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Veno-venous Extracorporeal Membrane Oxygenation in Coronavirus Disease 2019: A Case Series

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Take home message: VV-ECMO, when offered to COVID-19 patients in refractory respiratory failure, can be associated with favourable outcomes. We present a detailed case series of 43 COVID-19 patients requiring VV-ECMO from a UK centre. 67.4% survived to hospital discharge.

ABSTRACT

Rationale: The use of veno-venous extracorporeal membrane oxygenation (VV-ECMO) in severe hypoxaemic respiratory failure from Coronavirus disease 2019

(COVID-19) has been described, but reported utilisation and outcomes are variable, and detailed information on patient characteristics is lacking. We aim to report clinical characteristics, management, and outcomes of COVID-19 patients requiring VV-ECMO, admitted over two months to a high-volume UK centre.

Methods: Patient information, including baseline characteristics and clinical parameters, was collected retrospectively from electronic health records for COVID-19 VV-ECMO admissions between 3rd March and 2nd May 2020. Clinical management is described. Data are reported for survivors and non-survivors.

Results: We describe 43 consecutive patients with COVID-19 who received VV-ECMO. Median age was 46 years [IQR 35.5 - 52.5], 76.7% were male. Median time from symptom onset to VV-ECMO was 14 days [IQR 11 - 17.5]. All patients underwent computed tomography imaging, finding extensive pulmonary consolidation in 95.3%, and pulmonary embolus in 27.9%. 79.1% received immunomodulation with methylprednisolone for persistent maladaptive hyperinflammatory state. Vasopressors were used in 86%, and 44.2% received renal replacement therapy. Median duration on VV-ECMO was 13 days [IQR 8 - 20]. Fourteen patients died (32.6%) and 29 survived (67.4%) to hospital discharge. Non-survivors had significantly higher d-dimer (38.2 vs 9.5mg/L, Fibrinogen Equivalent Units; p = 0.035) and creatinine (169 vs 73umol/L; p=0.022) at commencement of ECMO.

Conclusions: Our data supports the use of VV-ECMO in selected COVID-19 patients. The cohort was characterised by high degree of alveolar consolidation, systemic inflammation, and intravascular thrombosis.

Abstract word count: 246

Indexing terms: COVID-19, extracorporeal membrane oxygenation (ECMO), severe respiratory failure, hyperinflammation, thrombosis

INTRODUCTION

A significant cohort of patients with Coronavirus disease 2019 (COVID-19) go on to develop severe respiratory failure, requiring critical care admission. Reports have described the use of veno-venous extracorporeal membrane oxygenation (VV-

ECMO) in a subset of critically ill patients, with utilisation ranging from 11% to 32% (1–3). VV-ECMO is indicated for patients with potentially reversible, refractory, life-threatening hypoxaemia or hypercapnia, or in patients where acceptable oxygenation or decarboxylation can be obtained only with injurious ventilatory settings. While VV-ECMO was associated with improved outcome during the H1N1 influenza pandemic(4, 5), COVID-19 demonstrates features unique from other respiratory infections and early case-series have reported high mortality in patients on ECMO(6–8).

Given the lack of detailed information about patient characteristics and their clinical course, balanced with the need for judicious use of resources in the context of a pandemic, it is important to understand the role of VV-ECMO in COVID-19. We aim to describe, in detail, the clinical characteristics, management and outcomes of COVID-19 VV-ECMO patients from a high-volume UK ECMO centre, over a two-month period of the pandemic.

METHODS

Case Selection

All COVID-19 patients admitted for VV-ECMO to Guy's and St Thomas' NHS Foundation Trust (GSTFT) in London, over a two-month period (3rd March 2020 to 2nd May 2020) covering the peak of the pandemic, are included. Suitability for VV-ECMO was assessed in line with UK national commissioning criteria(9), requiring a lung injury (Murray) score ≥3(10), or uncompensated hypercapnic acidosis with pH <7.2. National criteria were adapted for the COVID-19 pandemic on the 10th of April 2020(11) to include clinical frailty scale ≤3(12), the use of the Respiratory ECMO

Survival Prediction (RESP) score(13) to aid pre-ECMO decision-making (with RESP score ≤3 requiring agreement between at least two centres), and an exclusion of "refractory multi-organ failure". At the time of this series, detection of SARS-CoV-2 RNA on nose and throat swabs or bronchoalveolar lavage (BAL) using multiplexed-tandem polymerase chain reaction technology for detection of 2 gene targets, ORF 1a and ORF 8 (AusDiagnostics, Mascot, Australia), remained gold standard. All patients, at point of referral, had either laboratory confirmed or clinically suspected COVID-19 pneumonia; four patients without a positive result at time of referral subsequently tested positive from admission samples at GSTFT.

