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Age-dependent trends in survival after adult in-hospital cardiac arrest

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Abstract

Background—While survival after in-hospital cardiac arrest (IHCA) has improved in recent years, it remains unknown whether this trend primarily applies to younger IHCA victims. The aim of this study was to assess trends in survival to hospital discharge after adult IHCA across age groups from 2000 to 2016.

Methods—This is an observational study of IHCA patients included in the Get With The Guidelines®-Resuscitation registry between 2000 and 2016. The primary outcome was survival to hospital discharge. Patients were stratified into five age groups: <50 years, 50–59 years, 60–69 years, 70–79 years, and ≥80 years. Generalized linear regression was used to obtain absolute survival rates over time.

Results—A total of 234,767 IHCA patients were included. The absolute increase in survival per calendar year was 0.8% (95% CI 0.7–1.0%, $p < 0.001$) for patients younger than 50 years, 0.6% (95% CI 0.4–0.7%, $p < 0.001$) for patients between 50 and 59 years, 0.5% (95% CI 0.4–0.6%, $p < 0.001$) for patients between 60 and 69 years, 0.5% (95% CI 0.4–0.6%, $p < 0.001$) for patients between 70 and 79 years, and 0.5% (95% CI 0.4–0.6%, $p < 0.001$) for patients older than 80 years.

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Conflict of interest statement

The authors declare that they have no conflicts of interest in relation to this manuscript.

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.2020.03.008>.

We observed a significant interaction between calendar year and age group ($p < 0.001$), indicating that the rate of improvement in survival over time was significantly different between age groups.

Conclusions—For patients with IHCA, rates of survival to discharge have improved significantly from 2000 to 2016 across all age groups.

Keywords

In-hospital cardiac arrest; Age; Survival

Introduction

In-hospital cardiac arrest (IHCA) remains a leading cause of death, with approximately 290,000 annual treated cases reported from 2008 to 2017 in the United States.¹ While mortality remains high, overall survival to hospital discharge after IHCA increased from approximately 17% in 2000 to approximately 25% in 2016.²

Increasing age is a well-known determinant of poor outcome in critical illness, including out-of-hospital cardiac arrest (OHCA) and IHCA.^{3–7} While IHCA survival has improved over the past decade, it is unknown whether that trend applies primarily to younger IHCA patients or extends to older patients as well. Exploring the relationship between age and survival trends in IHCA is essential to the development of focused IHCA treatment and prognostication tools.

The aim of the current study was to assess and compare trends in survival to hospital discharge after adult IHCA across age groups from 2000 to 2016. We hypothesized that improved overall survival trends after IHCA would mainly be driven by improved survival in younger age groups. Secondly, we aimed to assess trends in return of spontaneous circulation (ROSC) and survival with good neurological outcome across age groups from 2000 to 2016.

Methods

This study was an analysis of data from the Get with the Guidelines®-Resuscitation (GWTG-R) registry from January 1, 2000 through December 31, 2016.

Data source

The GWTG-R is a prospective, quality improvement registry including data on IHCA in United States hospitals. The design of the registry has been described in detail previously.⁸ Briefly, trained personnel include all IHCA patients, who do not have a do-not-resuscitate (DNR) order. IHCA is defined as the absence of a palpable central pulse, apnea, and unresponsiveness with a hospital-wide or unit-based emergency response by trained personnel. Standardized definitions for patient variables and outcomes are applied in accordance with the Utstein criteria.⁹ Data integrity is ensured by certification of hospital staff and the use of standardized software for data checks for accuracy and completeness. The American Heart Association sponsors the registry. Hospital-level data were obtained from the 2013 American Hospital Association Annual Survey,¹⁰ which were linked to the

GWTC-R registry. IQVIA is the data collection coordination center for the American Heart Association and American Stroke Association Get With Guidelines programs. All participating hospitals are required to adhere to local regulatory guidelines. The local Institutional Review Board has confirmed that the use of GWTC-R data does not meet the definition for human subjects research in the absence of identifiable subject data.

Patients and outcomes

Adult patients (age ≥ 18 years) with an index cardiac arrest requiring chest compressions and/or defibrillation were included irrespective of initial rhythm. Hospital visitors and employees were excluded, and patients with missing data on the primary outcome and covariates were excluded from the primary analyses.

