Resuscitation 205 (2024) 110435

Contents lists available at ScienceDirect

Resuscitation

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

Clinical paper

Survival in relation to number of defibrillation attempts in out-of-hospital cardiac arrest

Linn Harrysson [a], Emma Blick [a], Akil Awad [a], Martin Jonsson [a], Andreas Claesson [a], Carl Magnusson [b], Lis Abazi [a], Johan Israelsson [c,d], Robin Hofmann [e], Per Nordberg [a], Gabriel Riva [a,*]

[a] *Center for Resuscitation Science, Department of Clinical Science and Education, Södersjukhuset (KI SÖS), Karolinska Institute, Stockholm, Sweden*
[b] *Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden*
[c] *Department of Internal Medicine, Division of Cardiology, Kalmar County Hospital, Region Kalmar County, Kalmar, Sweden*
[d] *Faculty of Health and Life Sciences, Linnaeus University, Kalmar, Sweden*
[e] *Department of Clinical Science and Education Södersjukhuset (KI/SÖS), Karolinska Institute, Stockholm, Sweden*

A R T I C L E I N F O

Keywords:
Cardiopulmonary resuscitation
Out of hospital cardiac arrest
Sudden cardiac death
Ventricular arrhythmia
Defibrillations
Survival

A B S T R A C T

Introduction/aim: Out-of-hospital cardiac arrest (OHCA) with shockable pulseless ventricular tachycardia or fibrillation not responding to defibrillation is a medical challenge. Novel treatment strategies have emerged for so-called refractory ventricular fibrillation not responding to three or more defibrillations but the evidence for optimal timing for these strategies is sparse. The primary aim of this observational study was to assess survival in relation to total numbers of defibrillations in OHCA.

Methods: This is a registry-based retrospective cohort study based on data reported by the emergency medical services to the Swedish Registry of Cardiopulmonary Resuscitation and the National Patient Registry. All OHCA patients aged 18 years or older with an initial shockable rhythm in Sweden from January 1, 2010 and December 31, 2020 were included. Exposure was total number of defibrillations, and primary outcome was survival to 30 days. Logistic regression was used to adjust for patient and resuscitation characteristics.

Results: Over the study period a total of 10,549 patients were included. Among them, 3,006 (28.5%) received only one shock, 1,665 (15.8%) two shocks, 1,336 (12.9%) three shocks, 1,064 (10.1%) four shocks and 3,478 (33.0%) five or more shocks. In the adjusted analysis an exponential decrease in the 30-day survival was found for each additional defibrillation. For patients receiving one, two, three and four defibrillations, the adjusted probability of survival was 42%, 36%, 30% and 25% respectively.

Conclusions: In this registry-based retrospective cohort study, additional defibrillations were associated with a lower survival. This association persisted after adjustments for patient and resuscitation characteristics.

Introduction

Out-of-hospital cardiac arrest (OHCA) is the third most common cause of mortality in Europe.[1] The annual incidence of OHCA where emergency medical services (EMS) attempted resuscitation is 19 – 97 / 100 000 person/years, with an average survival rate of only 8 %. Important factors that positively affect outcome are shockable rhythms (pulseless ventricular tachycardia (pVT) and ventricular fibrillation (VF)), early cardiopulmonary resuscitation (CPR), short time to first defibrillation, witnessed event, public location and early return of spontaneous circulation (ROSC).[2] However, even though an initial shockable rhythm is associated with better outcomes, only about 1 out of 3 patients survive to 30 days in Sweden.[3] Some OHCA patients with shockable rhythm do not respond to defibrillation at all,[4] whereas others might have a termination of pVT/VF but with recurrent episodes of VF.[5]

The term refractory ventricular fibrillation (RVF) is commonly used when the resuscitation does not result in a sustained ROSC after three or more consecutive defibrillations.[2,6–8] Advanced treatment involving drug administration, hospital admission to enable percutaneous coronary intervention (PCI) or extracorporeal membrane oxygenation (ECMO), finding reversible causes, maximizing defibrillator energy level and considering changing the placement of the pads are currently

* Corresponding author.
E-mail address: gabriel.riva@ki.se (G. Riva).

https://doi.org/10.1016/j.resuscitation.2024.110435
Received 1 September 2024; Received in revised form 3 November 2024; Accepted 11 November 2024
Available online 15 November 2024

recommended in patients with RVF (2). Patients with RVF have been found to have lower survival as compared to non-RVF,[7] but it has also been suggested that each additional defibrillation attempt is linked to worse survival even if the criteria for RVF are not met.[4] These findings suggest an opportunity to increase survival in OHCA by developing alternative strategies to increase defibrillation success. Novel approaches to defibrillation, such as double sequential defibrillation, have emerged as a treatment option for RVF.[8] However, further evaluation is needed before potential implementation[2] and additionally, the evidence for optimal timing for these interventions is sparse.

The primary aim of this observational study was to assess survival in relation to each additional defibrillation in OHCA. The secondary aim was to observe potential differences in patient and resuscitation characteristics based on the number of defibrillations received.

