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Clinical paper

Oxygen metabolism after cardiac arrest: Patterns and associations with survival

Meredith G. Shea[a], *Lakshman Balaji*[a], *Anne V. Grossestreuer*[a,b], *Mahmoud S. Issa*[a,b], *Jeremy Silverman*[a], *Franklin Li*[a], *Michael W. Donnino*[a,b,c], *Katherine M. Berg*[a,c,*]

Abstract

Aim: Whether changes in oxygen metabolism, as measured by oxygen consumption (VO_2), carbon dioxide production (VCO_2) and the respiratory exchange ratio (RER), are associated with survival after cardiac arrest is poorly understood. In this prospective observational study, we investigated the association between VO_2, VCO_2, and RER in the initial 12 and 24 h after return of spontaneous circulation (ROSC) and survival to hospital discharge.

Methods: Adults with ROSC after cardiac arrest, admitted to the intensive care unit, requiring mechanical ventilation and treated with targeted temperature management were included. VO_2 and VCO_2 were measured continuously for 24 h after ROSC, using a noninvasive anesthesia monitor. Area under the curve for VO_2, VCO_2 & RER was calculated using all available values over 12 and 24 h after ROSC. Using logistic regression, we evaluated the relationship between these metabolic variables and survival to hospital discharge. Analyses were adjusted for temperature, vasopressors, and neuromuscular blockade.

Results: Sixty four patients were included. Mean age was 64 ± 16 years, and 59% were women. There was no significant association between the area under the curve of VO_2 or VCO_2 and survival. A higher RER in the initial 12 h was associated with better survival (aOR = 3.97, 95% CI [1.01,15.6], p = 0.048). Survival was lower in those with median RER < 0.7 in the initial 12 h compared with those with a median RER $\geq$ 0.7 (25% vs 67%, p = 0.011).

Conclusion: Higher RER in the initial 12 h was associated with survival after cardiac arrest. The etiology of unusually low RERs in this patient population remains unclear.

Keywords: Respiratory exchange ratio, Oxygen consumption, Cardiac arrest, Post-cardiac arrest

Introduction

Cardiac arrest affects more than 500,000 Americans annually, and mortality remains extremely high.[1] Of those who achieve return of spontaneous circulation (ROSC), many will go on to die due to neurological deterioration, declining hemodynamic function, and organ failure.[1,2] Termed post-cardiac arrest syndrome, this process is thought to be driven by ischemia–reperfusion injury and resulting mitochondrial dysfunction.[3–6] Variability in the extent of mitochondrial injury likely contributes to the variability in survival, but there is currently no way to assess the degree of mitochondrial damage in the clinical setting. Cytopathic hypoxia, a term used to describe the breakdown of aerobic metabolism even when adequate oxygen is present, is thought to result from mitochondrial dysfunction and leads to low oxygen extraction, which will also lead to low oxygen consumption (VO_2).[7] Prior investigators, primarily using calculated values with use of a Swan Ganz catheter, have used the measurement of VO_2 as an indirect but measurable way to explore changes in oxygen metabolism from mitochondrial dysfunction in patients with septic shock, finding that lower VO_2 is associated with lower survival, with a single study reporting similar findings after cardiac arrest.[8–10]

Using a non-invasive anesthesia monitor that can measure continuous VO_2 and VCO_2 in mechanically ventilated patients, we previously reported an association between higher VO_2 in the first 12 h after ROSC and survival in a pilot cohort of 17 post-arrest patients.[11]

* Corresponding author at: Center for Resuscitation Science, Department of Emergency Medicine, Beth Israel Deaconess Medical Center, 1 Deaconess Road, Rosenberg 2, Boston, MA 02215, USA.

E-mail address: kberg@bidmc.harvard.edu (K.M. Berg).

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Respiratory quotient (RER) was also abnormally low in a majority of patients in that study, a finding that has also been reported in an animal model of cardiac arrest.[12] We conducted the current study to attempt to validate these findings in a larger cohort of post-cardiac arrest patients. We hypothesized that higher VO_2 would be associated with survival, and that an RER < 0.7 (generally considered the lower limit of normal) would be associated with mortality.

Methods

Design and setting

This was a single center, prospective observational study conducted at an urban, tertiary care medical center located in Boston, MA, USA. The study was approved by the institutional review board at Beth Israel Deaconess Medical Center. Legally authorized surrogates of all patients provided verbal informed consent prior to patient enrollment.