The primary outcome was survival to hospital discharge. The secondary outcome was sustained return of spontaneous circulation (ROSC), defined as the presence of a pulse and no further need for chest compressions for at least 20 min, including initiation of cardiopulmonary bypass or extracorporeal membrane oxygenation, and good neurological outcome at hospital discharge, defined as a cerebral performance category score of 1 to 2.¹¹

Statistical analysis

Throughout, categorical variables are presented as counts (frequencies), whereas continuous variables are presented as medians (25th percentile – 75th percentile). Patients were stratified *a priori* in 5 groups according to age: <50 years, 50–59 years, 60–69 years, 70–79 years, and ≥ 80 years. Age <50 years was chosen as the lowest age group based on previously published results suggesting that survival after OHCA begins to decrease at approximately 50 years.⁶

To assess unadjusted survival trends over time by age group, we applied linear regression models to obtain absolute survival estimates, presented as percent with 95% confidence intervals for each calendar year. We aimed to apply multivariable linear regression models to obtain adjusted risk estimated, but the models were not able to converge. Therefore, we applied multivariable modified Poisson regression models to obtain relative risk (RR) estimates with 95% confidence intervals using the year 2000 as the reference year.^{12,13} The modified Poisson regression models were adjusted for predefined suspected confounding and/or mediating variables, including demographics, admission diagnosis, pre-existing comorbidities, therapeutic interventions in place at time of arrest, arrest characteristics, and hospital characteristics (Table S1). For both the univariable linear regression models and for the multivariable modified Poisson regression models, we applied generalized estimating equations (GEE) to account for clustering of patients within individual hospitals.

The linear models and the modified poisson regression models were repeated with calendar year being included as a continuous covariate assuming a linear trend. These derived the change in survival per calendar year for each age group. In order to assess whether the change in survival per calendar year was significantly different between age groups, we included the interaction term ‘age group’*‘calendar year’ in linear as well as modified poisson regression models.

We repeated the described models for the secondary outcomes (ROSC and survival with a good neurological outcome at discharge). Further, we repeated the analyses in a subgroup of patients who achieved ROSC, as an indicator of survival in the postcardiac arrest phase.

To account for missing data in the primary analysis, we applied multiple imputations as a sensitivity analysis under the assumption that data were ‘missing at random’. Data were imputed using the fully conditional specification method,¹⁴ and a total of 20 imputed datasets were created.¹⁵ See Supplementary appendix for further details. A two-sided significance level of 0.05 was assumed throughout. All analyses were performed with the use of SAS software, version 9.4 (SAS Institute, Cary, NC, USA).

Results

Patient characteristics

The study population consisted of 234,767 IHCA patients (Fig. 1), of whom 36,306 (15%) were younger than 50 years at admission, 39,067 (17%) were between 50 and 59 years, 53,249 (23%) were between 60 and 69 years, 57,285 (24%) were between 70 and 79 years, and 48,860 (21%) were older than 80 years (Table 1). Patient characteristics, cardiac arrest characteristics, and hospital characteristics can be viewed in Tables 1–3, respectively.

Temporal trends in survival to hospital discharge

The absolute survival to discharge rate after IHCA in the year 2016 was 28.9% (27.0–31.0) for patients younger than 50 years, 28.3% (26.4–30.3) for patients between 50 and 59 years, 27.2% (25.7–28.8) for patients between 60 and 69 years, 23.6% (21.8–25.6) for patients between 70 and 79 years, and 18.0% (16.3–19.8) for patients older than 80 years (Fig. 2).

The absolute improvement in survival rates per calendar year were 0.8% (0.7–1.0%, $p < 0.001$) for patients younger than 50 years, 0.6% (0.4–0.7%, $p < 0.001$) for patients between 50 and 59 years, 0.5% (0.4–0.6%, $p < 0.001$) for patients between 60 and 69 years, 0.5% (0.4–0.6%, $p < 0.001$) for patients between 70 and 79 years, and 0.5% (0.4–0.6%, $p < 0.001$) for patients older than 80 years (Fig. 2). We observed a significant interaction between age group and calendar year ($p < 0.001$), indicating that the presented rates of improvement in survival over time were significantly different between age groups (Fig. 2).

