Available online at www.sciencedirect.com

Resuscitation

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

Clinical paper

The contribution of comorbidity and medication use to poor outcome from out-of-hospital cardiac arrest at home locations

Michiel Hulleman [a,*,1], Iris Oving [a,1], Paulien C.M. Homma [a], Stefanie G. Beesems [a], Hanno L. Tan [b], Rudolph W. Koster [a], Marieke T. Blom [a]

[a] Department of Clinical and Experimental Cardiology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands
[b] Netherlands Heart Institute, Utrecht, The Netherlands

Abstract

Introduction: Out-of-hospital cardiac arrest (OHCA) at home is associated with lower rates of shockable initial rhythm and survival than OHCA in a public location. We determined whether medical history and medication use explain the association between OHCA location and presence of shockable initial rhythm and survival rate.

Methods: Data from ARREST, an OHCA registry in the Netherlands, were used (January 2009–December 2012). We assessed if OHCA location remained associated with a) presence of shockable initial rhythm and b) survival when taking medical history, medication use, resuscitation characteristics and demographics into account in a multivariable regression analysis. The relative contributions of the above mentioned variables to variance in both outcome measures was estimated using the Nagelkerke test.

Results: We included 1404 patients (1034 [73.6%] home OHCA, 370 [26.4%] public OHCA). OHCA location remained significantly associated with shockable initial rhythm (home 42.7%, public 78.1%; $P < 0.01$) and survival to hospital discharge (home 14.0%, public 45.7%; $P < 0.01$). Adding resuscitation characteristics to models of shockable initial rhythm and survival rate resulted in an increase in explained variance (13.0%–23.6%), whereas adding medical history or medication use to these models resulted in only a limited increase in explained variance (medical history to 27.6%, medication use to 30.0%).

Conclusions: Comorbidity and medication use do not substantially contribute in explaining the poor outcome from out-of-hospital cardiac arrest occurring at home. Even when adjusted for medical history, medication use, resuscitation characteristics, and demographics, a large gap of unexplained variance in shockable initial rhythm and survival remains.

Keywords: Out-of-hospital, cardiac arrest, location, shockable rhythm, survival

Introduction

Approximately 70% of out-of-hospital cardiac arrests (OHCAs) occur at home[1,2] and survival rates after OHCA occurring at home are significantly lower than after OHCA occurring in public places.[2,3]

OHCA at home is known to be associated with a lower proportion of a witnessed arrest, bystander cardiopulmonary resuscitation (CPR), and automatic external defibrillator (AED) use. These resuscitation characteristics are considered to be the main explanation for the observed lower proportion of shockable initial rhythm and consequently a lower survival rate from OHCA occurring at home;[3–6] However, it has been suggested that patient factors may also play a role: OHCA patients at home are generally older, use more medication and have a higher disease burden when compared to patients with OHCA occurring in a public place.[4,7] Differences in shockable initial

* Corresponding author at: Department of Cardiology, Heart Center, Amsterdam UMC, University of Amsterdam, Meibergdreef 15, 1105 AZ Amsterdam, The Netherlands.
E-mail address: m.hulleman@amsterdamumc.nl (M. Hulleman).
[1] authors contributed equally.

https://doi.org/10.1016/j.resuscitation.2020.03.011
Received 14 November 2019; Received in revised form 26 February 2020; Accepted 18 March 2020

rhythm and survival between OHCA patients at home and OHCA patients in a public place might therefore also be explained by differences in prevalence of pre-existing disease or medication use.[3,8]

In the present study, differences in medical history, medication use and resuscitation characteristics between OHCA patients at home and in public were assessed in order to identify the relative contribution of these patient factors to the presence of shockable initial rhythm and survival rate.

Methods

Study, setting and patient selection

The study setting, described previously[9–11], was a population based cohort-study of patients in whom Emergency Medical Services (EMS) personnel attempted resuscitation during OHCA, in the study period January 2006–December 2012. OHCA cases were identified using data from the AmsteRdam REscustation STudies (ARREST), an on-going prospective community-based registry of all EMS-treated resuscitation attempts after OHCA since July 2005 in the study region. ARREST was set up in cooperation with all EMS in the study region to establish the determinants of occurrence and outcome of OHCA in the general population.

