Available online at www.sciencedirect.com

Resuscitation

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

Clinical paper

Bystander cardiopulmonary resuscitation and survival in patients with out-of-hospital cardiac arrest of non-cardiac origin

D.M. Christensen[a,*], S. Rajan[a], K. Kragholm[b,c,d], K.B. Søndergaard[a], O.M. Hansen[b], T.A. Gerds[e,f], C. Torp-Pedersen[b,c,d], G.H. Gislason[a,f], Freddy K. Lippert[g], C.A. Barcella[a]

[a] Department of Cardiology, Copenhagen University Hospital Herlev and Gentofte, Copenhagen, Denmark
[b] Department of Cardiology, Aalborg University Hospital, Aalborg, Denmark
[c] Unit of Epidemiology and Biostatistics, Aalborg University Hospital, Aalborg, Denmark
[d] Department of Health Science and Technology, Aalborg University, Aalborg, Denmark
[e] Department of Biostatistics, University of Copenhagen, Copenhagen, Denmark
[f] The Danish Heart Foundation, Copenhagen, Denmark
[g] Emergency Medical Services: The Capital Region of Denmark, Copenhagen, Denmark

Abstract

Background: Knowledge about the effect of bystander cardiopulmonary resuscitation (CPR) in out-of-hospital cardiac arrest (OHCA) of non-cardiac origin is lacking. We aimed to investigate the association between bystander CPR and survival in OHCA of presumed non-cardiac origin.

Methods: From the Danish Cardiac Arrest Registry and through linkage with national Danish healthcare registries we identified all patients with OHCA of presumed non-cardiac origin in Denmark (2001–2014). These were categorized further into OHCA of medical and non-medical cause. We analyzed temporal trends in bystander CPR and 30-day survival during the study period. Multiple logistic regression was used to examine the association between bystander CPR and 30-day survival and reported as standardized 30-day survival chances with versus without bystander CPR standardized to the prehospital OHCA-factors and patient characteristics of all patients in the study population.

Results: We identified 10,761 OHCAs of presumed non-cardiac origin. Bystander CPR was associated with a significantly higher 30-day survival chance of 3.4% (95% confidence interval [CI]: 2.9–3.9) versus 1.8% (95% CI: 1.4–2.2) without bystander CPR. A similar association was found in subgroups of both medical and non-medical OHCA. During the study period, the overall bystander CPR rates increased from 13.6% (95% CI: 11.2–16.5) to 62.7% (95% CI: 60.2–65.2). 30-day survival increased overall from 1.3% (95% CI: 0.7–2.6) to 4.0% (95% CI: 3.1–5.2).

Conclusion: Bystander CPR was associated with a higher chance of 30-day survival among OHCA of presumed non-cardiac origin regardless of the underlying cause (medical/non-medical). Rates of bystander CPR and 30-day survival improved during the study period.

Keywords: Bystander CPR, OHCA, Outcome, Registry, Non-cardiac, Non-medical, Medical, Aetiology, Cardiopulmonary resuscitation, Out-of-hospital cardiac arrest, Survival, Denmark

* Corresponding author at: Department of Cardiology, Copenhagen University Hospital Herlev and Gentofte, Post 635, Kildegaardsvej 28, 2900, Hellerup, Denmark.
E-mail address: daniel.ooi.moelager.christensen@regionh.dk (D.M. Christensen).

https://doi.org/10.1016/j.resuscitation.2019.05.014
Received 12 February 2019; Received in revised form 30 April 2019; Accepted 16 May 2019

Introduction

Out-of-hospital cardiac arrest (OHCA) is a leading cause of death worldwide and OHCA of cardiac origin has been extensively studied.[1,2] Notably, 20–40% of OHCAs are of non-cardiac origin[3–5] and are associated with poorer survival compared to OHCA of cardiac origin.[4,6–8]

OHCA of non-cardiac origin is a heterogeneous entity: the pathophysiological mechanisms vary among the distinctive causes, which include medical diseases such as respiratory or cerebrovascular disease, and non-medical causes such as trauma, asphyxia or drug overdose.[9–11]

Bystander cardiopulmonary resuscitation (CPR) is a fundamental link in improving survival from OHCA; therefore large-scale initiatives have been taken worldwide to improve bystander resuscitation attempts during the last decade.[12–14] However, the association between bystander CPR and favorable survival outcomes has primarily been investigated in OHCA of presumed cardiac origin.[15,16] Although guidelines recommend bystander CPR also in OHCA of non-cardiac origin,[11] knowledge regarding its benefits is lacking[17] and studies on this topic have achieved contrasting results.[3,5,18] Therefore, this study aimed to investigate the association between bystander CPR and 30-day survival in OHCA of non-cardiac origin, as well as the temporal trends in rates of bystander CPR and 30-day survival.

