Use of Volunteer First Responders and Automated External Defibrillators in Out-of-Hospital Cardiac Arrest

PhD THESIS

Laura Sarkisian Jangaard, MD

Date of Submission:
Oral Defence Session: November 26th 2021.

Thesis submitted to:
Institute of Clinical Research
Faculty of Health Sciences
University of Southern Denmark

Main author:

Laura Sarkisian Jangaard, MD

Research Unit of Cardiology, Odense University Hospital

J.B. Winsløws Vej 4, 5000 Odense C, Denmark

Tel.: +45 27 85 94 44

E-mail: Laura.Sarkisian2@rsyd.dk

Main supervisor:

Hans Mickley, Professor, MD, DMsc.

Research Unit of Cardiology, Odense University Hospital

Co-supervisors:

Finn Lund Henriksen, Associate Professor, MD, Ph.d.

Research Unit of Cardiology, Odense University Hospital

Jacob Eifer Møller, Professor, MD, DMsc.

Research Unit of Cardiology, Odense University Hospital

Members of assessment committee:

Jes Sandal Lindholt, Professor, MD, Ph.d. (Committee Chair)

Department of Cardiothoracic and Vascular Surgery, Odense University Hospital

Michael Müller, Professor, MD, DMsc.

Klinik f. Anästhesiologie, Intensiv- und Notfallmedizin, St. Josefskrankenhaus

Freiburg, Germany

Bo Løfgren, Professor, MD, Ph.d.

Department of Medicine, Randers Regional Hospital Hospital

Research Center for Emergency Medicine, Aarhus University Hospital

Table of Contents

ACKNOWLEDGEMENTS

First, I would like to thank my main supervisor, Professor Hans Mickley, for the tremendous work and support, he has put into the present PhD project. Our collaboration began many years ago, when I was a medical student, and I was quickly very impressed by your high work ethic, attention to detail and inspirational guidance in all research aspects. I could not have asked for a better mentor. Especially during the difficulties that came in our way during these recent years, you excelled in being objective, clear-sighted and patient, and provided support and motivation on many levels.

I am also very grateful for my co-supervisor, Dr. Finn Lund Henriksen, for the admirable footwork done prior to this research project. Your enthusiasm and passion for the first responder program, as well as your tremendous work for improving the conditions for people suffering out-of-hospital cardiac arrest has never ceased to inspire me. I am also thankful to Professor Jacob Eifer Møller, for the stimulating scientific discussions and help to launch this PhD program despite its challenges.

I would like to thank my collaborators: The Langeland Hjertestarterforening, its first responders, and Bruno and Birgitte for being available and assisting me throughout my first paper, and Henrik for helping me throughout all 3 papers. Also, thanks to the Emergency Medical Dispatch Center for collaboration and sharing of data, and Dr. Gitte Jørgensen, for providing me with knowledge concerning the prehospital emergency system. Finally, thanks to the national AED-network, and those involved for their collaboration. A special thanks to Henriette from Dialogue One for help and support.

I have had the privilege of supervising three talented young researchers during my PhD program, Sascha Lambrecht, Simon Michael Starck and Jonas Junghans Jensen, which has been a great pleasure and helped me become a better researcher.

I am grateful for spending my PhD years in the Forskerreden and becoming acquainted with the most amazing and fun research colleagues. Thank you all for your invaluable company, friendships, scientific as well as unscientific discussions and support during the years. I could not have done it without you.

Finally, the warmest thanks to my family and friends for your kind thoughts and support. A special thanks to my beloved husband, Nikolaj. Thank you for always making me laugh, and for always being patient and affectionate. Thank you for Agnes. You never fail to amaze me. You have my heart.

Sincerely, Laura

LIST OF PAPERS

The thesis is based on the three following papers:

Paper I (published)

Global Positioning System Alerted Volunteer First Responders Arrive Before Emergency Medical Services in More Than Four Out of Five Emergency Calls. Sarkisian L, Mickley H, Schakow H, Gerke O, Jørgensen G, Larsen ML, Henriksen FL. *Resuscitation. 2020 Jul;152:170-176. doi: 10.1016/j.resuscitation.2019.12.010.*

Paper II (published)

Use and Coverage of Automated External Defibrillators According to Location During Out-of-Hospital Cardiac Arrest. Sarkisian L, Mickley H, Schakow H, Gerke O, Møller JE, Jørgensen G, Henriksen FL. *Resuscitation. 2021 April. doi: 10.1016/j.resuscitation.2021.01.040.*

Paper III (work in progress)

Longer Retrieval Distances to the Automated External Defibrillator Reduces Survival After Out-of-Hospital Cardiac Arrest. Sarkisian L, Mickley H, Schakow H, Gerke O, Møller JE, Jørgensen G, Henriksen FL.

Additional papers (not included in thesis)

The Effect of Lay Responders' Experience on Response Time to Medical Emergencies in a Rural Area: An Observational Study. Starck SM, Jensen JJ, Sarkisian L, Schakow H, Andersen C, Henriksen FL. *(Work in progress)*

Different causes of Death in Patients with Myocardial Infarction Type 1, Type 2, and Myocardial Injury. Lambrecht S, Sarkisian L, Saaby L, Poulsen TS, Gerke O, Hosbond S, Diederichsen ACP, Thygesen K, Mickley H. *Am J Med. 2018 May ;131(5):548-554.doi:10.1016/j.amjmed.2017.Epub 2017 Dec 21.*

LIST OF ABBREVIATIONS

ACC: American College of Cardiology.

AED: Automated external defibrillator.

AHA: American Heart Association.

BLS: Basic life support.

CI: Confidence interval.

CPR: Cardiopulmonary resuscitation.

EMDC: Emergency medical dispatch center.

EMS: Emergency medical services.

ERC: European Resuscitation Council.

GPS: Global positioning system.

HEMS: Helicopter emergency medical service.

HRS: Heart Rhythm Society.

IQR: Interquartile range.

OHCA: Out-of-hospital cardiac arrest.

OR: Odds ratio.

OUH: Odense University Hospital.

PPJ: Prehospital Patient Journal.

QGIS: Quantum Geographic Information System.

ROSC: Return of spontaneous circulation.

RSD: Region of Southern Denmark.

SD: Standard deviation.

VFR: Volunteer first responders.

24/7: 24 hours a day 7 days a week.

BACKGROUND

Introduction

The abrupt loss of coordinated mechanical activity in the heart leading to absent circulation is known as cardiac arrest (1). When a cardiac arrest takes place outside of hospital, it is called an out-of-hospital cardiac arrest (OHCA). The symptoms of OHCA are loss of consciousness and absent or abnormal breathing (2), and the patient will either present with a shockable heart rhythm, defined as pulseless ventricular tachycardia (pVT) or ventricular fibrillation (VF), or a non-shockable heart rhythm, defined as asystole or pulseless electrical activity (PEA) (3). Studies have shown that shortly after collapse, the majority of OHCAs have a shockable heart rhythm (4-6). This can be treated by defibrillation, which means delivering an electrical shock through the heart to reestablish normal cardiac electric activity and thereby restoring the heart's ability to pump blood effectively (7). If a shockable rhythm is treated appropriately with defibrillation within 3 to 5 minutes, chances of survival can exceed >50% (8-11). In a casino study, dispatch of security officers trained in basic life support (BLS) including defibrillation demonstrated a remarkable survival rate of 74% in witnessed OHCAs defibrillated within 3 minutes (12). Similar results have been demonstrated in airports and other public places with use of on-site or nearby AEDs (8, 10). However, if the shockable rhythm remains untreated, it will deteriorate into a non-shockable rhythm (13, 14) with dismal survival rates of < 5% (15, 16). Overall, only about 10% of OHCA patients survive until hospital discharge (17-19).

The electrical devices used for defibrillation are called automated external defibrillators (AEDs), and they have proven to be safe and effective for bystander use (8, 20, 21), thereby gaining wide recognition (2, 7).

Incidence of out-of-hospital cardiac arrest

OHCA is the third leading cause of death in industrialized countries, affecting about 400,000 people in the US and 300,000 in Europe annually, with estimated incidences of 55-110 per 100,000 person-year (18, 22-24). In the last decade, the annual number of OHCAs in Denmark was approximately 4,000-5,000, resulting in an incidence of about 80 per 100,000 person-year (25, 26). The most common cause of OHCA is underlying coronary artery disease, which accounts for about two-thirds of cases (27, 28).

Chain of Survival

The four links in the Chain of Survival (Figure 1) encompass the main areas of focus for successful resuscitation after OHCA (29). In this thesis, our main focus will be on the 2nd (Early Cardiopulmonary Resuscitation (CPR)) and 3rd links (Early Defibrillation) in the chain.

Early CPR and defibrillation, either by a bystander or the professional EMS staff, is crucial for survival with good neurological outcome (17, 30-32). Using prediction models, previous OHCA studies have estimated a 7-10% decrease in the chance of survival per delayed minute from collapse-to-defibrillation (14, 33); this,

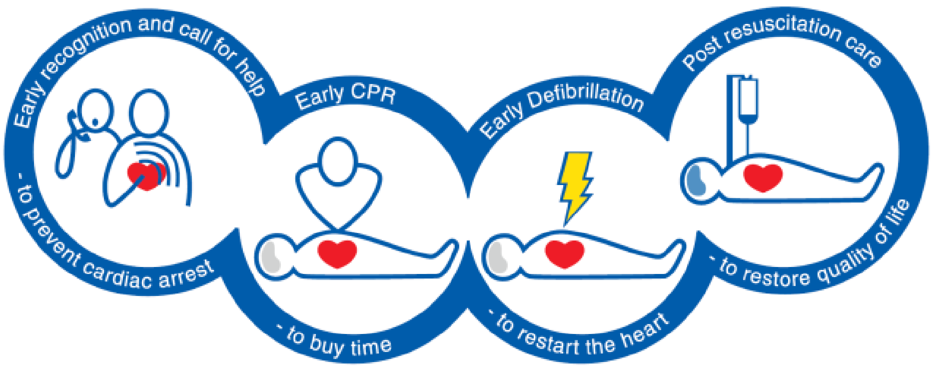


Figure 1. The Chain of Survival

however, can be reduced to 3-4% if the patient receives CPR (13, 14, 33). Therefore, both global (34, 35) and nationwide initiatives (36-38) have been made to increase public awareness and promote early bystander interventions. In Denmark, some of these efforts have included mandatory BLS training when acquiring a driver's license as well as BLS training in public schools (16, 39), the implementation of a national publically available AED-network (40, 41), the establishment of a set of recommendations regarding AED placement and accessibility by the national Danish Health Authority (42), and the implementation of a uniform national protocol used by all emergency medical dispatch centers (EMDC) to phone-assist bystanders to perform CPR and refer them to the nearest available AED, if conditions are appropriate (43). In recent years, the EMDC response in some parts of the country has also included mobile-phone activated first responders in cases of suspected OHCA (44, 45).

Public Access Defibrillation (PAD) Programs

In 1995 the American Heart Association (AHA) recommended the establishment of Public Access Defibrillation programs (PAD) to ensure available AEDs in public places, where OHCA is likely to occur, as means to shorten the collapse-to-defibrillation time (46, 47). So far, the only large-scale randomized controlled trial (RCT) of a PAD program was conducted in Northern America, involving 993 community units in 24 different regions (9). Each community unit was randomized to a CPR-only response system or a CPR+AED response system. In the study, Hallstrøm and colleagues found that the number of hospital survivors doubled in the CPR+AED group, compared to the CPR-only group. Ever since, there has been a large-scale dissemination of AEDs in industrialized countries (48) with >2,400,000 AEDs sold in the US alone (49). In 2016, the total number of AEDs sold in Denmark was 24,474 (50). Of these, 15,301 AEDs (63%) were registered in the national AED-network (50). Registering an AED in a PAD program increases the probability of use during OHCA (11), yet the full potential of this wide AED dissemination and PAD programs has not been achieved, since the overall rates of bystander defibrillation have remained low at 2-4% (6, 11, 31, 51, 52), and public AED placement largely remains unguided (40, 53-55).

International Recommendations for AED Placement

To increase bystander defibrillation, the AHA and the European Resuscitation Council (ERC) have proposed a number of recommendations regarding AED placement in PAD programs. In the previous 2006 guidelines, the AHA specifically addressed the expected AED coverage based on a number of studies (10, 12), and recommended AEDs to be placed within a short brisk walk of 1-1.5 minutes from areas with high risk of cardiac arrest (56). In most studies, this was translated as a straight-line (Euclidian) distance of 100 meter for a stationary AED (40, 53-55, 57). In the recent 2015 guidelines, however, the AHA and ERC recommendations abstained from recommending what AED coverage should entail. Instead the ERC recommended AEDs to be placed where one cardiac arrest can be expected per 5 years, and specifically called for AEDs to be placed "*in public places with high density and movement of citizens*", assuming that high pedestrian traffic pushes towards a higher incidence of witnessed cardiac arrests, as such seen in airports and shopping malls (2). The AHA stated the following recommendation: "*It is recommended that PAD programs for patients with OHCA be implemented in communities with individuals at risk of OHCA*" (34, 58), without further specifications. The current guidelines therefore seem insufficient, as they only address AED placement in public high-density urban centers, whereas the majority (60-80%) of OHCAs take place in residential areas and private homes (59, 60). Neither do they address AED placement in more rural areas with lower population densities and presumably longer distances to available AEDs. Consequently, the AHA and ERC in the current guidelines point out that there is a substantial knowledge gap surrounding AED placement strategies and call for research in this field.

Challenges for Early BLS during Cardiac Arrest

To create an overview of the bystander challenges for BLS interventions, it is important to point out some of the most important predictors of survival after OHCA. The predictors of survival can roughly be divided into spatial and non-spatial factors.

Spatial predictors of survival

The spatial factors that may affect survival include response time of the emergency medical service (EMS), AED retrieval distance, transport distance for hospital admission, type/level-of-care hospital, population density and rural-urban differences during OHCA.

In previous studies, longer EMS response times were found to be associated with lower survival after OHCA (61-63), and the length of EMS response times were also related to declining population density at the OHCA site (61, 64). Studies have also indicated that thinly populated areas were a marker of reduced survival (62, 63, 65), however, this must be interpreted with caution as population density could also be a proxy marker of higher residential OHCA rates and longer retrieval distances to the nearest available AED.

This, however, remains speculative. In two previous studies (66, 67), the transport distance to hospital admission was not associated with poorer survival; however, the type of hospital did affect survival, demonstrating improved outcomes for OHCAs admitted at invasive cardiac care units or tertiary centers, where they received a higher level of in-hospital care compared with admission at the nearest local hospital (66, 67). The effect of longer AED retrieval distance on survival after OHCA has, to the best of our knowledge, not been thoroughly investigated. In an observational study, Berdowski and colleagues compared survival outcomes in OHCAs defibrillated with an on-site versus dispatched AED (5). Not surprisingly, patients defibrillated with a dispatched AED had significantly longer collapse-to-defibrillation time than those with on-site use of AEDs, and demonstrated poorer survival. The bystanders, however, were restricted to firefighters and police officers, making it difficult to compare with present-day more widespread use by non-healthcare citizens.

Non-spatial predictors of survival

A number of non-spatial predictors of survival are patient-related, such as age, sex, comorbidity and cardiac arrest etiology (2, 7). These are partly non-modifiable (age and sex), and partly related to health promotion and prevention of cardiovascular disease initiatives (comorbidity and cardiac arrest etiology), which is beyond the scope of this thesis. Other non-spatial predictors of survival are; 1) The first three links in the Chain of Survival (the ability to early recognize a cardiac arrest and call for help, early CPR and early defibrillation, Figure 1) (2); 2) location of cardiac arrest (39, 68); 3) witnessed or non-witnessed cardiac arrest; 4) shockable or non-shockable heart rhythm (39, 59, 60); 5) AED availability (41, 50); 6) bystander ability and willingness to locate and retrieve an AED (69); and 7) AED functionality and effectiveness to treat a shockable rhythm (7, 70).

On a global scale, the rates of bystander CPR have increased, and this has been accompanied by an overall increase in survival (16, 71-74). However, the most significant changes have been observed for cardiac arrests that occur in public places (39, 68, 75). Here, OHCAs are more commonly witnessed, victims are younger, shockable heart rhythms are more frequent, and rates of bystander CPR and defibrillation are higher than in residential areas (59). Furthermore, public OHCAs more often occur in densely populated urban centers, where response times for emergency medical services are shorter (63, 65), which overall contributes to substantially better survival chances than in residential areas (39, 68, 75). As previously mentioned, the majority of all OHCAs are residential (59, 60), and survival rates have not changed significantly in this group over the recent years (68). Furthermore, while bystander defibrillation in public places has markedly increased, the numbers are dismal in residential areas (16, 39). So far, only few studies have evaluated the use of AEDs placed in residential areas (76, 77), and the results have been discouraging. Only one major randomized trial, the Home AED Trial, has been conducted in which a family member/spouse to patients with increased risk of sudden cardiac death were trained in CPR and assigned to either receive an AED for home use or no AED (78). The study found no significant survival effect of having access to an AED at home.

New Approaches for Increasing Bystander Defibrillation

In recent years, a number of studies have investigated the use of citizens trained in BLS as lay responders or volunteer first responders (VFRs), who are dispatched simultaneously with the EMS response when a cardiac arrest is suspected (79-84). In an observational study, Zijlstra and colleagues were able to demonstrate both an increase in bystander defibrillation in residential areas and a significant reduction in time-to-defibrillation, when VFRs were activated by text messages compared to the standard EMS response (84). The study, however, could not demonstrate an overall effect on survival after cardiac arrest. The only RCT study evaluating the effects of mobile-phone activated VFRs to facilitate BLS was conducted in central Stockholm, where VFRs within 500 meters of the emergency site were dispatched (85). The study found a significant increase in CPR rates, but was not designed to evaluate the effects on survival. Using mobile devices to activate nearby citizens and VFRs may be the missing link for increasing AED use for defibrillation purposes and reducing collapse-to-shock time during OHCA. There is, however, no clear-cut evidence on survival benefits of using VFRs, and the studies vary widely with inability to report important factors, such as VFR response times (81-84, 86), VFR response rates (80, 82), the response rates of VFRs bringing an

AED to the site, and their response times (79, 80, 82). Furthermore, the level of BLS training the VFRs are provided with and the type of rural-urban settings they are dispatched in varies widely between the studies (79-84).

Hypothesis

We hypothesized that;

Paper I: Mobile-phone-activated VFRs, that are geo-located through a global positioning system (GPS), will arrive to an emergency site before EMS in more than half of cases. Also, that using the GPS-system to activate VFRs, response times will be significantly shorter for VFRs compared with EMS response times

Paper II: The relative use of AEDs from public places is higher than that of AEDs placed in residential areas and other locations. AEDs are most often used at the same location type where they are placed. Also, AEDs placed in public places have shorter coverage than those placed in residential areas

Paper III: Survival after OHCA where an AED is used is lower in thinly populated areas compared with survival in densely populated areas. Also, longer AED retrieval distances reduce the chance of survival after OHCA.

AIMS OF THE THESIS

Paper I:

- To assess the response rates for mobile phone GPS-activated VFRs
- To compare VFR response times with EMS response times
- To evaluate survival after OHCA, when using the GPS-system to activate VFRs

Paper II:

- To evaluate the relative use of AEDs placed at seven types of locations: Residential areas; Public places; Nursing homes; Companies/workplaces; Institutions; Health clinics; and Sports facilities/Recreational areas
- To evaluate the extent of AEDs being transported from one location type to another for use during OHCA
- To investigate AED coverage distance during OHCA according to the AED location

Paper III:

- To evaluate and compare survival after OHCA in densely, moderately and thinly populated areas
- To evaluate the association between AED retrieval distance and survival after OHCA

METHODS – Paper I

Study Design and Settings

Paper I is a retrospective study conducted on the island of Langeland in Denmark. Langeland covers an area of ≈291 km^2, and is about 60 km long and 10 km at the widest point. Langeland does not have local hospitals, but is bridge-connected to Funen where there are two cardiac care units, one of which, the Odense University Hospital, serves as a tertiary referral center for the Region of Southern Denmark (RSD).

Demographic characteristics of Langeland

The island of Langeland has a population of ≈12,000. One-third of the population lives in the city of Rudkøbing. During the summer months the population grows substantially, as about 260,000 tourists visit the island (87). Langeland differs demographically from the rest of the RSD population; in 2012-2017 there was a higher proportion of ≥67 year-olds compared with the RSD (26.6% vs. 16.9%, respectively) (Statistics Denmark) (Figure 2).

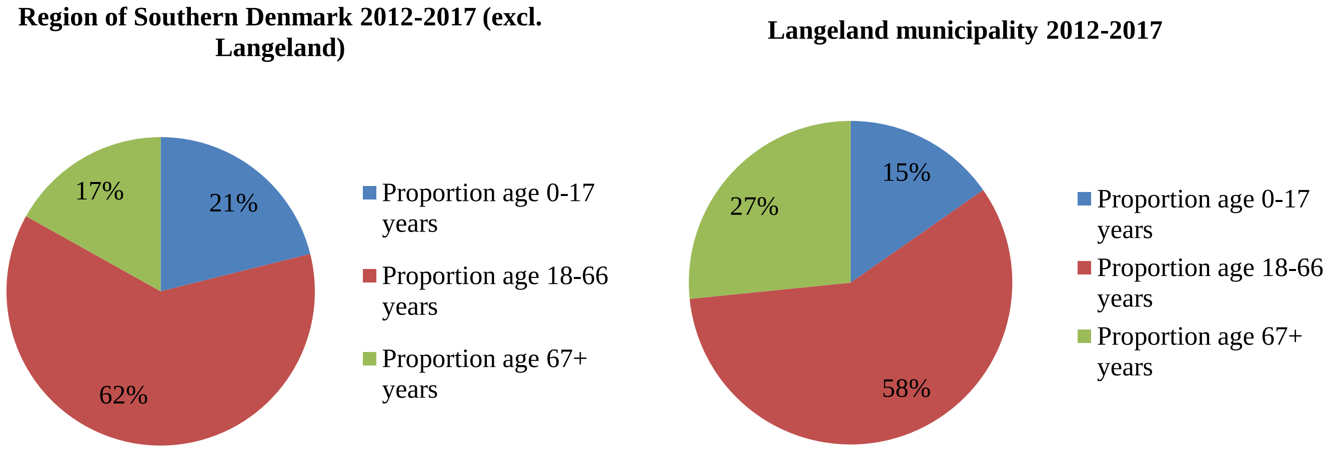


Figure 2. Age distribution in the Region of Southern Denmark and in the Langeland municipality (Statistics Denmark).

Moreover, the proportion of patients admitted or seen in an outpatient clinic (excluding visits at the general practitioners) was higher (38.8% vs. 36.5%, respectively), along with a higher socio-economic index (on average 1.29 vs 1.02, respectively) (Table 1, Figure 3).

Table 1. Socio-economic index

	2012	2013	2014	2015	2016	2017
RSD (excl. Langeland)	1.00	1.01	1.02	1.02	1.02	1.03
Langeland municipality	1.31	1.30	1.27	1.24	1.27	1.36
RSD: Region of Southern Denmark						

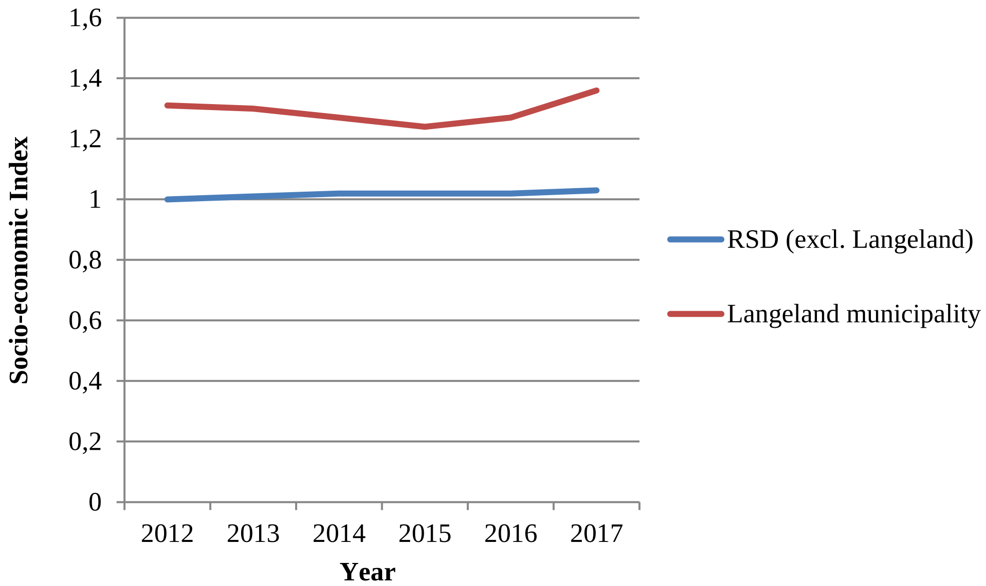


Figure 3. Shows that the socio-economic index in the Langeland municipality was consistently higher than in the rest of the RSD population. RSD: Region of Southern Denmark.

Data Collection

Data is collected using the Utstein-recommendations for reporting resuscitation outcomes (29). Neurological outcomes are reported using the five-point Cerebral Performance Category (CPC) score: CPC score 1-2 points denotes good to moderate cerebral disability, CPC score 3 points severe cerebral disability, CPC score

4 points comatose/vegetative state and CPC score 5 points dead/brain dead. The main outcome is reported as 30-day survival.

Shockable and non-shockable rhythms are defined according to the 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and a statement from the AHA Task Force on AEDs for PAD (70, 88).

The VFRs on Langeland

The VFRs were recruited through local advertisement and are mostly non-healthcare lay persons and a few off-duty healthcare professionals. They undergo a 12-hour course following the ERC-requirements for BLS training and a course in emergency first aid, which includes extensive training in e.g. drowning accidents, anaphylaxis and trauma management. When the course is completed, the VFRs download a smartphone application, (FirstAED, available for both Android and iOS), and must manually log on to the system to be available for dispatch. Afterwards, the VFRs undergo a yearly mandatory 3½ -hour training course to renew their certificate.

To become registered, the VFR must be at least 18 years of age, provide an updated criminal record certificate containing information on violations of the Penal Code's sexual offences against children less than 15 years of age, and sign a formal contract with the RSD to be health insured in the event of an injury.

The mobile-phone GPS-tracking system

The mobile phone GPS-tracking system (from now on called GPS-system), FirstAED, was introduced on the 21st of April 2012. The system is used for activating VFRs during all emergency calls on Langeland where an EMS is requested. However, VFRs were not activated in the city of Rudkøbing before the 21st of September 2015. When activated, the GPS-system localizes the nine closest available VFRs within a radius of 5000 meters from the emergency site and alerts them. The selected VFRs may accept or decline the emergency call. Of those that accept the call, three are chosen based on their position and the placement of the nearest available AED (Figure 4). The time-frame for this geo-localization is approximately 20 to 30 seconds, but the system is adaptive and awaits VFR response for up to 5 minutes, if not at least one VFR has accepted the call. The three dispatched VFRs are given distinct roles. The VFR closest to the AED must locate and collect it before approaching the emergency site (Figure 5). The two others must immediately rush to the emergency site to provide BLS, if necessary, guide the EMS, comfort bystanders etc. (Figure 4).

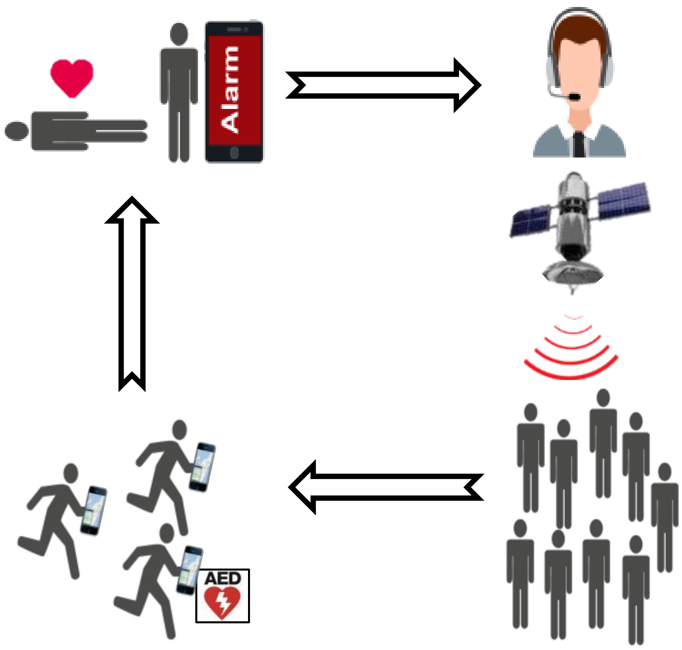


Figure 4. The GPS-system initially alerts nine volunteer first responders (VFRs) within a 5000 meter radius, and based on VFR response and their geographical location, the system selects and dispatches three VFRs.

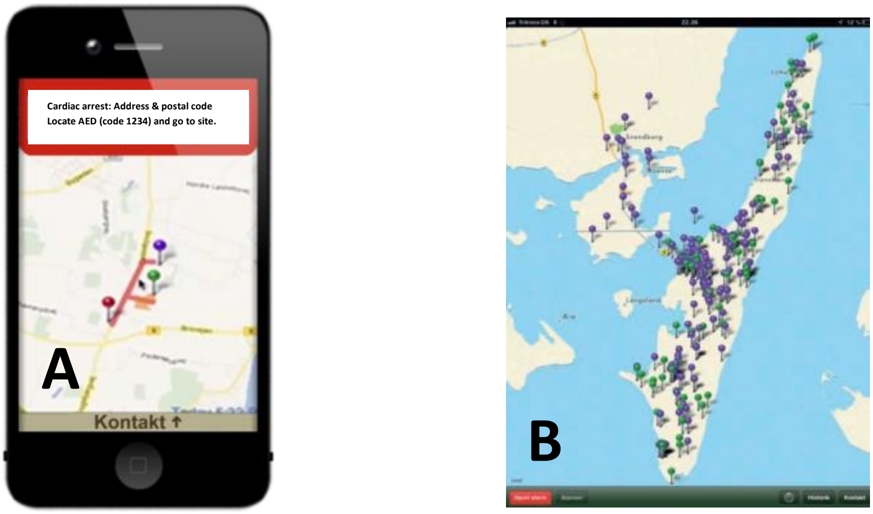


Figure 5. *A* is an example of the mobile phone map, which the volunteer first responder (VFR) receives after accepting the emergency call. The VFR (green pin) must collect the automated external defibrillator (AED) (purple pin) and go to the emergency site (red pin). *B* shows a snapshot of Langeland with the VFRs (green pins) and AEDs in the area (purple pins).

From April 2012 to August 2015 the health care professional at the EMDC used a separate tablet computer to activate the GPS-system. From September 2015 the GPS-system became an integrated part of the dispatch system and was activated simultaneously with the EMS-response.

The national Danish AED-network

In 2007, an AED-network for electronic registration of public access AEDs was established in Copenhagen, Denmark. In 2010, the AED-network was extended to nationwide registration, and in 2011 it became integrated with and accessible by the five EMDCs in Denmark (39, 40). Registration is voluntary, but encouraged by the national Danish Health Authorities (89) and most AED vendors. The general public can access information regarding placement and availability of registered AEDs through the network's homepage (www.hjertestarter.dk) or via a smartphone application ('Hjertestart').

