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Can Cerebral Regional Oxygen Saturation (rSO_2) be used as an Indicator of the Quality of Chest Compressions in Patients with Cardiopulmonary Arrest? A Study Evaluating The Association between rSO_2 and Mean Arterial Pressure: The PRESS Study

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Research Article

Keywords: arterial pressure, cardiopulmonary resuscitation, cerebral regional oxygen saturation, cerebrovascular circulation, prognosis

Posted Date: October 20th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-923130/v2

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Version of Record: A version of this preprint was published at Frontiers in Medicine on February 22nd, 2022. See the published version at https://doi.org/10.3389/fmed.2022.810449.

Abstract

Background: Sudden cardiac arrest causes numerous deaths worldwide. High-quality chest compressions are important for good neurological recovery. Arterial pressure is considered useful to monitor the quality of chest compressions by the American Heart Association. However, arterial pressure catheter might be inconvenient during resuscitation. Conversely, cerebral regional oxygen saturation (rSO_2) during resuscitation may be associated with a good neurological prognosis. Therefore, we aimed to evaluate the correlation between mean arterial pressure and rSO_2 during resuscitation to use rSO_2 as the indicator of the quality of chest compressions.

Methods: This study was a single-centre, prospective, observational study. Patients with out-of-hospital cardiac arrest who were transported to a tertiary care emergency centre between October 2014 and March 2015 in Japan were included. The primary outcome was the regression coefficient between MAP and rSO_2. MAP and rSO_2 were measured during resuscitation (at hospital arrival [0 min], 3 min, 6 min, 9 min, 12 min, 15 min), and MAP was measured by an arterial catheter inserted into the femoral artery. For analysis, we used the higher value of rSO_2 obtained from the left and right forehead of the patient and measured using a near-infrared spectrometer. Regression coefficients were calculated using the generalized estimating equation (GEE) with MAP and SAP as response variables and rSO_2 as an explanatory variable, because MAP and rSO_2 were repeatedly measured in the same patient. Since the confounding factors between MAP or SAP and rSO_2 were not clear clinically or from previous studies, the GEE was analysed using univariate analysis.

Results: Thirty-seven patients were analysed. rSO_2 and MAP during resuscitation from hospital arrival to 15 min later were expressed as follows (median [interquartile range]): rSO_2, 29.5 (24.3–38.8) %, and MAP, 36.5 (26–46) mmHg. The regression coefficient (95% confidence interval) of log-rSO_2 and log-MAP was 0.42 (0.03–0.81) (p=0.035).

Conclusion: rSO_2 and MAP showed a mild but statistically significant association. rSO_2 could be used to assess the quality of chest compressions during resuscitation as a non-invasive and simple method.

Trial registration: This study was registered in the University hospital Medical Information Network Clinical Trials Registry (UMIN000015479).

Introduction

Despite the advancements in medical technology, a good neurological recovery from sudden cardiac arrest remains low, and sudden cardiac arrest is responsible for numerous deaths worldwide.[1, 2] Although specific data are not yet available, it has been hypothesized that the social cost of these deaths is estimated to be enormous. To increase good neurological recovery after cardiopulmonary arrest, resuscitation procedures for sudden cardiac arrest have been studied, and high-quality chest compressions have been considered the most important factor for return of spontaneous circulation

(ROSC).[3] Moreover, we hypothesized that an improved ratio of ROSC is associated an improved neurological outcome; however, no previous study has examined this association.

The American Heart Association 2020 guidelines have considered the use of arterial pressure to monitor the quality of chest compressions.[4] Arterial pressure, especially mean arterial pressure (MAP), is often used to monitor organ perfusion in critically ill patients.[5] Previous studies have shown that high MAP during resuscitation might correlate with a good neurological prognosis in patients with cardiopulmonary arrest.[6] Therefore, the use of arterial pressure to monitor organ perfusion in patients with cardiopulmonary arrest may be reasonable. However, arterial pressure measurement requires an arterial pressure catheter, which cannot be inserted during emergency medical transportation to the hospital and requires a certain level of skill for insertion during resuscitation in hospitals. Therefore, it may not be considered a convenient device. In addition, the AHA 2020 guidelines refer to $ETCO_2$ as a non-invasive means of assessing the quality of chest compressions.[4] However, the measurement of $EtCO_2$ requires tracheal intubation, especially in pre-hospital situations, which might be difficult to use.