Methods

Data sources

In Denmark, all residents are assigned a unique Civil Registration Number, which enables linkage of information from different nationwide registries at an individual level. The Danish Cardiac Arrest Registry holds information on all OHCAs in Denmark with attempted resuscitation by bystanders or emergency medical services (EMS), excluding patients with obvious late signs of death. Details regarding the OHCA were filled in through case-report forms by EMS-personnel. The Danish Cardiac Arrest Registry has been described in detail previously.[12] The Danish Civil Registration System provides information on age and gender. Information on all hospital admissions is registered in the Danish National Patient Registry since 1978.[19] The assigned diagnoses are classified according to the *International Classification of Diseases* (ICD), ICD-8 prior to 1994 and ICD-10 following 1994. Data on dispensed medication prior to OHCA was obtained from the National Prescription Registry, where the drugs are classified by the Anatomical Therapeutic Classification code. The Danish Cause of Death Registry holds information from all death certificates, including data on underlying cause of death.[20]

Study population

We identified all OHCAs from June 2001 through December 2014. We categorized arrests according to presumed cardiac or non-cardiac origin: the underlying cause of OHCA was determined using diagnosis codes from hospital discharges or death certificates as previously done and in accordance with Utstein criteria.[9,10,12,21–23] Patients with cardiac disease, unknown disease or unexpected collapse were presumed to have arrest of cardiac origin. OHCA of presumed non-cardiac origin was defined if the underlying cause was either 1) a non-cardiac medical cause such as respiratory disease, cerebrovascular disease or cancer or 2) a non-medical cause. Non-medical causes were further divided into trauma, drug overdose, drowning and asphyxia as recommended in the 2015 update of the Utstein template.[9] Hanging was included in the definition of asphyxia. Data from the present study population have not been reported previously. The ICD-10 codes utilized in the definition of OHCA of medical and non-medical cause can be found in Supplemental Table 1.

Patients with EMS-witnessed OHCA, OHCA of presumed cardiac origin, and <18 years of age were excluded from the final study population (Fig. 1).

We estimated Charlson comorbidity index score using hospital discharge diagnoses up to 10 years before the date of OHCA.[24] Additionally, diabetes was defined by redemption of glucose-lowering medication within 180 days prior to OHCA.

Outcome measure

Our main outcome was 30-day survival. Secondary outcomes were bystander CPR and 30-day survival according to calendar year.

Statistics

We investigated calendar time trends of bystander CPR and 30-day survival overall as well as stratified by cause of OHCA (medical and non-medical) by using univariate logistic regression modeled with restricted cubic splines.[25]

Multiple logistic regression was used to describe the effect of bystander CPR on 30-day survival chance adjusted for sex, age, cause of OHCA (medical and non-medical), Charlson comorbidity index score, calendar year, location of arrest and witnessed status. The model was not adjusted for initial registered rhythm as this is an intermediate variable between bystander CPR and 30-day survival.[16] Reported were average 30-day survival chances separately for OHCA with and without bystander CPR and standardized to characteristics of all patients in the study population (g-formula), as well as average treatment effects as differences of standardized 30-day survival chances and corresponding number needed to treat (NNT).[26] Within the limitations of the data, the two standardized 30-day survival chances can be interpreted as what we would have observed if all the OHCA-patients had either received bystander CPR or not received bystander CPR.[27] We conducted several sensitivity analyses; (1) stratifying by cause of arrest (medical and non-medical), (2) stratifying by witnessed status (witnessed and unwitnessed arrests), (3) excluding traumatic arrests, (4) stratifying by Charlson Comorbidity Index score, and (5) replacing 30-day survival with return of spontaneous circulation (ROSC) upon hospital arrival in our outcome model.

Additionally, we reported predicted 30-day survival chances in best-case and worst-case scenarios defined by patient- and OHCA-characteristics and stratified by witnessed status. A best-case scenario was defined as a ≤65-year-old patient having an arrest in a public location with a Charlson comorbidity index score of 0; a worst-case scenario as a >65-year-old patient having an arrest in a private location with a Charlson comorbidity index score of ≥2. Both scenarios are shown for medical and non-medical arrests. Only for the analysis of predicted 30-day survival chances in best- and worst-case scenarios was age ([≤65 years] working age, [>65 years] retirement age) handled as a binary variable.[16]

All analyses were performed only among patients for whom all the information regarding OHCA was available (complete case analyses).

Table 1 – Patient and arrest characteristics according to cause of out-of-hospital cardiac arrest.

