Duration of Resuscitation and Long-Term Outcome After In-Hospital Cardiac Arrest

A Nationwide Observational Study

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Published in:
Resuscitation

DOI (link to publication from Publisher):
10.1016/j.resuscitation.2022.08.011

Publication date:
2022

Document Version
Publisher's PDF, also known as Version of record

RESUSCITATION 179 (2022) 267–273

Available online at ScienceDirect

Resuscitation

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

Clinical paper

Duration of resuscitation and long-term outcome after in-hospital cardiac arrest: A nationwide observational study

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Abstract

Background: Prior studies have investigated the association between duration of resuscitation and short-term outcomes following in-hospital cardiac arrest (IHCA). However, it remains unknown whether there is an association between duration of resuscitation and long-term survival and functional outcomes.

Method: We linked data from the Danish in-hospital cardiac arrest registry with nationwide registries and identified 8,727 patients between 2013 and 2019. Patients were stratified into four groups (A–D) according to quartiles of duration of resuscitation. Standardized average probability of outcomes was estimated using logistic regression.

Results: Of 8,727 patients, 53.1% (n = 4,604) achieved return of spontaneous circulation. Median age was 74 (1st–3rd quartile [Q1–Q3] 65–81 years) and 63.1% were men.

Among all IHCA patients the standardized 30-day survival was 62.0% (95% CI 59.8–64.2%) for group A (<5 minutes), 32.7% (30.8–34.6%) for group B (5–11 minutes), 14.4% (12.9–15.9%) for group C (12–20 minutes) and 8.1% (7.0–9.1%) for group D (21 minutes or more). Similarly, 1-year survival was also highest for group A (50.4%; 48.2–52.6%) gradually decreasing to 6.6% (5.6–7.6%) in group D.

Among 30-day survivors, survival without anoxic brain damage or nursing home admission within one-year post-arrest was highest for group A (80.4%; 78.2–82.6%), decreasing to 73.3% (70.0–76.6%) in group B, 67.2% (61.7–72.6%) in group C and 73.3% (66.9–79.7%) in group D.

Conclusion: Shorter duration of resuscitation attempt during an IHCA is associated with higher 30-day and 1-year survival. Furthermore, we found that the majority of 30-day survivors were still alive 1-year post-arrest without anoxic brain damage or nursing home admission despite prolonged resuscitation.

Keywords: In-Hospital Cardiac Arrest (IHCA), Cardiac arrest, Outcome, Duration of resuscitation, CPR, Epidemiology, Survival

Introduction

The decision to terminate resuscitation efforts are among one of the most challenging that in-hospital cardiac arrest (IHCA) teams must make and yet research on the appropriate length of resuscitation attempts is limited.[1] Most national as well as international guidelines provide limited guidance on this topic, and thus clinicians must base this crucial decision on lower level empirical evidence such as observational studies of selected patients, case reports and expert opinions.[2,3]

A previous study has shown that patients at hospitals with the longest median resuscitation attempts were more likely to achieve return of spontaneous circulation (ROSC) and survive to hospital discharge than patients at hospitals with the shortest median resuscitation attempt with no difference in neurological function at discharge.[4] This challenges the notion that longer resuscitation attempts are futile. However, several key questions remain unanswered such as

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https://doi.org/10.1016/j.resuscitation.2022.08.011
Received 8 June 2022; Received in Revised form 10 August 2022; Accepted 16 August 2022

the long-term follow-up of the cardiac arrest patients in terms of survival as well as functional status.

This study aimed to investigate the association between duration of resuscitation during an IHCA and 30-day as well as 1-year survival among all IHCA patients and ROSC patients only. Furthermore, we examined 1-year survival without anoxic brain damage or admission to a nursing home among 30-day IHCA survivors.

Methods

Data sources

The Danish registry for in-hospital cardiac arrest (DANARREST) is a clinical national registry that has previously been described in detail.[5] In short, it was started in 2013 and coverage has increased over the years and as of January 1st, 2017, 41 out of 43 hospitals with a rapid response team reported data to the registry. In DANARREST, cardiac arrest is defined as unconsciousness and abnormal breathing and for trained personnel, pulselessness.

