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Study protocol:

Sex-unique disparities in survival and resuscitation after out-of-hospital cardiac arrest – a Danish analysis

Study type
Observational study

Unique protocol identification number
ohcagd2022

Background
With the recent emphasis on research in womens´ health, sex differences in OHCA are nowadays more often investigated worldwide and mounting evidence revealed sex as a possible modifier of outcome in cardiovascular disease (CVD)[1 2 3 4 5]. Cardiovascular disease (CVD) is the leading cause of death in women, although conventionally, it has been considered as a male dominated disease[6]. In contrast to common beliefs, heart attacks occur almost as frequently in women as in men, but at an older age and with clinical manifestations that vary between, younger, premenopausal and older postmenopausal women[7 8 9]. Previous studies have investigated sex differences in OHCA, but with limited comprehensiveness and conflicting results regarding reported survival between sexes[10 11 12 13 14]. These discrepancies may be explained by the fact that data is assessed in different countries with different health care systems, with divergent inclusion criteria and subgroups of age, e.g. selection for only shockable initial rhythm (SIR)[14]. This suggests further investigations and cohesion to a standardized and comprehensive view on sex differences in OHCA outcomes.

In 2016 the Danish Emergency Medical Services introduced a nationwide electronic reporting system. This registry allows electronic searches to evaluate subgroups of OHCA (out-of-hospital cardiac arrest). Hence, it became possible to investigate characteristics in OHCA related to sex differences. Therefore, with this population-based cohort-study, we plan to analyze all emergency medical services treated resuscitations in Denmark between 2016 and 2021. This serves to achieve a better understanding and enhanced knowledge of the epidemiology of OHCA in between different sexes.

Aim

In this study we aim to describe possible differences in help provision by bystanders, cardiopulmonary resuscitation (CPR), pre-hospital treatment by emergency medical services (EMS), presence of SIR and survival rates after OHCA at successive stages of treatment for a six-year period in a Danish setting.

Methods

This study is a registry-based follow-up, including data on OHCA collected in the electronical prehospital medical registrations recorded by the Danish Emergency Medical Service over a 6-year period from 2016 to 2021.

Data

This analysis will be based on data from the national electronic based Danish OHCA registry. Data on OHCAs with resuscitative attempts in Denmark have been collected in the electronic based Danish Medical Service report system since 2016. The registry covers detailed data including the EMS report, executive entries, and advanced text searches of prehospital charts. All cases go through an elaborate validation process where all identified events are read through manually by an external verification team. This ensures high quality of data, collected according to the Utstein recommendations, throughout the approximately 5400 cases of OHCA in Denmark annually. During this verification process, supplementary sources of data are linked to each OHCA, among others information about survival, localization, initiation of bystander CPR and EMS personnel operation.

Variables included

- **Age:** Age will be defined as the patient´s age at the time of the event. Subjects will be stratified into six age-groups, including <40 years of age, 40-49 years of age, 50-59 years of age, 60-69 years of age, 70-79 years of age, over 80 years of age.

- **Sex:** Sex will be stated as either male, female or undetermined and derived from personal identification numbers. Gender will be defined based on EMS-charts, in cases where an

identification number is not found.

- **Initial rhythm:** The initial rhythm recorded by manual defibrillator or AED (whichever first) will be defined as the first rhythm observed by EMS personnel and categorized as either shockable initial rhythm ((SIR), ventricular tachycardia, ventricular fibrillation), non-shockable (asystole, pulseless electrical activity), non-shockable (other) or undetermined.

- **Etiology of cardiac arrest:** Presumed causes will be stated as either presumed cardiac, other medical cause, trauma, drug overdose, drowning, electrocution, or hypoxemia (external).

- **Location of Incidence:** Location will be characterized as either: privat home, public space, outdoor nature or other.

- **Observation of occurrence:** OHCAs will be defined as either unwitnessed, bystander witnessed or EMS-witnessed.

- **Cardio-pulmonary-resuscitation (CPR):** CPR will include bystander-initiated CPR and EMS treatment with CPR.

- **Deployment of automatic external defibrillators (AEDs)**: Defibrillation will include defibrillation by bystanders and/or EMS personnel. This includes using publicly available AEDs, which are fitted to the patient, have analysed the rhythm, but did not deliver a shock.

- **EMS-response time:** This will be defined as the time between a dispatcher receiving the emergency call and the arrival of the first EMS-personnel.

- **Hospitalization:** Hospitalization will be considered as either: transported to hospital or declared dead by EMS-personnel.

- **Return-of-spontaneous-circulation (ROSC):** ROSC will be classified as the achievement of ROSC anytime between recognition of the event and termination (defined as either hospital admission or declaration of death by EMS-personnel).

- **State at hospital admission:** State of the case upon arrival at the hospital will be defined as either ROSC or ongoing CPR.
- **Survival:** Survival will be defined as ROSC at the time of hospital admission, additionally 30-day survival will be included, this derived from data from the National Patient Registry. Survival will be calculated in total, per age decade and after selection for SIR. Survival will also be stratified according to location of OHCA (at non-public versus public location).

Analysis

Data is collected using the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement. All percentages will exclude missing values. Descriptive statistics includes the above-mentioned variables identified with absolute numbers and percentages. Comparative analyses will be carried out using non-parametric testing to examine subgroups. Forward logistic regression analysis will be performed for multivariate analysis. Odds ratio for survival will be calculated stratified by localization, bystander, SIR and EMS-actions.

Data storage

Data is stored on secure drive according to the regional instructions for safe conduct of data management.

Overall recruitment status

Completed.

Ethical considerations

GDPR will be followed according to Danish law, and the study is registered and approved at the Danish Data Protection Agency, capital region of Denmark. Since it is a registry-based study, no ethical approval is required.

Perspectives

This study will provide updated information regarding OHCA for the association of sex, bystander actions and survival, based on a reviewed, high-quality database. Findings might contribute to enhanced knowledge upon circumstances and potential modifiable factors associated with increased survival. Thus, it is our hope that this study will contribute to improve handling this type of arrests. This, eventually using educational campaigns targeted laypersons and healthcare personnel.

List of Abbreviations

AED: Automatic External Defibrillator

CPR: Cardio Pulmonary Resuscitation

EMS: Emergency Medical Services

GDPR: General Data Protection Regulation

OHCA: Out-of-Hospital Cardiac Arrest

ROSC: Return of Spontanous Circulation

SIR: Shockable Initial Rhythm

STROBE: STrengthening the Reporting of OBservational studies in Epidemiology

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