Relative long-term survival in out-of-hospital cardiac arrest: Is it really improving?

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Abstract

Aim: To describe the long-term survival of out-of-hospital cardiac arrest (OHCA) patients and to determine whether survival is improving in comparison to the general age- and sex-matched population.
Methods: We utilised the St John Western Australia (WA) OHCA database to retrospectively identify patients aged ≥16 years who experienced an OHCA within the Perth metropolitan area between 1998 and 2017 and survived for at least 30-days post arrest. Patients were excluded if their primary residence was not WA, they did not have an emergency medical services attempted resuscitation (or bystander defibrillation) or did not have an arrest of medical aetiology. Relative survival ratios stratified by decade of arrest were calculated by dividing observed survival of the study cohort by the expected survival of an age- and sex-matched cohort estimated from the Australian Bureau of Statistics life tables for WA.
Results: The OHCA patients who initially survived to 30-days experienced a modest reduction in long-term survival, with 84% (95% CI, 78-90) of patients surviving to 10-years relative to the age- and sex-matched general population. The 10-year relative survival increased from 76% (95% CI, 67-85) to 92% (95% CI, 84-100) between the first (1998-2007) and second (2008-2017) decade of our study.
Conclusion: Relative long-term survival prospects for initial OHCA survivors are moderately lower than that of the general population, however these differences have reduced over time and may be approaching those of the general population.

Introduction

Long-term survival outcomes (≥ 1 year) after out-of-hospital cardiac arrest (OHCA) have been reported to be improving.[1] However, it is unclear if these improvements are simply an artefact of increased life expectancy in the general population. Patients who initially survive an OHCA are subsequently exposed to two different potential sources of mortality. The first is the baseline mortality that all individuals within a population are exposed to irrespective of OHCA status (e.g. mortality due to; cancer, trauma, advanced age, etc.); while the second is the excess mortality hazard causally attributed to the OHCA event (e.g. major organ failure, brain damage, post OHCA treatment complications, etc.). Examining excess mortality allows us to address two important questions. Firstly, do OHCA patients who survive at least 30-days post arrest experience a reduction in long-term survival compared to their age- and sex-matched peers; and secondly, has long-term OHCA survival increased over time in excess of population life expectancy increases?

We applied a statistical method known as relative survival analysis[2] to determine whether the long-term survival of initial OHCA survivors is significantly different to that of the general population. Additionally, we aimed to assess whether the last decade has resulted in improvements in long-term survival of 30-day OHCA survivors, independent of any increases in population life expectancy.

Methods

Study Design
We conducted a population-based retrospective cohort study of patients aged ≥16 years who experienced an OHCA in the metropolitan city of Perth, Western Australia (WA), between 1st January 1998 and 31st December 2017. Patients were included if they: had an OHCA of medical aetiology[3]; received an attempted resuscitation by Emergency Medical Services (EMS) or bystander defibrillation; were a primary resident of WA; and survived at least 30 days following the arrest (referred to as 'initial survivors').

Study Setting
Perth is the capital and largest city of the state of WA. Metropolitan Perth covers 6,400 square kilometres and has a population of 2.06 million[4]. The sole provider of emergency ambulance services in Perth is St John WA (SJ-WA), which operates a single-tiered advanced life support (ALS) ambulance service, staffed by nationally registered paramedics. Patients who are not declared dead at the scene are transported to one of nine hospital emergency departments located within the Perth metropolitan area.

Data Sources
This study sourced data from the SJ-WA OHCA Database, which is maintained by the Prehospital, Resuscitation and Emergency Care Research Unit (PRECRU) at Curtin University. Data from patient care records, completed by SJ-WA paramedics, are automatically linked to the computer-aided dispatch data. The OHCA Database contains detailed information about patient demographics, arrest characteristics and EMS response and interventions. Date of death is determined from the WA Death Registry.