Cases with a clear non-cardiac cause according to the Utstein recommendations,[12] a “do not resuscitate” certificate, cases with signs of prolonged death, and EMS-witnessed cases were excluded from analysis. Moreover, we excluded cases with an incomplete medical or medication history, as well as surviving patients who did not consent to their data being used. Written informed consent was obtained from all participants who survived the OHCA. The Medical Ethics Review Board of the Academic Medical Center, Amsterdam, approved the study, including the use of data from patients who did not survive the OHCA.[13]

Data collection and definitions

Data collection was described previously.[9,14] Initial rhythm of the patient was categorized as[1] shockable (ventricular tachycardia (VT)/ ventricular fibrillation (VF)) or[2] non-shockable (asystole or pulseless electrical activity). Survival after OHCA was defined as survival to hospital discharge. Survival with neurologic favourable outcome was defined as having Cerebral Performance Category (CPC) score of 1 or 2 at hospital discharge. Location of collapse was classified based on the street address of collapse and retrieved from EMS dispatch form. Long term care facilities were classified as OHCA at home. All other non-home addresses were considered a public place. Resuscitation characteristics included in the present study were: presence/absence of witness, bystander CPR, AED connection, time of the day (8:00–15:59, 16:00–23:59, 24:00–07:59), and time from call-to-first ECG (from manual defibrillator or AED).

Medical history was derived by contacting the patient’s general practitioner (GP). In the Netherlands, every person has one single GP, and for non-life threatening medical problems the GP needs to be visited before seeking help from a medical specialist. If a patient is discharged from the hospital or visits a medical specialist, a discharge letter is sent to the GP, who is therefore aware of all medical history of the patient and records it in the patient’s records. The questionnaire is completed using the GP patient’s charts on the discretion of the GP. Included diseases on the questionnaire are described in supplementary data. Medication use was derived from drug dispensing records of the patient’s pharmacy, and were classified according to the Anatomical Therapeutic Chemical (ATC) code of the World Health Organization (WHO). Medication use was defined as a dispensing record in the six months preceding OHCA. The following ATC codes (main groups) were included in this study: A:Gastro-intestinal, B:Blood, C:Cardiac, H:Hormones, J:Anti-infectives, L:Oncolytics, N:Nervous system and R:Respiratory system.

Data analyses

Differences between OHCA patients at home and in public places were described using conventional descriptive statistics, reported as mean (Standard Deviation (SD)), median (interquartile range (IQR)), or number (N, %). Analyses were performed in complete cases (without any missing values on covariates).

First, we assessed whether the association between location of OHCA and a) the presence of a shockable initial rhythm and b) survival to hospital discharge was explained by demographics, resuscitation characteristics, medical history and medication use in a multivariable logistic regression analysis. Second, we estimated the relative contribution of the above mentioned variables to a) the presence of a shockable initial rhythm and b) survival to hospital discharge by determining the increase in explained variance (Nagelkerke test) while adding these variables to the model.

Analyses were performed in all patients, stratified according to sex, and according to shockable inital rhythm.

Long-term care facilities are often equipped with nurses and other staff with medical training (including training in resuscitation). Therefore, long-term care facilities may have other characteristics than regular homes. A sensitivity analysis was performed by excluding patients living in long-term care facilities in order to compare results.

All statistical tests were two-tailed, and a P of <0.05 was considered to be statistically significant. Statistics were performed in SPSS 24.0 for Mac, Chicago IL, USA.

Results

Complete medical history and medication use without missing data on covariates was available for 1404 OHCA patients (Fig. 1). Of these, 1034 patients (73.6%) had OHCA occurring at home and 370 patients (26.4%) had OHCA occurring at a public location. A shockable initial rhythm was less prevalent in patients with OHCA at home (42.7% vs. 78.1%, $P<0.01$), and survival to hospital discharge was lower (14.0% vs. 45.7%; $P<0.01$) (Table 1). Among patients surviving to hospital discharge, the percentage of neurologic favourable outcome was comparable between OHCA at home and in public. A missing case analysis is provided in eTable 1(Supplimentary material).

Differences between OHCAs at home and in public locations

OHCA patients at home were older, less often male and had less favorable resuscitation characteristics: less often a witnessed collapse and provision of bystander CPR, longer time from EMS call to defibrillator connection, and lower proportion of AED deployment (Table 1). OHCA patients at home were more often diagnosed with the following diseases: heart failure ($P<0.01$), diabetes type II ($P=0.03$), Stroke/TIA ($P=0.03$), depression ($P=0.02$), COPD ($P<0.01$) and