Upon registration, the owner must provide the following information; 1) Name and contact information for the person responsible for the AED; 2) address of AED placement including area-specific characteristics to help identify the location; 3) AED accessibility including open hours during weekdays and holidays/weekends; 4) AED serial number and model; and 5) expiry date for electrodes and batteries. A few days after registration, the contact person is telephoned by an employee from the AED-network to validate the information. This is repeated every six month as long as the AED is active for public access defibrillation. If the information cannot be validated, the AED is removed from the network.

The AED-network on Langeland

The majority of AEDs used by VFRs on Langeland are registered in the national AED-network and almost all are placed outdoors in heated cabinets. When the GPS-system is activated, the designated AED cabinet opens automatically, and turns on a siren alarm and a blue flashlight to enable rapid localization.

The settings and emergency response on Langeland

Emergency phone calls from Langeland are received at the EMDC in Odense. Rudkøbing has an EMS station with an ambulance and a paramedic in a non-transporting EMS vehicle on duty 24/7. The paramedic is able to perform advanced life support including intravenous drug administration in accordance with current guidelines (3).

If the health care professional at the EMDC receives a phone call and suspects a cardiac arrest, a two-tiered system is activated in the RSD, following the dispatch of the nearest available EMS-ambulance and a physician-staffed emergency vehicle. On Langeland, the GPS-system with VFRs is also activated alongside the two-tiered system. If the physician-staffed vehicle is unavailable, the paramedic is dispatched instead. If the ambulance in Rudkøbing is occupied elsewhere, an ambulance from Svendborg is activated 20-50 kilometers away, which potentially increases response times (87).

On 1st of June 2015, the ambulance provider in the RSD changed. During the transitional period from 1st of June to 21st of September 2015, EMS response times were not available and are missing in our data set.

VFR and EMS response times

VFR response time is measured from the activation of the GPS-system to arrival of each of the three VFRs. If more than one VFR arrives at the emergency site, the shortest arrival time will be used for analysis. The

GPS-system registers VFR arrival to the emergency site, when the VFR is within 50 meters of the site. Furthermore, the system cannot register VFR arrival if mobile battery life is less than 30%, or in the absence of mobile phone reception.

EMS response time is measured as the time from activation to arrival of the first EMS at the emergency site.

Study Population

All EMS-treated OHCAs that occurred on the island of Langeland from April 21st 2012 until December 31st 2017 are included. Patients with obvious late signs of death are excluded along with non-medical OHCAs due to trauma, suicide, accidents etc. Also, OHCAs in nursing homes are excluded as VFRs are not activated during these emergency calls.

Place of cardiac arrest is defined as residential (private homes, multiple dwelling houses and vacation houses/cottages) or public (public buildings, streets, workplaces, sports facilities).

From April 21st 2012 to May 31st 2015 patient information was filled out on paper forms by the EMS staff. To identify OHCA patients in this period, all paper forms from the EMS stations in Rudkøbing and Svendborg were systematically screened by one author (LS). From September 21st 2015 patient information was filled out electronically and stored in the Prehospital Patient Journal (PPJ). PPJ stores information about prehospital patient treatment by EMS, paramedics, physician-staffed vehicles and physicians from the helicopter emergency medical services (HEMS). To identify OHCA patients in the PPJ, all recordings describing problems involving airways, breathing and circulation were systematically screened, as these could potentially evolve to cardiac arrest from the time of the phone call to the arrival of EMS. Also, recordings reporting any form of cerebral derangement, e.g. unconsciousness, epileptic seizures, syncope, were also screened, as these could be misinterpreted cardiac arrest cases. To cross-check for potentially missing OHCAs, the EMDC withdrew a list of all patients that had any information written in the section “Cardiac Arrest” in the PPJ.

By using each patient's unique personal identification number (90), information regarding comorbidity, in-hospital treatment, results from blood analyses and imaging, and 30-day survival was collected.

Outcomes and Variables of Interest

The main outcome variables of interest are

1. Response rate for all VFRs
2. Response times for VFRs and EMS
3. Thirty-day survival after OHCA in residential and public places

Covariates of interest are number of VFRs arriving before EMS, number of VFRs arriving with an AED before EMS, rate of bystander CPR among OHCAs, first documented rhythm, defibrillation before EMS and CPC score at discharge.

Statistics

All categorical variables will be presented as frequencies and percentages. When comparing categorical variables, the Pearson's chi-square test or Fisher's exact test will be used, depending on sample size in each group.

We will visually inspect all continuous variables for normal distribution. The normally distributed continuous variables will be presented as means with standard deviations (SD). The non-normally distributed continuous variables will be presented as medians with 25th and 75th percentiles, also known as interquartile ranges (IQR).

When comparing groups of continuous variables, two or more normally distributed variables will be compared using the Student's T-test or one-way analysis of variance (ANOVA), respectively. Non-normally distributed variables will be compared using the non-parametric Mann-Whitney U-test for two groups and the non-parametric Kruskall-Wallis test in cases of more than two groups.

The statistical significance level is at 5%. Analysis will be performed by use of STATA version 15 (StataCorp LP, College Station, Texas).

Ethics and Data Protection

For this type of retrospective studies, Danish legislation has no formal requirements of ethical approval. The project was approved by The Danish Data Protection Agency (Journal no. 17/32047) and the Danish Patient Safety Authority under the administration of Danish Health Authority (no. 3-3013-2319/1 and 3-3013-2848/1, respectively).

RESULTS – Paper I

Key results from ***paper I*** are presented with additional data in this results section. More details can be found in ***paper I*** (45).

The number of registered VFRs in 2012 was 185 persons on Langeland, of which 54% were male. At the end of 2017 the number of VFRs had slightly decreased to 170, and the male fraction was unchanged (55%). The number of AEDs on Langeland that could be accessed by VFRs during emergencies was circa 100, of which 98% were available for use 24/7 in outdoors cabinets. Two AEDs were placed at general practitioners and only available during opening hours

VFR and EMS response times

Figure 6 shows a flow chart with the number of emergency calls on Langeland. Out of 2,774 emergency calls, at least one VFR responded in 2,662 cases. Of these, a VFR arrived before EMS in 2,266 cases (85%), and in 1,745 cases (66%) the VFR had brought an AED to the emergency site before EMS arrival.

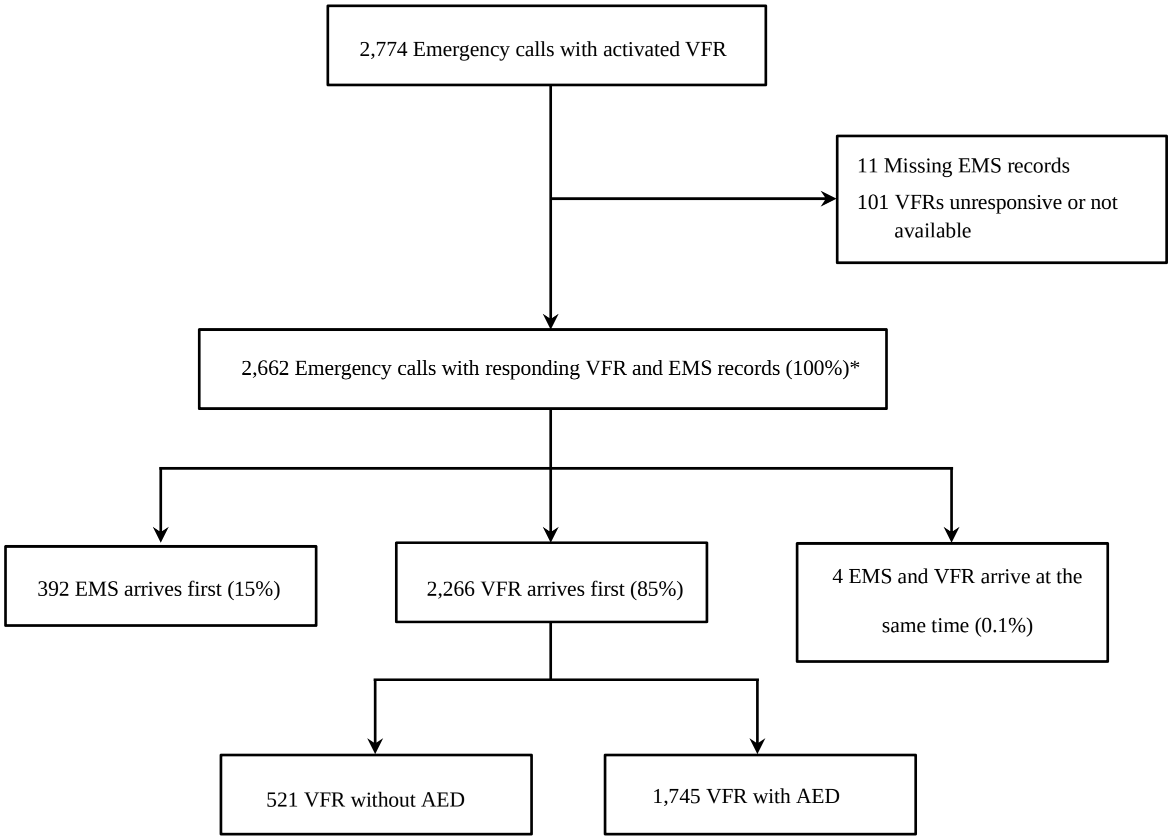


Figure 6. Flow-chart showing the number of emergency calls with activation of volunteer first responders (VFRs). *In 2,380 of the 2,662 cases, a VFR brought an AED to the site. AED: Automated external defibrillator. EMS: Emergency medical service. VFR: Volunteer first responder.

Table 2 shows the annual number of emergency calls, where VFRs were activated, and the corresponding VFR and EMS response times in the years 2012-2017. The annual response times are also shown in Figure 7. The median response times for all VFRs (N=2,662) was 4 minutes and 46 seconds, and the response time for a VFR bringing an AED to the site (N=2,380) was 6 minutes and 21 seconds, both significantly shorter than that of EMS, 10 minutes and 13 seconds ($p<0.0001$) (45).

Table 2. Annual VFR response times for 2012-2017.

		No. of VFR activations (%), (N=2,662)	VFR response time (min:sec), median (IQR)	EMS response time (min:sec), median (IQR)	P value*
Year					
-	2012	226 (8)	5:27 (3:34-7:42)	12:49 (8:38-16:13)	**<0.0001**
-	2013	360 (14)	4:53 (3:33-6:51)	13:17 (9:32-17:12)	**<0.0001**
-	2014	406 (15)	4:57 (3:31-6:58)	12:43 (8:42-16:39)	**<0.0001**
-	2015	314 (12)	5:10 (3:11-7:09)	11:04 (7:25-16:06)	**<0.0001**
-	2016	718 (27)	4:50 (3:22-7:11)	7:38 (4:34-14:13)	**<0.0001**
-	2017	638 (24)	4:06 (2:50-5:58)	7:16 (4:17-12:56)	**<0.0001**

*Non-parametric Mann-Whitney U-test. EMS: Emergency medical service. IQR: Interquartile range. RSD: Region of Southern Denmark. VFR: Volunteer first responder.

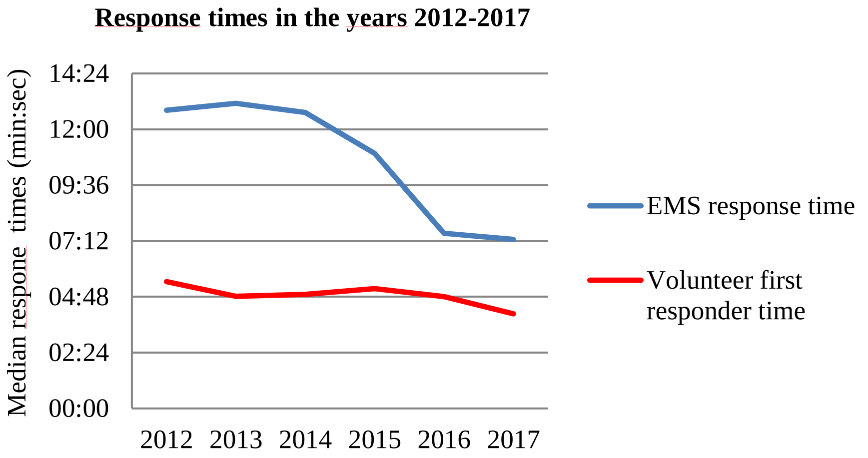


Figure 7. Annual response times for emergency medical services (EMS) and volunteer first responder (VFR).

Survival in residential and public places

Of the 243 presumed OHCAs identified during the inclusion period, 126 were excluded mainly due to signs of prolonged death (63 cases, 50%) and non-OHCAs (34 cases, 27%) (Figure 8). The latter group is further described in Table 3. Out of the 112 medical OHCAs, 65 took place in a residential area (58%) and 17 at a public place (15%).

OHCAs in residential areas and public places were comparable as regard to age, male sex distribution, proportion of shockable rhythm and pre-arrest cardiovascular risk factors (45). It seems, however, that public OHCAs more frequently had a cardiac cause of arrest, were more often witnessed and defibrillated prior to

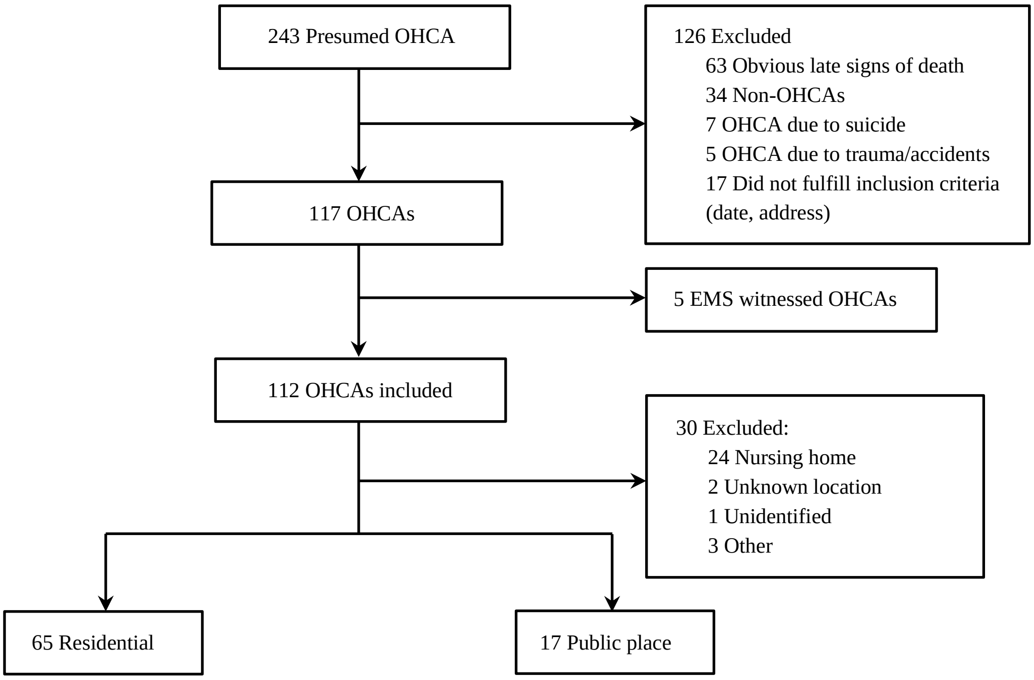


Figure 8. Flow-chart showing the inclusion-exclusion process in identifying out-of-hospital cardiac arrest (OHCA). EMS: Emergency medical service.

EMS arrival. In both groups, the occurrence of ROSC at hospital arrival was similar, yet 30-day survival appeared to be higher in the public OHCAs compared to the residential group (45).

Table 3. Causes of symptoms suggestive of cardiac arrest in non-out-of-hospital cardiac arrests (OHCA) (N=34)

	No. (%)
Epileptic seizure	14 (41)
Syncope	4 (12)
Medical cause	
- Subarachnoid hemorrhage.	2 (6)
- Cerebral stroke	2 (6)
- Cardiac arrhythmia	1 (3)
Cerebral confusion	4 (12)
Opioid overdose	3 (9)
Accident with head trauma	2 (6)
Alcohol intoxication	1 (3)
Choking accident	1 (3)

METHODS – Paper II & III

Study Design and Settings

Paper II and ***III*** are both cohort studies, where AED data was prospectively collected at the AED-center. The studies are designed retrospectively. The data is from AEDs used by bystanders in the RSD from January 1st 2014 to December 31st 2018.

The RSD consists partly of mainland and partly islands, of which the two largest, Funen and Langeland are connected to the mainland by bridges. The RSD covers an area of 12,191 km^2 and is a mixed rural-urban area with 1.2 million inhabitants, of which the ≈200,000 reside in the city of Odense (Statistics Denmark). The Odense University Hospital serves as a tertiary referral center for the RSD.

The emergency response in the RSD

The RSD has a total of 39 strategically placed EMS stations, six of which have a physician-staffed emergency vehicle. The EMDC for the RSD is located in Odense and is operated by health care professionals. If a health care professional receives a phone call and suspects a cardiac arrest, a two-tiered EMS system is activated following the dispatch of an ambulance and a physician-staffed emergency vehicle. The ambulance has BLS equipment including a defibrillator (LifePak 12/LifePak 15), and is staffed with an emergency medical technician (EMT) and an EMT assistant. The physician-staffed emergency vehicle is staffed with an anesthesiologist and an EMT, able to provide advanced life support (ALS) including endotracheal intubation. In 2013, a program with three helicopter emergency medical services (HEMS) was launched located in Ringsted, Skive and Billund serving the entire area of Denmark.

In cases where there are at least two bystanders present trained in CPR and a nearby available AED, the dispatcher may refer one of the bystanders to its location, in accordance with international guidelines (29).

In this study, EMS response times are measured as time from phone call to the EMDC to EMS arrival at the cardiac arrest site.

Data Collection

As in ***paper I***, data collection in both ***papers II*** and ***III*** are performed using the Utstein-recommendations for reporting resuscitation outcomes (29). Accordingly, reporting of neurological outcomes is done by use of the CPC score and 30-day survival is used to report the main survival outcome.

Cause of OHCA is defined according to the Utstein-guidelines (29), and is adjudicated by two authors (LS & FLH). Using hospital records and autopsy reports, those with a medical cause of cardiac arrest were further categorized into cardiac (presumed, confirmed and unknown cause) or non-cardiac cause of arrest. Shockable and non-shockable rhythms are defined according to the 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and AHA statement from the Task Force on AEDs for PAD (70, 88).

The AED-center and the Danish AED-network

In 2014, an AED-center was established at the Department of Cardiology, Odense University Hospital. If an AED is used on a person suspected of OHCA in the RSD, it is subsequently transported to the AED-center for further investigation. Using specialized software, the electrocardiogram recordings are retrieved and analyzed. Afterwards, the batteries, rescue kits and electrodes are replaced, and the AED is reset and send back to its owner. The information from the AED is stored in each patient's electronic hospital records for further diagnostic use.

The national Danish AED-network has been previously described (See 'The national Danish AED-network', p. 15). In cases where the AED-center cannot identify the owner/address of AED location, the serial number is used to trace this information via the AED-network, if the AED is registered in the network.

Definition and adjudication of location types

Location types are categorized using the 2015-Utstein template for uniform reporting of resuscitation outcomes (29) with addition of two location types that are not addressed in the template: 'Health clinics' and 'Institutions', as these have affiliated health care professionals with mandatory BLS training, but the population differs from that of nursing homes. Thus, the location types categorizing the OHCA site and AED placement are;

1) Residential areas (including private homes, multiple dwelling houses and vacation houses/cottages)

2) Public places (including all places freely accessible to the public e.g. shops and banks, as well as schools and educational facilities)

3) Nursing homes

4) Companies/workplaces

5) Institutions (defined as part time special care facilities and permanent community housings for people with mental or psychiatric disabilities)

6) Health clinics (defined as locations that employ authorized health care professionals registered under the Danish Health Authorities, e.g. medical doctors, nurses, dentists, physical therapists and occupational therapists. This does not include hospitals or outpatient clinics)

7) Sports facility/recreational area (including rowing and golf clubs)

When evaluating AED use, coverage and retrieval distances in ***paper II***, the above-mentioned location types will be used. However, when evaluating the demographic and prognostic results in ***paper II***, the groups 4-7 (companies/workplaces, institutions, health clinics and sports facilities/recreational areas) will be combined into one 'Mixed' group. The reason for this is that the these four locations have similar characteristics, as none are freely accessible to the public, but all are rallying points for rather large groups of people associated with that particular place.

At the end of 2018, the AED-network had a total of 4,359 AEDs registered in RSD. The registered information regarding the AED location types, however, was incomplete and validation was needed. Therefore, a random sample of 150 AEDs was selected and reviewed by three authors (LS, HM and FLH) to reach agreement regarding location type using the Utstein-template. Afterwards, one author (LS) systematically evaluated the remaining 4,209 AEDs and categorized them accordingly. In cases of ambiguity, the group was consulted to reach agreement.

Geocoding and QGIS

For ***paper III***, population densities are evaluated using a map with 1000 meter x 1000 meter (1 km^2) grid cells covering the entire RSD. The grid map used for this purpose is created by GEOSTAT (EUROSTAT) based on the population distribution in RSD in 2011 (91). Despite attempts to retrieve a more updated population map, this was not possible within the time frame of this PhD. To evaluate the population density in each grid cell, where an OHCA occurred and an AED was used, we will use the open source program, Quantum Geographic Information System (QGIS) (version A Coruña 3.10) (92). Using QGIS, each grid cell is color-graded according to the number of inhabitants, ranging from zero inhabitants (lightest green shade) to cells with ≥500 inhabitants (darkest green shade) (Figure 9).

Using QGIS, we will also integrate the addresses of the 4,359 AEDs in the GEOSTAT population map. This will help to visualize AED dissemination and to assess the number of AEDs in each cell at time of OHCA (Figure 10). When reporting the number of available AEDs at the time of OHCA, registration dates for all AEDs in the specific grid cell will be evaluated, and only AEDs registered before this date will be taken into account (Figure 10).

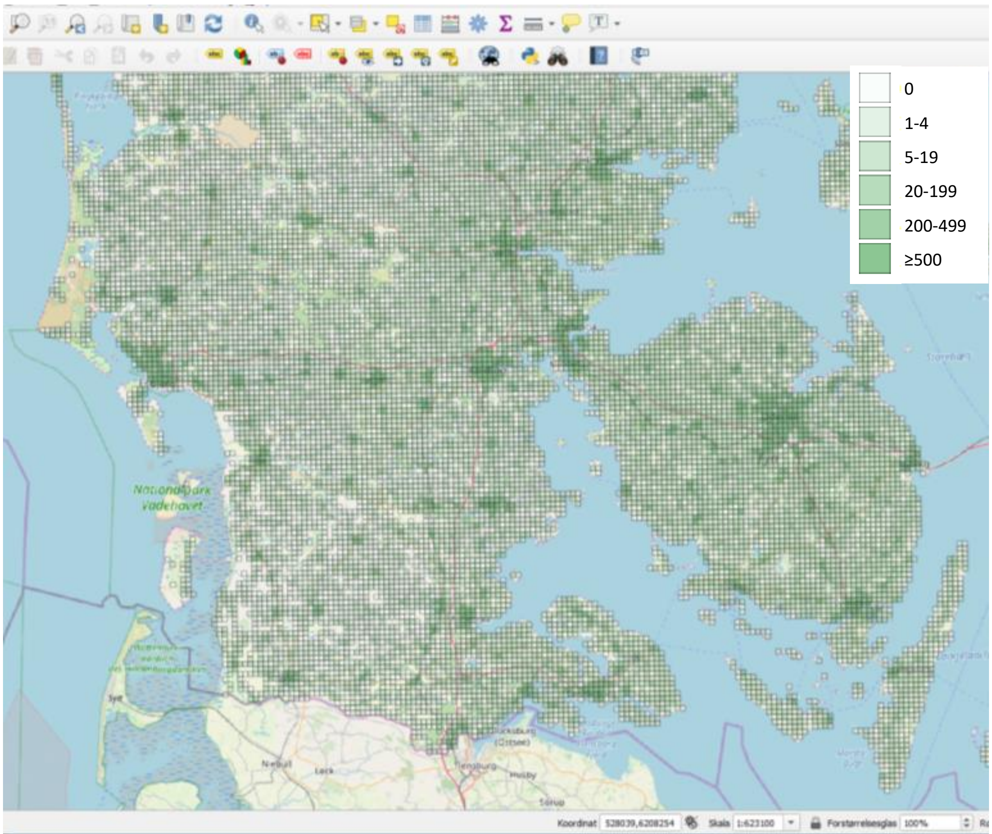


Figure 9. The GEOSTAT map showing the color-graded grid cells according to population density in each 1 km^2 cell. The upper right corner shows the color-grading according to the number of inhabitants in each cell.

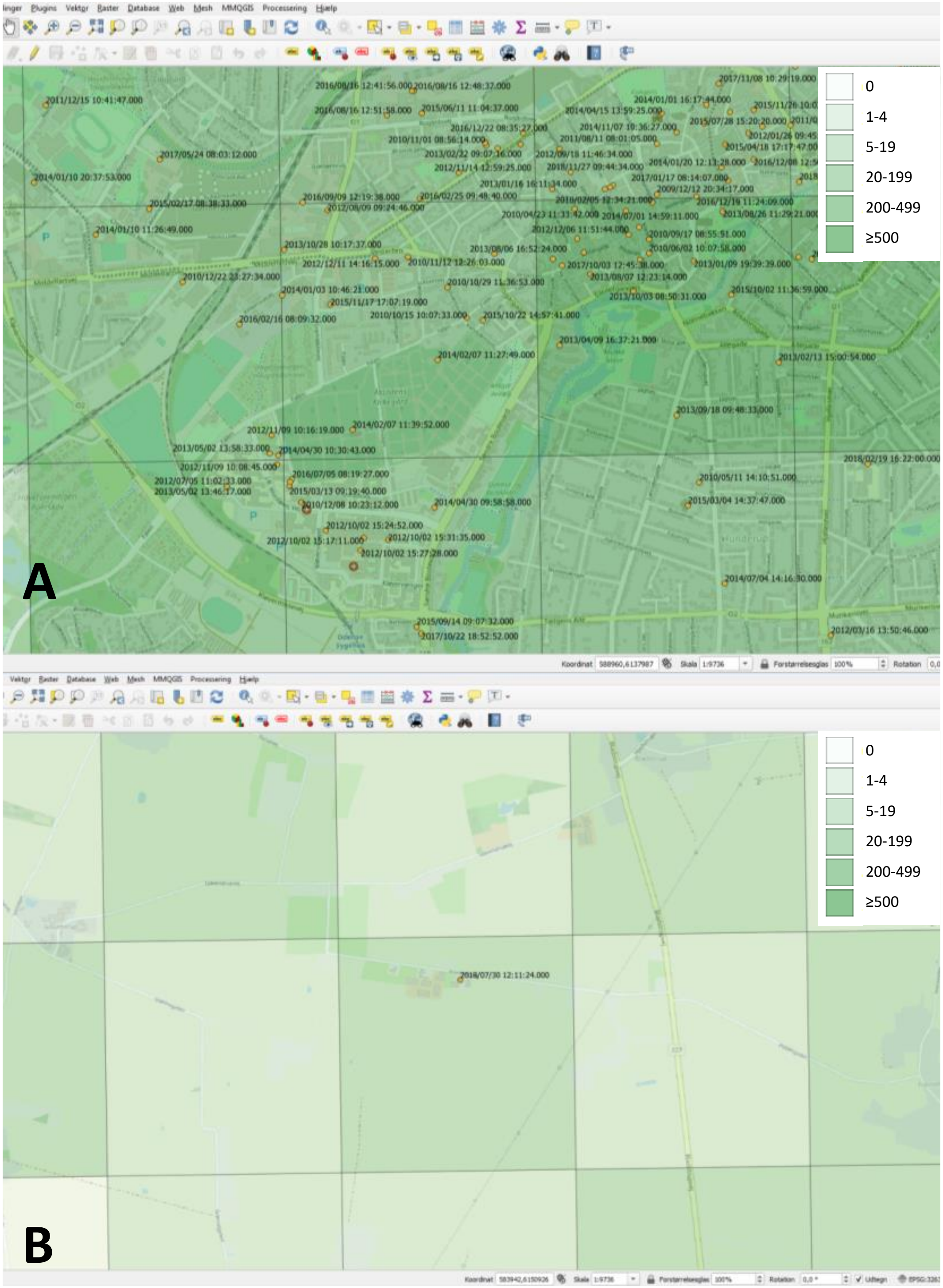


Figure 10. *A* shows the dark-green colored densely populated grid cells in urban Odense and the automated external defibrillators (AEDs) in the same area (yellow dots with registration dates). *B* shows a rural area approximately 15 kilometers outside of *A*. The area is less densely populated and only one AED is registered in several km^2.

Definition of population density

Based on the number of inhabitants in each grid cell, population density is categorized as follows:

1) Thinly populated: 0-19 inhabitants per km^2

2) Moderately populated: 20-199 inhabitants per km^2

3) Densely populated: ≥200 inhabitants per km^2.

To validate that population density in each grid cell approximates the population density in a given area, a random sample of 30 OHCA sites (10 in each population density group) was compared with the 'new definition of urbanization degree' by EUROSTAT, also called the LAU2 three-way classification (densely, intermediate and thinly populated) (93). Our definition of population density was consistent with the LAU2-definition in 28 out of 30 cases (in two cases, the moderately/intermediate density groups was categorized as thinly populated according to the LAU2-definition).

Definition of AED coverage and AED retrieval distances

The definition of AED coverage is the median distance an AED is carried from its stationary location to the OHCA site, thus the distance covered from that AED location. The definition of AED retrieval distance is the distance a bystander must walk from the OHCA site to collect an AED. For example, the expected AED coverage of an AED placed in a public place with high-pedestrian traffic may be a shorter distance, while during a rural cardiac arrest in a private home, the bystander may travel a longer distance to retrieve the nearest AED.

All coverage and retrieval distances are calculated using Google Maps, and presented as one-way walking distances. Google Maps is a valid mapping tool for measuring shorter horizontal-spatial distances within the scope of this study (94). If the site of cardiac arrest and AED location is the same (on-site AED), an arbitrarily distance of 5 meters will be used for distance calculations.

Study Population

OHCA cases, where an AED is used, and the AED is subsequently transported to the AED-center are evaluated for inclusion, if information about the OHCA site is available.

Paper II: OHCA due to medical causes are included. OHCA patients with prolonged signs of death are excluded along with those who did not have cardiac arrest.

Paper III: OHCA due to both medical and non-medical causes are included (trauma/drug overdose/drowning/electrocution/asphyxia). However, for non-medical OHCAs, only information regarding EMS response times, OHCA and AED, distance calculations and population density is reported. OHCA patients with prolonged signs of death, who did not have cardiac arrest or those that occurred at nursing homes are excluded.

Outcomes and Variables of Interest

For ***paper II*** the main outcome variables of interest are

1. AED use relative to proportion of registered AEDs according to location type
2. The percentage of AEDs transported from one to another location type during OHCA
3. AED coverage distance according to location type

Secondary outcome variables of interest for ***paper II*** are; AED retrieval distances and 30-day survival according to location type. Covariates of interest are; Rates of shockable first rhythm according to location type, number of registered AEDs and 24 hour AED availability according to location.