Participants and outcomes

Patients included in the study were a convenience sample of adults (age $\geq$ 18 years) who were admitted to the intensive care unit for cardiac arrest, required mechanical ventilation, and were receiving target temperature management. For this observational study, all patients enrolled in one of our ongoing cardiac arrest trials were also screened for this observational study. Patients were excluded if they had: 1) factors known to artifactually alter VO_2 such as air-leak, fever or agitation, 2) positive end-expiratory pressure (PEEP) > 15 cm H_2O, due to the potential risk of a brief disconnection from the ventilator, 3) fraction of inspired oxygen (FiO_2) > 60% due to the monitor being validated for FiO_2 of 60% or less and 4) equipment or personnel for metabolic data collection not available. The GE monitor reports all FiO_2 values to two decimal places. Therefore an FiO_2 cut-off of < 61% was used to capture all available data for the FiO_2 of 60%. Patient data were only included if they had at least 60 min of post-ROSC metabolic data collected within the first 24 h after ROSC. Trials that participants in this study were co-enrolled in included randomized trials of thiamine, ubiquinol and neuromuscular blockade administered after ROSC (NCT03450707, NCT02974257, NCT02934555, NCT02260258).[13–16] The primary outcome was the area under the curve of VO_2 (AUC-VO_2). Secondary outcomes included the area under the curve of VCO_2 (AUC-VCO_2) and of the RER (AUC-RER), and survival to hospital discharge.

Data collection

Demographics, cardiac arrest data and basic clinical information such as temperature, ventilator settings, vasopressors, sedatives and neuromuscular blockade were recorded at the bedside or abstracted from the medical record prospectively. Temperature was recorded hourly, and assumed to be the same as the measured value for the next hour or until the next measured value. Vasopressors, sedation and neuromuscular blockade were entered as a yes/no variable every hour that metabolic data was collected. For each hour, a yes meant the medication was in use for at least 50% of the hour in question. For collection of metabolic data, a GE Healthcare Carescape Monitor B650 with the Carescape respiratory module E-sCOVX (GE Healthcare, Helsinki, Finland) was connected as soon as possible after ROSC, after consent was obtained. In addition to metabolic data, this monitor also records PEEP and FiO_2 continuously and provides these values. Ventilator settings were also collected from the record and any changes cross-checked between the record and the GE monitor.

The Carescape Monitor connects in-line with the patient's ventilator tubing and measures spirometry and gas exchange from a gas sampling port and flow sensor. The gas exchange module measures the flow of exhaled gasses as well as the difference in oxygen and carbon dioxide content during inhalation and exhalation using a pneumotachograph and rapid paramagnetic analyzer. VO_2 and VCO_2 are measured with each breath, and values averaged over 60-second intervals are continuously recorded for up to 24 h using the GE Healthcare S/5 Collect Software. The RER is reported by the monitor but for analytic purposes was calculated by dividing VCO_2 by VO_2 at every time point after cleaning the data to remove artifactual values.

The Carescape Monitor B650 has been approved for use in critically ill, mechanically ventilated patients to measure oxygen consumption and carbon dioxide production and the respiratory exchange in mechanically ventilated patients with an FiO_2 of 605 or less.

