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# Skeletal muscle oxygenation during cardiopulmonary resuscitation as a predictor of return of spontaneous circulation: a pilot study

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## Abstract

**Background** Near-infrared spectroscopy (NIRS) provides regional tissue oxygenation ( $rSO_2$ ) even in pulseless states, such as out-of-hospital cardiac arrest (OHCA). Brain  $rSO_2$  seems to be important predictor of return of spontaneous circulation (ROSC) during cardiopulmonary resuscitation (CPR). Aim of our study was to explore feasibility for monitoring and detecting changes of skeletal muscle  $rSO_2$  during resuscitation.

**Methods** Skeletal muscle and brain  $rSO_2$  were measured by NIRS (SenSmart Model X-100, Nonin, USA) during CPR in adult patient with OHCA. Start (basal)  $rSO_2$ , maximal during CPR (maximal) and difference between maximal–minimal  $rSO_2$  ( $\Delta rSO_2$ ), were recorded. Patients were divided into ROSC and NO-ROSC group.

**Results** 20 patients [age: 66.0ys (60.5–79.5), 65% male] with OHCA [50% witnessed, 70% BLS, time to ALS 13.5 min (11.0–19.0)] were finally analyzed. ROSC was confirmed in 5 (25%) patients. Basal and maximal skeletal muscle  $rSO_2$  were higher in ROSC compared to NO-ROSC group [49.0% (39.7–53.7) vs. 15.0% (12.0–25.2),  $P = 0.006$ ; 76.0% (52.7–80.5) vs. 34.0% (18.0–49.5),  $P = 0.005$ , respectively]. There was non-linear cubic relationship between time of collapse and basal skeletal muscle  $rSO_2$  in witnessed OHCA and without BLS ( $F$ -ratio = 9.7713,  $P = 0.0261$ ). There was correlation between maximal skeletal muscle and brain  $rSO_2$  ( $n = 18$ ,  $\rho = 0.578$ ,  $P = 0.0121$ ).

**Conclusions** Recording of skeletal muscle  $rSO_2$  during CPR in patients with OHCA is feasible. Basal and maximal skeletal muscle  $rSO_2$  were higher in ROSC compared to NO-ROSC group.

*Clinical trial registration number* ClinicalTrials.gov, NCT04058925, registered on: 16th August 2019. URL of trial registry record: <https://www.clinicaltrials.gov/ct2/show/NCT04058925?titles=Tissue+Oxygenation+During+Cardiopulmonary+Resuscitation+as+a+Predictor+of+Return+of+Spontaneous+Circulation&draw=2&rank=1>.

**Keywords** Near-infrared spectroscopy, Tissue oxygenation, Skeletal muscle, Brain, cardiac arrest, Return of spontaneous circulation

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## Background

Out of hospital cardiac arrest (OHCA) is a major cause of morbidity and mortality around the world [1]. Despite the progress in medicine, new devices and research, there was no great breakthrough in recent years [2]. There are numerous factors that have influence on the outcome of cardiopulmonary resuscitation (CPR) in OHCA. It is usually impossible to predict whether the resuscitation will be successful or not, especially in early stages of cardiac arrest [3].

Near-infrared spectroscopy (NIRS) is a noninvasive optical technique that uses light in near-infrared spectrum of electromagnetic wave (700–1300 nm) [4, 5]. NIRS can be used to assess tissue oxygenation, oxygen consumption and blood flow in various tissues, including brain and skeletal muscle [6–8]. NIRS has an advantage over pulsatile oximetry, because it can be used in situations, where there is no blood flow [9]. With NIRS we measure oxygen saturation in all vessels that are smaller in diameter than 1 mm (arterioles, capillaries, venules) [4, 10]. Most of the signal comes from capillaries, because they represent majority of vessels in the tissue [6].

During cardiac arrest and during CPR the blood flow through the brain is absent or significantly reduced. Brain injury is major cause for neurologic disability after successful resuscitation [4, 7, 10]. With the placement of NIRS probes on the forehead region, regional tissue oxygen saturation ( $rSO_2$ ) in superficial areas of frontal brain lobes is measured. Current data confirms that increase of brain  $rSO_2$  is associated with higher probability of return of spontaneous circulation (ROSC) [4, 7, 9–12]. Different values of basal brain  $rSO_2$  or different values of brain  $rSO_2$  increase were associated with higher probability of ROSC. Genbrugge et al. reported that absolute increase of  $rSO_2$  for 15% or more was associated with ROSC. They also noticed that increase in  $rSO_2$  beyond 1 min after initiation of  $rSO_2$  measurement was associated with more favorable long-term neurologic outcome [13]. Parnia et al. have shown that all patients with ROSC had mean brain  $rSO_2$  of 35% or higher. A rise of brain  $rSO_2$  from baseline was associated with ROSC and values remaining below 30% most of the period of CPR predicted that ROSC will not be achieved [12]. Recent meta-analysis has confirmed prognostic value of brain tissue oxygenation [14].