For ***paper III*** the main outcome variables of interest are

1. Thirty-day survival after OHCA in densely, moderately and thinly populated areas
2. The effect of AED retrieval distance on 30-day survival after OHCA

Covariates of interest are; EMS response times, proportion of residential OHCAs according to population density, and AEDs per km^2 according to population density.

Statistics

All categorical variables will be presented as frequencies and percentages. When comparing two or more categorical variables, the Pearson's chi-square test or Fisher's exact test will be used, depending on the sample size. Continuous variables will be visually inspected for normal distribution. The normally distributed continuous variables will be presented as means with SD, and non-normally distributed continuous variables as medians with 25th and 75^{th} percentiles (IQR). In group comparisons, two or more normally distributed variables will be compared using the student's T-test or one-way ANOVA, respectively. Non-normally distributed variables will be compared using the non-parametric Mann-Whitney U-test and the non-parametric Kruskall-Wallis test in cases of two or more group comparisons, respectively.

In ***paper II*** we will use a scatter plot to graphically display the association between the proportion of registered AEDs at the seven different types of locations (X axis) and the proportion of AEDs that are used from the same locations (Y axis). An upward shift in the scatter plot (Y value > X value) will be interpreted as a relatively higher use of AED from that specific location. Also, in ***paper II***, we will use a box plot to visually compare AED coverage distances according to location type.

In ***paper III,*** a multivariable logistic regression analysis will be used to evaluate the association between AED retrieval distance and survival after cardiac arrest.

The statistical significance level is at 5% in both ***paper II*** and ***III***. Analysis will be performed by use of STATA version 15 (StataCorp LP, College Station, Texas).

Ethics and Data Protection

For this type of retrospective studies ***(paper II & III)*** Danish legislation has no formal requirements of ethical approval. The project was approved by The Danish Data Protection Agency (Journal no. 17/32047) and the Danish Patient Safety Authority under the administration of Danish Health Authority (no. 3-3013-2319/1 and 3-3013-2848/1, respectively).

RESULTS – Paper II & III

Table 5. Cumulative numbers and proportions of registered AEDs according to location type

	2014	2015	2016	2017	2018	**Total %**	24/7 h no.	24/7 h %
Residential areas	194	282	363	430	501	**11.5**	494	98.6
Public places	767	902	1,073	1,259	1,408	**32.3**	79	66.0
Nursing homes	36	49	76	84	86	**1.9**	929	91.9
Companies/workplaces	644	767	931	1,103	1,228	**28.2**	248	39.7
Institutions	283	367	441	537	586	**13.4**	345	58.9
Health clinics	86	111	125	142	159	**3.6**	487	29.6
Sports facilities/recreational	278	306	336	366	391	**9.0**	47	63.4
Total number	**2,288**	**2,784**	**3,345**	**3,921**	**4,359**	**100.0**	**2,629**	**60.3**

AED: Automated external defibrillator. 24/7 h: 24 hours a day seven days a week.

Key results from ***paper II*** and ***paper III*** are presented in this results section with some additional data. More details can be found in the papers.

From 2014-2018 the AED-center received 621 AEDs for analysis. The annual number of AEDs is shown in Table 4.

Table 4. No. of AEDs received at the AED-center 2014-2018

	No. (%)
Year	
- 2014	93 (15)
- 2015	104 (17)
- 2016	111 (18)
- 2017	139 (22)
- 2018	174 (28)
Total	**621 (100)**

AED: Automated external defibrillator.

During the study period, the number of registered AEDs in the AED-network almost doubled from 2,288 in 2014 to 4,359 in 2018, with AEDs at public places (32%) and companies/workplaces (28%) comprising the majority (Table 5). The highest 24/7 h availability was observed among residential AEDs (98%) (Table 5).

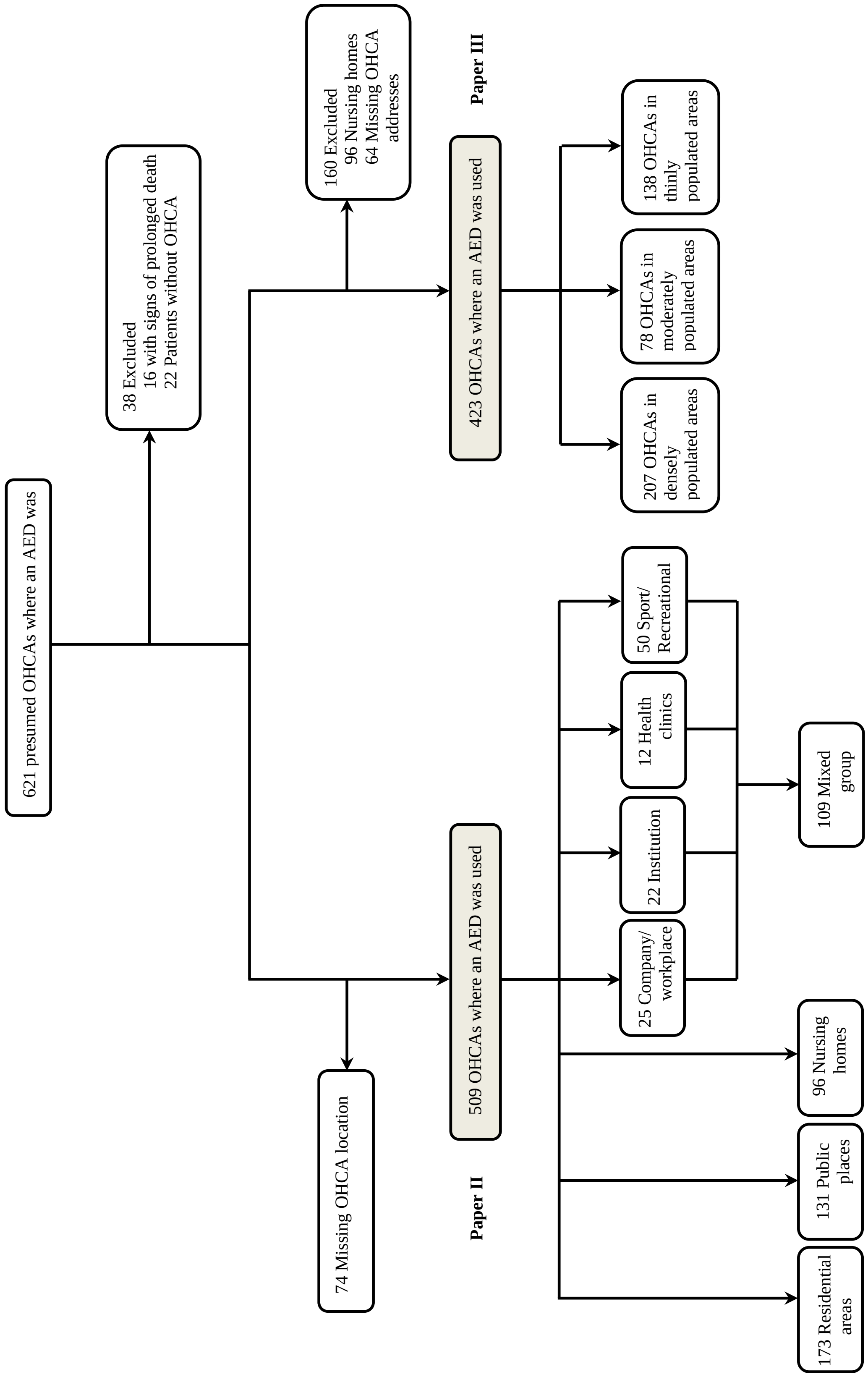


Figure 11. Flow-chart showing the inclusion-exclusion process for ***paper II & III.*** AED: Automated external defibrillator. OHCA: Out-of-hospital cardiac arrest.

Figure 11 shows the inclusion-exclusion process for ***paper II & III***. The figure shows that 509 OHCAs fulfilled the inclusion criteria for the purpose of ***paper II***, and 423 OHCAs for the purpose of ***paper III***.

Due to an unfortunate misclassification of OHCAs when entering data into the database, 5 non-medical OHCAs (all due to suicide) were included in the 509 patients in ***paper II***. In ***paper III***, all non-medical OHCAs (5 suicides and 17 other non-medical OHCAs) were appropriately included.

In 7 OHCA cases, the OHCA location type was known while the specific OHCA address remained unknown. These 7 cases were therefore included in ***paper II*** and excluded in ***paper III***.

Demographic and prognostic results (*Paper II*)

The 509 OHCAs were subdivided according to the seven OHCA location types (Figure 11). OHCAs in residential areas comprised the majority (173 out of 509, 34%), followed by OHCAs in public places (131 out of 509, 26%) (95). OHCAs in residential areas and nursing homes were more commonly female, more often unwitnessed, and had lower rates of shockable rhythms compared to the other groups (95). OHCAs in public areas and in the 'Mixed' group had the highest 30-day survival (45% and 64%, respectively), whereas survival was markedly lower in residential areas and nursing homes (13% and 2%, respectively).

AED use from different location types (*Paper II*)

The relative AED use from public places, nursing homes, sport facilities/recreational areas and health clinics was high, and the relative use from companies/workplaces, residential areas and institutions was low (95). We also found that during cardiac arrest in residential areas, AEDs were most commonly collected from public places.

AED coverage and AED retrieval distances (*Paper II)*

Of the 509 included OHCAs, the AED location was available in 416 cases (82%) for distance calculations. The widest AED coverage was observed for AEDs placed in residential areas, with a median coverage distance of 575 meters (IQR 130-1110), followed by public areas with a median coverage distance of 250 meters (IQR 5-550) (95). When an OHCA occurred in a residential area, the AED retrieval distance was almost the same as the coverage distance for a residentially placed AED (550 meters (IQR 280-1200) & 575 meters (IQR 130-1110), respectively) (95). However, during public OHCAs, a bystander travelled a median of 40 meters (IQR 5-230) to retrieve an AED compared to the more wider AED coverage distance of 250 meters (IQR 5-550) for a publically placed AED.

Demographic and prognostic results (*Paper III*)

Of the 423 OHCAs included in ***paper III***, 207 (49%) occurred in densely populated areas, while 78 (18%) and 138 (33%) occurred in moderately and thinly populated areas, respectively. Patient characteristics were comparable across the groups (Table 1, p. 3). When comparing thinly populated areas with densely populated areas, EMS response times were significantly longer (12 minutes (IQR 8-15) vs. 8 minutes (IQR 5-12), respectively (P=0.0001)), and the proportion of residential OHCAs was higher (50% vs. 36%, respectively (P=0.01)). Despite longer AED retrieval distances in thinly populated areas, survival did not differ among the groups (40%, 31% and 34% in densely, moderately and thinly populated areas, respectively).

The effect of AED retrieval distance on survival (*Paper III)*

About one-third of AEDs used during OHCA were on-site, and about two-thirds were collected from different addresses (Figure 3, p. 110). A multivariable logistic regression analysis was performed using 10 clinically relevant covariates and confounders (age, male sex, cardiac cause of arrest, bystander witnessed, public place of arrest, shockable rhythm, bystander defibrillation before EMS arrival, time of day, population density and EMS response time), and as part of a backward elimination, three variables (public place of arrest and bystander defibrillation before EMS arrival and population density) were excluded. In the final multivariable analysis, AED retrieval distance was regressed on 30-day survival. The analysis demonstrated an OR of 1.0010 (95% CI 1.0004-10016), which is translated into a 0.1% increase in risk of death per meter, corresponding to a 10% increase in risk of death per 100 meters an AED was placed further away from the OHCA site (Table 2, p. 107).

DISCUSSION

The results from ***paper I*** show that GPS-activation of trained VFRs during OHCA leads to the arrival of at least one VFR in 96% of cases and demonstrates that a VFR arrived before EMS in more than four out of five cases. Furthermore, the GPS-system resulted in a VFR response time that was significantly shorter than the EMS response time. The study also shows a trend towards improved survival after OHCA in both residential and public areas compared with results reported in earlier OHCA studies. However, this study was not designed to evaluate causative effects of VFRs, and the results are therefore only hypothesis generating.

The results from ***paper II*** show that there was a high relative use of AEDs placed in public places, nursing homes, health clinics and sports facilities, and a low relative use of AEDs placed in residential areas, companies/workplaces and institutions, considering the number of registered AEDs at each location. Also, the majority of AEDs used during residential OHCAs were collected from public places. Lastly, the study demonstrated significantly longer coverage distances of AEDs placed in public places and in residential areas than proposed in current literature and previous guidelines.

The results from ***paper III*** demonstrate that survival after OHCA, where an AED was used, did not seem to differ in thinly, moderately and densely populated areas. The length of the AED retrieval distance, however, was associated with reduced survival, even after adjusting for covariates and potential confounders.

The implications of VFR use during cardiac arrest

Although most cardiac arrests occur in private homes, the results from ***paper II*** revealed that only one in three AEDs was used at this location (173 out of 509 OHCAs) (95), and ***paper III*** further demonstrated that most OHCAs occur outside the densely populated areas. These two groups, residential and OHCAs outside densely populated urban areas, share similarities that give rise to the same challenges for improving survival; both have longer EMS response times (39, 60, 62-65, 96), fewer shockable rhythms (59, 60, 63, 64, 68), and overall reduced survival, when compared with public cardiac arrests and OHCAs in densely populated areas

(39, 59, 62, 65, 96). ***Paper III*** also reported a higher rate of residential OHCAs in thinly populated areas compared with high-density areas, consistent with the findings of Nehme and colleagues (63). Here, however, the study evaluated the use of firefighters dispatched as first responders. In order to improve AED use, an increasing number of communities have used different mobile phone systems to activate VFRs during OHCA. The results so far have been promising, but have raised new challenges that need to be addressed. In the PAD Trial, only 60% of the 19,000 BLS trained VFRs responded by giving appropriate CPR in the event of a cardiac arrest, and an AED was only used in about one-third of cases (9). The study, however, was conducted more than a decade ago, and the results could reflect a more restrained approach among first-responder towards providing BLS during OHCA. As previously mentioned, bystander CPR rates have increased substantially, and according to the most recent report from the Danish Resuscitation Council, bystander CPR rates exceeded that of first-responders in the PAD trial (79% vs. 60%, respectively) (26). The findings in ***paper I*** also suggest that citizen volunteers in a rural area can be effectively trained to become a part of the EMDC response during OHCA, with an impressive response rate of 96% and a median response time of 4:32 (IQR 3:07-6:21) among the 82% of VFRs that arrived before EMS. The response time, however, is measured from the time point of VFR activation until arrival. Unfortunately, it was not possible to report the time delay from phone call to VFR/EMS activation, or the collapse-to-call delay for the 2,662 emergency calls, where at least one VFR accepted the call. However, this time delay was calculated for the 43 witnessed OHCAs included in ***paper I***, and showed an average delay of 1:14 min:secs (data not shown), which means that for VFRs arriving before EMS, response times will not exceed the 5-6 minutes endorsed by current guidelines (2).

In the RSD, it is expected for an EMS to reach the emergency site within 15 minutes for 95% of all EMS responses (97). In ***paper I***, the median EMS response time was 10:13 min:secs (IQR 6:14-13:41). Even with the collapse-to-call and call-to-dispatch delay, this is within the expected time frame for the RSD (97). This is also close to the EMS responses of 10-12 minutes observed in other studies (52, 65, 81, 98). However, without proper bystander intervention, almost none would survive a cardiac arrest (14, 33). Perhaps the markedly shorter VFR response times affect survival rates after OHCA on Langeland (14 out of 82 OHCAs alive after 30 days, 17%), which is encouraging compared with 5-10% overall survival among OHCAs in other studies (17-19). Yet, the number of OHCAs in ***paper I*** is relatively small and cannot be used for evaluating causative effects. Also, as mentioned in ***paper I***, the GPS-system used on Langeland markedly differs from other types of alert systems used in other communities (45), and a head-to-head comparison with standard EMS response in a randomized trial has only been conducted in one study (85). The study, however, only involved OHCAs in central Stockholm, a densely populated area, and it is therefore unknown whether the alert system with untrained VFRs will perform as effectively outside an urban center.

AED use from different location types

The results from ***paper II*** showed that the relative use of AEDs from public places, nursing homes, health clinics and sport facilities/recreational sites was high compared to the number of AEDs registered at those location types. Vice versa, there was a low relative use of AEDs placed in residential areas, company/workplaces and institutions. As regards to the ERC recommendation of placing AEDs on public places where an OHCA is expected to occur every 5 years (2), this is considered to be cost-effective compared to other interventions (54, 99). However, on-site cardiac arrest incidence cannot stand alone when considering AED placement, but must be evaluated in relation to the population at the specific location amongst other factors. The incidence at e.g. nursing homes is expected to be relatively high, due to higher age and comorbidity among nursing home residents (100-102). However, a Danish registry study found that 30-day survival was only 1.7% among 2,519 nursing home OHCAs (100). This is similar to the results found in ***paper II*** (2%), which also found a relatively high use of AEDs at this location. For comparison, the relative AED use from companies/workplaces was low in ***paper II*** (only 1 in 20 of used AEDs). However, cardiac arrests that occur in companies/workplaces tend to affect a younger and healthier population with a much higher survival rate after OHCA (103), which ***paper II*** also confirmed. Hence, the expected number of life-years gained after AED use in companies/workplaces is higher compared to other locations, which must be weighed against the relatively low AED use and low cardiac arrest incidence found there. These are among the factors that should accompany the on-site incidence rates, when deciding the optimal location for AED placement and forming future recommendations in this field.

AED coverage distances

The recent ERC recommendation mentioned above does not specify the area size used for incidence measurements (occurrence of every 5 years), however, most studies interpret this as the reoccurrence of OHCA at the same address (53-55, 104). This recommendation was evaluated in a Danish study by Folke and colleagues. By using addresses of historical OHCAs, the study found that AED placement in these 'high-risk' public places would only be able to cover about one-fifth of public OHCAs, or 5% of all OHCAs (248 of a total of 4828 OHCAs) (54), if residential OHCAs are included. The study emphasizes that the majority of OHCAs occur in areas that are not addressed in the guidelines. Moreover, in current literature an AED is only expected to cover a distance of ≈100 meters (53-56, 104, 105), which is mainly applicable to urban centers with a high density of AEDs (40, 53-55, 105, 106). The results in ***paper II***, however, reveal that the real-life coverage distance of AEDs in public places was far longer than the 100 meters expected (250 meters (IQR 5-550), and that the coverage distance of a residential AED was almost six times the expected (575 meters (IQR 130-1300). So far, ***paper II*** is the first study to distinguish between AED coverage distance and AED retrieval distances during OHCA. The term "AED coverage", when used in the literature and previous AHA guidelines (53-56, 104, 105), refers to the one-way distance a bystander is expected to travel to collect an AED. In ***paper II***, this term ("AED coverage") was renamed to the "AED retrieval distance" and the term "AED coverage" was instead applied to the median distance an AED was transported from its stationary location. While the AED retrieval distance of 40 meters (IQR 5-230) for public OHCAs confirms that bystanders at public OHCAs only are willing to travel a short distance for AED retrieval, the AEDs placed in public places were able to cover a much larger area (0.23 km^2 for public places and 1.0 km^2 for residential areas vs. 0.03 km^2 for a radius of 100 meters).

AED retrieval distances and travel speed

The bystander retrieval distance during a residential OHCA was 550 meters (IQR 280-1200 m) in ***paper II***. If the travel speed used in previous guidelines is applied here (1-1.5 minutes to travel 100 meters or ≈1.5 m/sec), the additional time delay from collapse-to-defibrillation would be 6 to7 minutes. In the HeartRunner study by Jonsson and colleagues, VFRs were able to travel at a median speed of 2.3 m/sec (IQR 1.4-4.0

m/sec) (57). Furthermore, the study demonstrated that travel speed in rural areas exceeded that of densely populated urban areas (3.1 m/sec versus 1.8 m/sec). In a Swiss study, Auricchio and colleagues found that VFRs travelled at a median speed of 6.9 m/sec, which implies the use of motorized vehicles, as only 4% of VFRs travelled with a speed equivalent to brisk walking (79). Both studies were conducted in mixed rural-urban settings, requiring longer distances (median of 1196 meters (IQR 596-2314) and 956 meters (IQR 480-1661), respectively) for VFRs to reach the emergency site. For comparison, two other studies in urban Stockholm had VFR distances of 250 meters (IQR unavailable) and 560 meters (IQR 332-860) (80, 86), respectively. However, the VFR distances are not directly comparable with the bystander AED retrieval distances, which is used in both ***paper II & III***. While a bystander must travel a two-way distance to collect an AED and bring it to the emergency site, a VFR is located by GPS, receives coordinates for the nearest AED and is advised the shortest one-way route to the emergency site. Furthermore, the aforementioned distance measurements (57, 79, 80, 86) are for VFRs reaching the emergency site to provide CPR, and not bring an AED. So far, only one study has evaluated the additional distance a VFR must travel to collect and AED before approaching the emergency site. The one-way travel distance of 560 meters (IQR 332-860) reported by Berglund and colleagues almost doubled (1280 meters (IQR 748-1776), when the VFR was assigned to collect an AED (80). In ***paper I*** we were not able to report VFR travel distances. However, we found a time delay of 1 minutes and 35 seconds between the first VFR to reach the emergency site and the VFR bringing an AED to the site (4:46 min:sec versus 6:21 min:sec). The GPS-system on Langeland had a substantially larger radius of 5000 meters for activating VFRs, compared to other mobile phone systems (11, 79, 80, 84, 85), however, the maximum distance to reach an available AED at any place on Langeland is 1000 m. The reason for this is that the ≈100 available AEDs on the island were purchased by the Langeland Hjertestarterforening, which opted for a unified strategic decision of placing AEDs no longer than 2 km apart. Therefore there is an upper limit for the additional collapse-to-defibrillation time on Langeland compared with other areas in the RSD, where AED placement is largely unguided (Figure 9). Perhaps, this strategic placement of AEDs in rural areas is the optimal approach for reducing collapse-to-defibrillation time, especially if a first-responder system is available. This, however, needs further research as it would require buying an additional large number of AEDs or efforts into relocation the existing AEDs that are registered in the AED-network to reduce retrieval distances in the RSD.

AED retrieval distance and survival after cardiac arrest

The results in ***paper III*** show that the chance of survival is reduced with increasing AED retrieval distances, regardless of heart rhythm, witnessed status, EMS response time and other confounders. This is in line with the findings of Sondergaard and colleagues, who demonstrated that the overall chance of survival was associated with the distance to the nearest available AED (107). They also found that the probability of bystander defibrillation during cardiac arrests in residential areas remained low at all distances, compared to public areas. However, the study by Sondergaard and colleagues was a registry study where only defibrillation status was recorded, and not whether an AED was used, and the results could in fact reflect the decreasing number of shockable rhythms which deteriorated due to longer collapse-to-defibrillation time. In continuation of this line of thought, one could argue that the AED retrieval distance is a proxy marker of collapse-to-defibrillation time. However, the time it takes for a bystander to locate and retrieve an AED can be modified by several factors, including EMS response times, bystander use of motorized vehicles or brisk walking, the accessibility of an AED during day/evening/night times, whether the AED cabinet is open for quick access or only by code, whether the bystander uses the shortest available route or not. These factors, along with a more guided AED placement approach and an optimized use of VFRs should accompany future efforts to optimize this field.

STRENGTHS AND LIMITATIONS

All papers were retrospective observational studies, where selection bias cannot be ruled out.

Paper I

Our study was limited by the use of data from a small, confined area as regards to EMS response times and OHCA survival outcomes. During the 6-year inclusion period, several time-related factors could have contributed to improved survival after OHCA, which may involve both pre- and in-hospital treatment after cardiac arrest. Another limitation is the inability to report travel distances for VFRs and the time-delay from collapse-to-phone call and from phone call-to-dispatch of EMS/VFRs. This would help make the results more comparable with other VFR studies in this field. However, during 2012-2015, the VFRs were dispatched by the EMDC via a separate tablet computer, which meant an additional median time-delay that could not be accounted for. The GPS-system used on Langeland was developed based on real-life settings found here, as well as the establishment of an intrinsic AED-network with predetermined distances between AEDs. The impressive response times may therefore be difficult to achieve in other Danish regions or outside of Denmark. Lastly, the number of OHCAs in this study was limited, making the results susceptible to variation. Lastly, the study was, as mentioned, not designed for evaluating neither causative effects nor associations, and the results must therefore be interpreted with caution.

A strength of this study is that all EMS paper and electronic journals were screened to identify OHCA cases during the inclusion period, which is not possible for registry studies in this field. The extensive information gathered from both EMS journals was cross-checked with hospital journals, making it possible to identify additional OHCA cases, further adding to the data completeness in this study.

Paper II & III

The papers have several limitations that need to be addressed: The number of AEDs that were used during OHCA, but not transported to the AED-centre for analysis, is unknown. We may speculate that the EMS staff would feel more inclined to deliver a used AED for analysis as a part of the in-hospital treatment, if the resuscitation efforts were successful, which would give rise to selection bias. We do not know the number of used AEDs not brought to the AED-centre. However, in the event of AED deployment, the EMDC is required to inform both the AED-centre and EMS staff to ensure transportation to the AED-centre, which should limit this issue.When evaluating the number of registered AEDs per location type, we did not account for multiple AEDs registered at the same address or the potential number of unregistered AEDs. For example, large, public educational facilities (e.g. universities) or large corporate buildings could use the same address for registering multiple AEDs. The extent of registering multiple AEDs at the same address and its impact is unknown.

Distance calculations may have been underestimated, as Google Maps does not take into account vertical-spatial changes in the terrain, when calculating walking distances. Neither did we account for vertical distances in multiple dwelling houses. When evaluating the number of AEDs that were used from each location, the calculations assume that unregistered AEDs are dispersed in the same way as registered AEDs in the community, however, this is also unknown. The number of AEDs reaching the emergency site simultaneously with EMS is unknown. Finally, both studies are observational, which means that the results may imply associations and not causative effects. The results are therefore hypothesis generating and should be further investigated.

The AED data used in ***paper II & III*** were prospectively collected during the entire study period. When the idea for the two papers emerged in 2017, it helped to increase the detail extensiveness for both studies. Furthermore, ***paper II*** is the first to evaluate actual en-route distances between OHCA site and AED location, and to assess real-life coverage of AEDs placed in different types of locations. An additional strength that further added to data completeness was the possibility to cross-link AEDs from the AED-centre to those registered at the national AED-network, which helped gain information regarding AEDs that would otherwise have remained unidentified.

CONCLUSION

Using a mobile phone GPS-system to locate and dispatch VFRs on a rural island resulted in high response rates, and demonstrated that a VFR was able to arrive before EMS in four out of five cases. Furthermore, VFR response times were significantly shorter than EMS response times, and 30-day survival in patients with OHCA in residential and public places was better than expected compared to survival in other OHCA studies.

The relative use of AEDs placed in public places, nursing homes, sport facilities and health clinics was high and the relative use of AEDs placed in residential areas, company/workplaces and institutions was low, compared with the number of registered AEDs at these locations. During residential OHCAs, an AED was most often collected from a public place. The coverage distance of AEDs located in public places and residential areas was longer than proposed in current literature.

Survival after OHCA where an AED was used in densely, moderately and thinly populated areas was largely comparable. Finally, in a multivariable regression analysis, AED retrieval distance was associated with reduced survival after OHCA.

PERSPECTIVES

However challenging the conditions may seem for improving bystander defibrillation and AED use, especially in residential and rural areas, even a small increase may have a great impact in absolute numbers due to the higher incidences in these areas. Alerting VFRs for providing BLS during OHCA has been implemented in many communities. While bystander CPR and defibrillation have an definite effect on survival after OHCA, the benefits of using VFRs are less clear. So far, only one randomized trial has investigated the use of VFRs to provide CPR before EMS arrival (85). The study, however, was not designed to evaluate the effect on survival after OHCA, and with the wide dissemination of different alert systems across communities, it is difficult to imagine that the effects of VFRs to improve survival after OHCA can be evaluated in a randomized setting. The mounting evidence of survival benefits when providing CPR and defibrillation before EMS arrival may give rise to ethical dilemmas. However, by not testing VFR+EMS response vs. the standard EMS response, it will be difficult to evaluate which alert system, VFR training level, number of alerted VFRs should be used to optimize prehospital cardiac arrest treatment, and how the rural-urban settings affect VFR responses. Conclusively, it may be impossible to evaluate which alert system is the most feasible. Also, if VFRs are able to increase survival rates after OHCA, it must be investigated whether or not these survivors are neurologically intact. Furthermore, the human factor must be considered.

Due to increasing public awareness and societal expectation that ordinary citizens must step forward and provide treatment as early as possible, or even become trained VFRs as a part of the EMDC response, citizens/VFRs could potentially face incomprehensible consequences themselves. Eager citizens and VFRs could risk being injured or become involved in accidents themselves at or before reaching the emergency site, or risk suffering from severe psychological trauma after resuscitation efforts that were unsuccessful. It is therefore important to weigh the human aspects of using citizens/VFRs against the potential survival benefits, when using non-healthcare professionals to treat cardiac arrest.

The large AED dissemination across communities has independently been associated with an increase in bystander defibrillation and improved outcomes after OHCA. Kitamura et al showed that when the density of AEDs increased from 1 AED per km^2 to 4 AED per km^2, it was associated with a four times higher survival with good neurological outcome (38). However, the overall rate of bystander defibrillation was less than 10% in this study (38), consistent with the findings in other OHCA studies, which calls for new strategies for optimizing the conditions for bystander defibrillation. ***Paper II*** demonstrated that the AED coverage areas in public places and residential areas are more than 2 to 5 times higher, respectively, than the 100 meters proposed in current literature and earlier guidelines. This calls for further research to examine whether these findings can be confirmed by other research groups, as they may imply a revision in current literature and future guidelines for AED placement strategies. Some studies have advocated for mathematical optimization of AED placement in urban centers (53, 105, 108). The authors used prediction models identifying areas, where AEDs were scarce, and where AED placement could potentially benefit OHCA patients, which could be a costly approach. However, by using a novel relocation approach, Tierney and colleagues evaluated a large mixed rural-urban area, and found that the AED relocation model could potentially increase AED coverage in both residential and rural areas, and at the same time markedly reduce retrieval distances during OHCA (109). Though many factors – both spatial and non-spatial – affect AED use, perhaps the next efforts for nationwide strategies would be to relocate existing registered AEDs and extent the use of VFRs. The latter is already underway with the Danish Trygfond's "Hjerteløber"-mobile phone application for recruiting VFRs. After all, AED registration for PAD purposes implies a wish to help co-citizens during lifethreatening illness, and a more extensive national collaboration between AED vendors, private and corporate AED owners and the Danish AED-network could be the next step to radically improve this field.

English summary

Out-of-hospital cardiac arrest (OHCA) is one of the leading causes of death, affecting annually ≈5,000 people in Denmark. Early cardiopulmonary resuscitation (CPR) and defibrillation by an automated external defibrillator (AED) can markedly increase survival, and an increasing a number of communities have started using volunteer first responders (VFRs) to reduce time to CPR and defibrillation. Despite increases in bystander CPR, defibrillation rates have remained low at ≈5%, and survival after OHCA is ≈10%.