From the DANARREST registry, we obtained information on date and year of arrest; witness and monitored status; time to alert, time to arrival of the rapid response team; time to cardiopulmonary resuscitation (CPR); CPR performed prior to arrival of the rapid response team; initial rhythm and detailed rhythm analysis on arrival of the rapid response team; defibrillation; administration of adrenaline and/or amiodarone; use of mechanical CPR (device performing chest compressions) and status on resuscitative efforts with time to termination or return of spontaneous circulation (ROSC).

The IHCA data was linked to other national registries through the Civil Registration Number which is a unique personal identification number that is assigned to all Danish residents upon immigration or birth. Patient's age, sex and date of death was retrieved from the Danish Civil Personal Register. The burden of comorbidities was assessed using Charlson Comorbidity Index (CCI) which was also retrieved from the DANARREST database.[6]

Data on anoxic brain damage and nursing home admissions were retrieved from the Danish National Patient Register, Statistics Denmark and a nursing home registry from the Danish Health Authorities. Anoxic brain damage was defined using ICD-10 code ('DG931') at hospital discharge within the first 12 month of the cardiac arrest.

Study design and population

This study is a register-based cohort study conducted in Denmark with a population of approximately 5.8 million inhabitants.[7] All IHCA patients with an index cardiac arrest registered in the DANARREST registry between January 1st, 2013 and December 31st, 2019 were identified. We excluded patients for whom there was no clinical indication for a resuscitation attempt on arrival of the rapid response team because of a do-not-resuscitate order (DNAR). Patients with incomplete data on the duration of resuscitation were excluded. In a subset of the study population, patients who did not survive to day 30 after IHCA and who, prior to arrest, already lived in a nursing home, and/or had anoxic brain damage were excluded from analyses of onset of anoxic brain damage or nursing home admission (Fig. 1).

Exposure

Based on median and quartiles of duration of resuscitation all patients were stratified into four groups: group A (<5 minutes); group B (5–11 minutes); group C (12–20 minutes) and group D (more than 21 minutes) (Fig. 1). Duration of resuscitation was defined as onset of cardiac arrest to termination of resuscitation resulting in either ROSC or death.

Outcome

We studied the following outcomes: 30-day survival and 1-year survival among all IHCA patients and for ROSC patients alone. Among 30-day survivors, we studied 1-year survival without anoxic brain damage or nursing home admission post-arrest.

Statistical analysis

Patient and cardiac arrest related characteristics were evaluated for all IHCA patients stratified by duration of resuscitation attempt with a univariate analysis. Categorical variables were summarized using counts and frequencies while continuous variables were summarized by medians and 1st to 3rd quartiles (Q1–Q3).

For each outcome, the average probability of an event, standardized to the whole population, was calculated using logistic regression with 95% confidence intervals (95% CI). Based on previous work, the regression models were adjusted for patient and cardiac arrest related covariates that could affect the outcome and exposure: Age treated as a categorical variable (<60, 60–70, 70–80, >80), sex, Charlson Comorbidity Index, witnessed arrest and monitored arrest.[8] Patients with missing data for these covariates were excluded prior to analysis (Fig. 1).

A two-sided p-value <0.05 was considered statistically significant. All statistical analyses and data management were conducted using R, version 4.0.3 (R Foundation for Statistical Computing).

Ethics

Register-based studies do not require ethical approval or informed consent by Danish law.[9] The study has been approved by both the DANARREST registry committee and data responsible unit in the Capital Region of Denmark (approval number: P-2019-400). The study was conducted in compliance with the Declaration of Helsinki.

Results

Patient and cardiac arrest characteristics

Between January 1st, 2013, to December 31st, 2019, 9,301 patients were identified with an in-hospital cardiac arrest. Data on duration of resuscitation was missing for 4.6% (n = 425) of patients, who were excluded as well as 1.6% (n = 149) because of missing data on covariates, leaving the study population with 8,727 patients. Overall, the median age was 74 (Q1–Q3 65–81 years) and 63.1% (n = 5,509) were men. The cardiac arrest was witnessed by healthcare personnel in 76.9% (n = 6,713) of patients. The initial rhythm on arrival of the rapid response team was ventricular tachycardia or fibrillation in 18.4% (n = 1,526) of patients and pulseless electrical activity or asystole in 75.4% (n = 6,266). In total, 53.1% (n = 4,604) of patients achieved ROSC. The overall median duration of resuscitation was 12 min (Q1–Q3 5–21 min) (Table 1).