Patient Clinical Pathway

GSTFT is a national VV-ECMO centre commissioned to provide regional ECMO retrieval and provision(9). At the start of the pandemic, GSTFT ECMO capacity was doubled through adaptation of each bedspace to accommodate two patients on ECMO. Patients were retrieved from referring hospitals via a previously described standard pathway(14), with no deviation in practice aside from use of recommended personal protective equipment. Standard GSTFT practice is bifemoral percutaneous cannulation at the referring hospital, and use of Maquet Cardiohelp (Maquet, Rastatt, Germany) consoles. Following retrieval, all patients underwent computed tomography (CT) imaging of head, thorax (including CT pulmonary angiogram), abdomen and pelvis. Lung recruitment CT imaging at ventilator pressures of 5 cmH_2O and 45 cmH_2O were performed, unless pneumothorax was detected on initial scan or pulmonary air leak was suspected, to assess lung recruitment potential and delineate underlying lung parenchyma(15). Diagnostic bronchoscopy and BAL for bacterial culture, viral and SARS-CoV-2 PCR was performed on all patients within

the first 24 hours. Patients without haemorrhagic complications were anticoagulated with unfractionated heparin infusion, targeting anti-Xa levels (0.3-0.7 UI/mL).

Patients were ventilated with protective lung parameters. Mechanical ventilation was generally initiated using standardised settings: PEEP 10-15 cmH_2O, tidal volume 2-4 ml/kg of predicted body weight provided that driving pressure (plateau minus PEEP total) could be kept at 10 cmH_2O, and plateau pressure < 25 cmH_2O. Initial respiratory rate was generally maintained at 10 breaths/minute to limit overall mechanical power(15). In patients with high potential for lung recruitment – as demonstrated on low/high pressure CT imaging – higher PEEP (near 15 cmH_2O) or TCAV (time-controlled adaptive ventilation) was used, with mean airway pressures of 23-26 cmH_2O depending on body mass index and small airway closures (following assessment of a low-flow pressure-volume loop). Fraction of inspired oxygen (FiO2) on the ventilator was kept at 30-40%, and ECMO support titrated to achieve PaO_2 > 60mmHg and pH 7.35-7.40.

Patients received a course of broad-spectrum antibiotics on arrival, targeted to known microbiology where possible. A subset of patients with failure to progress and signs of a sustained hyperinflammatory state (fevers, persistently elevated C-reactive protein and/or ferritin, sustained organ dysfunction and hypoxaemia), in the absence of untreated active infection (bacteria or fungal species detected on blood culture and BAL, low procalcitonin and galactomannan), were treated with low dose methylprednisolone regimens of 1-2mg/kg/day for 5-7 days, with halving in dose every 5-7 days, similar to published protocol (16). This dosing regimen was chosen for its relative safety profile(17, 18). Patients with persistent hyperinflammatory disease behaviour despite corticosteroids, or those with an “H score” greater than

169 suggesting secondary haemophagocytic lymphohistiocytosis (19, 20) were considered for treatment with the IL-1 receptor antagonist anakinra(21, 22). Patients with persistent hypoxaemia and radiological abnormality despite low dose corticosteroids, or patients who demonstrated early fibrosis on CT, were treated with high dose “pulsed” methylprednisolone at doses of 1g for 3 days, followed by 1mg/kg per day, followed by a weaning regimen. Treatments were given in consultation with local lung inflammation specialists.

Patients generally remained paralysed for an initial 24 hours, particularly if strong inspiratory efforts persisted despite adequate sedation, or if asynchronies due to deep sedation were noted (e.g. reverse triggering). Daily sedation wean was then undertaken in stable patients to maximise wakefulness. A specialist physiotherapy team assessed patients on a daily basis for both secretion clearance, and early rehabilitation. Ventilation weaning was based on daily assessment of lung mechanics, as well as ability to spontaneously ventilate without injurious tidal volumes, respiratory rate and inspiratory effort (including measurements of P0.1 – 100ms airway occlusion pressure), that might contribute to patient self-inflicted lung injury (P-SILI). Criteria for decannulation from VV-ECMO in this cohort included maintained fractional inspired oxygen < 0.5 and non-injurious ventilatory effort, with ECMO sweep gas turned off for at least 24 hours. The full protocol of weaning from VV-ECMO is described and available(23).

