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Interventional strategies associated with improvements in survival for out-of-hospital cardiac arrests in Singapore over 10 years

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ABSTRACT

Aim: We aim to study if there has been an improvement in survival for Out-of-Hospital Cardiac Arrest (OHCA) in Singapore, the effects of various interventional strategies over the past 10 years, and identify strategies that contributed to improved survival.

Methods: Rates of OHCA survival were compared between 2001–2004 and 2010–2012, using nationwide data for all OHCA presenting to EMS and public hospitals. A multivariate logistic regression model for survival to discharge was constructed to identify strategies with significant impact.

Results: A total of 5453 cases were included, 2428 cases from 2001 to 2004 and 3025 cases from 2010 to 2012. There was significant improvement in Utstein (witnessed, shockable) survival to discharge from 2001–2004 (2.5%) to 2010–2012 (11.0%), adjusted odds ratio (OR) 9.6 [95% CI: 2.2–41.9]). Overall survival to discharge increased from 1.6% to 3.2% (adjusted OR 2.2 [1.5–3.3]). Bystander CPR rates increased from 19.7% to 22.4% ($p = 0.02$). The multivariate regression model (adjusted for important non-modifiable risk factors) showed that response time <8 min (OR 1.5 [1.0–2.3]), bystander AED (OR 5.8 [2.0–16.2]), and post-resuscitation hypothermia (OR 30.0 [11.5–78.0]) were significantly associated with survival to hospital discharge. Conversely, pre-hospital epinephrine (OR 0.6 [0.4–0.9]) was associated negatively with survival.

Conclusions: OHCA survival has improved in Singapore over the past 10 years. Improvement in response time, public AEDs and post-resuscitation hypothermia appear to have contributed to the increase in survival. Singapore's experience might suggest that developing EMS systems should focus on reducing times to basic life support, including bystander defibrillation and post-resuscitation care.

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1. Introduction

Out of Hospital Cardiac Arrest (OHCA) is defined as cessation of cardiac mechanical activity that occurs outside of the hospital setting and is confirmed by the absence of signs of circulation. In the concept of the "chain of survival", mortality from cardiac arrests can be reduced with early access, early cardiopulmonary resuscitation (CPR), early defibrillation, early advanced care and post resuscitation care.[1] However developing EMS systems with limited resources often face a dilemma on which interventions to prioritize.

The majority of OHCA sufferers, irrespective of aetiology, do not receive timely bystander-assisted CPR or other interventions thought to improve the likelihood of survival to hospital discharge (e.g., defibrillation). Nearly half of cardiac arrest events are witnessed and efforts to increase survival rates should focus not only on Emergency Medical Services (EMS) but also timely delivery of effective interventions by bystanders.[2] In Singapore, the previously published OHCA survival rate is 2% (2001–2002)[3] as compared to 16.3% in 10 North American sites, suggesting that there is still much room for improvement.[4]

Singapore is a city-state with a land area of 712.4 square kilometres and a population that has increased from 4.1 million (in 2002) to 5.3 million (in 2012).[5] The Singapore EMS is activated by a centralized, enhanced '995' dispatch system run by the Singapore Civil Defence Force (SCDF) and utilizing Computer Aided Dispatch, Medical Dispatch protocols, Global Positioning Satellite (GPS) Automatic Vehicle Locating Systems and road traffic monitoring systems.

From 2001 to 2012, there were several improvements in Singapore's EMS pre-hospital system in terms of equipment, paramedic skills and in-hospital care of OHCA patients. For example, public access defibrillators have started to be introduced, the number of ambulances was increased from 36 in 2001 to 46, paramedics were certified to give epinephrine intravenously and use laryngeal mask airway devices in 2004 and therapeutic hypothermia was introduced for post-resuscitation care in 2008. Public education on CPR has helped create more awareness and encouraged the public to learn CPR.

We aim to study if there has been an improvement in survival, the effects of various interventional strategies over the past 10 years, and to identify the strategies that contributed to improved survival. We hypothesize that survival to discharge for OHCA in Singapore has improved in the last 10 years, and that this improvement is due to improvements in several modifiable factors.

2. Methods

We conducted a nationwide retrospective cohort analysis of all OHCA cases presenting to EMS and public hospitals. We utilized data from the Singapore Cardiac Arrest and Resuscitation Epidemiology (CARE) project from 2001 to 2004 and 2010 to 2012. Singapore has a comprehensive, single provider, fire-based EMS system which only sends cases to public hospitals. Both cohorts covered exactly the same population-base over different time periods and used the same case ascertainment, data definitions, data collection methods and data variables.