Statistical analysis

A power calculation was not done a priori due to the very limited nature of prior data in post-arrest patients and as the number of patients included in this exploratory study was dictated by feasibility at our single center. Baseline characteristics were summarized with descriptive statistics, with means ± standard deviations (SD), sample size and percents, and medians and interquartile ranges (IQR) as appropriate. Continuous variables were compared using either the two sample Student's *t*-test or Wilcoxon rank sum test, depending on the distribution of the data. Categorical and dichotomous variables were compared using either a chi-square test or a Fisher's exact test. Prior to unblinding or analysis, all metabolic data were cleaned using an algorithm designed by our research team in R version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria), which has been described previously.[17] The automated algorithm excludes a VO_2 datapoint (and the corresponding value for VCO_2) if one or more of the following criteria is met: 1) all values recorded in the 10 min following a change in FiO_2 of $\geq$ 10%, 2) all values recorded while FiO_2 is > 61%, (61% used in order to capture all situations when the ventilator is set for an FiO_2 > 60%, as the monitor reports this number to two decimal places, and a set number of 60% may be recorded as 60.54%, for example), 3) all values deviating 15% or more from the mean of the previous five values and the next five values (i.e, deviating 15% from the mean of the ten neighboring data points), and 4) values out of physiologic range unless these were persistent for more than 30 min, as these measurements were considered artifacts. Values considered out of physiologic range were VO_2 < 80 mL/kg/min or > 800 mL/kg/min. These values were allowed if they persisted for $\geq$ 30 min and if they were not excluded per the algorithm for other reasons, as critically ill patients can have values well outside of standard normal range due to medication use such as sedatives and neuromuscular blockade and/or alterations in metabolic function. The respiratory quotient (RER) was calculated as the ratio of VCO_2 to VO_2 at each minute. After data was run through the algorithm, and still prior to unblinding, there was a final visual review of a graphical print-out of all data points for each patient to provide a secondary confirmation that values were kept or dropped appropriately. Prior to analysis, VO_2 and VCO_2 values were adjusted for bodyweight by dividing total mL/min by weight in kilograms.

The area under the curve (AUC) was calculated using all available values in the first 12 and 24 h after ROSC for VO_2, VCO_2, and the RER. Median AUCs in the first 12 and 24 h were calculated and compared between groups by survival status. The AUC calculation was adjusted for the number of minutes of data available, which varied between individual patients. Odds ratios and 95% confidence intervals were calculated to determine the association between metabolic variables and survival. Logistic regression was used to provide an adjusted odds ratio adjusting for temperature, sedation, and vasopressors.[18–21] Survival of patients with a normal or high (>0.7) and low (<0.7) median AUC-RER was compared using a Chi square test. Based on results from our earlier study, survival was also compared between patients with median RER < 0.7 or ≥ 0.7 in the first hour of data collection.

Results

A total of 64 patients were included in analysis of the first 24 h after ROSC, and 43 of these had sufficient data (at least 60 min) for analysis of the first 12 h (Fig. 1). The number of patients with available metabolic data at each hour after ROSC is presented by survival group in Table S1. Individual patient graphs of raw VO_2 measurements, and all values after data were cleaned with our algorithm to remove artifactual values, are provided in the supplement. The mean age was 64 ± 16 years and 59% were women. Survivors were statistically significantly more likely to have a shockable rhythm and a shorter median duration of resuscitation before ROSC and were less likely to be on vasopressors at any time post-arrest. Other characteristics were not significantly different between groups (Table 1).

In the initial 12 h after ROSC, the median number of minutes of usable metabolic data in the subset of 43 patients with sufficient data to be included was 293 (IQR 200–365). Over 24 h the median number of minutes of data for all 64 patients was 905 (IQR 753–1031). Only a small number of patients had data collected before 6 h after ROSC, largely due to the need to obtain informed consent. Median values in survivors and nonsurvivors for the AUC of all 3 metabolic parameters are shown in Table 2. With the exception of the AUC-RER over 12 h, there was considerable overlap in interquartile ranges between groups. Trends over time are presented visually in Fig. 2.

There was no significant association between the AUC of VO2 ($AUC\text{-}VO_2$) during the first 12 h after ROSC and survival (OR = 1.33, 95%CI [0.78, 2.26], p = 0.296). The relationship did not change after adjustment (aOR = 1.21, 95% CI [0.68, 2.16], p = 0.523, Fig. 3) or when including data over 24 h (OR = 1.12, 95% CI [0.73, 1.73], p = 0.592, and aOR = 1.12, 95% CI [0.66,1.89], p = 0.680, Fig. 4).

There was no significant association between AUC of VCO_2 ($AUC\text{-}VCO_2$) in the first 12 h and survival in unadjusted analysis (OR = 2.06, 95% CI [0.87, 4.87], p = 0.102). This relationship did not change with adjustment (aOR = 1.79, 95% CI [0.70, 4.55], p = 0.225, Fig. 3) or when including data over 24 h (OR = 1.34, 95%CI [0.71, 2.55], p = 0.370, and aOR = 1.36, 95% CI [0.61, 3.04], p = 0.450, Fig. 4).