Conversely, high cerebral regional oxygen saturation (rSO_2), which is a measure of cerebral perfusion that is obtained non-invasively via near-infrared spectroscopy (NIRS),[7] during resuscitation of patients with cardiopulmonary arrest may be associated with a good neurological prognosis.[8, 9] We hypothesized that higher MAP increases rSO_2 and, accordingly, improves neurological prognosis when considering the association between MAP and neurological prognosis. However, no previous study has examined the association between MAP and rSO_2. If the association between MAP and rSO_2 could be demonstrated, it would be possible to evaluate the quality of chest compressions in any situation during resuscitation using rSO_2, which is a non-invasive and easy method, and it might help to improve the neurological prognosis of patients with cardiopulmonary arrest. Therefore, our study aimed to evaluate the association between MAP and rSO_2 during resuscitation of patients with cardiopulmonary arrest.

Methods

Design and patients

This was a single-centre, prospective, observational study. Patients transported to the Japanese Red Cross Musashino Hospital, a tertiary care emergency centre in Japan, between October 2014 and March 2015 were enrolled. This study was registered in the University hospital Medical Information Network Clinical Trials Registry (UMIN000015479) and approved by the ethics committee of the Japanese Red Cross Musashino Hospital (ethical review no. 642). In addition, this study was based on the STrengthening the Reporting of OBservational studies in Epidemiology statement.[10] Informed consent was not needed because the data could be collected during normal resuscitation care, and the information was revealed by opt-outs.

Patients with out-of-hospital cardiac arrest who were transported to the Japanese Red Cross Musashino Hospital were included in this study. However, the following patients were excluded from this study: patients (1) aged less than 18 years, (2) with trauma, (3) introduced with extracorporeal membrane oxygenation (ECMO), (4) with a maximum measured rSO_2 value of 15%, (5) with a do-not-resuscitate (DNAR) order, or (6) not eligible to participate in the study based on the attending physician's discretion. Since the lower limit of rSO_2 measurement of the measurement device was 15%, if the maximum value of rSO_2 measured was 15%, it was not possible to distinguish whether the measured value was 15% or less than 15%. In such a case, the use of the measured value of 15% would cause measurement bias and was therefore excluded.

Data collection

The following data were collected: age, sex, whether or not the cardiac arrest was witnessed, whether or not bystander-initiated cardiopulmonary resuscitation (CPR) was performed, cause of cardiac arrest (cardiogenic, non-cardiogenic), initial rhythm at the time of emergency medical services (EMS) contact (ventricular fibrillation [VF]/pulseless ventricular tachycardia [VT], pulseless electrical activity [PEA], cardiac arrest), time from EMS call to hospital arrival, rSO_2 and arterial pressure (systolic arterial pressure [SAP], MAP) during resuscitation (at hospital arrival [0 min], 3 min, 6 min, 9 min, 12 min, 15 min), and with or without ROSC of patients. Arterial pressure was measured by the arterial catheter in the femoral artery, because arterial catheter insertion into the radial artery during resuscitation is difficult with a high probability of complications and requires a long time. Chest compressions were performed by selecting the site where the arterial pressure measured by the arterial catheter was highest. rSO_2 values were collected from the left and right forehead of the patient using a near-infrared spectrometer (INVOSTM5100C; Medtronic, Boulder, CO, USA), and the higher value of rSO_2 between the left and right value was used for analysis. Data follow-up was terminated when the patient was discharged, died, or was transferred to another hospital.

The data collection was unmasked because the physicians in charge collected the data individually, and the outcome assessors were unblinded. Missing data were not completed, and patients with missing MAP or rSO_2 data were excluded.

Outcome

The primary outcome was the regression coefficient between MAP and rSO_2. The secondary outcome was the regression coefficient between SAP and rSO_2.

Statistical analyses

Continuous variables are described using median and interquartile range (IQR), and categorical variables are described using absolute values and percentages (%). Initially, rSO_2 and arterial pressures (MAP, SAP) were log-transformed, and the Kolmogorov-Smirnov test was used to confirm that each factor was normally distributed. Since rSO_2 and arterial pressures (MAP, SAP) were repeated-measured data, we hypothesized that the data measured at different points within the same patient were correlated.