The aims of ***paper I*** was to evaluate response rates of GPS-activated VFRs and compare response times of VFRs with the emergency medical service (EMS). Also, to evaluate survival after OHCA when using GPS-activated VFRs on a rural island. In ***paper II & III*** the aims were 1) to evaluate relative use of AEDs placed at different location types, 2) to evaluate the extent of AEDs transported from one location type to another, 3) to assess AED coverage from different location types, 4) to compare survival after OHCA where an AED was used in densely, moderately and thinly populated areas, and 5) to evaluate the association between AED retrieval distance and survival after OHCA.

Methods & Results

Paper I: During 2012-2017, a GPS-system was used to activate VFRs during emergency calls on a rural island. Response times from VFRs and EMS were collected and compared. Information about OHCAs was collected from EMS and hospital records. The GPS-system was activated during 2,774 emergency calls, and at least one VFR arrived in 2,662 of cases (96%). Response times for VFRs and EMS were 4:46 min:sec (IQR 3:16-6:52) and 10:13 min:sec (6:14-13:41) , respectively (P<0.0001). In 2,266 cases (85%) a VFR arrived first to the emergency site. A total of 82 OHCAs were identified, with 65 occurring in residential areas and 17 in public places. Survival in the two groups were 15% and 24%, respectively.

Paper II & III: From 2014-2018, a central AED-center collected AEDs used during OHCA in the region of Southern Denmark. Patients with a known OHCA site were included. In ***paper III*** OHCAs in nursing homes were excluded. Information regarding registered AEDs was obtained from the national AED-registry.

Location of OHCA and AED was categorized into residential area, public place, nursing home, company/workplace, institution, health clinic and sport facility. To evaluate population density, a map with 1000x1000 meter grid cells was used with each cell color-graded according to the number of inhabitants. Densely, moderately and thinly populated areas were defined as ≥200 inhabitants, 20-199 inhabitants and 0-19 inhabitants per km^2, respectively. Primary outcome was 30-day survival. In ***paper II***, a total of 509 OHCAs were included. The relative AED use was high in public places, nursing homes, health clinics and sports facilities, and low in residential areas, companies/workplaces and institutions. During residential OHCAs, 39% of AEDs were collected from public places. AED coverage distance was 250 meters (IQR 5-550) for AEDs placed in public places and 575 meters (IQR 130-1300) for AEDs in residential areas. In ***paper III,*** 423 OHCAs were included, of which 49% occurred in densely populated areas, while 18% and 33% occurred in moderately and thinly populated areas, respectively. Median AED retrieval distances were 105 meters (IQR 5-450), 220 meters (IQR 5-450) and 350 meters (IQR 5-1500) in densely, moderately and thinly populated areas ($p<0.001$), and 30-day survival in the three groups were 40%, 31% and 34%, respectively ($P=0.3$). In a multivariable regression analysis, the risk of death increased 10% for every 100 meters an AED was placed further away from the cardiac arrest site.

Conclusion

A GPS-system can effectively activate VFRs, and significantly reduce response times compared with EMS. Using the GPS-system on a rural island, survival was found to be higher than expected in both residential and public places compared to other OHCA studies. Relative to the number of registered AEDs per location type, AED use was high from public places, nursing homes, sport facilities and health clinics. During residential OHCAs, AEDs were most frequently collected from public places. The AED coverage in public places and residential areas was 2 to 5 times higher than expected and proposed in current literature. Survival after OHCA where an AED was used was largely comparable in densely, moderately and thinly populated areas, however, AED retrieval distance was associated with reduced survival after OHCA.

Dansk resumé

Hjertestop uden for hospital er en af de hyppigste dødsårsager, der årligt rammer ≈5,000 mennesker i Danmark. Tidlig hjertelungeredning (HLR) og defibrillering med en hjertestarter eller en automatiseret ekstern defibrillator (AED) kan markant øge overlevelsen. I et stigende antal lande er man begyndt at anvende frivillige førstehjælpere (FF) i forsøg på at give hurtig HLR og defibrillere inden ambulancens ankomst. Man anbefaler, at AED'er placeres på offentlige steder med mange forbipasserende. På trods af stigninger i andelen, som får HLR, er antallet som defibrilleres fortsat lav (ca. 5%), og overlevelse efter hjertestop uden for hospital er blot 10%. Formålet med ***Artikel 1*** var at evaluere responsrater for GPS-aktiverede FF'ere, at sammenligne FF's responstider med ambulance-responstider, samt at evaluere overlevelse efter hjertestop på offentlige steder og i private hjem. I ***Artikel 2 og 3*** var formålene; 1) at evaluere den relative anvendelse af AED'er placeret på forskellige lokalisationer, 2) at evaluere omfanget af AED'er, som transporteres fra en lokalisation til en anden, 3) at vurdere AED-dækning fra forskellige lokalisationer, 4) at sammenligne overlevelse efter hjertestop uden for hospital, hvor der anvendes AED i tæt, moderat og tyndtbefolkede områder, og 5) at evaluere associationen mellem afstand til den AED, som blev anvendt, og overlevelse efter hjertestop uden for hospital.

Metode og resultater

Artikel 1: I årene 2012-2017 blev et GPS-system brugt til at aktivere FF'ere på en tyndtbefolket ø. Responstider for FF'ere og ambulance blev systematisk registreret. Oplysninger omkring personer med hjertestop uden for hospital blev indhentet fra ambulance- og sygehusjournaler. GPS-systemet blev aktiveret i 2,774 tilfælde af 1-1-2-nødopkald, og mindst én FF'er ankom til skadested i 2,662 af tilfældene (96%). Responstider for FF'ere og ambulance var henholdsvis 4:46 min:sek (IQR 3: 16-6: 52) og 10:13 min:sek (6: 14-13: 41) (P <0,0001). I 2,266 tilfælde (85%) ankom en FF til skadestedet før ambulancen. I alt fandt der 82 hjertestop sted, hvoraf 65 skete i private hjem og 17 på offentlige steder. Overlevelse i de to grupper var henholdsvis 15% og 24%. ***Artikel 2 og 3***: Fra 2014-2018 modtog et centralt AED-center alle AED'er, som havde været anvendt ved hjertestop uden for hospital i Region Syddanmark. Patienter med kendt skadested

blev inkluderet. I ***Artikel 3*** blev hjertestop på plejehjem ekskluderet. Oplysninger om registrerede AED'er blev hentet fra hjertestarter-netværket. Skadested for hjertestop og placering af AED'er blev kategoriseret som følger: Privat hjem, offentligt sted, plejehjem, virksomhed/arbejdsplads, institution, sundhedsklinik og sportsfacilitet. For at evaluere befolkningstætheden på skadestedet, blev der anvendt et kort med 1000x1000 meter gitterceller, hvor hver celle blev farvelagt efter antal indbyggere. Tæt-, moderat- og tyndtbefolkede områder blev defineret som henholdsvis ≥200, 20-199 og 0-19 indbyggere pr. km^2. Primære outcome var 30-dages overlevelse. I ***Artikel 2*** blev i alt 509 personer med hjertestop inkluderet. Den relative AED-anvendelse fra offentlige steder, plejehjem, sundhedsklinikker og sportsfaciliteter var høj, mens anvendelsen fra private hjem, virksomheder/arbejdspladser og institutioner var lav. Ved hjertestop i private hjem blev 39% af AED'er hentet fra offentlige steder. Dækningsafstanden for en AED var 250 meters (IQR 5-550) på offentlige steder og 575 meters (IQR 130-1300) for AED'er placeret ved private hjem. I ***Artikel 3*** blev 423 hjertestop inkluderet. Heraf forekom 49% i tætbefolkede områder, mens 18% og 33% fandt sted i henholdsvis moderat- og tyndtbefolkede områder. Afstanden fra skadested til AED var 105 meters (IQR 5-450), 220 meters (IQR 5-450) og 350 meters (IQR 5-1500) i tæt-, moderat- og tyndtbefolkede områder (P <0,001), og 30-dages overlevelse i de tre grupper var 40%, 31% og 34% (P = 0,3). I en multivariabel regressionsanalyse øgedes mortalitetsrisikoen med 10% per 100 meter en AED var placeret væk fra skadestedet.

Konklusion

Et GPS-system kan effektivt aktivere FF'ere på en tyndtbefolket ø, og markant reducere responstider for FF'ere sammenlignet med ambulanceresponstider. Overlevelsen efter hjertestop i private hjem og på offentlige stede på øen var betydeligt højere end forventet, sammenlignet med overlevelsen i lignende tidligere studier. Den relative anvendelse af AED'er fra offentlige steder, plejehjem, sportsfaciliteter og sundhedsklinikker var høj, og den relative anvendelse af AED'er fra private hjem, virksomheder/arbejdspladser og institutioner var lav, set i forhold til antallet af registrerede AED'er på lokalisationerne. Ved hjertestop i private hjem blev en AED oftest hentet fra et offentligt sted. Overlevelsen efter hjertestop, hvor der blev anvendt AED, i tæt-, moderat- og tyndtbefolkede områder, var sammenlignelig. Dog var afstanden fra skadested til en AED associeret med lavere overlevelse efter hjertestop.

REFERENCES

1. Jacobs I, Nadkarni V, Bahr J, Berg RA, Billi JE, Bossaert L, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries. A statement for healthcare professionals from a task force of the international liaison committee on resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa). Resuscitation. 2004;63(3):233-49.
2. Perkins GD, Handley AJ, Koster RW, Castrén M, Smyth MA, Olasveengen T, et al. European Resuscitation Council Guidelines for Resuscitation 2015: Section 2. Adult basic life support and automated external defibrillation. Resuscitation. 2015;95:81-99.
3. Callaway CW, Soar J, Aibiki M, Böttiger BW, Brooks SC, Deakin CD, et al. Part 4: Advanced Life Support: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. Circulation. 2015;132(16 Suppl 1):S84-145.
4. Sedgwick ML, Dalziel K, Watson J, Carrington DJ, Cobbe SM. The causative rhythm in out-of-hospital cardiac arrests witnessed by the emergency medical services in the Heartstart Scotland Project. Resuscitation. 1994;27(1):55-9.
5. Berdowski J, Blom MT, Bardai A, Tan HL, Tijssen JG, Koster RW. Impact of onsite or dispatched automated external defibrillator use on survival after out-of-hospital cardiac arrest. Circulation. 2011;124(20):2225-32.
6. Weisfeldt ML, Sitlani CM, Ornato JP, Rea T, Aufderheide TP, Davis D, et al. Survival after application of automatic external defibrillators before arrival of the emergency medical system: evaluation in the resuscitation outcomes consortium population of 21 million. J Am Coll Cardiol. 2010;55(16):1713-20.
7. Link MS, Atkins DL, Passman RS, Halperin HR, Samson RA, White RD, et al. Part 6: electrical therapies: automated external defibrillators, defibrillation, cardioversion, and pacing: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2010;122(18 Suppl 3):S706-19.
8. Caffrey SL, Willoughby PJ, Pepe PE, Becker LB. Public use of automated external defibrillators. N Engl J Med. 2002;347(16):1242-7.
9. Hallstrom AP, Ornato JP, Weisfeldt M, Travers A, Christenson J, McBurnie MA, et al. Public-access defibrillation and survival after out-of-hospital cardiac arrest. N Engl J Med. 2004;351(7):637-46.
10. Page RL, Joglar JA, Kowal RC, Zagrodzky JD, Nelson LL, Ramaswamy K, et al. Use of automated external defibrillators by a U.S. airline. N Engl J Med. 2000;343(17):1210-6.
11. Ringh M, Jonsson M, Nordberg P, Fredman D, Hasselqvist-Ax I, Hakansson F, et al. Survival after Public Access Defibrillation in Stockholm, Sweden--A striking success. Resuscitation. 2015;91:1-7.
12. Valenzuela TD, Roe DJ, Nichol G, Clark LL, Spaite DW, Hardman RG. Outcomes of rapid defibrillation by security officers after cardiac arrest in casinos. N Engl J Med. 2000;343(17):1206-9.

13. Chan PS, Krumholz HM, Nichol G, Nallamothu BK. Delayed time to defibrillation after in-hospital cardiac arrest. N Engl J Med. 2008;358(1):9-17.

14. Larsen MP, Eisenberg MS, Cummins RO, Hallstrom AP. Predicting survival from out-of-hospital cardiac arrest: a graphic model. Ann Emerg Med. 1993;22(11):1652-8.

15. Rajan S, Folke F, Hansen SM, Hansen CM, Kragholm K, Gerds TA, 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. 2017;114:157-63.

16. Wissenberg M, Lippert FK, Folke F, Weeke P, Hansen CM, Christensen EF, et al. Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest. JAMA. 2013;310(13):1377-84.

17. Sasson C, Rogers MA, Dahl J, Kellermann AL. Predictors of survival from out-of-hospital cardiac arrest: a systematic review and meta-analysis. Circ Cardiovasc Qual Outcomes. 2010;3(1):63-81.

18. Gräsner JT, Wnent J, Herlitz J, Perkins GD, Lefering R, Tjelmeland I, et al. Survival after out-of-hospital cardiac arrest in Europe - Results of the EuReCa TWO study. Resuscitation. 2020;148:218-26.

19. Daya MR, Schmicker RH, Zive DM, Rea TD, Nichol G, Buick JE, et al. Out-of-hospital cardiac arrest survival improving over time: Results from the Resuscitation Outcomes Consortium (ROC). Resuscitation. 2015;91:108-15.

20. Hoke RS, Heinroth K, Trappe HJ, Werdan K. Is external defibrillation an electric threat for bystanders? Resuscitation. 2009;80(4):395-401.

21. Fromm RE, Jr., Varon J. Automated external versus blind manual defibrillation by untrained lay rescuers. Resuscitation. 1997;33(3):219-21.

22. Berdowski J, Berg RA, Tijssen JG, Koster RW. Global incidences of out-of-hospital cardiac arrest and survival rates: Systematic review of 67 prospective studies. Resuscitation. 2010;81(11):1479-87.

23. Nichol G, Thomas E, Callaway CW, Hedges J, Powell JL, Aufderheide TP, et al. Regional variation in out-of-hospital cardiac arrest incidence and outcome. JAMA. 2008;300(12):1423-31.

24. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart Disease and Stroke Statistics-2016 Update: A Report From the American Heart Association. Circulation. 2016;133(4):e38-360.

25. (DHR) DH. Hjertestop uden for hospital i Danmark: Sammenfatning af resultater fra Dansk Hjertestopregister 2001-2016. 2019.

26. Genoplivning DRf. Faktaark om Hjertestop. December 2020.

27. State-specific mortality from sudden cardiac death--United States, 1999. MMWR Morb Mortal Wkly Rep. 2002;51(6):123-6.

28. Saxon LA. Sudden cardiac death: epidemiology and temporal trends. Rev Cardiovasc Med. 2005;6 Suppl 2:S12-20.

29. Perkins GD, Jacobs IG, Nadkarni VM, Berg RA, Bhanji F, Biarent D, 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. Circulation. 2015;132(13):1286-300.

30. Holmberg M, Holmberg S, Herlitz J. Factors modifying the effect of bystander cardiopulmonary resuscitation on survival in out-of-hospital cardiac arrest patients in Sweden. Eur Heart J. 2001;22(6):511-9.

31. McNally B, Robb R, Mehta M, Vellano K, Valderrama AL, Yoon PW, et al. Out-of-hospital cardiac arrest surveillance --- Cardiac Arrest Registry to Enhance Survival (CARES), United States, October 1, 2005--December 31, 2010. MMWR Surveill Summ. 2011;60(8):1-19.

32. Kragholm K, Wissenberg M, Mortensen RN, Hansen SM, Malta Hansen C, Thorsteinsson K, et al. Bystander Efforts and 1-Year Outcomes in Out-of-Hospital Cardiac Arrest. N Engl J Med. 2017;376(18):1737-47.

33. Valenzuela TD, Roe DJ, Cretin S, Spaite DW, Larsen MP. Estimating effectiveness of cardiac arrest interventions: a logistic regression survival model. Circulation. 1997;96(10):3308-13.

34. Kronick SL, Kurz MC, Lin S, Edelson DP, Berg RA, Billi JE, et al. Part 4: Systems of Care and Continuous Quality Improvement: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2015;132(18 Suppl 2):S397-413.

35. Lerner EB, Rea TD, Bobrow BJ, Acker JE, 3rd, Berg RA, Brooks SC, et al. Emergency medical service dispatch cardiopulmonary resuscitation prearrival instructions to improve survival from out-of-hospital cardiac arrest: a scientific statement from the American Heart Association. Circulation. 2012;125(4):648-55.

36. Colquhoun MC, Chamberlain DA, Newcombe RG, Harris R, Harris S, Peel K, et al. A national scheme for public access defibrillation in England and Wales: early results. Resuscitation. 2008;78(3):275-80.

37. Fleischhackl R, Roessler B, Domanovits H, Singer F, Fleischhackl S, Foitik G, et al. Results from Austria's nationwide public access defibrillation (ANPAD) programme collected over 2 years. Resuscitation. 2008;77(2):195-200.

38. Kitamura T, Iwami T, Kawamura T, Nagao K, Tanaka H, Hiraide A. Nationwide public-access defibrillation in Japan. N Engl J Med. 2010;362(11):994-1004.

39. Hansen SM, Hansen CM, Folke F, Rajan S, Kragholm K, Ejlskov L, et al. Bystander Defibrillation for Out-of-Hospital Cardiac Arrest in Public vs Residential Locations. JAMA cardiology. 2017;2(5):507-14.

40. Hansen CM, Lippert FK, Wissenberg M, Weeke P, Zinckernagel L, Ruwald MH, et al. Temporal trends in coverage of historical cardiac arrests using a volunteer-based network of automated external defibrillators accessible to laypersons and emergency dispatch centers. Circulation. 2014;130(21):1859-67.

41. Hansen CM, Wissenberg M, Weeke P, Ruwald MH, Lamberts M, Lippert FK, et al. Automated external defibrillators inaccessible to more than half of nearby cardiac arrests in public locations during evening, nighttime, and weekends. Circulation. 2013;128(20):2224-31.

42. Sundhedsstyrelsen. Hjertestartere (AED) placeret uden for sygehus. 2011.

43. Regioner D. Dansk Indeks for Akuthjælp. 2020;Landsudgaven, version 1.9 - revised December 2020:88.

44. Andelius L, Malta Hansen C, Lippert FK, Karlsson L, Torp-Pedersen C, Kjær Ersbøll A, et al. Smartphone Activation of Citizen Responders to Facilitate Defibrillation in Out-of-Hospital Cardiac Arrest. J Am Coll Cardiol. 2020;76(1):43-53.

45. Sarkisian L, Mickley H, Schakow H, Gerke O, Jørgensen G, Larsen ML, et al. Global positioning system alerted volunteer first responders arrive before emergency medical services in more than four out of five emergency calls. Resuscitation. 2020;152:170-6.

46. Weisfeldt ML, Kerber RE, McGoldrick RP, Moss AJ, Nichol G, Ornato JP, et al. Public access defibrillation. A statement for healthcare professionals from the American Heart Association Task Force on Automatic External Defibrillation. Circulation. 1995;92(9):2763.

47. Weisfeldt ML, Kerber RE, McGoldrick RP, Moss AJ, Nichol G, Ornato JP, et al. American Heart Association Report on the Public Access Defibrillation Conference December 8-10, 1994. Automatic External Defibrillation Task Force. Circulation. 1995;92(9):2740-7.

48. Kiyohara K, Kitamura T, Sakai T, Nishiyama C, Nishiuchi T, Hayashi Y, et al. Public-access AED pad application and outcomes for out-of-hospital cardiac arrests in Osaka, Japan. Resuscitation. 2016;106:70-5.

49. Nichol G, Elrod JA, Becker LB. Treatment for out-of-hospital cardiac arrest: is the glass half empty or half full? Circulation. 2014;130(21):1844-6.

50. Karlsson L, Malta Hansen C, Wissenberg M, Moller Hansen S, Lippert FK, Rajan S, et al. Automated external defibrillator accessibility is crucial for bystander defibrillation and survival: A registry-based study. Resuscitation. 2019;136:30-7.

51. Agerskov M, Nielsen AM, Hansen CM, Hansen MB, Lippert FK, Wissenberg M, et al. Public Access Defibrillation: Great benefit and potential but infrequently used. Resuscitation. 2015;96:53-8.

52. Kitamura T, Kiyohara K, Sakai T, Matsuyama T, Hatakeyama T, Shimamoto T, et al. Public-Access Defibrillation and Out-of-Hospital Cardiac Arrest in Japan. N Engl J Med. 2016;375(17):1649-59.

53. Chan TC, Li H, Lebovic G, Tang SK, Chan JY, Cheng HC, et al. Identifying locations for public access defibrillators using mathematical optimization. Circulation. 2013;127(17):1801-9.

54. Folke F, Lippert FK, Nielsen SL, Gislason GH, Hansen ML, Schramm TK, et al. Location of cardiac arrest in a city center: strategic placement of automated external defibrillators in public locations. Circulation. 2009;120(6):510-7.

55. Sun CL, Demirtas D, Brooks SC, Morrison LJ, Chan TC. Overcoming Spatial and Temporal Barriers to Public Access Defibrillators Via Optimization. J Am Coll Cardiol. 2016;68(8):836-45.

56. Aufderheide T, Hazinski MF, Nichol G, Steffens SS, Buroker A, McCune R, et al. Community lay rescuer automated external defibrillation programs: key state legislative components and implementation strategies: a summary of a decade of experience for healthcare providers, policymakers, legislators, employers, and community leaders from the American Heart Association Emergency Cardiovascular Care Committee, Council on Clinical Cardiology, and Office of State Advocacy. Circulation. 2006;113(9):1260-70.

57. Jonsson M, Berglund E, Djärv T, Nordberg P, Claesson A, Forsberg S, et al. A brisk walk-Real-life travelling speed of lay responders in out-of-hospital cardiac arrest. Resuscitation. 2020;151:197-204.

58. Kleinman ME, Brennan EE, Goldberger ZD, Swor RA, Terry M, Bobrow BJ, et al. Part 5: Adult Basic Life Support and Cardiopulmonary Resuscitation Quality: 2015 American Heart

Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2015;132(18 Suppl 2):S414-35.

59. Folke F, Gislason GH, Lippert FK, Nielsen SL, Weeke P, Hansen ML, et al. Differences between out-of-hospital cardiac arrest in residential and public locations and implications for public-access defibrillation. Circulation. 2010;122(6):623-30.

60. Herlitz J, Eek M, Holmberg M, Engdahl J, Holmberg S. Characteristics and outcome among patients having out of hospital cardiac arrest at home compared with elsewhere. Heart. 2002;88(6):579-82.

61. Gnesin F, Møller AL, Mills EHA, Zylyftari N, Jensen B, Bøggild H, et al. Rapid dispatch for out-of-hospital cardiac arrest is associated with improved survival. Resuscitation. 2021.

62. Masterson S, Wright P, O'Donnell C, Vellinga A, Murphy AW, Hennelly D, et al. Urban and rural differences in out-of-hospital cardiac arrest in Ireland. Resuscitation. 2015;91:42-7.

63. Nehme Z, Andrew E, Cameron PA, Bray JE, Bernard SA, Meredith IT, et al. Population density predicts outcome from out-of-hospital cardiac arrest in Victoria, Australia. Med J Aust. 2014;200(8):471-5.

64. Stapczynski JS, Svenson JE, Stone CK. Population density, automated external defibrillator use, and survival in rural cardiac arrest. Acad Emerg Med. 1997;4(6):552-8.

65. Mathiesen WT, Bjørshol CA, Kvaløy JT, Søreide E. Effects of modifiable prehospital factors on survival after out-of-hospital cardiac arrest in rural versus urban areas. Crit Care. 2018;22(1):99.

66. Cudnik MT, Schmicker RH, Vaillancourt C, Newgard CD, Christenson JM, Davis DP, et al. A geospatial assessment of transport distance and survival to discharge in out of hospital cardiac arrest patients: Implications for resuscitation centers. Resuscitation. 2010;81(5):518-23.

67. Tranberg T, Lippert FK, Christensen EF, Stengaard C, Hjort J, Lassen JF, et al. Distance to invasive heart centre, performance of acute coronary angiography, and angioplasty and associated outcome in out-of-hospital cardiac arrest: a nationwide study. Eur Heart J. 2017;38(21):1645-52.

68. Sondergaard KB, Wissenberg M, Gerds TA, Rajan S, Karlsson L, Kragholm K, et al. Bystander cardiopulmonary resuscitation and long-term outcomes in out-of-hospital cardiac arrest according to location of arrest. Eur Heart J. 2019;40(3):309-18.

69. Brooks B, Chan S, Lander P, Adamson R, Hodgetts GA, Deakin CD. Public knowledge and confidence in the use of public access defibrillation. Heart. 2015;101(12):967-71.

70. Kerber RE, Becker LB, Bourland JD, Cummins RO, Hallstrom AP, Michos MB, et al. Automatic external defibrillators for public access defibrillation: recommendations for specifying and reporting arrhythmia analysis algorithm performance, incorporating new waveforms, and enhancing safety. A statement for health professionals from the American Heart Association Task Force on Automatic External Defibrillation, Subcommittee on AED Safety and Efficacy. Circulation. 1997;95(6):1677-82.

71. Chan PS, McNally B, Tang F, Kellermann A. Recent trends in survival from out-of-hospital cardiac arrest in the United States. Circulation. 2014;130(21):1876-82.

72. Kitamura T, Iwami T, Kawamura T, Nitta M, Nagao K, Nonogi H, et al. Nationwide improvements in survival from out-of-hospital cardiac arrest in Japan. Circulation. 2012;126(24):2834-43.

73. Ro YS, Shin SD, Song KJ, Lee EJ, Kim JY, Ahn KO, et al. A trend in epidemiology and outcomes of out-of-hospital cardiac arrest by urbanization level: a nationwide observational study from 2006 to 2010 in South Korea. Resuscitation. 2013;84(5):547-57.

74. Wong MK, Morrison LJ, Qiu F, Austin PC, Cheskes S, Dorian P, et al. Trends in short- and long-term survival among out-of-hospital cardiac arrest patients alive at hospital arrival. Circulation. 2014;130(21):1883-90.

75. Weisfeldt ML, Everson-Stewart S, Sitlani C, Rea T, Aufderheide TP, Atkins DL, et al. Ventricular tachyarrhythmias after cardiac arrest in public versus at home. N Engl J Med. 2011;364(4):313-21.

76. Levy MJ, Seaman KG, Millin MG, Bissell RA, Jenkins JL. A poor association between out-of-hospital cardiac arrest location and public automated external defibrillator placement. Prehosp Disaster Med. 2013;28(4):342-7.

77. Winkle RA. The effectiveness and cost effectiveness of public-access defibrillation. Clin Cardiol. 2010;33(7):396-9.

78. Bardy GH, Lee KL, Mark DB, Poole JE, Toff WD, Tonkin AM, et al. Home use of automated external defibrillators for sudden cardiac arrest. N Engl J Med. 2008;358(17):1793-804.

79. Auricchio A, Gianquintieri L, Burkart R, Benvenuti C, Muschietti S, Peluso S, et al. Real-life time and distance covered by lay first responders alerted by means of smartphone-application: Implications for early initiation of cardiopulmonary resuscitation and access to automatic external defibrillators. Resuscitation. 2019;141:182-7.

80. Berglund E, Claesson A, Nordberg P, Djarv T, Lundgren P, Folke F, et al. A smartphone application for dispatch of lay responders to out-of-hospital cardiac arrests. Resuscitation. 2018;126:160-5.

81. Caputo ML, Muschietti S, Burkart R, Benvenuti C, Conte G, Regoli F, et al. Lay persons alerted by mobile application system initiate earlier cardio-pulmonary resuscitation: A comparison with SMS-based system notification. Resuscitation. 2017;114:73-8.

82. Pijls RW, Nelemans PJ, Rahel BM, Gorgels AP. A text message alert system for trained volunteers improves out-of-hospital cardiac arrest survival. Resuscitation. 2016;105:182-7.

83. Smith CM, Wilson MH, Ghorbangholi A, Hartley-Sharpe C, Gwinnutt C, Dicker B, et al. The use of trained volunteers in the response to out-of-hospital cardiac arrest - the GoodSAM experience. Resuscitation. 2017;121:123-6.

84. Zijlstra JA, Stieglis R, Riedijk F, Smeekes M, van der Worp WE, Koster RW. Local lay rescuers with AEDs, alerted by text messages, contribute to early defibrillation in a Dutch out-of-hospital cardiac arrest dispatch system. Resuscitation. 2014;85(11):1444-9.

85. Ringh M, Rosenqvist M, Hollenberg J, Jonsson M, Fredman D, Nordberg P, et al. Mobile-phone dispatch of laypersons for CPR in out-of-hospital cardiac arrest. N Engl J Med. 2015;372(24):2316-25.

86. Ringh M, Fredman D, Nordberg P, Stark T, Hollenberg J. Mobile phone technology identifies and recruits trained citizens to perform CPR on out-of-hospital cardiac arrest victims prior to ambulance arrival. Resuscitation. 2011;82(12):1514-8.

87. Henriksen F, Schorling P, Hansen B, Schakow H, Larsen M. FirstAED emergency dispatch, global positioning of community first responders with distinct roles - a solution to reduce the response times and ensuring an AED to early defibrillation in the rural Langeland. Int J Networking and Virtual Organisations. 2016;16(1):86-102.

88. Al-Khatib SM, Stevenson WG, Ackerman MJ, Bryant WJ, Callans DJ, Curtis AB, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Executive summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. Heart Rhythm. 2018;15(10):e190-e252.

89. Authority TnDH. Hjertestartere (AED) placeret uden for sygehus (2011) URL: https://www.sst.dk/da/udgivelser/2011/hjertestartere-aed-placeret-uden-for-sygehus. Accessed Mar 20, 2020. [

90. Pedersen CB. The Danish Civil Registration System. Scand J Public Health. 2011;39(7 Suppl):22-5.

91. EUROSTAT G-SE. https://ec.europa.eu/eurostat/statistics-explained/index.php/Population_grids#Grid_statistics (Accessed Mar 24, 2020). [

92. GIS Q-TLOSD. https://www.qgis.org/en/site/about/index.html (Accessed Mar 24, 2020). [

93. H. DLaP. Regional Working Paper 2014: "A harmonised definition of cities and rural areas: the new degree of urbanisation". 2014.

94. Cipeluch B JR, Mooney PWinstanley A, et al. . Comparison of the accuracy of OpenStreetMap for Ireland with Google Maps and Bing Maps Proceedings of the Ninth International Symposium on Spatial Accuracy Assessment in Natural Resuorces and Enviromental Sciences 20-23rd July 2010. 2010.

95. Sarkisian L, Mickley H, Schakow H, Gerke O, Starck SM, Jensen JJ, et al. Use and coverage of automated external defibrillators according to location in out-of-hospital cardiac arrest. Resuscitation. 2021;162:112-9.

96. Chen CC, Chen CW, Ho CK, Liu IC, Lin BC, Chan TC. Spatial Variation and Resuscitation Process Affecting Survival after Out-of-Hospital Cardiac Arrests (OHCA). PLoS One. 2015;10(12):e0144882.

97. Denmark RoS. Responstider/wm515376 2021 [Available from: https://www.regionsyddanmark.dk/wm515376.

98. Moller SG, Wissenberg M, Moller-Hansen S, Folke F, Malta Hansen C, Kragholm K, et al. Regional variation in out-of-hospital cardiac arrest: Incidence and survival - A nationwide study of regions in Denmark. Resuscitation. 2020;148:191-9.