Statistical Analysis
Observed (or absolute) survival is an estimate of the probability of survival in a cohort of OHCA patients while expected survival is an estimate of the survival probability in a comparable cohort of patients from the general population. Expected survival was estimated using the Ederer II method[5, 6] with WA population life tables (provided by the Australian Bureau of Statistics) matched by year of arrest, patient age at arrest and patient sex. Relative survival has been used extensively in cancer research7 to quantify long-term survival and identify improvements in survival across calendar time.8

To determine if long-term survival had improved over the study period, relative survival ratios were compared for each decade in the study (1998-2007 vs 2008-2017). Relative survival ratios were also compared by sex (male/female) and age at arrest (16-39, 40-64, 65- 79 and ≥ 80 years). Absolute long-term survival was examined using Kaplan-Meir curves. Statistical analysis was performed using R v3.5.3 (R Core Team; Vienna, Austria) using the 'relsurv' package for estimating relative survival. Group differences were assessed using the Log-Rank test with a statistical significance of <0.05.

Ethics

This study was approved by the Human Research Ethics Committee of Curtin University as a sub-study of the Western Australian Pre-hospital Care Record Linkage Project (HR128/2013).

Results

Between 1998 and 2017 there were 27,069 OHCAs in the Perth metropolitan area attended by SJ-WA. After excluding cases where patients were <16 years old (n=647), had no EMS attempted resuscitation or bystander defibrillation (n=15,223), were non-residents of WA (n=210) or had a non-medical arrest aetiology (n=1,661), 9,328 OHCA cases remained. Of these, 871 (9.3%) survived at least 30 days following their arrest and formed the study cohort. The mean patient age at time of arrest was 60.7 years (standard deviation, 15.5), with 79% between the ages of 40 and 79 years; with 75% males. Supplementary table 1 shows the baseline characteristics of our initial survivor cohort stratified by decade of arrest.

Figure 1a shows the 10-year Kaplan Meier survival curve while figure 1b shows the 10-year relative survival curve. The Kaplan-Meier estimates for absolute OHCA survival show lower survival compared to the age- and sex-matched general population at one (91% vs 94%), five (81% vs. 91%) and ten (62% vs. 84%) years (Table 1). There was a significant increase (log-rank p=0.03) in 10-year survival between the first (1998-2007) and second (2008-2017) decade of our study, with the relative survival ratio at 10-years increasing from 0.76 to 0.92 (figure 2). Neither patient age (at time of arrest) nor sex were found to be associated with relative long-term OHCA survival (supplementary figure 1).

Discussion

In this retrospective cohort study of 871 initial (30-day) OHCA survivors, we found the long-term survival prospects were modestly lower than that of the general population. The 10-year relative survival of OHCA patients was 84% (95% CI, 78-90). Our findings are novel as they estimate the mortality of OHCA patients that is in excess of the general population mortality. In contrast, most other OHCA studies report long-term survival in 'absolute' terms; where continued survival is influenced by both the mortality risk imparted by the arrest itself *and* the underlying background mortality risk (unrelated to the OHCA). The large difference between relative and absolute survival estimates can be seen in our study where 10-year relative survival was 84% and 10-year absolute survival (obtained using Kaplan Meier) was only 62%.

We found that long-term survival has increased over time, with the 10-year relative survival ratio increasing from 0.76 (95% CI, 0.67-0.85) to 0.92 (95% CI, 0.84-1.00) between the first (1998-2007) and second (2008-2017) decade of our study. Importantly, the 10-year relative survival in the second decade of our study was not statistically significant (95% CI includes '1'); suggesting that long-term survival may be improving to a point where initial OHCA survivors experience similar life spans to their age-and sex-matched peers (without OHCA). Although other studies[9] have also reported increasing trends in long-term survival, ours is the first to find this increase is in excess of any population life expectancy increases. Our results are consistent with previous research[1, 10] that the 'fine-tuning' of resuscitation guidelines (and increasing bystander CPR) over the years has yielded substantial benefits in OHCA survival, although clearly there may be other underlying causal factors such as change in case-mix.[11]