Therefore, we calculated regression coefficients using the generalized estimating equation (GEE), with MAP and SAP as response variables and rSO_2 as an explanatory variable. Since the confounding factors between MAP or SAP and rSO_2 were not clear clinically or from previous studies, the GEE was analysed using univariate analysis. EZR version 1.38, R version 3.5.2.tar.gz, and SAS version 9.4 (SAS Institute, Cary, North Carolina, USA) were used for analysis, and $p<0.05$ was considered statistically significant by two-sided test.

Results

A total of 222 patients were included, and 37 patients were analysed (Fig. 1). The reasons for exclusion were as follows: 88 for physicians' decision, 37 for DNAR order, 25 for ECMO, 24 for maximum rSO_2 measured at 15%, 7 for missed MAP, and 4 for missed rSO_2. MAP and rSO_2 were measured 98 times.

The patient's backgrounds are shown in Table 1. The median age (IQR) was 75 (69–82) years, 26 patients (70.3%) had witnessed cardiac arrest, 12 patients (32.4%) had bystander-initiated CPR, 5 patients (13.5%) had VF/pulseless VT, 15 patients (40.5%) had PEA, and 17 patients (46.0%) had asystole. The time to hospital arrival was 36 (range, 30–44) min. The maximum rSO_2 value during resuscitation was 29.5% (24.3–38.8%), MAP was 36.5 (26–46) mmHg, and there were 34 (91.9%) deaths during resuscitation.

Table 1. Baseline characteristics of all the analysed patients

Variables	Patients (n=37)
Age, years (median [IQR])	75 (69–82)
Male sex, no. (%)	31 (83.8)
Bystander witness, no. (%)	26 (70.3)
Bystander-initiated CPR, no. (%)	12 (32.4)
Origin of cardiac arrest, no. (%)	
Cardiac	21 (56.8)
Noncardiac	16 (43.2)
Initially documented rhythms on the scene of the cardiac arrest, no. (%)	
VF/pulseless VT	5 (13.5)
PEA	15 (40.5)
Asystole	17 (46.0)
Emergency call to arrival at the hospital in min, (median [IQR])	36 (30–44)
rSO_2 during resuscitation†, (median [IQR])	29.5 (24.3–38.8)
MAP during resuscitation, (median [IQR])	36.5 (26–46)
SAP during resuscitation, (median [IQR])	69 (47–105)
Death in the emergency room, no. (%)	34 (91.9)

†The highest value during resuscitation

Abbreviations: CPC, cerebral performance category; CPR, cardiopulmonary resuscitation; IQR, interquartile range; MAP, mean arterial pressure; PEA, pulseless electrical activity; OHCA, out-of-hospital cardiac arrest; rSO_2, regional saturation of oxygen; VF, ventricular fibrillation; VT, ventricular tachycardia

The trends of rSO_2, MAP, and SAP during resuscitation from hospital arrival to 15 min later are shown in Fig. 2. Although statistical tests were not performed, rSO_2, MAP, and SAP remained generally unchanged from 0 to 15 min after resuscitation, and all factors showed similar trends.

MAP, SAP, and rSO_2 were log-transformed and tested for normality distribution using the Kolmogorov-Smirnov test for each factor. The results of the Kolmogorov-Smirnov test were as follows: log-MAP, $p=0.14$; log-SAP, $p=0.98$; and log-rSO_2, $p=0.25$. Therefore, each factor was considered normally distributed. Next, the association between MAP or SAP and rSO_2 at each time point from 0 to 15 min later is shown in a scatterplot, and a scatterplot summarizing these repeated measurement data was created (Supplementary Fig. 1-a, 1-b, Fig. 3-a, 3-b).

The regression coefficients were calculated using GEE with log-MAP and log-SAP as the response variables and log-rSO_2 as the explanatory variable. The regression coefficients (95% confidence interval) between log-MAP and log-rSO_2 and log-SAP and log-rSO_2 were 0.43 (0.029–0.83) (p=0.035) and 0.42 (0.03–0.81) (p=0.037), respectively (Table 2-a, 2-b).

Table 2-a. Regression coefficients with MAP and rSO_2

Log-MAP	Regression coefficient	95% CI (lower)	95% CI (upper)	p value
Log-rSO_2†	0.43	0.029	0.83	0.035

Table 2-b. Regression coefficients with SAP and rSO_2

Log-SAP	Regression coefficient	95% CI (lower)	95% CI (upper)	p value
Log-rSO_2†	0.42	0.03	0.81	0.037

†The highest value during resuscitation

Abbreviations: CI, confidence interval; MAP, mean arterial pressure; rSO_2, regional saturation of oxygen; SAP, systolic arterial pressure

MAP, SAP, and rSO_2 were log-transformed, and we used an univariate generalized estimating equation.