Patient and cardiac arrest characteristics across different durations of resuscitation

Comparing across the different time groups, we found that patients in group A had a lower Charlson index score compared to group B–D. fewer cardiac arrests were witnessed by healthcare personnel in

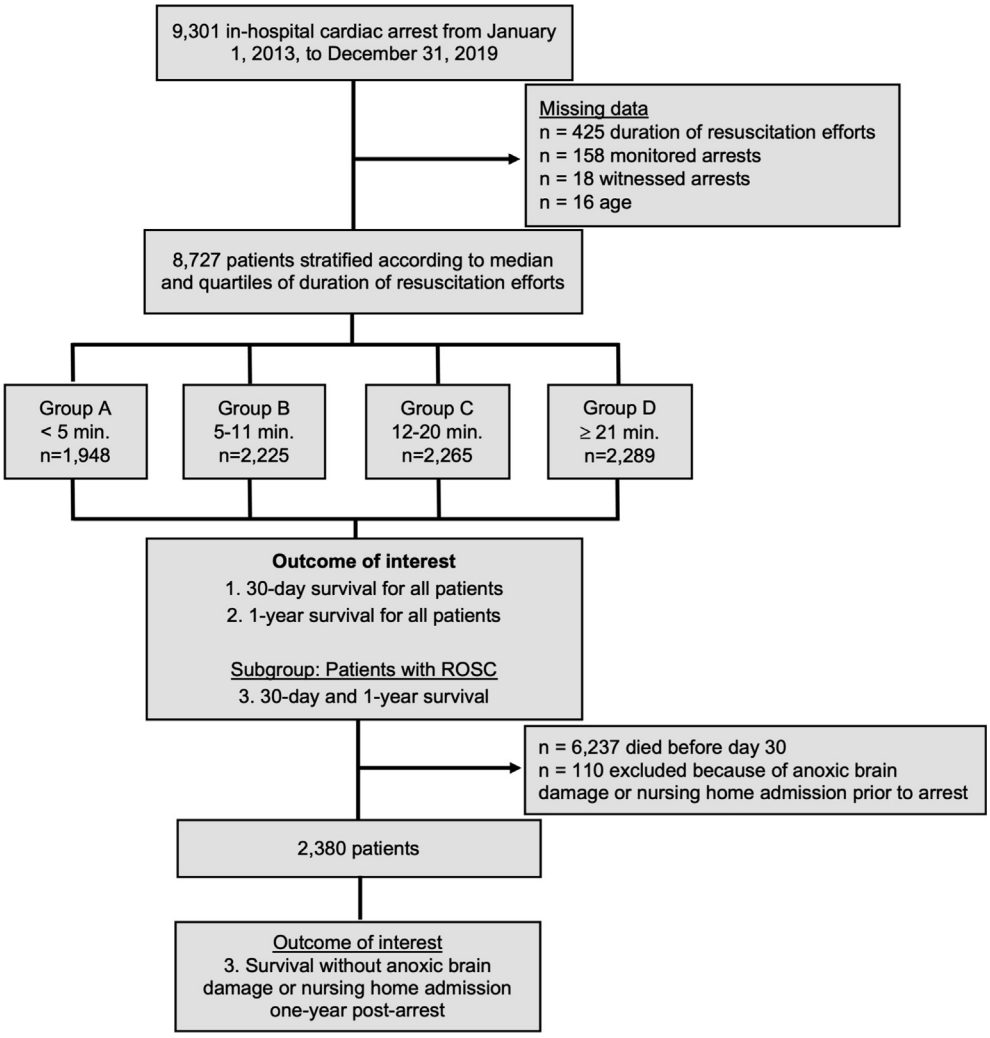

Fig. 1 – Flowchart over the patient selection process and outcome of interest. Min indicates minutes; ROSC indicates return of spontaneous circulation.

group D compared to group A (75.8% vs 91.7%) and fewer patients were monitored (43.4% vs 66.8%). Median time of arrival of the rapid response team was 180 seconds for group B–D while it was 120 seconds for group A. Proportion of patients with an initial non-shockable rhythm was also higher for group B–D (ranging between 77.9–87.9%) compared to group A (44.5%).