Data Collection and Analysis

Data was collected retrospectively from electronic records, including the IntelliVue Clinical Information Portfolio (Phillips, Eindhoven, The Netherlands). Pre-ECMO data were obtained from ECMO referral systems(24), paper records, or direct interview with members of retrieval teams. RESP score was calculated at the time of referral.

Sequential Organ Failure Assessment score was calculated from pre-ECMO clinical parameters, day 0 ECMO laboratory results, with Glasgow Coma Scale presumed to be 15 unless deranged consciousness pre-intubation was confirmed. Data were collected until all patients had reached either death (non-survivors) or discharge from hospital (survivors). Quantitative variables are presented with median and interquartile range (IQR), and categorical variables are presented as frequencies and percentages. Missing data were not imputed and are recognised in tables by adjusted n-values. Comparison on non-parametric continuous variables used Mann-Whitney U tests with significance at $p<0.05$ (Python: package *SciPy v1.4.1*). The study had institutional approval and waiver of individual informed consent (reference number: 10796), qualifying as service evaluation defined by the UK NHS Health Research Authority (http://www.hra.nhs.uk).

RESULTS

Demographic and Pre-ECMO Characteristics

Forty-three patients with COVID-19 were accepted and admitted for VV-ECMO based on the listed criteria, out of 215 patients referred to GSTFT during the study period. Patient characteristics are shown in *table 1*. Median age was 46 years [IQR 35.5 - 52.5], ranging from 26 to 66. Most patients were male (33, 76.7%), 28 (65.1%) patients came from a Black, Asian and Minority Ethnic background and (21, 48.8%) were obese. Refractory and life-threatening hypoxia was an indication for VV-ECMO in all: median partial pressure of oxygen to fraction of inspired oxygen ratio (PaO_2/FiO_2) was 67.5mmHg [IQR 58.9 – 77.8] at referral. Eleven (25.6%) patients additionally had uncompensated respiratory acidosis with pH <7.20. Median static

compliance was 30 mL/cmH_2O [IQR 21.5 - 33.6] in 24 patients with sufficient data for the calculation. Airway pressure release ventilation (APRV) was used widely pre-ECMO (24 patients, 55.8%). Forty (93%) patients had undergone prone positioning prior to ECMO, and all patients had received neuromuscular blockade. Twenty-one (48.8%) patients received vasopressors at referral, and 3 (7%) required acute renal replacement therapy. Excluding one patient who acquired COVID-19 nosocomially, the median time from hospital admission to VV-ECMO was 7 [IQR 5 - 9] days. Median time from reported start of COVID-19 symptoms to VV-ECMO was 14 [IQR 11 - 18] days, and median from invasive ventilation to VV-ECMO was 5 days [2 – 6].

Clinical Diagnostics and Features

The majority of patients (41, 95.3%) had extensive pulmonary consolidation on CT in either all lobes (*figure 1a*), or in a dependent distribution (*figure 1b*) with minimal sparing. Nineteen patients underwent lung recruitment imaging, 17 (89.5%) showed at least moderate recruitability as assessed visually by a radiologist. Twelve (27.9%) patients had pulmonary embolism (PE), five involving at least one main pulmonary artery. Five (11.6%) additional patients demonstrated areas of pulmonary infarction without PE. Left ventricular (LV) impairment on admission echocardiography was rare, in one patient (2.3%) with mild-moderate impairment only. In six (14%) patients, right ventricular dysfunction was found concurrently with PE. Six (14%) patients had small foci of subarachnoid haemorrhage on CT head, 2 of which demonstrated local mass effect. Three (7%) patients had ischaemic infarction. Patients on day 0 of VV-ECMO had severe lymphopenia (median 0.6 x 10^9/L [IQR 0.5 - 1.1]), elevated neutrophil:lymphocyte ratio (median 12.8 [IQR 9.2 – 22.5]), and high C-reactive protein (median 326 mg/L [IQR 245 - 368]), ferritin (median 1907 ug/L [IQR 1153 -

4083]), and d-dimer (median 11.7 mg/L Fibrinogen Equivalent Units [IQR 6.4 - 41.7]. Acute kidney injury (creatinine ≥105umol/L) was a common feature (21 patients, 48.8%). Data is shown in *table 2*.

