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A "NIRS" Death Experience: A Reduction in Cortical Oxygenation by Time-Resolved Near-Infrared Spectroscopy Preceding Cardiac Arrest

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Introduction

Near-infrared spectroscopy (NIRS) derived measurements of regional tissue oxygen saturation (StO_2) have been studied both during and after cardiac arrest. Changes in StO_2 can detect recovery of spontaneous circulation (ROSC) during chest compressions[1] and can predict the likelihood of achieving ROSC during cardiopulmonary rescusitation.[2] High StO_2 is associated with survival and more favorable neurological outcomes in the post-arrest setting.[3,4] However, preempting hemodynamic collapse is preferable to achieving ROSC through advanced cardiac life support (ACLS). Minimizing "time down" without end-organ perfusion has always been a central pillar of ACLS.[5] In many critically ill patients there is a prolonged phase of end-organ hypoperfusion preceding loss of palpable pulses and initiation of ACLS.

Here we report a young man who suffered a pulseless electrical activity (PEA) arrest while cortical oxygenation was monitored using time-resolved near-infrared spectroscopy (TRS-NIRS; NIRO-TRS1, Hamamatsu Photonics K.K., Japan). The onset of cortical deoxygenation preceded the loss of palpable pulses by 15 minutes despite otherwise stable measures of perfusion, reflecting falling cortical microvascular hemoglobin concentration and oxygenation minutes before PEA arrest. This finding suggests that TRS-NIRS monitoring might provide a means of detecting and preempting PEA arrest.

Report of Case

A 48 year old male with congestive heart failure, type 2 diabetes mellitus, hypothyroidism and morbid obesity was admitted to Harbor-UCLA Medical Center with gradually progressive

dyspnea due to pulmonary edema. He was diuresed, but dyspnea failed to improve as aggressive fluid removal was limited by hypotension. After two days, his respiratory status declined further, and he was transferred to the medical ICU with hypercapnic respiratory failure (P_aCO_2=62mmHg). After emergent endotracheal intubation, his respiratory status improved, but he became hypotensive (MAP=59mmHg). Subsequent chest CT revealed pulmonary consolidations consistent with pneumonia and he was treated for septic shock.

On ICU admission the patient was enrolled into a pilot study of TRS-NIRS in sepsis and septic shock, which compares traditional clinical markers of perfusion adequacy with cortical StO_2 and other TRS-NIRS variables. LA BioMed Institutional Review Board approved the study (#21307-01). The patient's legally authorized representative provided written informed consent. A cortical TRS-NIRS probe was fixed with adhesive tape to the left forehead (emission/detection optode spacing 3cm) and shielded from ambient light with thick black rubber holders and an optically dense bandage.

On hospital day seven, the patient suffered a bradycardic PEA arrest. Immediately before arrest, mean arterial pressure (from upper extremity sphygmomanometer) was stable for several hours (60-85mmHg) with four vasoactive medications (norepinephrine, vasopressin, epinephrine, dopamine). Phenylephrine was initiated ~22 minutes prior to arrest and subsequent MAP, and standard perfusion-related variables, were stable until arrest (Table 1). Invasive arterial catheterization for continuous measurement of MAP was contra-indicated because of the presence of coagulopathy due to disseminated intravascular coagulation (DIC).

Figure 1 shows that cortical StO_2 began to decline 15 minutes prior to PEA arrest. The fall in StO_2 first reached the lower limit of normal (LLN) 8 minutes prior to arrest (where the local LLN was calculated over 30 minutes using 1.96*SD with a 10 minute delay). A precipitous decline in cortical oxyhemoglobin concentration ($[O_2Hb]$) slightly preceded a progressive increase in deoxyhemoglobin concentration ([HHb]). Combined, this resulted in a subtle, but clear, 5% drop in total hemoglobin concentration ($[tHb]=[O_2Hb]+[HHb]$). Initiation of ACLS temporarily halted the decline in cortical StO_2, but did not reverse it. The NIRS probe was dislodged during CPR, 8 minutes after the arrest. Because of the patient's extremely poor prognosis and prolonged pulseless time (>16 minutes), and despite achieving ROSC, the family elected to transition the patient to comfort measures. Therefore, the NIRS probe was not replaced and the patient was withdrawn from the research study.