30-day survival across different durations of resuscitation

Thirty-day survival was highest for the group of patients with the shortest duration of resuscitation (group A) with a standardized absolute survival of 62.0% (95% CI 59.8–64.2%). This decreased to 32.7% (95% CI 30.8–34.6%) for group B (5–11 minutes), 14.4% (95% CI 12.9–15.9%) for group C (12–20 minutes) while the group with the longest duration of resuscitation (group D) had a standardized absolute survival of 8.1% (95% CI 7.0–9.1%) (Fig. 2). The standardized relative ratio (RR) of 30-day survival for group D was 0.13 (95% CI 0.11–0.15, *p*-value <0.001) compared to group A.

One-year survival across different durations of resuscitation

Similar to 30-day survival, one-year survival was highest in group A with a standardized absolute survival of 50.4% (95% CI 48.2–52.6%) decreasing to 25.1% (95% CI 23.3–26.9%) in group B, 11.1% (95% CI 9.7–12.5%) in group C and 6.6% (95% CI 5.6–7.6%) in group D (Fig. 3). The one-year survival was halved for patients who were resuscitated for 5–11 minutes (group B) compared to patients resuscitated for less than 5 minutes (group A) (RR 0.50; 95% CI 0.46–0.54, *p*-value <0.001) and one-fifth for patients resuscitated for 11–20 minutes compared with group A (RR 0.22; 95% CI 0.19–0.25, *p*-value <0.001).

One-year survival without anoxic brain damage or nursing home admission among 30-day survivors across different durations of resuscitation

This study population of 2,380 patients consisted of 30-day IHCA survivors without anoxic brain damage or nursing home admission prior to arrest. Among these, the standardized absolute survival without anoxic brain damage or nursing home admission within one-year post-arrest was highest for patients resuscitated in less than five minutes (group A) (80.4%; 95% CI 78.2–82.6%), 73.3% (95% CI 70.0–76.6%) for patients whom duration of resuscitation lasted 5–11 minutes (group B), 67.2% (95% CI 61.7–72.6%) for group C and 73.3% (95% CI 66.9–79.7%) for group D (Fig. 4).

Table 1 – Baseline patient and cardiac arrest characteristics for the primary population (n = 8,727).