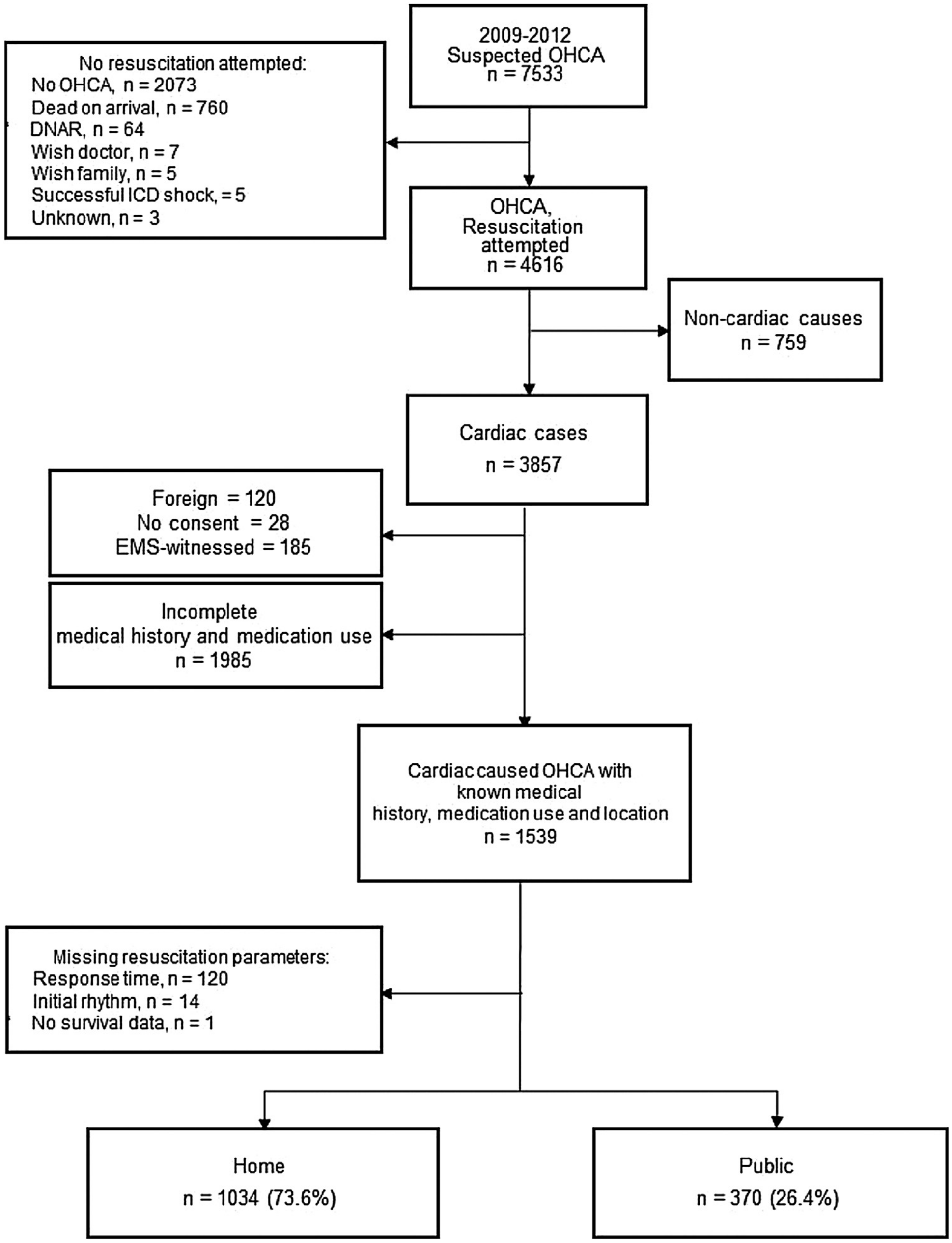

Fig. 1 – Patient inclusion, 2009−2012.
Abbreviations: DNAR, do not attempt to resuscitate; EMS, Emergency Medical Services; ICD, implantable cardioverter defibrillator; OHCA, out-of-hospital cardiac arrest.

renal dysfunction ($P = 0.04$) (Table 1). Also, patients at home used all studied ATC medication groups more often (all $P < 0.05$; Table 1).

Differences between patients with shockable and non-shockable initial rhythm are shown in eTable 2.

Location of OHCA in relation to presence of shockable initial rhythm and survival

When adjusted for resuscitation characteristics, sex, age and medical history or medication use, the location of collapse was still significantly associated with presence of shockable initial rhythm ($P < 0.001$) (Fig. 2A) and survival to hospital discharge ($P < 0.001$) (Fig. 2B).

Location of collapse explained 13.0% of the variance in shockable initial rhythm. Adding resuscitation characteristics to the model resulted in an increase in explained variance from 13.0%−23.6%. Adding age and sex to this model increased explained variance to 26.2%. Finally, adding medical history or medication use resulted in a limited additional increase in explained variance (medical history to 27.6%, medication use to 30.0%) (Fig. 2A).

