European Registry of Cardiac Arrest - Study One

(EuReCa ONE)

An international, prospective, multi-centre, one month survey of epidemiology, treatment and outcome of patients suffering an out-of-hospital cardiac arrest in Europe

Study protocol

*Version 1.3**

May 2014

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* National Coordinator list and ERC address updated (17th September 2014)

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ClinicalTrials.gov Registration Number

NCT02236819 (added 11th Sept 2014)

Contents

1. Introduction

Cardiovascular disease is the leading cause of death in Europe and accounts for approximately 40% of all deaths in patients younger than 75 years [1]. The incidence of out-of-hospital cardiac arrests treated by EMS systems for all rhythms is between 38-86 per 100,000 inhabitants (data from a selection of communities scattered over Europe [2, 3]). In common with the United States [5], the incidence of cardiac arrest, treated or not-treated by EMS-systems may vary between European regions and communities [4] due to different lifestyle, nutrition and prevalence of coronary heart disease. Local policies on whether or not to start a resuscitation attempt also influence this incidence.

It has been suggested that in recent years, developments in pre-hospital as well as early in-hospital care might have increased the ratio of admission to hospital and survival [6].

Several research projects have been undertaken to improve the outcome after out-of-hospital cardiac arrest. Nevertheless it is assumed that there is potential for further improvement. To uncover factors associated with better outcome, more knowledge about cardiac arrest is required [7]. An international multi-centre study provides the opportunity to uncover differences in epidemiology, treatment and outcome in out-of-hospital cardiac arrest throughout Europe and may help find explanations for these differences. Study results might also support a certain quality benchmarking between EMS services.

It is highly likely that besides epidemiological factors, differences in data collection methodologies might influence variability among regions and countries. This international study provides a common methodology within the same period and with common criteria for all and therefore potentially increases comparability [3, 8].

The lack of a uniform data template often makes it difficult to compare systems. For cardiac arrest the Utstein template has existed since 1991, and is widely accepted as the uniform data template for cardiac arrest [9]. The template has been updated in 2004 [10]. The EuReCa ONE study will facilitate the inclusion of the Utstein core variables into national, regional or local participating registries. This will facilitate future research on more specific questions in resuscitation science.

Documenting differences in the populations, organisation or practice may result in improved care for this large group. Reliable and robust data must be available to support changes in the current approach to cardiac arrest and to improve quality of care.

2. Research questions

- What is the incidence of out-of-hospital cardiac arrest in different European regions?
- What is the incidence of any CPR (cardiopulmonary resuscitation) attempted in out-of-hospital cardiac arrest throughout Europe?
- In out-of-hospital cardiac arrest, what is the initial presenting rhythm of the patients where bystanders or EMS starts CPR or any other resuscitation intervention - shockable or non-shockable?
- In patients where CPR was started by bystanders or EMS, what is the incidence and rate of any return of spontaneous circulation (ROSC) after out-of-hospital cardiac arrest?
- What is the patient status at handover from EMS to emergency department or hospital system with ongoing additional treatment in the next step of care (ROSC, ongoing CPR, dead)?
- What is the incidence of patients who are still alive 30 days (whether in-hospital or discharged) after their cardiac arrest event and/or what is the incidence of patients who are discharged alive from hospital?
- In patients with a witnessed collapse (witnessed by bystanders and/or EMS), found in a shockable rhythm and with an event of suspected cardiac cause (i.e. Utstein comparator group):
    - What is the incidence of ROSC at hospital admission (at time of being handed over from EMS to to emergency department or hospital system with ongoing additional treatment e.g. PCI
    - What is the incidence of patients who are still alive 30 days (whether in-hospital or discharged) after their cardiac arrest event and/or what is the incidence of patients who are discharged alive from hospital?
- What factors determine ROSC, admission and survival (as defined in questions above)?

3. Methods

Inclusion criteria: All patients who suffer an out of hospital cardiac arrest * and are attended by the EMS at any stage during the event. This study will include all events that occur between 00:00 on 1st October 2014 and 23:59 on 31st October 2014. Patients will be included irrespective of their age, gender or personal factors.

*A cardiac arrest that occurs in any location other than an acute hospital .