The study was approved by the local Institutional Review Boards. It was classified as minimal risk research with waiver of informed consent.

The CARE project is a prospective registry of cardiac arrests, with initial data collection from October 2001 to October 2004 involving the six (at the time) major hospitals in Singapore. There was no nationwide data collection between 2005 and 2009 due to a lapse of research funding. Subsequently with restored funding, all OHCA cases from April 2010 to May 2012 were included for analysis in the 'after' phase.

In both cohorts, all patients with OHCA as confirmed by the absence of a pulse, unresponsiveness and apnoea were included. Exclusion criteria were those 'obviously dead' as defined by the presence of decomposition, rigour mortis or dependant lividity and traumatic arrests. Patient characteristics, cardiac arrest circumstances, ECG rhythms, EMS response times and outcomes were recorded in a standard report according to the Utstein template.[6] Aetiology of arrests were determined by coroner's report and inpatient discharge records for survivors.

Data were drawn from prospectively filled study forms, EMS records, Emergency Department (ED) notes as well as hospital discharge records. EMS response timings were extracted from a centralized dispatch system and ambulance records. In Singapore, time at patient's side is routinely radioed to dispatch, which captures the timing electronically. Data was managed using a secure, online electronic data-capture platform. Data entered in the system was periodically checked by research coordinators for accuracy and completeness. Incomplete data variables were sent back to respective site principal investigators for clarification and verification. Utstein survival refers to survival to hospital discharge of those cardiac patients whose arrest events were witnessed by a bystander and who had an initial rhythm of ventricular fibrillation or pulseless ventricular tachycardia.

To test the various hypotheses, the survival rate was first compared by logistic regression and second the distribution of resuscitation factors was compared by Chi-squared test or Mann–Whitney test, between the 2 datasets corresponding to the 2 time periods. Finally, the effect on survival outcome, of non-modifiable factors such as age, gender, past medical history, as well as modifiable factors such as bystander AED was investigated using univariate logistic regression followed by multivariate logistic regression using the a merged dataset. For each factor, both unadjusted and adjusted odds ratios (95% confidence intervals) for the univariate and multivariate analysis respectively were reported. The multivariate logistic regression model for survival to discharge was implemented adjusting for age, witnessed/unwitnessed arrest, initial rhythm, bystander CPR, bystander AED, response time, ambulance defibrillation, ambulance mechanical CPR, pre-hospital advanced airway, IV epinephrine administration and therapeutic hypothermia. The selection of variables for the model was based on factors known from the literature which were previously associated with cardiac arrest survival.[7,8] All data analyses were performed using SPSS version 17.0.

3. Results

From October 2001 to October 2004, 2428 cases were included. From April 2010 to May 2012, 3025 cases were included, for a total of 5453 cases. Despite an increase in the population between 2002 and 2012, the number of cardiac arrests per 100,000 population remained similar between the two time periods (59.2 in 2002 vs. 57.1 in 2012). The mean age of the 2001–2004 patients was 60.6 years with 63.0% male and 63.5 years for 2010–2012 with 65.7% male. The top 3 locations of arrests for both 2001–2004 and 2010–2012 were home residence (70.1% vs. 70.0%), public/commercial building (7.1% vs. 7.8%) and street/highway (4.4% vs. 5.9%) (Table 1).

Table 2 shows resuscitation factors for the two time periods. Bystander CPR rates increased from 19.7% in 2001–2004 to 22.4% in 2010–2012 ($p = 0.02$). Bystander AED applied rates (layperson defibrillator applied) increased from 0.0% in 2001–2004 to 1.8% in 2010–2012 ($p < 0.01$) while the Public Access Defibrillation (PAD) rate (layperson defibrillation-shock given) increased from 0.0% to 1.0% ($p < 0.01$) for all arrests. Pre-hospital drug administration increased from 13.4% to 46.8% ($p < 0.01$).

Table 1
Characteristics of patients 2001–2004 vs. 2010–2012.