Patient characteristics	Overall	Medical OHCA	Non-medical OHCA	P value
Total patients	10761	7625	3136	
Median age, years (IQR)	67.00 [53.00, 78.00]	70.00 [60.00, 80.00]	50.00 [37.00, 66.00]	<0.001
Male, n (%)	6357 (59.1)	4153 (54.5)	2204 (70.3)	<0.001
Age group, n (%)				
Working age 18–65 years, n (%)	5138 (47.7)	2822 (37.0)	2316 (73.9)	<0.001
Retirement age 66–79 years, n (%)	3481 (32.3)	2970 (39.0)	511 (16.2)	<0.001
Senior 80+years, n (%)	2142 (20.0)	1833 (24.0)	309 (9.9)	<0.001
Civil status - unmarried, n (%)	5488 (51.0)	3726 (48.9)	1762 (56.2)	<0.001
Charlson comorbidity index score, n (%)				
0	4218 (39.2)	2070 (27.1)	2148 (68.5)	<0.001
1	1987 (18.5)	1542 (20.2)	445 (14.2)	<0.001
≥2	4557 (42.3)	4013 (52.7)	543 (17.3)	<0.001
OHCA-factors				
Arrest in private location, n (%)	6979 (64.9)	5494 (72.1)	1485 (47.4)	<0.001
Data missing, n (%)	1355 (12.6)	870 (11.4)	485 (15.5)	
Bystander-witnessed arrests, n (%)	4306 (40.0)	3574 (46.9)	732 (23.3)	<0.001
Data missing, n (%)	682 (6.3)	455 (6.0)	227 (7.2)	
Bystander CPR, n (%)	3963 (36.8)	2755 (36.1)	1208 (38.5)	0.027
Data missing, n (%)	605 (5.6)	437 (5.7)	168 (5.4)	
Bystander defibrillation, n (%)	60 (0.6)	42 (0.6)	18 (0.6)	0.98
Data missing, n (%)	1231 (11.4)	862 (11.3)	369 (11.8)	
Median ambulance response time, min (IQR)	13.00 [7.00, 22.00]	12.00 [7.00, 20.00]	14.00 [8.00, 29.00]	<0.001
Shockable initial rhythm, n (%)	537 (5.0)	441 (5.8)	96 (3.1)	<0.001
Data missing, n (%)	1000 (9.3)	672 (8.8)	328 (10.5)	
Outcomes				
ROSC upon hospital arrival, n (%)	972 (9.0)	730 (9.6)	242 (7.7)	0.002
Data missing, n (%)	1406 (13.1)	1006 (13.2)	400 (12.8)	
30-day survival, n (%)	328 (3.0)	229 (3.0)	99 (3.2)	0.81
One-year survival, n (%)	258 (2.4)	180 (2.4)	78 (2.5)	0.75

OHCA, out-of-hospital cardiac arrest. IQR, interquartile range. CPR, cardiopulmonary resuscitation. ROSC, return of spontaneous circulation.

The level of statistical significance was set at 5%. Data management and statistical analyses were performed with the use of SAS version 9.4 (SAS Institute Inc.) and R version 3.2.2 (R Development Core Team).[28]

Ethics

The study has been approved by the Danish Data Protection Agency (Ref.no. 2007-58-0015, local ref.no. GEH-2014-017, I-Suite.nr. 02735). For register studies based on anonymous data in Denmark ethical approval is not required.

Results

Patients

A total of 10,761 patients with OHCA of presumed non-cardiac origin were included in our study: 7625 (70.9%) with a medical and 3136 (29.1%) with a non-medical cause of arrest, Fig. 1.

Characteristics

Table 1 displays baseline characteristics according to cause of OHCA. Compared to patients with medical cause of arrest, patients with non-medical cause of arrest were younger, had a lower Charlson comorbidity index score and were more often men. Patients with non-medical cause of arrest were less likely to have witnessed arrest, yet more often had arrest in a public location. The most frequent non-medical cause of arrest was trauma followed by drug overdose, asphyxia and drowning, Fig. 1.

Temporal trends

During the study period, a large increase in the rates of bystander CPR was observed overall and among OHCA of both medical and non-medical cause: from 13.6% (95% confidence interval [CI]: 11.2–16.5) to 62.7% (95% CI: 60.2–65.2) overall, from 13.4% (95% CI: 10.5–16.9) to 62.9% (95% CI: 60.0–65.7) in medical cause and from 14.1% (95% CI: 10.0–19.7) to 62.5% (95% CI: 57.3–67.5) in non-medical cause, Fig. 2A and C. 30-day survival also rose during the study period: from 1.3% (95% CI: 0.7–2.6) to 4.0% (95% CI: 3.1–5.2) overall, from 1.6% (95% CI: 0.8–3.3) to 3.7% (95% CI: 2.7–5.0) in medical cause and from 0.9% (95% CI: 0.2–3.8) to 5.1% (95% CI: 3.2–8.0) in non-medical cause, Fig. 2B and 2D.

A similar temporal increase in rates of bystander CPR was observed among all specific causes in both non-medical and medical arrests, Supplemental Fig. 1.

Standardized 30-day survival chances with and without bystander CPR

Fig. 3 depicts the adjusted standardized 30-day survival chances with and without bystander CPR. Overall the 30-day survival chance was

