

Is the perfusion index an accurate predictor of return of spontaneous circulation in cardiac arrest?

NCT: pending

STUDY SUMMARY

Title

Is the perfusion index an accurate predictor of return of spontaneous circulation in cardiac arrest?

Methodology

A perspective observational double blind study

Outcomes

Return of spontaneous circulation in a mixed population of out-of-hospital and in-hospital cardiac arrest

Study Duration

Estimated duration for the main protocol (e.g. from start of screening to last subject processed and finishing the study) is approximately 2.5 years

Study Center

Monocentric: Centre Hospitalier Universitaire Saint Pierre, Brussels, Belgium

Objectives

Primary Objective: To evaluate the sensibility and specificity of the perfusion index in predicting further return to spontaneous circulation

Secondary Objectives: To compare perfusion index specificity and sensibility in predicting further return to spontaneous circulation compared to end-tidal CO₂

Number of Subjects

92 non-randomized patients in one arms

Main Inclusion Criteria

Inclusion Criteria

- Male and female patients, 12-99 years old, in any distribution.
- Cardiac arrest with an indication to reanimate
- Consent and compliance with all aspects of the study protocol, methods, providing data during the cardiac arrest management

Exclusion Criteria

- Male and female patients younger than 12 years old or older than 99 years old.
- Prisoners
- Pregnant women

Study parameter

- Perfusion index during cardiac arrest

Statistical

Methodology

Primary Endpoint:

Sensitivity and specificity of the perfusion index in predicting a return of spontaneous circulation (ROSC)

Secondary Endpoints:

Comparison of receiver operator curves from the perfusion index and the end-tidal CO₂ in predicting ROSC

Determination of the receiver operating characteristic curve of an index combining perfusion index with ETCO₂ and current rhythm

Tertiary Endpoints:

Sensitivity and specificity of the perfusion index in predicting further arrest following an initial ROSC

Purpose:

The primary objective is to evaluate the sensibility and specificity of the perfusion index, measured during chest compressions for cardiac arrest, in predicting ROSC.

Background:

Cardiac arrest prognostication is important in to inform the decision to cease resuscitation or, in the prehospital setting, to inform the decision on transport to hospital. Currently the only intra-arrest monitoring tools widely available with proven prognostic value are the underlying cardiac rhythm identified on electrocardiogram and end-tidal CO₂ (ETCO₂) measurement. Shockable rhythms, namely ventricular fibrillation and pulseless ventricular tachycardia, are associated with better outcomes than non-shockable rhythms such as pulseless electrical activity and asystole.

ETCO₂, so far, is considered the best tool available for prognostication during in or out-of-hospital cardiac arrest. Previous studies have examined ETCO₂ readings and trends at various times during cardiac arrest as a possible predictor of ROSC, survival to admission, and survival to hospital discharge. Nonetheless, ETCO₂ values have numerous limitations and no value alone can safely and accurately predict the chances of return to a spontaneous circulation (ROSC) or can safely inform on the futility of further reanimation. It would be therefore interesting for the clinician on the ground to be able to rely on a panel of different parameters to assess the chances of ROSC in a multimodal way.

Goals of the study:

1. To examine the association between absolute values of the perfusion index during resuscitation and ROSC.
2. To examine the association between the change in perfusion index values during resuscitation and ROSC.
3. To compare the performance of the perfusion index to ETCO₂ in predicting the chances of ROSC.
4. To study a combined index including rhythm, ETCO₂ and perfusion index achieves in predicting ROSC.
5. To study the ability of perfusion index to predict further arrests in patients further re-arrests in patients that achieved an initial ROSC

Duration of the Study:

The study is estimated to complete enrollment within 12 months from study initiation;

however, enrolment will remain open until the study goal is met. The duration of this

study for each subject will be a maximum of two years.

Product Description:

Perfusion index will be measured at the finger tip using a Radical 97 monitor (Masimo, Irvine, California). Masimo Signal Extraction Technology (SET[®]) pulse oximetry yields continual and simultaneous absolute values and trends.

Perfusion index (PI) is an assessment of the pulsatile strength at a specific monitoring site, and as such PI is an indirect and noninvasive measure of peripheral perfusion. It is calculated by means of pulse oximetry by expressing the pulsatile signal as a percentage of the nonpulsatile signal, both of which are derived from the amount of infrared (940 nm) light absorbed. The PI value is relative to a particular monitoring site, (e.g. the fingertip or toe), of each patient as physiological conditions vary between monitoring sites and individual patients.

