Sublingual microcirculation predicts survival after out-of-hospital cardiac arrest

Fabian Voß1 | Matthias Karbenn1 | Till Hoffmann2 | Julian Schweitzer1 | Christian Jung1 | Michael Bernhard3 | Peter Kienbaum4 | Malte Kelm1,5 | Ralf Westenfeld1

1Division of Cardiology, Pulmonology and Vascular Medicine, Medical Faculty, Heinrich-Heine University, Düsseldorf, Germany
2Institute of Transplantation Diagnostics and Cell Therapeutics, Medical Faculty, Heinrich Heine University, Düsseldorf, Germany
3Emergency Department, Medical Faculty, University Hospital, Heinrich-Heine University, Düsseldorf, Germany
4Department of Anesthesiology, Medical Faculty, Heinrich-Heine University, Düsseldorf, Germany
5CARID (Cardiovascular Research Institute Düsseldorf), Düsseldorf, Germany

Abstract

Background: Despite successful resuscitation with return of spontaneous circulation (ROSC), the prediction of survival in patients suffering out-of-hospital cardiac arrest (OHCA) remains difficult. Several studies have shown alterations in sublingual microcirculation in the critical ill. We hypothesized that early alterations in sublingual microcirculation may predict short-term survival after OHCA.

Methods: We prospectively included all adults admitted to our university hospital between April and September 2019 with ROSC following OHCA. Sidestream dark-field microscopy to obtain sublingual microcirculation was performed at admission and after 6, 12 and 24 hours. Primary outcome was survival until discharge.

Results: Twenty-five patients were included. Six hours after ROSC, the proportion of perfused small vessels (PPV_{small}) was lower in non-survivors than in survivors (85 ± 7.9 vs. 75 ± 6.6%; p = .01). PPV_{small} did not correlate with serum lactate. Stratification for survival with cutoff values >78.4% for PPV_{small} 6 h post-admission and <5.15 mmol/l for initial serum lactate as suggested by ROC-Analyses results in a positive predictive value of 100% and a negative one of 67% for our study population.

Conclusion: Estimating short-term prognosis of OHCA patients with ROSC may be supported by measuring the PPV_{small} at the sublingual microcirculation 6 hours after admission.

KEYWORDS
microcirculation, out-of-hospital cardiac arrest, survival

Abbreviations: aPTT, activated partial thromboplastin time; AU, arbitrary unit; AUC, area under the curve; CPR, cardiopulmonary resuscitation; ERC, European Resuscitation Council; GFR, glomerular filtration rate; ICU, intensive care unit; INR, international normalized ratio; MFI, microcirculatory flow index; NSE, neuron specific enolase; OHCA, out-of-hospital cardiac arrest; PEA, pulseless electric activity; PPV, proportional perfused vessels; PPV_{small}, proportional perfused small vessels; PVD, Perfused small vessel density; PVD_{small}, perfused small vessel density; ROC, receiver operating characteristics; ROSC, return of spontaneous circulation; SDF, sidestream dark-field illumination; STEMI, ST-segment elevation myocardial infarction; T1-T4, time points 1-4; TTM, target temperature monitoring; TVD, total vessel density; TVD_{small}, total small vessel density.

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1 | INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) remains a frequent cause of death worldwide with an incidence between 28 and 55 per 100,000 residents.1,4

After return of spontaneous circulation (ROSC), most patients are admitted comatose to an intensive care unit (ICU) where, according to current guidelines, target temperature monitoring (TTM), including the need for deep sedation, is initiated.5–7 During that time, prediction of short-term survival and neurological outcome remains challenging, creating stressful uncertainty among treating physicians and the patients' relatives, resulting in increased costs and extended use of rare resources of our health care systems.4,5

In the last decades, different biomarkers such as neuron specific enolase (NSE), initial serum lactate, initial serum pH or serum potassium levels were introduced as predictors of short-term survival.6–8 Additionally, electrophysiological tests as well as various imaging techniques provided information about the patient's neurological outcome.9,10 None of those for its own was able to predict survival or favorable neurologic outcome reliable. Furthermore, many of these parameters are only available after a time period of 48 to 72h post-cardiac arrest.12