The AUC of the RER (AUC-RER) was < 0.7 in 49% of patients. The unadjusted association between the AUC-RER and survival in the first 12 h after ROSC did not reach statistical significance (OR = 3.00, 95% CI [0.98, 9.13], p = 0.053), but this became significant after adjustment (aOR = 3.97, 95% CI [1.01, 15.6], p = 0.048, Fig. 3). There was no association between AUC-RER and survival when including data from the 24 h after ROSC (OR = 1.85, 95% CI [0.61, 0.5.63], p = 0.278; aOR = 1.92, 95% CI [0.54, 6.78], p = 0.312, Fig. 4).

Survival was significantly higher in patients with a median AUC-RER of ≥ 0.7 over the first 12 h, compared with patients with a median AUC-RER of < 0.7 in the first 12 h (68% compared with 25%, p = 0.011). The initial RER measurement was obtained at a median of 8 h (IQR: 7, 9) after ROSC. Using the first one hour of available data only, 64% of patients with a median RER ≥ 0.7 survived, compared with 17% of patients with a median RER of < 0.7 (p < 0.001).

Discussion

In this observational study we found no statistically significant differences in VO_2 or VCO_2 between survivors and nonsurvivors over 12 or 24 h. We did find a significantly higher rate of survival in patients

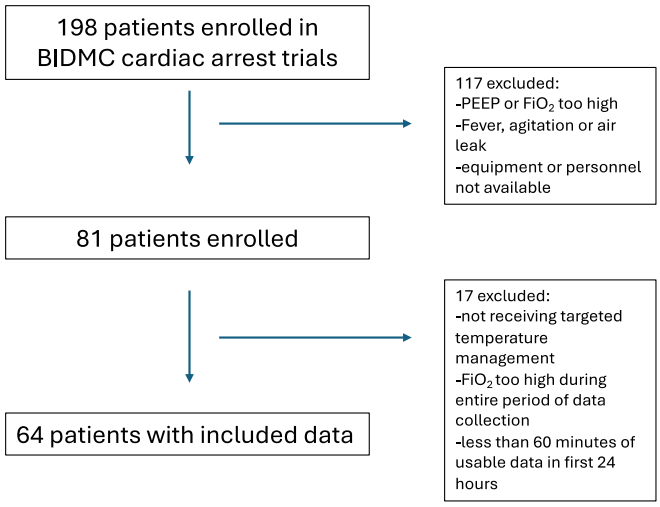

Fig. 1 – Screening and enrollment flow chart.

Table 1 – Characteristics of 64 patients contributing 60 min or more of clean VO2 monitor data in the first 24 h after ROSC.