For both men and women, location of collapse remained independently associated with a lower proportion of shockable initial rhythm, although in women adjustment for resuscitation characteristics, medical history and medication use did not increase explained variance as much as in men (P for interaction 0.04; Fig. 3).

Table 1 – Patient and resuscitation characteristics by location of collapse.

	Home n = 1034	Public n = 370	*P*
Demographics			
Mean age ± SD, years	69.2 ± 14.0	64.4 ± 14.9	<0.01
Male sex†	762 (68.1)	359 (85.5)	<0.01
Resuscitation characteristics			
Initial shockable rhythm†	44.2 (42.7)	289 (78.1)	<0.01
Bystander CPR†	723 (69.9)	322 (87.0)	<0.01
Witnessed collapse†	719 (69.5)	309 (83.5)	<0.01
General practitioner	37 (5.1)	13 (4.2)	
Spouse	421 (58.6)	37 (12.0)	
Other bystanders	261 (36.3)	259 (83.8)	
AED connected†	403 (39.0)	216 (58.4)	<0.01
Time from call to initial rhythm‡	9.4 (7.2–12.1)	7.3 (5.0–9.9)	<0.01
Survived to discharge†	145 (14.0)	169 (45.7)	<0.01
Medical history (n)			
Myocardial infaction† (322)	240 (23.2)	82 (22.2)	0.68
Atrial fibrillation† (238)	177 (17.1)	61 (16.5)	0.78
Valvular pathology† (22)	13 (1.3)	9 (2.4)	0.10
Hypercholesteremia† (418)	288 (27.9)	130 (35.1)	<0.01
Cardiomyopathy† (105)	77 (7.4)	28 (7.6)	0.94
Hypertension† (661)	496 (48.0)	165 (44.6)	0.27
Heart failure† (281)	226 (21.9)	55 (14.9)	<0.01
Diabetes I† (7)	5 (0.5)	2 (0.5)	0.89
Diabetes II† (290)	224 (21.7)	66 (17.8)	0.03
Stroke/TIA† (179)	144 (13.9)	35 (9.5)	0.03
Depression† (120)	99 (9.6)	21 (5.7)	0.02
Asthma† (53)	37 (3.6)	16 (4.3)	0.52
COPD† (198)	167 (16.2)	31 (8.4)	<0.01
Cancer† (239)	188 (18.2)	51 (13.8)	0.05
Liver dysfunction† (42)	31 (3.0)	11 (3.0)	0.98
Rheumatic disease† (65)	51 (4.9)	14 (3.8)	0.37
Renal dysfunction† (142)	115 (11.1)	27 (7.3)	0.04
Medication use by ATC classification (n)			
A: Gastro-intestinal† (626)	486 (47.0)	140 (37.8)	<0.01
B: Blood† (614)	472 (45.6)	142 (38.4)	0.02
C: Cardiac† (857)	654 (63.2)	203 (54.9)	0.01
H: Hormones† (146)	128 (12.4)	18 (4.9)	<0.01
J: Anti-infectives† (283)	236 (22.8)	58 (13.1)	<0.01
L: Oncolytics† (51)	45 (4.4)	6 (1.6)	0.02
N: Nervous system† (409)	346 (33.5)	63 (17.0)	<0.01
R: Respiratory system† (1013)	766 (74.1)	247 (66.8)	0.01

*Data are N (%) unless indicated otherwise; †Differences tested using Chi-square statistic. ‡Time intervals are presented in median in minutes (25th to 75th percentile), differences tested using Mann-Whitney *U* test
**Abbreviations AED, automated external defibrillator; ATC, Anatomical Therapeutic Chemical; COPD, Chronic obstructive pulmonary disease; CPR, cardiopulmonary resuscitation; CPR, cardiopulmonary resuscitation; SD, standard deviation; TIA, Transient Ischemic Attack.

Location of collapse alone explained 14.9% of the variance in survival to hospital discharge. Adding resuscitation characteristics to the model resulted in an increase in explained variance from 14.9% to 43.5%. Adding age and sex to this model, the explained variance increased to 48.2%. Finally, adding medical history or medication use to the models resulted in a limited increase in explained variance (medical history to 48.2%, medication use to 49.2%) (Fig. 2B).

When medical history or medication use were added to the model while resuscitation characteristics were left out, again only a limited increase in explained variance was observed for both initial rhythm (medical history 15.2%, medication use 18.2%) and survival to hospital discharge (medical history 17.2%, medication use 18.8%, eFig. 1 in Supplimentary material).