In their 2015 guidelines, the European Resuscitation Council (ERC) summarized these findings in an algorithm to predict neurological outcome.5

Subsequent analyses showed a good prediction of poor outcome, but with a lack of sensitivity, creating large numbers of patients at "intermediate" risk, without clear-cut prognosis.13 No statement concerning short-term survival due to other reasons (e.g., persisting shock) is made by this algorithm. Taken together, we still lack robust parameters to improve decision making in treatment of patients after suffering an OHCA according to the projected outcome.

Post-cardiac arrest syndrome is characterized by alterations in blood coagulation and microvascular perfusion.14,15 Alterations of the sublingual microcirculation, assessed by sidestream dark-field illumination (SDF), were shown in the critical ill and also in patients after suffering a cardiac arrest.16,17

In this study, we hypothesized that early changes in sublingual microcirculation predict short-term survival after OHCA. In addition, we aimed to correlate alterations in sublingual microcirculation with observed parameters of the coagulation system.

2 | METHODS

2.1 | Study design and population

This study was a prospective observational, single-center study performed between April and October 2019 at university hospital Dusseldorf. The study was approved by the local institutional ethics board (2018–153-KFoGU). We included all consecutive adults with ROSC following OHCA for non-traumatic reason who were admitted to the intensive care unit. Patients were included if two independent physicians did not see any contraindication to assess the sublingual microcirculation. Written consent was obtained later if patients were able to consent or if available, from authorized relatives. In the remaining cases, it was proceeded according to the patient's suspected will after enlightenment of relatives.

2.2 | Cardiopulmonary resuscitation and target temperature monitoring

Cardiopulmonary resuscitation (CPR) was performed according to the 2015 Guidelines published by the European Resuscitation Council. After reaching ROSC, TTM was performed with a target temperature between 32 and 34°C for 24 h followed by 48h of fever avoidance (body temperature <37°C as measured via urinary catheter) using a central venous catheter via femoral access with the Thermoguard XP System (ZOLL, Cologne, GER) if no contraindications existed.

2.3 | Assessment of the sublingual microcirculation

Sublingual microcirculation was assessed via SDF using the MicroScan Device (MicroVision Medical) following current recommendations.18 In short, at least five videos per measurement, at 30 frames each, were recorded by an experienced investigator at the sublingual area. If assessment of the sublingual area was not possible, due to medical circumstances (e.g., bleedings in mouth or fractures of the cervical spine with indication for restraint), patients were excluded.

Videos were recorded after admission (T1 to the ICU (with a maximum delay of 4 h), 6 (T2), 12 (T3) and 24 (T4) hours after reaching ROSC. Videos were selected by manual quality scoring, as described elsewhere,19 and to obtain Mean Flow Index (MFI). Videos with a quality score >6 were discarded. Offline analysis was performed using AVA Software 4.3 (MicroVision Medical) reporting results for proportional perfused small vessels (PPVsmall), proportional perfused vessels (PPV), total vessel density (TVD), total small vessel density (TVDsmall), perfused small vessel density (PVDsmall) and perfused vessel density (PVD).

2.4 | Blood samples and assessment of clinical course

Blood samples were taken as part of routine clinical care, including blood gas analysis at least every four hours. Additional samples for platelet count, d-dimers, fibrinogen, international normalized ratio (INR) and activated partial thromboplastin time (aPTT) were collected at admission as well as 6, 12 and 24 h post-admission to the ICU. Data were collected from the clinical data information system to assess outcome parameters such as SOFA scores (1, 3, 5 and 7 days after admission), renal function (creatinine, glomerular filtration rate (GFR) and serum urea), death or discharge.
2.5 Outcome variables

A posteriori, we divided patients into two groups in dependence of death (non-survivors) or hospital discharge (survivors). Differences between the two groups concerning CPR data, sublingual microcirculation, coagulation parameters, NSE, initial serum lactate, renal function and SOFA scores were calculated.

