Extracorporeal membrane oxygenation in South Africa: Experience from a single centre in the private sector

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Background. Extracorporeal membrane oxygenation (ECMO) is an advanced, resource-intensive technology used in a limited capacity in South Africa (SA). Minimal data on the use of ECMO in SA are available.
Objectives. To describe the indications, early outcome and comorbidities of patients placed on ECMO in the highest-volume ECMO centre in SA.
Methods. We performed a single-centre retrospective review of all adult patients supported with any form of ECMO from August 2016 to December 2018. Operative and clinical records were reviewed. The primary objective of this study was to review the outcome of patients placed on ECMO in the form of survival to hospital discharge. The secondary objectives were to identify population-specific comorbidities and indications for ECMO that could be associated with non-survival and to compare outcome with known risk scores in the form of the Respiratory ECMO Survival Prediction (RESP) and Survival After Venoarterial ECMO (SAVE) scores.
Results. One hundred and seven patients were identified. The primary indication for ECMO was respiratory support in 78 patients and cardiac support in 29 patients. Forty-seven patients were discharged from hospital, with a 44.0% overall survival rate. Gender (p=0.039), age (p=0.019) and hypertension (p=0.022) were associated with death in univariate logistic regression analysis. However, after adjusting for potential confounding in multivariate logistic regression analysis, the association was no longer significant. In the all respiratory support group, patients in risk class IV had better than predicted survival according to the RESP score, while risk classes I, II and III had worse than predicted survival. In the circulatory support group, all risk classes had worse than predicted survival according to the SAVE score.
Conclusion. We report ECMO outcomes in SA for the first time. We identified very high mortality rates for patients transferred on ECMO from other facilities and for patients converted from venovenous ECMO to venoarterial ECMO. Although our outcomes were comparable in some of the risk classes, further external validation of the SAVE and RESP scores will be needed to compare our outcomes with these scores.
Keywords. Extracorporeal membrane oxygenation, ECMO, venovenous ECMO, venoarterial ECMO, ECMO indications, ECMO outcomes, lung transplant, circulatory support.

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Study synopsis
What the study adds. We report on extracorporeal membrane oxygenation (ECMO) outcomes in South Africa for the first time. We identified a high mortality rate in patients transferred on ECMO from other facilities, and in patients converted from venovenous ECMO to venoarterial ECMO.
Implications of the findings. Transferred patients had a high mortality rate. The reason for this should be further investigated and may highlight the need for possible protocols to assist with appropriate timing of patient transfers and possible earlier intervention or transfer.

Extracorporeal membrane oxygenation (ECMO), also known as extracorporeal life support (ECLS), is a mechanical support system used in patients with inadequate oxygenation, ventilation or perfusion. ECMO may be used to provide physiological support until recovery of the failing organ or as a bridge to definitive treatment.

There are two major types of ECMO: venovenous (VV-ECMO) and venoarterial (VA-ECMO). In VV-ECMO, only venous access is needed and mainly respiratory support is provided, while both venous and arterial access are required in VA-ECMO in order to facilitate both gas exchange and mechanical cardiac output support.[1]

ECMO technology has advanced considerably in recent times, with circuits becoming smaller and safer. With these advances, ECMO use worldwide has seen a marked increase.[2,3] While ECMO is commonly used in most developed countries, its use in the developing world is

extremely limited owing to its high cost and a scarcity of dedicated ECMO intensive care units (ICUs) with the highly specialised and skilled staff needed to care for the patients.

South Africa (SA) currently only has three Extracorporeal Life Support Organization (ELSO)-registered centres that provide ECMO for adults. Only one of the centres provides care to the public sector.

With advances in ECMO technology, the indications for ECMO are also expanding. Some of the indications are hypoxaemic respiratory failure with a mortality risk >50%, hypercapnic respiratory failure with a pH <7.2, bridge to transplantation, refractory cardiogenic shock, massive pulmonary embolism, and failure to wean from cardiopulmonary bypass after cardiac surgery.[3-6]

Although ECMO is certainly lifesaving in some patients, it is an invasive treatment option with a significant potential for complications. The need to predict which patients would benefit from this resource-intensive technology has given rise to multiple risk prediction scores in the ELSO literature. The Respiratory ECMO Survival Prediction (RESP) and Survival After Venoarterial ECMO (SAVE) scores are two of the most frequently used.[7,8] Risk models use multiple variables, are sometimes diagnosis specific, and need to be externally validated to assess their accuracy in different cohorts.[9,10]

We present the experience of an ELSO-registered ECMO centre in SA.