Previous studies have reported on absolute long-term survival in OHCA cohorts, however few have provided relative measures of survival. A small (n=79 patients) 2003 study[12] reported reduced long-term survival in OHCA patients compared to age- and sex-matched general population. Interestingly, this study noted that if patients were also matched for comorbidity, survival was statistically not different to that of the general population. The negative association between pre-arrest comorbidity and OHCA outcomes has been described in a recent systematic review.[13] A 2017 study[14] from Melbourne, Australia reported that long-term relative mortality rates in initial OHCA survivors was initially higher than that of the general population but ceased to be significantly different after five years. Our relative long-term survival model found that older age was not significantly associated with survival, suggesting that the significant associations reported in previous studies may be a result of the background mortality risk of age (irrespective of OHCA).

Our study has some limitations. Firstly, our relative survival model assumes that the cohort under consideration is a representative sample of general population from which the population life tables are derived. We were unable to match for other factors potentially influencing outcome, such as comorbidity (or neurological status) as such life tables are not available. However, assuming OHCA patient comorbidity is higher than that of the age- and sex-matched general population the bias introduced would tend to result in reduced relative survival. Secondly, our cohort contained few individuals over 80 years of age, meaning that our relative survival ratios by age group may have low statistical power. Lastly, as Perth metropolitan area life tables were unavailable, we used WA state life tables to determine expected survival. However, this is unlikely to bias our results as the majority (92%) of the state's population resides in the Perth metropolitan area.

Conclusion

Despite the pessimism surrounding OHCA survival, our study shows that patients who survive 30-days post arrest experience only a moderate reduction in 10-year survival compared to the general population. Additionally, we found that long-term OHCA survival was improving over time.

Conflicts of Interest

Professor Judith Finn receives research support from SJ-WA. A/Prof. Paul Bailey is Clinical Services Director at SJ-WA. None of the other authors have any conflicts of interest to declare.

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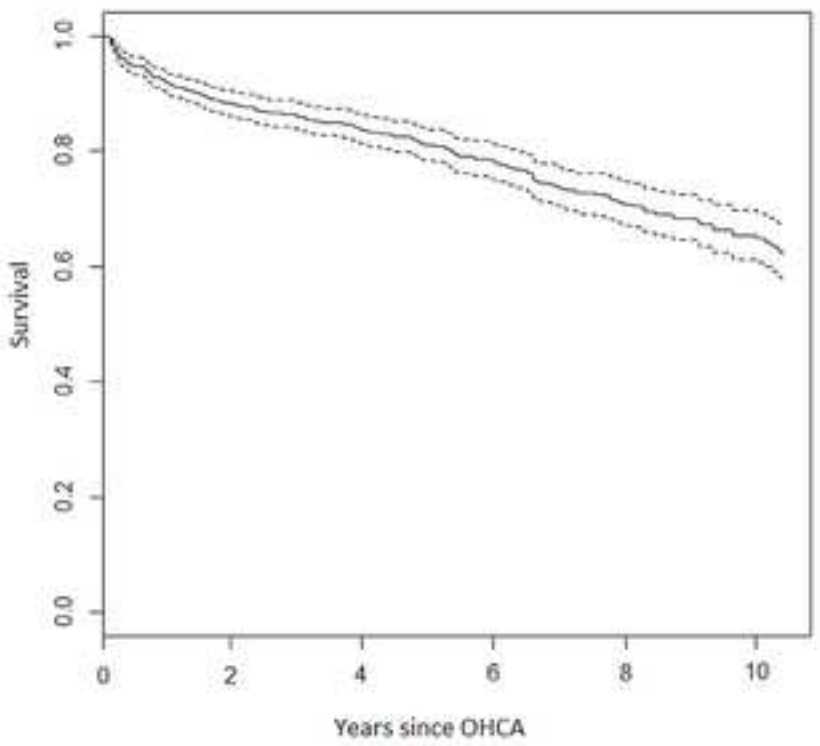
Figure 1. a) Ten year Kaplan-Meier survival (with 95% confidence interval), and b) the 10-year relative survival (with 95% confidence interval) of initial (30-day) OHCA survivors.