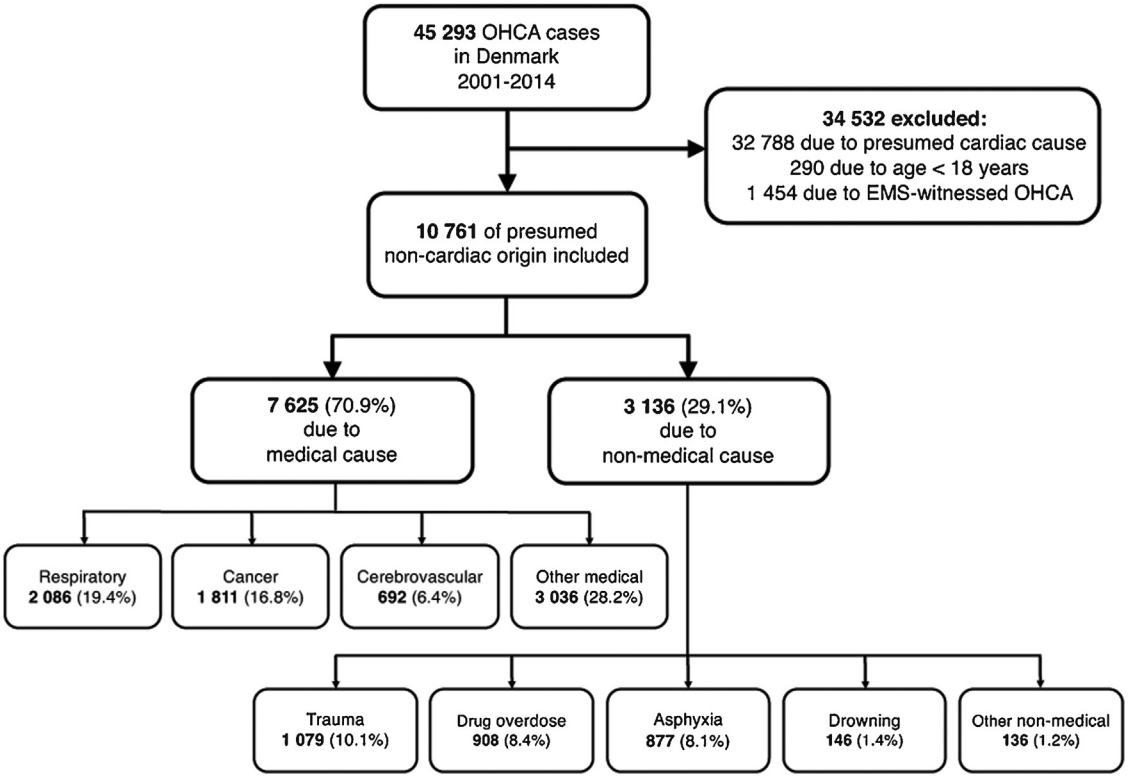

Fig. 1 – Flowchart of patient selection process for the study population. OHCA, out-of-hospital cardiac arrest. EMS, Emergency Medical Services.

3.4% (95% CI: 2.9–3.9) for bystander CPR versus 1.8% (95% CI: 1.4–2.2) for no bystander CPR equal to a 1.9 times higher relative chance of survival. There was a significant difference in standardized 30-day survival chance of 1.6% (95% CI: 0.9–2.3) corresponding to an NNT of 64.

The association between bystander CPR and increased survival persisted when we stratified according to cause of arrest (medical/non-medical), Fig. 3.

Furthermore, we observed bystander CPR to be associated with enhanced survival only among witnessed arrests Supplemental Fig. 2.

Repeating the main analysis only among non-traumatic arrests, as well as stratified by Charlson Comorbidity Index score (0, 1, ≥2), yielded similar results, Supplemental Figs. 3 and 4.

Bystander CPR was associated with a similar absolute increase in chance of ROSC upon hospital arrival; however, the relative increase was less marked compared to 30-day survival (Supplemental Table 2).

Best- and worst-case scenarios

Fig. 4 displays predicted survival chances for patients with witnessed arrest in a best-case scenario (≤65 years old, public location of arrest, Charlson comorbidity index score of 0) and a worst-case scenario (>65 years old, arrest in a private location, Charlson comorbidity index score of ≥2) among both medical and non-medical cause of OHCA. Among witnessed arrests in the study population, 9.1% of patients presented with the best-case scenario and 27.7% presented with the worst-case scenario.

In all scenarios, receiving bystander CPR was associated with a higher predicted 30-day survival chance. In the best-case scenario the predicted 30-day survival chance was 15.3% (95% CI: 10.8–19.9) with bystander CPR versus 6.8% (95% CI: 3.9–9.6) without (2.3 times higher with bystander CPR) for medical OHCA and 14.9% (95% CI: 10.3–19.5) with bystander CPR versus 5.0% (95% CI: 1.8–8.2) without (3.0 times higher with bystander CPR) for non-medical OHCA. In the worst-case scenario the predicted 30-day survival chance was 2.9% (95% CI: 1.9–3.9) with bystander CPR versus 1.2% (95% CI: 0.7–1.6) without (2.4 times higher with bystander CPR) and 2.8% (95% CI: 1.3–4.3) with bystander CPR versus 0.9% (95% CI: 0.2–1.5) without (3.1 times higher with bystander CPR) for medical and non-medical OHCA, respectively.

Best- and worst-case scenarios for unwitnessed arrests did not show a significant association (Supplemental Fig. 5).

Discussion

In this nationwide study, bystander CPR was associated with an almost two-fold improvement in 30-day survival chances overall among patients suffering from OHCA of presumed non-cardiac origin. The findings applied to both medical and non-medical causes of arrest. During the study period overall rates of bystander CPR more than quadrupled and rates of 30-day survival more than tripled. In best-case and worst-case scenarios, bystander CPR remained associated with a higher 30-day survival chance among witnessed OHCAs.