Methods

A retrospective review was conducted of all patients who underwent any form of ECMO at Netcare Milpark Hospital in Johannesburg from August 2016 to December 2018. The study was approved by the Research Operations Committee of Stellenbosch University (ref. no. UNIV-2019-0004). Informed consent for individual patients was waived. The primary objective of the study was to review our outcomes with ECMO in the form of survival to hospital discharge. The secondary objectives were to identify population-specific comorbidities and indications for ECMO that could be related to mortality and to compare our outcomes with known risk scores in the form of the RESP and SAVE scores.

All adult patients (≥18 years of age) who underwent ECMO, had hospital files available for review and were discharged or died before 31 December 2018 were included. The primary outcome was defined as death or discharge from hospital before 31 December 2018. The duration of ECMO treatment was calculated from the time of ECMO cannulation until decannulation or death. These data were also compared with data captured by the Milpark Cardiothoracic Centre. Other data collected included age, sex, days in the ICU, days on ventilator prior to ECMO placement, type of ECMO (VV or VA), indication for ECMO (respiratory failure or cardiogenic shock), injury type, surgery prior to ECMO placement, ECMO circuit changed or replaced, site of cannulation, whether tracheostomy was performed, whether patients were transferred on ECMO from another facility, and risk assessment in the form of a risk score.

To analyse our primary outcomes, the patients with respiratory failure were divided into an all respiratory support group and a respiratory support without lung transplant group. Patients with cardiogenic shock were divided into a circulatory support group and a circulatory support without cardiac transplant group.

To assess our secondary outcomes, patients were grouped into three categories according to the type of ECMO support received, namely VV-ECMO, VA-ECMO, or VV+VA-ECMO if changed from one type to another.

In patients with cardiogenic shock, the SAVE score was used, and for primarily adult respiratory failure, the RESP score was calculated.[7,8]

Statistical analysis

Descriptive data were presented as either means with standard deviations (SDs) for normal distribution or medians with interquartile ranges (IQRs) for skewed distribution. Data were analysed using Pearson's χ^2 test and Fisher's exact test. We tested associations between clinical characteristics using logistic regression analysis. We controlled for potential confounding using multivariate logistic regression analysis. We report the odds ratio as measures of association with the corresponding confidence intervals. Statistical significance was set at $p<0.05$.

Results

There were 107 patients in the study. Forty-three patients were transferred from other hospitals prior to ECMO placement at Milpark Hospital, and 6 patients were placed on ECMO at the referring hospital and retrieved on ECMO. The mean (SD) age of patients placed on ECMO was 47 (13.3) years. The mean age of ECMO survivors was lower than that of non-survivors (44 (13.8) v. 50 (12.4) years, respectively; $p=0.019$). The study population comprised slightly more male than female patients (53.3% male; $n=57$).

In the total group, the primary indication for ECMO placement was respiratory support in 78 patients and cardiac support in 29. VV-ECMO was initiated in 58 patients, 40 patients received VA-ECMO, and 9 patients received VV+VA-ECMO. Forty-seven patients were discharged from hospital, with a 44.0% overall survival rate. The patients on VA-ECMO and VV-ECMO had similar survival rates of 45.8% and 46.5%, respectively, while the VV+VA-ECMO group had a 22.2% survival rate. Four patients were changed from VV-ECMO to VA-ECMO, all of whom died ($p=0.13$).

A total of 60 patients died in hospital, 45 while still on ECMO. The median (IQR) duration of ECMO treatment was 8 (4 - 18) days, the median time in hospital was 33 (14 - 60) days, and the median time on ECMO after lung transplant was 4 (0 - 11) days. The longest duration of ECMO recorded was 83 days; unfortunately, this patient died. The longest duration of ECMO after which the patient was successfully discharged was 48 days, and the longest hospital stay with successful discharge was 197 days.

Sixty-three patients had surgery performed prior to ECMO placement. Bilateral sequential lung transplant and single-lung transplant were the most common procedures performed prior to ECMO placement, and accounted for 22 of the participants. A further breakdown of procedures performed is presented in Table 1. Indications for lung transplant were interstitial lung disease ($n=7$), cystic fibrosis ($n=3$), chronic obstructive pulmonary disease (COPD) ($n=4$), pulmonary arterial hypertension ($n=3$) and miscellaneous ($n=5$).