ECMO Course and Outcomes

Twenty-nine patients (67.4%) were successfully decannulated from VV-ECMO and survived until hospital discharge. Twelve (27.9%) patients died on ECMO, and two (4.7%) died following decannulation. Causes of death and complications are summarised in *table 3*. Median days on ECMO was 14 [IQR 8 – 21] for survivors. Non-survivors had significantly greater procalcitonin (6.30 vs 1.24ng/ml; p = 0.028), d-dimer (38.2 vs 9.5mg/L Fibrinogen Equivalent Units; p = 0.035) and creatinine (169 vs 73umol/L; p = 0.022) at admission. Common complications were haemorrhage requiring ≥1 packed red blood cell transfusion (8, 18.6%) including two bleeds after tracheostomy and two spontaneous retroperitoneal haemorrhages (one leading to death), and tension pneumothorax (5, 11.6%) that contributed to mortality in three patients. One patient developed myocarditis, with cardiac tamponade resulting in death. Nineteen (44.2%) patients required renal replacement therapy and the majority (86%) required noradrenaline at moderate doses during ECMO (peak dose median 0.19mcg/kg/min [IQR 0.11 – 0.35]). Seventeen (39.5%) patients required at least one circuit change during their ECMO for membrane thrombosis; mean ECMO days per each circuit change (numerator as sum of all days on ECMO of entire cohort) was 29.6. In thirty-one patients decannulated from ECMO, seventeen (54.8%) demonstrated cannula-related peripheral venous thrombosis on Doppler imaging. The majority of patients (79.1%) received immunomodulation, typically

methylprednisolone at 1-2mg/kg/day although 9 (20.9%) received higher “pulsed” doses and 10 (23.3%) received anakinra.

Microbiology

During their period of ECMO support, 15 (34.9%) patients developed bacterial respiratory infection with *Klebsiella spp (aerogenes (6), oxytoca (1), and pneumoniae (8))*. In two patients this grew from BAL on day 0 of ECMO, whilst later infection was detected in thirteen. The most frequent fungal isolate was *Candida spp* (15 patients, 34.9%), all light or scanty growth from BAL. There were four significant bloodstream infections, two with *Klebsiella oxytoca*, one with *P. mirabilis,* and a persistent vancomycin resistant enterococcus secondary to a deep-seated focus (retroperitoneal haematoma). *Aspergillus fumigatus* grew from BAL in two patients, and two others developed Cytomegalovirus viraemia with IgG positivity.

DISCUSSION

The mortality described in this VV-ECMO series (14 of 43, 32.6%) is lower than in early descriptions. Patients exhibited particular characteristics including poor lung compliance, persistent hyperinflammation, and high incidence of thrombosis. Survival in this series is comparable to more recent data from the USA(25) and France(26). Since the study period, a further 13 patients have completed VV-ECMO at GSTFT, with overall survival to ICU discharge at 71.4%.

The pattern of disease seen in our cohort has been previous described. Exudative lung disease with poor compliance (as described by Gattinoni et al(27)), persistent hyperinflammation(28, 29), and increased thrombosis incidence may demonstrate a

particular phenotype that defines a later stage of the disease process. Median ferritin and d-dimer seen at ECMO initiation were comparable to values seen after two weeks in a cohort of non-surviving hospitalised patients(30). A majority of our patients were given immunomodulation(19) after risks of immunosuppressing critically ill patients(31) were weighed against lack of clinical progress and on-going inflammatory lung insult. Recent trial data showing benefits of dexamethasone in ventilated COVID-19 patients may support the wider use of steroids, although their role in patients on ECMO is unclear(32).

The incidence of PE (27.9%) was substantially higher than in pre-COVID-19 (9.6%) in the same centre(33), carrying substantial morbidity in our cohort with RV dysfunction in 50%. Cannula-related thrombosis rates (54.8%) were greater than baseline prevalence(34), and ECMO membrane complication rate was similarly high. Thrombosis risk is a known entity in severe COVID-19(35), but adjusted anticoagulation targets must be balanced against higher risk of haemorrhagic complication in ECMO(36), the cause of multiple complications and one death in our cohort.