After adjustment for demographics, admission diagnosis, pre-existing comorbidities, therapeutic interventions in place at time of arrest, arrest characteristics, and hospital characteristics (Table S1), the relative risk of survival per calendar year ranged from 1.02 to 1.03 through all age groups (Fig. S1). We observed a significant interaction between age group and calendar year ($p < 0.001$) in the adjusted model, indicating that the presented rates of improvement in survival over time were significantly different between age groups (Fig. S1).

Temporal trends in ROSC

The absolute improvement in ROSC rates per calendar year was 1.5% (1.4–1.7%, $p < 0.001$) for patients younger than 50 years, 1.4% (1.2–1.5%, $p < 0.001$) for patients between 50 and 59 years, 1.3% (1.1–1.4%, $p < 0.001$) for patients between 60 and 69 years, 1.3% (1.1–1.5%,

$p < 0.001$) for patients between 70 and 79 years, and 1.5% (1.3–1.7%, $p < 0.001$) for patients older than 80 years (Fig. 3). The improvement in ROSC rates over time were significantly different between age groups ($p < 0.001$, Fig. 3).

After adjustment, the relative risk of ROSC per calendar year was 1.02 through all age groups (Fig. S2), with no significant difference between age groups.

Temporal trends in rates of good neurological outcome

The absolute improvement in rates of good neurological outcome per calendar year were 0.5% (0.3–0.7%, $p < 0.001$) for patients younger than 50 years, 0.2% (0.03–0.4%, $p = 0.02$) or patients between 50 and 59 years, 0.2% (0.01–0.3%, $p = 0.04$) for patients between 60 and 69 years, 0.2% (0.03–0.3%, $p = 0.02$) for patients between 70 and 79 years, and 0.2% (0.07–0.3%, $p = 0.002$) for patients older than 80 years (Fig. S3). The improvement in good neurological outcome over time was significantly different between age groups ($p < 0.001$, Fig. S3).

After adjustment, the relative risk of good neurological outcome per calendar year ranged from 1.02–1.03 through all age groups (Fig. S4), with a significant difference between age groups ($p < 0.001$).

Temporal trends in survival in patients achieving ROSC

In the 150,570 (64%) patients achieving ROSC, the absolute improvement in survival rates per calendar year was 0.4% (0.2–0.6%, $p < 0.001$) for patients younger than 50 years, 0.08% (–0.1 to 0.3%, $p = 0.41$) for patients between 50 and 59 years, 0.05% (–0.1 to 0.2%, $p = 0.53$) for patients between 60 and 69 years, 0.1% (–0.03 to 0.3%, $p = 0.10$) for patients between 70 and 79 years, and 0.2% (0.01–0.4%, $p = 0.04$) for patients older than 80 years (Fig. S5). The improvement in survival over time in patients achieving ROSC was significantly different between age groups ($p < 0.001$, Fig. S3).

After adjustment, the relative risk of survival per calendar year in patients having achieved ROSC ranged from 1.01 to 1.02 ($p < 0.001$) through all age groups (Fig. S6), with a significant difference between age groups ($p < 0.001$).

Discussion

The present study found that rates of ROSC, survival to hospital discharge, and survival to discharge with good neurological outcome after IHCA have improved between 2000 and 2016 across all age groups from patients younger than 50 years to patients older than 80 years. These findings were robust to statistical adjustment for potential confounding and/or mediating factors.

The ongoing effort to improve survival after cardiac arrest is manifest in the recommendations published by the International Liaison Committee on Resuscitation (ILCOR) every fifth year since 2000. The recommendations focus on all aspects of cardiac arrest treatment from early detection and treatment to post resuscitation care.¹⁶ While in-hospital survival after IHCA^{17,18} and OHCA^{19–21} has been improving in recent years, and

previous retrospective studies have suggested improved survival after guideline updates,^{22,23} any possible causality between implementation of guidelines and survival is unknown.