Characteristics	2001–2004 (N = 2428)	2010–2012 (N = 3025)
Age		
Mean (SD)	60.6 (19.3)	63.5 (18.2)
Median (IQR)	63.4 (50.4–74.4)	65.0 (53.0–77.0)
Gender (%)		
Male	1652 (63.0)	1988 (65.7)
Race (%)		
Chinese	1687 (69.5)	2009 (66.4)
Malay	365 (15.0)	459 (15.2)
Indians	267 (11.0)	343 (11.3)
Others	108 (4.5)	214 (7.0)
Medical history (%)		
No	282 (11.6)	383 (12.6)
Unknown	482 (19.9)	289 (9.4)
Heart disease	788 (32.5)	1090 (35.9)
Diabetes	569 (23.4)	869 (28.7)
Hypertension	752 (31.0)	1430 (47.1)
Other	436 (18.0)	1057 (35.0)
Witnessed arrest		
Bystander	1318 (54.3)	1483 (49.0)
EMS/private ambulance	255 (10.5)	239 (7.9)
Not witnessed	845 (34.8)	1303 (43.1)
First arrest rhythm		
Asystole	1162 (47.8)	1586 (52.4)
PEA	640 (26.3)	805 (26.6)
VF/VT	436 (18.0)	541 (17.9)
Unknown shockable rhythm	4 (0.2)	14 (0.5)
Unknown unshockable rhythm	2 (0.08)	24 (0.8)
Unknown	19 (0.8)	5 (0.2)
Cause of arrest		
Presumed cardiac aetiology	1598 (65.8)	2253 (74.5)
Non-cardiac aetiology	830 (34.2)	673 (22.2)
Location (%)		
Home residence	1703 (70.1)	2128 (70.0)
Healthcare facility	103 (4.2)	110 (3.6)
Public/commercial building	173 (7.1)	237 (7.8)
Industrial place	43 (1.8)	63 (2.1)
Nursing home	35 (1.4)	111 (3.7)
Place of recreation	22 (0.9)	57 (1.9)
Street/highway	108 (4.4)	155 (5.9)
Transport centre	36 (1.5)	37 (1.2)
[a]In EMS/private ambulance	67 (2.8)	69 (2.3)
Other	86 (3.5)	60 (2.0)

EMS, emergency medical services; PEA, pulseless electrical activity; VF, ventricular fibrillation; VT, ventricular tachycardia.
[a] EMS witnessed arrest.

In 2010–2012, mechanical CPR device applied by the EMS was 8.3%.

The EMS factors and timing intervals are described in Table 2. There was a decrease in time of call to EMS arrival at scene from 9.0 in 2001–2004 to 8.0 min in 2010–2012 ($p < 0.01$). Time from arrival at patient's side to time to leave the scene was found to increase from 10.0 min to 12.1 min ($p < 0.01$).

Table 3 compares the primary outcomes for 2010–2012 in reference to the earlier dataset of 2001–2004, before and after adjusting for age, gender and the various medical histories found significantly different between the 2 datasets. For all arrests, the EMS return of spontaneous circulation (ROSC) increased from 1.9% in 2001–2004 to 5.0% in (2010–2012 vs. 2001–2004: adjusted OR 6.3 [2.8–13.9]) and from 3.2% to 10.1% (2010–2012 vs. 2001–2004: adjusted OR 5.0 [1.7–14.8]) for Utstein (witnessed, shockable, cardiac aetiology) arrests. Overall survival to discharge increased from 1.6% to 3.2% (adjusted OR 2.2 [1.5–3.3]) and Utstein survival increased from 2.5% to 11.0% (adjusted OR 9.6 [2.2–41.9]). Neurological outcome as defined by Cerebral Performance Category (CPC) 1 and 2 for Utstein survival increased from 2.1% to 7.0% (adjusted OR 6.0 [1.3–27.0]).

The multivariate regression model of all arrests is presented in Table 4. Age 65 years and below (adjusted OR 1.6 [1.1–2.4]), witnessed arrest (adjusted OR 2.0 [1.3–3.3]), initial rhythm (adjusted OR 7.8 [3.3–18.0]), bystander defibrillation/AED (adjusted OR 5.8 [2.0–16.2]), response time <8 min (adjusted OR 1.5 [1.0–2.3]), pre-hospital epinephrine (adjusted OR 0.6 [0.4–0.9]) and hypothermia (adjusted OR 30 [11.5–78.0]) were shown to be significant predictors of survival to hospital discharge. There were no multi-collinearity issues encountered in the multivariate logistic regression. The standard errors (SE) of all the parameter coefficients, including the constant term in the regression were all lower than 0.53. The correlation matrix of the estimates also verified that there was no large correlation between any 2 parameter estimates.