VV-ECMO was mostly established with a dual-lumen cannula. The most frequent site of cannulation in the VV-ECMO group was the right jugular vein (81.0% of cases), followed by the left jugular vein (13.7%) and the femoral vein (5.2%). Tracheostomy was performed in 42 of the patients.

A total of 24 different cardiopulmonary injury types leading to ECMO placement, or indications for placement, were identified in our study (Table 2). The main indications for ECMO support were after bilateral lung transplant (*n*=21), followed by bacterial and viral pneumonia (*n*=18 and 12, respectively). One patient was treated with extracorporeal cardiopulmonary resuscitation (ECPR), but died.

Age and sex were compared between survivors and non-survivors, and many comorbidities were identified and compared (Table 3). Non-survivors were older (49 years v. 43 years, respectively; *p*=0.019), and more males than females did not survive (64.9% v. 46.0%; *p*=0.039). Acute kidney injury was diagnosed in 34 patients at the time of ECMO placement, ranging from an Acute Kidney Injury Network (AKIN) classification of 1 (*n*=13) to AKIN 2 (*n*=11) and AKIN 3 (*n*=10). Only 4 patients were known to have asthma prior to ECMO placement, and all survived (*p*=0.035). Asthma was only a concomitant comorbidity and not the primary indication for ECMO placement in any of the patients. For the patients known to have asthma, the indications for ECMO were bacterial pneumonia (*n*=1), fungal pneumonia (*n*=1) and post bilateral lung transplant (*n*=2).

The ECMO outcome prediction scores for the likelihood of survival in the form of a SAVE score for patients with adult cardiogenic shock and a RESP score for adult respiratory failure were compared with our data. Two patients in the all respiratory support group did not have all the variables needed to generate an accurate RESP score.

In the all respiratory support group (*n*=76), 46.1% survived. The respiratory support without lung transplant group (*n*=54) had a survival rate of 42.5%. In the circulatory support group (*n*=29), the survival rate was 34.4%. In the circulatory support group without transplant (*n*=20), 35.0% survived.

The predicted survival likelihood compared with actual survival is shown in Table 4. In the all respiratory support group, patients in risk class IV had better than predicted survival according to the RESP score, while risk classes I, II and III had worse than predicted survival. In the circulatory support group, all risk classes had worse than predicted survival.

Overall survival for the transferred patients and the patients retrieved on ECMO was 44.2% (*n*=19/43) and 16.7% (*n*=1/6), respectively.

Table 1. Procedures performed prior to ECMO placement

	n (% of total procedures)
Bilateral sequential lung transplant and single-lung transplant	22 (34.9)
Coronary artery bypass grafting	3 (4.8)
Valve replacement and coronary artery bypass grafting	2 (3.2)
Valve replacement or repair	6 (9.5)
Heart transplant	9 (14.2)
Coronary artery stenting	1 (1.6)
General surgical	8 (12.7)
Thoracic surgery	7 (11.1)
Bilateral pulmonary endarterectomy	4 (6.3)
Redo cardiac surgery	1 (1.6)
Total procedures	63

ECMO = extracorporeal membrane oxygenation.

Discussion

ECMO is an expensive, specialised technology with a high mortality rate, but it can be lifesaving for certain patients with reversible cardiopulmonary failure. ECMO circuits are continuously improving and are becoming smaller, safer to manage, and hopefully more accessible. Identifying which patients would benefit from ECMO support, and the development of risk scores to assist with this process, are therefore of the utmost importance.

To our knowledge this is the first study to report on ECMO outcomes in SA.

Milpark Hospital is the only ELSO-registered ECMO referral centre for adults in the northern part of SA.[3] Although improved outcomes have been documented at specialist referral centres, delays in transfer could lead to a delay in ECMO initiation and possibly an increase in mortality.[3] The outcomes in the patients retrieved on ECMO could possibly reflect the increased mortality in critically ill patients who are far from specialised facilities, and also the increased risk of transporting them. The protocols and indications for the retrieval of these patients will need to be reviewed to improve outcomes in this specific group.