Arrests of non-cardiac origin differ from those of cardiac origin by being more heterogeneous and by having a lower chance of survival. In accordance with previous studies, we observed an

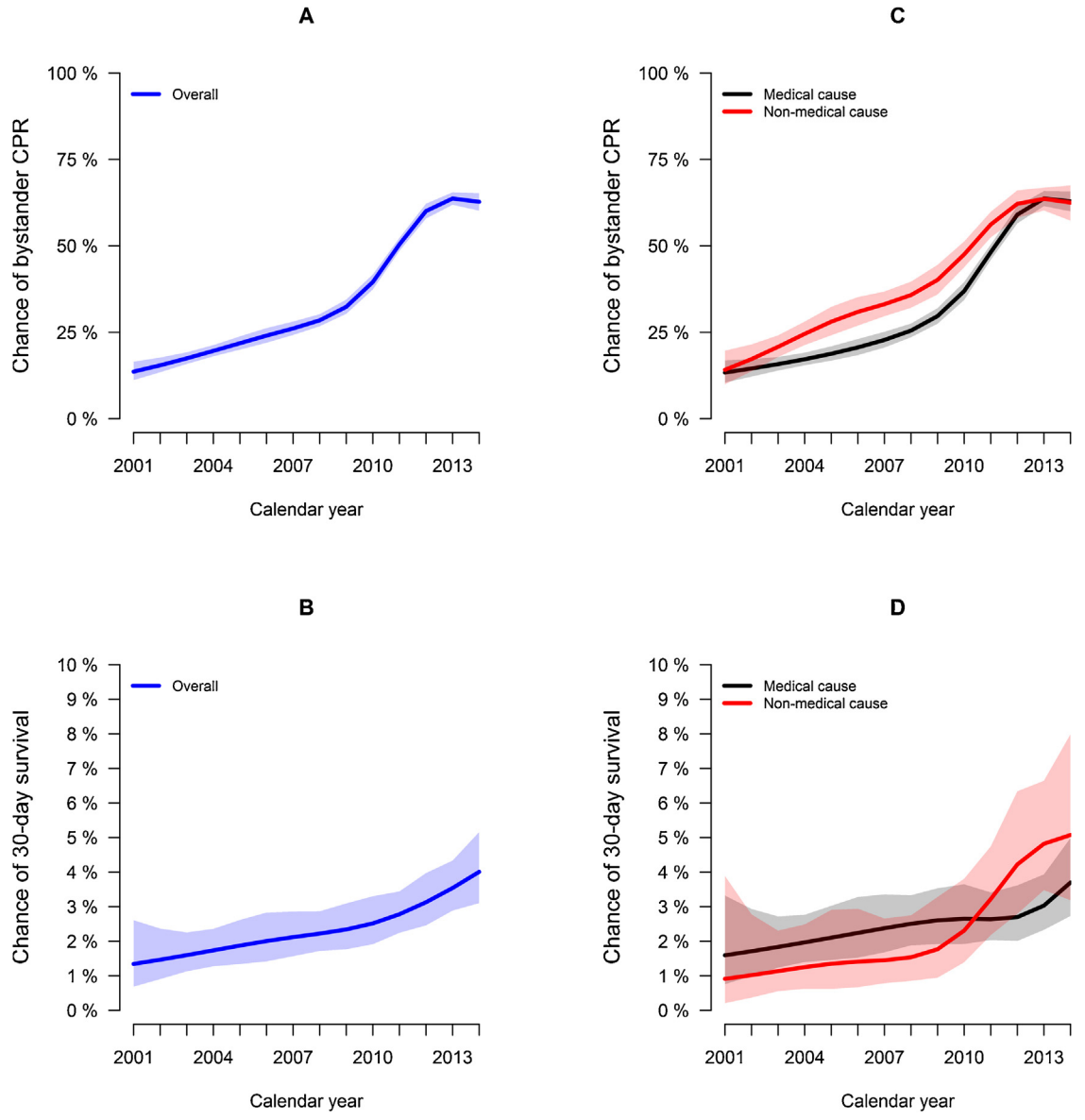

Fig. 2 – Temporal trends from 2001 to 2014 in rates of: (A) bystander cardiopulmonary resuscitation, (B) 30-day survival, (C) bystander cardiopulmonary resuscitation for medical and non-medical arrests, (D) 30-day survival for medical and non-medical arrests. CPR, cardiopulmonary resuscitation.

overall low 30-day survival following OHCA of presumed non-cardiac origin.[4,6,8] This may be due to the low occurrence of reversible causes of arrest, low rate of shockable rhythm and limited in-hospital treatment options. Despite that, CPR is still crucial in providing blood flow to vital organs in arrest of non-cardiac origin. Accordingly, we found bystander CPR to be associated with 1.9 times higher relative chance of survival overall in our cohort, and thus the associated benefit of bystander CPR is comparable to that observed in OHCA of cardiac origin.[15,29] Moreover, we found that when bystander CPR was performed, the survival chances in our best-case scenario prediction were similar to the overall survival rates following OHCA of cardiac origin.[15] However, in our sensitivity analysis among only unwitnessed arrests, we do not observe an associated survival benefit of bystander CPR. This may be explained by the fact that unwitnessed arrests have a prolonged time from the moment of collapse to commencement of bystander resuscitation, as it is known that a prompt bystander intervention is vital in securing a favorable outcome following OHCA.[3,16]

Our findings are in contrast with a study from Osaka, Japan, which observed no association between bystander CPR and 30-day survival in OHCA of non-cardiac origin.[5] A plausible explanation of the conflicting results may be the different average EMS response times (8 min in the study from Osaka, 13 min in our study), which could imply that bystanders were only able to provide CPR for a short duration, thus diminishing its influence on survival. Further, the distribution of causes of OHCA differed in the two study populations: in the study from Osaka, more than half of the arrests were of non-medical cause and specifically, the difference compared to our study was mainly driven by a higher rate of asphyxial arrests.