At time of writing, no published literature specifically addresses secondary or co-infection in COVID-19 ECMO. These individuals may represent a distinct cohort microbiologically. The unusual predominance of *Klebsiella spp* has been seen elsewhere, as has *Candida spp*(37, 38), but remains a focus of further analysis in GSTFT regarding infection control consequences of doubling bedspace usage. Admission procalcitonin was elevated in all patients, but significantly greater procalcitonin in the non-survivor group may have limited earlier use of steroids.

Reactivation or flares of chronic viral infections including CMV must also be considered, especially in those receiving immunomodulation.

Following new commissioning criteria in the UK, the threshold for acceptance of patients onto VV-ECMO has been reinforced by the inclusion of the RESP score. This predictive score is validated in patients already on ECMO(13, 39), but not as a pre-ECMO decision tool. The RESP score was one component of a multi-tool assessment process when deciding which patients should be offered VV-ECMO, and cases with low RESP scores were discussed with a second centre if ECMO was felt to be indicated. Validation of this tool in the UK ECMO population may help guide future usage.

This series has the inherent limitations of a single-centre study, conducted in a well-resourced and experienced centre, during the early stages of our understanding in a new disease. It is likely that aspects of management will differ over time and between centres, as our understanding of how to treat particular phenotypes improves in any future pandemic waves.

This case series suggests that VV-ECMO, when offered to patients with COVID-19 respiratory failure refractory to conventional ventilatory management, can be associated with a favourable outcome. In COVID-19 patients with severe respiratory failure, early consultation with an ECMO centre and joint decision-making on suitable support modality is a key strategy.

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APPENDIX (TABLES AND FIGURES)

Table 1: baseline and pre-ECMO characteristics

	Survivors (n=29)	Non-survivors (n=14)	Total (n=43)
Age* (median [IQR])	45 [35 – 49]	52.5 [43.8 – 53]	46 [35.5-52.5]
Sex (n (%))			
- Female	9 (31.0)	1 (7.1)	10 (23.3)
- Male	20 (69.0)	13 (92.9)	33 (76.7)
BMI† (median [IQR])	29 [28 – 34]	31 [26 – 34]	29 [27 – 34]
Ethnicity (ISARIC) (n (%))			
- White	9 (31.0)	6 (42.9)	15 (34.9)
- Black	7 (24.1)	3 (21.4)	10 (23.3)
- South Asian	11 (37.9)	2 (14.3)	13 (30.2)
- East Asian	2 (6.9)	2 (14.3)	4 (9.3)
- Mixed	0 (0)	1 (7.1)	1 (2.3)
Comorbidity (n (%))			
- Obesity‡	14 (48.3)	7 (50.0)	21 (48.8)
- Hypertension	5 (17.2)	5 (35.7)	10 (23.3)
- Diabetes	2¥¥ (6.9)	6¥¥ (42.9)	8 (18.6)
- Asthma	2 (6.9)	3 (21.4)	5 (11.6)
Cardiac arrest (n (%))	0 (0)	1 (7.1)	1 (2.3)
RESP score§ (median [IQR])	4 [3 – 5]	3 [3 – 5]	4 [3 – 5]
PaO_2/FiO_2‖ (median [IQR])	67.5 [61.6 – 77.6]	61.5 [53.7 – 79.5] (n=13)	67.5 [58.9 – 77.8] (n=42)
pH (median [IQR])	7.34 [7.23 – 7.39] (n=28)	7.25 [7.17 – 7.30] (n=13)	7.30 [7.19 – 7.36] (n=41)
$PaCO_2$** (median [IQR])	66.5 [52.5.0 – 70.5]	69.8 [60.3 – 78.4]	67.5 [53.1 – 75.8]
Ventilation days before ECMO (median [IQR])	5 [2 – 6]	4 [1 – 6]	5 [2 – 6]
SOFA score†† (median [IQR])	6 [4 – 8]	9 [6 – 12]	7 [4 – 10]

**Age in years*; †*BMI = body mass index;* ‡*Obesity defined as BMI ≥ 30;* §*RESP score = Respiratory ECMO Survival Prediction score;* ‖PaO_2/FiO_2*= partial pressure of oxygen to fraction of inspired*

*oxygen ratio in mmHg at point of referral; **$PaCO_2$ in mmHg; ††SOFA score = Sequential Organ Failure Assessment score; ¥¥p-value <0.01;*