Discussion

In this study, MAP and SAP during resuscitation of patients with cardiopulmonary arrest showed a mild but statistically significant association with rSO_2.

It is considered that rSO_2 increased as MAP and SAP increased since rSO_2 might reflect the increased cerebral blood flow (CBF) caused by chest compressions during resuscitation. In general, MAP was considered to be related to organ perfusion including CBF.[5] Previous studies in patients with sepsis have shown that both lower MAP and SAP were likely to correlate with poor prognosis.[5] MAP and SAP were associated with organ perfusion, and it was considered that the prognosis was exacerbated by organ failure as a result of decreased organ perfusion.[5] In contrary, rSO_2 was considered to reflect regional local tissue perfusion and might reflect CBF. rSO_2 was expressed as the oxygen saturation (%) of local tissue and considered to be strongly influenced by venous blood oxygen saturation because the local vascular area was larger in veins than that in arteries.[7] Jugular venous oxygen saturation (SjO_2) was an example of venous blood saturation and expressed by an equation that includes CBF. Therefore, it has been considered that SjO_2 was associated with CBF.[11] In fact, previous studies have shown that SjO_2 decreased in a situation as follows, where CBF seems to have decreased: intracranial hypertension, hypocarbia, systemic hypotension, and cerebral vasospasm.[11] Therefore, although no previous study has examined the association between rSO_2 and SjO_2, rSO_2 might be associated with CBF and SjO_2, which was venous oxygen saturation. In summary, chest compressions might have increased CBF, which was reflected in the increase in MAP, SAP, and rSO_2. Therefore, MAP and SAP showed a mild but statistically significant association with rSO_2.

To the best of our knowledge, this is the first study to demonstrate the significant association between MAP or SAP and rSO_2 during resuscitation in patients with cardiopulmonary arrest. In other words, as MAP or SAP increases, so does rSO_2; therefore, rSO_2 can be used to evaluate the quality of chest compressions during resuscitation as a non-invasive and simple method instead of measuring arterial pressure, which might help improve neurological prognosis.

However, this study has several limitations. First, the clinical use of rSO_2 to assess the quality of chest compressions might be difficult because the association between MAP or SAP and rSO_2 was mild. It is possible that MAP, SAP, and rSO_2 were not elevated; therefore, there was a weak association since we included only patients with a poor prognosis. If patients with good neurological prognosis are included, MAP, SAP, and rSO2 will be higher, and it is possible that stronger associations can be shown. Therefore, further studies are required in patient groups with good neurological outcome that are more likely to have higher MAP, SAP, and rSO_2 during resuscitation, such as those with an initial rhythm other than asystole, shorter time to sick arrival, and higher percentage of undergoing bystander-initiated CPR. Second, since the analysis in this study was performed by logarithmic transformation, it might be difficult to consider the quantitative significance of rSO_2 and MAP increase. For example, although the regression coefficient between log-MAP and log-rSO_2 was 0.43 (0.029–0.83) in this study, it was not easy to calculate how much MAP was increased when rSO_2 was increased by 1%. Since a positive correlation has been shown in this study, it was possible to evaluate the quality of chest compressions using increased values as an index, but quantitative assessment might be difficult in clinical setting. Third, the tissue oxygenation index (TOI) measured by a different NIRS mechanism than rSO_2 might be more accurate in assessing CBF. Therefore, the regression coefficients evaluated by rSO_2 might not be correct. Although there were no studies comparing rSO_2 with TOI as a measure of CBF, using TOI other than rSO_2 might have stronger association with MAP and SAP. Fourth, the results of the regression coefficients might be underestimated because the number of patients analysed were small. In this study, there were only 37 patients who were analysed. This might have led to a lack of statistical power.

Conclusion

In this study, MAP and SAP during resuscitation of patients with cardiopulmonary arrest and rSO_2 showed a mild but statistically significant association. rSO_2 could be used to assess the quality of chest compressions during resuscitation as a non-invasive and simple method, which might help improve neurological prognosis.