Methods

Study design and study population

This registry-based retrospective cohort study is based on data from the Swedish Registry of Cardiopulmonary Resuscitation (SRCR) and the National Patient Registry (NPR). The study population comprised all patients 18 years and older suffering OHCA with an initial shockable rhythm from January 1, 2010 and December 31, 2020. Exposure was defined as the total number of defibrillations during resuscitation and primary outcome 30-day survival.

Patients with missing data on the number of defibrillations (exposure) and 30-day survival (primary outcome) were excluded.

The Swedish registry of cardiopulmonary resuscitation

SRCR is a nationwide quality registry in Sweden launched in 1990.[3] The registry includes all patients with OHCA where treatment was initiated by the EMS.[9] It consists of data reported from all EMS organizations in Sweden's 21 regions.[9] Data is reported by the EMS team using a modified Utstein style standard form.[10] To prevent incomplete individual reporting, data is also filled in retrospectively from EMS charts.[11]

The National patient registry

The NPR has been described thoroughly elsewhere.[12,13] It is a nationwide registry in Sweden launched in 1964 consisting of data on inpatients from hospitals and specialist clinics, and outpatients from private and public healthcare. It is estimated that the registry covers 99

Table 1
Patient and Resuscitation Characteristics.

Variables	Total (n = 10,549)	1 shock (n = 3,006)	2 shocks (n = 1,665)	3 shocks (n = 1,336)	4 shocks (n = 1,064)	5 or more shocks (n = 3,478)	Missing, n (%)
Age, median (Q1, Q3)	71 (61, 79)	71 (61, 80)	72 (62, 80)	72 (62, 80)	70 (62, 78)	70 (61, 78)	802 (7.6)
Female sex, n (%)	2,168 (20.6)	771 (25.7)	395 (23.7)	255 (19.1)	195 (18.3)	552 (15.9)	6 (<0.1)
Witnessed OHCA, n (%)	8,733 (84.3)	2,522 (86.0)	1,402 (85.7)	1,125 (85.4)	877 (83.8)	2,807 (81.8)	184 (1.7)
OHCA at home, n (%)	6,066 (57.6)	1,520 (50.7)	874 (52.5)	755 (56.6)	634 (59.6)	2,283 (65.7)	12 (0.1)
Treatment before EMS arrival, n (%)							
Bystander CPR	6,546 (63.6)	1,650 (57.6)	1,059 (65.3)	886 (67.0)	722 (68.8)	2,229 (65.0)	260 (2.5)
Bystander Defibrillation*	464 (4.4)	147 (4.9)	88 (5.3)	64 (4.8)	35 (3.3)	130 (3.7)	10,009 (94.9)
Advancedtreatment, n (%)							
Adrenaline	7,829 (75.0)	1,434 (48.6)	1,030 (62.9)	1,058 (80.0)	954 (90.0)	3,353 (96.7)	112 (1.1)
Amiodarone	4,191 (40.7)	87 (3.0)	106 (6.7)	489 (37.9)	615 (58.7)	2,894 (83.7)	261 (2.5)
Intubation**	3,089 (29.8)	647 (22.0)	406 (24.8)	393 (30.0)	361 (34.6)	1282 (37.4)	187 (1.8)
Laryngeal mask airway**	3,462 (60.0)	727 (43.6)	512 (56.7)	457 (62.9)	379 (67.2)	1,387 (72.5)	4,776 (45)
Mechanical chest compression	4,489 (44.1)	840 (29.0)	659 (41.0)	641 (49.4)	527 (51.4)	1,822 (54.2)	361 (3.4)
Time intervals,median (Q1, Q3) – min							
Detection of OHCA to start of CPR	2.0 (0.0, 6.0)	1.0 (0.0, 4.0)	1.0 (0.0, 5.0)	2.0 (0.0, 7.0)	2.0 (0.0, 7.0)	3.0 (0.0, 8.0)	1,403 (13.3)
Detection of OHCA tofirst shock	12.0 (6.0, 17.0)	9.0 (2.0, 15.0)	11.0 (6.0, 16.0)	12.0 (8.0, 17.0)	13.0 (8.0, 18.0)	13.0 (8.0, 18.0)	1,510 (14.3)
Detection of OHCA to EMS arrival	10.0 (5.0, 16.0)	8.0 (−0.75, 14.0)	9.0 (5.0, 15.0)	10.0 (6.0, 15.0)	11.0 (7.0, 16.0)	11.0 (7.0, 17.0)	1,975 (18.7)
Emergency call toEMS arrival	9.0 (6.0, 14.0)	9.0 (6.0, 15.0)	8.0 (5.0, 13.0)	8.0 (6.0, 13.0)	8.0 (6.0, 13.0)	9.0 (6.0, 14.0)	1,153 (10.9)
Outcomes, n (%)							
30-day survival	3,419 (32.4)	1,407 (46.8)	690 (41.4)	442 (33.1)	302 (28.4)	578 (16.6)	0.0 (0)
ROSC at any time	6,010 (57.5)	2,071 (70.6)	1,111 (67.0)	840 (63.0)	609 (57.5)	1379 (39.9)	105 (1.0)
Comorbidities prior to the event, n (%)***							0 (0)
Atrial fibrillation	2,562 (24.3)	645 (21.5)	379 (22.8)	310 (23.2)	270 (25.4)	958 (27.5)	
Heart failure	2,736 (25.9)	646 (21.5)	414 (24.9)	340 (25.4)	293 (27.5)	1,043 (30.0)	
Diabetes type 1	652 (6.2)	177 (5.9)	99 (5.9)	81 (6.1)	79 (7.4)	216 (6.2)	
Diabetes type 2	1,837 (17.4)	489 (16.3)	273 (16.4)	207 (15.5)	224 (21.1)	644 (18.5)	
Myocardial infarction	2,737 (25.9)	764 (25.4)	432 (25.9)	324 (24.3)	294 (27.6)	923 (26.5)	
Stroke	1,010 (9.6)	303 (10.1)	147 (8.8)	117 (8.8)	96 (9.0)	347 (10.0)	
Ischemic heart disease	3,052 (28.9)	767 (25.5)	479 (28.8)	374 (28.0)	329 (30.9)	1,103 (31.7)	