During cardiac arrest there is no blood flow, the consequence is lower oxygen values in all tissues [15, 16]. Skeletal muscles are not part of vital organs and flow through them is decreased in critical states. In critically ill we currently monitor skeletal muscle  $rSO_2$  in patients with shock or in patients on different types of circulatory mechanical support [8, 17]. We have previously shown

that skeletal muscle  $rSO_2$  can predict adequacy of flow (i.e., mixed venous oxygenation) in patients with shock with preserved oxygen extraction; it can also be used to track effects of therapy [8, 18]. Despite new NIRS technologies and design of probes, skeletal muscle  $rSO_2$  monitoring remains technically more reliably compared to brain  $rSO_2$ , because skeletal muscle is covered with a thin layer of skin and subcutis compared to brain, which is hidden in the skull and floating in the cerebrospinal fluid [19]. A short paper already reported an illustrative case series of skeletal muscle  $rSO_2$  use in five patients in the emergency department, showing fast response of skeletal muscle  $rSO_2$  value to loss or return of pulse [15].

Aim of our study is to test feasibility to monitor skeletal muscle  $rSO_2$  during CPR after OHCA and to assess changes of skeletal muscle  $rSO_2$  during CPR and after ROSC. In addition, we want to explore the relationship between skeletal muscle and brain  $rSO_2$ .

## Methods

### Study design and setting

The single-center, prospective, non-randomized and observational study was conducted at a prehospital area that is covered by the Emergency Unit of Community Health Centre Ljubljana and the Rescue station of University Medical Centre Ljubljana during September 2019 and May 2022. The prehospital area has 1670 km<sup>2</sup> and provides emergency services for around 450.000 inhabitants and additionally over 60.000 daily working migrants.

The research protocol received approval by Slovenian Medical Ethics Committee (No. 0120-334/2019/3); patients' consent was waived because of the observational nature of the study and emergency setting. Study protocol was registered at clinicaltrials.gov (NCT04058925).

### Study intervention

All patients with non-traumatic cardiac arrest aged 18 or more were eligible for inclusion. Excluded patient were as follows: age below 18 years, pregnant women, traumatic cardiac arrest, hypothermic patient, drowned patient, patient who had additional extracorporeal CPR, patients who had achieved ROSC before the placement of NIRS device probes on the skin and if it was not possible to place NIRS probes on the patient within 5 min after start of ALS algorithm. Criteria for additional extracorporeal CPR are (all must be fulfilled): age < 55 years, witnessed cardiac arrest, appropriate BLS before ALS, primary shockable rhythm, unsuccessful advance life support resuscitation for at least 30 min (i.e., sustained/resistant ventricular fibrillation), estimated time to implantation of extracorporeal device less than 60 min from the time of collapse.

The team of doctor and two medical rescuers were dispatched by a health dispatcher after receiving information of a patient not showing signs of life. The doctor led resuscitation according to European Resuscitation Council guidelines for Advanced Life Support (ALS) [20, 21]. Immediately upon arrival, the prehospital team started with the ALS algorithm.

**Tissue oxygenation measurement**

As soon as possible, one of the team members placed NIRS probes on the patient. NIRS device (SenSmart Model X-100, Nonin Medical, Inc. Plymouth, Minnesota, USA), which records rSO<sub>2</sub> every 4 s, and disposable self-adhesive probes (SenSmart Nonin Medical, Inc. Plymouth, Minnesota, USA) were used. Each probe was marked with color and always placed on the same part of the body: blue probe for brain and yellow for skeletal muscle. The blue probe for measuring brain rSO<sub>2</sub> was placed on the patient’s right side of forehead and the yellow probe to the patient’s right hand thenar to measure skeletal muscle rSO<sub>2</sub>. The patient’s thenar was used due to our previous experimental and clinical experience [8]. The probes were additionally fixed with medical grade adhesive tape to avoid discontinuation of measurements. The NIRS device screen was not covered, so the team members could fix probe position in case of bad contact. As consequence this study was unblinded. However, teams had instructions that measured rSO<sub>2</sub> values must not influence decisions made by the resuscitation team regarding termination of resuscitation or continuing one. The measurement stopped when the patient was admitted to the Emergency department or when the doctor declared death of the patient and CPR was terminated [22]. Return of spontaneous circulation (ROSC) was defined as return of spontaneous palpable

pulse and or breathing, coughing, movement of the patient, rise of etCO<sub>2</sub> for more than 30 s [22].