After selecting patients with a shockable initial rhythm, adding medical history or medication use to the models resulted in a similar limited increase in explained variance of survival to hospital discharge (eFig. 2 in Supplimentary material). Stratified analyses for sex were not performed, as there was no significant interaction between location and sex and survival (*P* for interaction 0.53).

Finally, when excluding long-term care patients from the analyses, similar results were observed (eTable 3, eFig. 3 in Supplimentary material).

Discussion

Main findings

Patients experiencing an OHCA at home had a larger disease burden, used more medication, were older, more often female and had less

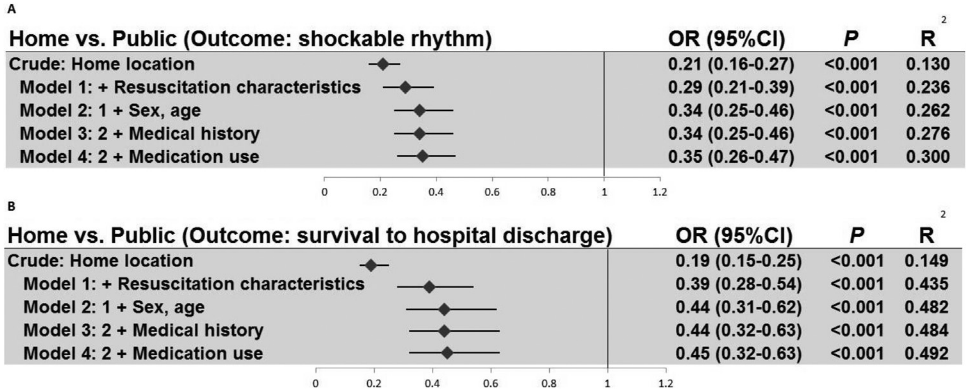

Fig. 2 – Association of location of collapse (Home vs. Public location), adjusted for resuscitation characteristics, age, sex and medical history or medication use with shockable initial rhythm and survival to hospital discharge, including explained variance of the models.
Abbreviations: AED, automated external defibrillator; CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest.
A Variables contributing to presence of shockable rhythm
B Variables contributing to survival to hospital discharge after OHCA
Crude: Home location; Model 1: location, resuscitation characteristics (Panel A: initial rhythm was not included); Model 2: location, resuscitation characteristics, age, sex; Model 3: location, resuscitation characteristics, age, sex, medical history; Model 4: location, resuscitation characteristics, age, sex, medication use.

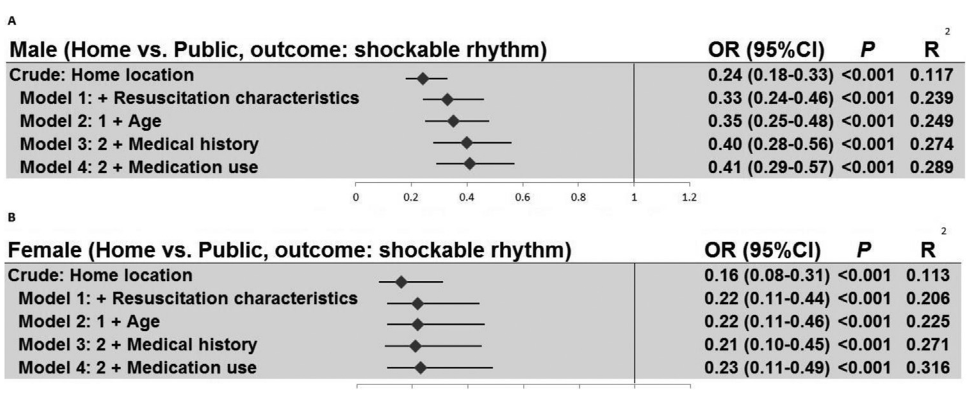

Fig. 3 – Figure 3: Association of location of collapse (Home vs. Public location), adjusted for resuscitation characteristics, age and medical history or medication use with shockable initial rhythm, stratified by sex, including explained variance of the models.
Abbreviations: AED, automated external defibrillator; CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest.
A Males
B Females
Crude: Home location; Model 1: location, resuscitation characteristics (initial rhythm was not included);
Model 2: location, resuscitation characteristics, age; Model 3: location, resuscitation characteristics, medical history; Model 4: location, resuscitation characteristics, medication use.

favorable resuscitation characteristics. However, these factors together explained less than 50% of the variance in the lower proportion of shockable initial rhythm and survival rate. Moreover, medical history and medication use only contributed slightly to explaining the differences in proportion of shockable initial rhythm or survival rate between OHCAs at home and public. Resuscitation characteristics remain the main predictor of outcome, for both OHCA at home and in public, but a large gap of unexplained variance in shockable initial rhythm and OHCA survival remains.