* Missing values for bystander defibrillation were assumed as no defibrillation.
** Intubation or laryngeal mask airway at any time during the prehospital treatment by the EMS.
*** Patients with missing values for the comorbidities were considered to not have the diagnosis. CPR, cardiopulmonary resuscitation; EMS, emergency medical service; OHCA, out-of-hospital cardiac arrest; ROSC, return of spontaneous circulation; SMD, standardized mean difference; Q, quartile.

% of these patients. However, no primary care is included. The registry data consists of diagnoses and surgical procedure codes, according to the International Classification of Diseases (ICD)-10 codes.

Data collection

Patients and resuscitation characteristics were retrieved from the SRCR, see Table 1. Initial shockable rhythm was defined as either pVT or VF detected by the emergency medical services (EMS) upon arrival, or if defibrillation had been performed by bystanders using an automated external defibrillator (AED) before EMS arrival. We assumed that patients who received bystander defibrillation by an AED before EMS arrival had an initial shockable rhythm even if an initial non-shockable rhythm (asystole or pulseless electrical activity (PEA)) or missing data were registered at ambulance arrival. ICD-diagnoses prior to the OHCA were retrieved from the NPR. The following ICD-diagnoses were collected; atrial fibrillation (I48), heart failure (I50), diabetes type 1 (E10), diabetes type 2 (E11), myocardial infarction (I21, I22), stroke (I69, I63, I64) and ischemic heart disease (I25). These diagnoses were included since they are common in this study population with prevalences from 6.2 % to 28.9 % and were considered relevant in the OHCA group with shockable rhythm.

The Swedish emergency medical system

In suspected OHCA, generally two EMS units are dispatched, staffed with nurses trained in prehospital care, performing advanced cardiovascular life support (ACLS) in accordance with the European Resuscitation Council guidelines.[2] In addition, there has been a dual dispatch system in many regions in Sweden since 2005, where first responders i.e. trained firefighters and police officers are also dispatched to the site of the OHCA with an AED.[14] In 2016, a mobile application was launched in Stockholm where CPR-trained volunteers sign up to be dispatched as responders to OHCA if they are close to the location.[15] In 2024, this system was active in 14 out of 21 regions in Sweden. The aim for these volunteers is either to perform CPR or fetch and use an AED. Drones are also used as an additional way of delivering an AED to the site of OHCA as fast as possible, but the use of drones is still limited to one region.[16]

Statistical analysis

All patients were stratified by the total number of defibrillations performed. Continuous variables were presented as median and quartiles (Q1, Q3), and categorical variables as counts and percentages (n, %). In Table 1, missing values for bystander defibrillation were assumed as no defibrillation before EMS arrival to address the substantial amount of missing data. Multivariable logistic regression was used to adjust for potential confounders in the natural spline analysis and was presented as a curve. The outputs, odds ratio and 95 % confidence interval, from this regression were presented in the supplementary Table 5. Adjustments were made for age (years), sex (male/female), witnessed status (yes/no), location (home/other), bystander CPR (yes/no), time from emergency call to EMS arrival in minutes and year of cardiac arrest as a continuous variable. We also adjusted for comorbidities (yes/no); atrial fibrillation, heart failure, diabetes type 1, diabetes type 2, myocardial infarction, stroke and ischemic heart disease. Patients with missing values for the comorbidities were considered to not have the diagnosis.

Variables were treated as potential confounders if they were present before the first defibrillation, with the potential to affect both exposure and outcome. Bystander defibrillation was not included due to the substantial amount of missing data. Patients with unreliable data in the estimated time to EMS arrival, with negative values and extremely long delays of more than 60 min, were excluded from the regression analysis. A bubble chart with counts and cumulative percentages was used to display the distribution of OHCA patients for each additional shock.

Additionally, a separate analysis of patient and resuscitation characteristics was performed dividing patients into two groups non-RVF (1 or 2 shocks) and RVF (3 or more shocks), and the 30-day survival rate in these groups was compared over time. Patients who had an initial non-shockable rhythm (or missing data on initial rhythm) but received at least one defibrillation due to conversion to shockable rhythm at any time during the resuscitation, were not included in the primary analysis, but analyzed separately. Finally, the main analysis was repeated with stratification by patient sex. R V.4.3.2 for Mac OSx was used in all statistical analyses.