Variable	Level	<5 min. (*n* = 1948)	5–11 min. (*n* = 2225)	11–20 min. (*n* = 2265)	>21 min. (*n* = 2289)
Age	Median [iqr]	72.1 [62.1, 79.7]	74.9 [66.4, 82.5]	74.5 [66.3, 82.0]	72.9 [63.7, 80.2]
Sex	Male	1209 (62.1)	1376 (61.8)	1431 (63.2)	1493 (65.2)
Charlson Index score	1	636 (32.6)	505 (22.7)	474 (20.9)	617 (27.0)
	2	703 (36.1)	761 (34.2)	801 (35.4)	793 (34.6)
	≥3	609 (31.3)	959 (43.1)	990 (43.7)	879 (38.4)
Witnessed arrest	By health care personnel	1,786 (91.7)	1,709 (76.8)	1,483 (65.5)	1,735 (75.8)
	By layman	33 (1.7)	69 (3.1)	57 (2.5)	68 (3.0)
	No	129 (6.6)	447 (20.1)	725 (32.0)	486 (21.2)
Monitored arrest	No	646 (33.2)	1273 (57.2)	1518 (67.0)	1296 (56.6)
Place of arrest	Internal medicine/surgical ward	943 (48.5)	1,380 (62.1)	1,597 (70.5)	1,425 (62.3)
	Emergency department	337 (17.3)	331 (14.9)	297 (13.1)	370 (16.2)
	Outpatient department	31 (1.6)	25 (1.1)	16 (0.7)	18 (0.8)
	Cardiac cath lab	210 (10.8)	60 (2.7)	53 (2.3)	115 (5.0)
	Operating room	93 (4.8)	52 (2.3)	27 (1.2)	41 (1.8)
	Recovery room	37 (1.9)	26 (1.2)	16 (0.7)	17 (0.7)
	Intensive care unit	214 (11.0)	234 (10.5)	179 (7.9)	177 (7.7)
	Other	81 (4.2)	115 (5.2)	79 (3.5)	124 (5.4)
	Missing	2 (0.1)	2 (0.1)	1 (0.04)	2 (0.1)
Time to alert of the rapid response team	Median, sec. [iqr]	0 [0, 60]	0 [0, 60]	0 [0, 60]	0 [0, 120]
	Missing	215 (11.0)	134 (6.0)	114 (5.0)	148 (6.5)
Time to arrival of the rapid response team	Median, sec. [iqr]	120 [60, 180]	180 [120, 240]	180 [120, 300]	180 [120, 300]
	Missing	218 (11.2)	120 (5.4)	87 (3.8)	123 (5.4)
Time to CPR	Median, sec. [iqr]	0 [0, 0]	0 [0, 0]	0 [0, 0]	0 [0, 0]
	Missing	217 (11.1)	46 (2.1)	36 (1.6)	31 (1.4)
CPR prior to arrival of rapid response team	Yes	336 (17.2)	556 (25.0)	529 (23.4)	526 (23.0)
Initial rhythm on arrival of the rapid response team	Non-shockable	779 (44.5)	1,631 (77.9)	1,945 (87.9)	1,911 (85.0)
	Shockable	630 (36.0)	363 (17.3)	234 (10.6)	299 (13.3)
	ROSC	343 (19.6)	99 (4.7)	35 (1.6)	38 (1.7)
	missing	196 (10.1)	132 (5.9)	51 (2.3)	41 (1.8)
Detailed rhythm analysis	Asystole	355 (21.0)	713 (35.3)	1,008 (46.5)	753 (34.0)
	Pulseless electrical activity	376 (22.2)	863 (42.8)	895 (41.3)	1134 (51.2)
	Ventricular fibrillation	393 (23.2)	240 (11.9)	163 (7.5)	213 (9.6)
	Ventricular tachycardia	227 (13.4)	103 (5.1)	65 (3.0)	77 (3.5)
	ROSC	343 (20.2)	99 (4.9)	35 (1.6)	38 (1.7)
	missing	254 (13.3)	207 (9.3)	99 (4.4)	74 (3.2)
Defibrillated	Yes	391 (22.3)	228 (11.3)	180 (8.8)	239 (12.7)
	missing	194 (10.0)	205 (9.2)	225 (9.9)	405 (17.7)
Amiodarone given	Yes	155 (8.0)	139 (6.2)	177 (7.8)	335 (14.6)
Adrenaline given	Yes	441 (22.6)	1559 (70.1)	2054 (90.7)	2171 (94.8)
Mechanical CPR	Yes	30 (1.5)	66 (3.0)	129 (5.7)	409 (18.0)
	missing	7 (0.4)	12 (0.5)	16 (0.7)	20 (0.9)
Status after termination of resuscitation	ROSC	1,844 (95.1)	1,445 (65.4)	807 (35.8)	508 (22.3)
	Death	88 (4.5)	753 (34.1)	1432 (63.6)	1715 (75.3)
	ECMO	6 (0.3)	11 (0.5)	14 (0.6)	54 (2.4)
	missing	10 (0.5)	16 (0.7)	12 (0.5)	12 (0.5)

All proportions exclude missing data.

*min. – minutes, † iqr – interquartile range, ‡ – Charlson comorbidity score explained: 1 (patients scoring 0), 2 (patients scoring 1 or 2), 3 (patients scoring > 2), § – sec. - seconds, ¶ - CPR – cardiopulmonary resuscitation.

Compared with group A, the relative ratio of 1-year survival without anoxic brain damage or nursing home admission was lower for group B (RR 0.91; 95% CI 0.86–0.96, *p*-value <0.001) and group C (RR 0.84; 95% CI 0.76–0.91, *p*-value <0.001). It was also lower for group D (RR 0.91; 95% CI 0.83–99, *p*-value 0.037).