These inclusion criteria include all patients who receive resuscitation (chest compression and / or defibrillation of any type)

- by the EMS,
- by bystanders before the arrival of the EMS with continued resuscitation by the EMS
- by bystanders before the arrival of the EMS, that is immediately stopped (for any reason) when the EMS arrives
- by bystanders with ROSC before the arrival of the EMS

It also includes patients found or declared dead (for any reason).

Some countries or registries may not be able to provide all necessary data to answer every research question. These registries will not be included in the analysis of the related research questions.

Participating registries/centres:

All Registries throughout Europe, able to provide at least the core data demanded (see appendix 1), are invited to participate in this study. Requirements are a written letter of intent to participate in this study, a written consent to follow this study protocol and a valid ethical approval (see below) if needed. Should there be more than one registry serving the same region and population, the national coordinator is responsible for avoiding multiple submissions of patients' data. The national coordinator will be required to submit all the data for the whole country to the study management team.

Written approval of participation: All participating registries must guarantee the existence of written approvals from the EMS organisations they serve to use and submit data for the EuReCa ONE study. These approvals may follow local policy and do not need to have a specific format but must include terms clearly describing the permission to use and transmit defined data for research purposes on an international basis. The national coordinator is responsible for obtaining this approval.

Ethical approval: Ethical approval will be applied for by national coordinators (see above) if necessary. Ethical approval may not be required in every nation of the participating registries. Participants are not allowed to report data unless ethical approval or a documented waiver (stating there is no requirement for ethical approval) exists for their country. The ethical approval or the documented waiver must be sent to the study management team. As only anonymised data will be reported and the data is recorded as part of routine care, a requirement for patient consent is not expected. It is however the role of the national coordinator to ensure that patient consent is not required in his/her jurisdiction.

There are no interventions in this study other than the effort required by EMS personnel or systems to report the required information to the study. There is no reported or estimated risk related to participation in this study, and since the treatment is not changed, there is no increased risk involved for the patient. The benefit to the patient is that countries get to benchmark their results and compare with best practice. The national coordinator will decide if the protocol needs to be submitted to the national research ethical committee.

4. Data collection

To maximise the extent of population coverage, participating national, regional or local registries should encourage EMS centres that may not regularly participate in existing registries to collect and provide data.

The participating registries will transfer unprocessed anonymised data. Transmission of aggregated data should be avoided whenever possible; only in case of limitations due to national laws or ethical requirements should a participating registry transmit aggregated data.

Every single case requires a data sheet (DS). Data will be collected within the national, regional or local participating registries (either as a computer-based export from the national, regional or local registry or as a paper-based DS. After validation and anonymisation of data by participating registries the data will then be transferred only via the national coordinator (computer-based) to the study centre.

National coordinators are responsible for quality control i.e. the completeness reliability and accuracy of the of data, including timely submission of data to the study management group.

Every DS will be identified by a unique number, including the country and region of origin.

Registries that cannot transfer unprocessed original data due to the reasons mentioned above will collect data themselves. These registries will then send aggregated data to the study centre.

Participating registries must collect basic EMS data on the region and population served. This registry-specific information must only be transmitted once during the study period.

Data (computer and paper-based) will be handled according to national laws concerning data security; the national coordinator is responsible for maintaining the necessary standards. Access to the data will be protected by username and password.

5. Dataset

A consistent and uniform dataset is fundamental to the success of this study. The Utstein dataset has been developed and refined over decades, therefore core Utstein variables will provide the basis for the mandatory data variables to be transmitted to the study centre. Registries must ensure that their collected data variables are in exact concordance with the nomenclature and descriptions of the items (see appendix 1). Participating registries will be furthermore requested to extend their regular data collection to at least the items of this dataset for at least the length of the study period of EuReCa One. Participating EMS systems should be informed about the extension of the registry´s dataset and support the data collection.

For this study, the items are divided into core and optional. It is hoped that by using a simple and user-friendly dataset that the study group will encourage participation in the study while ensuring the data quality required is attained.

National coordinators and the study management team will ensure local monitoring of EMS data return and local manual check of all recorded cases. If any missing information is uncovered later, this will be reported retrospectively.

6. Statistical Analysis

The statistical analysis of the data collected will be provided by the German Resuscitation Registry (GRR)®.