Ethics

All patients reported to the SRCR who survive to 3 months receive a mail with information that they are included in the register, the type of data that is stored and their full right to withdraw from further participation if they so wish. The current study using pseudonymized data from the register was approved by the Swedish Ethical Review authority (DNR 2023–05406-01, submitted 2023/09–29).

Results

Overall, 55,108 patients were registered in SRCR between January 1, 2010 and December 31, 2020. 11,445 patients remained after the exclusion of those aged below 18 years (n = 635, 1.2 %), without shockable rhythm (n = 36,801, 66.8 %) and missing data on first rhythm (n = 6,227, 11.3 %). After further exclusion of patients with missing data on the number of shocks (n = 896, 7.8 %) a total of 10,549 patients remained and were included in the final analysis. There was no missing data on 30-day survival. Among the included patients, 3,006 (28.5 %) received one shock, 1,665 (15.8 %) two shocks, 1,336 (12.9 %) three shocks, 1,064 (10.1 %) four shocks and 3,478 (33.0 %) 5 or more shocks (Fig. 1, flowchart).

Patient and resuscitation characteristics

Overall, the median age was 71 (Q1-Q3, 61–79) years and 20.6 % were females. Most OHCA were witnessed (84.3 %) and most occurred at home (57.6 %) compared to public locations. Of all patients, 63.6 % received bystander CPR and 4.4 % received bystander defibrillation before EMS arrival. The overall median time delay from the emergency call to EMS arrival was 9 (Q1-Q3, 6–14) minutes. The study population was fairly evenly distributed throughout the decade, with around 9.5 % of all patients each year, except for the last two years which contained lower proportions of 8.2 % in 2019 and 5.2 % in 2020 (Supplementary, Table 1). Several differences could be observed in patient and resuscitation characteristics based on the number of defibrillations received. The proportion of females and witnessed OHCA was lower for each additional shock. On the contrary, a higher proportion of OHCA at home, administration of adrenaline/amiodarone, intubation and mechanical chest compressions was observed for each additional shock. The time from OHCA detection to CPR initiation, first defibrillation and EMS arrival was observed to be longer as the number of shocks increased. The delay from emergency call to EMS arrival followed a more stable and no-changing trend. For a detailed presentation of the patient characteristics and missing data on respective variables, see Table 1.

Survival to 30 days

In total, 32.4 % of all included patients survived to 30 days (Table 1). There was a negative association between survival and the total number of shocks delivered. The adjusted survival rates for each additional shock were observed as an exponential decrease. For patients receiving one, two, three and four shocks, the adjusted probability of survival was 42 %, 36 %, 30 % and 25 % respectively (Fig. 2, panel A). In this adjustment analysis, the total number of patients was 8,376. As the

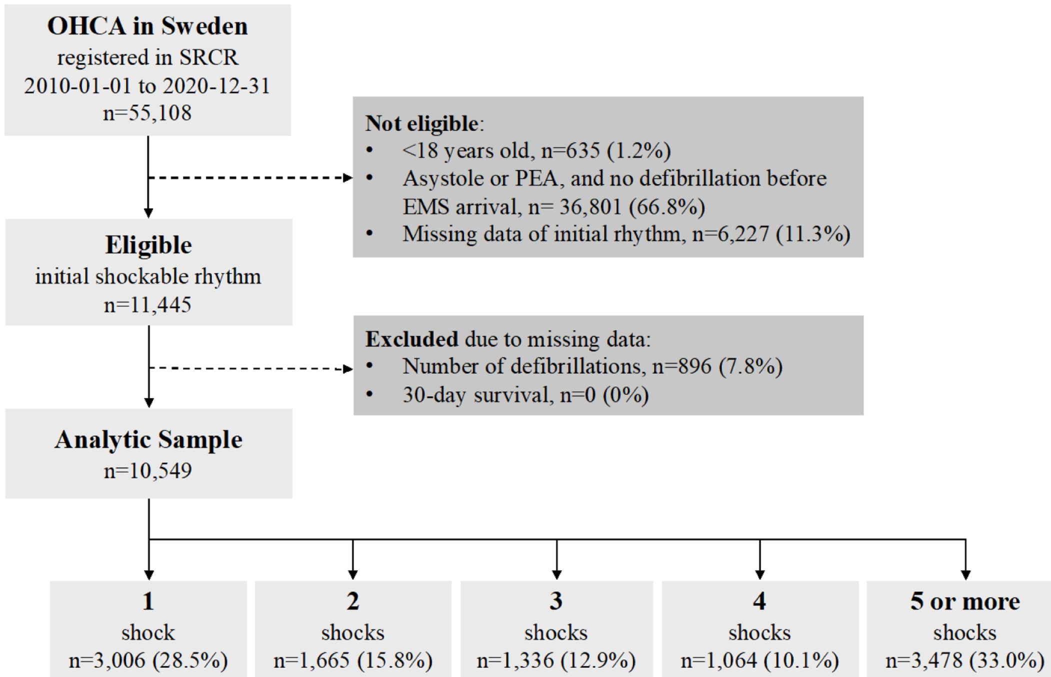

Fig. 1. Flowchart with patient selection. OHCA, out-of-hospital cardiac arrest; SRCR, Swedish Registry of Cardiopulmonary Resuscitation; PEA, pulseless electrical activity; EMS, emergency medical service.

number of shocks delivered increased, the number of patients decreased (Fig. 2, panel B).