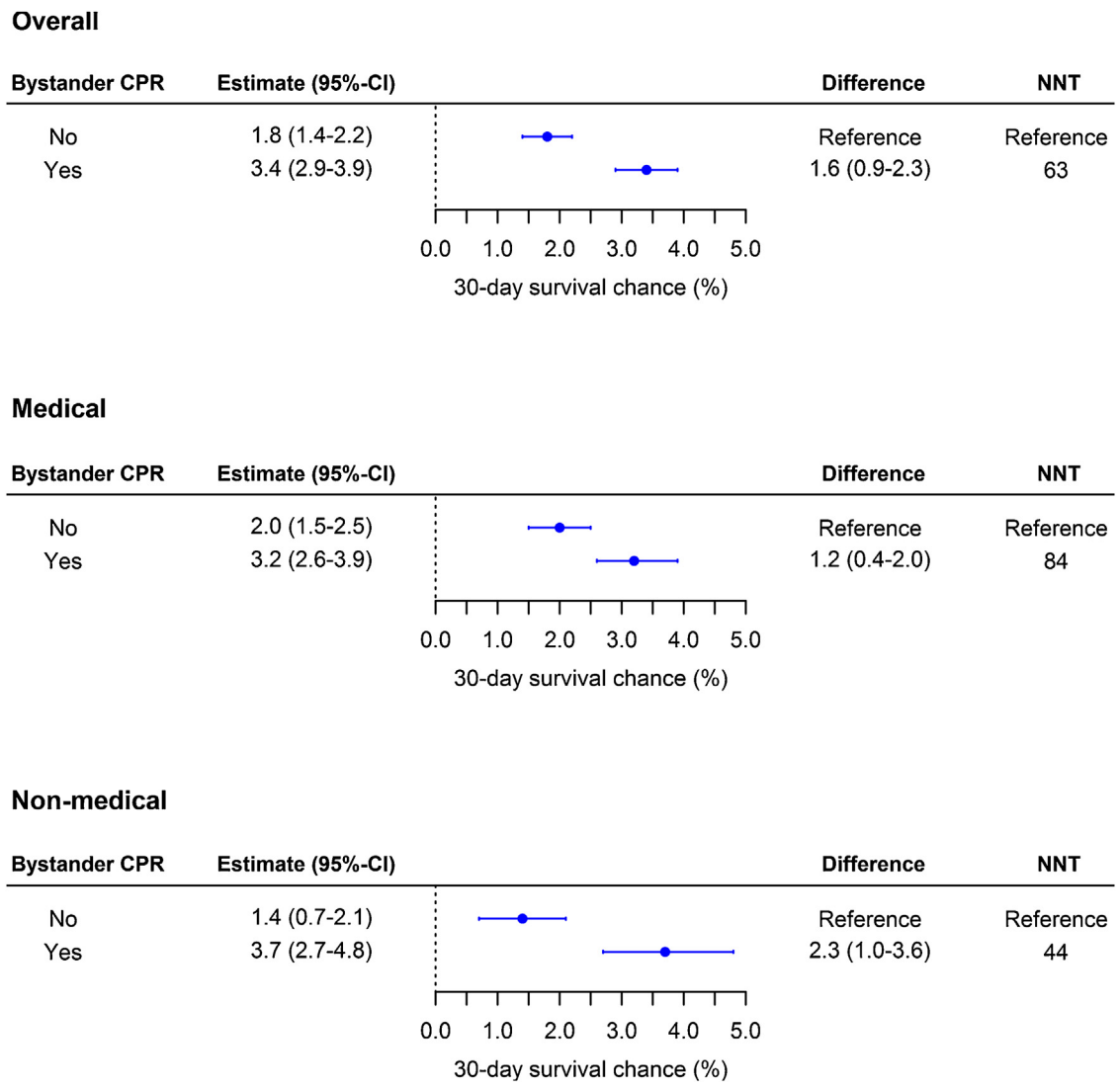

Fig. 3 – Standardized 30-day survival chance with and without bystander cardiopulmonary resuscitation overall and according to medical and non-medical cause of arrest. CPR, cardiopulmonary resuscitation. CI, confidence interval. NNT, number needed to treat.

Notably, a separate nationwide Japanese study, which only included witnessed arrests and had an EMS response time similar to ours (average 12.5 min), found bystander CPR to be associated with improved 30-day survival in OHCA of non-cardiac origin.[18] Similarly, a Swedish study also found bystander CPR for OHCA of non-cardiac origin to be univariately associated with improved survival in a subgroup analysis.[3] With the present study, we were able to confirm these previous findings and expand the current knowledge about the topic showing an association between bystander CPR and improved 30-day survival chance regardless of the underlying cause of OHCA (medical, non-medical, only among non-traumatic arrests).

We demonstrated a large temporal increase in rates of bystander CPR in our study population, which was comparable to that observed for OHCA of cardiac origin in another Danish study.[12] Despite some studies indicating that bystanders may be hesitant to provide resuscitation for patients with disagreeable characteristics,[30] the increase was present among different causes, including arrests caused by trauma, asphyxia, drug overdose and drowning. Particularly, we observed a sharp increase in 30-day survival among non-medical arrests beginning in 2009, which coincides with the implementation of dispatcher assisted CPR in Denmark.[12] Dispatchers may have been able to guide bystanders that were previously hesitant to provide CPR in special incidents of non-medical cardiac arrest. In contrast to the static rates of 30-day survival observed in the aforementioned study from Osaka,[5] we found that 30-day survival for OHCA of presumed non-cardiac origin more than tripled in Denmark during the study period, which underlines the importance of the national initiatives to improve bystander resuscitation.