Fig. 1 presents the Utstein flow chart for 2001–2004 and 2010–2012. There were 2267 and 2975 resuscitations attempted in 2001–2004 and 2010–2012 respectively. In 2001–2004, 16 cases (5.7%) were admitted to hospital vs. 82 (25%) in 2010–2012. 7 cases (2.5%) in 2001–2004 were discharged alive or remained alive at 30 days vs. 35 (11%) in 2010–2012. 6 cases (2.1%) in 2001–2004 vs. 22 (7%) in 2010–2012 had CPC score of 1 or 2. Fig. 2 presents the EMS time intervals between the time cardiac arrest occurred and the time ambulance reached hospital in both periods.

4. Discussion

In this study, we found Utstein survival for OHCA increased from 2.5% to 11.0% (adjusted OR 9.6 [2.2, 41.9]) over 10 years. In general, reported cardiac arrest survival has remained unchanged in North America and Europe over the last decades. However there have been a few examples of improved survival related to EMS system changes in Japan, Denmark and the state of Arizona in USA.[9–11]

There were several changes to the EMS system in Singapore from the period of 2001 to 2012. There was an increase of 14 ambulances from 32 to 46 from 2001 to 2010. Motorcycle Fast Response Paramedics (FRPs) were progressively introduced starting in 2001, leading to faster response times. Intravenous epinephrine and laryngeal mask airways were implemented in 2004, mechanical CPR was implemented in ambulances in 2011. In 2006, Extra-Corporeal Membrane Oxygenation (ECMO) therapy was started at one of the tertiary hospitals. Hypothermia was implemented in 2008 at one of the tertiary hospitals, and subsequently spread to 4 other hospitals. Acute Percutaneous Coronary Intervention (PCI) post cardiac arrest has also become common since 2008, unfortunately the PCI data is not available in our registry.

Based on our literature review, previously reported modifiable factors for better outcomes included bystander CPR, defibrillation, EMS response time, and post resuscitation care.[7,12,13] After multivariate analysis, only age, witnessed arrest, initial rhythm, bystander AED, response time, epinephrine (negative association) and post-resuscitation hypothermia remained significant. These variables were associated with almost a twofold increase in survival rate in the 2nd time period as compared to the 1st time period.

Singapore's experience might suggest that developing EMS systems should focus on reducing times to basic life support, including bystander defibrillation. It also suggests the value of investing in post-resuscitation care. In contrast, there seems to be limited outcome improvements associated with ambulance based advanced life support like drugs and advanced airways. These findings echo the OPALS study in Canada.[7]

Despite various efforts to increase public awareness and train the public in CPR over the last 10 years, the increase in bystander CPR seen was only slight. It was also surprising that in the

Table 2
Resuscitation factors for 2001–2004 vs. 2010–2012.

	2001–2004	2010–2012	*p* value
Resuscitation – community factors (%)			
All arrests:			
Bystander CPR present	478 (19.7)	678 (22.4)	0.02
Bystander AED applied	0 (0.0)	55 (1.8)	0.00
Public access defibrillation	0 (0.0)	29 (1.0)	0.00
Bystander witnessed arrest ONLY:			
Bystander CPR present	370 (28.1)	416/1483 (28.1)	0.67
Bystander AED applied	0 (0.0)	32/1483 (2.2)	0.00
Public access defibrillation	0 (0.0)	16 (1.1)	0.00
Mechanical CPR device used	0 (0.0)	252 (8.3)	0.00
Pre-hospital defibrillation	508 (22.4)	698 (23.1)	0.70
Pre-hospital advanced airway	0 (0.0)	2389 (79.0)	0.00
Pre-hospital drug administration	303 (13.4)	1416 (46.8)	0.00
Post-resuscitation care (%)			
ECMO therapy	0 (0.0)	2 (0.1)	0.00
Hypothermia therapy	0 (0.0)	29 (1.0)	0.00
Mechanical CPR device used			
EMS time intervals in minutes, median (IQR)			
For arrests that occurred before EMS arrival			
Time of arrest – Time of call[a]	6.4 (2.7–13.0) *n* = 1546	5.8 (2.3–12.5) *n* = 2148	<0.20
For arrests that occur after EMS arrival:			
Time of call – Time of arrest	7.7 (2.8–18.0) *n* = 627	6.3 (1.81–15.8) *n* = 720	0.04
Call-dispatch[*]	–	0.6 (0.28–0.9)	–
FRP dispatch – FRP arrival at scene[*]	–	5.0 (4–7)	–
Call to arrival at scene	9 (6.8–11.4)	8.0 (6.0–10.3)	<0.001
Call to arrival at patient side	11.1 (9.0–14.0)	9.9 (7.8–12.6)	<0.001
Arrival at scene to arrival at patient side	2.0 (1.0–3.0)	1.7 (1.0–2.7)	<0.001
Arrival at patient side to leave scene	10.0 (7.0–12.6)	12.1 (10.0–14.7)	<0.001
Arrival at patient side to time CPR started[*]	–	0.5 (0.0–1.9)	–
Arrival at patient side to time of first shock	3.0 (2.0–4.9)	3.3 (2–4)	<0.001
Arrival at patient side to Time AED applied[*]	–	2.0 (1.0–3.2)	–
Leave scene to arrival at hospital	10.0 (7.0–14.2)	10.0 (7.0–13.9)	0.10
Call to ED	32.3 (27.4–38.1)	33.2 (28.4–38.5)	0.02