When patients were divided into non-RVF (1–2 shocks) and RVF (3 or more shocks) survival was 49.9 % for non-RVF and 22.5 % for RVF (Supplementary, Table 2). Survival was higher in the later years of the study for RVF, whereas survival was higher for 1 or 2 shocks during all years but with no apparent trend over time (Fig. 3). In the separate analysis on excluded patients that did not have initial shockable rhythm or bystander defibrillation, but still received a defibrillation at any point during resuscitation, we found a 30-day survival of 6.3 % (Supplementary, Table 4). In sex-specific analyses, an exponential decrease in adjusted survival rates for each additional shock was also found for males, but was less distinct in females (Supplementary, Fig. 2 panels A and B).

Return of spontaneous circulation

Among all patients, 57.5 % achieved ROSC at any time (Table 1). The proportion of ROSC decreased as the number of shocks increased. The ratio between survival to 30 days and ROSC was 0.68 among those receiving only one shock, 0.62 for two shocks, 0.53 for three shocks, 0.50 for four shocks and 0.42 for five or more shocks.

Discussion

In this nationwide registry study over 11 years including all adult OHCA with an initial shockable rhythm, the main finding was a lower 30-day survival for each additional defibrillation attempt, which followed the appearance of an exponential decrease. This association persisted after adjustment for age, sex, witnessed status, location, bystander CPR, EMS response time, year of OHCA and several important comorbidities.

Previous studies have also found a lower survival rate for each additional shock in line with our findings.[4,17] Holmén et al.[4] assessed the association between 30-day survival and the number of shocks in Sweden in the period from 1990 to 2015. Holmén et al.[4] reported lower survival rates compared to our findings (33.7 % vs. 42 % one shock, 27.6 % vs. 36 % two shocks, 19 % vs. 30 % three shocks and 18 % vs. 25 % four shocks).

Moreover, in the comparison of 30-day survival between non-RVF (1 or 2 shocks) and RVF (3 or more shocks), we found substantially lower survival rates among RVF patients (22.5 % vs. 44.9 %, Supplementary Table 2). Alhenaki et al.[7] recently found similar results with the same division of groups during similar years. This definition of RVF has clinical implications since advanced treatment such as intravenous drugs, transportation and alternative defibrillation strategies should be considered after the third shock.[2] In our study about 1 out of 2 patients (Supplementary, Table 2) would be considered as RVF and qualify for advanced treatment.

However, our study highlights a clinically important decrease in survival before the third shock, and there is no apparent cut-off point.

The reason for a lower survival rate for each additional shock is probably multifactorial. A longer resuscitation attempt as a consequence of the need for more defibrillations may impact survival. Previous studies have found an association between longer resuscitation time and lower survival.[7,18] Another speculation is that differences in patient characteristics, such as previous disease burden or severity of the acute cardiac condition, could affect both defibrillation success and survival. In other words, the disease burden may act as a confounder of the association between the number of defibrillations and survival.

Our study also found a gradual decline in the ratio between 30-day survival and ROSC. This suggests that longer resuscitation time translates to lower survival even after ROSC. This may be a consequence of brain injury or organ failure due to the extended period without spontaneous circulation leading to hypoperfusion. Conversely, survival may increase if sustained ROSC can be obtained with fewer defibrillations.

We also found several differences regarding patient and resuscitation characteristics in relation to the number of defibrillations. Suffering OHCA at home is well known to be associated with a worse chance of survival,[2] and this is in line with our finding of an increased proportion of OHCA at home as the number of shocks increased. Well-known positive prognostic factors were observed with fewer defibrillations, perhaps most importantly time from recognition to first shock (9 min for 1 shock vs. 13 min for 4 and 5 or more shocks). This highlights the