Discussion

Continuous wave, spatially resolved or frequency domain NIRS methods have received considerable attention for their potential to provide a non-invasive window on cerebral microcirculatory function and oxygenation in the clinical setting.[6,7] Time-resolved NIRS differs from 'standard' NIRS methods in that it provides an absolute quantification of absorption and scattering coefficients of light transiting a tissue bed based on photon diffusion theory[8] rather than on light intensity. Laser diodes produce light pulses at an emitter, which are diffused in tissues and received at a Peltier-cooled multi-pixel photon counter. Because the absorption of NIR light is high in large blood vessels, the [HHb] and $[O_2Hb]$ derived from NIRS reflects

chromophore concentration in small arterioles, capillaries and venules. Signals derive from ~1.5 cm depth below the skin, and because bone has extremely low NIR absorption, NIRS probes placed on the forehead assesses oxygenated and deoxygenated hemoglobin in the frontal lobe of the cerebral cortex. Using these measurements microvascular [tHb] and StO_2 may be calculated. StO_2 reflects the ratio of oxygen delivery to tissue O_2 utilization. Typical values of StO_2 of 60-70% in health reflect well the expected mean-capillary StO_2.[8] Capillary hemoglobin concentration ([tHb]) provides an index of O_2 diffusive capacity, as it is quantitatively related to the surface area of juxtaposed red blood cells and capillary endothelia.

The cortical StO_2 value of ~30-40% in our patient during the hours preceding arrest is extremely low and similar to values achieved during manual CPR. StO_2 <40%, in itself, may be a potential risk index for mortality. StO_2 measurement cannot distinguish between increased tissue O_2 consumption ($\dot{V}O_2$) and decreased O_2 delivery ($\dot{Q}O_2$). In our patient, S_pO_2 was stable at 92%, and increased $\dot{V}O_2$ is unlikely. Therefore, the likely causes of falling StO_2 were falling microvascular [Hb] and blood flow, which began to fail some minutes before PEA arrest.

We estimated cortical fractional blood volume to tissue volume ratio (BTVR) using [tHb] to be 4.3%: BTVR=[tHb]/((10^6*[Hb]*10/MW)*CLVHR)*100; where MW is hemoglobin molecular weight (64500) and CLVHR is cerebral to large vessel hematocrit ratio (a typical value is 0.69). This estimate is very close to reported values in humans of 4-5% using PET,[9] supporting that TRS-NIRS-derived [tHb] is accurate. The 5% drop in [tHb] in our patient 15 minutes before PEA arrest indicates a fall in capillary-to-neuron O_2 diffusive capacity at a time when capillary PO_2 was already approaching critical limits. Thus, reduced [tHb] may have further exacerbated the influence of inadequate convective O_2 delivery.

To our knowledge, cortical oxygenation has not been observed in the period immediately prior to cardiac arrest in humans. As continuous monitoring of palpable pulses is not feasible, a dramatic change in MAP, heart rate or SpO_2 is used to trigger assessment of palpable pulses. Increased duration of CPR is associated with worse neurologic outcomes[10] and mortality[11] in patients that achieve ROSC. In our case, cortical StO_2 began to decline some minutes before PEA arrest; an alarm based on StO_2 falling below LLN could be implemented to identify an impending state of inadequate perfusion and limit pulseless time.

Due to the relative rarity of in hospital cardiac arrest, capturing TRS-NIRS data in a large number of actively arresting patients is extremely challenging. Most studies examining NIRS in cardiac arrest enroll patients post-arrest during ACLS. This single case is inadequate to draw conclusions regarding the prognostic value of TRS-NIRS on outcome, but suggests the need for further assessment of the utility of TRS-NIRS in the inpatient critical care setting where the period prior to arrest is perhaps more important than the resuscitation itself.

Conclusion

TRS-NIRS predicted impending PEA arrest before other standard measures of perfusion in this critically ill patient. As a noninvasive and continuous measure of cortical perfusion adequacy, this finding will be of future value in the intensive care setting where preempting cardiac arrest is preferable to re-establishing perfusion after the arrest has occurred.