Abbreviations

CBF, cerebral blood flow; CPR, cardiopulmonary resuscitation; DNAR, do-not-resuscitate; ECMO, extracorporeal membrane oxygenation; EMS, emergency medical services; GEE, generalized estimating equation; SjO_2, jugular venous oxygen saturation; MAP, mean arterial pressure; NIRS, near-infrared spectroscopy; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; rSO_2, cerebral regional oxygen saturation; SAP, systolic arterial pressure; VF, ventricular fibrillation; VT, pulseless ventricular tachycardia

Declarations

Ethics approval and consent to participate

This study was registered in the University hospital Medical Information Network Clinical Trials Registry (UMIN000015479) and approved by the ethics committee of the Japanese Red Cross Musashino Hospital (ethical review no. 642). Informed consent was not needed because the data could be collected during normal resuscitation care, and the information was revealed by opt-outs.

Consent for publication

Not required.

Availability of data and materials

All data and materials are available in the manuscript. And all data and materials are available on reasonable request to the corresponding author.

Competing interests

Not applicable.

Funding

Not applicable.

Authors' contributions

HY conceived the study. YK and HY undertook the data collection. YK and HY performed the statistical analysis of the data. YK interpreted the data and drafted the manuscript. All authors contributed substantially to the study design and revision of the manuscript with supervision from HY. All authors have approved the manuscript and agree to be accountable for the work.

Acknowledgement

The authors acknowledge the support of Editage (www.editage.jp) for English language editing.