Characteristic*	All patients (n = 64)	Non-survivors (n = 32)	Survivors (n = 32)	p-value	Nmiss (%)
Age (years), mean ± SD	63.64 ± 15.50	66.59 ± 15.58	60.69 ± 15.08	0.13	–
Female n(%)	38 (59.4)	20 (62.5)	18 (56.2)	0.80	–
BMI (kg/m^2), Median IQR	27.70 [23.55, 32.15]	26.20 [23.62, 32.47]	28.45 [23.58, 31.92]	0.62	–
Race n(%)					14 (21.9)
Asian	3 (6.0)	1 (4.3)	2 (7.4)	0.23	
Black	10 (20.0)	2 (8.7)	8 (29.6)		
Other	13 (26.0)	8 (34.8)	5 (18.5)		
White	24 (48.0)	12 (52.2)	12 (44.4)		
Hispanic	1 (2.9)	0 (0.0)	1 (4.8)	>0.99	30 (46.9)
PMH n(%)					
Diabetes	10 (15.9)	4 (12.9)	6 (18.8)	0.77	1 (1.6)
Hypertension	37 (58.7)	19 (61.3)	18 (56.2)	0.88	1 (1.6)
COPD	13 (20.6)	6 (19.4)	7 (21.9)	>0.99	1 (1.6)
CVA	4 (6.3)	1 (3.2)	3 (9.4)	0.63	1 (1.6)
Any Cardiac Disease	21 (35.6)	8 (27.6)	13 (43.3)	0.32	5 (7.8)
Liver Disease	6 (10.3)	4 (14.3)	2 (6.7)	0.60	6 (9.4)
Kidney Disease	12 (19.0)	5 (16.1)	7 (21.9)	0.80	1 (1.6)
Cancer	12 (19.0)	7 (22.6)	5 (15.6)	0.70	1 (1.6)
Arrest characteristics					
Presumed Cardiac Etiology n(%)	36 (61.0)	14 (48.3)	22 (73.3)	0.09	5 (7.8)
Location, OHCA n(%)	52 (81.2)	24 (75.0)	28 (87.5)	0.34	–
Arrest Witnessed n(%)	44 (74.6)	20 (69.0)	24 (80.0)	0.50	5 (7.8)
Bystander CPR provided n(%)	50 (82.0)	25 (83.3)	25 (80.6)	>0.99	3 (4.7)
Shockable Rhythm n(%)	29 (45.3)	8 (25.0)	21 (65.6)	<0.01	–
STEMI present n(%)	12 (21.4)	4 (14.8)	8 (27.6)	0.40	8 (12.5)
First post ROSC lactate (mmol/L) Median IQR	3.76 (3.26)	3.35 [2.23, 4.65]	2.50 [1.35, 4.00]	0.09	3 (4.6)
Duration of CPR (minutes) Median IQR	15.0 [9.0, 22.0]	18.50 [10.50, 30.00]	14.00 [8.75, 19.25]	0.04	–
Post-arrest care					
Sedation on at anytime n(%)	64 (100.00%)	32 (100.0)	32 (100.0)	NA	
Proportion of time on sedation %(median, IQR)**	100.00 (100.00, 100.00)	100.0(100.0, 100.0)	100.0 (100.0, 100.0)	0.06	
Pressors on at anytime n(%)	45 (70.3%)	28 (87.5%)	17 (53.1%)	0.01	
Proportion of time on pressor %(median, IQR)	90.0 (43.0, 100.0), n = 45	96.8 (55.4, 100.0), n = 28	89.1 (33.9, 100.0) n = 17	0.45	
Temperature °C(median, IQR)	35.0 (34.2, 35.9)	35.0 (33.8, 36.0)	35.1 (34.6, 35.9)	0.86	
Mean pH (SD) over 24 h	7.34 (0.08)	7.32 (0.09)	7.35 (0.07)	0.14	–
Receiving enteral nutrition	0	0	0	NA	–
Receiving bicarbonate infusion	0	0	0	NA	–

* All percentages exclude missing values. For the variable race 9 nonsurvivors and 5 survivors were missing and not taken into account. Ethnicity was missing data from 19 nonsurvivors and 11 survivors. The following variables had missing information from the non survivor group only: hypertension, COPD, and CVA. Information on cardiac disease, cardiac etiology, witnessed arrest, and reperfusion was missing from 3 non survivors and 2 survivors. Only 1 non survivor was missing information on cancer history. There was missing information bystander CPR and lactate for 2 nonsurvivors and 1 survivor. Lastly, there was missing information on STEMI from 5 nonsurvivors and 3 survivors.

** Out of 64, 55 patients were on sedation 100% of the time. Of the remaining 9 patients who were not on sedation 100% of the time, 7 were from the non-survivor group (with a mean proportion of time on sedation = 71%), and 2 were from the survivor group (with a mean proportion of time on sedation = 92%).

with higher adjusted AUC-RER over the first 12 h after ROSC, compared with patients with a lower AUC-RER. This association did not persist over 24 h. Survival was also significantly higher in patients with a median AUC-RER > 0.7 compared with patients with a median AUC-RER < 0.7, both in the initial hour of data collection and in the first 12 h after ROSC.

We previously reported findings from a 17-person pilot study utilizing the same methodology as the current study, suggesting that both higher AUC-VO_2 in the first 12 h after ROSC from cardiac arrest and an initial RER measurement $\geq$ 0.7 were associated with better survival.[11] The aim of the present study was to validate our earlier findings. While we were not able to validate the association between VO_2 and survival in the current study, we again found a high rate of very low RER in this post-arrest cohort, with almost 50% of patients having median values below 0.7, which is generally regarded as the lower limit of normal. We also found that an RER > 0.7 in the initial hours post-ROSC was associated with survival.

The physiology underlying these findings and their clinical significance are not clear. While some past investigators have excluded metabolic measurements outside of the normal physiologic range, we only kept such values if steady state was maintained for at least 30 min, and similar findings have been reported in an animal model of cardiac arrest using technology for metabolic measurements designed specifically for the rat model.[12] In that study, the investiga-

Table 2 – Medians and interquartile ranges for the area under the curve for metabolic parameters over the first 12 and 24 h after ROSC.