30-day and 1-year survival among patients with return of spontaneous circulation across different durations of resuscitation

As mentioned previously, 4,604 patients achieved ROSC and among these, the standardized absolute 30-day survival was 69.8% (95% CI

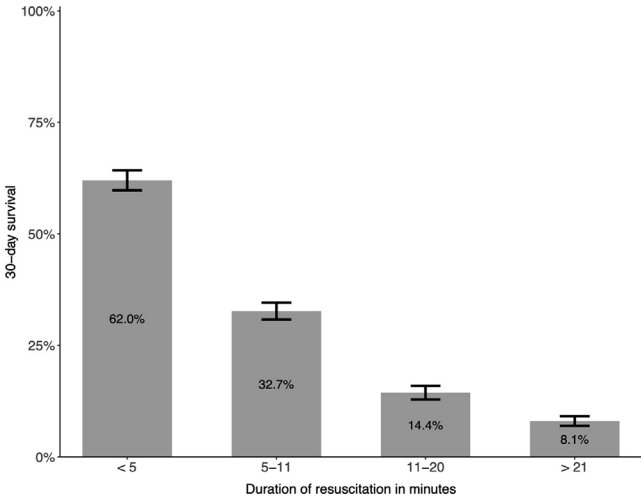

Fig. 2 – Standardized absolute 30-day survival according to duration of resuscitation. Error bars show 95% confidence intervals. N = 8,727.

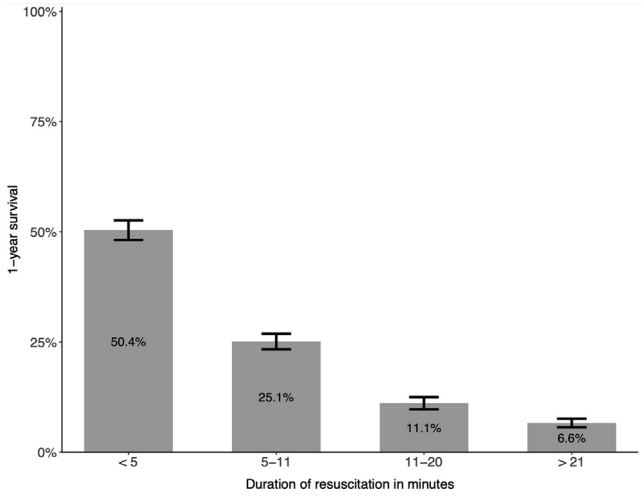

Fig. 3 – Standardized absolute 1-year survival according to duration of resuscitation attempt. Error bars show 95% confidence intervals. N = 8,727.

67.7–71.9%) for group A, 48.5% (95% CI 46.0–51.0%) for group B, 33.9% (95% CI 30.7–37.1%) for group C and 31.1% (95% CI 27.2–35.0%) for group D (Fig. 5 in Supplemental Material).

The standardized 1-year survival was 57.7% (95% CI 55.5–60.0%) for group A, 37.4% (95% CI 34.9–39.8%) for group B, 25.9% (95% CI 22.9–28.9%) for group C and 24.6% (95% CI 21.0–28.3%) for group D (Fig. 6 in Supplemental Material).

Discussion

The main result of this study was that among 8,727 in-hospital cardiac arrest patients we found that the overall 30-day and 1-year survival was highest for patients with the shortest duration from cardiac arrest to ROSC. Furthermore, we found that, among 30-day survivors of an IHCA, the 1-year survival without anoxic brain damage

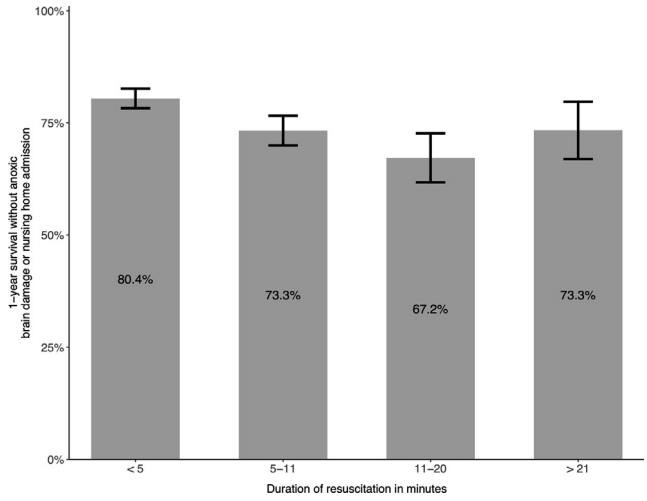

Fig. 4 – Standardized absolute 1-year survival without anoxic brain damage or nursing home admission among 30-day survivors according to duration of resuscitation. Error bars show 95% confidence intervals. N = 2,380.

