# **ARTICLE IN PRESS**

Resuscitation xxx (2016) xxx-xxx



Contents lists available at ScienceDirect

# Resuscitation



journal homepage: www.elsevier.com/locate/resuscitation

## 2 Clinical paper

- Incidence and survival outcome according to heart rhythm during
- <sup>4</sup> resuscitation attempt in out-of-hospital cardiac arrest patients with
- $_{\rm s}$  presumed cardiac etiology  $^{\star}$
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#### 36 ARTICLE INFO

21 Article history:

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- 23 Received 3 October 2016
- 24 Received in revised form
- 25 22 December 2016
- Accepted 24 December 2016
- 28 Keywords:
- 29 Out-of-hospital cardiac arrest
- 30 Arrhythmia
- 31 Survival
- 32 Epidemiology
- 33 Converted rhythm

#### 34 Defibrillation

## ABSTRACT

*Background:* Knowledge about heart rhythm conversion from non-shockable to shockable rhythm during resuscitation attempt after out-of-hospital cardiac arrest (OHCA) and following chance of survival is limited and inconsistent.

*Methods:* We studied 13,860 patients with presumed cardiac-caused OHCA not witnessed by the emergency medical services from the Danish Cardiac Arrest Register (2005–2012). Patients were stratified according to rhythm: shockable, converted shockable (based on receipt of subsequent defibrillation) and sustained non-shockable rhythm. Multiple logistic regression was used to identify predictors of rhythm conversion and to compute 30-day survival chances.

*Results:* Twenty-five percent of patients who received pre-hospital defibrillation by ambulance personnel were initially found in non-shockable rhythms. Younger age, males, witnessed arrest, shorter response time, and heart disease were significantly associated with conversion to shockable rhythm, while psychiatric- and chronic obstructive pulmonary disease were significantly associated with sustained non-shockable rhythm. Compared to sustained non-shockable rhythms, converted shockable rhythms and initial shockable rhythms were significantly associated with increased 30-day survival (Adjusted odds ratio (OR) 2.6, 95% confidence interval (CI): 1.8–3.8; and OR 16.4, 95% CI 12.7–21.2, respectively). From 2005 to 2012, 30-day survival chances increased significantly for all three groups: shockable rhythms, from 16.3% (CI: 14.2%–18.7%) to 35.7% (CI: 32.5%–38.9%); converted rhythms, from 2.1% (CI: 1.6%–2.9%) to 5.8% (CI: 4.4%–7.6%); and sustained non-shockable rhythms, from 0.6% (CI: 0.5%–0.8%) to 1.8% (CI: 1.4%–2.2%).

Conclusion: Converting to shockable rhythm during resuscitation attempt was common and associated with nearly a three-fold higher odds of 30-day survival compared to sustained non-shockable rhythms. © 2017 Published by Elsevier Ireland Ltd.

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- A Spanish translated version of the abstract of this article appears as Appendix in the final online version at http://dx.doi.org/10.1016/j.resuscitation.2016.12.021.
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http://dx.doi.org/10.1016/j.resuscitation.2016.12.021 0300-9572/© 2017 Published by Elsevier Ireland Ltd.

Please cite this article in press as: Rajan S, et al. Incidence and survival outcome according to heart rhythm during resuscitation attempt in out-of-hospital cardiac arrest patients with presumed cardiac etiology. Resuscitation (2016), http://dx.doi.org/10.1016/j.resuscitation.2016.12.021 37

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### Introduction

Successful resuscitation following out-of-hospital cardiac arrests (OHCA) highly depends on the presenting heart rhythm, with shockable rhythms (ventricular fibrillation and pulseless ventricular tachycardia) linked to higher survival rates than initial non-shockable heart rhythms (pulseless electrical activity and asystole).1-3 4403

During the past two decades, the incidence of OHCA patients 45 presenting with shockable rhythms has decreased in several coun-46 tries, and due to the link between non-shockable rhythms and 47 poor success rates of resuscitation, the falling incidence of shock-48 able rhythms challenges efforts to improve survival outcome after 49 OHCA.<sup>4–6</sup> Yet, in some cases, first-recorded non-shockable rhythms 50 can convert into shockable rhythms during the course of car-51 diopulmonary resuscitation (CPR) and advanced treatment. While 52 previous studies indicate that converting to a shockable rhythm 53 is linked to a better outcome than remaining in a non-shockable 54 rhythm, little is known about which pre-hospital factors, including 55 patient demographics (age, sex and comorbidities), that are asso-56 ciated with conversion to a shockable rhythm.<sup>7-11</sup> Furthermore, 57 while it is well known that overall survival rates after OHCA has 58 increased over time in several countries,<sup>1,12,13</sup> the temporal trend 59 in survival for converted shockable rhythms is unknown. 60

Using data from the nationwide Danish Cardiac Arrest Regis-61 ter, we described baseline characteristics and survival associated 62 to: (1) initial shockable rhythm, (2) conversion from initial non-63 shockable to shockable rhythm and (3) sustained non-shockable 64 rhythm, and identified pre-hospital factors associated with conver-65 sion of rhythm. We also developed predictive models (best-worst 66 case scenarios) highlighting situations giving rise to the largest and 67 lowest survival rate for each rhythm. 68

### Methods

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#### Data source and definitions 70

All OHCA cases were identified from the nationwide Danish Cardiac Arrest Register (2005-2012). The register and the Danish emergency medical services (EMS) system and linkage to other nationwide registers has been described in detail elsewhere.<sup>1</sup> There are no structured first-responder automated external defibrillator programs in Denmark (police or firefighters bringing a defibrillator).