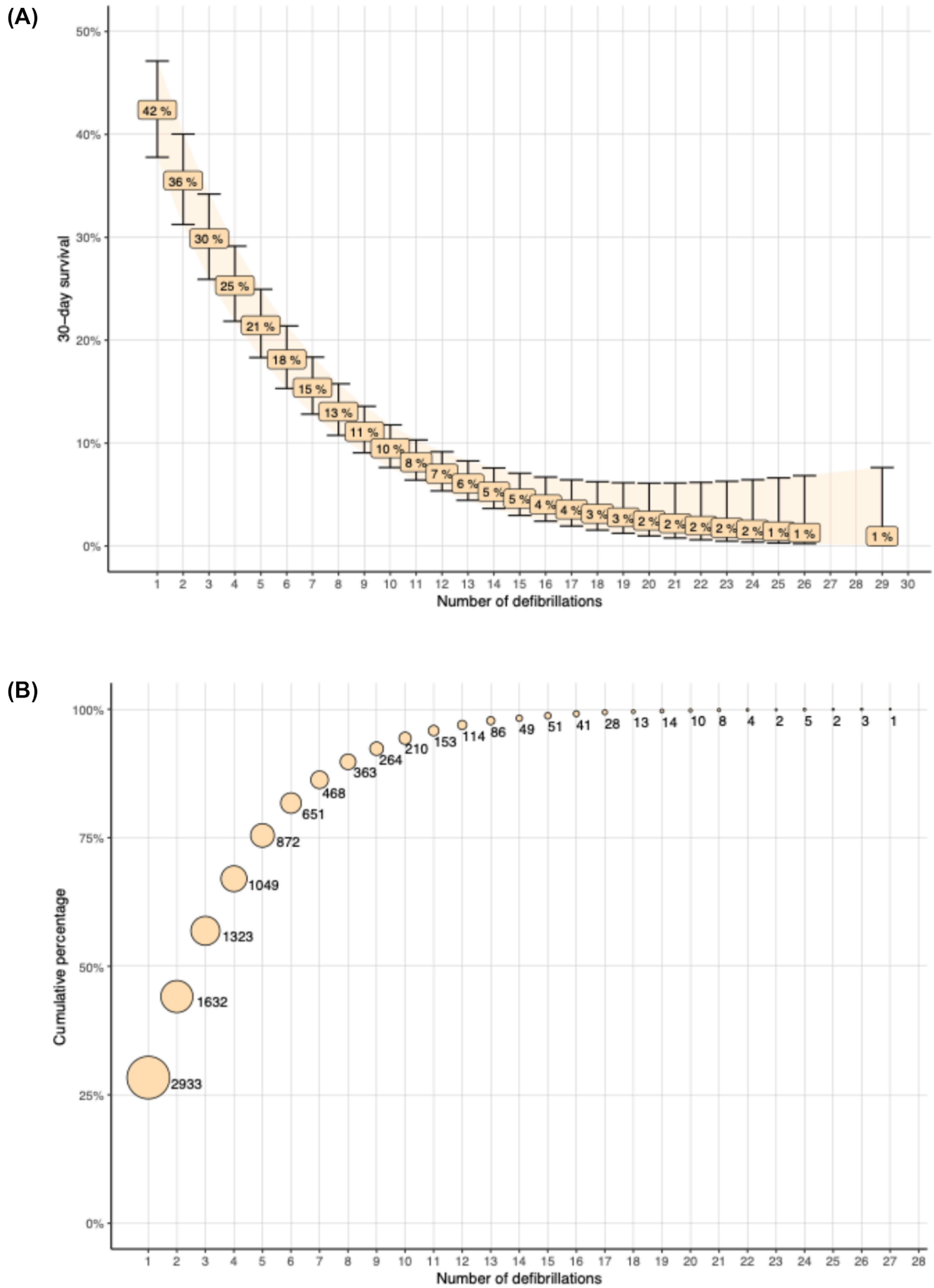

Fig. 2. Adjusted survival rates and patient distribution for each additional shock. Panel A. Adjusted natural spline. Adjustment with logistic regression for age, sex, witnessed status, location, bystander cardiopulmonary resuscitation, emergency medical services response time, year of out-of-hospital cardiac arrest, atrial fibrillation, heart failure, diabetes type 1, diabetes type 2, myocardial infarction, stroke and ischemic heart disease. 8,376 patients were included. 1,973 patients were excluded due to missing data and 200 patients due to unreliable data in the estimated time for emergency medical services arrival (negative values and extremely long delays of more than 60 min). Odds ratios and 95% confidence interval from this regression analysis are presented in Supplementary, Table 5. **Panel B.** Bubble Chart. Cumulative percentage of all cases in y-axis. Counts of varying sizes of yellow circles represent the total number of patients who received each defibrillation. 10,349 patients were included. 200 patients were excluded for the same reason as in Panel A. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