	12 h (n = 43)	24 h (n = 64)
	($n_{survived}$ = 19, $n_{non\text{-}survivor}$ = 24)	($n_{survived}$ = 32, $n_{non\text{-}survivor}$ = 32)
AUC-VO2		
	Median (IQR)	
Survivors	3.7 (3.1, 4.4)	3.2 (2.9, 4.0)
Non-survivors	3.4 (3.0, 4.2)	3.4 (2.9, 4.1)
AUC-VCO2		
	Median (IQR)	
Survivors	2.6 (2.3, 3.1)	2.4 (2.0, 2.9)
Non-survivors	2.4 (2.1, 2.9)	2.4 (1.9, 2.7)
AUC-RER		
	Median (IQR)	
Survivors	0.72 (0.70, 0.77)	0.69 (0.68, 0.73)
Non-survivors	0.68 (0.67, 0.70)	0.68 (0.65, 0.71)

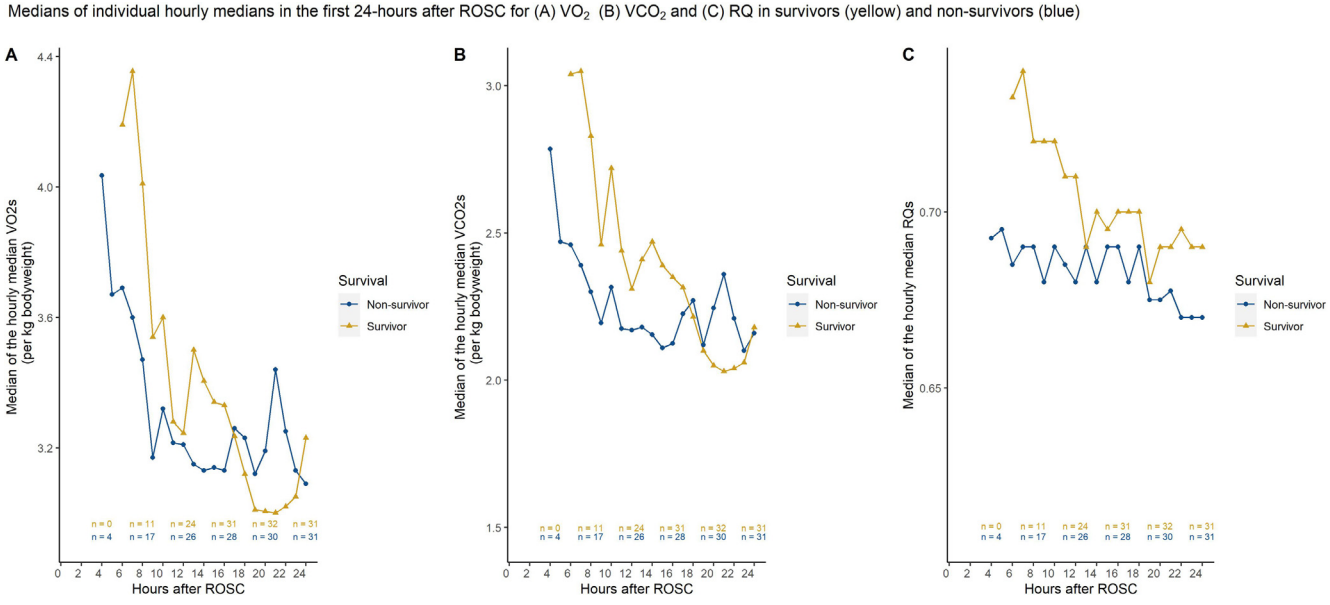

Fig. 2 – Metabolic data in survivors and nonsurvivors over time, presented as medians at each hour after ROSC. The number (n) of participants with metabolic data at each time point is presented at the bottom of each graph.

tors found a high proportion of RER measurements < 0.7 in rats after cardiac arrest. Post-resuscitation VO_2 in rats was elevated, while VCO_2 did not rise in equal measure, leading to decreased RER, a finding the authors hypothesized could reflect an increase in nonmitochondrial respiration. Associations between VO_2, RER, and survival were not examined in that study.