Older age has previously been associated with poor outcome after OHCA as well as IHCA,^{6,7} and our analyses confirmed this finding. However, information on whether IHCA survival is improving over time in older age groups has been limited. Our results demonstrate that while survival rates are lower among older patients, even octogenarians have experienced a significant improvement in survival rate since the year 2000. Furthermore, successful resuscitation is feasible, with 18% of patients in this age group surviving to hospital discharge in the year 2016. The likelihood of survival with good neurological outcome at discharge in this group was 11%, however, the rate of neurological recovery likely improves over time similarly to what has been reported in OHCA patients.²⁴

The improvement in survival, ROSC rates, and good neurological outcome was seen in unadjusted as well as adjusted analyses, which suggests that the outcome after IHCA has improved irrespective of temporal changes in patient, event, and hospital-related characteristics, such as comorbidity, shockable rhythm, type of hospital, etc. (Table 1–3). In the proportion of patients who did achieve ROSC, improved survival over time was seen in all age groups only in adjusted analyses. One potential explanation for this could be that ROSC has been achieved in patients with less favorable demographics and/or cardiac arrest characteristic over time, which accordingly could have biased the unadjusted analyses towards the null.

Survival rates were significantly higher in the youngest patients compared to the remainder of the cohort, a finding which was robust to adjustment for potential confounding and mediating variables. This suggests that survival improved at a faster rate in younger patients, irrespective of temporal changes in patient, event, and hospital-related characteristics, such as comorbidity, shockable rhythm, type of hospital, etc. (Table 1–3). Overall, the temporal differences in increased survival rates between age groups could be related to a combination of changing population characteristics, changing treatment protocols, and/or changing attitudes towards initiation and completion of resuscitative efforts. Although speculative, the faster increase in survival among younger patients could indicate that this age group to a higher extent has benefitted from novel treatment modalities and guidelines throughout all phases from pre- to post-arrest. The slower rate of improvement in older patients may also be due to less reversibility of the disease process in elderly patients.

The presented results should be interpreted in light of the following limitations. While we were able to adjust the analyses for a number of potential confounding and mediating variables, residual confounding or mediation including the underlying pathophysiology of the cardiac arrest, the quality of care and post resuscitation treatment may be present. For example, patients with a DNR order are not included in the GWTG-R register, and temporal changes in DNR orders could change the selection of GWTG-R patients over time. Accordingly, improved survival trends may not wholly represent a treatment effect, but could be caused by a gradual selection of healthier patients with a higher treatment potential, not captured by the included confounders/ mediators. Finally, the hospitals providing data to the GWTG-R registry may not be representative of other hospitals in the US or hospitals in

other countries, which may limit generalizability. While we show that survival has improved at a significantly faster rate in younger age groups, even after adjustment for potential confounding and mediating factors, the present study does not address potential modifiable causes for improved survival, which could be the focus for future studies.

In conclusion, rates of ROSC, survival to discharge, and good neurological outcome after IHCA have improved significantly from 2000 to 2016, across all age groups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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Fig. 1 -

Consort diagram displaying exclusion and inclusion for the primary analysis. Between 2000 and 2017, 333,295 adult in-hospital cardiac arrests were registered in the Get With The Guidelines-Resuscitation registry. We included 234,767 for the primary analysis.

Fig. 2 -

Survival trends, stratified by age group. The figure illustrates trends in survival to hospital discharge from 2000 to 2016. Results are reported as absolute risks with 95% confidence intervals.

Fig. 3 -
Return of spontaneous circulation, stratified by age group. The figure illustrates trends in return of spontaneous circulation from 2000 to 2016. Results are reported as absolute risks with 95% confidence intervals.

Table 1 –

Patient characteristics, stratified according to age group.