In our cohort, there was 100% survival in the patients known to have asthma as a comorbidity. However, we had no patients placed on ECMO for status asthmaticus in our cohort. ECMO has been shown

Table 2. Injury types/indications for ECMO placement

	n (% of total patients)
Post lung transplant	22 (20.6)
Bacterial pneumonia	18 (16.8)
Viral pneumonia	12 (11.2)
Post cardiotomy	9 (8.4)
Burns	2 (1.9)
Myocardial infarction	2 (1.9)
Bridge to transplant	2 (1.9)
Post cardiac transplant	8 (7.4)
Aspiration pneumonia	3 (2.8)
Pulmonary embolism	4 (3.7)
Haemorrhagic shock	1 (0.9)
Cardiac shock	3 (2.8)
Trauma	1 (0.9)
Graft failure	1 (0.9)
Transfusion-related lung injury	2 (1.9)
Cardiomyopathy	2 (1.9)
Left ventricular assist device placement	1 (0.9)
Fungal pneumonia	1 (0.9)
Tracheal surgery	2 (1.9)
Reperfusion injury post pulmonary endarterectomy	4 (3.7)
Pulmonary contusion	2 (1.9)
Post lung resection	3 (2.8)
Chronic graft rejection	1 (0.9)
ECPR	1 (0.9)
Total	107

ECMO = extracorporeal membrane oxygenation;
ECPR = extracorporeal cardiopulmonary resuscitation.

to improve survival in patients with status asthmaticus.[11] Asthma was also found to be a protective factor during the development of the RESP score. Pre-ECMO asthma diagnosis was associated with 17.7 increased odds of survival to hospital discharge ($p<0.0001$) in the Predicting Survival after ECMO for Severe Acute Respiratory Failure study, and carries the highest weighting of 11 in the RESP score.[7] It is interesting that in our study, patients with asthma as a comorbidity showed statistically significant survival. However, this was in the setting of a retrospective review, and a further prospective study will be necessary to evaluate this finding.

ECPR refers to the rapid deployment of VA-ECMO during efforts to resuscitate a patient during cardiac arrest. ECPR is the most rapidly growing indication for ECMO use, with 8 558 runs during 2020.[2] ECPR has also been associated with the worst outcomes, with only 29% of patients surviving to discharge or transfer according to the ECLS registry report of 2020. Only one patient in our study received ECPR, and unfortunately died. The increased mortality rate of 83.3% for patients transferred on ECMO and poor survival for patients placed on ECMO during ECPR should be considered in non-ELSO-registered hospitals in SA.

The role of ECMO in lung transplantation has expanded considerably. ECMO can be used as a bridge to transplant, for intraoperative support during transplantation, and for postoperative support. The main indications for lung transplantation are idiopathic interstitial pneumonia, COPD, cystic fibrosis, pulmonary arterial hypertension and retransplant.[12,13] These indications correlated with our cohort.

Pulmonary donor graft dysfunction continues to play a large part in postoperative morbidity of transplant patients.[14] The use of intraoperative ECMO support during lung transplantation with the option to extend support postoperatively has multiple benefits and should continue to rise in view of excellent results achieved by some groups.[15,16] It is therefore not surprising that the most common postoperative indication for ECMO use in the present study was in the setting of lung transplantation.

Although the primary aim of this study was not to externally validate the RESP and SAVE scores, it did provide us with information regarding the predicted survival likelihoods for our cohort. In the all respiratory support group, risk class IV had better than predicted survival according to the RESP score, while risk classes I, II and III had worse than predicted survival. In the circulatory support group, all risk classes had worse than predicted survival. However, these groups were small and inadequately powered to make definitive conclusions. A possible reason for the worse than predicted survival for the circulatory support group is that with the initial development of the SAVE score, patients who received VA-ECMO during CPR and patients on their second run of ECMO were excluded,[8] while these patients were included in our cohort. Further external validation of the risk scores will be needed to assess their accuracy in our population group.

Conversion from VV-ECMO to VA-ECMO is associated with decreased survival.[17] Our patient cohort included 4 patients who were placed on VA-ECMO after initial VV-ECMO. Although all 4 patients died, this did not reach statistical significance owing to the small number of patients in this group.

