14.8 (8.3–23.4)	9.1 (7.0–12.7)	0.301
Duration of ventilation, days, median (IQR)	18.8 (13.3–46.0)	31.2 (17.1–54.0)	16.7 (10.1–31.0)	0.043
ICU length of stay, days, median (IQR)	30.4 (19.5–50.1)	48.0 (33.0–106.1)	23.8 (15.8–35.0)	0.004
▶ In survivors, days, median (IQR)	34.6 (24.2–56.3)	49.9 (41.8–123.9)	27.0 (18.9–35.0)	0.008
Hospital length of stay, days, median (IQR)	40.5 (23.7–59.2)	57.2 (48.9–143.9)	30.7 (19.0–46.1)	0.005
▶ In survivors, days, median (IQR)	49.0 (32.1–78.2)	66.6 (55.0–169.9)	36.1 (21.2–46.1)	0.006
▶ ICU mortality	11 (31.4%)	3 (23.1%)	8 (36.4%)	0.478
▶ Hospital mortality	11 (32.4%)	3 (23.1%)	8 (38.1%)	0.465
▶ 180-day mortality	11 (33.3%)	3 (25.0%)	8 (38.1%)	0.703
Long term outcomes at 6 months				
WHODAS score, %, median (IQR)	22.9 (4.2–50.0)	32.3 (8.3–56.2)	22.9 (3.1–42.7)	0.392
▶ Disability	8 (47.1%)	3 (50.0%)	5 (45.5%)	0.999
▶ New disability	8 (61.5%)	4 (66.7%)	4 (57.1%)	0.999
EQ-5D-5L utility score, median (IQR)	0.8 (0.4–0.8)	0.6 (0.3–0.8)	0.8 (0.7–0.9)	0.339

APACHE = Acute Physiology and Chronic Health Evaluation; CNS = central nervous system; EQ-5D-5L = Five-level EuroQol five dimensions questionnaire; FiO₂ = fraction of inspired oxygen; ICU = intensive care unit; IQR = interquartile range; PaCO₂ = arterial partial pressure of carbon dioxide; PaO₂ = arterial partial pressure of oxygen; PEEP = positive end-expiratory pressure; PBW = predicted body weight; SOFA = Sequential Organ Failure Assessment; SpO₂ = oxygen saturation measured by pulse oximetry; VA-ECMO = veno-arterial extracorporeal membrane oxygenation; VV-ECMO = venovenous extracorporeal membrane oxygenation; WHODAS = World Health Organization Disability Assessment Schedule.

intubation. Traditionally, VV-ECMO outcomes have been worse for this late initiation group,² and recent COVID-19 Extracorporeal Life Support Organization (ELSO) guidelines suggest late (> 7 days mechanical ventilation) initiation is a relative contraindication.³ However, we found that 6-month mortality and disability were comparable for COVID-19 and viral pneumonitis patients, and compared favourably with other recently published data,⁴ suggesting that acceptable survival can occur in this late initiation group. In contrast, ECMO duration, ICU and hospital length of stay were longer with COVID-19, which may have significant resource implications during the COVID-19 pandemic and in periods

of ICU strain. The findings of this study are preliminary, with small patient numbers and relatively few patients who were prone, and reflect a health care system that was not overwhelmed.

In conclusion, our data show that 6-month survival, disability, and quality of life for COVID-19 were similar to other viral pneumonitis, despite ECMO being initiated much later. However, the prolonged length of stay for these patients may have significant resource implications. These findings require further validation in larger datasets.

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Competing interests

All authors declare that they do not have any potential conflict of interest in relation to this manuscript.

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