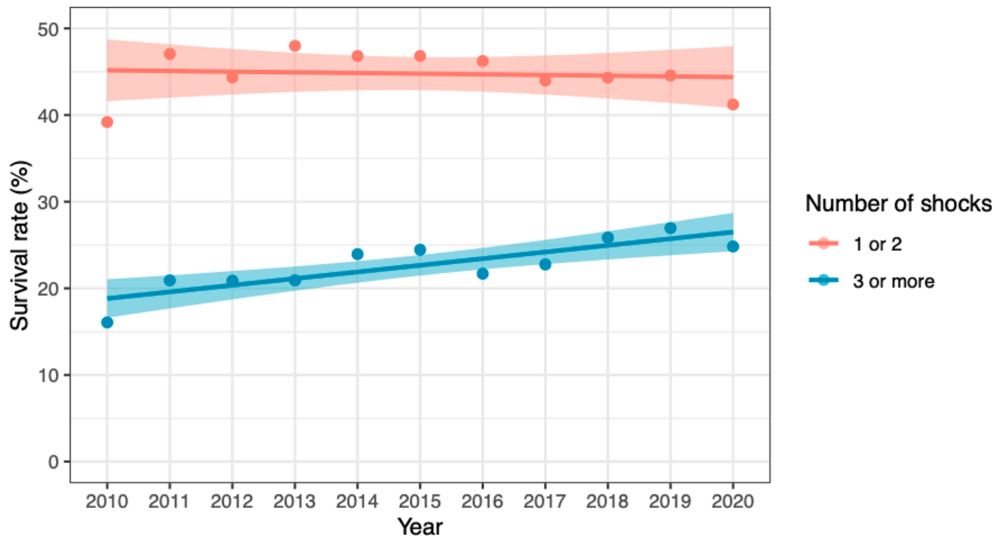

Fig. 3. Unadjusted survival trends stratified by 1 or 2 vs. 3 or more shocks. The y-axis represents the percentage of 30-day survival in the two study groups. Linear regression was used to fit a trend line for the plots. The background color presents the standard error.

importance of reducing time to first defibrillation.

Early defibrillation could be affected by public access defibrillation programs,[9] usage of the mobile application to recruit volunteers to fetch AEĎs and perform CPR[15] and initiation of dual dispatch systems.[14] These interventions could also act synergistically since early CPR has been found to prevent the deterioration of shockable rhythms into non-shockable rhythms over time.[19]

Another important finding was a temporal trend of unadjusted 30-day survival over time. The trend among those who received 3 or more shocks was associated with a higher survival rate in the later years of the study period, while the survival rate was higher and stable for all years among those with 1 or 2 shocks. We can only speculate on the reasons for this finding but improved post-resuscitation care during the later years of the study period may be one possible explanation.

Regarding clinical implications, the findings of this study may be informative on when to consider advanced treatment such as antiarrhythmics or alternative electrode pad placement (e.g. vector change or double sequential defibrillation) when VF persists despite defibrillation. The only randomized trial on double sequential defibrillation[8] found a survival benefit with either vector change or double sequential external defibrillation among patients in refractory VF defined as VF as initial rhythm that persisted despite three consecutive shocks. Our study suggests a poor and rapidly decreasing survival even among patients classified as non-refractory, which raises the question of whether it would be favorable to initiate advanced treatment or alternative defibrillation strategies earlier, after 1 or 2 failed defibrillations. Prospective studies of alternative defibrillations strategies are needed regarding when, and after how many shocks, it may be beneficial to change defibrillations strategy. Currently there is one ongoing pilot trial comparing double sequential defibrillation as soon as possible after one failed defibrillation to standard treatment (clinical trials NCT06447805) and hopefully others will follow.

Strengths and limitations

This is a large study including all OHCA with shockable rhythm over more than a decade from a mandatory national register which increases power and generalizability. We also consider the adjusted analysis to be a strength, where we adjusted for both resuscitation and patient characteristics including comorbidities. However, there are also several limitations to consider. First, the registry-based study design implies limitations due to potential bias and risk for residual or unknown confounders. Second, we only had data on the total number of defibrillations and lacked granularity on transitions of rhythms or re-fibrillation. Among patients who have successful defibrillation after one shock, more than 50 % will have recurrent ventricular fibrillation after successful shock.[2] Therefore, the observed decrease in survival with additional shocks could in part be due to recurrent arrhythmia and not related to defibrillation failure. Third, even though we adjusted for previous comorbidities, the exact cause of cardiac arrest such as primary ischemia, chronic ischemia with or without heart failure, arrhythmogenic cardiomyopathies or channelopathies was unknown and these conditions may confound the association between the number of defibrillations and survival.

Conclusions

In this registry-based retrospective cohort study, additional defibrillations were associated with a lower survival. This association persisted after adjustments for patient and resuscitation characteristics. The result from the adjusted analysis suggests a poor and rapidly decreasing survival before the third shock. It is therefore warranted for future studies to assess outcomes in shockable OHCA when advanced treatment and novel strategies are initiated before the third shock.

Sources of Funding

This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. RH was supported by research appointments from the Region Stockholm and the Swedish Heart-Lung Foundation. GR was supported by research appointments from the Region Stockholm.

CRediT authorship contribution statement

Linn Harrysson: Writing – review & editing, Writing – original draft, Visualization, Formal analysis, Data curation, Conceptualization. **Emma Blick:** Writing – review & editing, Writing – original draft. **Akil Awad:** Writing – review & editing, Conceptualization. **Martin Jonsson:** Writing – review & editing, Supervision, Data curation. **Andreas Claesson:** Writing – review & editing. **Carl Magnusson:** Writing – review & editing. **Lis Abazi:** Writing – review & editing. **Johan Israelsson:** Writing – review & editing. **Robin Hofmann:** Writing – review & editing. **Per Nordberg:** Writing – review & editing. **Gabriel Riva:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: RH received lecture and consulting fees to institutions from Pfizer/BMS and AstraZeneca.

Acknowledgments

We want to express our sincerest gratitude to all the EMS teams, for treating OHCA patients and collecting invaluable registry data. This type of registry-based study would not be possible without their dedicated work.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resuscitation.2024.110435.