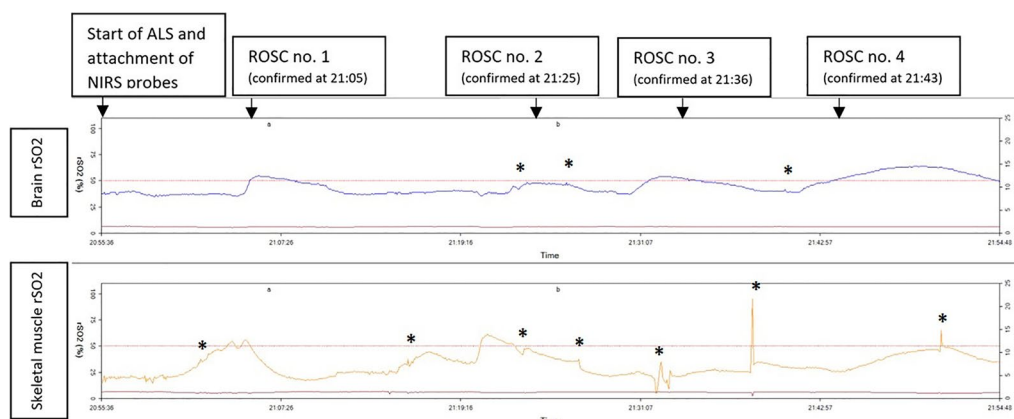
After intervention data were downloaded from the NIRS device by especially dedicated software (SenSmart, Version 1.0.1.0, Nonin Medical Inc., Minneapolis, MN USA) and paired with information from the intervention protocol. One of the graphs with measurements is presented in Fig. 1. Basal rSO<sub>2</sub> was defined as an average of 4 measurements (average of rSO<sub>2</sub> values in 16 s) of brain and skeletal muscle rSO<sub>2</sub> after signal stabilization (approximately 12–16 s) after NIRS probes placement. We also recorded maximal rSO<sub>2</sub> value during the CPR, difference between maximal–minimal rSO<sub>2</sub> value (delta-rSO<sub>2</sub>), value of rSO<sub>2</sub> at ROSC or the end of CPR with no-ROSC (end-CPR rSO<sub>2</sub>). rSO<sub>2</sub> value of end-CPR rSO<sub>2</sub> was average of 4 (16 s) measurements just before ROSC was confirmed or the resuscitation was terminated. Spiking signals, which were out of trend of the NIRS measurements, were considered as artefacts (Fig. 1) and we not included in analysis.

**Additional data**

The following additional data were recorded: basic demographic data (age, gender), the time of call to emergency telephone number (112), the time of arrival of the emergency team on scene, the time of ROSC/time of death, duration of CPR, was cardiac arrest witnessed, were eyewitnesses doing BLS (basic life support), the first ECG rhythm, use of AED, intubation status, number of defibrillations, cumulative dose of used adrenaline, ECG rhythm at the end of CPR/intervention and 28-day survival.

**Primary outcome**

Primary outcome was feasibility of skeletal muscle rSO<sub>2</sub> measurement; how demanding is it to apply NIRS probes



**Fig. 1** Graph example from one of CPRs with several ROSC (\* marks artefact)

on two sites, what are the main problems of losing signal, how to fix the probes not to lose the signal.

**Secondary outcome**

The secondary outcome was to find out if there are any changes in measured skeletal muscle rSO<sub>2</sub> during CPR and before/after ROSC. We also want to test the relationship between basal skeletal muscle rSO<sub>2</sub> and time to start ALS in patients with witnessed cardiac arrest and without BLS. We also want to test relationship between skeletal muscle and brain rSO<sub>2</sub>.

Power analysis: no previously published data were available for specific NIRS device used in our study, that is why absolute difference of mean skeletal muscle rSO<sub>2</sub>=20% (SD 10%) between patients with ROSC and no-ROSC (ratio of sample size 1:3) was estimated in the first 10 recruited patients. For estimated error (Type I. error of 0.05, Type II. error of 0.20) total sample size of 16 patients (4 in ROSC, 12 in no-ROSC group) would be necessary.

**Statistical analysis**

The study population was divided into 2 groups according to outcome: ROSC and no-ROSC group. Continuous data were summarized as median (25th–75th quartile) compared by Mann–Whitney test for independent and Wilcoxon test for paired samples. Non-continuous data were summarized as the count (percentage). Chi-square test was used to compare non-continuous data. Rank correlation with Spearman’s coefficient (rho) was used to test relationships between variables. Linear and non-linear regression methods was also used to test relationship between variables. MedCalc® ver. 20.104 (MedCalc Software Ltd) software was used for the statistical analysis. *P* value<0.05 was regarded as statistically significant.