	Age group				
	<50 years	50–59 years	60–69 years	70–79 years	80 years
	36,306 (15%)	39,067 (17%)	53,249 (23%)	57,285 (24%)	48,860 (21%)
<i>Patient characteristics</i>					
Male sex	21,421 (59)	24,206 (62)	32,303 (61)	33,311 (58)	25,519 (52)
Age in years, median (IQR) ^a	41 (33–46)	55 (53–57)	65 (62–67)	75 (72–77)	84 (82–88)
<i>Illness category:</i>					
<i>Medical</i>					
Cardiac	9,482 (26)	13,457 (34)	19,819 (37)	22,141 (39)	19,960 (41)
Non-cardiac	17,995 (50)	18,087 (46)	22,563 (42)	22,527 (29)	19,805 (41)
<i>Surgical</i>					
Cardiac	1,482 (4.0)	2,352 (6.0)	4,160 (7.8)	4,903 (8.6)	2,797 (5.7)
Non-cardiac ^b	3,785 (10)	4,007 (10)	5,740 (11)	6,791 (12)	5,341 (11)
Trauma	3,562 (9.8)	1,164 (3.0)	967 (1.8)	923 (1.6)	957 (2.0)
<i>Pre-existing conditions:</i>					
<i>Acute stroke</i>					
	960 (2.6)	1,431 (3.7)	2,162 (4.1)	2,531 (4.4)	2,111 (4.3)
<i>Acute non-stroke CNS^c event</i>					
	3,527 (9.7)	2,954 (7.6)	3,480 (6.5)	3,683 (6.4)	3,258 (6.7)
<i>Baseline depression in CNS^c</i>					
	3,960 (11)	3,754 (9.6)	4,747 (8.9)	6,169 (11)	6,643 (14)
<i>Heart failure prior admission</i>					
	4,150 (11)	6,769 (17)	11,580 (22)	14,395 (25)	13,190 (27)
<i>Heart failure this admission</i>					
	3,760 (10)	5,528 (14)	9,047 (17)	11,143 (19)	9,890 (20)
<i>Myocardial infarction prior admission</i>					
	2,278 (6.3)	5,183 (13)	9,081 (17)	11,068 (19)	8,965 (18)
<i>Myocardial infarction this admission</i>					
	3,460 (9.5)	6,225 (16)	9,524 (18)	10,560 (18)	8,660 (18)
<i>Diabetes</i>					
	7,365 (20)	12,675 (32)	20,210 (38)	20,508 (36)	12,812 (26)
<i>Metastatic malignancy</i>					
	3,600 (9.9)	5,012 (13)	7,162 (13)	7,309 (13)	4,508 (9.2)
<i>Hypotension</i>					
	10,999 (30)	10,908 (28)	14,274 (27)	14,979 (26)	11,792 (24)
<i>Respiratory insufficiency</i>					
	16,425 (45)	17,309 (44)	23,785 (45)	25,015 (44)	19,053 (39)
<i>Hepatic insufficiency</i>					
	4,322 (12)	5,033 (13)	4,209 (7.9)	2,675 (4.7)	1,347 (2.8)
<i>Renal insufficiency</i>					
	11,233 (31)	13,516 (35)	19,255 (36)	20,603 (36)	15,762 (32)

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	Age group				
	<50 years	50–59 years	60–69 years	70–79 years	80 years
Metabolic abnormality	8,123 (22)	7,960 (20)	9,680 (18)	9,580 (17)	7,028 (14)
Pneumonia	5,058 (14)	5,055 (13)	6,923 (13)	7,927 (14)	7,365 (15)
Septicemia	7,318 (20)	7,490 (19)	9,156 (17)	8,666 (15)	6,671 (14)

^aInter quartile range.
^bIncludes non-cardiac surgical patients, and obstetric patients.
^cCentral nervous system.

Table 2 –

Cardiac arrest characteristics, stratified according to age group.