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Figures

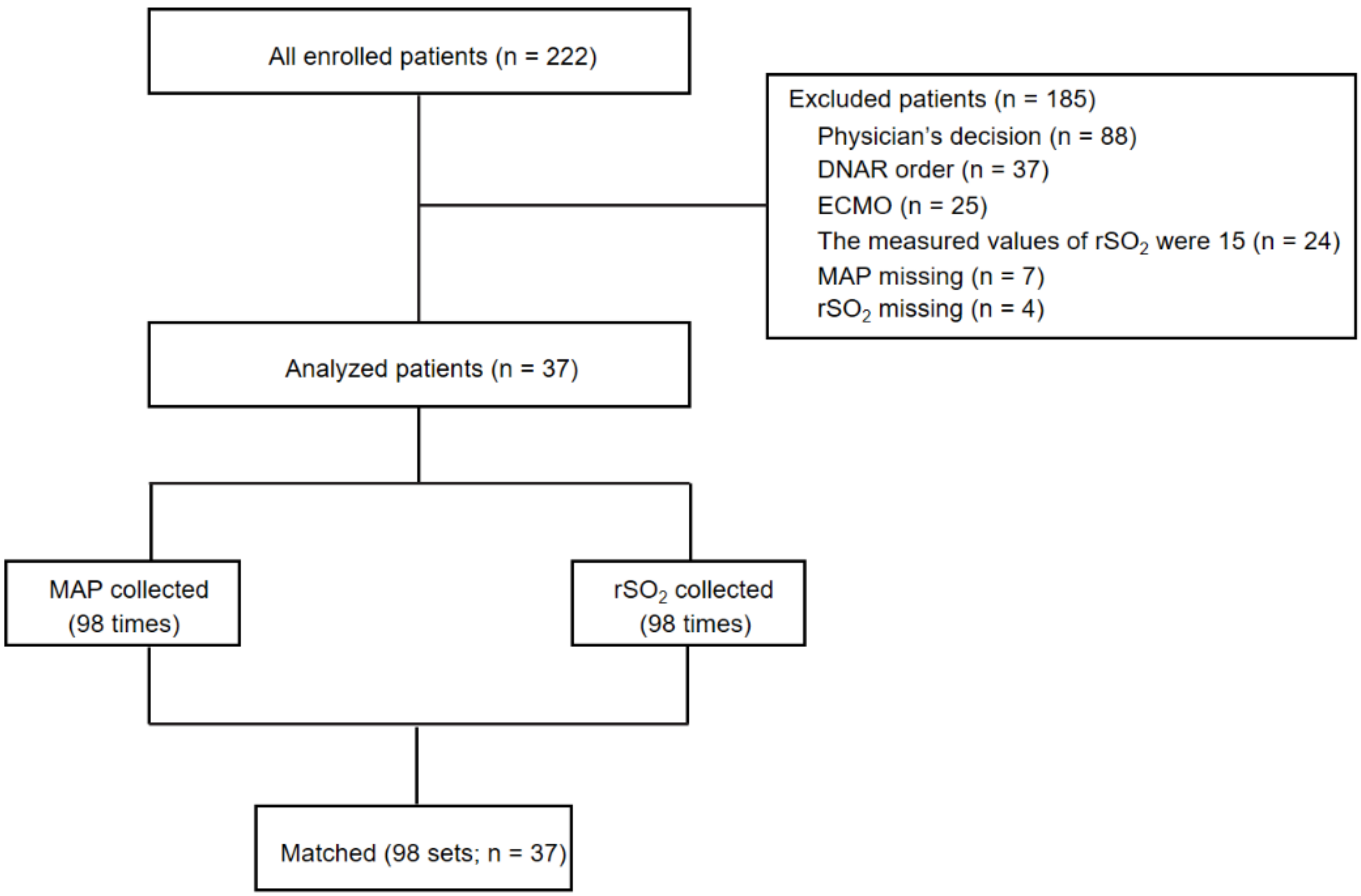
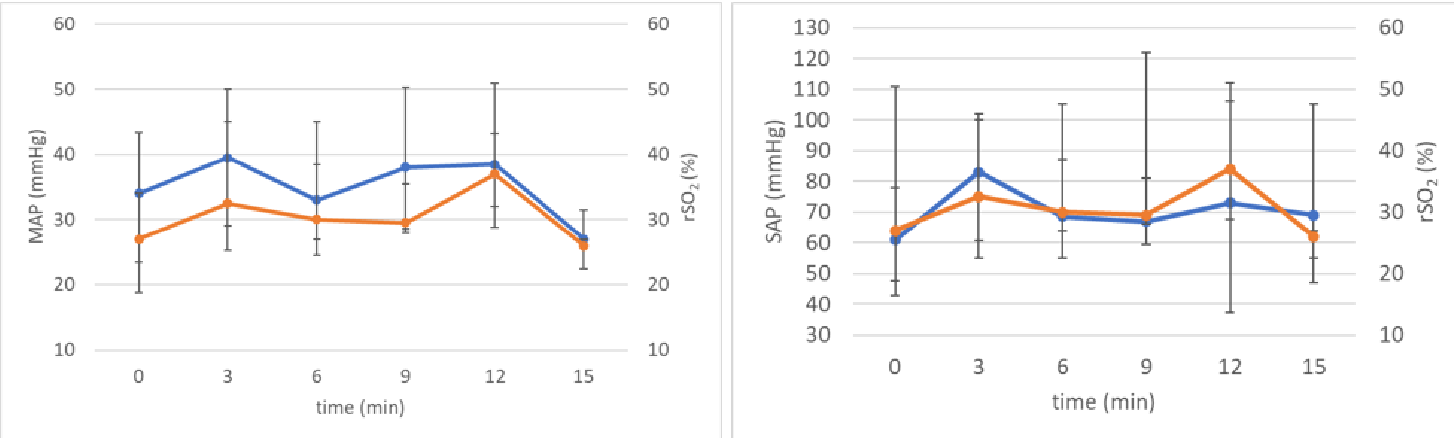


Figure 1

Flowchart of patients' screening and enrolment in this study Abbreviations: DNAR, do not resuscitate; ECMO, extracorporeal membrane oxygenation; MAP, mean arterial pressure; rSO2, regional saturation of oxygen; SAP, systolic arterial pressure



	0 min	3 min	6 min	9 min	12 min	15 min	All times
MAP (mmHg) (median [IQR]), n	34 (23.5—45.3), 28	39.5 (29—50), 30	33 (24.5—45), 23	38 (28.5—50.3), 10	38.5 (32—43.2), 4	27 (22.5—31.5), 3	36.5 (26—46), 98
SAP (mmHg) (median [IQR]), n	61 (43—111), 27	83 (55—102), 29	68.5 (55—105), 20	67 (59.5—122), 10	73 (37.3—106), 4	43 (36.5—53.5), 3	69 (47—105), 93
rSO_2 (%) (median [IQR]), n	27 (18.8—34) ,28	32.5 (25.3—45) ,30	30 (27—38.5) ,23	29.5 (28—35.5) ,10	37 (28.8—51) ,4	26 (22.5—27) ,3	29.5 (24.3—38.8) ,98

Figure 2

Changes in MAP, SAP, and rSO2 over 15 min Abbreviations: IQR, interquartile range; MAP, mean arterial pressure; rSO2, regional saturation of oxygen; SAP, systolic arterial pressure