Comparison with previous literature

Multiple studies (as early as in 1987) implied that patients at home differ from patients having OHCA in public places, and that this might explain the differences in outcome from OHCA compared to patients collapsing in public places.[1,2,7,15–19] These studies suggested that patients at home might be older and have more comorbidities that limit participation in outside acitivities; OHCA at home might therefore only be a proxy for higher age and combordity.[16] Although often suggested, few studies actually investigated comorbidities and medication use according to location of collapse and the relation with initial rhythm and survival.[4] In the present study, we confimed the observations from a Danish group that location of OHCA, when corrected for chronic disease and medication, remained an independent predictor of the presence of a non-shockable rhythm and worse survival from OHCA.[4] However, this study did not quantify how much of the association between OHCA at home and non-shockable rhythm could be attributed to chronic disease and medication use. The novelty of the present study is the quantification of the contribution of medical history and medication use to this association. We observed that adding medical history and medication use to the regression models has only limited effect on the explained variance in initial shockable rhythm and survival.

Treatment of OHCAs at home and resuscitation characteristics Being witnessed at the time of collapse is extremely important. Patients with OHCA at home are less likely to be witnessed, causing a delay in resuscitation measures resulting in lower rates of shockable initial rhythm and survival.[3,4] Accordingly, as OHCA patients at home differ unfavourably from OHCA patients in public locations, the question has been raised whether early defibrillation initiatives are worthwhile for OHCA patients at home.[3,20,21] In the Home Automated External Defibrillator Trial it was tested whether placing an AED in the home of patients at risk of sudden cardiac death (SCD) would improve survival.[22] No favourable effect of such placement was found, partly caused by the lower than expected risk of SCD of less than 1% per year which left the study underpowered. Furthermore, almost half of the resuscitated patients were admitted to a hospital or long term care facility at the time of the cardiac arrest, and unwitnessed arrest occurred frequently. In both cases, no benefit from an home AED could therefore be expected.

In recent years, citizen rescuer systems have been developed in several countries.[23–26] These systems do not aim to identify a high risk population (as in the Home AED Trial), but aim to reach all patients, by dispatching trained volunteers in the vicinity of the victim either to the OHCA location to perform BLS or to collect a nearby AED. Citizen rescuers systems have the benefit that they can reach patients at home as easily as patients in a public setting. Still, few AEDs are available in home areas, where the majority of OHCA occurs. The present study confirms that also in OHCAs at home resuscitation characteristics remain the most important predictors of initial rhythm and outcome, even though patients at home are older and have higher disease burden. It shows that the largest increase in explained variance is caused by adding resuscitation characteristics to the model, and not by adding medical history or medication use. This suggests that improving pre-hospital response by organizing a rapid first response system in residential areas would be of benefit to OHCA victims at home.

Unexplained variance: missing factors?

Only approximately one third of the variance in presence of shockable initial rhythm and half or the variance in survival could be explained in the fully adjusted model (including medication use, medical history and resuscitation characteristics). Although resuscitation characteristics are of primary importance in OHCAs at both home and public locations, there must be missing factors that explain the remaining variance.

An unknown factor in resuscitation research is what happens before first contact with EMS. The delay from collapse to EMS-call is not recorded, nor the quality of bystander CPR; these factors might be different at home compared to public locations. The average age of patients at home was 69 years, and the witness of the OHCA at home (and the person that performed CPR) is often the spouse of a similar age.[27] It could be that quality of CPR by a spouse is lower than that provided by a presumably younger person in public. Late recognized OHCA, delayed EMS-call or late start of bystander CPR (of uncertain quality) decrease the chance of a registered shockable rhythm or survival, but such factors could not be included in our models.

Furthermore, sex differences shown in the present study might also be part of the unexplained variance. For women, the effect of adding resuscitation characteristics, medical history and medication use to the models was less pronounced than for men, and the independent effect of location of collapse was larger. Multiple studies show that women who experience an OHCA are more likely to have unfavourable resuscitation characteristics and have associated lower survival rates.[28–32]

Implications from the present study

We aimed to construct a comprehensive picture of the outcome differences in OHCA patients at home and in a public location, taking resuscitation and patient characteristics into account.