Table 2: ECMO admission investigation findings

	Survivors (n=29)	Non-survivors (n=14)	Total (n=43)
CT Thorax* (n (%))			
- Alveolar consolidation	29 (100)	14 (100)	43 (100)
- Ground glass opacities	29 (100)	14 (100)	43 (100)
- Pneumothorax	3 (10.3)	2 (14.3)	5 (11.6)
- Pneumomediastinum	4 (13.8)	4 (28.6)	8 (18.6)
- Pulmonary embolism	7 (24.1)	5 (35.7)	12 (27.9)
Echocardiogram (n (%))			
- Left ventricular impairment	1 (3.4)	0 (0)	1 (2.3)
- Right ventricular impairment	3¥ (10.3)	5¥ (35.7)	8 (18.6)
CT Head (n (%))			
- Subarachnoid haemorrhage	3 (10.3)	3 (21.4)	6 (14.0)
- With sulcal effacement	0¥ (0)	2¥ (14.3)	2 (4.7)
- Subdural haemorrhage	1 (3.4)	0 (0)	1 (2.3)
- Ischaemic infarction	0¥¥ (0)	3¥¥ (21.4)	3 (7.0)
Laboratory values† (median [IQR])			
- Haemoglobin	99 [92 – 102]	95 [86 – 107]	97 [89 – 106]
- Lymphocyte count	0.8 [0.5 – 1.3]	0.6 [0.4 – 0.8]	0.6 [0.5 – 1.1]
- Neutrophil:Lymphocyte ratio	11.2 [9.2 – 19.3]	17.8 [12.1 – 24.2]	12.8 [9.2 – 22.5]
- Platelet count	247 [203 – 344]	214 [121 – 329]	245 [163 – 339]
- Creatinine	73¥ [53 – 192]	169¥ [98 – 347]	96 [66 – 237]
- Bilirubin	16 [9 – 22]	15 [12 – 20]	15 [11 – 22]
- Ferritin	1903 [904 – 3800]	2251[1308 – 5435]	1907 [1153 – 4083]
- C-reactive Protein	291 [217 – 388]	344 [328 – 361]	326 [245 – 368]
- Procalcitonin	1.24¥ [0.76 – 6.43] (n=28)	6.3¥ [2.99 – 16.27]	3.96 [1.15 – 9.01] (n=42)
- D-dimer	9.5¥ [5.2 – 31.7]	38.2¥ [10.9 – 60.5]	11.7 [6.4 – 41.7]
- Troponin	26 [16 – 40] (n=24)	98 [25 – 132] (n=7)	28 [15 – 70] (n=31)

**CT = computed tomography; †Units for laboratory values: Haemoglobin in g/dl, lymphocyte count in 10^9/L, platelet count per microlitre, creatinine/bilirubin umol/L, ferritin in ug/L, C-reactive protein in mg/L, procalcitonin in ng/mL, d-dimer in mg/L Fibrinogen Equivalent Units, and troponin in ng/L, ¥p-value 0.01-0.05; ¥¥p-value <0.01;*

Table 3: Time course, causes of death, and complications on ECMO

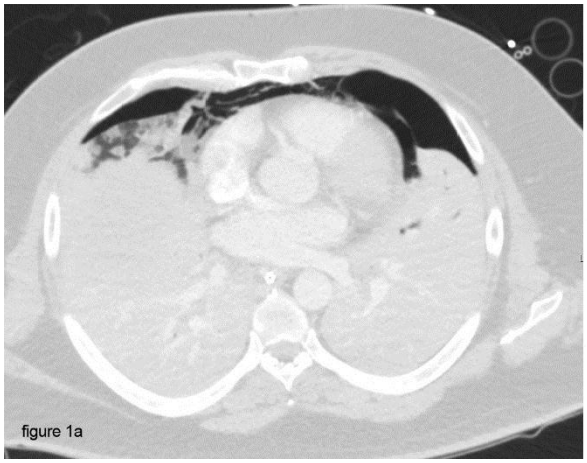
	Survivors (n=29)	Non-survivors (n=14)	Total (n=43)
Days on ECMO (median [IQR])	14 [8 – 21]	12.5 [5.75 – 18]	13 [8 – 20]
Causes of death (n (%))			
- On ECMO		6 (42.9)	
- Full active treatment*	-	2 (33.3)	-
- Limits of care	-	4 (66.7)	-
- Withdrawal of ECMO	-	6 (42.9)	-
- Progression of ICH† with brainstem herniation	-	1 (16.7)	-
- Extensive cerebral infarction and multi-organ failure	-	2 (33.3)	-
- Poor respiratory prognosis and multi-organ failure	-	3 (50.0)	-
- Post-ECMO	-	2 (14.3)	-
- Progression of extensive cerebral infarction and multi-organ failure	-	1 (50.0)	-
- Refractory respiratory failure with severe fibrotic lung disease	-	1 (50.0)	-
Complications on ECMO (n (%))			
- Bleeding leading to transfusion	4 (13.8)	1 (7.1)	5 (11.6)
- Bleeding leading to transfusion and intervention	3 (10.3)	0 (0)	3 (7.0)
- Bacteraemia	3 (10.3)	1 (7.1)	4 (9.3)
- Tension pneumothorax	2 (6.9)	3 (21.4)	5 (11.6)
- Myocarditis and cardiac tamponade	0 (0)	1 (7.1)	1 (2.3)