99. Nichol G, Valenzuela T, Roe D, Clark L, Huszti E, Wells GA. Cost effectiveness of defibrillation by targeted responders in public settings. Circulation. 2003;108(6):697-703.

100. Pape M, Rajan S, Hansen SM, Mortensen RN, Riddersholm S, Folke F, et al. Survival after out-of-hospital cardiac arrest in nursing homes - A nationwide study. Resuscitation. 2018;125:90-8.

101. Swor RA, Jackson RE, Tintinalli JE, Pirrallo RG. Does advanced age matter in outcomes after out-of-hospital cardiac arrest in community-dwelling adults? Acad Emerg Med. 2000;7(7):762-8.

102. Wissenberg M, Folke F, Hansen CM, Lippert FK, Kragholm K, Risgaard B, et al. Survival After Out-of-Hospital Cardiac Arrest in Relation to Age and Early Identification of Patients With Minimal Chance of Long-Term Survival. Circulation. 2015;131(18):1536-45.

103. Descatha A, Dagrenat C, Cassan P, Jost D, Loeb T, Baer M. Cardiac arrest in the workplace and its outcome: a systematic review and meta-analysis. Resuscitation. 2015;96:30-6.

104. Fan M, Fan KL, Leung LP. Walking Route-Based Calculation is Recommended for Optimizing Deployment of Publicly Accessible Defibrillators in Urban Cities. J Am Heart Assoc. 2020;9(2):e014398.

105. Dahan B, Jabre P, Karam N, Misslin R, Bories MC, Tafflet M, et al. Optimization of automated external defibrillator deployment outdoors: An evidence-based approach. Resuscitation. 2016;108:68-74.

106. Deakin CD, Anfield S, Hodgetts GA. Underutilisation of public access defibrillation is related to retrieval distance and time-dependent availability. Heart. 2018;104(16):1339-43.

107. Sondergaard KB, Hansen SM, Pallisgaard JL, Gerds TA, Wissenberg M, Karlsson L, et al. Out-of-hospital cardiac arrest: Probability of bystander defibrillation relative to distance to nearest automated external defibrillator. Resuscitation. 2018;124:138-44.

108. Brooks SC, Hsu JH, Tang SK, Jeyakumar R, Chan TC. Determining risk for out-of-hospital cardiac arrest by location type in a Canadian urban setting to guide future public access defibrillator placement. Ann Emerg Med. 2013;61(5):530-8.e2.

109. Tierney NJ, Reinhold HJ, Mira A, Weiser M, Burkart R, Benvenuti C, et al. Novel relocation methods for automatic external defibrillator improve out-of-hospital cardiac arrest coverage under limited resources. Resuscitation. 2018;125:83-9.

PAPERS

Paper I

RESUSCITATION 152 (2020) 170 –176

Available online at www.sciencedirect.com

Resuscitation

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

Clinical paper

Global positioning system alerted volunteer first responders arrive before emergency medical services in more than four out of five emergency calls

Laura Sarkisian [a,b,*], *Hans Mickley* [a], *Henrik Schakow* [c], *Oke Gerke* [d], *Gitte Jørgensen* [c], *Mogens Lytken Larsen* [e], *Finn Lund Henriksen* [a]

[a] *Research Unit of Cardiology, Department of Cardiology, Odense University Hospital, J.B. Winsløws Vej 4, Odense C, 5000, Denmark*
[b] *OPEN, Odense Patient Data Explorative Network, Odense University Hospital, Odense, Denmark*
[c] *Emergency Medical Services, Region of Southern Denmark, Damhaven 12, Vejle, 7100, Denmark*
[d] *Department of Nuclear Medicine, Odense University Hospital, J.B. Winsløws Vej 4, Odense C, 5000, Denmark*
[e] *Department of Clinical Medicine, Aalborg University Hospital, Søndre Skovvej 15, Aalborg, 9000, Denmark*

Abstract

Aim: To evaluate response rates for volunteer first responders (VFRs) activated by use of a smartphone GPS-tracking system and to compare response times of VFRs with those of emergency medical services (EMS). Furthermore, to evaluate 30-day-survival after out-of-hospital cardiac arrest (OHCA) on a rural island.

Methods: Since 2012 a GPS-tracking system has been used on a rural island to activate VFRs during all emergency calls requesting an EMS. When activated, three VFRs were recruited and given distinct roles, including collection of the nearest automatic external defibrillator (AED). We retrospectively investigated EMS response data from April 2012 to December 2017. These were matched with VFR response times from the GPS-tracking system. The 30-day survival in OHCA patients was also assessed.

Results: In 2266 of 2662 emergency calls (85%) at least one VFR arrived to the site before EMS. Median response times for VFRs (n = 2662) was 4:46 min:sec (IQR 3:16–6:52) compared with 10:13 min:sec (6:14–13:41) for EMS ($p < 0.0001$). A total of 17 OHCAs took place in public locations and 65 in residential areas. Thirty-day survival in these were 24% and 15%, respectively.

Conclusion: Use of a smartphone GPS-tracking system to dispatch VFRs ensures that in more than four of five cases, a VFR arrives to the site before EMS. Response times for VFRs were also found to be lower than EMS response times. Finally, the 30-day survival of OHCA patients in a rural area, based on these results, surpass our expectations.

Keywords: First responder, Volunteer, Automated external defibrillator, AED, Smartphone, App, Application, Cardiopulmonary resuscitation, Out-of-hospital cardiac arrest, OHCA, Bystander, GPS, Survival

Introduction

Out-of-hospital cardiac arrest (OHCA) is a leading cause of sudden death in industrialized countries.[1] In Denmark, public initiatives have increased awareness and early action during cardiac arrest, which may have contributed to the substantial increase in bystander cardiopulmonary resuscitation (CPR).[2,3] Also, the number of onsite available automated external defibrillators (AEDs) has grown and a national volunteer-based AED-network has been created to increase

* Corresponding author at: Research Unit of Cardiology, Department of Cardiology, Odense University Hospital, J.B. Winsløws Vej 4, Odense C, 5000, Denmark.

E-mail addresses: Laura.Sarkisian2@rsyd.dk (L. Sarkisian), Mickley@rsyd.dk (H. Mickley), schakow@pc.dk (H. Schakow), Oke.Gerke@rsyd.dk (O. Gerke), Gitte.Jorgensen@rsyd.dk (G. Jørgensen), mogenslytkenlarsen@dadlnet.dk (M.L. Larsen), Finn.L.Henriksen@rsyd.dk (F.L. Henriksen).
https://doi.org/10.1016/j.resuscitation.2019.12.010
; Accepted 15 December 2019

AED usage.[2,4] Still, survival remains low at about 10% after OHCA.[2,5,6] In previous studies, bystander defibrillation before the arrival of the emergency medical service (EMS) has shown to increase survival up to 74%,[7–9] but these studies were performed in selected high-risk public areas, making it difficult to extrapolate to real-life settings. Further, about three-quarters of OHCAs occur in residential areas,[6,10] where CPR performance, defibrillation and survival are markedly lower compared with OHCAs in public areas.[11] Recently, studies have examined the use of GPS or text-message based systems to alert volunteer first responders (VFRs)[12–14] during suspected cardiac arrest. These studies, however, did not measure the number of on-site VFRs, response-times, nor did they demonstrate prognostic effects of the systems used. In 2012, on the island of Langeland, Denmark, a smartphone application was developed, which used global positioning system (GPS) to locate and dispatch VFRs to emergency sites along with standard EMS response. In each emergency call the selected VFRs were given one of three different tasks.

In this study we aim to investigate the response rates and response times for trained VFRs compared to EMS when using a smartphone GPS-tracking system on a rural island. Our secondary aim is to evaluate the 30-day survival after OHCA.

Methods

Settings and study design

This is a retrospective study conducted on the island of Langeland, Denmark. Langeland covers approximately 291 km^2 (about 60 km long and 10 km at the widest point) and has a population of about 12,000 of which one-third live in the city of Rudkøbing. During summer months the population grows substantially.[15] Rudkøbing has an EMS station with an ambulance and a paramedic in a non-transporting EMS vehicle. Langeland has no local hospitals, but is bridge-connected to Funen, where there are two hospitals that both have cardiac care units and one has invasive cardiac facilities.

Emergency medical dispatch centre and AED network

In Denmark, if the emergency medical dispatch centre receives a call and suspects cardiac arrest, the health care professional follows a standardized national protocol to phone-assist the bystander in performing CPR. Also, a two-tiered EMS system is activated following the dispatch of an ambulance and a physician-manned vehicle. On Langeland, a paramedic is always activated when cardiac arrest is suspected.

GPS system and volunteer first responders

The VFRs in this study are citizens that undergo a European Resuscitation Council (ERC)-certified basic life support (BLS) course and a course in emergency first aid. Afterwards they undergo yearly mandatory training to renew their certificates. When the course is completed, the individual VFR downloads a smartphone application (FirstAED), which must be manually activated, when the VFR is available for dispatch.

The GPS-tracking system was introduced in April 2012. On Langeland, the system is activated during all emergency calls, where an EMS is requested. Activation is followed by GPS localization and alert of the nine closest VFRs within 5000 m of the emergency site, who may choose to accept or reject the call. Of all VFRs accepting the call, three are selected based on their location and the placement of the nearest AED. Each of the VFRs is given a distinct role, of which one of the responders is guided to the nearest AED before approaching the emergency site. The AEDs are placed in heated cabinets and when GPS-activated, the cabinet turns on a blue flashlight and a siren alarm. Information about AED location and availability is retrieved through the nationwide AED-network (www.hjertestarter.dk). The other two VFRs must immediately rush to the emergency site and start CPR, assist the EMS staff, comfort bystanders etc. Fig. 1 shows the activation of the GPS-tracking system.

Variables of interest

The main outcome variables of interest are response rates and response times for VFRs vs. EMS. The secondary outcome is 30-day survival after OHCA in residential areas and on public locations.

Covariates of interest are location, bystander CPR, first documented rhythm, VFR arriving with AED before EMS, bystander/VFR/EMS defibrillation and Cerebral Performance Category score.

Study population

The OHCA study population includes EMS-treated OHCAs that occurred on Langeland from 21st of April 2012 until 31th of December 2017. Location of cardiac arrest was defined according to the Utstein-style recommended guidelines.[16]

Patients with obvious late signs of death, non-OHCAs and OHCA due to non-medical causes (suicide, trauma, accidents etc.) were excluded.[16] Also, patients with OHCAs occurring in nursing homes were excluded. Cardiac and non-cardiac causes of cardiac arrest were defined according to the 2015 updated Utstein guidelines.[17]

Data collection

Data was collected following the Utstein-recommendations for reporting resuscitation outcomes.[16] Information about the response times of EMS and VFRs was collected from the emergency medical dispatch centre in the Region of Southern Denmark.

From April 2012 to September 2015 patient data retrieved by EMS personnel was filled out on paper reports, which were systematically screened to identify OHCAs. From September 2015 EMS information was filled out and stored electronically (Elektronisk Patient Journal), and therefore all journals reporting problems involving airways/breathing/circulation were screened along with those reporting cerebral derangement (unconsciousness, epileptic seizures etc.). To cross-check for missing OHCAs, the medical dispatch centre in the Region of Southern Denmark provided a data extraction on all patients that had any information written in the field "Cardiac Arrest". Information about in-hospital treatment and survival was retrieved from hospital records using each patient's unique personal identification number.[18]

Statistics

The categorical variables will be presented as frequencies and percentages. Comparison between categorical groups will be performed using the Pearson's chi-square test or Fisher's exact test, depending on sample size. Continuous variables, e.g. response times, will be visually inspected for normal distribution and displayed using mean ($\pm$standard deviations), and in group comparisons Student's t-test or a one-way analysis of variance (ANOVA) will be used, depending on the number of independent groups in the comparison. If more than one VFR arrives at the emergency site, the

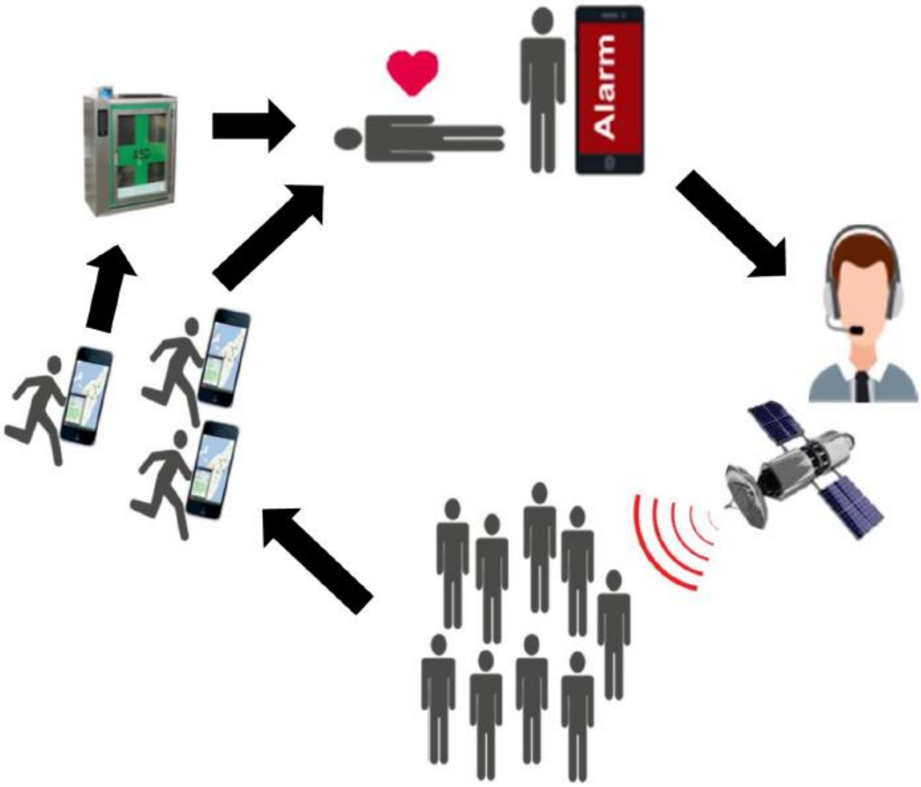


Fig. 1 – Shows how the global positioning system activates nine volunteer first responders (VFRs) and dispatched three VFRs based on their geographical location. The EMS is dispatched simultaneously (not portrayed).

shortest response time will be used. This also applies if more than one EMS arrives to the emergency site. To describe non-normally distributed continuous variables, medians with 25th and 75th percentiles will be presented. To perform group comparisons between non-normally distributed variables, the non-parametric Mann Whitney U-test and Kruskall-Wallis test will be used in cases of two or more group comparisons, respectively. The statistical significance level is 5%. Analysis will be performed by use of STATA version 15 (StataCorp LP, College Station, Texas).

Ethics and data protection

The study was approved by The Danish Data Protection Agency (Journal no. 17/32047) and the Danish Patient Safety Authority under the administration of Danish Health Authority (no. 3-3013-2848/1, ref. LOSC). In Denmark, ethical approval is not necessary for this type of study.

Results

In 2012, 185 citizens of Langeland were registered as VFRs; in 2017 this number had slightly decreased to 170. During the 5½-year inclusion period, 96 AEDs were registered on Langeland.[15]

The GPS-tracking system was activated in 2774 emergency calls (Fig. 2). In 101 calls (4%) none of the VFRs responded. In 2662 calls (96%) at least one VFR arrived to the emergency site, and in 2266 of these (85%), the VFR arrived before the EMS. In 1745 of 2662 cases (66%) the VFR brought an AED to the emergency site before EMS arrival (Fig. 2). In nearly two-thirds of the 2662 emergency calls, all three VFRs arrived to the emergency site (n = 1648, 62%) (Supplementary Appendix I).

The median response time for all VFRs (n = 2662) was 4 min and 46 s (Table 1). The response time for VFRs bringing an AED to the emergency site (n = 2380) was 6 min and 21 s. In comparison, the response time for EMS (n = 2763) was 10 min and 13 s, which was significantly higher compared with both VFR groups ($P < 0.0001$) (Table 1).

We identified 243 patients with presumed OHCA (Fig. 3), and further assessment revealed that 112 were true OHCAs. Of these, 65 OHCAs occurred in residential areas (58%) and 17 OHCAs occurred in public areas (15%). Thirty patients were excluded as they were located in nursing homes or had unknown/imprecise location of cardiac arrest (Fig. 3). Table 2 shows the demographic and survival data concerning the 82 patients of relevance. The two groups were comparable in age, sex distribution and cardiac disease. Comorbidity occurred more frequently in patients from residential areas than in those from public areas.

Thirty-day survival in OHCA patients from residential areas was 15% (10 of 65) vs. 24% (4 of 17) in OHCA patients from public areas ($p = 0.47$) (Table 2).

Discussion

In this retrospective study, we found that a smartphone GPS-tracking system that locates and activates VFRs results in a 96% response rate and significantly reduces VFR response times compared to response

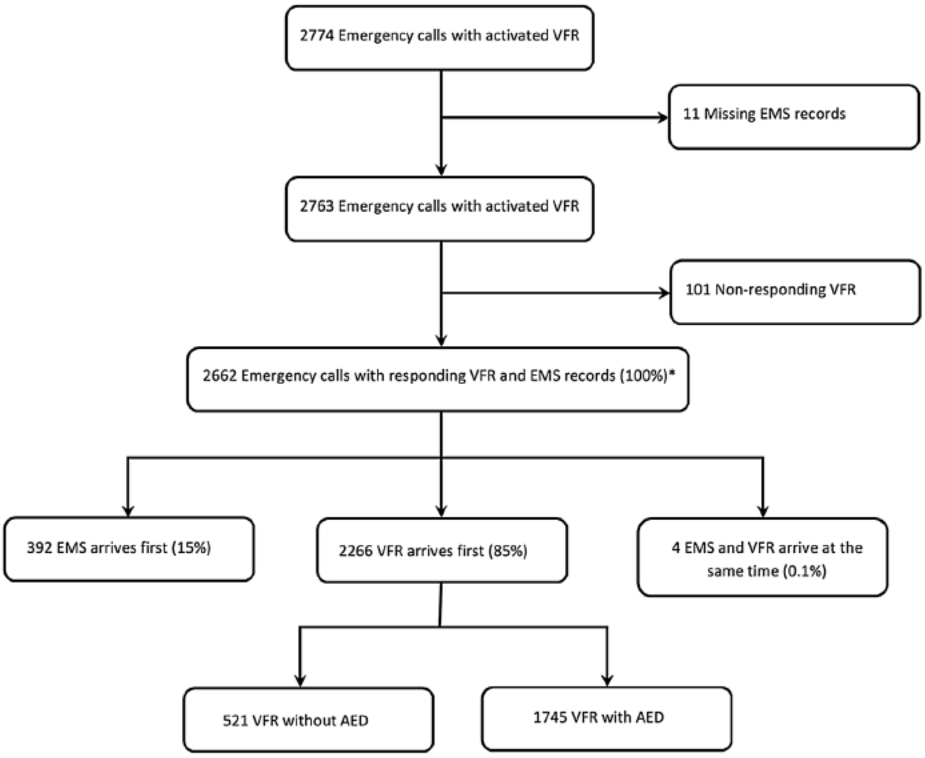


Fig. 2 – Flow-chart showing the number of emergency calls with activation of volunteer first responders (VFR). EMS: Emergency medical service. * 2380 brought an AED.

Table 1 – Response times for the volunteer first responders (VFR) compared with emergency medical service (EMS). AED: automated external defibrillator. IQR: interquartile range.

	Time (min:sec), median (IQR)	P value
EMS (N = 2763)	10:13 (6:14–13:41)	Ref
All VFRs (N = 2662)	4:46 (3:16–6:52)	<0.0001
All VFRs with an AED (N = 2380)	6:21 (4:29–8:49)	<0.0001
VFR with AED on site before EMS (N = 1745)	4:32 (3:07–6:21)	<0.0001

times for EMS. In more than four of five cases a VFR arrives to the emergency site before the arrival of the EMS. Our observations may suggest that the 30-day survival was higher in both residential and public areas, in comparison with the results reported in earlier OHCA studies.

In Denmark, bystander CPR has increased substantially, probably due to large-scale public initiatives in promoting BLS training and increased awareness concerning early action during cardiac arrest.[2,3] Bystander defibrillation, on the other hand, mainly takes place at public cardiac arrests, and defibrillation in residential areas occurs in less than 5% in most register studies.[2,19,20] Recent studies have evaluated the use of different mobile devices to activate citizens and health professionals and facilitate early BLS in cases of presumed OHCA. In a randomized controlled trial, Ringh et al found that 65% of VFRs within a 500 m diameter accepted the emergency call and 59 % of these arrived before EMS, which lead to a significant increase in bystander CPR.[13] In an observational study, Caputo et al found that using a mobile application to activate VFR increased the response rate up to 70 % compared to 15% using a text-message activating system.[21] In contrast, a survey among VFRs using the PulsePoint system reported that 23% responded to the notification but only 11% arrived at the scene.[22] In our study a 96% response rate was found, and in most of these (85%) the VFR arrived before the EMS. The reasons for the large variation in VFR response rates observed in different studies are unknown. However, we may speculate that different levels of education and training could result in varying commitment among VFRs; as in this study, the first two studies required updated ERC-certification in BLS with annual mandatory certificate renewal,[13,21] which was not the case in the latter study.[22] Also, response rates may vary due to differences in the geographical location and the degree of urbanization in the different studies. Perhaps, in rural areas a stronger feeling of commitment among the local citizens to join a VFR network exists, because AEDs are less common and EMS response times are longer than in densely populated areas.

The number of dispatched VFRs in earlier studies varies markedly. In three different studies,[12–14] VFRs within 500–1000 m of the emergency site were activated. This may be suitable in an urban setting with a high population density. However, it may be difficult to recruit VFRs in a rural area, with longer distances to the nearest available EMS, which may also require that VFRs use transport

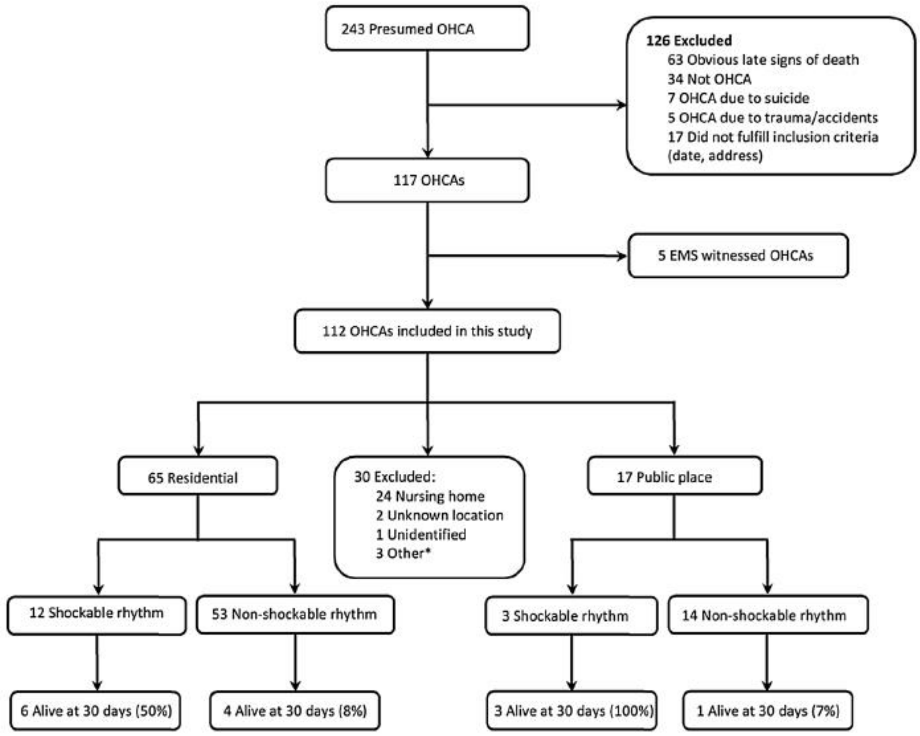


Fig. 3 – Flow-chart showing the inclusion-exclusion process in identifying out-of-hospital cardiac arrest (OHCA).

vehicles to reach the emergency site. This issue has been addressed by Auricchio et al, where VFRs covered a median distance of 1196 m to reach the emergency sites.[23] The VFRs travelled with an average speed of 24 km/h, suggesting the usage of motorized vehicles. The study, however, reported a 100% response rate among eligible VFRs, which has been yet unseen. Also, the study could not describe the alert strategy in selecting VFRs to either locate the nearest AED or to reach the site immediately, nor could they describe the number of AEDs arriving to the site before EMS. The island of Langeland consists mainly of rural countryside, and to reach a wider VFR and AED coverage, the smartphone GPS-tracking system in this study used a 5000 m radius. This did not appear to reduce VFR response rates in this study, where at least two of three VFRs responded to the emergency call in the majority of emergency calls (Supplementary Appendix I). Moreover, only three VFRs were dispatched per emergency call, which is a relatively low number compared to other studies,[12–14,24,25] but neither this appeared to affect the response rates among VFRs (Supplementary Appendix I). Perhaps, this is an important consideration in the efforts to optimize the response rate for VFRs. If a high number of VFRs arrive to the emergency site only to find that other VFRs are already present, they may feel demotivated and become less eager to accept future calls. Of course, this is speculative, but should perhaps be a concern when designing future studies in this field.

So far, only one study has compared VFR response times with the conventional EMS response times.[24] Berglund et al used a smartphone application to activate CPR-trained lay volunteers in all cases of suspected OHCA. A significant reduction in response time (6:17 min for first arriving responder versus 9:36 min for EMS) was found. However, the study only covered greater Stockholm and was not active during night hours.[24] This issue is of major importance when evaluating the actual reduction in time to CPR and defibrillation. It is well established that survival after OHCA is extremely time-sensitive, and the minute-to-minute mortality risk until defibrillation can be reduced to 3–4 % per minute with early CPR.[26] In the present study, we demonstrate that the GPS-tracking system has the potential to increase rates of bystander CPR as well as to reduce the time to CPR in OHCA patients, which ultimately may lead to improved survival.

Cardiac arrest in residential areas comprises three-quarters of OHCAs in most studies.[6,10] Yet, survival in these patients remains low compared to cardiac arrest in public areas. The reasons for the discrepancy is multifactorial; cardiac arrest in residential areas are more frequently unwitnessed, have lower rates of bystander CPR, the population is older with more comorbidity and has more often non-shockable rhythm.[2,11] Also, the number of available on-site AEDs is skewed in favour of public locations[2], which further complicate AED use in residential areas. A study by Hansen et al demonstrated a higher frequency of shockable first rhythm from AED data compared with EMS data,[27] perhaps due to shorter time from collapse to rhythm analysis. In the study by Zijlstra et al, a text-message based alert system resulted in a reduction in time to defibrillation in residential areas, compared with defibrillation by conventional EMS personnel.[14] However, the number of VFRs actually reaching the site was unknown and the study did not evaluate the prognostic impact.[14] In 2014, only 0.8% of residential OHCAs in Denmark underwent bystander defibrillation,[10] which, in this study took place in 13% of OHCAs in private homes. Also, we demonstrated an increase in 30-day survival after OHCA in both residential and public areas, with a combined survival of 17% (14 out of 82 patients), which is markedly higher compared to other studies in this field.[10,28,29] It remains uncertain whether these findings is a direct effect

Table 2 – Demographic and survival results for patients with out-of-hospital cardiac arrest in residential areas and public areas.

	Residential area (N = 65)	Public area (N = 17)
Age, median (IQR)	70 (63–82)	71 (59–77)
Male sex, no. (%)	46 (71)	13/16 (81)
Cardiac cause, no. (%)	51 (78)	16 (94)
Witnessed, no. (%)	32/64 (50)	11 (65)
Bystander CPR, no. (%)	53 (82)	17 (100)
Shockable first rhythm, no. (%)	11/64 (17)	3 (18)
Defibrillation before EMS, no. (%)	8/62 (13)	4/16 (25)
Defibrillation by EMS, no. (%)	12 (18)	3 (18)
VFR activated, no. (%)	54 (83)	16 (94)
VFR arrives before EMS, no. (%)	43 (80)	14 (88)
VFR with AED arrives before EMS, no. (%)	36 (67)	11 (69)
Response time, min:sec	5:13 (3:44–6:29)	4:31 (2:39–8:29)
Pre-arrest comorbidity, no. (%)		
Ischaemic heart disease	11/59 (19)	1/13 (8)
Diabetes	11/59 (19)	2/13 (15)
Hypertension	29/58 (50)	4/13 (31)
Ejection fraction ≤45%	10/59 (17)	0/12 (0)
Chronic obstructive pulmonary Disease	22/59 (37)	0/12 (0)
Chronic kidney disease	3/59 (5)	0/12 (0)
Prior stroke	7/59 (12)	0/12 (0)
Psychiatric disease	8/57 (14)	1/12 (8)
Active cancer	6/59 (10)	0/12 (0)
ROSC at hospital arrival, no. (%)	20 (31)	5 (29)
Alive at 30 days, no. (%)	10 (15)	4 (24)
Cerebral Performance Category Score 1–2 at discharge after OHCA, no. (%)	9/10 (90)	4(100)

CPR: cardiopulmonary resuscitation. EMS: emergency medical service. IQR: Interquartile range. ROSC: return of spontaneous circulation. VFR: volunteer first responder.

of the VFR efforts, however, the rapid VFR response rates and response times combined with early AED use may be favourable for opting early BLS and creating better survival outcomes.

Strengths and limitations

A A strength of this study is the use of a well-established national AED-register that provides VFRs with updated information taking into account the specific availability of AEDs in the nearby area.[23] It is also novel for being the first to provide VFRs with distinct roles, which strengthens team structure during emergency calls. Unlike other studies in this field our study is not register-based, and is characterized by the thorough case ascertainment to identify OHCA subjects in the inclusion period. Also, we cross-checked OHCA data by extracting information from the dispatch centre in the Region of Southern Denmark and thereby identified further two missing OHCA subjects. The civil registration system used in Denmark provides a unique opportunity to identify and collect patient data by matching them across different electronic systems, adding even further to data completion in this study.[18] However, the study has several limitations. It is a single-centre study conducted retrospectively with a small number of OHCAs, and the study is not designed to evaluate causality between the smartphone GPS-tracking system used and its impact on survival after cardiac arrest. Also, this study has a 5½-year inclusion period, and we cannot account for an expected time-dependent rise in 30-day survival after cardiac arrest; there may have been additional citizen BLS training programs and other public initiatives, as well as improvements in prehospital and in-hospital advanced treatment that may have influenced the increase in 30-day survival. This remains speculative.

Conclusion

In this retrospective study, we found that the use of a smartphone GPS-tracking system to alert and dispatch trained VFRs during emergency calls results in a high VFR response rate and significantly reduces response times for VFRs compared to EMS response times. In more than four out of five cases, a VFR arrived to the emergency site before EMS. Finally, our results show a trend towards improved 30-day survival in OHCA patients, however; this calls for further causal research in this field.

Funding

The present study has received grants from the Odense University Hospital's PhD Fund, a grant from the Southern University of Denmark and a grant from TV2 Funen/Odense University Hospital.

