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Clinical Paper

Myocardial infarction is a frequent cause of exercise-related resuscitated out-of-hospital cardiac arrest in a general non-athletic population

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ABSTRACT

Background: Performing exercise is shown to prevent cardiovascular disease, but the risk of an out-of-hospital cardiac arrest (OHCA) is temporarily increased during strenuous activity. We examined the etiology and outcome after successfully resuscitated OHCA during exercise in a general non-athletic population.
Methods: Consecutive patients with OHCA were admitted with return of spontaneous circulation (ROSC) or on-going resuscitation at hospital arrival (2002–2011). Patient charts were reviewed for post-resuscitation data. Exercise was defined as moderate/vigorous physical activity.
Results: A total of 1393 OHCA-patients were included with 91(7%) arrests occurring during exercise. Exercise-related OHCA-patients were younger (60 ± 13 vs. 65 ± 15, $p < 0.001$) and predominantly male (96% vs. 69%, $p < 0.001$). The arrest was more frequently witnessed (94% vs. 86%, $p = 0.02$), bystander CPR was more often performed (88% vs. 54%, $p < 0.001$), time to ROSC was shorter (12 min (IQR: 5–19) vs. 15 (9–22), $p = 0.007$) and the primary rhythm was more frequently shock-able (91% vs. 49%, $p < 0.001$) compared to non-exercise patients. Cardiac etiology was the predominant cause of OHCA in both exercise and non-exercise patients (97% vs. 80%, $p < 0.001$) and acute coronary syndrome was more frequent among exercise patients (59% vs. 38%, $p < 0.001$). One-year mortality was 25% vs. 65% ($p < 0.001$), and exercise was even after adjustment associated with a significantly lower mortality (HR = 0.40 (95%CI: 0.23–0.72), $p = 0.002$).
Conclusions: OHCA occurring during exercise was associated with a significantly lower mortality in successfully resuscitated patients even after adjusting for confounding factors. Acute coronary syndrome was more common among exercise-related cardiac arrest patients.

1. Introduction

Although the beneficial effects of regular exercise have been proven for both secondary and primary prevention of cardiovascular disease, it is well known that the risk of an acute cardiac event is temporarily increased during strenuous physical activity – termed the paradox of exercise.[1–3] Sudden cardiac death is tragic and cardiac arrests occurring during exercise and sport activities frequently draw attention. The extensive attention of exercise-related cardiac arrest and the following concern may refrain some from exercising. Survival after out-of-hospital cardiac arrest (OHCA) has increased in recent years, however OHCA remains associated with a poor prognosis.[4] Most current studies on OHCA during sport and exercise focus on sudden death in young professional athletes and the discussion of screening prior to participation in elite sports is ongoing in many countries.[5–8]

Myocardial infarction is the most common cause of malignant arrhythmias leading to cardiac arrest and minimizing the delay from symptom onset to first medical contact in the pre-hospital setting is recognized as a major factor for outcome.[9,10] The establishment of emergency medical teams educated in basic life support (BLS) and equipped with an AED in sport stadiums and athletic settings have been suggested to improve fast response

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in case of an acute cardiac event as a benefit for both spectators and athletes.[11–15] Risk factors such as prior cardiovascular events, smoking, and a recent episode of fatigue or flu-like symptoms are associated with an increased risk of an acute cardiac event, however the association between exercise and susceptibility of a fatal myocardial infarction has not been thoroughly investigated.[16–20]

We aimed at reporting a large urban experience with outcome and prognosis after resuscitated OHCA occurring in relation to exercise in the general non-athletic population. Furthermore, we investigated the incidence of acute coronary syndrome as a cause of the arrest in both patients with exercise- and non-exercise-related cardiac arrests.

2. Materials and methods

2.1. Patients and study area

From June 2002 through 2011 consecutive patients (≥18 years) with OHCA of all causes in the greater Copenhagen area and emergency medical services (EMS) dispatched and attended were included in the cohort study. Pre-hospital resuscitation was attempted in all included patients, and if treatment was terminated before hospital admission the patients were excluded from the study.[21] Patients with return-of-spontaneous circulation (ROSC) or ongoing CPR at hospital admission were included. Patients with obvious signs of death (e.g. rigor/livor mortis) were excluded, as were non-Danish residents due to unavailable outcome data.