Potential Benefits and Risks to Patients:

No foreseeable benefit can be expected on included patients.

Given the observational design and the well studied effects of continuous non-invasive infrared pulse oximetry monitoring we can reliably declare that we expect no possible harm to the patients included in the study.

Methods:

Study Design.

Double-blind study involving ninety two subjects treated with advanced life support according to the European Resuscitation Council (ERC) recommendations will be included in one observatory arms. Patient treatment during resuscitation will be determined by the treating clinician within the frame of ERC recommendations. Monitoring of perfusion index will be initiated as soon as possible and recorded until the end of the resuscitation efforts. ETCO₂ will be placed as soon as possible and recorded until the end of the resuscitation irrespectively if measured while the patient is ventilated through a bag-valve-mask or through a advanced infraglottic airway.

Study population and selection criteria.

All aspects of the study and consent forms will be approved by our Ethical Board prior to implementation. All patients in cardiac arrest, after application of the inclusion and exclusion criteria, with an indication to initiate an advanced life support will be included in the study. Included participants that will be successfully reanimated and that will regain a sufficient level of consciousness will be required to sign a full informed consent.

Inclusion criteria will be a cardiac arrest in a subject aged between 12 to 99 years old with an indication to start an ALS.

Subjects will be excluded from the study if younger than 12 years old, if pregnant or if prisoners at study inclusion.

We aim to recruit 90 patients in cardiac arrest for whom an ALS has been initiated.

Recruitment methods.

All subjects that will be treated by the mobile intensive care unit of CHU Saint Pierre during study period will be screened for eligibility. Subjects having regained a sufficient neurological awareness to sign an informed consent for the study will review and undergo informed consent.

This study will be listed at www.clinicaltrials.gov.

Data collection and reporting.

Data will be collected throughout the intervention up until death or hospital admission or intensive care admission whichever comes first.

Expected outcomes.

It is the sponsor's expectation that higher perfusion index and upwards trends will be associated with higher chances of ROSC during ALS. Moreover, the sponsor expectation is that lower perfusion index following ROSC will be associated with higher chances of re-arrest. Finally the sponsor expect that a combined index including PI, ETCO2 and rhythm would overperform each of these items in terms of capacity of predicting ROSC chances.

Adverse reactions.

There is no expectation of any adverse outcomes or reactions due to a patient being monitored with a Radical 97 monitor. Any adverse reactions should be reported immediately to the principal investigator or co-investigators

Reasons for Withdrawal or Termination

A subject may be discontinued from the study at any time if the subject, the Investigator, or the Sponsor feels that it is not in the subject's best interest to continue.

The following is a list of possible reasons for study treatment discontinuation:

- Screening Failure
- Subject withdrawal of consent
- The treating clinician is not compliant with study or ERC procedures
- Adverse Event that in the opinion of the Investigator would be in the best interest of the subject to discontinue study participation
- Protocol violation requiring discontinuation
- Mechanical – technical failure of the monitor

Handling of Participant Withdrawals or Termination:

Although subjects may withdraw from the study at any time and for any reason, (or may be withdrawn according to the abovementioned pre-specified cases), subject withdrawal should be avoided as much as reasonably possible.

Premature Termination or Suspension of Study:

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to the Investigator, and the Sponsor.

SAMPLE SIZE JUSTIFICATION

Sample Size Calculations

We an expected sensitivity and specificity of 90% for PI to predict ROSC, an expected prevalence of ROSC of 40%, a precision of 10% and a type I error rate of 0.05 we calculated a required sample size of 87. Including a possible dropout of 5% we calculated a final sample size of 92.

STATISTICAL ANALYSIS PLAN

Primary Endpoint

We will determine the predictive value of PI measures for ROSC. We will calculate the sensitivity and specificity at multiple different PI thresholds along with corresponding 95% confidence intervals. Overall discrimination of PI for ROSC will be presented as area under the receiver operator characteristic curve (AUC/ROC). PI values will be averaged on two minutes. Each value will be tested for its ability to predict ROSC during the following ALS cycle (2 minutes). To assess the trending ability of PI to detect ROSC we will measure the difference (Δ PI) between initial PI and PI values of the cycle preceding ROSC or the last cycle in the absence of ROSC. We will then examine the association between Δ PI and ROSC through a multivariable logistic regression while adjusting for predetermined baseline confounders such as age, initial rhythm, noflow time, bystander CPR and sex.