Conflicts of interest

The co-investigators and co-authors Finn Lund Henriksen and Henrik Schakow have stock ownership in the GPS-tracking system, FirstAED, which has been used in this study. All other authors have no conflicts of interest to declare.

Acknowledgements

We thank the Langeland AED Association and the volunteer first responder corps for contribution in data collection. We also thank the medical staff at the medical coordination centre in the Region of Southern Denmark for the assistance in acquisition of data.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2019.12.010.

REFERENCES

1. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics-2016 update: a report from the American Heart Association. Circulation 2016;133:e38–360.

2. Hansen SM, Hansen CM, Folke F, et al. Bystander defibrillation for out-of-hospital cardiac arrest in public vs residential locations. JAMA Cardiol 2017;2:507–14.
3. Wissenberg M, Lippert FK, Folke F, et al. Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest. JAMA 2013;310:1377–84.
4. Hansen CM, Lippert FK, Wissenberg M, et al. Temporal trends in coverage of historical cardiac arrests using a volunteer-based network of automated external defibrillators accessible to laypersons and emergency dispatch centers. Circulation 2014;130:1859–67.
5. Kragholm K, Wissenberg M, Mortensen RN, et al. Bystander efforts and 1-year outcomes in out-of-hospital cardiac arrest. N Engl J Med 2017;376:1737–47.
6. Ringh M, Hollenberg J, Palsgaard-Moeller T, et al. The challenges and possibilities of public access defibrillation. J Intern Med 2018;283:238–56.
7. Caffrey SL, Willoughby PJ, Pepe PE, Becker LB. Public use of automated external defibrillators. N Engl J Med 2002;347:1242–7.
8. Page RL, Joglar JA, Kowal RC, et al. Use of automated external defibrillators by a U.S. Airline. N Engl J Med 2000;343:1210–6.
9. Valenzuela TD, Roe DJ, Nichol G, Clark LL, Spaite DW, Hardman RG. Outcomes of rapid defibrillation by security officers after cardiac arrest in casinos. N Engl J Med 2000;343:1206–9.
10. Sondergaard KB, Wissenberg M, Gerds TA, et al. Bystander cardiopulmonary resuscitation and long-term outcomes in out-of-hospital cardiac arrest according to location of arrest. Eur Heart J 2019;40:309–18.
11. Folke F, Gislason GH, Lippert FK, et al. Differences between out-of-hospital cardiac arrest in residential and public locations and implications for public-access defibrillation. Circulation 2010;122:623–30.
12. Pijls RW, Nelemans PJ, Rahel BM, Gorgels AP. A text message alert system for trained volunteers improves out-of-hospital cardiac arrest survival. Resuscitation 2016;105:182–7.
13. Ringh M, Rosenqvist M, Hollenberg J, et al. Mobile-phone dispatch of laypersons for CPR in out-of-hospital cardiac arrest. N Engl J Med 2015;372:2316–25.
14. Zijlstra JA, Stieglis R, Riedijk F, Smeekes M, van der Worp WE, Koster RW. Local lay rescuers with AEDs, alerted by text messages, contribute to early defibrillation in a Dutch out-of-hospital cardiac arrest dispatch system. Resuscitation 2014;85:1444–9.
15. Henriksen F, Schorling P, Hansen B, Schakow H, Larsen M. FirstAED emergency dispatch, global positioning of community first responders with distinct roles - a solution to reduce the response times and ensuring an AED to early defibrillation in the rural Langeland. Int J Networking Virtual Organ 2016;16:86–102.
16. Jacobs I, Nadkarni V, Bahr J, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update and simplification of the Utstein templates for resuscitation registries: a statement for healthcare professionals from a task force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian Resuscitation Council, New Zealand Resuscitation Council, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Councils of Southern Africa). Circulation 2004;110:3385–97.
17. 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. Circulation 2015;132:1286–300.
18. Pedersen CB. The Danish Civil Registration System. Scand J Public Health 2011;39:22–5.
19. Berdowski J, Blom MT, Bardai A, Tan HL, Tijssen JG, Koster RW. Impact of onsite or dispatched automated external defibrillator use on survival after out-of-hospital cardiac arrest. Circulation 2011;124:2225–32.
20. Weisfeldt ML, Sitlani CM, Ornato JP, et al. Survival after application of automatic external defibrillators before arrival of the emergency medical system: evaluation in the resuscitation outcomes consortium population of 21 million. J Am Coll Cardiol 2010;55:1713–20.
21. Caputo ML, Muschietti S, Burkart R, et al. Lay persons alerted by mobile application system initiate earlier cardio-pulmonary resuscitation: a comparison with SMS-based system notification. Resuscitation 2017;114:73–8.
22. Brooks SC, Simmons G, Worthington H, Bobrow BJ, Morrison LJ. The PulsePoint Respond mobile device application to crowdsource basic life support for patients with out-of-hospital cardiac arrest: challenges for optimal implementation. Resuscitation 2016;98:20–6.
23. Auricchio A, Gianquintieri L, Burkart R, et al. Real-life time and distance covered by lay first responders alerted by means of smartphone-application: Implications for early initiation of cardiopulmonary resuscitation and access to automatic external defibrillators. Resuscitation 2019;141:182–7.
24. Berglund E, Claesson A, Nordberg P, et al. A smartphone application for dispatch of lay responders to out-of-hospital cardiac arrests. Resuscitation 2018;126:160–5.
25. Smith CM, Wilson MH, Ghorbangholi A, et al. The use of trained volunteers in the response to out-of-hospital cardiac arrest — the GoodSAM experience. Resuscitation 2017;121:123–6.
26. Larsen MP, Eisenberg MS, Cummins RO, Hallstrom AP. Predicting survival from out-of-hospital cardiac arrest: a graphic model. Ann Emerg Med 1993;22:1652–8.
27. Hansen MB, Lippert FK, Rasmussen LS, Nielsen AM. Systematic downloading and analysis of data from automated external defibrillators used in out-of-hospital cardiac arrest. Resuscitation 2014;85:1681–5.
28. Kiyohara K, Nishiyama C, Matsuyama T, et al. Out-of-hospital cardiac arrest at home in Japan. Am J Cardiol 2019;123:1060–8.
29. Weisfeldt ML, Everson-Stewart S, Sitlani C, et al. Ventricular tachyarrhythmias after cardiac arrest in public versus at home. N Engl J Med 2011;364:313–21.

Paper I Supplement

Appendix I	**VFR arriving at site (N=2662)**
One VFR, no. (%)	294 (11)
Two VFRs, no. (%)	720 (27)
Three VFRs, no. (%)	1648 (62)

AED: automated external defibrillator. IQR: interquartile range.

Appendix I: Number of volunteer first responders (VFRs) arriving at the emergency site. AED: automated external defibrillator. IQR: interquartile range.

Paper II

RESUSCITATION 162 (2021) 112 –119

Available online at www.sciencedirect.com

Resuscitation

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

Clinical paper

Use and coverage of automated external defibrillators according to location in out-of-hospital cardiac arrest

Laura Sarkisian [a,b,*], *Hans Mickley* [a], *Henrik Schakow* [c], *Oke Gerke* [d,e], *Simon Michael Starck* [a], *Jonas Junghans Jensen* [a], *Jacob Eifer Møller* [a], *Gitte Jørgensen* [c], *Finn Lund Henriksen* [a]

[a] *Research Unit of Cardiology, Department of Cardiology, Odense University Hospital, J.B. Winsløws Vej 4, 5000 Odense C, Denmark*
[b] *OPEN, Odense Patient Data Explorative Network, Odense University Hospital, Odense, Denmark*
[c] *Emergency Medical Services, Region of Southern Denmark, Damhaven 12, 7100 Vejle, Denmark*
[d] *Department of Nuclear Medicine, Odense University Hospital, J.B. Winsløws Vej 4, 5000 Odense C, Denmark*
[e] *Research Unit of Clinical Physiology and Nuclear Medicine, Department of Clinical Research, University of Southern Denmark, J.B. Winsløws Vej 19, 5000 Odense C, Denmark*

Abstract

Aims: To evaluate 1) the relative use of automated external defibrillators (AEDs) at different types of AED locations 2) the percentage of AEDs crossing location types during OHCA before use 3) the AED coverage distance at different types of AED locations, and 4) the 30-day-survival in different subgroups.

Methods: From 2014–2018, AEDs used by bystanders during out-of-hospital cardiac arrest (OHCA) in the Region of Southern Denmark were collected. Data regarding registered AEDs was retrieved from the national AED-network. The OHCA site and AED placement was categorized into; 1) Residential; 2) Public; 3) Nursing home, 4) Company/workplace; 5) Institution; 6) Health clinic and 7) Sports facility/recreational. To evaluate 30-day-survival, groups 4–7 were pooled into one Mixed group.

Results: In total 509 OHCAs were included. There was high relative usage of AEDs from public places, nursing homes, health clinics and sports facilities, and low relative usage from companies/workplaces, residential areas and institutions. Of AEDs used during residential OHCAs 39% were collected from public places. AEDs placed in residential areas and public places had a coverage of 575 m (IQR 130–1300) and 270 m (IQR5-550), respectively. Thirty-day- survival in public, residential and mixed groups were 49%, 14% and 67%, respectively.

Conclusion: The relative use of AEDs from public places, nursing homes, sports facilities and health clinics was high, and AEDs used during OHCA in residential areas were most frequently collected from public places. AEDs placed in both residential areas and public places may have a wider coverage area than proposed in current literature.

Keywords: Out-of-hospital cardiac arrest, OHCA, Automated external, Defibrillator, AED, Bystander, Defibrillation, Coverage

* Corresponding author.
E-mail addresses: sarkisian86@hotmail.com (L. Sarkisian), Hans.Mickley@rsyd.dk (H. Mickley), schakow@pc.dk (H. Schakow), Oke.Gerke@rsyd.dk (O. Gerke), simon.michael.starck@rsyd.dk (S.M. Starck), JonasJunghansJensen@gmail.com (J.J. Jensen), Jacob.Moeller1@rsyd.dk (J.E. Møller), Gitte.Jorgensen@rsyd.dk (G. Jørgensen), Finn.L.Henriksen@rsyd.dk (F.L. Henriksen).

https://doi.org/10.1016/j.resuscitation.2021.01.040
Received 24 November 2020; Received in revised form 20 January 2021; Accepted 27 January 2021
0300-9572/

Introduction

Cardiac arrest means abrupt cessation of cardiac activity and will inevitably lead to death if not treated immediately. Out of-hospital cardiac arrest (OHCA) is a major public health concern and annually strikes approximately 700,000 people in Northern America and Europe combined.[1] Early cardiopulmonary resuscitation (CPR) and defibrillation within the first minutes with an automated external defibrillator (AED) may increase survival to more than 50%.[2,3] In recent years, AEDs have gained widespread dissemination in many communities[4,5] and in Denmark several national initiatives have been undertaken to increase bystander AED use, including the establishment of a national AED-network.[6] Bystander defibrillation, however, remains low ranging from 1 to 5%.[5–8] Prior studies have indicated that to increase AED use, AEDs must be placed in close proximity to the site of cardiac arrest,[8–10] they must be available at all times[10–12] and bystanders must be aware of AED locations and be willing to use them.[13] Also, the most optimal AED placement appears to be in public places with high pedestrian traffic.[12,14] Indeed, AEDs are recommended to be placed in public places with high likelihood of OHCA that can be reached within 1–1.5 minutes of brisk walking or approximately 100 m.[15–17] However, international recommendations regarding specific AED placement are scarce, resulting in unguided AED placement in most cases.[6,7,18] So far, AED use from specific locations remains largely unknown. Also, data addressing the actual distances AEDs are carried to OHCA sites is limited, making it difficult to assess the coverage of AEDs placed at different locations.

The aim of this study was three-fold: 1) to assess the relative use of AEDs placed at different types of locations; 2) to assess whether AEDs are carried across different location types before they are used; and 3) to assess the AED coverage distances at different AED locations.

Methods

Settings and study design

This is a retrospective cohort study with prospectively collected data from AEDs used by bystanders in the Region of Southern Denmark from January 1st 2014 to December 31st 2018. The region is mixed rural-urban and covers an area of 12,191 km^2. It has 39 Emergency Medical Service (EMS) stations and one emergency medical dispatch centre (EMDC). The region has 1.2 million inhabitants. During the years 2009–2014, a total of 4350 OHCAs occurred in the region, resulting in 42.4 OHCAs per 100,000 inhabitants per year.[19] Of these, 52.9% received bystander CPR and 3.5% were defibrillated prior to EMS arrival.

Data collection

Data was collected following the Utstein-recommendations for reporting resuscitation outcomes.[16]

AED-centre and the Danish AED-network

Information regarding AEDs was collected from the AED-centre at Odense University Hospital. In cases where the AED-centre received an AED from an unknown site/owner, the serial number was used to track additional information from the Danish AED-network. The AED-centre collects both registered and unregistered AEDs used during OHCA. Upon receiving an AED, data is retracted, analysed and stored in each patient's electronic medical record.

In 2010 a national AED-network was established. In 2011 the AED-network became integrated with the five Danish EMDCs. The network gives AED-owners the opportunity to electronically register AED address, location type, availability, serial number and model. The information is available for the public via a homepage and a smartphone application.

Emergency medical dispatch centre in the region of Southern Denmark

When the EMDC receives a call and suspects OHCA, the dispatcher phone-assists the bystander in performing CPR. If more than one bystander is present, the dispatcher can refer to a nearby AED via the AED-network, in accordance with international guidelines.[17] Also, a two-tiered EMS system is activated followed by the dispatch of an ambulance and a physician-staffed emergency vehicle both equipped with a defibrillator.

Adjudication of location types

We used the Utstein-template location types[16]; 1) Residential; 2) Public; 3) Nursing home; 4) Company/workplace; 5) Institution; 6) Health clinic and 7) Sports facility/recreational (Table S1 in the Supplement). When presenting the demographic and prognostic results and AED coverage, groups 4–7 will be pooled into one 'Mixed' group.

To adjudicate AED location type, a random sample of 150 registered AEDs was reviewed by three authors (LS, HM and FLH) to reach consensus. The remaining 4209 AEDs were systematically evaluated by one author (LS), and HM and FLH were consulted in cases of ambiguity.

Study population

Patients with OHCA were included if 1) an AED was used before the arrival of EMS, 2) the AED was subsequently transported to the AED-centre and 3) information regarding the site of OHCA was available. Data addressing previous medical history and in-hospital treatment was collected from medical records using each patient's personal identification number.[20] Patients with obvious signs of prolonged death were excluded. Cause of cardiac arrest was defined according to the Utstein-guidelines.[16] The Cerebral Performance Category (CPC) score at hospital discharge was used to report neurologic outcomes.[16]

Definition of AED coverage and retrieval distances

AED coverage distance according to AED location type was defined and measured as the shortest one-way walking distance from AED location to OHCA site. AED retrieval distance according to OHCA location was defined and measured as the shortest one-way walking distance from OHCA site to AED location.

Distance calculations were done using Google Maps.

Outcomes

The main outcomes were: 1) the relative use of AEDs at different types of AED locations 2) the percentage of AEDs crossing location types during OHCA before use; and 3) the AED coverage distance at different types of AED locations.

The secondary outcomes were: 1) AED retrieval distance according to OHCA location; 2) CPC score at discharge; and 3) 30-day survival.

When evaluating primary outcomes 2) and 3), and secondary outcome 1) information regarding both registered and unregistered AEDs was used.

Statistics

Categorical variables were presented as frequencies and percentages. When comparing categorical variables, Pearson's chi-square test or Fisher's exact test were used, depending on sample size. Continuous variables were visually inspected for normal distribution. Normally distributed continuous variables were presented as means with standard deviations (SD), and non-normally distributed variables as medians with interquartile ranges (IQR). In group comparisons, two or more normally distributed variables were compared using Student's *t*-test or one-way analysis of variance, respectively. Non-normally distributed variables were compared using the non-parametric Mann-Whitney *U* test and the non-parametric Kruskall-Wallis test in cases of two or more group comparisons, respectively.

A scatter plot was used to graphically display the association between percentage of registered AEDs at specific locations and the percentage of AEDs used from the same locations. An upward shift in the scatter plot will suggest increased AED use at that specific location. A box-and-whisker plot was used to visually compare AED coverage distances.

The statistical significance level was at 5%. All analyses were performed by use of STATA version 15 (StataCorp LP, College Station, Texas).

Ethics and data protection

The study was approved by The Danish Data Protection Agency (Journal no. 17/32047) and the Danish Patient Safety Authority under the administration of Danish Health Authority (no. 3-3013-2319/1 and 3-3013-2848/1).

Results

Baseline characteristics and outcomes

During the study period, the AED-centre collected 621 AEDs. As illustrated in Fig. 1, 509 OHCA-patients fulfilled the inclusion criteria. Table 1 shows the demographic and prognostic results. OHCAs in public places and in the 'Mixed' group were more often male and more frequently had a witnessed cardiac arrest. Shockable first AED rhythm was less frequent in OHCAs in residential areas and nursing homes. Survival after OHCA in public places and the 'Mixed' group was three to four times higher than in residential areas. Survivors in all groups demonstrated a high proportion of favourable neurological outcomes.

Use of AEDs at different location types

From 2014–2018 the number of registered AEDs increased from 2288 to 4359 (Fig. S1 in the Supplement). Twenty-four hour AED availability was highest in residential areas followed by nursing homes and public places (Table S2 in the Supplement). Forty percent of all AEDs did not have 24 h availability. In 416 of the 509 OHCAs (82%), the AED location was available for distance measurements.

Fig. 2 shows a relatively high use of AEDs in public areas, nursing homes, sports facilities/recreational areas and health clinics, as opposed to a relatively low use of AEDs from companies/workplaces, residential areas and institutions.

Table 2 shows that during OHCA in public places, nursing homes, companies/workplaces, institutions, health clinics and sports facilities, the AEDs were most commonly retrieved from the same type of area During OHCA in residential areas the most commonly used AEDs were retrieved from public places.

AED coverage and AED retrieval distances according to different location types

The widest AED coverage distances were observed in residential areas and public places (575 m (IQR 130–1100) and 250 m

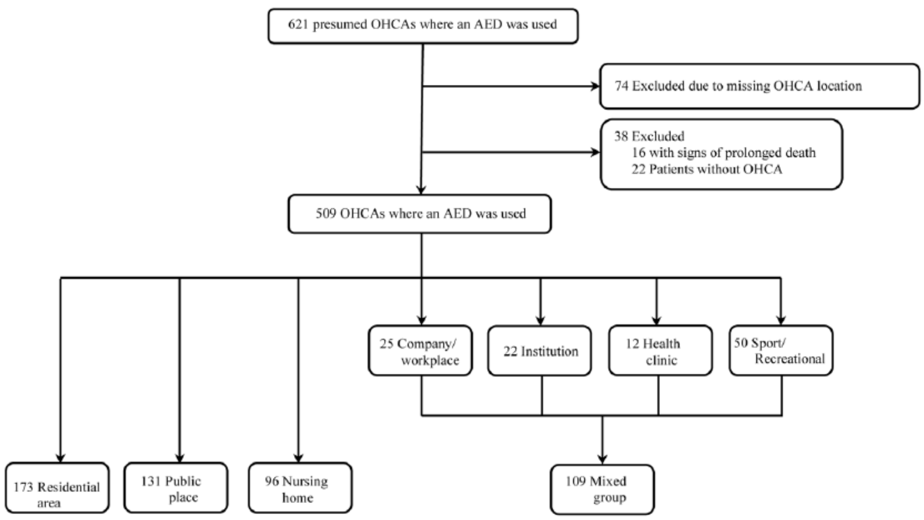


Fig. 1 – Flow-chart showing the inclusion-exclusion.

Table 1 – Demographic and prognostic results.

	Location of OHCA					
	Residential (N = 173)	Public place (N = 131)	Nursing home (N = 96)	Mixed[1] (N = 109)	P value Residential vs Public	P value All groups
Age, year, mean (SD)	68 (14)	69 (13)	79 (11)	61 (12)	0.7[2]	**<0.001**[3]
Male sex, no. (%)	122 (70.5)	102 (81.0)	50 (55.6)	96 (91.4)	**0.04**[4]	**<0.001**[4]
Data missing, no. (%)	0 (0.0)	5 (3.8)	6 (6.3)	4 (3.7)		
Cause of cardiac arrest, no. (%)						
Cardiac*	155 (89.6)	121(97.8)	81 (84.4)	98 (89.9)		
Non-cardiac	18 (10.4)	7 (5.4)	14 (14.6)	10 (9.2)	**0.04**[7]	0.09[7]
Trauma/suicide/accident	0 (0.0)	3 (2.3)	1 (1.0)	1 (0.9)		
Data missing, no. (%)	0 (0.0)	2 (1.5)	0 (0.0)	0 (0.0)		
AED registered at AED-network, no. (%)	129 (75.9)	94 (74.0)	78 (82.1)	83 (76.9)	0.7[4]	0.5[4]
Data missing, no. (%)	3 (1.7)	4 (3.1)	1 (1.0)	1 (0.9)		
Witnessed cardiac arrest	91 (54.5)	100 (84.0)	46 (51.7)	88 (83.0)	**<0.001**[4]	**<0.001**[4]
Data missing, no. (%)	6 (3.5)	12 (9.2)	7 (7.3)	3 (2.8)		
AED with shockable first rhythm, n. (%)	50 (34.0)	82 (70.1)	8 (8.8)	79 (79.0)	**<0.001**[4]	**<0.001**[4]
First rhythm unknown, no. (%)	26 (15.0)	14 (10.7)	5 (5.2)	9 (8.3)		
AED shock and ROSC before EMS arrival, n. (%)	11 (6.5)	30 (25.4)	4 (4.5)	48 (46.6)	**<0.001**[7]	**<0.001**[7]
Data missing, no. (%)	4 (2.3)	13 (9.9)	7 (7.3)	6 (5.5)		
Comorbidity						
Known ischemic heart disease	32 (22.4)	33 (31.4)	15 (18.3)	15 (15.2)	0.1[4]	**0.03**[4]
Congestive heart failure	19 (13.3)	16 (15.2)	13 (15.9)	10 (10.1)	0.6[4]	0.6[4]
Prior stroke	17 (11.9)	10 (9.5)	21 (25.6)	7 (7.1)	0.6[4]	**0.001**[4]
Diabetes	30 (21.0)	23 (21.9)	15 (18.3)	13 (13.1)	0.8[4]	0.4[4]
COPD	26 (18.2)	10 (9.5)	14 (17.1)	14 (14.1)	0.07[4]	0.3[4]
Malignancy	15 (10.5)	11 (10.4)	7 (8.5)	0 (0.0)	0.9[4]	**0.001**[7]
Data missing, no. (%)	30 (17.3)	26 (19.8)	14 (14.6)	10 (9.2)		
ROSC at hospital arrival, no. (%)	38 (22.6)	68 (55.3)	18 (19.8)	76 (73.1)	**<0.001**[4]	**<0.001**[4]
Cerebral Performance Category Score 1–2 at discharge	23/24 (95.8)	57/58 (98.3)	2/2 (100.0)	69/70 (98.6)	0.5[7]	0.6[7]
Data missing, no. (%)	0 (0.0)	1 (0.8)	0 (0.0)	0 (0.0)		

AED: Automated external defibrillator. COPD: Chronic obstructive pulmonary disease. CPR: Cardiopulmonary resuscitation. EMS: Emergency medical services. IQR: Interquartile ranges. OHCA: Out-of-hospital cardiac arrest. ROSC: Return of spontaneous circulation. SD: Standard deviation.
[1]Company/workplace, institutions, health clinic and sports facility/recreational.
[2]Student's *t*-test.
[3]One-way ANOVA.
[4]Pearson's chi-square test.
[5]Mann-Whitney *U* test.
[6]Kruskall-Wallis test.
[7]Fisher's exact test. *Deceased with late signs of death, cases of epileptic seizures/syncope etc.
*Includes OHCAs with presumed, confirmed and unknown cause of cardiac arrest.

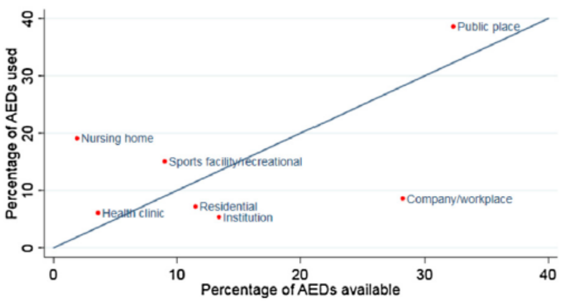


Fig. 2 – Percentage of automated external defibrillators (AEDs) used during OHCA (Y axis) relative to the percentage of registered AEDs at different locations (X axis).

(IQR 5–550), respectively) (Fig. 3). AED retrieval distances in residential areas were significantly higher compared to the other groups (Table 3). In 212 of the 416 OHCA cases (51%), the retrieval distance was ≤100 m.

Discussion

This study presents novel data addressing real life use of AEDs in patients with OHCA from a mixed rural-urban area. A relative high use was observed of AEDs placed in public places and nursing homes, whereas a low use was observed in residential areas. The majority of AEDs were placed and used in the same type of location. Thirty-nine percent of AEDs used in residential areas were retrieved from public places. AEDs placed in residential areas and at public places had a

Table 2 – Cross-table showing wherefrom automated external defibrillators (AEDs) were retrieved and carried to during out-of-hospital cardiac arrest (OHCA).

Location from which AED is collected	Location of OHCA: Residential (N=173)	Public places (N=131)	Nursing homes (N=96)	Companies/ workplaces (N=25)	Institutions (N=22)	Health clinics (N=12)	Sports facilities (N=50)
Residential	19 (11.0)	5 (3.8)	4 (4.2)	3 (12.0)	0 (0.0)	0 (0.0)	0 (0.0)
Public places	66 (38.2)	71 (54.2)	8 (8.3)	2 (8.0)	4 (18.2)	1 (8.3)	9 (18.0)
Nursing homes	4 (2.3)	3 (2.3)	66 (68.8)	1 (4.0)	6 (27.3)	0 (0.0)	0 (0.0)
Companies/ workplaces	16 (9.2)	5 (3.8)	2 (2.1)	11 (44.0)	0 (0.0)	0 (0.0)	1 (2.0)
Institutions	7 (4.1)	4 (3.1)	2 (2.1)	2 (8.0)	6 (27.3)	0 (0.0)	2 (4.0)
Health clinics	1 (0.6)	5 (3.8)	4 (4.2)	0 (0.0)	2 (9.1)	10 (83.3)	1 (2.0)
Sports facilities	17 (9.8)	10 (7.6)	1 (1.0)	2 (8.0)	1 (4.6)	0 (0.0)	32 (64.0)
Unknown AED location	43 (24.9)	28 (21.4)	9 (9.4)	4 (16.0)	3 (13.6)	1 (8.3)	5 (10.0)

25.0 % or higher: Frequent AED use from other locations

25.0 % or higher: Frequent AED use from same location

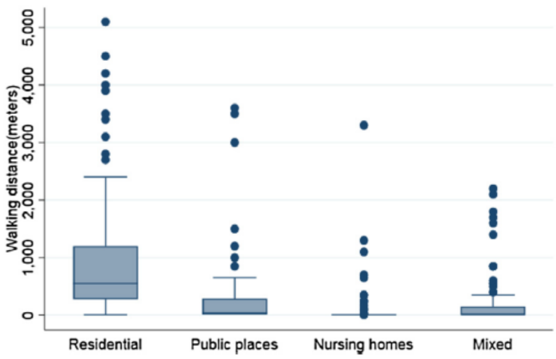


Fig. 3 – Automated external defibrillator (AED) coverage distances according to location.

median coverage distance of more than 500 and 250 m, respectively, indicating that AEDs may have wider coverage than expected.

In recent years, there has been a wide dissemination of AEDs across communities. Approximately 75% of all OHCAs occur in residential areas, where bystander defibrillation consistently has remained low, compared with public places.[6,21–23] Several factors reduce the chance of survival and bystander defibrillation during residential OHCAs, including older age, higher comorbidity, more frequent unwitnessed arrests and a higher proportion of non-shockable rhythms.[22,24] It has also been shown that bystanders at residential OHCAs more often are alone compared with bystanders in public places, reducing the possibility of AED use.[25] Contrary to previous studies,[22,24] we found that patients with OHCA in residential areas and public places were comparable in age and comorbidity (Table 1). This attenuates that OHCAs in residential areas where an AED is applied differ from those where an AED is not applied. Younger age in these OHCA patients makes it more likely that other relatives share the same residence that may put efforts into AED retrieval. It may also imply younger bystanders, who are physically capable of locating and retrieving an AED, compared to their older counterparts. Furthermore, some studies categorize cardiac arrest in nursing homes as residential OHCAs, which may explain the higher age and poorer survival observed in these.[9,21] In a large registry study it was shown that AED application, irrespective of first rhythm, defibrillation status, location and age resulted in an overall increased survival compared to those where an AED was not applied.[5] Perhaps, AED

Table 3 – Automated external defibrillator (AED) coverage and retrieval distances in meters (N = 416).

	Residential	Public place	Nursing home	Mixed[1]	P value
AED coverage distance, median (IQR)	575 (130–1100)	250 (5–550)	5 (5–5)	36 (5–450)	<0.001*
Total no. (%)	31 (7.5)	159 (38.2)	80 (19.2)	146 (35.1)	
AED retrieval distance, median (IQR)	550 (280–1200)	40 (5–230)	5 (5–5)	5 (5–155)	<0.001*
Total no. (%)	129 (31.0)	104 (25.0)	87 (20.9)	96 (23.4)	

[1] Company/workplace, institution, health clinic and sports facility/recreational.
* Kruskall-Wallis test. IQR: Interquartile range.

applications itself indicates other unseen opportune factors, such as more efficient resuscitation efforts due to voice prompts resulting in fewer CPR breaks, or more aggressive in-hospital treatment. This, however, remains speculative.

According to international guidelines, an AED should be placed where there has been an OHCA every 5 years,[16] and "in public locations where there is a relatively high likelihood of witnessed cardiac arrest".[17] In these settings, an AED is expected to cover a radius of approximately 100 m walking range (≈0.03 km^2).[15–17] Some studies have opted for mathematical optimization of AED placement based on prior OHCA sites.[7,12,26,27] These strategies, however, were based on geographically confined, densely populated urban areas, making it difficult to extrapolate to suburban and rural areas. Moreover, OHCAs in residential areas were excluded.[7,12,26,27] So far, no recommendations regarding AED placement in residential areas exist. Also, the actual AED coverage at different locations remains unknown, resulting in an arbitrarily based assumption of coverage limited to a 100 m walking distance. In the present study, AEDs placed in residential areas were carried a median distance of 575 m, corresponding to a coverage area of ≈1 km^2. Furthermore, the observed median retrieval distance of 550 m in residential OHCAs indicates that bystanders were willing to move greater distances to retrieve AEDs than previously proposed in the literature.[9,15,18,21] A study in urban Toronto found a median distance of 281 m between historic OHCAs and the closest AED.[7] This is potentially within the walking range presented here. However, only public OHCAs were included, and distances were measured using straight line calculations, a method known to underestimate actual walking distances.[28] Regarding publicly placed AEDs, the present study showed shorter coverage distances compared with residential AEDs (250 vs. 575 m), but still longer than the 100 m proposed.[9,12,15,18,21] The reason for the observed difference is most likely multifactorial; perhaps during public OHCAs, bystanders are less prone to walk longer distances, in unfamiliar surroundings with unknown AED locations, or they may retrieve an AED, but find that the EMS arrived first due to shorter EMS response times.[7,22] Conversely, bystanders at residential OHCAs are likely residents themselves, potentially making them more inclined to seek out an AED in familiar surroundings despite longer distances.