ECMO, extracorporeal membrane oxygenation; CPR, cardiopulmonary resuscitation; FRP, fast response paramedics; AED, automated external defibrillator; EMS, emergency medical services.

[*] *p*-value could not be computed when count was zero in one of the comparison group.

[a] Unwitnessed arrests were excluded from this analysis.

Table 3
Comparing outcomes between all arrests, Utstein, presumed cardiac aetiology and EMS witnessed groups (2001–2004 vs. 2010–2012).

	2001–2004 *x*/*n* (%)	2010–2012 *x*/*n* (%)	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)
Utstein survival (witnessed, shockable rhythm, presumed cardiac and resuscitation attempted)				
EMS ROSC	9/280 (3.2)	32/317 (10.0)	3.4 (1.5–7.2)	5.0 (1.7–14.8)
ED ROSC	43/276 (15.6)	98/317 (30.9)	2.5 (1.6–3.7)	2.7 (1.5–4.8)
Admitted	16/280 (5.7)	82/317 (26.8)	5.8 (3.3–10.1)	9.6 (3.9–23.3)
Discharged alive or remain alive at 30 days	7/280 (2.5)	35/317 (11.0)	5 (2.2–11.4)	9.6 (2.2–41.9)
Post arrest CPC 1/2	6/280 (2.1)	22/317 (7.0)	3.4 (1.4–8.5)	6.0 (1.3–27.0)
Survival – presumed cardiac aetiology				
EMS ROSC	28/1598 (1.8)	109/2253 (4.8)	2.8 (1.9–4.3)	2.9 (1.9–4.4)
ED ROSC	239/1598 (15.0)	526/2253 (23.2)	1.7 (1.5–2.0)	1.7 (1.4–2.0)
Admitted	111/1598 (6.9)	323/2253 (14.3)	2.2 (1.8–2.8)	2.2 (1.8–2.8)
Discharged alive or remain alive at 30 days	26/1598 (1.6)	81/2253 (3.6)	2.2 (1.4–3.5)	2.3 (1.5–3.6)
Post arrest CPC 1/2	22/1598 (1.4)	47/2253 (2.1)	1.5 (0.9–2.5)	1.6 (0.9–2.6)
Survival – EMS witnessed				
EMS ROSC	18/255 (7.1)	24/239 (10.0)	1.5 (0.8–2.8)	1.6 (0.9–3.1)
ED ROSC	81/255 (31.8)	106/239 (44.4)	1.7 (1.2–2.5)	1.7 (1.2–2.4)
Admitted	48/255 (18.8)	79/239 (33.1)	2.1 (1.4–3.2)	2.2 (1.4–3.3)
Discharged alive or remain alive at 30 days	16/255 (6.3)	21/239 (8.8)	1.4 (0.7–2.8)	1.7 (0.8–3.3)
Post arrest CPC 1/2	15/255 (5.9)	16/239 (6.7)	1.1 (0.6–2.4)	1.3 (0.6–2.8)
Survival – all arrests				
EMS ROSC	43/2267 (1.9)	151/2975(5.0)	1.9 (1.6–2.2)	6.3 (2.8–13.9)
ED ROSC	398/2428 (16.4)	867/3025 (28.7)	1.8 (1.6–2.1)	1.8 (1.6–2.1)
Admitted	215/2428 (9.0)	514/3025 (17.0)	2.1 (1.8–2.5)	2.2 (1.8–2.6)
Discharged alive or remain alive at 30 days	38/2428 (1.6)	97/3025 (3.2)	2.1 (1.4–3.0)	2.2 (1.5–3.3)
Post arrest CPC 1/2	28/2428 (1.2)	53/3025 (1.8)	1.6 (1.0–2.6)	1.7 (1.1–2.8)

EMS, emergency medical services; ED, emergency department; ROSC, return of spontaneous circulation; CPC, cerebral performance category.