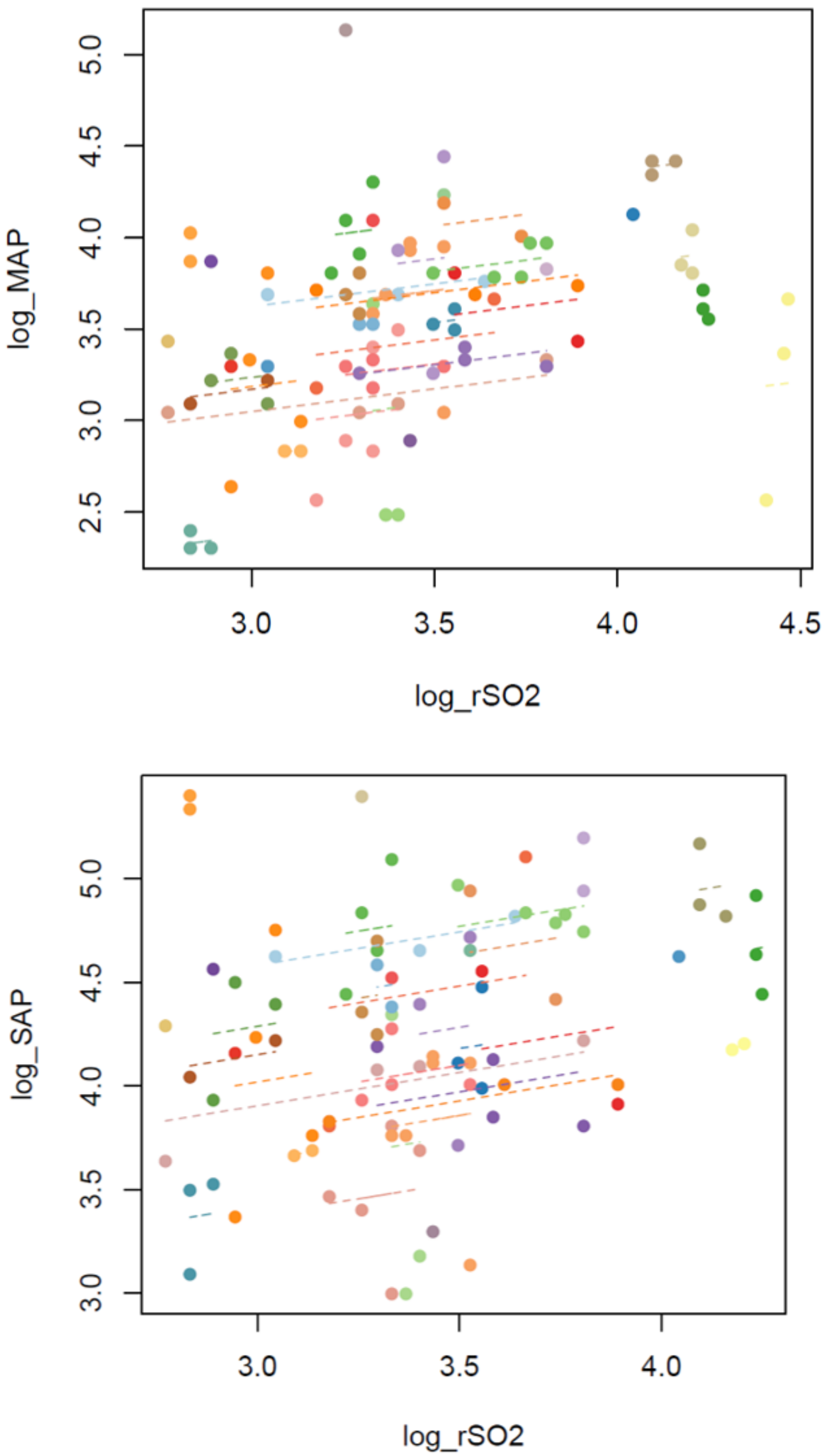


Figure 3

a. Scatterplot of MAP and rSO2 in repeated measurements b. Scatterplot of SAP and rSO2 in repeated measurements Abbreviations: MAP, mean arterial pressure; rSO2, regional oxygen saturation; SAP, systolic arterial pressure The repeated measurements of MAP and rSO2 from 0 to 15 min are plotted.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryFigures.pptx