2.6 Statistical analyses

Multiple t-tests corrected with Holm–Sidak method and Fisher’s exact tests were used for comparisons between groups. ROC-Analyses were performed by Wilson/Brown method, and cutoff was chosen by optimal Youden’s Index.20 Statistical significance was assumed for p < .05. All tests were performed with GraphPad Prism 9 for Windows.

3 RESULTS

3.1 Study population

During the 6-month study period, 68 patients with ROSC after OHCA were admitted to our university hospital, of whom 48 fulfilled the inclusion criteria and 25 were finally included in our analysis. Unsuitable patients for SDF measurement, mainly because oral bleedings or constant oral motions were the main reason for exclusion, further reasons are described in Figure 1. Patient characteristics are depicted in Table 1: Mean age of the patients was 66 ± 2 years and 80% of them were male. Thirteen patients (52%) survived until discharge from hospital, and the remaining 12 (48%) died in the ICU (Table 1).

In 36% (54% in survivors vs. 18% in non-survivors, p = .24), a myocardial infarction with ST-segment elevation (STEMI) was the assumed reason for OHCA. Immediate coronary angiography was performed in 56% of all patients and was associated with higher chance of survival (77 vs. 33%, p = .05).

3.2 CPR characteristics and TTM

Cardiac arrest was witnessed in 76% (92% in survivors vs. 58% in non-survivors, p = 0.07), bystander CPR was initiated in 60% (76 vs. 41%, p = .11), and thereof, in 24% compression only CPR was performed (Table 1).

An initial non-shockable rhythm (asystole or pulseless electric activity (PEA)) and a longer duration of resuscitation (13 ± 6.2 vs. 26 ± 17.4%, p = .01) associated with lower chance of survival (23 vs. 75%, p = .02).

Mean body temperature was 35.3 ± 0.17°C at admission and 34.6 ± 0.19°C 6 h, 34.5 ± 0.25°C 12 h and 34.5 ± 0.23°C 24 h post-admission to the ICU.

3.3 Sublingual microcirculation

Sublingual microcirculation has been assessable in 12 patients at admission (T1), in 19 patients at T2 and T3 and in 17 patients at T4 (Table 2). At admission, sublingual microcirculation was not assessable when patients were directly transferred to the catheterization laboratory; afterward, the main reason for incomplete data was the patients’ death.

Six hours after admission (T2) survivors demonstrated a higher proportion of small perfused vessels (PPVsmall) than non-survivors (85 ± 7.9 vs. 75 ± 6.8%, p = .01). MFI, PPV, TVD, TVDsmall, PVD and PVDsmall did not differ between the groups (Table 2, Figure 2). PPVsmall did not correlate with serum lactate (Figure 3A) or d-dimers (Figure 3B).

ROC-Analysis of PPVsmall 6 h post-admission revealed an area under the curve of 0.84 with p = .013 (Figure 4A). No differences were observed after 12 h post-admission (T3 and T4). At admission (T1), no differences between survivors and non-survivors were present in MFI (2.5 ± 0.3 vs. 2.3 ± 0.7 arbitrary units (AU), p = .56), PPV (92 ± 3.9 vs. 88 ± 9.6%, p = 0.47), PPVsmall (79 ± 14.2 vs. 77 ± 12.6%, p = .8), PVD (8.3 ± 1.17 vs. 7.9 ± 0.18 mm²/mm², p = .69) and PVDsmall (2.6 ± 1.57 vs. 3.1 ± 0.14 mm²/mm², p = .47). At T3 and T4, no differences between the groups were detected; further information is listed in Table 2.