Observational studies have found that higher RER during or immediately after high-risk surgery is associated with a higher risk of post-operative complications and predictive of higher serum lactate.[22,23] Prior study authors have hypothesized that the RER is a point-of-care, noninvasive way to assess for the shift to anerobic metabolism, by detecting a relative decrease in VO_2 compared with CO_2 production. Trial data is more limited, but in at least one randomized trial, intraoperative management informed by RER measurements did not affect patient outcomes.[24] Our postarrest data, suggesting a possible association between higher RER and *better* outcome differs from the prior surgical data, pointing to possible important differences in postarrest oxygen metabolism compared with metabolism in surgical patients. Whether mitochondrial injury after cardiac arrest might lead to adaptive or maladaptive changes in oxygen metabolism is not clear, but the unusual prevalence of low RER warrants exploration of this possibility.

The RER provides insight into substrate utilization and mitochondrial respiration, and the frequency of RER values lower than the normal range suggests either a shift to different substrate utilization or reliance on alternative pathways for oxygen utilization. One possible explanation for RER values < 0.7 is ketosis, a metabolic state that is known to cause RERs in this range as fat is the primary fuel source in the ketotic state.[25–27] Ketosis has been found to be neuroprotective in animal models of stroke and cardiac arrest, but this does not necessarily contradict the finding that lower RER is associated with worse survival if the shift to ketosis is an adaptive response to more

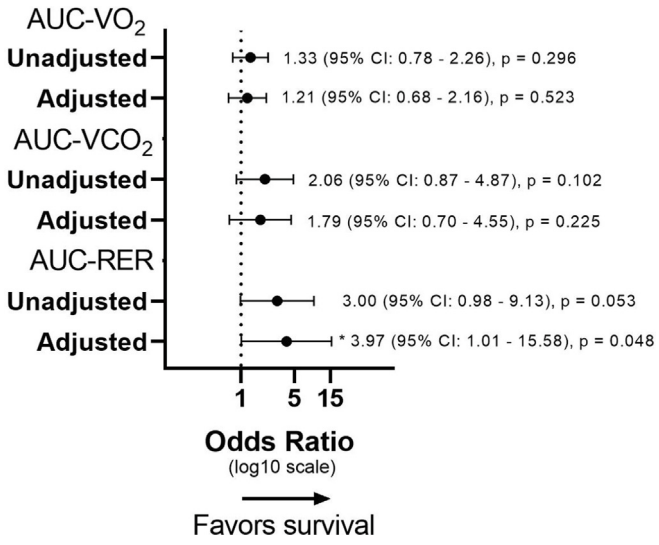

Fig. 3 – The unadjusted and adjusted odds ratio for survival status for unit increases in AUC-VO_2, AUC-VCO_2, and 0.1 unit increase in AUC-RER over 12 h after return of spontaneous circulation. * Indicates statistical significance. AUC-VO_2; area under the curve oxygen consumption, AUC-VCO_2; area under the curve carbon dioxide production, AUC-RER; area under the curve respiratory quotient, CI; Confidence interval.

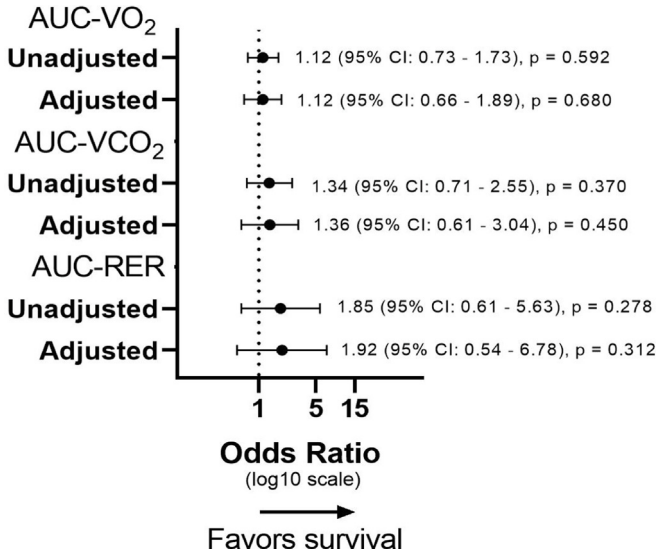

Fig. 4 – The unadjusted and adjusted odds ratio for survival status for unit increases in AUC-VO_2, AUC-VCO_2, and 0.1 unit increase in AUC-RER over 24 h after return of spontaneous circulation. AUC-VO_2; area under the curve oxygen consumption, AUC-VCO_2; area under the curve carbon dioxide production, AUC-RER; area under the curve respiratory quotient, CI; Confidence interval.

severe injury. An increased reliance on non-mitochondrial respiration in patients with significant mitochondrial injury has also been suggested, as noted above.