**Results**

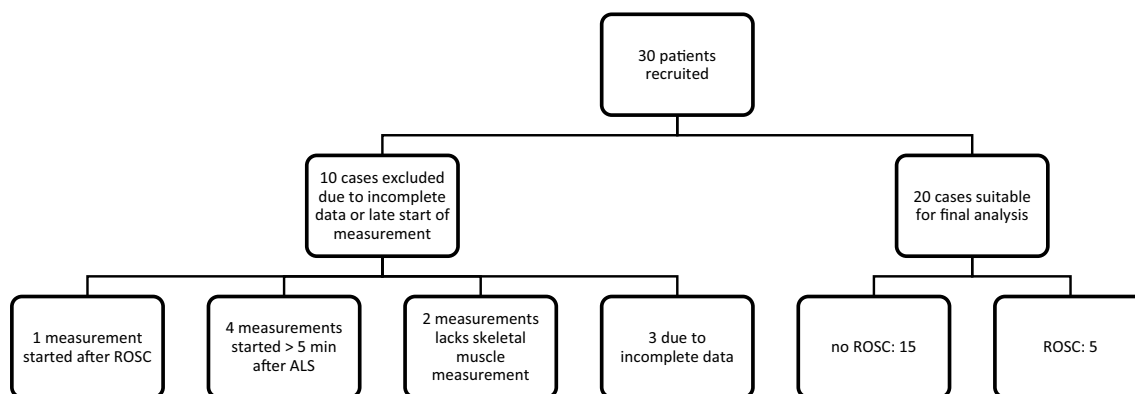
Thirty patients were recruited. Ten patients were excluded due to different technical problems or violation of study protocol (Fig. 2): two patients due to disconnection of NIRS probe and consequent loss of skeletal muscle rSO<sub>2</sub> signal during CPR; in four patients the probes were applied more than 5 min after arrival to the patient; in one patient probes were applied after ROSC; three patients were excluded due to irregular rSO<sub>2</sub> signals, which have not allowed to determine predefined checkpoints.

Twenty patients with skeletal muscle rSO<sub>2</sub> data were finally analyzed. In these patients, one patient had only skeletal muscle and no brain rSO<sub>2</sub> recordings. Both skeletal muscle and brain rSO<sub>2</sub> were recorded in 19 patients.

Basic demographic data, data about arrest and CPR are presented in Table 1. Twenty patients [age: 66.0 years (60.5–79.5), 65% male] with OHCA (50% witnessed, 70% with BLS), time to advance life support (ALS) 13.5 min (11.0–19.0) were finally analyzed. Cumulative dose of adrenaline was higher in no-ROSC group.

Measurement of skeletal muscle rSO<sub>2</sub> and brain rSO<sub>2</sub> are presented in Table 2. There was no statistically significant difference between the basal skeletal muscle and the basal brain rSO<sub>2</sub> (17.5 (12.8–26.0) vs. 31.0 (15.8–41.6), *P*= 0.1674, respectively). Basal, maximal and end-CPR skeletal muscle rSO<sub>2</sub> were higher in ROSC compared to no-ROSC group (49.0% (39.7–53.7) vs. 15.0% (12.0–25.2), *P*= 0.006; 76.0% (52.7–80.5) vs. 34.0% (18.0–49.5), *P*= 0.005; 72.0% (48.7–74.7) vs. 16.0% (12.0–35.0), *P*= 0.002, respectively) (Fig. 3). Delta rSO<sub>2</sub> for skeletal muscle was not significantly different in patients with ROSC and no-ROSC group.

Basal brain rSO<sub>2</sub> did not differ between ROSC and no-ROSC (38.0% vs. 29.5% (14.5–42.5), *P*= 0.4). Maximal, delta-rSO<sub>2</sub> and end-CPR brain rSO<sub>2</sub> were



