

# **Validity of ICU Clinician's Appraisal of Proportionality in CPR (VICAP-CPR)**

## **Study Protocol**

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## **Background**

An international multicenter survey of emergency clinicians found that one in five perceived their last CPR attempt as inappropriate, or reported uncertainty about its appropriateness.<sup>1</sup> In patients 80 years of age or older, this was the case for one in two CPR attempts.<sup>2</sup> The perception of a disproportionate CPR attempt was largely concordant with patient outcome. The most important factors associated with perception of inappropriate CPR were patient-related factors such as non-shockable initial rhythm, non-witnessed cardiac arrest, older age, and a poor first physical impression of the patient. However, even in subgroups with a very low to zero percent survival, most emergency clinicians still considered such a resuscitation appropriate.

While high quality databases show improvement of OHCA survival, this is mainly due to the subgroup of shockable rhythms.<sup>3,4</sup> In the last decade survival and neurological outcome of OHCA remain unchanged.<sup>5</sup> Clinical decision rules such as the Bokutoh criteria, the NUE rule, and the Australian 15/5/0 rule show that unwitnessed asystolic OHCA patients with age 73 years or older have an extremely poor prognosis regardless of the intensity and duration of the resuscitation attempt.<sup>6-9</sup>

In the ERC guidelines 2021 it is acknowledged that apart from criteria related to the cardiac arrest circumstances, additional criteria can be used to support resuscitation decisions. For instance, the presence of severe chronic comorbidities or a very poor quality of life prior to cardiac arrest are allowed to support decisions to stop or not start resuscitation in unwitnessed cardiac arrest with an initial non-shockable rhythm.<sup>10</sup> In current clinical practice, these factors are often not taken into account and patients with severe underlying comorbidities and poor general condition are also resuscitated.<sup>11</sup> In intensive care, a wait-and-see approach is then usually adopted until additional information is gathered about the patient's likely prognosis based on repetitive clinical neurological examination, electrophysiological tests such as electro-encephalography and somatosensory evoked potentials, biomarker analysis and cerebral imaging (multimodal neuroprognostication).

At the ICU level, both physicians and nurses can have valuable insights into what the likely prognosis is of the OHCA patients they are treating. In subgroups with a poor prognosis (e.g. non-shockable unwitnessed arrest in older patient) the added value of the multimodal ICU neuroprognostication is potentially very limited or absent. The implication for intensive care could be that policy decisions could perhaps be made earlier in several situations. Exploring the prognostic value of the clinical perception of ICU physicians and ICU nurses regarding appropriateness of CPR and their prognostication of neurological outcome and

quality of life relative to multimodal ICU neuroprognostication might help to refine the ethical guidance towards resuscitation decision making and towards ICU management after ROSC in general.

### **Study aims**

1. To assess whether and to what extent the following factors are associated with ICU clinician's perception regarding appropriateness of CPR: perceived presence of frailty, poor quality of life and severe comorbidities, as well as objective factors related to the OHCA (shockable rhythm, bystander CPR, witnessed arrest) and clinician characteristics (age, gender, years of experience and professional background).
2. To assess the concordance between clinicians' combined perception of inappropriateness of CPR (i.e. whether or not at least 2 clinicians perceive CPR as inappropriate) and multimodal ICU neuroprognostication as performed in STEPCARE. The STEPCARE trial is an international, investigator-initiated, randomised trial on three different aspects of standard care after out-of-hospital cardiac arrest. In a 2x2x2 factorial design the effect of continuous sedation vs. minimal sedation, fever management with a device vs. without a device and a higher blood pressure target vs. a lower blood pressure target are compared. The primary outcome of the trial will be survival at 180 days with secondary outcomes including neurological function and health-related quality of life.
3. To investigate the prognostic value of clinicians' combined perception of inappropriateness of CPR, the clinician's prognostication (functional outcome and quality of life after 6 months) and the added prognostic value of the multimodal ICU neuroprognostication with regard to the long-term composite outcome (alive with a good functional outcome and good quality of life as defined in STEPCARE) above and beyond the prognostic value of clinicians' combined perception of inappropriateness of CPR and the clinician's prognostication within subgroups of initial non-shockable/shockable rhythm.

### **Primary and secondary endpoints**

Primary endpoint: composite endpoint of survival, good functional outcome and good quality of life 6 months after OHCA

Secondary endpoint: assessment of a likely poor neurological outcome (yes/no) based on the multimodal ICU neuroprognostication (>72h after randomisation)

## **Eligibility**

Inclusion criteria:

Doctors and nurses working in the Intensive Care Unit who treat a patient included in STEPCARE during the first 24 hours after admission to Intensive Care.

Exclusion criteria:

Doctors and nurses who do not have a direct treatment relationship with the patient in Intensive Care cannot participate in the study.