Secondary Endpoints

Superiority analysis of PI compared to ETCO₂ in predicting ROSC. Initial and final values of both PI and ETCO₂ will be assessed for their ability to predict ROSC. Moreover averaged values per 2 min cycle will be assessed for their ability to predict ROSC in the following cycle. The constructed ROC curves will be compared using the algorithm suggested by De Long.

Tertiary Endpoints

As a tertiary endpoint we will study the predictive value of PI to predict further re-arrest following a ROSC. Overall discrimination of PI for re-arrest will be presented as area under the receiver operator characteristic curve (AUC/ROC). PI values will be averaged on two minutes. Each value will be tested for its ability to predict a re-arrest during the following 2 minutes.

ASSESSMENT OF SAFETY

Adverse events (AE) will be monitored and collected by the study team during the monitoring phase of the study. For each AE, a detailed explanation will be obtained from the treating physician and medical record. All AEs will be recorded on the CRFs.

Definition of Adverse Event

An AE is defined as any unanticipated medical occurrence regardless to relationship of the investigative arm of the trial. An AE can be any unintended sign symptom, or disease associated with the trial

Definition of Serious Adverse Event

An adverse event is considered serious if it results in any of the following:

1. Death
2. A life-threatening AE
3. Prolong existing hospitalization
4. Persistent disability/incapacity
5. Medically important event by the Investigator

Severity of Event

The Investigator will be asked to assess the severity of the AE using the following categories:

Mild: Events require minimal or no treatment and do not interfere with the participant's daily activities.

Moderate: Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.

Severe: Severe events are usually potentially life-threatening or incapacitating.

Relationship to Study Products

For all collected AEs, the clinician who examines and evaluates the participant will determine the AE's causality based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

Definitely: The relationship of the AE and the study device or the study procedure can definitely be established.

Probably: While a clear relationship to the study device or to the study procedure cannot be established, the AE is associated with an expected AE or there is no other medical condition or intervention, which could explain the occurrence of such an event.

Possibly: There is no clear relationship between the AE and the study device or study procedure; however, one cannot definitely conclude that there is no relationship.

Unrelated: There is no relationship between the AE and the study device or study procedure. This may include but is not limited to the incident being an expected outcome of a previously existing or concurrent disease, concomitant medication or procedure the subject experienced.

SAE Reporting

In the case of a SAE, the Investigator must notify the Sponsor within 1 working day after the Investigator first learns of the event.

Data Safety Monitoring

As the monitor technique implemented in the study are currently being used as standard of care, the study team does not anticipate subjects experiencing any adverse events solely due to being in the study. Therefore, a formal Data Safety Monitoring Board will not be needed for this study.

DATA MONITORING

The Principal Investigator will be responsible to ensure the study is conducted in accordance with the protocol, Good Clinical Practice (GCP), applicable regulatory requirements, and that the data recorded is valid. To achieve this objective, the study will be continuously monitored and reviewed on a two-month basis by the study team. Clinical site monitoring is conducted to ensure that the rights and well-being of human subjects are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with applicable regulatory requirement(s).

A Clinical Monitoring Plan will be created by the Sponsor and describe in detail who will conduct the monitoring, at what frequency monitoring will be done, at what level of detail monitoring will be performed, and the distribution of monitoring reports.

DATA HANDLING AND RECORD KEEPING

The collection of personal patient information will be limited to the amount necessary to achieve the aims of the research, so that no unneeded sensitive information is being collected. Only study

personnel will collect data. Hard copy documents will be retained for the duration of the study until data entry. All hard copy documents will be kept in a locked cabinet in the nurse research coordinator's office. Data will be exported into Excel format (password protected), which will then be used for data analysis. Only de-identified data will be used for data analysis. All hard copy documents will be shredded within ten years after completion of the study upon Sponsor approval. Collected de-identified data will be sent to a biostatistician for statistical analysis.

INSTITUTIONAL ETHICAL REVIEW BOARD

The protocol, informed consent form(s), and all participant materials will be submitted to the Ethical Board for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the Ethical Board before the changes are implemented to the study. All changes to the consent form will be approved by the Ethical Board; a determination will be made regarding whether previously consented participants need to be re-consented.

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PUBLICATION AND DATA SHARING POLICY

The preparation and submittal for publication of manuscripts containing the study results shall be in accordance with a process determined by mutual written agreement among the study Sponsor and participating institutions. The publication or presentation of any study results shall comply with all applicable privacy laws, including, but not limited to, the Health Insurance Portability and Accountability Act of 1996.