The results of this study provide a lead in the development of treatment strategies aimed at reducing the survival gap between OHCA at home and OHCA in a public location. We established that resuscitation characteristics remain the main predictor of outcome at home, even though patients at home are generally older and have on average higher disease burden. If delay between OHCA and defibrillator connection is short, shockable initial rhythm is still observed in a large proportion of OHCA patients at home. Thus, results from this study provide the incentive for an adequate organization of first response resuscitation care, e.g., development of systems facilitating early defibrillation for OHCAs occurring in a residential setting. Moreover, the suggestion that there are factors currently unidentified that contribute to outcome differences between OHCAs at home and in public places, shows the need for future research.

Strengths and limitations

One of the strengths of the present study is the completeness of data from EMS-dispatch center, paramedics, hospital, general practitioner, and pharmacy. This provides a comprehensive picture of the circumstances and outcome of the OHCA, both from surviving and non-surviving patients. By using data from GPs, we were able to collect information regarding pre–OHCA morbidity for all patients included in the study. We also collected complete medication dispensing records for all patients included in the study, providing a reliable insight in the medication use.

A number of important limitations need to be considered. First, to identify the patients' comorbidity, we gathered data using a questionnaire completed by the GP. In this questionnaire, the GP was limited to provide information on the diseases that were included in the questionnaire. Other diseases could be present that were not included in the questionnaire, thereby underestimating the disease burden. Second, we also did not determine the severity of the different medical conditions, but treated these as binary variables. This might have caused under- or overestimation of total disease burden, although previous studies showed inconclusive results with regard to the association between disease severity and initial rhythm or outcome.[33–35] Thirdly, we stratified the data to home or public, ignoring the difference between the patients' home residence and someone else's home. The latter may be associated with unfavourable resuscitation characteristics or worse outcome to a lesser extent. However, combining residency with other homes might skew the data towards more favourable resuscitation characteristics. Finally, our missing case analysis showed that missing cases had a lower survival and shockable initial rhythm rate compared to complete cases. This should be taken into account while interpreting the results. We assume however that our primary conclusions (limited contribution of medical history and medication use to explaining variance in initial rhythm and survival) would not have changed if missing cases were included.

Conclusion

Comorbidity and medication use do not substantially contribute in explaining the poor outcome from out-of-hospital cardiac arrest occurring at home. Even when adjusted for medical history, medication use, resuscitation characteristics, and demographics, a large gap of unexplained variance remains. Both medical history and medication use only explain a modest proportion of the variance of shockable initial rhythm and survival.

Conflict of interest

None declared.

Grantsupport

This work has received funding from the European Union's Horizon 2020 research and innovation programme under acronym ESCAPE-NET (IO, MTB, HLT, PCMH), registered under grant agreement No 733,381), and the Netherlands CardioVascular Research Initiative (Dutch Heart Foundation, Dutch Federation of University Medical Centers, Netherlands Organization for Health Research and Development, and Royal Netherlands Academy of Sciences) grant CVON-2018–30 Predict 2 (MTB, HLT). The Arrest registry is supported by an unconditional grant of Stryker Emergency Care, Redmond, Wa, USA (RWK). The funders had no access to the data and did not contribute to the preparation of this manuscript.

Acknowledgements

We are greatly indebted to all participating EMS dispatch centers (Amsterdam, Haarlem and Alkmaar), regional ambulance services (Ambulance Amsterdam, GGD Kennemerland, Witte Kruis and Veiligheidsregio Noord-Holland Noord Ambulancezorg), fire brigades, and police departments, as well as Schiphol airport, for their cooperation and support. We greatly appreciate the contributions of Remy Stieglis (MSc) of the Academic Medical Center (Amsterdam, The Netherlands), to the data collection, data entry, and patient follow-up. We thank all the students of the University of Amsterdam who helped collect the AED data.

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.2020.03.011.

REFERENCES

1. Eisenburger P, Sterz F, Haugk M, Scheinecker W, Holzer M, Koreny M, et al. Cardiac arrest in public locations–an independent predictor for better outcome? Resuscitation 2006;70(3):395–403.
2. 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.
3. 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.
4. 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.
5. 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.
6. 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 cardiol 2017;2(5):507–14.
7. Granfeldt A, Wissenberg M, Hansen SM, Lippert FK, Torp-Pedersen C, Christensen EF, et al. Location of cardiac arrest and impact of pre-arrest chronic disease and medication use on survival. Resuscitation 2017;114:113–20.
8. Herlitz J, Engdahl J, Svensson L, Young M, Angquist KA, Holmberg S. Decrease in the occurrence of ventricular fibrillation as the initially observed arrhythmia after out-of-hospital cardiac arrest during 11 years in Sweden. Resuscitation 2004;60(3):283–90.
9. Berdowski J, Schulten RJ, Tijssen JG, van Alem AP, Koster RW. Delaying a shock after takeover from the automated external defibrillator by paramedics is associated with decreased survival. Resuscitation 2010;81(3):287–92.
10. 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.
11. Blom MT, van Hoeijen DA, Bardai A, Berdowski J, Souverein PC, De Bruin ML, et al. Genetic, clinical and pharmacological determinants of out-of-hospital cardiac arrest: rationale and outline of the AmsteRdam Resuscitation Studies (ARREST) registry. Open Heart 2014;1(1):e000112.
12. 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.
13. Bak MAR, Blom MT, Tan HL, Willems DL. Ethical aspects of sudden cardiac arrest research using observational data: a narrative review. Critical care (London, England) 2018;22(1):212.
14. Blom MT, van Hoeijen DA, Bardai A, Berdowski J, Souverein PC, De Bruin ML, et al. Genetic, clinical and pharmacological determinants of out-of-hospital cardiac arrest: rationale and outline of the AmsteRdam resuscitation studies (ARREST) registry. Open Heart 2014;1(1):e000112.