**Fig. 2** Flowchart of patients included in the study

**Table 1** Basic demographic and cardiac arrest data

	All (n = 20)	ROSC (n = 5)	No ROSC (n = 15)	Statistics p
Age (years), median (interquartile range)	66.0 (60.5–79.5)	54.0 (48.75–69.75)	67.0 (63.5–80.25)	0.1152
Gender, male, n (%)	13 (65%)	5 (100%)	8 (53%)	0.0648
Witnessed arrest, n (%)	10 (50%)	1 (20%)	9 (60%)	0.1311
Bystander BLS, n (%)	14 (70%)	4 (80%)	10 (67%)	0.5829
Time to ALS (min), median (interquartile range)	13.5 (11.0–19.0)	18 (9.5–21.0)	13 (11.25–16.75)	0.7263
Primary rhythm				
VF	7 (35%)	1 (20%)	6 (40%)	0.95
Asystole	10 (50%)	3 (60%)	7 (47%)	0.88
PEA	3 (15%)	1 (20%)	2 (13%)	0.69
Cumulative dose of adrenalin (mg), median (interquartile range)	4,5 (3.0–6.5)	2 (0.75–4.5)	5 (3.25–7.0)	0.0432
Number of defibrillators, median (interquartile range)	1 (0–3)	1 (0–2.25)	1 (0–3.75)	0.8186
Orotracheal intubation, median (interquartile range)	1 (1–2)	1 (1–2)	1 (1–2)	1.0
Duration of ALS (min), median (interquartile range)	30 (15–47.5)	11 (5.5–16)	34 (24–54.75)	0.0034
28-Day survival, number (%)	1 (5%)	1 (20%)	0 (0%)	0.08

BLS, basic life support; ALS, advanced life support; VF, ventricular fibrillation; PEA, pulseless electrical activity

**Table 2** Skeletal muscle and brain regional tissue oxygenation during CPR

	Skeletal muscle				Brain			
	All (n = 20)	ROSC (n = 5)	No ROSC (n = 15)	p	All (n = 19)	ROSC (n = 3)	No ROSC (n = 16)	p
Basal rSO <sub>2</sub> (%)	20.5 (14.0–32.0)	49.0 (39,7–53,7)	15.0 (12.0–25.2)	0.006	31.0 (15.8–41.6)	38.0	29.5 (14.5–42.5)	0.4
Maximal rSO <sub>2</sub> (%)	44.0 (27.0–54.0)	76.0 (52.7–80.5)	34.0 (18.0–49.5)	0.005	45.0 (32.0–58.6)	77	42.0 (30.5–53.0)	0.01
Delta rSO <sub>2</sub> (%)	15.5 (6.0–26.0)	26.0 (13.2–32.2)	9.0 (5.0–24,5)	0.3	14.0 (7.8–18.2)	27	10.5 (6.0–15.0)	0.007
End-CPR rSO <sub>2</sub> (%)	31.0 (13.0–47.0)	72.0 (48.7–74.7)	16.0 (12.0–35.0)	0.002	47.5 (32.5–54.6)	77	39.0 (29.7–52.7)	0.01

Data are presented as median (interquartile range)

Basal rSO<sub>2</sub>, rSO<sub>2</sub> at the beginning of CPR; Maximal rSO<sub>2</sub>, the highest rSO<sub>2</sub> during CPR; Delta rSO<sub>2</sub>, difference between maximal and minimal rSO<sub>2</sub> during CPR; end-CPR rSO<sub>2</sub>, rSO<sub>2</sub> at the end of CPR

higher in ROSC compared to no-ROSC group (77% vs. 42.0% (30.5–53.0),  $P = 0.01$ ; 27% vs. 10.5% (6.0–15.0),  $P = 0.007$ ; 77% vs. 39.0% (29.7–52.7),  $P = 0.01$ , respectively) (Table 2).