3.4 Biomarkers after cardiac arrest

Lower initial serum lactate (4.4 ± 2.54 vs. 10.3 ± 5.4 mmol/l, p < .01) was associated with a higher chance of survival, whereas serum lactate 6, 12 and 24 h post-admission did not differ between the groups (Table 1, Figure 5A). ROC-Analysis of initial serum lactate levels revealed an area under the curve of 0.84 with p < .01

![FIGURE 1](Image)

Sixty-eight patients after out-of-hospital cardiac arrest (OHCA) presented to our university hospital, 20 did not meet inclusion criteria and 23 were excluded because of missing possibility to perform sidestream dark-field (SDF) imaging, missing possibility for inclusion, patients underwent emergency surgery or withdrawal of consent. Twenty-five patients were included.
### Table 1: Characteristics of included patients in dependence of survival or non-survival

| Mean ± SD       | Total (n = 25) | Survivors (n = 13) | Non-survivors (n = 12) | p-value |
|-----------------|----------------|-------------------|------------------------|---------|
| **Population**  |                |                   |                        |         |
| Age [years]     | 66 ± 15.95     | 60.4 ± 12.50      | 71.4 ± 17.76           | .08     |
| Male sex [%]    | 80             | 100               | 58.33                  |         |
| **Hemodynamic data at admission** | |                   |                        |         |
| Mean arterial pressure [mmHg] | 81.2 ± 16.53 | 82.2 ± 14.37 | 80 ± 19.18            | .74     |
| Heart rate [bpm] | 88 ± 29.8    | 84 ± 21.4         | 94 ± 37.2              | .41     |
| Norepinephrine infusion [mg*h⁻¹] | 0.9 ± 1.6    | 0.5 ± 0.68        | 2.7 ± 3.49            | .054    |
| **CPR characteristics** | |                   |                        |         |
| STEMI [%]       | 36             | 54                | 18                     | .24     |
| Direct coronary angiography [%] | 56         | 77                | 33                     | .05     |
| PCI of a culprit lesion [%] | 36         | 46                | 25                     | .41     |
| Witnessed arrest [%] | 76          | 92                | 58                     | .07     |
| Bystander CPR [%] | 60           | 77                | 42                     | .11     |
| Compression only CPR [%] | 24       | 23                | 25                     | >.99    |
| Non-shockable rhythm [%] | 48        | 23                | 75                     | .02     |
| No flow time [min] (n = 22) | 2.7 ± 3.9   | 2.3 ± 3           | 3.7 ± 5                | .43     |
| Cumulative resuscitation time [min] | 19.6 ± 14.32 | 13.2 ± 6.18      | 26.7 ± 17.39           | .01     |
| **Initial laboratory parameters** | |                   |                        |         |
| pH              | 7.2 ± 0.17     | 7.3 ± 0.14        | 7.2 ± 0.19             | .38     |
| Lactate [mmol/l] | 7.2 ± 5.05    | 4.4 ± 2.54        | 10.3 ± 5.4             | .002    |
| Potassium [mmol/l] | 4.2 ± 0.79   | 4.1 ± 0.92        | 4.3 ± 0.65             | .31     |
| Creatinine [mg/dl] | 1.4 ± 1.17   | 1.1 ± 0.33        | 1.8 ± 1.62             | .19     |
| Phosphate [mmol/l] | 2 ± 0.84     | 1.5 ± 0.54        | 2.6 ± 0.75             | <.001   |
| NSE Peak [µg/l] (n = 20) | 72.3 ± 60.95 | 39.2 ± 26.31      | 133.9 ± 59.79          | <.001   |
| Troponin T hs [ng/l] | 208.7 ± 416.7 | 283.2 ± 571.9 | 127.9 ± 91.77          | .36     |
| Hemoglobin [g/dL] | 12.9 ± 2.62 | 13.2 ± 1.92       | 12.6 ± 3.27            | .57     |
| **Initial coagulation parameters** | |                   |                        |         |
| Thrombocytes [×1000/µl] | 235 ± 78.2   | 260 ± 78.8        | 207 ± 70.5             | .09     |
| Fibrinogen [mg/dl] (n = 22) | 291.5 ± 89.87 | 284.7 ± 79.32 | 298.3 ± 102.8          | .73     |
| INR             | 1.7 ± 1.17    | 1.6 ± 0.78        | 1.8 ± 1.51             | .66     |
| aPTT [s]        | 68 ± 48.3     | 73 ± 52.3         | 63 ± 45.3              | .63     |
| D-Dimer [mg/l]  | 40.1 ± 46.61  | 13.4 ± 14.51      | 66.7 ± 52.73           | <.001   |

Note: Data are shown as mean ± standard deviation. Bold values indicate statistical significance with p< 0.05 between survivors and non-survivors.