Figure 2. Ten year relative survival of initial (30-day) OHCA survivors stratified by decade of arrest.

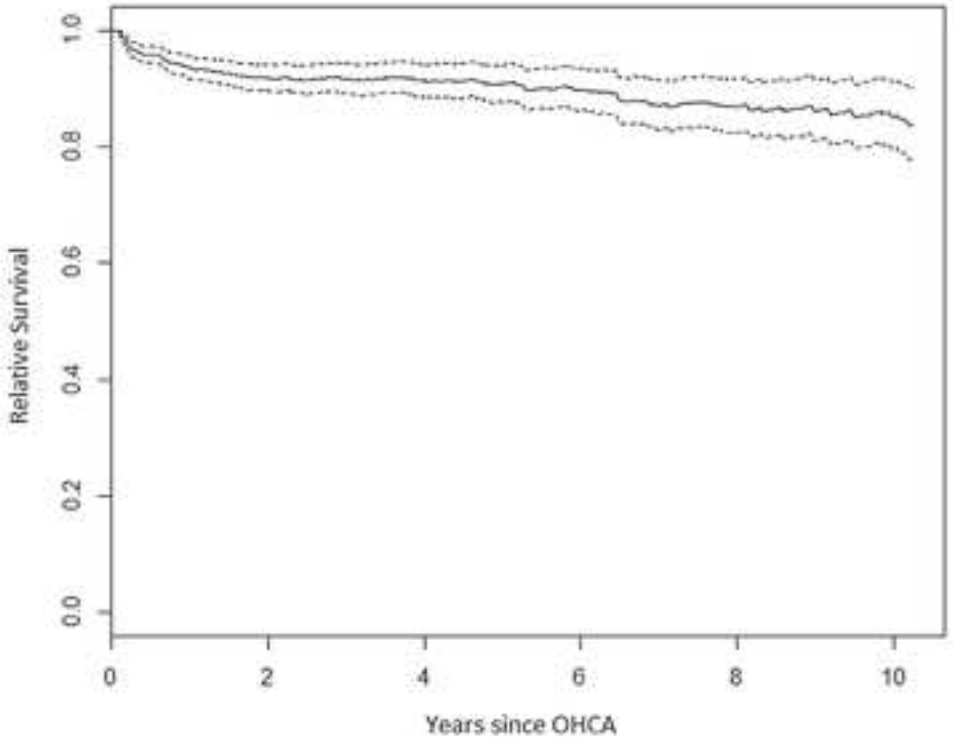
Table 1. Relative survival ratios for one, five and ten years post OHCA in those who survive to 30-days.

Relative survival ratio	**1 -year**		**5-year**		**10-year**	
	Ratio	**95% CI**	**Ratio**	**95% CI**	**Ratio**	**95% CI**
Overall	0.94	(0.92-0.95)	0.91	(0.88-0.94)	0.84	(0.78-0.90)
Sex						
Male	0.94	(0.92-0.97)	0.92	(0.89-0.96)	0.87	(0.80-0.94)
Female	0.91	(0.87-0.95)	0.87	(0.80-0.94)	0.75	(0.63-0.88)
Age Group						
16-39	0.93	(0.88-0.99)	0.87	(0.79-0.95)	0.84	(0.75-0.94)
40-64	0.97	(0.95-0.96)	0.93	(0.90-0.97)	0.89	(0.84-0.95)
65-79	0.94	(0.90-0.97)	0.92	(0.86-0.99)	0.81	(0.70-0.94)
≥80	0.80	(0.71-0.90)	0.81	(0.64-1.03)	0.66	(0.37-1.21)
Decade of arrest						
1998-2007	0.92	(0.88-0.96)	0.85	(0.79-0.91)	0.76	(0.67-0.85)
2008-2017	0.94	(0.92-0.96)	0.93	(0.89-0.97)	0.92	(0.84-1.00)

Figure 1



(a)



(b)

Figure 2