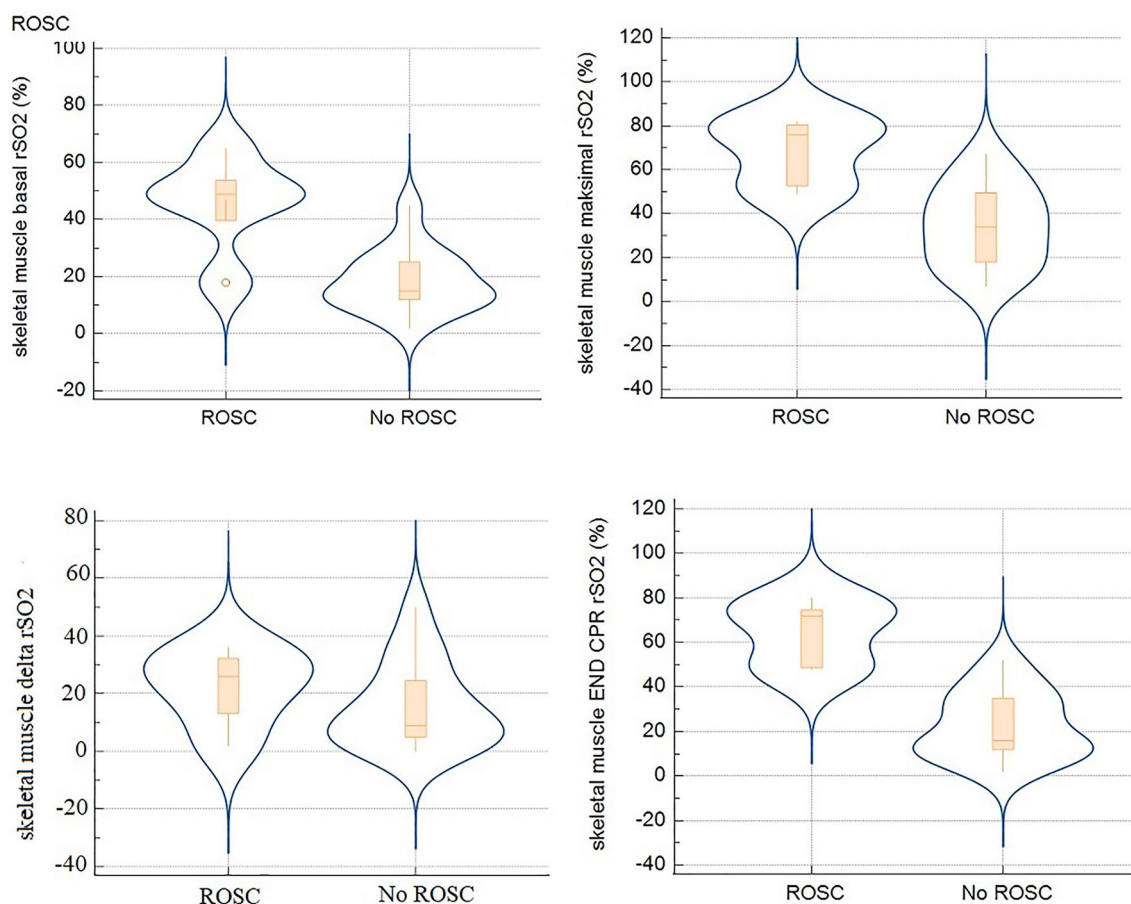
There was non-linear cubic relationship between duration of collapse to establishment of NIRS monitoring and basal skeletal muscle rSO<sub>2</sub> in witnessed OHCA and without BLS (F-ratio = 9.7713,  $P = 0.0261$ ) (Fig. 4).

There was no correlation between basal rSO<sub>2</sub>, delta-rSO<sub>2</sub> and end-CPR rSO<sub>2</sub> of skeletal muscle and brain. There was a correlation between maximal skeletal muscle and brain rSO<sub>2</sub> ( $n = 18$ , rho: 0.578,  $P = 0.0121$ ), which was confirmed also in linear regression model ( $y = 25.245 + 0.499 x$ ,  $r = 0.63$ ,  $P = 0.005$ ) (Fig. 5).

## Discussion

The study confirmed the feasibility of monitoring skeletal muscle rSO<sub>2</sub> in OHCA. Patients with ROSC had higher skeletal muscle rSO<sub>2</sub> at the start of ALS (basal rSO<sub>2</sub>) and during CPR (maximal rSO<sub>2</sub>). There was a non-linear cubic relationship between basal rSO<sub>2</sub> and time from collapse to start of rSO<sub>2</sub> monitoring. There was also a linear relationship between the maximal values of skeletal muscle and brain rSO<sub>2</sub>.

During cardiac arrest there is decrease of rSO<sub>2</sub>, the value of decrease depends on the duration of no-flow/low flow and oxygen consumption of the tissue [8]. Basal skeletal muscle rSO<sub>2</sub> is a surrogate for estimating the time of tissue low/no flow. Our study has shown a relationship between duration of witnessed cardiac



**Fig. 3** Skeletal muscle tissue oxygenation (rSO<sub>2</sub>) at the beginning, during and at the end of CPR. basal rSO<sub>2</sub>—rSO<sub>2</sub> at the beginning of CPR, maximal rSO<sub>2</sub>—the highest rSO<sub>2</sub> during CPR, delta rSO<sub>2</sub>—difference between maximal and minimal rSO<sub>2</sub> during CPR, end-CPR rSO<sub>2</sub>—rSO<sub>2</sub> at the end of CPR

arrest and basal skeletal muscle rSO<sub>2</sub>, which was, however, not significant due to low number of patients, because only patients with witnessed cardiac arrest and without BLS were include in that analysis. Basal skeletal muscle rSO<sub>2</sub> were significantly different between ROSC and No ROSC groups, when all included patients were analyzed.

By rapid cuff inflation it is possible to stop flow through the arm, such as simulation of cardiac arrest, and evaluate skeletal muscle oxygen consumption. We have done this in patients with sepsis/septic shock and controls, aiming skeletal muscle rSO<sub>2</sub> to decrease to 40% [23]. The rate of StO<sub>2</sub> decrease during rapid cuff occlusion test was lower in septic shock patients compared to severe sepsis and controls (− 5 ± 2%/min vs. − 12 ± 2%/min vs. − 37 ± 7%/min, respectively; *P* < 0.001). In healthy volunteers we could measure rate of skeletal muscle rSO<sub>2</sub> decrease during no-flow for longer period of time without any major risk, to explore skeletal muscle rSO<sub>2</sub> kinetics and construct a normogram for estimating the duration of cardiac arrest for different age and gender groups.