or admission to a nursing home was high regardless of the duration of the resuscitation attempt, ranging from 67% to 80%. These findings are interesting as there are few studies on the effect of resuscitation duration on outcome and even fewer on long-term outcome measures such as survival and functional status of patients in the months and years after cardiac arrest. Until now, previous research has primarily reported survival and neurological function at hospital discharge, however such short-term outcome measures are not adequate as it is known that the risk of death as well as fluctuations in neurological function are highest in the first three months post-arrest.[4,10–12] It is important to look at the neurological function beyond this period and our study contributes with this and provides new insight into the association between duration of resuscitation and long-term outcomes.

In an observational study from Sweden, Rohlin and colleagues investigated the impact of CPR duration on 30-day survival for patients achieving ROSC.[13] Similar to this study, they found that shorter CPR duration was associated with higher odds for 30-day survival. However, more interestingly they found that, among patients with the longest duration of resuscitation (≥13 minutes), survival ratio was still up to 30%, concluding that CPR duration is a poor prognostic marker for patients achieving ROSC [13]. In our study, we found the absolute 30-day survival to be 31.1% and 1-year survival of 24.6% in the group of patients resuscitated for 21 or more minutes (Figs. 2 and 3). Furthermore, we were also able to show that, among 30-day survivors, 1-year survival without long-term complications such as anoxic brain damage or nursing home admission was high even with longer duration of resuscitation.

One of the key areas for future research to increase survival after IHCA is identifying which patients will benefit from prolonged resuscitation and, just as important, to identify patient- and cardiac arrest characteristics that are associated with a worse outcome. The need to identify these factors to support clinical bedside decision-making was highlighted in a study which found that under half of medical students, residents and attending physicians were able to accurately assess the probability of survival after an IHCA.[14]

In a study by Khan et al., factors associated with duration of resuscitation were investigated.[15] They found that lower age and female sex was associated with longer duration of resuscitation in patients who did not experience ROSC. This could possibly be related to a perception among clinicians that these groups have a higher likelihood of survival. However, previous research shows conflicting results with regard to the association between sex and outcome after IHCA, warranting further research into this topic.[16–18]

This study has limitations. First of all, this was an observational study and therefore, the reported associations may not be causal.

The diagnosis code of anoxic brain damage has not been validated previously. However, the majority of hospitals included in this study have neurological wards and all hospitals have the possibility to acquire a neurologist for prognostication and evaluation. A strength of the study was the low number of missing data on the exposure measure which was the duration of resuscitation. While this variable has not been validated before, data on the cardiac arrest is usually registered by a team member of the rapid response team once the resuscitation attempt has ended.

Conclusion

In conclusion, shorter duration of resuscitation attempt during an IHCA is associated with higher 30-day and 1-year survival. Furthermore, we found that the large majority of 30-day survivors were still alive 1-year post-arrest without anoxic brain damage or nursing home admission despite prolonged resuscitation.

CRediT authorship contribution statement

Kragholm: Conceptualization, formal analysis, methodology, supervision, writing - review and editing.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: 'Dr. Kragholm reports having received research grants from the Laerdal foundation. All other authors declare no conflict of interest.'.

Acknowledgements

We would like to acknowledge the national Danish In-Hospital Cardiac Arrest Registry (DANARREST) which is managed by the Danish Clinical Quality Program (RKKP) for access to data.

Sources of Funding

This study was supported by the Danish foundation TrygFonden (Grant No.: 154943) which has no commercial interests in the field of cardiac arrest. TrygFonden had no influence on the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the article for submission.

Appendix A. Supplementary material

Supplementary material to this article can be found online at https://doi.org/10.1016/j.resuscitation.2022.08.011.

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