	Age group				
	<50 years	50–59 years	60–69 years	70–79 years	80 years
	36,306 (15%)	39,067 (17%)	53,249 (23%)	57,285 (24%)	48,860 (21%)
<i>Cardiac arrest characteristics</i>					
Interventions in place before arrest:					
Assisted or mechanical ventilation	15,463 (43)	13,865 (35)	17,484 (33)	16,755 (29)	11,469 (23)
Vasopressor support	10,347 (29)	10,621 (27)	14,026 (26)	14,082 (25)	9,800 (20)
Implantable cardiac defibrillator	485 (1.3)	701 (1.8)	1,124 (2.1)	1,180 (2.1)	666 (1.4)
Dialysis	1,586 (4.4)	1,526 (3.9)	2,073 (3.9)	1,851 (3.2)	804 (1.7)
Location:					
Emergency department	5,229 (14)	4,663 (12)	5,487 (10)	5,127 (9.0)	4,918 (10)
Intensive care unit	20,048 (55)	20,391 (52)	27,172 (51)	27,657 (48)	19,832 (41)
Operating room	2,418 (6.7)	2,699 (6.9)	3,608 (6.8)	3,597 (6.3)	2,732 (5.6)
Floor					
With telemetry	3,519 (9.7)	5,044 (13)	8,318 (16)	10,812 (19)	10,917 (22)
Without telemetry	4,400 (12)	5,604 (14)	7,714 (14)	8,976 (16)	9,550 (20)
Other ^a	692 (1.9)	666 (1.7)	950 (1.8)	1,116 (2.0)	911 (1.9)
Time:					
Weekend ^b	11,764 (32)	12,173 (31)	16,069 (30)	17,355 (30)	15,301 (31)
Nighttime ^c	11,845 (33)	12,407 (32)	16,522 (31)	17,926 (31)	15,877 (32)
Witnessed arrest	31,719 (87)	33,511 (86)	45,607 (86)	48,149 (84)	39,203 (80)
Hospital response team activated	11,823 (33)	10,581 (27)	12,985 (24)	11,856 (21)	8,985 (18)
Initial shockable rhythm	6,579 (18)	8,336 (21)	11,396 (21)	11,487 (20)	8,314 (17)

^aIncluding ambulatory or outpatient clinics, diagnostic or interventional areas, operating room, post-anesthesia recovery room, rehabilitation unit, same-day surgical area, and delivery room.^bFriday 11 PM to Monday 7 AM.^c11:00 PM to 6:59 AM.

Table 3 –

Hospital characteristics, stratified according to age group.

	Age group			
	<50 years	50–59 years	60–69 years	70–79 years
	36,306 (15%)	39,067 (17%)	53,249 (23%)	57,285 (24%)
				48,860 (21%)
<i>Hospital characteristics</i>				
Geographic region:				
Northeast	4,919 (14)	5,337 (14)	7,934 (15)	8,935 (16)
				8,944 (18)
Southeast	9,802 (27)	10,651 (27)	15,188 (29)	16,600 (29)
				13,860 (28)
Midwest	7,826 (22)	8,594 (22)	11,399 (21)	12,811 (22)
				10,603 (22)
Southwest	8,328 (23)	8,753 (22)	11,112 (21)	10,801 (19)
				8,316 (17)
West	5,431 (15)	5,732 (15)	7,617 (14)	8,138 (14)
				7,137 (15)
Geographic location:				
Urban	34,951 (96)	37,384 (96)	50,778 (95)	54,136 (95)
				46,191 (95)
Rural	1,355 (3.7)	1,683 (4.3)	2,471 (4.6)	3,149 (5.5)
				2,669 (5.5)
Ownership:				
Private	3,698 (10)	4,105 (11)	5,601 (11)	6,141 (11)
				5,649 (12)
Government	7,736 (21)	7,280 (19)	8,499 (16)	7,536 (13)
				5,648 (12)
Non-profit	24,613 (68)	26,886 (69)	37,910 (71)	42,540 (74)
				36,793 (75)
Military	259 (0.7)	796 (2.0)	1,239 (2.3)	1,068 (1.9)
				770 (1.6)
Teaching status:				
Major	17,683 (49)	17,209 (44)	21,511 (40)	19,519 (34)
				14,668 (30)
Minor	9,444 (26)	10,985 (28)	15,719 (30)	18,184 (32)
				16,249 (33)
Non-teaching	9,179 (25)	10,873 (28)	16,019 (30)	19,582 (34)
				17,943 (37)
Size:				
<250 beds	5,361 (15)	6,390 (16)	9,181 (17)	10,615 (19)
				9,955 (20)
250–499 beds	12,677 (35)	14,378 (37)	20,428 (38)	23,477 (41)
				20,786 (43)
500 beds	18,268 (50)	18,299 (47)	23,640 (44)	23,193 (40)
				18,119 (37)