In order to examine the comorbidities of the patients, dis-78 charge diagnoses up to ten years prior to OHCA were examined in 79 accordance with previously described methods.<sup>14</sup> Included cardiac 80 comorbidities were ischemic heart disease, myocardial infarction, 81 and heart failure. Included non-cardiac comorbidities were chronic 82 obstructive pulmonary disease, diabetes, malignancy, renal disease 83 and psychiatric disease. All diagnoses have been coded using the 84 International Classification system (ICD). Before 1994, the 8th revi-85 sion is applied (ICD-8), and from 1994 onwards the 10th revision 86 is applied (ICD-10) (Supplemental Table 1). 87

#### Study population 88

All OHCA patients of presumed cardiac cause and  $\geq$ 18 years 89 at the time of OHCA were identified.<sup>1</sup> Patients defibrillated by a 90 bystander were excluded from the study population. The first regis-91 tered rhythm was defined as the presenting rhythm when the EMS 92 arrived and connected a defibrillator. The defibrillator determined 93 whether the rhythm was classified as shockable or not. The study population was stratified into three groups according to rhythm analysis: (1) first-recorded shockable rhythm, (2) non-shockable

http://dx.doi.org/10.1016/j.resuscitation.2016.12.021

rhythm converted to shockable during resuscitation efforts by the EMS, and (3) sustained non-shockable rhythm. The second group, "converted to shockable rhythm", was defined as patients who initially had non-shockable rhythm at the time of EMS arrival but who subsequently received pre-hospital defibrillation from the EMS.

#### Study endpoints/outcomes

The primary outcome measure was 30-day survival. Secondary outcome measure was return of spontaneous circulation (ROSC) (pulse or other signs of restored circulation) at hospital arrival.

Statistics

Baseline characteristics were summarized as counts and percentages for categorical variables and as medians and interguartile range for continuous variables. In order to identify patient- and cardiac arrest characteristics associated with converting to a shockable rhythm, we analysed the subset of patients that had first-recorded non-shockable rhythms. We used multiple logistic regression with rhythm as outcome (converted shockable vs. sustained nonshockable) to investigate the following patient characteristics: age, sex, the selected comorbidities, location of arrest, witnessed status, bystander CPR, and time from recognition of arrest to rhythm analysis by the EMS. Reported were odds ratios with corresponding 95% confidence intervals. Multiple logistic regression was also performed in all patients to examine the association between heart rhythm and 30-day survival. This model was adjusted for age, sex, comorbidities, location of arrest, witnessed status, bystander CPR, time from recognition of arrest to rhythm analysis by the EMS, and year of arrest (Supplemental Fig. 1). Missing data was handled using the multiple imputations by chained equation method. Hundred imputed datasets were constructed using all covariates in Table 1, and estimates from observed and imputed datasets were compared. Temporal 30-day survival chances were reported as crude relative frequencies as well as predictions from a logistic regression model where the relationship between 30-day survival chances and calendar year was modelled by restricted cubic splines with prespecified knots at years 2007, 2009 and 2011.<sup>15</sup> The analyses were repeated with ROSC as outcome instead of 30-day survival. Linear calendar time trends in data were examined by using the Cochran Armitage Trend Test. The level of statistical significance was set at 5%.

To illustrate the variation in 30-day survival for specific individuals in subgroups defined by rhythm we also report 30-day survival chances from fully adjusted logistic regression for selected specific combinations of patient- and OHCA characteristics: for a person without known comorbidities, of working age  $\leq 65$  years, with a non-residential witnessed arrest and who had received bystander cardiopulmonary resuscitation (best-case scenario), and for a person with one or more comorbidities, age >65 years, a residential unwitnessed arrest and who had not received bystander cardiopulmonary resuscitation (worst-case scenario). These results are presented as predicted 30-day survival percentages with 95% confidence intervals.

All statistical analyses were performed using SAS, version 9.4 (SAS Institute Inc., Cary, NC, USA) and R, version 3.2.3.<sup>16</sup>

#### Ethics

Please cite this article in press as: Rajan S, et al. Incidence and survival outcome according to heart rhythm during resuscitation attempt in out-of-hospital cardiac arrest patients with presumed cardiac etiology. Resuscitation (2016),

This study was approved by The Danish Data Protection Agency (J. ref: 2007-58-0015/local J ref: GEH-2014-017/I-Suite: 02735). Ethical approval is not required for retrospective register-based studies in Denmark.

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