The EMS in Copenhagen, the capital of Denmark, covers the Copenhagen area of 675 km^2 (260 Mi^2), which is inhabited by approximately 1.2 million people. The standard response to cardiac arrest is an emergency ambulance with BLS equipment, a defibrillator and a mobile emergency care unit staffed with a physician (anesthesiologist) and a paramedic. The EMS was dispatched to all patients with presumed OHCA with the treatment protocol adherent to the advanced life support guidelines from the European Resuscitation Council.[22,23] The attending physician used an Utstein registration sheet as documentation and data were entered in the OHCA-database immediately after end of each case.[24–26] Patients were admitted for post-resuscitation care at one of eight hospitals in the greater Copenhagen area. The OHCA incidence was calculated as number of arrests per year divided with number of citizens in the EMS coverage area.

A single investigator comprehensively reviewed the individual patient charts with definition of registered parameters prior to chart review. Included variables were pre-arrest co-morbidity assessed by the Charlson Comorbidity Index that takes the severity of 22 conditions into account and is used to predict short-term mortality.[27,28] Moreover data regarding in-hospital post-resuscitation care, place of arrest (public/non-public) and whether the OHCA-patient were exercising at time of OHCA were recorded. Exercise-related OHCA was defined as OHCA occurring during or within 15 min of cessation of moderate to vigorous physical activity. Activities such as lawn mowing, housekeeping and sexual intercourse were not defined as exercise. The etiology of the arrest was determined after review of the full disease course, and cardiac etiology was defined as acute coronary syndrome (ACS), primary arrhythmia, aortic stenosis or cardiomyopathy (dilated or hypertrophic). ACS was defined as ST-segment elevation myocardial infarction (STEMI) with ST-segment elevation in two contiguous electrocardiogram leads of >0.1 mV in V4–V6 or limb leads, or >0.2 mV in lead V1–V3 or non-ST-segment elevation myocardial infarction (NSTEMI) with or without changes in the electrocardiogram. If cardiac biomarkers or the coronary angiography did not confirm the diagnosis, patients were not categorized as having ACS.[29] The diagnosis of ACS was validated in 100 patients in the cohort by a second investigator blinded to previous assessment.

The regional ethics committee waived informed consent to the study with the reference number: H-2-2012-053, and the study was approved by the Danish Data Protection Agency.

2.2. Outcome

The primary endpoint of this study was survival to discharge from hospital and after 1 year. Patients were followed up to May 1st, 2013 with a maximum follow-up time of 11.1 years and with 99.6% completion. Patients who survived the OHCA but afterwards emigrated were censored at time of emigration ($n = 6$). Mortality data were acquired from the Danish National Patient Registry, which holds vital status on all Danish citizens, all of whom are registered by a unique personal identification number. Neurological outcome was assessed with the Cerebral Performance Category score (CPC) at hospital discharge, and CPC 1 or 2 were categorized as favorable neurological outcome, 3 or 4 were categorized as non-favorable and 5 as dead.[24]

2.3. Statistics

Continuous variables are presented as mean ± standard deviation for normally distributed data and as median and interquartile ranges (IQR) for non-normal distributed data. Differences were analyzed with Student's unpaired *t*-test or Wilcoxon rank sum test as appropriate. Categorical variables are presented as number (n) and percent and differences are analyzed with χ^2-test. Kappa statistics were applied for inter-observatory agreement.

Mortality is presented as Kaplan–Meier plots and differences are tested using log-rank test. Univariate and multiple proportional hazard regression analysis (COX-regression) were performed estimating hazard ratios (HR) and 95% confidence intervals (CI) adjusting for potential confounders (age, sex, rhythm, witnessed arrest, bystander CPR, time to ROSC, initiated therapeutic hypothermia, acute coronary angiography, cardiac etiology, public arrest, Charlson Comorbidity Index and arrest during nighttime (midnight to 8 AM) after checking for the underlying assumptions of proportionality and lack of interactions. All statistical analysis was carried out in SAS Statistics version 9.3 (Cary, NC, USA) with a level of significance defined as $p < 0.05$.

3. Results

3.1. Patient characteristics

In the study period a total of 1393 consecutive patients suffered from OHCA, and were attempted resuscitated by the EMS in Copenhagen and admitted to hospital with ROSC or ongoing CPR (Fig. 1) (incidence approximately 0.01% per year). Of those were 7% ($n = 91$) of the arrests occurring during exercise (Fig. 1). Mean age was 60 ± 13 years for OHCA during exercise and 65 ± 15 years in non-exercise OHCA-patients ($p < 0.001$) with no differences in the number of patients younger than 40 years (Table 1). Patients experiencing OHCA during exercise were almost exclusively male (96% vs. 69%, $p < 0.001$) (Table 1). Charlson co-morbidity index was significantly lower in patients with exercise-related arrests ($p < 0.001$), however risk factors for an acute cardiac event (smoking, hypercholesterolemia, known ischemic heart disease, congestive heart failure and/or hypertension) were not different in the two groups (Table 1).