When studying best-case and worst-case scenarios, large differences in predicted survival chances were observed. These findings demonstrate that OHCA is a multifactorial situation where many pre-hospital and patient characteristics influence the outcome. However, bystander CPR remained associated with a similar relative increase in predicted 30-day survival in all scenarios, highlighting the robustness of this single factor in improving survival following OHCA.

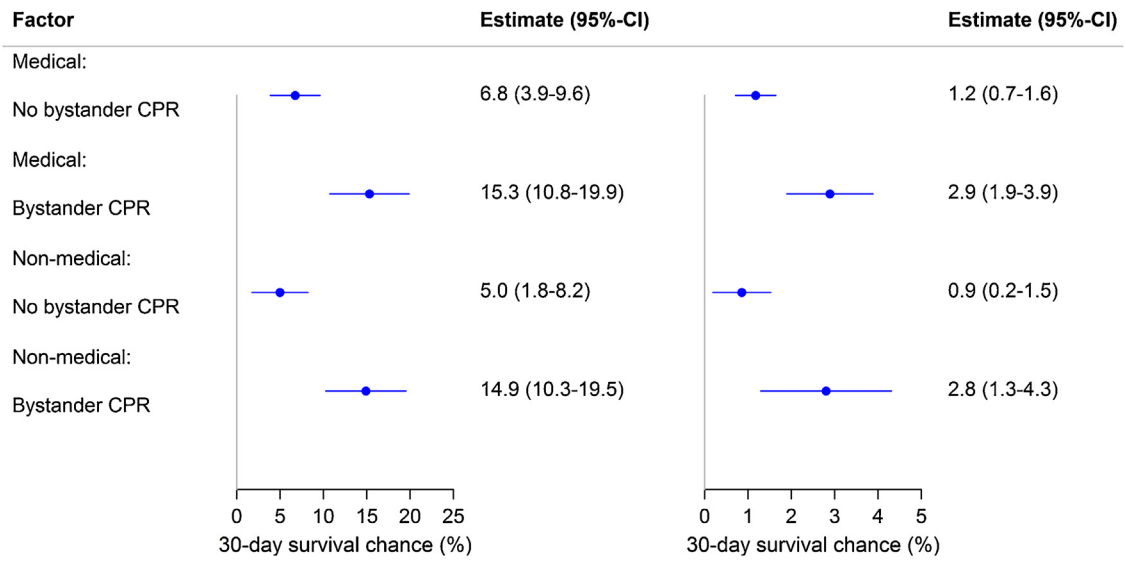

Fig. 4 – Predicted 30-day survival chance among witnessed out-of-hospital cardiac arrests of medical and non-medical cause with and without bystander cardiopulmonary resuscitation in: (left) a best-case scenario, (right) a worst-case scenario. CPR, cardiopulmonary resuscitation. CI, confidence interval.

Limitations

The main limitation of our study subsisted in its observational nature, which did not permit us to draw conclusions on causality. Moreover, although we did adjust for potential confounders, we cannot rule out the effect of residual confounding on our results, as the Danish registries did not include information on some important clinical features, such as alcohol consumption or weight. Furthermore, the ambulance response times were only estimates, and thus may not precisely reflect the exact duration of the patients' cardiac arrest.

We did not have information on quality, duration or type of CPR (i.e. chest-compression-only or chest compressions with rescue breaths). Rescue breathing may be beneficial compared to chest-compression-only CPR during special circumstances, such as in arrest caused by drowning or asphyxia.[18,31]

Lastly, we did not have complete information about treatment in intensive care units, such as therapeutic hypothermia, which is not adequately registered in the Danish National Patient Registry. The association that we observed may have been influenced by differences in in-hospital treatment, as there might be a bias towards more exhaustive treatment of those patients who received bystander CPR. However, to exclude the effect of in-hospital treatment, we conducted a sensitivity analysis which showed an increased chance of ROSC upon hospital arrival associated with bystander CPR.

Conclusion

In this nationwide study, we demonstrated a significant association between bystander CPR and improved 30-day survival among patients suffering from OHCA of presumed non-cardiac origin. Overall, we observed a more than four-fold increase in rates of bystander CPR, as well as a three-fold increase in 30-day survival during the study period. The present study underlines the effectiveness and importance of initiatives that are aimed at improving bystander CPR, including among arrests of non-cardiac origin. A continuing effort to support a prompt bystander intervention, also for arrests of non-cardiac origin, is warranted, as a higher rate of bystander CPR among these patients may likely to lead to more lives saved.

Conflicts of interests

Dr. Kragholm reports receiving research grant from The Laerdal Foundation, and lecture fees from Novartis Healthcare. Dr. Hansen reports receiving lecture fees from AstraZeneca. Dr. Lippert reports receiving research grants from the Danish foundation TrygFonden and from The Laerdal Foundation. Dr. Torp-Pedersen reports receiving grant support and honoraria from Bayer and grant support from Biotronik. Dr. Gislason is supported by an unrestricted clinical research scholarship from the Novo Nordisk Foundation. No other potential conflict of interest relevant to this article was reported.