Abbreviations: aPTT, activated partial thromboplastin time; CPR, cardiopulmonary resuscitation; INR, international normalized ratio; NSE, neuron specific enolase; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.
TABLE 2 Sublingual microcirculation in dependence of survival

| Parameter of the microcirculation | T1 (admission) | T2 (6 h) | T3 (12 h) | T4 (24 h) |
|----------------------------------|---------------|---------|----------|---------|
| MFI [AU]                         |               |         |          |         |
| Survivors                        | 2.5 ± 0.3     | 2.6 ± 0.24 | 2.7 ± 0.23 | 2.7 ± 0.17 |
| Non-survivors                    | 2.3 ± 0.67    | 2.5 ± 0.36 | 2.7 ± 0.13 | 2.8 ± 0.15 |
| PPV [%]                          |               |         |          |         |
| Survivors                        | 91.8 ± 3.86   | 91.8 ± 3.09 | 89 ± 5.46  | 88.1 ± 4.74 |
| Non-survivors                    | 88 ± 9.64     | 88.8 ± 6  | 89.6 ± 5.48 | 91 ± 3.89 |
| PPV\_small [%]                   |               |         |          |         |
| Survivors                        | 79 ± 14.21    | 84.6 ± 7.87* | 80.9 ± 9.88 | 81.6 ± 8.03 |
| Non-survivors                    | 76.9 ± 12.6   | 74.8 ± 6.75* | 83.9 ± 8.65 | 84.1 ± 6.55 |
| PVD [mm²/mm²]                    |               |         |          |         |
| Survivors                        | 8.3 ± 1.17    | 9.6 ± 4.84 | 7.9 ± 0.8  | 8.2 ± 1.68 |
| Non-survivors                    | 7.9 ± 1.81    | 8.2 ± 0.98 | 8 ± 1.67   | 8.5 ± 0.25 |
| PVD\_small [mm²/mm²]             |               |         |          |         |
| Survivors                        | 2.6 ± 1.57    | 3.5 ± 1.08 | 3.3 ± 0.88 | 3.9 ± 1.11 |
| Non-survivors                    | 3.1 ± 1.14    | 3.1 ± 1.03 | 3.6 ± 1.59 | 3.4 ± 1.27 |
| TVD [mm²/mm²]                    |               |         |          |         |
| Survivors                        | 8.9 ± 1.32    | 8.9 ± 1.22 | 8.9 ± 0.59 | 9.3 ± 1.69 |
| Non-survivors                    | 8.8 ± 1.48    | 9.1 ± 0.94 | 9 ± 1.66   | 9.4 ± 0.69 |
| TVD\_small [mm²/mm²]             |               |         |          |         |
| Survivors                        | 3.2 ± 1.94    | 4.2 ± 1.35 | 4.1 ± 1.07 | 4.8 ± 1.37 |
| Non-survivors                    | 4 ± 1.3       | 4 ± 1.3   | 4.4 ± 1.93 | 4.3 ± 1.64 |

n

Note: Measures of the sublingual microcirculation are shown in dependence of survival ad admission (T1), after 6 (T2), 12 (T3) and 24h (T4). Data are shown as mean ± standard deviation.

* indicates p < 0.05 between survivors and non-survivors.

Abbreviations: MFI, microcirculatory flow index; PPV, proportional perfused vessel; small, vessels <20 μm; PVD, perfused vessel density; TVD, total vessel density; AU, arbitrary unit.