In current study increase of skeletal muscle during resuscitation (delta rSO<sub>2</sub>) was not different between ROSC and No ROSC groups, this additionally emphasize the importance to start the resuscitation early as possible, when the basal skeletal muscle rSO<sub>2</sub> (tissue oxygenation) is also still relatively high.

By additional fixation we have improved the position of NIRS probe on the thenar allowing more stable signal monitoring. The problem was big probe size, compared to thenar and higher possibility of detachment while manipulating patient’s hand. This fixation completely removed the possibility of losing contact and consequently signal during rSO<sub>2</sub> monitoring even during different manipulations around and with the patient.

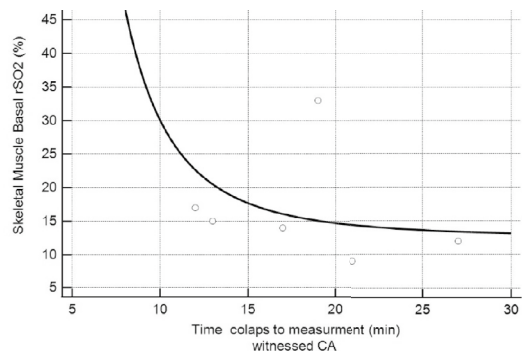
Despite the end of resuscitation (end-CPR rSO<sub>2</sub>) was different between ROSC and No-ROSC group, it is a very biased measure, since end-CPR by definition occurs much later in the no-ROSC group. This is a similar problem to the resuscitation-time bias seen in previous observational studies of the use of adrenaline during resuscitation from cardiac arrest [24–26]. End-CPR

Regression Equation (Analysis of Variance)

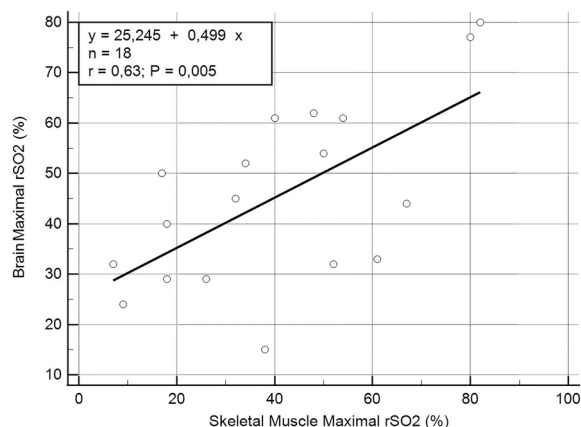
a/x^3+c			
Parameter	Coefficient	Std. Error	95% CI
a	17561,2552	5617,9575	3119,8356 to 32002,6749
c	12,5173	4,4711	1,0241 to 24,0106

F-ratio	9,7713
Significance level	P=0,0261



**Fig. 4** Relationship between time between collapse and Basal skeletal muscle rSO<sub>2</sub> in witnessed cardiac arrest. Regression Equation (Analysis of Variance)



**Fig. 5** Correlation between Maximal skeletal muscle and brain rSO<sub>2</sub> (n = 18, Spearman's coefficient of rank correlation (rho): 0.578, P = 0.0121, 95% CI for rho: 0.152 to 0.823)

rSO<sub>2</sub>, furthermore, is an impracticable measure that cannot be used in a clinical relevant setting, because of the obvious fact that we cannot predict ROSC.

Brain rSO<sub>2</sub> seems to be physiologically superior compared to other regional tissues. However, other rSO<sub>2</sub>, like kidney, are tested to give additional value to brain rSO<sub>2</sub> during resuscitation in pediatric population [27, 28]. Monitoring of skeletal muscle rSO<sub>2</sub> seem to

be technically more reliably compared to brain rSO<sub>2</sub>, especially due to brain location in the body [19].