The calculation of incidence rates (for of out-of-hospital cardiac arrests and CPR) will be done per 100,000 population.

All variables collected for the project will be uniformly checked prior to analysis. These checks will include range checks, cross checks, and plausibility checks (participating centres are free to suggest such plausibility checks). In cases where the integrity of data is questionable, queries will be sent to the respective registry.

Statistical analysis will be based on the research questions listed previously. As a first step, the specific population will be defined (e.g. patients for whom CPR was started). Further analyses will be performed for the whole group as well as for each participating registry (or country) separately. Descriptive analysis will be performed with adequate measures of statistical analysis: for both, categorical and continuous variables, 95% confidence intervals (CI95) will be calculated.

Formal statistical testing comparing the different participants will be avoided due to the large number of participants (multiple pairwise tests). The study was neither planned nor powered for detecting significant differences. Non-overlapping CI95 will be interpreted as significant.

For certain endpoints like ROSC, admission or survival, multivariate logistic regression analysis will be performed in the whole dataset. Independent predictor variables were selected from the Utstein Core Dataset for this study if their relevance was proven by published data. The source of data (participating country, or registry) may be included in these analyses in order to adjust for local variations. Country-specific effects (like bystander CPR) may be evaluated for interactions. Alternatively, a core model will be applied separately for each participating registry, resulting in a range of effectiveness measures (odds ratios) for each predictor.

7. Organisation

The “European Registry of Cardiac Arrest - Study One (EuReCa ONE)” will be conducted by the EuReCa ONE study group on behalf of the European Resuscitation Council (ERC).

The members of the steering committee were determined during the meeting in Hamburg, Germany, on *28 February-1 March 2014.* The steering committee will be chaired by the chief investigator. The steering committee is responsible for the scientific conduct.

The study management team has been appointed by the steering committee during the above-mentioned meeting in Hamburg. This team is responsible for the administration of all project tasks.

National coordinators. There will only be one national coordinator in every country. National coordinators will be responsible for: ensuring that mandatory approvals (e.g. ethical approval) exist; communication with the participating registry or registries; measures to generate good data quality; supervision of data collection and complete transmission of the data of their country. National coordinators will be approved by the steering committee.

8. Data management, ownership

The University Hospital Schleswig-Holstein, Department of Anaesthesiology and Intensive Care Medicine / The University of Kiel, faculty of medicine, will act as custodian of the data. Data will be handled according to national laws concerning data security; the national coordinator is responsible for maintaining the necessary standards.

The local, regional or national registries will keep the ownership of their data. They will provide the data (by submission) to the study management group for the evaluation of the research questions listed previously. Submitted data cannot be revoked. When submitting data the local, regional or national registries must undertake not to publish submitted data before acceptance of the EuReCa ONE paper. Members of the EuReCa ONE study group will have the right to access the data for scientific and other purposes after the study proposal has been reviewed. The steering committee has provided written approval for this measure.

All participants (registries, national coordinators, steering group, SMT, writing group) have committed to dealing in a confidential manner with data and unpublished results.

9. Publication plan

Publications will be organized by the writing group. The writing group comprises the chief investigator, a statistician and the steering committee and the study management team. The chief investigator is the first author followed by the steering committee, the statistician, the study management group and the national coordinators. All other contributors and all other representatives of all other countries will appear in the appendix and “medline”.

All publications should be in accordance to the STROBE-Statement [11].

Possible target journals for the publication of the study results are “Resuscitation” and “The Lancet”. The study protocol will be published separately (possible target journal: “Resuscitation”, “BMC Health Science”, “Trials”). The major results may be re-published in the different countries. Publication of regional or local data in participating countries may only be undertaken after the publication of the EuReCa-ONE study results; exceptions to this requirement would need the approval of the steering committee.

10. Timeline

October 1, 2014	Begin study period, first patient in
October 31, 2014	Last patient, end of study period
November 30, 2014	Last patient in for 30-day-survival
January 31, 2015	Last data submitted (incl. for 30-day-survival) by national coordinator
Up to March 2015	Analysis and first draft
End of March 2015	Presentation to the group
April 30, 2015	Submission

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Appendix 1 – Dataset