15. Litwin PE, Eisenberg MS, Hallstrom AP, Cummins RO. The location of collapse and its effect on survival from cardiac arrest. Ann Emerg Med 1987;16(7):787–91.
16. 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.
17. Swor RA, Jackson RE, Compton S, Domeier R, Zalenski R, Honeycutt L, et al. Cardiac arrest in private locations: different strategies are needed to improve outcome. Resuscitation 2003;58(2):171–6.
18. 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.
19. Fordyce CB, Hansen CM, Kragholm K, Dupre ME, Jollis JG, Roettig ML, et al. Association of public health initiatives with outcomes for out-of-hospital cardiac arrest at home and in public locations. JAMA cardiology 2017;2(11):1226–35.
20. Bardy GH. A critic's assessment of our approach to cardiac arrest. N Engl J Med 2011;364(4):374–5.
21. Kiguchi T, Kiyohara K, Kitamura T, Nishiyama C, Kobayashi D, Okabayashi S, et al. Public-access defibrillation and survival of out-of-hospital cardiac arrest in public vs. residential locations in Japan. Circ J 2019;83(8):1682–8.
22. 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.
23. 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.
24. Hansen SM, Brondum S, Thomas G, Rasmussen SR, Kvist B, Christensen A, et al. Home care providers to the rescue: a novel first-responder programme. PLoS One 2015;10(10):e0141352.
25. 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.
26. Pijls RWM, Nelemans PJ, Rahel BM, Gorgels APM. Characteristics of a novel citizen rescue system for out-of-hospital cardiac arrest in the Dutch province of Limburg: relation to incidence and survival. Neth Heart J 2019;27(2):100–7.
27. Grasner 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.
28. Morrison LJ, Schmicker RH, Weisfeldt ML, Bigham BL, Berg RA, Topjian AA, et al. Effect of gender on outcome of out of hospital cardiac arrest in the resuscitation outcomes consortium. Resuscitation 2016;100:76–81.
29. Mumma BE, Umarov T. Sex differences in the prehospital management of out-of-hospital cardiac arrest. Resuscitation 2016;105:161–4.
30. Lewis JF, Zeger SL, Li X, Mann NC, Newgard CD, Haynes S, et al. Gender differences in the quality of EMS care nationwide for chest pain and out-of- hospital cardiac arrest. Women's Health Issues 2018.
31. Safdar B, Stolz U, Stiell IG, Cone DC, Bobrow BJ, deBoehr M, et al. Differential survival for men and women from out-of-hospital cardiac arrest varies by age: results from the OPALS study. Acad Emerg Med 2014;21(12):1503–11.
32. Blom MT, Oving I, Berdowski J, van Valkengoed IGM, Bardai A, Tan HL. Women have lower chances than men to be resuscitated and survive out-of-hospital cardiac arrest. Eur Heart J 2019.
33. Søholm H, Hassager C, Lippert F, Winther-Jensen M, Thomsen JH, Friberg H, et al. Factors associated with successful resuscitation after out-of-hospital cardiac arrest and temporal trends in survival and comorbidity. Ann Emerg Med 201565(5) 523-31.e2.
34. Hirlekar G, Jonsson M, Karlsson T, Hollenberg J, Albertsson P, Herlitz J. Comorbidity and survival in out-of-hospital cardiac arrest. Resuscitation 2018;133:118–23.
35. Beesems SG, Blom MT, van der Pas MHA, Hulleman M, van de Glind EMM, van Munster BC, et al. Comorbidity and favorable neurologic outcome after out-of-hospital cardiac arrest in patients of 70 years and older. Resuscitation 2015;94:33–9.