3.5 Survival stratified by combination of initial serum lactate and PPV\_small

To stratify survival by combination of initial serum lactate and PPV\_small at 6 h post-admission, ROC analysis was performed and revealed rational cutoffs with <5.15 mmol/l for initial serum lactate and >78.4% for PPV\_small (Figure 3 (A and B), Table 3).

Applying these cutoffs yielded a positive predictive value for survival of 100% and negative predictive value of 67% has been calculated in our study population, which is associated with a sensitivity of 64% and a specificity of 100% (Table 3).

3.6 Global Hemodynamics and SOFA scores

Global hemodynamics were similar in survivors and non-survivors, as the dosages of norepinephrine, did not differ between the groups, but showed a trend toward higher dosages of norepinephrine in non-survivors at admission (0.5 ± 0.68 vs. 2.6 ± 3.5 mg h\(^{-1}\), p = .054). This trend vanished during the following time course (data not shown). Heart rate and blood pressure at admission did not differ between the groups (Table 1). SOFA scores did not differ between the groups, but on day 3 after admission survivors tended...
to lower scores (7 ± 3.5 vs. 11.31 pts, \( p = .056 \)) (supplemental data, table 4).

4 | DISCUSSION

Our study demonstrates that early evaluation of sublingual microcirculation may add valuable information to characterize prognosis in patients after OHCA. Our main findings were as follows:

1. PPV\(_{\text{small}}\) 6h after ICU admission predicted survival to discharge.
2. Initial serum lactate and PPV\(_{\text{small}}\) 6h after ICU admission were equal in their ability to prognosticate patients’ survival after OHCA.
3. Combination of PPV\(_{\text{small}}\) 6h after ICU admission and initial serum lactate resulted in a good positive predictive value for survival after ROSC following OHCA.
4. Increased d-dimer levels at admission strongly correlated with death before discharge from the hospital.

4.1 | Microcirculatory changes following OHCA

Our results go in line with previous investigations which highlighted the important role of the microcirculation in critical ill patients independently of global hemodynamics,\(^ {16,21,22} \) e.g., in septic or cardiogenic shock.

Following cardiac arrest, several studies demonstrated microcirculatory alterations\(^ {14,17} \) but none revealed data on the relationship between sublingual microcirculation and survival. Omar et al.\(^ {14} \) reported alterations of the sublingual microcirculation six hours after cardiac arrest by comparing the MFI to healthy controls and patients suffering a septic shock. Reported MFI values six hours after cardiac arrest were similar to our cohort, but PPV\(_{\text{small}}\) has not been investigated in their study and there were no differences between survivors and non-survivors in MFI. Van Genderen et al.\(^ {23} \) described a poor survival after suffering an OHCA with persistent microcirculatory perfusion alterations during TTM, but excluded patients with unstable systemic circulation, e.g., due to a severe myocardial infarction, who represent an important subgroup among resuscitated patients. In our cohort, with an average dose of 1.5 ± 0.98 mg/h norepinephrine and only 20% of patients free of vasopressors, most patients met the definition of ongoing hemodynamic shock. But only at T1 survivors showed a trend to a lower need of vasopressors than non-survivors, which vanished 6h post-admission. To our best knowledge, this is the first study deciphering early differences in sublingual microcirculation, particularly in PPV\(_{\text{small}}\), between survivors and non-survivors in a real-world cohort of patients with ROSC following OHCA.

Among the various parameters assessed, only PPV\(_{\text{small}}\) distinguished survivors and non-survivors six hours post-admission. Since PPV\(_{\text{small}}\) represents the proportion of perfused capillaries it is, as the MFI, a variable for convective blood flow and is reported to play a crucial role in states of cardiogenic shock,\(^ {18} \) which may be similar to patients after resuscitation. TVD and consequently PVD are described as variables of diffusive capacity, which may be
more relevant in states of septic or distributive shock. In our analysis, MFI did not show statistical differences between the groups, but six hours post-admission, MFI in survivors was considered to be normal (2.6 ± 0.24), whereas in non-survivors (2.5 ± 0.36) it was not.