## **Statistical analysis**

Associations between the perception of ICU physicians and ICU nurses regarding appropriateness of CPR, on the one hand, and the ICU clinician's perceived presence of frailty, severe comorbidities, quality of life, as well as objective factors related to the OHCA (shockable rhythm, bystander CPR, witnessed arrest) and clinician characteristics (age, gender, years of experience and professional background), on the other hand, will be estimated (in terms of conditional odds ratios) using a generalised linear mixed effects model (with 'logit' link and a random intercept for center and for patient) to allow statistical inference (estimation of corresponding standard errors and confidence intervals) that correctly accounts for the multilevel structure of the data (i.e. clinicians clustered within patients, patients clustered within centers).

Subsequently, the concordance between clinicians' combined perception of inappropriateness of CPR (A) and the result of the multimodal ICU neuroprognostication (Y) will be assessed by estimating the following predictive metrics with Y being the outcome and A being the predictor:

- Positive Predictive Value (PPV)
- Negative Predictive Value (NPV)
- Sensitivity
- Specificity
- Area Under the Receiver-Operator Curve (AUC)

The PPV expresses the percentage of poor multimodal ICU neuroprognostications among cases where at least two clinicians perceive CPR to have been inappropriate, while the NPV expresses the percentage of good multimodal ICU neuroprognostications among cases where less than two clinicians perceive CPR to have been inappropriate. Results of the multimodal ICU neuroprognostication will be imputed as 'good' or 'poor' whenever, respectively, patients were discharged alive or died before the multimodal ICU neuroprognostication could be

conducted or completed. This enables calculation of the PPV and NPV in the population of patients originally included in the study and gives prospective insight into the extent to which clinicians' combined perception of inappropriateness of CPR in these patients is prognostic for the results of their multimodal ICU neuroprognostication. The sensitivity expresses the percentage of cases where at least two clinicians perceive CPR to have been inappropriate among poor multimodal ICU neuroprognostications, while the specificity expresses the percentage of cases where less than two clinicians perceive CPR to have been inappropriate among good multimodal ICU neuroprognostications. The latter two metrics will be calculated only in patients still hospitalized by the time the multimodal ICU neuroprognostication could be completed. This gives retrospective insight into the extent to which good or poor multimodal ICU neuroprognostication could already be anticipated by clinicians' combined perception of inappropriateness of CPR. Ideally, the multilevel nature of the data will be accounted for when estimating these metrics and their respective confidence intervals.

Subsequently, the prognostic value of clinicians' combined perception of inappropriate CPR and the clinician's prognostication with respect to the primary composite endpoint (alive with a good functional outcome and good quality of life as defined in STEPCARE) will be assessed in terms of the PPV, NPV and AUC. Additionally, the added or incremental prognostic value of the multimodal ICU neuroprognostication above and beyond that of ICU clinicians' combined perception of inappropriate CPR and the clinician's prognostication will be assessed in terms of increase in AUC. More specifically, two logistic regression models will be fitted: a logistic regression model for the primary outcome with clinicians' combined perception of inappropriate CPR, the clinician's prognostication as only predictor (model 1), and a logistic regression model for the primary outcome with clinicians' combined perception of inappropriate CPR, the clinician's prognostication and the result of the multimodal ICU neuroprognostication (and their interaction) as predictors (model 2). The AUCs of these models will be reported, as well as their respective PPV and NPV. AUC of model 2 minus AUC of model 1 will be estimated and used as a metric to quantify the added prognostic value. These analyses will be conducted for the entire study population, as well as in separate subgroups of patients with shockable versus non-shockable initial rhythms. For this analysis, whenever patients were discharged alive or died before the multimodal ICU neuroprognostication could be conducted or completed, results of the multimodal ICU neuroprognostication will be imputed in such a way that their coding is identical to that of the corresponding clinicians' combined perception of inappropriate CPR to reflect the fact that, in such cases, multimodal ICU neuroprognostication can by definition not have any added prognostic value. Ideally, the multilevel nature of the data will be accounted for when estimating these metrics and their respective confidence intervals.

### **What this study might add**

1. More knowledge on which factors ICU physicians and ICU nurses take into account regarding perception of appropriateness of CPR and prognostication of OHCA patients in real-life practice
2. More knowledge on the prognostic value of objective factors (OHCA characteristics, comorbidities, frailty) and subjective factors (perception of appropriateness of CPR, quality of life, clinical assessment by ICU doctors and ICU nurses)
3. Potential refinement of the ethical guidance toward resuscitation decision making and ICU management after ROSC in general

### **What additional data are needed apart from the existing STEPCARE database?**

ICU doctors and nurses treating the patient in the first 24 hours after ICU admission are requested to complete a short (**less than 3 minutes**) survey, ideally as soon as possible since we are interested in the predictive value of *clinical* appraisal of the ICU doctor and ICU nurse.

The survey comprises questions regarding clinician characteristics, perception regarding frailty, quality of life, comorbidities, appropriateness of CPR and prognostication of the outcome 6 months after OHCA.

### **Ethics approval**

Depending on national regulations healthcare professionals and/or patients or their legal representative will have to consent before completing the survey.

### **Authorship**

Authorship will be granted using the Vancouver definitions and depending on personal involvement and fulfilment of the author's respective roles.

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