The association between a higher adjusted AUC-RER and survival after cardiac arrest raises the question of whether treatments that could restore or support disrupted metabolic pathways would be beneficial. Alternatively, if the decrease in RER indicates an adaptive shift in metabolism in patients with severe injury, then trying to reverse that process may not alter outcomes or could even be harmful. RER, as a ratio of VCO_2:VO_2, may be a better tool than either individual measurement for detecting subtle but possibly clinically important differences in gas metabolism. The early difference that disappears after 12 h suggests that a larger study focusing data collection over the first 12 or even 6 h after ROSC could be informative. Similar to what has been posited for temperature control after cardiac arrest, it is possible that metabolic changes are most apparent, and perhaps have most potential as a therapeutic target, very early in the post-arrest period. Notably, our prior trials of ubiquinol, thiamine and neuromuscular blockade after cardiac arrest have not been able to demonstrate an effect of these agents on VO_2 or RER, so whether these metabolic values are modifiable with treatment in critically ill postarrest patients is not clear.[13–16]

This study has several limitations. First, due primarily to the need to obtain informed consent, we were only able to collect metabolic

data on a small number of patients in the iitial 6–8 h after ROSC, and future studies conducted with a waiver of consent to facilitate early data collection would be useful. There are many patient and monitor level factors that can cause artifact within the data and lead to erroneous metabolic measurements, some of which may not have been fully accounted for by our cleaning algorithm. Due to sample size we were also limited in the number of variables we could adjust for, and it is possible that some patient or cardiac arrest characteristics for which we could not adjust drove both the RER differences and the mortality. Many patients were coenrolled in randomized trials of ubiquinol, thiamine or continuous neuromuscular blockade, agents that theoretically could affect metabolic data. However, in all of these trials no significant difference in metabolic values was found between study groups.[13–16] Additionally, although none of the participants were receiving enteral nutrition or TPN during metabolic data collection, differences in prearrest nutritional status could affect metabolic data. Similarly, although mean pH was similar over 24 h in both groups and no patients were documented to receive intravenous bicarbonate, variations in some of these physiologic parameters over time could potentially have an effect on metabolic measurements as well.

Conclusion

There were no significant associations between median AUC-VO_2 or AUC-VCO_2 and survival in the first 12 and 24 h after ROSC. RER was unusually low in nearly half of the patients and higher AUC-RER in the first 12 h after ROSC was associated with survival in adjusted analysis. Survival was significantly lower in patients with median AUC-RER < 0.7, compared with patients with values above this range. The etiology and clinical significance of this finding remain unclear.

Conflicts of interest

Use of monitors and modest project support for this investigator-initiated study was provided by a grant from General Electric.

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Ethics board approval

This study was approved by the Beth Israel Deaconess Medical Center Internal Review Board.

CRediT authorship contribution statement

Meredith G. Shea: Writing – review & editing, Writing – original draft, Conceptualization. **Lakshman Balaji:** Writing – review & editing, Methodology, Formal analysis, Data curation. **Anne V. Grossestreuer:** Writing – review & editing, Methodology, Formal analysis, Data curation, Conceptualization. **Mahmoud S. Issa:** Writing – review & editing, Investigation, Data curation. **Jeremy Silverman:** Writing – review & editing, Investigation, Data curation. **Franklin Li:** Writing – review & editing, Investigation, Data curation. **Michael W. Donnino:** Writing – review & editing, Methodology, Funding acquisition, Conceptualization. **Katherine M. Berg:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resplu.2024.100667.

Author details

[a]*Center for Resuscitation Science, Department of Emergency Medicine, Beth Israel Deaconess Medical Center, 1 Deaconess Road, Rosenberg 2, Boston, MA 02215, USA* [b]*Department of Emergency Medicine, Beth Israel Deaconess Medical Center, 1 Deaconess Road, Rosenberg 2, Boston, MA 02215, USA* [c]*Division of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, Beth Israel Deaconess Medical Center, 1 Deaconess Road, Rosenberg 2, Boston, MA 02215, USA*

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