This retrospective study has several limitations. We were unable to collect accurate data on complications and causes of death. Patients

Table 3. Demographics and comorbidities of all ECMO patients*

	All ECMO (*N*=107), *n* (%)†	Survivors (*n*=47), *n* (%)†	Non-survivors (*n*=60), *n* (%)†	*p*-value
Age (years), mean (SD)	47 (13.2)	43 (13.8)	49 (12.4)	0.019
Sex male	57 (53.3)	20 (42.6)	37 (61.7)	0.039
Hypertension	37 (34.5)	11 (23.4)	26 (43.3)	0.022
COPD	11 (10.2)	5 (10.6)	6 (10.0)	0.884
Diabetes	21 (19.6)	8 (17.0)	13 (21.7)	0.585
Asthma	4 (3.7)	4 (8.5)	0	0.035
Chronic pulmonary hypertension	27 (25.2)	12 (25.5)	15 (25.0)	0.899
Sarcoidosis	1 (0.9)	1 (2.1)	0	0.256
Epilepsy	2 (1.8)	0	2 (3.3)	0.206
Fungal pneumonia	5 (4.7)	2 (4.2)	3 (5.0)	0.462
Trauma/burn	7 (6.5)	3 (6.4)	4 (6.7)	0.619
Interstitial lung disease	17 (15.9)	10 (21.3)	7 (11.7)	0.640
Tracheostomy	42 (39.2)	15 (31.9)	27 (45.0)	0.373
Cystic fibrosis	4 (3.7)	2 (4.2)	2 (3.3)	0.802
Chronic thromboembolic pulmonary hypertension	4 (3.7)	3 (6.4)	1 (1.7)	0.201
Cancer	2 (1.8)	0	2 (3.3)	0.502
Acute kidney injury upon initiation	34 (31.7)	10 (21.3)	24 (40.0)	0.368
AKIN 1	13 (12.1)	4 (8.5)	9 (15.0)	0.185
AKIN 2	11 (10.2)	3 (6.4)	8 (13.3)	0.147
AKIN 3	10 (9.3)	3 (6.4)	7 (11.7)	0.219

ECMO = extracorporeal membrane oxygenation; COPD = chronic obstructive pulmonary disease; AKIN = Acute Kidney Injury Network classification.
*Some patients had more than one comorbidity.
†Except where otherwise indicated.

Table 4. Predicted survival compared with actual survival

	N	Grade	Predicted survival, %	Mortality, *n*	Survival per grade, %
All respiratory support					
RESP score					
≤6	4	I	92	1	75.0
3 - 5	26	II	76	12	53.9
–1 - 2	33	III	57	19	42.5
–2 - –5	8	IV	33	5	37.5
≥–6	5	V	18	4	20.0
Total	76			41	46.1
Respiratory support without lung transplant					
RESP score					
≤6	4	I	92	1	75.0
3 - 5	16	II	76	8	50.0
–1 - 2	23	III	57	14	29.1
–2 - –5	7	IV	33	5	28.6
≥–6	4	V	18	3	25.0
Total	54			31	42.5
All circulatory support					
SAVE score					
>5	3	I	75	1	66.6
1 - 5	8	II	58	4	50.0
–4 - 0	10	III	42	8	20.0
–9 - –5	8	IV	30	6	25.0
≤–10	0	V	18	-	-
Total	29			19	34.4
Circulatory support without cardiac transplant					
SAVE score					
>5	2	I	75	1	50.0
1 - 5	5	II	58	3	40.0
–4 - 0	6	III	42	4	33.3
–9 - –5	7	IV	30	5	28.6
≤–10	0	V	18	-	-
Total	20			13	35.0

RESP = Respiratory ECMO Survival Prediction; SAVE = Survival After Venoarterial ECMO.

who undergo ECMO patients have prolonged ICU stays with complex diagnoses and multiple factors impacting on their outcomes. Owing to the wide variation in ECMO indications in our cohort, the subgroups became too small to make deductions regarding specific indications and mortality.

Conclusion

We report ECMO outcomes in SA for the first time. We identified very high mortality rates for patients transferred on ECMO from other facilities and for patients converted from VV-ECMO to VA-ECMO. Although our outcomes were comparable in some of the risk classes, further external validation of the SAVE and RESP scores will be needed to compare our outcomes with these scores.

Declaration. The research for this study was done in partial fulfilment of the requirements for NLFvZ's MMed (Thor Surg) degree at Stellenbosch University.

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