The strength of PPV<sub>small</sub> in prediction of short-term survival in OHCA patients is highlighted when compared to initial serum lactate, which may be the most common biomarker in clinical practice for early outcome prognostication. Both PPV<sub>small</sub> 6 h post-admission and initial serum lactate showed similar receiver operating characteristic as indicated by an AUC of 0.84. Neither initial serum lactate levels nor lactate levels 6 h post-admission showed any correlation to the measured PPV<sub>small</sub> values, indicating an additional use in clinical practice. In contrast to that other widely used biomarkers like initial serum pH or serum potassium did not predict in hospital mortality in our cohort. NSE Peak was higher in non-survivors but was available only 24 to 48 h post-cardiac arrest.

However, in our collective DIC was not common, but non-survivors had higher levels of d-dimer than survivors. Since no relevant changes of platelet counts or fibrinogen levels existed, this state may be described as coagulopathic state without DIC.

Our results support previous observations describing d-dimer levels as predictor of survival following cardiac arrest.

Impaired microcirculation may be caused or even intensified by these coagulopathic changes. However, so far, all efforts toward therapeutic interventions, such as thrombolytic therapies during cardiac arrest, failed to improve survival after OHCA, despite promising preclinical results. A recent retrospective analysis of the German Resuscitation Register pointed out a potential benefit of out-of-hospital aspirin and heparin administration, but clearly warrants further investigation.

The connection between post-cardiac arrest coagulopathies and a disturbed microcirculation as potential key for new therapeutic options in the cardiac arrest syndrome, clearly needs further investigation.

### 4.3 | Limitations

Our study has several limitations: Due to its monocentric observational nature, further external validation is needed, generality cannot be assumed, and association cannot be proved as causality by significant correlations. Furthermore, due to its small sample size it can only serve for generating further hypothesis. Farther, as a consequence of
the methodical limitations of SDF imaging, patients with oral bleedings or multiply tongue movements had to be excluded.

Additionally, potential effects of TTM have not been assessed by our study, due to its focus on the very early post-resuscitation period and consequently only minimal fluctuations in body temperature during our investigation.

Finally, due to dropouts, caused by death or medical interventions, the number of patients differs between the time points, which may have biased our results. But nevertheless, for the first time, our study points out PPV\textsubscript{small} as predictive parameter for survival after ROSC following OHCA independent of known parameters such as serum lactate.

5 | CONCLUSION AND PERSPECTIVES

Estimating short-term prognosis of OHCA patients after achieving ROSC may be supported by measuring the PPV\textsubscript{small} at the sublingual microcirculation six hours after admission. Combining PPV\textsubscript{small} with established parameters (e.g., lactate) may further improve prediction of patients’ outcome. Furthermore, we deciphered d-dimer serum levels on admission as predictive values for survival. Thus, a link between alterations in coagulation and sublingual microcirculation is conceivable. Further investigations will help to expand the knowledge about sublingual microcirculatory alterations in patients with ROSC following OHCA and may promote its role in predicting survival.

ACKNOWLEDGMENTS

This work was performed in partial fulfillment of the requirements of an MD thesis of Matthias Karbenn. Open Access funding enabled and organized by Projekt DEAL.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

FV, TH and RW had contributed to concept, design, analysis and interpretation of the study and to drafting of the manuscript including revision and final approval. MKa, JS, CJ, MB, PK and MK had contributed to analysis and interpretation of the study and to drafting of the manuscript including revision and final approval.

DATA AVAILABILITY STATEMENT

Data that support the findings of this study are available on request from the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher’s website.

How to cite this article: Voß F, Karbenn M, Hoffmann T, et al. Sublingual microcirculation predicts survival after out-of-hospital cardiac arrest. *Microcirculation*. 2021;28:e12729. [https://doi.org/10.1111/micc.12729](https://doi.org/10.1111/micc.12729)