Table

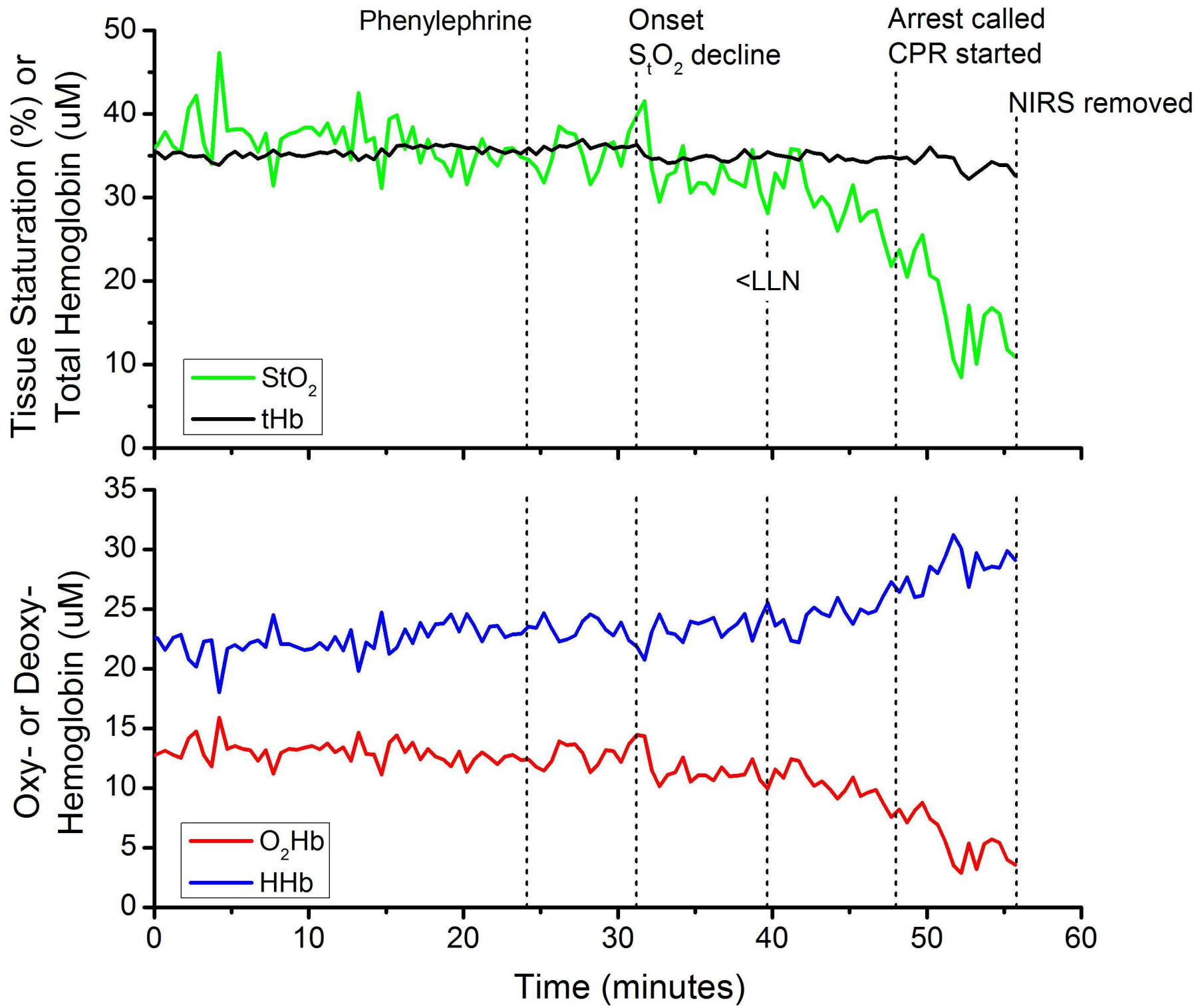
Table 1. Time-resolved near-infrared spectroscopic derived cortical oxygen saturation and standard clinical measures of perfusion adequacy 82 minutes before pulseless electrical activity arrest in a patient with septic shock.

Variable	Unit	Value
Cortical oxygen saturation (StO_2)	%	33
SOFA		16
Lactate	mg/dL	9.3
Mean arterial pressure	mm Hg	75
Hemoglobin	g/dL	7.6
Heart rate	beats/min	80
SpO_2	%	92

Values averaged over 10 minutes before and after sampling of blood for lactate and hemoglobin. SOFA is the Sequential Organ Failure Assessment.

Figure Legend

Figure 1. Time-resolved near-infrared spectroscopic (TRS-NIRS) measurement of cortical saturation (StO_2) and hemoglobin concentration ([tHb]) in a patient with septic shock during the hour prior to a pulseless electrical activity arrest and cardiopulmonary resuscitation (CPR). StO_2 and [tHb] are calculated from direct measurement of [O_2Hb] and [HHb] by TRS-NIRS using photon diffusion theory. The lower limit of normal (LLN) was calculated using a 30 minute rolling measurement of 1.96 * standard deviation, with a 10 minute delay.


Phenylephrine
Onset
S_tO_2 decline
Arrest called
CPR started
NIRS removed
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Tissue Staturation (%) or
Total Hemoglobin (uM)
StO_2
tHb
Oxy- or Deoxy-
Hemoglobin (uM)
O_2Hb
HHb
Time (minutes)

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