References

1. Gräsner JT, Herlitz J, Tjelmeland IBM, et al. European Resuscitation Council Guidelines 2021: Epidemiology of cardiac arrest in Europe. *Resuscitation*. 2021 Apr;1(161):61–79.
2. Soar J, Böttiger BW, Carli P, et al. European Resuscitation Council Guidelines 2021: Adult advanced life support. *Resuscitation*. 2021 Apr;1(161):115–151.
3. Jerkeman M, Sultanian P, Lundgren P, et al. Trends in survival after cardiac arrest: a Swedish nationwide study over 30 years. *Eur Heart J*. 2022 Aug 4;43(46):4817–4829.
4. Holmén J, Hollenberg J, Claesson A, et al. Survival in ventricular fibrillation with emphasis on the number of defibrillations in relation to other factors at resuscitation. *Resuscitation*. 2017 Apr;1(113):33–38.
5. White RD, Russell JK. Refibrillation, resuscitation and survival in out-of-hospital sudden cardiac arrest victims treated with biphasic automated external defibrillators. *Resuscitation*. 2002 Oct 1;55(1):17–23.
6. Hasegawa M, Abe T, Nagata T, Onozuka D, Hagihara A. The number of prehospital defibrillation shocks and 1-month survival in patients with out-of-hospital cardiac arrest. *Scand J Trauma Resusc Emerg Med*. 2015 Apr;17(23):34.
7. Alhenaki A, Alqudah Z, Williams B, Nehme E, Nehme Z. Temporal trends in the incidence and outcomes of shock-refractory ventricular fibrillation out-of-hospital cardiac arrest. *Resusc plus*. 2024 Mar;8(18), 100597.
8. Cheskes S, Verbeek PR, Drennan IR, et al. Defibrillation Strategies for Refractory Ventricular Fibrillation. *N Engl J Med*. 2022 Nov 24;387(21):1947–1956.
9. Hasselqvist-Ax I, Riva G, Herlitz J, et al. Early Cardiopulmonary Resuscitation in Out-of-Hospital Cardiac Arrest. *N Engl J Med*. 2015 Jun 11;372(24):2307–2315.
10. Perkins GD, Jacobs IG, Nadkarni VM, et al. Cardiac Arrest and Cardiopulmonary Resuscitation Outcome Reports: Update of the Utstein Resuscitation Registry Templates for Out-of-Hospital Cardiac Arrest: A Statement for Healthcare Professionals From a Task Force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian and New Zealand Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia); and the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care. *Perioperative and Resuscitation. Resuscitation*. 2015 Nov;1(96):328–340.
11. Strömsöe A, Svensson L, Axelsson ÅB, Göransson K, Todorova L, Herlitz J. Validity of reported data in the Swedish Cardiac Arrest Register in selected parts in Sweden. *Resuscitation*. 2013 Jul 1;84(7):952–956.
12. Miedel C, Jonsson M, Dragas M, et al. Underlying reasons for sex difference in survival following out-of-hospital cardiac arrest: a mediation analysis. *Europace*. 2024. May 2;26(5):euae126.
13. Ludvigsson JF, Andersson E, Ekbom A, et al. External review and validation of the Swedish national inpatient register. *BMC Public Health*. 2011 Jun;9(11):450.
14. Nordberg P, Hollenberg J, Rosenqvist M, et al. The implementation of a dual dispatch system in out-of-hospital cardiac arrest is associated with improved short and long term survival. *Eur Heart J Acute Cardiovasc Care*. 2014 Dec;3(4):293–303.
15. Berglund E, Hollenberg J, Jonsson M, et al. Effect of Smartphone Dispatch of Volunteer Responders on Automated External Defibrillators and Out-of-Hospital Cardiac Arrests: The SAMBA Randomized Clinical Trial. *JAMA Cardiol*. 2023 Jan 1;8(1):81–88.
16. Schierbeck S, Nord A, Svensson L, et al. Drone delivery of automated external defibrillators compared with ambulance arrival in real-life suspected out-of-hospital cardiac arrests: a prospective observational study in Sweden. *Lancet Digital Health*. 2023 Dec 1;5(12):e862–e871.
17. Tateishi K, Saito Y, Kitahara H, et al. Impact of number of defibrillation attempts on neurologically favourable survival rate in patients with Out-of-Hospital cardiac arrest. *Resuscitation*. 2023 May;1(186), 109779.
18. Goto Y, Funada A, Goto Y. Relationship Between the Duration of Cardiopulmonary Resuscitation and Favorable Neurological Outcomes After Out-of-Hospital Cardiac Arrest: A Prospective, Nationwide, Population-Based Cohort Study. Mar 18 [cited 2024 Feb 28]; Available from: *J Am Heart Assoc [internet]*.; 2016. https://www.ahajournals.org/doi/abs/10.1161/JAHA.115.002819.
19. Waalewijn RA, Nijpels MA, Tijssen JG, Koster RW. Prevention of deterioration of ventricular fibrillation by basic life support during out-of-hospital cardiac arrest. *Resuscitation*. 2002 Jul 1;54(1):31–36.