In both the present and earlier studies,[6,29,30] the placement of AEDs was consistently skewed in favour of public places. Correspondingly, the present study showed a relatively higher AED use in public places, and found that AEDs were frequently transported from public places to other locations as well, including residential areas. In another study from urban Toronto, the likelihood of OHCA in different building and location types was assessed.[30] Here, a large number of AEDs were placed at public schools where OHCA incidences were very low, and the authors concluded that AED placement in these public buildings was improper. This conclusion is in contrast with our observations, which demonstrated frequent deployment of publically placed AEDs to other cardiac arrest sites. Therefore, we suggest that future AED placement should not only take into account the risk of "on-site" cardiac arrest, but also consider AED placements, that are known and accessed by the public, as these may have wider coverage distances than previously assumed.

Despite great 24 h availability (Table S2 in the Supplement), AEDs placed in residential areas were seldom used (Fig. 2). An explanation could be that residential areas are less congested and AEDs therefore less visual for the general public. Low use of AEDs from residential areas was also found in a previous study,[5] despite residential AEDs comprising surprisingly four out of ten of total registered AEDs. Perhaps other methods are needed to improve AED use in residential areas.

Strengths and limitations

The study has some limitations. First, we do not know the number of AEDs not brought to the AED-centre after being used. Second, we have not taken into account multiple AEDs registered at the same location. The extent of this and its impact is unknown. Third, we assume that unregistered AEDs in the region are dispersed in the same way as registered AEDs, however, this also remains unknown. Fourth, the organizational and logistical settings in Denmark can make it difficult to extrapolate the results to other countries. A final limitation is the observational nature of this study. The strength of this study is the prospectively collected AED data, which provides information about both registered and unregistered AEDs. By cross-linking AED data to the national AED-network, we were able to collect additional information regarding unidentified AEDs, adding to the extensive data completeness. Also, this study is the first to measure and report en-route distances between AED locations and OHCA sites and to thereby evaluate the actual AED coverage distances at various locations.

Conclusion

By collecting data from AEDs that were used during OHCAs in a mixed rural-urban area, we observed high AED use from public places, nursing homes, sports facilities/recreational areas and health clinics, and low use from companies/workplaces, residential areas and institutions. The majority of AEDs were placed and used in the same type of location, except for residential OHCAs, where AEDs more frequently were retrieved from public places. By measuring en-route distances from AED location to OHCA site, we found that AEDs placed in residential areas and public places had wider coverage than proposed in the current literature. These observations impose new aspects that may be considered in future guidelines addressing AED placement.

Conflicts of interest

Doctor Møller has received grants and personal fees from Abiomed, and personal fees from Orion Pharma and Novartis. All other authors declared no conflict of interests.

CRediT authorship contribution statement

Laura Sarkisian: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing - original draft, Writing - review & editing, Visualization, Project administration, Funding acquisition. **Hans Mickley:** Conceptualization, Methodology, Validation, Formal analysis, Writing - original draft, Writing - review & editing, Supervision, Project administration, Funding acquisition. **Henrik Schakow:** Conceptualization, Methodology, Investigation, Resources, Data curation, Writing - review & editing. **Oke Gerke:** Conceptualization, Methodology, Validation, Formal analysis, Writing - review & editing, Supervision. **Simon Michael Starck:** Methodology, Validation, Investigation, Data curation, Writing - review & editing. **Jonas Junghans Jensen:** Methodology, Validation, Investigation, Data curation, Writing - review & editing. **Jacob Eifer Møller:** Conceptualization, Methodology, Validation, Writing - review & editing, Supervision. **Gitte Jørgensen:** Methodology, Validation, Investigation, Resources, Writing - review & editing. **Finn Lund Henriksen:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing - original draft, Writing - review & editing, Supervision, Project administration, Funding acquisition.

Acknowledgements

We thank the health care professionals at the EMDC for the assistance in data acquisition and collaboration with the AED-centre. Also, we thank the AED-network for sharing data for the purpose of this study.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2021.01.040.

REFERENCES

1. Berdowski J, Berg RA, Tijssen JG, Koster RW. Global incidences of out-of-hospital cardiac arrest and survival rates: Systematic review of 67 prospective studies. Resuscitation. 2010;81:1479–87.
2. Valenzuela TD, Roe DJ, Nichol G, Clark LL, Spaite DW, Hardman RG. Outcomes of rapid defibrillation by security officers after cardiac arrest in casinos. N Engl J Med. 2000;343:1206–9.
3. Caffrey SL, Willoughby PJ, Pepe PE, Becker LB. Public use of automated external defibrillators. N Engl J Med. 2002;347:1242–7.
4. Kitamura T, Kiyohara K, Sakai T, et al. Public-Access Defibrillation and Out-of-Hospital Cardiac Arrest in Japan. N Engl J Med. 2016;375:1649–59.
5. Weisfeldt ML, Sitlani CM, Ornato JP, et al. Survival after application of automatic external defibrillators before arrival of the emergency medical system: evaluation in the resuscitation outcomes consortium population of 21 million. J Am Coll Cardiol. 2010;55:1713–20.
6. Hansen SM, Hansen CM, Folke F, et al. Bystander Defibrillation for Out-of-Hospital Cardiac Arrest in Public vs Residential Locations. JAMA cardiology. 2017;2:507–14.
7. Chan TC, Li H, Lebovic G, et al. Identifying locations for public access defibrillators using mathematical optimization. Circulation. 2013;127:1801–9.
8. Sondergaard KB, Hansen SM, Pallisgaard JL, et al. Out-of-hospital cardiac arrest: Probability of bystander defibrillation relative to distance to nearest automated external defibrillator. Resuscitation. 2018;124:138–44.
9. Karlsson L, Hansen CM, Vourakis C, et al. Improving bystander defibrillation in out-of-hospital cardiac arrests at home. Eur Heart J Acute Cardiovasc Care. 2020;2048872619891675.
10. Deakin CD, Anfield S, Hodgetts GA. Underutilisation of public access defibrillation is related to retrieval distance and time-dependent availability. Heart. 2018;104:1339–43.
11. Hansen CM, Wissenberg M, Weeke P, et al. Automated external defibrillators inaccessible to more than half of nearby cardiac arrests in public locations during evening, nighttime, and weekends. Circulation. 2013;128:2224–31.
12. Sun CL, Demirtas D, Brooks SC, Morrison LJ, Chan TC. Overcoming Spatial and Temporal Barriers to Public Access Defibrillators Via Optimization. J Am Coll Cardiol. 2016;68:836–45.
13. Brooks B, Chan S, Lander P, Adamson R, Hodgetts GA, Deakin CD. Public knowledge and confidence in the use of public access defibrillation. Heart. 2015;101:967–71.
14. Hallstrom AP, Ornato JP, Weisfeldt M, et al. Public-access defibrillation and survival after out-of-hospital cardiac arrest. N Engl J Med. 2004;351:637–46.
15. Aufderheide T, Hazinski MF, Nichol G, et al. Community lay rescuer automated external defibrillation programs: key state legislative components and implementation strategies: a summary of a decade of experience for healthcare providers, policymakers, legislators, employers, and community leaders from the American Heart Association Emergency Cardiovascular Care Committee, Council on Clinical Cardiology, and Office of State Advocacy. Circulation. 2006;113:1260–70.
16. 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. Circulation. 2015;132:1286–300.
17. Kleinman ME, Brennan EE, Goldberger ZD, et al. Part 5: Adult Basic Life Support and Cardiopulmonary Resuscitation Quality: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2015;132:S414–35.
18. Hansen CM, Lippert FK, Wissenberg M, et al. Temporal trends in coverage of historical cardiac arrests using a volunteer-based network of automated external defibrillators accessible to laypersons and emergency dispatch centers. Circulation. 2014;130:1859–67.
19. Moller SG, Wissenberg M, Moller-Hansen S, et al. Regional variation in out-of-hospital cardiac arrest: Incidence and survival - A nationwide study of regions in Denmark. Resuscitation. 2020;148:191–9.
20. Pedersen CB. The Danish Civil Registration System. Scand J Public Health. 2011;39:22–5.
21. Folke F, Gislason GH, Lippert FK, et al. Differences between out-of-hospital cardiac arrest in residential and public locations and implications for public-access defibrillation. Circulation. 2010;122:623–30.
22. Herlitz J, Eek M, Holmberg M, Engdahl J, Holmberg S. Characteristics and outcome among patients having out of hospital cardiac arrest at home compared with elsewhere. Heart. 2002;88:579–82.
23. Kiyohara K, Nishiyama C, Matsuyama T, et al. Out-of-Hospital Cardiac Arrest at Home in Japan. Am J Cardiol. 2019;123:1060–8.
24. Murakami Y, Iwami T, Kitamura T, et al. Outcomes of out-of-hospital cardiac arrest by public location in the public-access defibrillation era. J Am Heart Assoc. 2014;3:e000533.
25. Fredman D, Svensson L, Ban Y, et al. Expanding the first link in the chain of survival - Experiences from dispatcher referral of callers to AED locations. Resuscitation. 2016;107:129–34.
26. Folke F, Lippert FK, Nielsen SL, et al. Location of cardiac arrest in a city center: strategic placement of automated external defibrillators in public locations. Circulation. 2009;120:510–7.

27. Dahan B, Jabre P, Karam N, et al. Optimization of automated external defibrillator deployment outdoors: An evidence-based approach. Resuscitation. 2016;108:68–74.
28. Fan M, Fan KL, Leung LP. Walking Route-Based Calculation is Recommended for Optimizing Deployment of Publicly Accessible Defibrillators in Urban Cities. J Am Heart Assoc. 2020;9:e014398.
29. Karlsson L, Malta Hansen C, Wissenberg M, et al. Automated external defibrillator accessibility is crucial for bystander defibrillation and survival: A registry-based study. Resuscitation. 2019;136:30–7.
30. Brooks SC, Hsu JH, Tang SK, Jeyakumar R, Chan TC. Determining risk for out-of-hospital cardiac arrest by location type in a Canadian urban setting to guide future public access defibrillator placement. Ann Emerg Med. 2013;61:530-8.e2.

Paper II Supplement

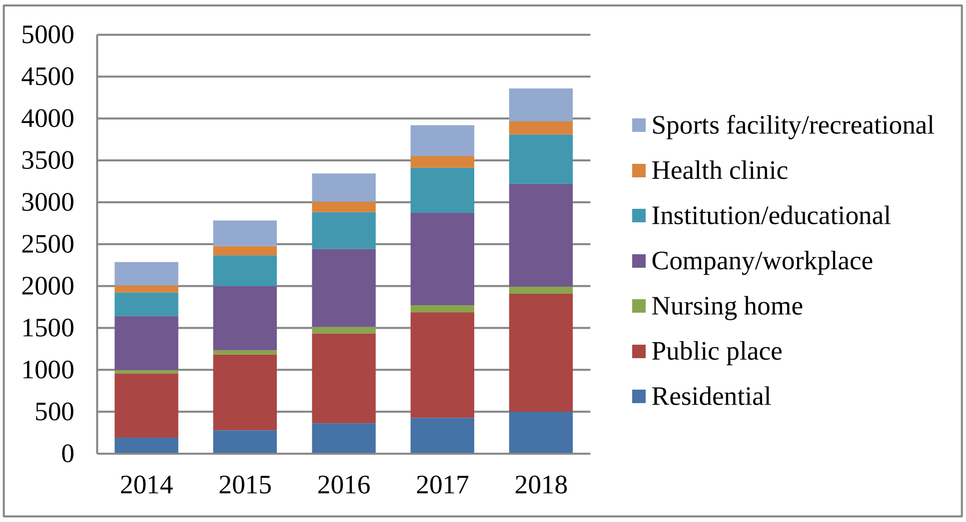


Figure S1. Cumulative distribution of AEDs registered in the AED-network

Supplemental Table S1. Description of types of location

Types of location	Definition
Residential area	Private homes, multiple dwelling houses and vacation houses/cottages.
Public place	All places freely accessible to the public, including schools and educational facilities.
Nursing home	-
Company/workplace*	-
Institution*	Part-time special care facilities and permanent housings for people with mental or psychiatric disabilities.
Health clinic*	Clinics that employ authorized health care professionals registered under the Danish Health Authorities, e.g. nurses, dentists, physical therapists. Hospitals and outpatient clinics excluded.
Sports facility/ recreational area*	All sports facilities and recreational areas including rowing and golf clubs

* These four location types are pooled into one 'Mixed' group, as they are somewhat similar in being a rallying point for a specific group of people, but not freely accessible to the public.

Supplemental Table S2. Cumulative number and percentage of registered automated external defibrillators (AEDs) and 24 h availability at different locations by 2018

	No. AEDs (%) (N=4,359)	24 h availability, no. (%)
Residential	501 (11.5)	494 (98.6)
Public place	1,408 (32.3)	929 (66.0)
Nursing home	86 (1.9)	79 (91.9)
Company/workplace	1,228 (28.8)	487 (39.7)
Institution	586 (13.4)	345 (58.9)
Health clinic	159 (3.6)	47 (29.6)
Sports facility/recreational	391 (9.0)	248 (63.4)

Paper III

Longer Retrieval Distances to the Automated External Defibrillator Reduces Survival After Out-of-Hospital OHCA

Laura Sarkisian, M.D.[1,2 *], Laura.Sarkisian2@rsyd.dk

Hans Mickley, M.D., DMSc[1], Hans.Mickley@rsyd.dk

Henrik Schakow, EMT[3], schakow@pc.dk

Oke Gerke, MSc, PhD[4,5], Oke.Gerke@rsyd.dk

Simon Michael Starck, M.D.[1], simon.michael.starck@rsyd.dk

Jonas Junghans Jensen, M.D.[1], JonasJunghansJensen@gmail.com

Jacob Eifer Møller, M.D., DMSc[1], Jacob.Moeller1@rsyd.dk

Gitte Jørgensen, M.D.[3], Gitte.Jorgensen@rsyd.dk

Finn Lund Henriksen, M.D., PhD[1], Finn.L.Henriksen@rsyd.dk

Word count: 3,068

[1]Research Unit of Cardiology, Department of Cardiology, Odense University Hospital, J.B. Winsløws Vej 4, 5000 Odense C, Denmark **(primary site of research)**.

[2]OPEN, Odense Patient data Explorative Network, Odense University Hospital, Odense, Denmark **(affiliation)**.

[3]Emergency Medical Services, Region of Southern Denmark, Damhaven 12, 7100 Vejle, Denmark

[4]Department of Nuclear Medicine, Odense University Hospital, J.B. Winsløws Vej 4, 5000 Odense C, Denmark.

[5]Research Unit of Clinical Physiology and Nuclear Medicine, Department of Clinical Research, University of Southern Denmark, J.B. Winsløws Vej 19, 5000 Odense C, Denmark.

* Corresponding author: Laura Sarkisian, phone no. +45 27 85 94 44, fax no. +45 65 41 30 02.

Abstract: (250 words)

Aims: To evaluate and compare survival after out-of-hospital OHCA (OHCA), where an automated external defibrillator (AED) was used, in densely, moderately and thinly populated areas. Also, to evaluate the association between AED retrieval distance and survival after OHCA.

Methods: From 2014 to 2018, AEDs used during OHCA in the region of Southern Denmark were systematically collected. OHCAs were included if the OHCA address was known. OHCAs at nursing homes were excluded. To evaluate population density, a map with 1000x1000 meter grid cells was used with each cell color-graded according to the number of inhabitants. Densely, moderately and thinly populated areas were defined as ≥200 inhabitants, 20-199 inhabitants and 0-19 inhabitants per km^2, respectively. Primary outcome was 30-day survival.

Results: A total of 423 cases of OHCA were included, of which 207 (49%) occurred in densely populated areas, while 78 (18%) and 138 (33%) occurred in moderately and thinly populated areas, respectively. AED retrieval distances were; densely populated 105 meters (IQR 5-450), moderately populated 220 meters (IQR 5-450) and thinly populated 350 meters (IQR 5-1500) (P=0.0002). Thirty-day survival was 40%, 31% and 34%, respectively (P=0.3). In a multivariable regression analysis, the risk of death increased with 10% per 100 meters an AED was placed further away from the site

Conclusion: Survival after OHCA, where an AED was used, did not seem to differ in thinly, moderately and densely populated areas. The length of the AED retrieval distance, however, was correlated with reduced survival, even after adjusting for other potentially explanatory variables.

Introduction

Out-of-hospital OHCA (OHCA) is the third leading cause of death in Europe and remains a significant public health problem with only about 5% surviving to hospital discharge (1). Early cardiopulmonary resuscitation (CPR) and bystander defibrillation is pivotal for OHCA outcomes (2-4), and though bystander CPR has become widespread in recent years (5, 6), the rates of bystander defibrillation have remained relatively low at 2-10% (7-9). To improve the use of automated external defibrillator (AED), the European Resuscitation Council and the American Heart Association (AHA) have recommended public access defibrillation (PAD) programs where AEDs are placed "in public places with a high density and movement of citizens", and where one OHCA can be expected per 2-5 years (10, 11). Accordingly, great effort has been put into identifying high-risk locations for AED placement in urban areas (12-14). Guidelines regarding AED placement in thinly populated areas remain scarce. Here, the response times for emergency medical services (EMS) are longer than in urban areas, which is associated with reduced survival after OHCA (7, 15-17). Also, the incidence of residential OHCAs in rural areas is higher than in dense urban areas (16), making the effects of PAD in rural areas more uncertain. According to international guidelines, an AED is expected to cover an area reachable within 1-2 minutes of brisk walking (11), translated to a Euclidian distance of approximately 100 meters. However, in rural areas, distances to the nearest available AED may be longer (18), further inhibiting AED use, and the effects of longer AED retrieval distances on survival after OHCA remains unknown.

The aims of the study were 1) to evaluate and compare 30-day survival during OHCA, where an AED was used in densely, moderately and thinly populated areas, and 2) to evaluate the association between AED retrieval distance and 30-day survival after OHCA.

Methods

Study design and patient population

This is a retrospective cohort study, where AED data was prospectively collected. Data was collected using the 2014 Utstein recommendations for reporting resuscitation outcomes (19).

Patients were included from January 1st 2014 to December 31st 2018. The study includes all consecutive cases of OHCA that were attempted resuscitated by the EMS staff, where an AED was used before EMS arrival, and the AED was subsequently transported to the AED-center at the Odense University Hospital. OHCAs with unknown AED address and at nursing homes were excluded along with OHCAs with signs of prolonged death such as rigor mortis.

Definition of primary endpoint

The primary endpoint was 30-day survival after the index OHCA event.

Study settings

The study was conducted in the region of Southern Denmark. The region covers 12,191 km^2 and has 1.2 million inhabitants. It has 39 Emergency Medical Service (EMS) stations, organized and dispatched by one Emergency Medical Dispatch Center (EMDC). According to Statistics Denmark, 16% of the population (≈200,000 inhabitants) in this region lives outside urban areas, which comprise 94% of the entire area (20). Urban areas are defined as "built-up areas" with at least 200 inhabitants and where the distance between the buildings is not more than 200 meters, unless due to e.g. parks, cemeteries facilities (Statistics Denmark) (21). According to Statistics Denmark, the population density in rural areas is <200 inhabitants per km^2.

If the EMDC receives a call and suspects an OHCA, a two-tiered system is activated. The first tier involves an ambulance equipped with a defibrillator, and the second tier is an anesthesiologist-staffed emergency vehicle with means to provide advanced life.

Data collection

AED data was collected from the AED-center at Odense University Hospital and the Danish national AED-network.

Since 2014 the AED-center has collected AEDs used during OHCA in the region of Southern Denmark. The AED-center has been described previously in detail (22). The Danish national AED-network was established in 2010 and is a voluntary based registry containing information regarding publically available AEDs. The information is accessible via a homepage (www.hjertestarter.dk) and a smartphone application.

Information regarding previous medical history and in-hospital treatment was collected from the medical records using each patients' personal civil registration number (23). Information regarding the prehospital treatment was retrieved from the electronic Prehospital Patient Journals.

Geocoding, population density and AED retrieval distance

The exact addresses of OHCA sites, registered AEDs and AEDs used during OHCA were geocoded using the open source Quantum Geographic Information System (QGIS). An AED was defined as publically available if it was registered at the AED network at the time of OHCA. Information regarding population density was retrieved from Statistics Denmark (2011) and integrated into QGIS, which thereby provided a map with 1000 x 1000 meter grid cells color-graded according to the number of inhabitants in each grid cell (Figure S1 in the Supplement).

Population density was defined as densely populated (≥200 inhabitants per km^2), moderately populated (20-199 inhabitants per km^2) and thinly populated (0-19 inhabitants per km^2) areas according to the site of OHCA. Information regarding population density in the region was retrieved from Statistics Denmark using the 2014 GEOSTAT 'New Degree of Urbanisation' (24). Distance measurements for AED retrieval distance were obtained using Google Maps and represent the shortest one-way walking distance from AED location to OHCA site.

On-site AED use was defined as an AED retrieval distance of 0-5 meters and applied to cases where the OHCA and AED location had the same address.

Statistics

Categorical variables were presented as percentages and their respective frequencies. Categorical data were compared using either Pearson's chi-squared test or Fisher's exact test, depending on sample size.

Continuous variables were presented as means (± standard deviations) or medians (interquartile ranges), after visually inspecting for normal distribution. If normally distributed, two or more groups were compared using

Student's t-test or one-way analysis of variance (ANOVA), respectively. Non-normally distributed variables were compared using the non-parametric Mann-Whitney U test and the non-parametric Kruskall-Wallis test in cases of two or more group comparisons, respectively.

To evaluate aim 1) Pearson's chi-squared test was used to compare survival in the three groups. To evaluate aim 2) we conducted a multivariable logistic regression analysis where the primary endpoint was regressed on AED retrieval distance, while adjusting for the following prognostic factors: Age, sex, cardiac cause of arrest, bystander witnessed OHCA, public place of arrest, shockable first rhythm, bystander defibrillation before EMS arrival, time of day, population density and EMS response time. Backward variable selection was applied with a p-stay of 0.4 while age and sex were kept in the model due to suspected prognostic value, irrespective of statistical significance.

Hypothesis tests were two-sided and the statistical significance level was set at 5%.

All statistical analyses were performed using Stata 15 (StataCorp LP, College Station, Texas).

Ethics and data protection

This study was approved by the Danish Safety Patient Authority (under Danish Health Authority) (no. 3-3013-2319/1 & 3-3013-2484/1) and the Danish Data Protection Agency (Journal no. 17/32047).

Results

Clinical characteristics and outcomes according to population density

During the 5-year period, an AED was taken into use during 621 cases of presumed OHCA. A total of 423 (68%) cases fulfilled the inclusion criteria (Figure 1). Of these, 207 (49%) took place in densely populated areas, while 78 (18%) and 138 (33%) occurred in moderately and thinly populated areas, respectively.

Table 1 shows patient characteristics and clinical outcomes. The groups were comparable in age, sex distribution, pre-arrest comorbidity and predictors of OHCA survival, including bystander witnessed arrest, bystander CPR and bystander defibrillation. In thinly populated areas, EMS response times were significantly longer and residential OHCAs occurred more frequently than in densely populated areas. Also, AED retrieval distance became longer with the declining population density (105 m (IQR 5-450) vs. 350 m

(IQR 5-1500) in densely and thinly populated areas, respectively). When evaluating 30-day survival, patients from densely populated areas appeared to have the most favorable outcome (40% versus 34% in thinly populated areas), however, the result did not reach the level of statistical significance (Table 1).

AED retrieval distance and survival outcome

In 348 out of 423 OHCAs (82%) the AED location was known, and AED retrieval distances were calculated. Figure 2 illustrates the distribution of four predictors of survival and the AED retrieval distance. It confirms that the proportion of residential OHCAs increases with higher AED retrieval distances, but seems unchanged in the proportion of shockable first rhythm, witnessed OHCAs and OHCAs older than 65 years. Figure 3 illustrates the cumulative distribution of AED retrieval distances. It shows that about one-third of AEDs were collected on-site (Figure 3A) and confirms that distances were longer in thinly populated areas compared with the two other groups (Figure 3B). Figure 4 shows that the number of OHCAs with ROSC at hospital arrival and the number of patients alive after 30 days decreased with longer AED retrieval distances.

Multivariable logistic regression

After adjusting for 10 clinically relevant variables (Table S1 in the Supplement), the variables ‘population density’, ‘public place of arrest’ and ‘bystander defibrillation before EMS arrival’ were excluded as part of the backward elimination process. This was done due to these variables’ high correlation with ‘EMS response time’ and ‘shockable first rhythm’, respectively, and due to the non-significant effect that these three had in the initial regression analysis.

In the following multivariable analysis, AED retrieval distance was regressed on 30-day survival adjusting for the remaining seven explanatory variables of interest (Table 2). The regression showed that the risk of death increased with 0.1% per meter (OR 1.0010 (95% CI 1.0004-1.0016)), corresponding to a 10% (95% CI 4-16%) increased risk of death per 100 meters an AED was placed further away from the site. Younger age, bystander witnessed arrests and OHCAs with shockable first rhythms were associated with better survival outcomes.

Discussion

The present study involves consecutive patients with OHCA where an AED was used before EMS arrival. The study had two main findings. Firstly; 30-day survival in thinly, moderately and densely populated areas were largely comparable, and secondly; in a multivariate regression analysis, increasing AED retrieval distance was significantly associated with increased mortality. More specifically, there was a 10% increase in risk of death per 100 meters distance from OHCA site to the retrieved AED.

During OHCA, reducing time-to-shock has proven crucial for survival. Despite many initiatives (25), research efforts and recommendations have mainly concerned urban centers and public places (10-14, 26). As a result, there is a knowledge gap concerning AED placement and use in rural areas. The region of Southern Denmark is a mixed rural-urban area, where the population majority live in urban areas, which only comprises 6% of the total area (21). Despite this, about half of OHCA cases, where an AED was used, occurred outside the densely populated urban areas (216 out of 423 cases from moderately and thinly populated areas). Masterson et al found similar results with a higher chance of bystander CPR and bystander defibrillation in rural OHCAs (15). This seems surprising considering that OHCAs occur more frequently in urban areas due to higher population densities and the influx of working people during daytime (27); however, with shorter urban EMS response times, the professional staff is more likely to arrive before a bystander with an AED. Perhaps, in smaller rural communities where there is a higher proportion of residential OHCAs (16), bystanders are more likely to know the OHCA patient, making them more inclined to put efforts into retrieving and using an AED during OHCA (28). Another possible explanation for the higher AED use observed in rural areas in the present study may be attributed to volunteer first responders (VFRs). Use of VFRs has been an integrated part of the region's EMDC response in rural areas since 2012 (29), and has previously been shown to increase defibrillation rates in residential areas (30).

As expected, AED retrieval distances became longer with decreasing population densities (Table 1). According to guidelines, a retrieval distance of 350 meters, which was the case in rural areas, can be translated into a time-to-shock delay of ≈4 minutes if the brisk walking speed of ≈1.5 m/sec is used (11). In a survival prediction model (31), survival chances were reduced by 7-10% per minute to defibrillation during OHCA, but could be altered to 3-4% per minute if CPR was given. With this delay and counting the 1-2 minute delay from collapse to phone call (32), we would expect a survival rate of ≈40% (31). The 30-day survival of 34% in this group is therefore comparable, and is likely to also be affected by the higher rate of residential OHCAs in rural areas, or the bystanders traveling a longer distance by a motorized vehicle to retrieve an AED (Table 1). However, with the limited number of OHCAs in this observational study, the results are susceptible to variation and must be interpreted with caution. If an AED had not been retrieved by a bystander, however, time-to-shock would have increased substantially due to the eleven minute EMS response time (Table 1), and the shockable rhythms would likely have deteriorated to non-shockable rhythms in many cases, causing poorer survival outcomes (33). To counteract prolonged EMS responses, recent studies have examined the effects of VFRs retrieving AEDs and approaching the emergency site for early defibrillation purposes (34-36). In the aforementioned study by Zijlstra et al, VFRs significantly increased defibrillation rates among OHCAs, of which about 80% occurred in residential areas (30). Furthermore, by only travelling one-way and using GPS-coordinates to rapidly geo-locate AEDs, VFRs may further reduce time-to-shock (37), and could therefore be an important link for increasing AED use and OHCA survival in both rural and residential areas.

Previous studies have demonstrated that areas with low population density are associated with prolonged EMS response times, longer AED retrieval distances and higher rates of residential OHCAs in thinly populated areas (15, 16, 38, 39), also confirmed in the present study (Table 1), but we could not establish the previously found adverse effect on 30-day survival. Perhaps our number of included cases was too small to detect a true difference, causing a type II error. Furthermore, a direct comparison between earlier all-comer OHCA studies and our selected AED-OHCA population preferably must be done with caution. After all, despite longer AED retrieval distances, the rate of shockable first rhythm in the rural group was comparable with the two other groups (Table 1 & Figure 2), which could be due to fewer interruptions in chest-compression due to AED voice prompts, or an indicator of younger and physically more able bystanders (6) performing sufficient CPR. Perhaps, having an AED applied itself is a marker of better outcome, as suggested by Weisfeldt et al (8).

The survival benefits of on-site use of public AEDs within the first minutes after collapse are overwhelming (2, 4, 40). The impact of dispatched AEDs, however, and the effects of retrieval distances on survival are less clear. In a Dutch registry study, Berdowski et al found that that time-to-shock using a dispatched AED was significantly longer compared with use of on-site AEDs (8.5 minutes vs. 4.1 minutes, respectively) (41), and accordingly, survival benefits of on-site AED use exceeded that of dispatched AEDs (50% vs. 17%, respectively). However, the use of dispatched AEDs was restricted to firefighters and police officers, making these observations difficult to compare with present day widespread bystander use. The present study is the first to establish an adjusted correlation between the AED retrieval distance and survival after OHCA. This observation, however, may raise more questions than answers concerning AED placement in both high-risk and in low-risk, rural areas. With the 10% survival reduction per 100 meter of retrieval distance in mind, it is critical to weigh all premises in order to decide which retrieval distance – as a proxy of mortality risk – is acceptable in a given situation. For example, in a rural setting with prolonged AED retrieval distances; when should a bystander be activated by the EMDC health care professional for AED retrieval, if the alternative is to ensure high-quality CPR by taking turns in chest-compression until EMS arrival? Likewise, when utilizing the one-way travel strategy for VFRs, it is crucial to establish the optimal retrieval distance for collecting and bringing an AED to the OHCA site, instead of directing the VFR directly to the emergency site to perform early CPR. It must be emphasized that the 10% reduction per 100 meter added distance to bystander retrieval may be modified by travel speed, one-way retrieval for VFRs or two-way for bystanders, whether VFR/bystander choose the shortest walking route and EMS response times. The results of this study call for more research to establish what the optimal and acceptable distance between AEDs in high-density urban centers and low-density rural areas should be.