[a] Adjusted for age, gender, and the medical histories found significantly different in the 2 datasets.

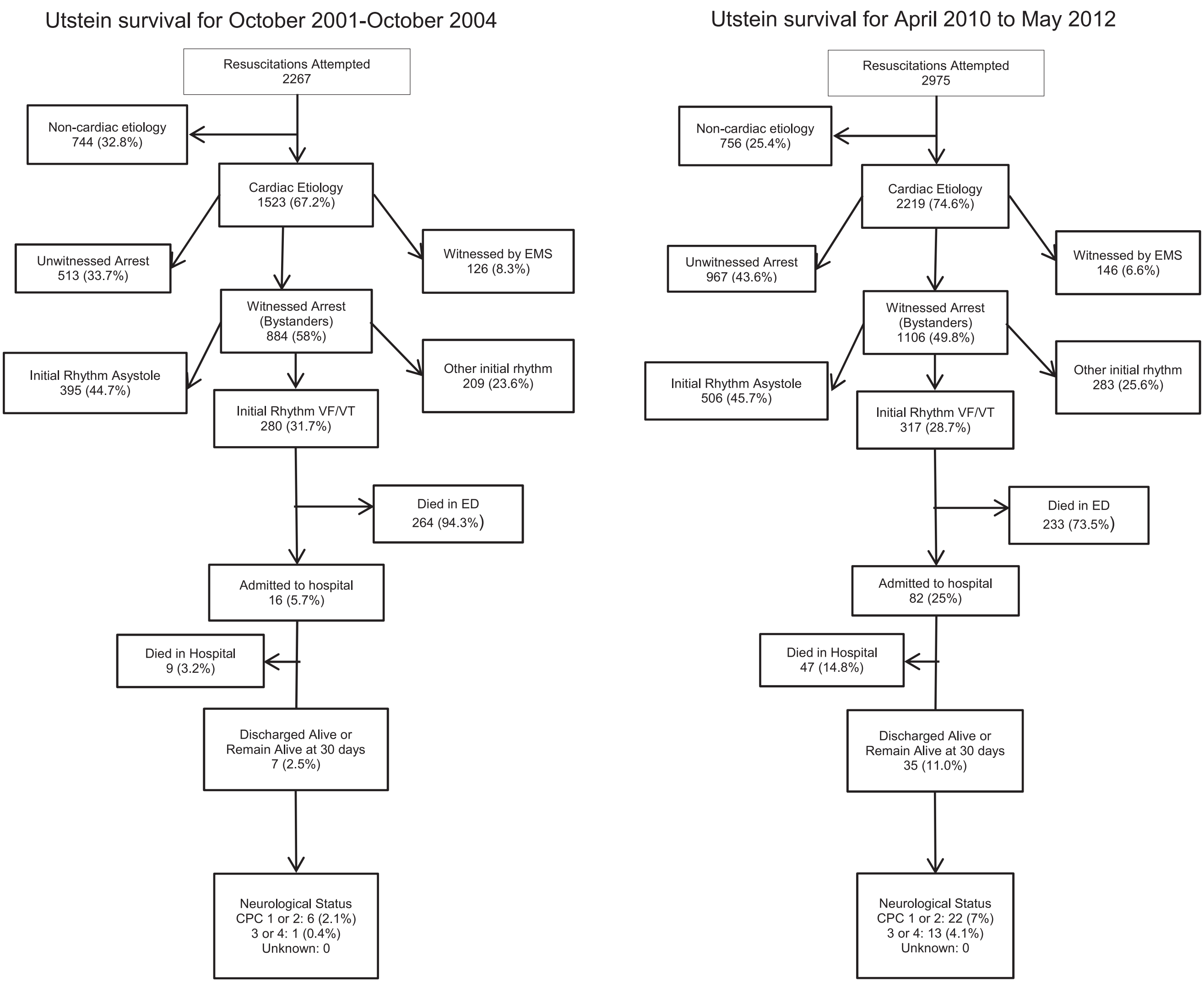

Fig. 1. Utstein flow charts for 2001–2004 and 2010–2012.