**Causes of deaths on ECMO: 1) spontaneous retroperitoneal haemorrhage 2) myocarditis with cardiac tamponade; †ICH = intracerebral haemorrhage.*

Table 4: Organ support, therapeutics, other interventions

	Survivors (n=29)	Non-survivors (n=14)	Total (n=43)
Organ support (n (%))			
- Noradrenaline	23 (79.3)	14 (100)	37 (86.0)
- Peak dose (median [IQR])	0.15 [0.09 – 0.32]	0.23 [0.18 - 0.41]	0.19 [0.11 – 0.35]
- Milrinone	4 (13.8)	5 (35.7)	9 (20.9)
- Renal replacement therapy	11 (37.9)	8 (57.1)	19 (44.2)
- Persisting requirement at step-down	6 (20.7)	-	-
Immunomodulation (n (%))	25 (86.2)	9 (64.3)	34 (79.1)
- Methylprednisolone 1-2mg/kg	24 (82.8)	8 (57.1)	32 (74.4)
- Anakinra	7 (24.1)	3 (21.4)	10 (23.3)
- Methylprednisolone 1g “pulsed”	5 (17.2)	4 (28.6)	9 (20.9)
- Hydrocortisone	1 (3.4)	0 (0)	0 (0)
Pharmacological intervention (n (%))			
- Remdesivir	4 (13.8)	0 (0)	0 (0)
- Hydroxychloroquine	2 (6.9)	0 (0)	0 (0)
ECMO circuit change (n (%))	11 (37.9)	6 (42.9)	17 (39.5)
- ECMO days per circuit change (mean)	33	29	30
Tracheostomy (n (%))	20[¥] (69.0)	5[¥] (35.7)	25 (58.1)
Post-decannulation lower limb DVT (n (%))	16 (55.2)	1 (50.0) (n=2)	17 (54.8) (n=31)
- Occlusive thrombus	1 (6.3)	0 (0)	1 (3.2)
- Non-occlusive thrombus	12 (75.0)	1 (100)	13 (41.9)
- Mural thrombus only	3 (18.8)	0 (0)	3 (9.7)

[¥]*p-value 0.01-0.05*



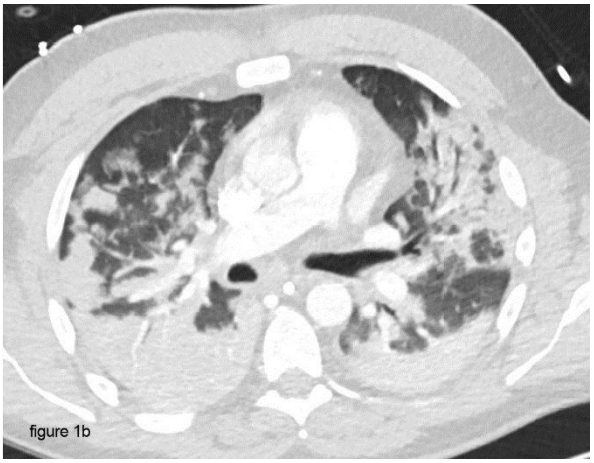


Figure 1a - Almost completely consolidated lungs, with minor sparing at the right middle lobe periphery where there is scattered ground glass. Bilateral small pneumothoraces and moderate pneumomediastinum.

Figure 1b – Dense consolidation involving most of the lower lobes, further areas of consolidation seen in all other lobes in a patchy distribution, with ground glass opacification.