Limitations & strengths

This study has some limitations that must be addressed: 1) The observational nature of the data presented can be addressed only in an observational context; 2) the lack of information regarding time-to-shock. This was not possible to obtain since date and time information from the AEDs varied widely, creating too much uncertainty; 3) the number of AEDs that failed to be retrieved by the bystanders due to logistic barriers is unknown; 4) the number of used AEDs that did not reach the AED-center is also unknown. However, in the event of AED deployment, the EMDC is required to inform both the AED-centre and EMS staff to ensure transportation to the AED-centre, which should limit this issue.

So far, studies evaluating OHCA survival in relation to population density have used local, administrative unites or geographical districts (15, 16, 38, 39, 42), resulting in varying rural-urban definitions that are difficult to reproduce. A strength of this study is that population density was evaluated by using the exact number of inhabitants in each km^2 grid cell (24) using information from Statistics Denmark with specific information about number of inhabitants in each grid cell. Another strength is the prospectively collected data material and the cross-linkage of information from EMS and hospital records using each patient's personal identification number (23), which further adds to the data completeness in this study.

Conclusion

Patients with OHCA where an AED was used before EMS arrival had a favorable 30-day survival, which was comparable in densely, moderately and thinly populated areas. When evaluating the effect of AED retrieval distance on 30-day survival, we found a 10% reduction in survival per 100 meters an AED was placed further away from the OHCA site. These results call for more research regarding the potential impact of AED retrieval distance on survival after OHCA. Ultimately, it may help guide future AED placement.

1. Gräsner JT, Wnent J, Herlitz J, Perkins GD, Lefering R, Tjelmeland I, et al. Survival after out-of-hospital OHCA in Europe - Results of the EuReCa TWO study. Resuscitation. 2020;148:218-26.
2. Caffrey SL, Willoughby PJ, Pepe PE, Becker LB. Public use of automated external defibrillators. N Engl J Med. 2002;347(16):1242-7.
3. Hasselqvist-Ax I, Riva G, Herlitz J, Rosenqvist M, Hollenberg J, Nordberg P, et al. Early cardiopulmonary resuscitation in out-of-hospital OHCA. N Engl J Med. 2015;372(24):2307-15.
4. Valenzuela TD, Roe DJ, Nichol G, Clark LL, Spaite DW, Hardman RG. Outcomes of rapid defibrillation by security officers after OHCA in casinos. N Engl J Med. 2000;343(17):1206-9.
5. Shao F, Li H, Ma S, Li D, Li C. Outcomes of out-of-hospital OHCA in Beijing: a 5-year cross-sectional study. BMJ Open. 2021;11(4):e041917.
6. Sondergaard KB, Wissenberg M, Gerds TA, Rajan S, Karlsson L, Kragholm K, et al. Bystander cardiopulmonary resuscitation and long-term outcomes in out-of-hospital OHCA according to location of arrest. Eur Heart J. 2019;40(3):309-18.
7. Gnesin F, Møller AL, Mills EHA, Zylyftari N, Jensen B, Bøggild H, et al. Rapid dispatch for out-of-hospital OHCA is associated with improved survival. Resuscitation. 2021.
8. Weisfeldt ML, Sitlani CM, Ornato JP, Rea T, Aufderheide TP, Davis D, et al. Survival after application of automatic external defibrillators before arrival of the emergency medical system: evaluation in the resuscitation outcomes consortium population of 21 million. J Am Coll Cardiol. 2010;55(16):1713-20.
9. Kitamura T, Iwami T, Kawamura T, Nagao K, Tanaka H, Hiraide A. Nationwide public-access defibrillation in Japan. N Engl J Med. 2010;362(11):994-1004.
10. Perkins GD, Handley AJ, Koster RW, Castrén M, Smyth MA, Olasveengen T, et al. European Resuscitation Council Guidelines for Resuscitation 2015: Section 2. Adult basic life support and automated external defibrillation. Resuscitation. 2015;95:81-99.
11. Aufderheide T, Hazinski MF, Nichol G, Steffens SS, Buroker A, McCune R, et al. Community lay rescuer automated external defibrillation programs: key state legislative components and implementation strategies: a summary of a decade of experience for healthcare providers, policymakers, legislators, employers, and community leaders from the American Heart Association Emergency Cardiovascular Care Committee, Council on Clinical Cardiology, and Office of State Advocacy. Circulation. 2006;113(9):1260-70.
12. Chan TC, Li H, Lebovic G, Tang SK, Chan JY, Cheng HC, et al. Identifying locations for public access defibrillators using mathematical optimization. Circulation. 2013;127(17):1801-9.
13. Folke F, Lippert FK, Nielsen SL, Gislason GH, Hansen ML, Schramm TK, et al. Location of OHCA in a city center: strategic placement of automated external defibrillators in public locations. Circulation. 2009;120(6):510-7.
14. Sun CL, Demirtas D, Brooks SC, Morrison LJ, Chan TC. Overcoming Spatial and Temporal Barriers to Public Access Defibrillators Via Optimization. J Am Coll Cardiol. 2016;68(8):836-45.
15. Masterson S, Wright P, O'Donnell C, Vellinga A, Murphy AW, Hennelly D, et al. Urban and rural differences in out-of-hospital OHCA in Ireland. Resuscitation. 2015;91:42-7.
16. Nehme Z, Andrew E, Cameron PA, Bray JE, Bernard SA, Meredith IT, et al. Population density predicts outcome from out-of-hospital OHCA in Victoria, Australia. Med J Aust. 2014;200(8):471-5.
17. Stapczynski JS, Svenson JE, Stone CK. Population density, automated external defibrillator use, and survival in rural OHCA. Acad Emerg Med. 1997;4(6):552-8.
18. Tierney NJ, Reinhold HJ, Mira A, Weiser M, Burkart R, Benvenuti C, et al. Novel relocation methods for automatic external defibrillator improve out-of-hospital OHCA coverage under limited resources. Resuscitation. 2018;125:83-9.
19. Perkins GD, Jacobs IG, Nadkarni VM, Berg RA, Bhanji F, Biarent D, et al. OHCA and cardiopulmonary resuscitation outcome reports: update of the Utstein Resuscitation Registry Templates for Out-of-Hospital OHCA: 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. Circulation. 2015;132(13):1286-300.
20. Denmark S. BY3: Population 1. January by urban, rural areas and population, area and population density 2017 [Available from: https://www.statbank.dk/BY3.
21. H. C. Documentation of Statistics for Urban Areas 2020 2020 [03.05.2021]. Available from: https://www.dst.dk/Site/Dst/SingleFiles/kvaldeklbilag.aspx?filename=4bf94914-9b33-4104-83e2-0de59083f2d5Urban_Areas_2020.
22. Sarkisian L, Mickley H, Schakow H, Gerke O, Starck SM, Jensen JJ, et al. Use and coverage of automated external defibrillators according to location in out-of-hospital OHCA. Resuscitation. 2021;162:112-9.
23. Pedersen CB. The Danish Civil Registration System. Scand J Public Health. 2011;39(7 Suppl):22-5.
24. H. DLaP. Regional Working Paper 2014: "A harmonised definition of cities and rural areas: the new degree of urbanisation". 2014.
25. Hansen SM, Hansen CM, Folke F, Rajan S, Kragholm K, Ejlskov L, et al. Bystander Defibrillation for Out-of-Hospital OHCA in Public vs Residential Locations. JAMA cardiology. 2017;2(5):507-14.
26. Folke F, Gislason GH, Lippert FK, Nielsen SL, Weeke P, Hansen ML, et al. Differences between out-of-hospital OHCA in residential and public locations and implications for public-access defibrillation. Circulation. 2010;122(6):623-30.
27. Ströhle M, Paal P, Strapazzon G, Avancini G, Procter E, Brugger H. Defibrillation in rural areas. Am J Emerg Med. 2014;32(11):1408-12.
28. Chow SKY. Bystanders' Views on the Use of Automated External Defibrillators for Out-of-Hospital OHCA: Implications for Health Promotions. Int J Environ Res Public Health. 2021;18(3).
29. Sarkisian L, Mickley H, Schakow H, Gerke O, Jørgensen G, Larsen ML, et al. Global positioning system alerted volunteer first responders arrive before emergency medical services in more than four out of five emergency calls. Resuscitation. 2020;152:170-6.
30. Zijlstra JA, Stieglis R, Riedijk F, Smeekes M, van der Worp WE, Koster RW. Local lay rescuers with AEDs, alerted by text messages, contribute to early defibrillation in a Dutch out-of-hospital OHCA dispatch system. Resuscitation. 2014;85(11):1444-9.
31. Larsen MP, Eisenberg MS, Cummins RO, Hallstrom AP. Predicting survival from out-of-hospital OHCA: a graphic model. Ann Emerg Med. 1993;22(11):1652-8.
32. Takei Y, Nishi T, Kamikura T, Tanaka Y, Wato Y, Kubo M, et al. Do early emergency calls before patient collapse improve survival after out-of-hospital OHCAs? Resuscitation. 2015;88:20-7.
33. Chan PS, Krumholz HM, Nichol G, Nallamothu BK. Delayed time to defibrillation after in-hospital OHCA. N Engl J Med. 2008;358(1):9-17.
34. Auricchio A, Gianquintieri L, Burkart R, Benvenuti C, Muschietti S, Peluso S, et al. Real-life time and distance covered by lay first responders alerted by means of smartphone-application: Implications for early initiation of cardiopulmonary resuscitation and access to automatic external defibrillators. Resuscitation. 2019;141:182-7.
35. Pijls RW, Nelemans PJ, Rahel BM, Gorgels AP. A text message alert system for trained volunteers improves out-of-hospital OHCA survival. Resuscitation. 2016;105:182-7.
36. Ringh M, Rosenqvist M, Hollenberg J, Jonsson M, Fredman D, Nordberg P, et al. Mobile-phone dispatch of laypersons for CPR in out-of-hospital OHCA. N Engl J Med. 2015;372(24):2316-25.
37. Jonsson M, Berglund E, Djärv T, Nordberg P, Claesson A, Forsberg S, et al. A brisk walk-Real-life travelling speed of lay responders in out-of-hospital OHCA. Resuscitation. 2020;151:197-204.
38. Chen CC, Chen CW, Ho CK, Liu IC, Lin BC, Chan TC. Spatial Variation and Resuscitation Process Affecting Survival after Out-of-Hospital OHCAs (OHCA). PLoS One. 2015;10(12):e0144882.
39. Mathiesen WT, Bjørshol CA, Kvaløy JT, Søreide E. Effects of modifiable prehospital factors on survival after out-of-hospital OHCA in rural versus urban areas. Crit Care. 2018;22(1):99.

40. Hallstrom AP, Ornato JP, Weisfeldt M, Travers A, Christenson J, McBurnie MA, et al. Public-access defibrillation and survival after out-of-hospital OHCA. N Engl J Med. 2004;351(7):637-46.
41. Berdowski J, Berg RA, Tijssen JG, Koster RW. Global incidences of out-of-hospital OHCA and survival rates: Systematic review of 67 prospective studies. Resuscitation. 2010;81(11):1479-87.
42. Strömsöe A, Svensson L, Claesson A, Lindkvist J, Lundström A, Herlitz J. Association between population density and reported incidence, characteristics and outcome after out-of-hospital OHCA in Sweden. Resuscitation. 2011;82(10):1307-13.

Table 1: Demographic and prognostic results with inter-group comparisons

	Population density at cardiac arrest site					
	A) Densely populated (N=207)	B) Moderately populated (N=78)	C) Thinly populated (N=138)	**A vs. B P value**	**B vs. C P value**	**A vs. C P value**
Age, year, mean (SD)	66 (14)	68 (14)	66 (11)	0.5[1]	0.3[1]	0.6[1]
Male sex, % (n/valid cases)	78 (151/194)	77 (59/77)	83 (102/123)	0.8[2]	0.3[2]	0.3[2]
Comorbidity, % (n/valid cases)						
- Known ischemic heart disease	24 (41/172)	20 (14/70)	23 (23/101)	0.5[2]	0.7[2]	0.8[2]
- Congestive heart failure	16 (28/174)	7 (5/70)	12 (12/101)	0.06[2]	0.3[2]	0.3[2]
- Prior stroke	10 (18/175)	11 (8/70)	7 (7/100)	0.8[2]	0.3[2]	0.4[2]
- Diabetes	18 (31/175)	19 (13/70)	20 (20/101)	0.9[2]	0.8[2]	0.7[2]
- COPD	15 (27/175)	24 (17/70)	6 (6/101)	0.1[2]	**0.001[2]**	**0.02[2]**
- Malignancy	7 (12/175)	9 (6/70)	8 (8/100)	0.6[2]	0.9[2]	0.7[2]

Cause of cardiac arrest, % (n/valid cases)						
- Cardiac[a]	83 (146/176)	83 (53/64)	86 (103/120)	0.9[2]	0.6[2]	0.5[2]
- Non-cardiac	10 (18/176)	17 (11/64)	6 (7/120)	0.1[2]	**0.01[2]**	0.2[2]
- Trauma/suicide/accident	7 (12/176)	0 (0/64)	8 (10/120)	**0.03[3]**	**0.02[3]**	0.6[2]
Time of day, % (n/valid cases)						
- Day (8 am to 3.59 pm)	63 (127/202)	65 (48/74)	59 (78/132)	0.8[2]	0.4[2]	0.5[2]
- Evening (4 pm to 11.5 pm)	28 (56/202)	27 (20/74)	30 (39/132)	0.9[2]	0.7[2]	0.7[2]
- Night (12 pm to 7.59 am)	9 (19/202)	8 (6/74)	11 (15/132)	0.7[2]	0.5[2]	0.6[2]
Bystander witnessed, % (n/valid cases)	71 (143/202)	71 (53/75)	66 (84/128)	0.9[2]	0.5[2]	0.3[2]
Bystander CPR, % (n/valid cases)	99 (202/205)	100 (77/77)	100 (132/132)	0.3[3]	0.9[3]	0.2[3]
AED with shockable first rhythm, % (n/valid cases)	59 (110/186)	46 (29/63)	55 (69/125)	0.07[2]	0.2[2]	0.5[2]
Bystander defibrillation, % (n/valid cases)	56 (104/186)	49 (31/63)	59 (72/122)	0.4[2]	0.2[2]	0.6[2]
Bystander defibrillation and ROSC before EMS arrival, % (n/valid cases)	24 (47/197)	16 (12/76)	22 (29/130)	0.1[2]	0.3[2]	0.7[2]

AED registered at AED-network, % (n/valid cases)	75 (154/205)	81 (62/77)	74 (101/137)	0.3[2]	0.3[2]	0.8[2]
- Available 24/7	67 (103/154)	85 (53/62)	77 (78/101)	**0.006[2]**	0.2·	0.08[2]
No. of AEDs in grid cell of cardiac arrest, median (IQR)	3.5 (2.0-7.5)	1.0 (1.0-2.0)	0.0 (0.0-1.0)	**0.0001[4]**	**0.0001[4]**	**0.0001[4]**
AED one-way retrieval distance one-way, median (IQR)	105 (5-450)	220 (5-450)	350 (5-1500)	0.1[4]	**0.04[4]**	**0.0001[4]**
EMS response time, minutes, median (IQR)	8 (5-12)	11 (8-14)	12 (8-15)	**0.0001[4]**	0.5[4]	**0.0001[4]**
Location of cardiac arrest, % (n/valid cases)						
– Residential area	36 (71/199)	48 (37/77)	50 (62/125)	0.06[2]	0.8[2]	**0.01[2]**
– Public place	34 (67/199)	32 (25/77)	24 (30/125)	0.8[2]	0.2[2]	0.06[2]
– Mixed group[b]	31 (61/199)	19 (15/77)	26 (33/125)	0.06[2]	0.3[2]	0.4[2]
ROSC at hospital arrival, % (n/valid cases)	50 (102/203)	43 (33/77)	36 (47/130)	0.3[2]	0.3[2]	**0.01[2]**
30-day survival, % (n/valid cases)	40 (82/203)	31 (24/77)	34 (44/128)	0.2[2]	0.6[2]	0.3[2]
Cerebral Performance Category Score 1-2 at discharge, % (n/valid cases)	98 (79/81)	100 (23/23)	98 (44/45)	0.9[3]	0.5[3]	0.9[3]

[1]Student's t-test. [2]Pearson's chi-square test. [3]Fisher's exact test. [4]Non-parametric Wilcoxon signed-rank test. [a] Includes OHCAs with presumed, confirmed and unknown cause of cardiac arrest. [b]Mixed group: Company/workplace, institutions, health clinic and sports facility/recreational. AED: Automated external defibrillator. COPD: Chronic obstructive

pulmonary disease. CPR: Cardiopulmonary resuscitation. EMS: Emergency medical services. IQR: Interquartile ranges. OHCA: Out-of-hospital cardiac arrest. ROSC: Return of spontaneous circulation. SD: Standard deviation.

Table 2: Multivariable logistic regression of 30-day survival after the index OHCA event on AED retrieval distance and other prognostic factors

	Odds Ratio	95% CI	P value
AED retrieval distance	1.0010	1.0004-1.0016	**0.001**
Age	1.070	1.034-1.11	**<0.001**
Male sex	0.82	0.30-2.25	0.7
Cardiac cause of arrest	0.48	0.10-2.27	0.4
Bystander witnessed	0.16	0.05-0.58	**0.005**
Shockable first rhythm	0.06	0.02-0.19	**<0.001**
EMS response time	1.065	0.99-1.15	0.09
Time of day			
- Day (8 am to 3.59 pm)	1	-	-
- Evening (4 pm to 11.5 pm)	1.41	0.61-3.27	0.4
- Night (12 pm to 7.59 am)	2.15	0.54-8.49	0.3

AED: Automated external defibrillator. CI: Confidence interval. EMS: Emergency medical service.

OHCA: Out-of-hospital cardiac arrest.

Figure 1. Flow-chart showing the inclusion-exclusion

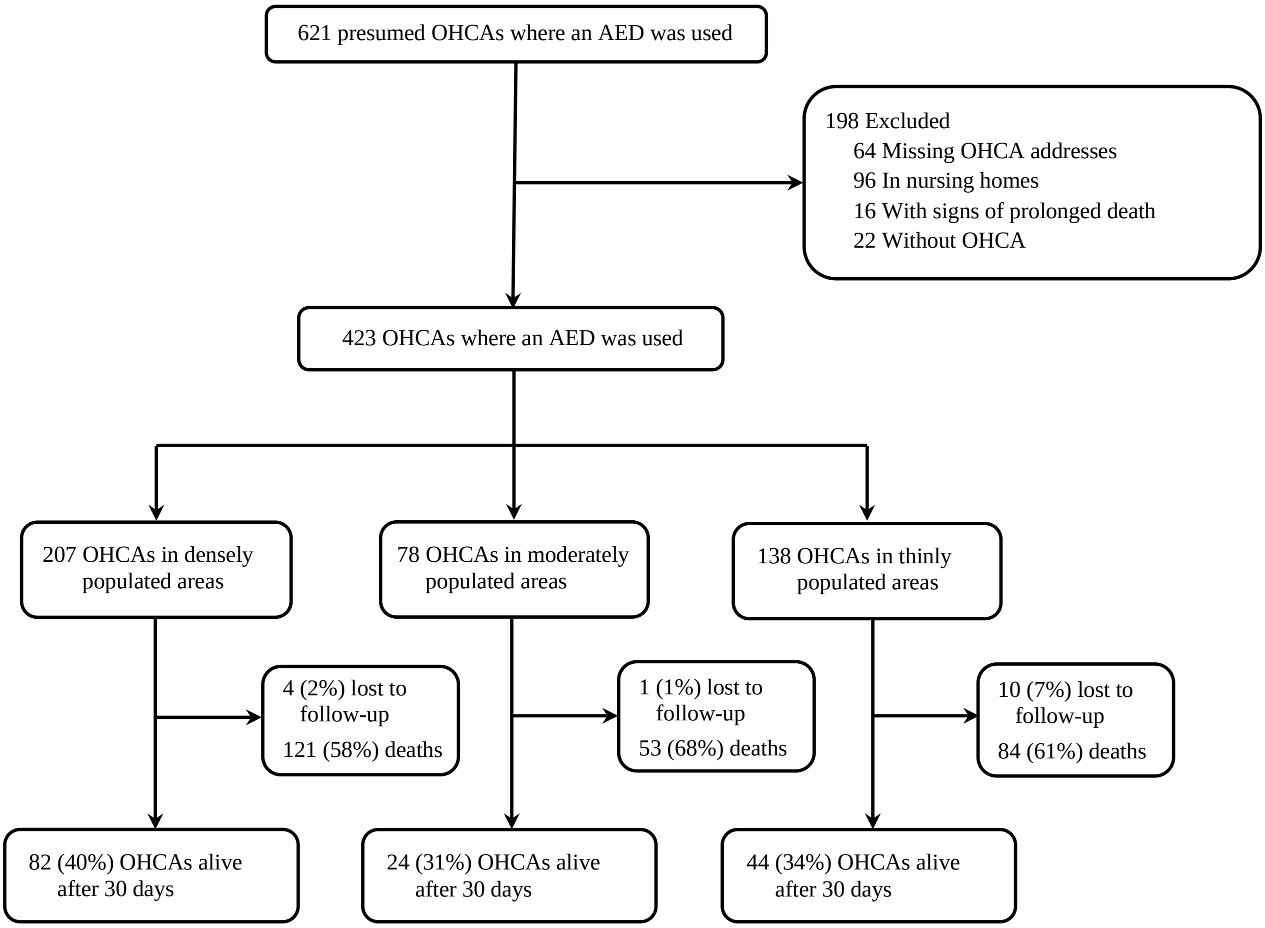


Figure 2. The four figures showing the distribution of four different variables, from on-site AED use (0-5 meters) to >500 meters AED retrieval distance.

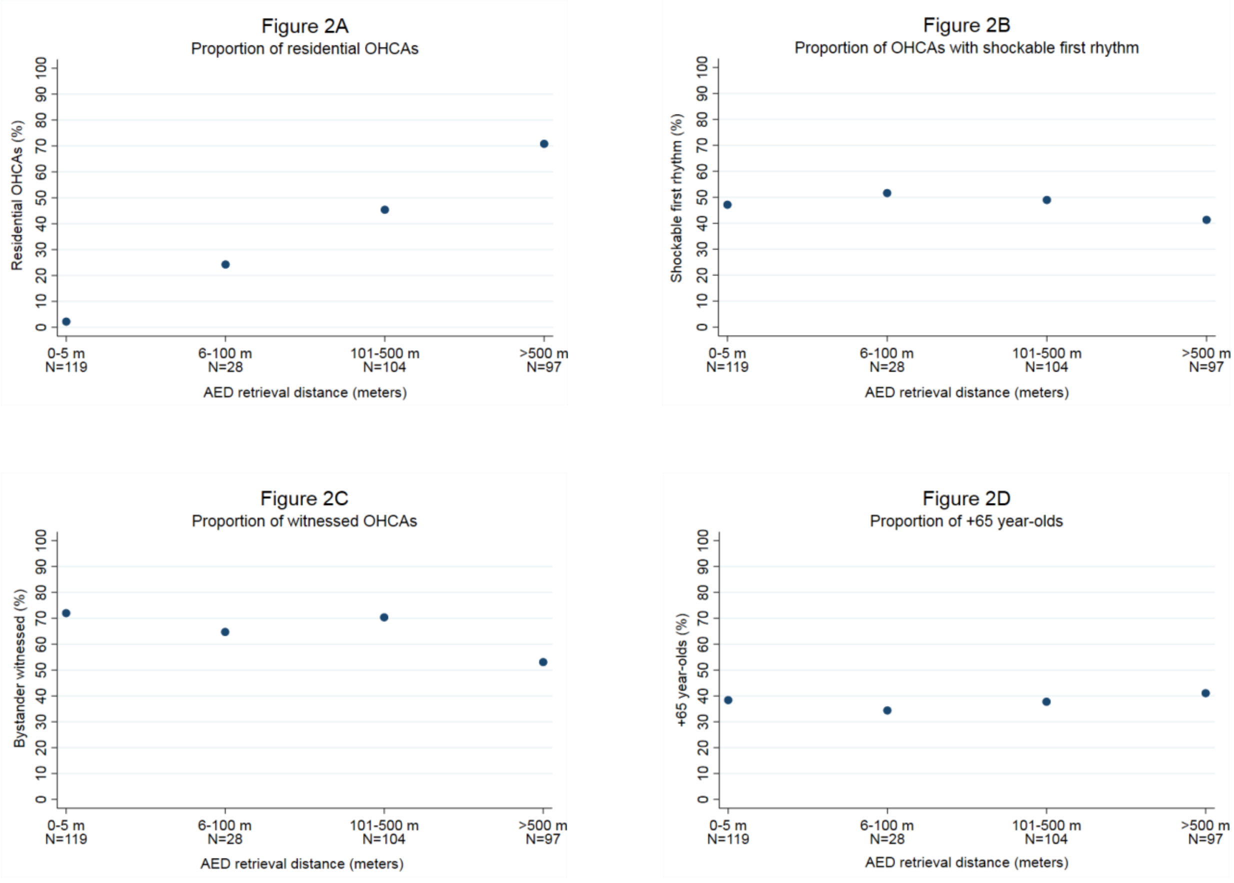
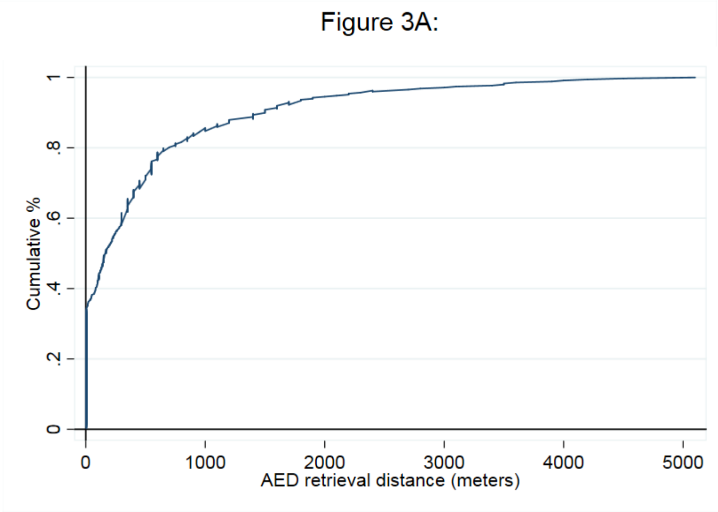


Figure 3. 3A shows the cumulative distribution of AED retrieval distance, and 3B shows the cumulative distribution of AED retrieval distance according to population density.



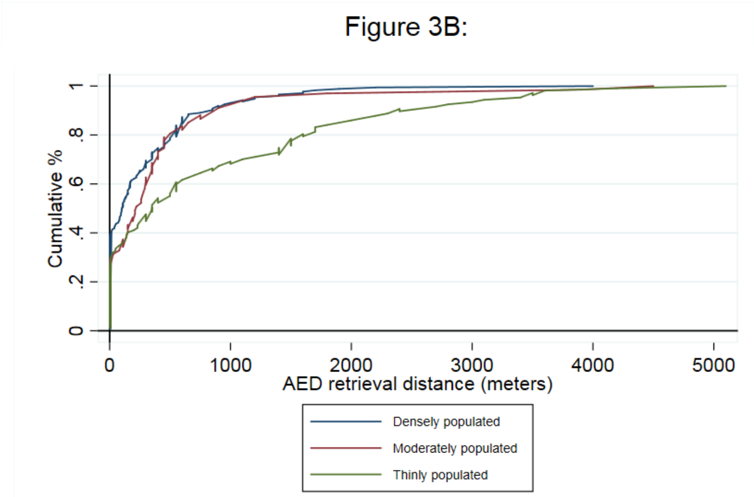


Figure 4 shows the proportion of OHCAs that had ROSC at hospital arrival and were alive after 30 days in relation to the AED retrieval distance.

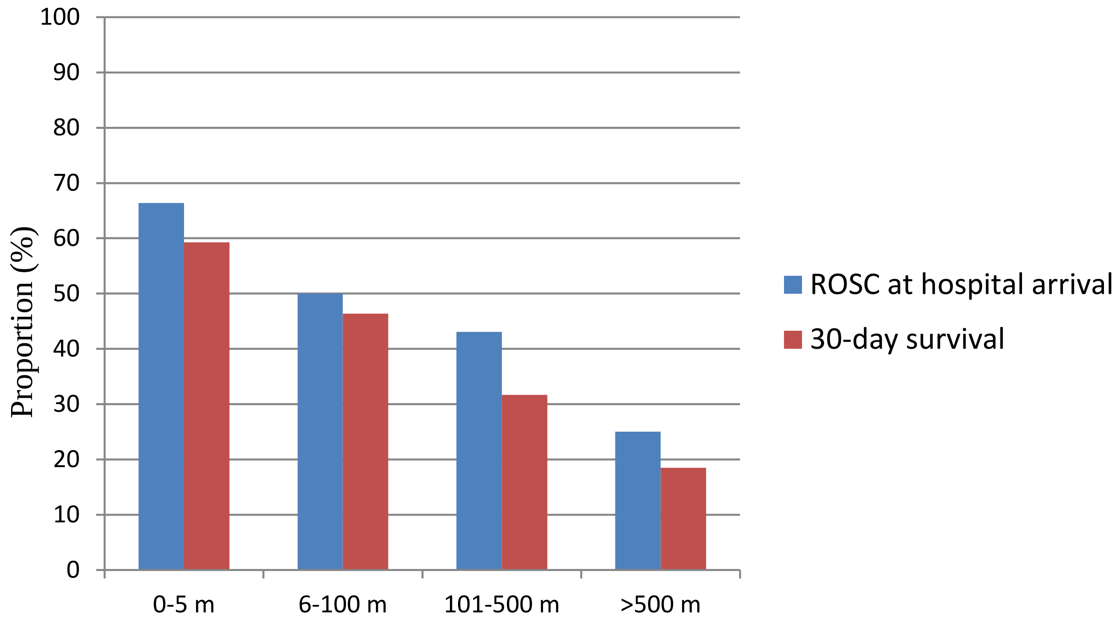


Table S1 (Supplement): Multivariable logistic regression of 30-day survival after the index OHCA event on AED retrieval distance and other prognostic factors, full model (i.e. before backward variable selection)

	Odds Ratio	95% CI	P value
AED retrieval distance	1.0016	1.00074-1.0025	**<0.001**
Age	1.096	1.052-1.14	**<0.001**
Male sex	0.99	0.33-2.93	0.9
Cardiac cause of arrest	0.67	0.12-3.61	0.6
Bystander witnessed cardiac arrest	0.17	0.040-0.70	**0.01**
Public place of arrest	1.26	0.41-3.86	0.7
Shockable first rhythm	0.02	0.0013-0.35	**0.007**
Bystander defibrillation before EMS arrival	1.54	1.13-18.00	0.7
Time of day			
- Day (8 am to 3.59 pm)	1	-	-
- Evening (4 pm to 11.5 pm)	1.62	0.62-4.21	0.3
- Night (12 pm to 7.59 am)	2.95	0.67-13.00	0.2
Population density			
- Densely populated (≥200 inhabitant per km^2)	1	-	-
- Moderately populated (20-199 inhabitants per km^2)	2.32	0.75-7.19	0.1
- Thinly populated (0-19 inhabitants per km^2)	0.36	0.12-1.12	0.08
EMS response time	1.074	0.99-1.17	0.1

AED: Automated external defibrillator. CI: Confidence interval. EMS: Emergency medical service. OHCA: Out-of-hospital cardiac arrest.