Acknowledgements

TrygFonden supports The Danish Cardiac Arrest Registry and did not influence the study design, data collection and interpretation, nor preparation and approval of this manuscript.

We commend the Danish Emergency Medical Services for their work in completing the case report forms for the Danish Cardiac Arrest Registry.

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.2019.05.014.

REFERENCES

1. Perkins GD, Handley AJ, Koster RW, et al. European Resuscitation Council guidelines for resuscitation 2015: section 2. Adult basic life support and automated external defibrillation. Resuscitation 2015;95:81–99.
2. Kronick SL, Kurz MC, Lin S, 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:S397–413.
3. Hasselqvist-Ax I, Riva G, Herlitz J, et al. Early cardiopulmonary resuscitation in out-of-hospital cardiac arrest. N Engl J Med. 2015;372:2307–15.
4. Engdahl J, Bång A, Karlson BW, Lindqvist J, Herlitz J. Characteristics and outcome among patients suffering from out of hospital cardiac arrest of non-cardiac aetiology. Resuscitation 2003;57:33–41.
5. Kitamura T, Kiyohara K, Sakai T, et al. Epidemiology and outcome of adult out-of-hospital cardiac arrest of non-cardiac origin in Osaka: a population-based study. BMJ Open 2014;4:e006462.
6. Kuisma M, Alaspaa A. Out-of-hospital cardiac arrests of non-cardiac origin: Epidemiology and outcome. Eur Heart J 1997;18:1122–8.
7. Claesson A, Djarv T, Nordberg P, et al. Medical versus non medical etiology in out-of-hospital cardiac arrest-Changes in outcome in relation to the revised Utstein template. Resuscitation 2017;110: 48–55.
8. Hess EP, Campbell RL, White RD. Epidemiology, trends, and outcome of out-of-hospital cardiac arrest of non-cardiac origin. Resuscitation 2007;72:200–6.
9. 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.
10. 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.
11. Truhlar A, Deakin CD, Soar J, et al. European resuscitation council guidelines for resuscitation 2015: section 4. Cardiac arrest in special circumstances. Resuscitation 2015;95:148–201.
12. 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.
13. Kitamura T, Iwami T, Kawamura T, et al. Nationwide improvements in survival from out-of-hospital cardiac arrest in Japan. Circulation 2012;126:2834–43.
14. Chan PS, McNally B, Tang F, Kellermann A, Group CS. Recent trends in survival from out-of-hospital cardiac arrest in the United States. Circulation 2014;130:1876–82.
15. Malta Hansen C, Kragholm K, Pearson DA, et al. Association of bystander and first-responder intervention with survival after out-of-hospital cardiac arrest in North Carolina, 2010-2013. JAMA. 2015;314:255–64.
16. Rajan S, Wissenberg M, Folke F, et al. Association of bystander cardiopulmonary resuscitation and survival according to ambulance response times after out-of-hospital cardiac arrest. Circulation 2016;134:2095–104.
17. Olasveengen TM, de Caen AR, Mancini ME, et al. International consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations summary. Circulation 2017;136:e424–40.
18. Kitamura T, Iwami T, Kawamura T, et al. Bystander-initiated rescue breathing for out-of-hospital cardiac arrests of noncardiac origin. Circulation 2010;122:293–9.
19. Lynge E, Sandegaard JL, Rebolj M. The Danish national patient register. Scand J Public Health 2011;39:30–3.
20. Helweg-Larsen K. The Danish register of causes of death. Scand J Public Health 2011;39:26–9.
21. Kragholm K, Wissenberg M, Mortensen RN, et al. Return to work in out-of-hospital cardiac arrest survivors: a nationwide register-based follow-up study. Circulation 2015;131:1682–90.
22. Wissenberg M, Folke F, Hansen CM, 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;131:1536–45.
23. 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.
24. Thygesen S, Christiansen C, Christensen S, Lash T, Sørensen H. The predictive value of ICD-10 diagnostic coding used to assess Charlson comorbidity index conditions in the population-based Danish national registry of patients. BMC Med Res Methodol 2011;11:83-.
25. Harrell F. Regression modelling strategies. New York: Springer; 2001.
26. Taubman SL, Robins JM, Mittleman MA, Hernan MA. Intervening on risk factors for coronary heart disease: an application of the parametric g-formula. Int J Epidemiol 2009;38:1599–611.
27. Hernán MA, Robins JM. Causal inference. Boca Raton: Chapman & Hall/CRC; 2019. . forthcoming https://www.hsph.harvard.edu/miguel-hernan/causal-inference-book/.
28. R Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2018.
29. 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;3:63–81.
30. Axelsson Å, Herlitz J, Ekström L, Holmberg S. Bystander-initiated cardiopulmonary resuscitation out-of-hospital. A first description of the bystanders and their experiences. Resuscitation 1996;33:3–11.
31. Panchal AR, Bobrow BJ, Spaite DW, et al. Chest compression-only cardiopulmonary resuscitation performed by lay rescuers for adult out-of-hospital cardiac arrest due to non-cardiac aetiologies. Resuscitation 2013;84:435–9.