Several NIRS devices are available for clinical use. They differ according to numerous aspects, which include the algorithms adopted, the type of light source, the wavelengths of light emitted, the number and distance between the light emitters and detectors [19]. For example, INVOS system (5100C Cerebral/Somatic Oximeter; Medtronic, MN, USA) uses near-infrared light at two wavelengths [29]. Light travels from the light emitting diode of the sensor to either a proximal or distal detector, which allows separate data processing of shallow and deep optical signals. Data from the scalp and the surface tissue are subtracted and suppressed by spatial resolution, which reflects the rSO<sub>2</sub> in deeper tissues [30]. The EQUANOX 7600 and also the SenSmart Model X-100 (Nonin Medical, MI, USA), the model that we have used, uses a dual light emitting and detecting sensor architecture, which has been shown to more effectively target the cerebral cortex and eliminate extracranial contamination from the scalp and skull. The Nonin system uses four wavelengths of near-infrared light. These added third and fourth wavelengths increase the accuracy of reporting the actual percent of oxygenated hemoglobin in the targeted tissues and can compensate for tissue factors that might otherwise reduce the accuracy of the measurements. This also allows the algorithm to reduce inter-subject variability, regardless of age, weight or skin color [30, 31]. We have previously shown high grade diversity of brain rSO<sub>2</sub>, with different NIRS devices, in patients with alkaptonuria, who had widespread tissue deposition of black pigment [19, 32, 33]. To guide our resuscitation efforts, we should probably not focus on only one modality, i.e., brain rSO<sub>2</sub>. Especially, because there is a report when good neurological outcome was achieved after prolonged CPR despite very low brain rSO<sub>2</sub> [34].

Skeletal muscle rSO<sub>2</sub> could also guide post-resuscitation care [17]. Continuous monitoring skeletal muscle rSO<sub>2</sub> is already used in trauma patients and identifies the severity of shock [35]. Skeletal muscle rSO<sub>2</sub> can track changes of systemic oxygen delivery during and after resuscitation of trauma patients or in patients heart failure patients/cardiogenic shock, who have preserved oxygen extraction [36]. New methods, such as near-infrared spectroscopy, which measures venous oxygen saturation in tissue from the near-infrared spectrum of the amplitude of respiration-induced absorption oscillations, may lead to the design of a non-invasive optical instrument capable of providing simultaneous and real-time measurements of local arterial, tissue and venous oxygen saturation.[37].

There was no statistically significant difference between the basal skeletal muscle and the basal brain  $rSO_2$ , despite we would expect lower basal brain  $rSO_2$  due to higher cerebral oxygen consumption in normal human subjects compared to resting skeletal muscle oxygen consumption [38, 39]. There was also a very wide spread of basal  $rSO_2$ . In pre-arrest state the patient could have centralization of flow to vital organ, and skeletal muscle  $rSO_2$  would be already low before cardiac arrest, as we previously have shown in patients with cardiogenic shock [8]. In our study, during resuscitation, there was lineal correlation between the maximal brain and skeletal muscle  $rSO_2$ .

Repeatability of skeletal muscle  $rSO_2$  with NIRS during vascular occlusion test was confirmed in previous studies [40].

### Limitations

Current study has at least four major limitations. First, the number of recruited patients is low despite long recruiting period. The main cause is the SARS-CoV-2 epidemics, during which the study was temporally stopped to minimize workload of staff in protective clothing. Second, the study was only single center study. Our data should be confirmed in a bigger prospective multicenter study. Third, low number of patients with ROSC, did not allow to study time change of skeletal muscle  $rSO_2$  during resuscitation and prognostic value of skeletal muscle  $rSO_2$  for good neurological outcome. The fourth, study was not designed to study use of skeletal muscle  $rSO_2$  as post-resuscitation therapy guide and non-invasive estimation of adequacy of flow. It should be done in other multicenter study.

### Conclusions

Recording of skeletal muscle  $rSO_2$  during CPR in patients with OHCA is feasible. Basal and maximal skeletal muscle  $rSO_2$  were higher in ROSC compared to no-ROSC group. Skeletal muscle  $rSO_2$  during cardiac arrest could provide additional data to brain  $rSO_2$  on duration of arrest and efficiency of resuscitation efforts.

### Abbreviations

NIRS	Near-infrared spectroscopy
OHCA	Out of hospital cardiac arrest
ROSC	Return of spontaneous circulation
CPR	Cardiopulmonary resuscitation
BLS	Basic life support
ALS	Advanced life support
$rSO_2$	Regional tissue oxygen saturation

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### Author contributions

Author contributions are as follows: primary author MK was involved in idea and setting the protocol, recruiting patients, analyzing data and drafting the manuscript; MP was involved in idea and setting the protocol, analyzing data and finalizing the manuscript; HM was involved in idea and setting the protocol, supervised the study, applied for funding and finalizing the manuscript. All authors read and approved the final manuscript.

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### Availability of data and materials

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Declarations

#### Ethics approval and consent to participate

The research protocol received approval by Slovenian Medical Ethics Committee (No. 0120-334/2019/3); patients' consent was waived because of the observational nature of the study and emergency setting.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare that they have no competing interests.

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