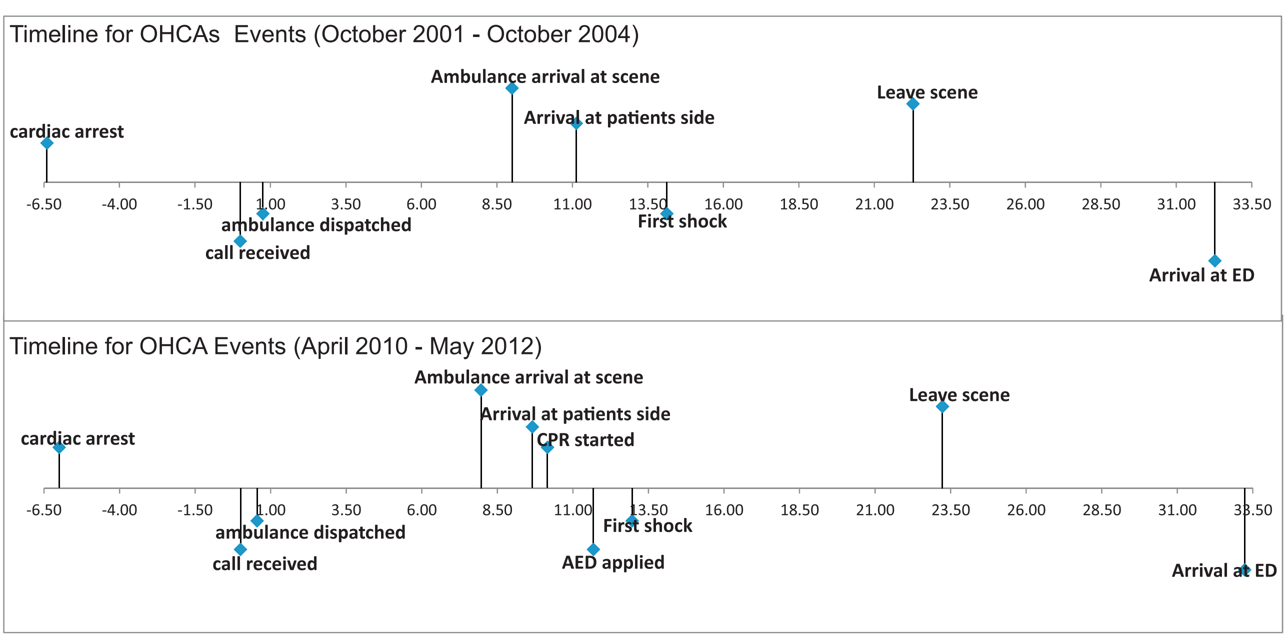

Fig. 2. Timeline of OHCAs in Singapore for 2001–2004 and 2010–2012 from time of arrest to arrival at ED.

Table 4
Univariate and multivariate analysis of factors important for survival to discharge.

Variables	Unadjusted OR (95% CI)	Nagelkerke R^2 (in %)[a]	Adjusted OR (95% CI)	Nagelkerke R^2 (in %)[b]
Age 65 years and below	2.1 (1.4–3.0)	14	1.6 (1.1–2.4)	
Witnessed arrest	2.7 (1.7–4)	2.2	2.0 (1.3–3.3)	
Initial rhythm	10.7 (7.3–15.7)	14.8	7.8 (3.3–18.0)	
Bystander CPR	1.9 (1.3–2.8)	1	1.0 (0.7–1.6)	
Bystander defibrillation/AED	5.0 (2.1–11.9)	0.8	5.8 (2.0–16.2)	
Response time 8 min or less	1.8 (1.3–2.6)	0.9	1.5 (1.0–2.3)	21
Ambulance defibrillation	7.8 (5.4–11.3)	11.5	1.2 (0.5–2.9)	
Mechanical CPR by EMS	1.7 (0.9–3.2)	0.2	1.7 (0.8–3.6)	
Pre-hospital advanced airway	1.0 (0.7–1.4)	0	0.8 (0.6–1.3)	
Epinephrine	0.7 (0.5–1.1)	0.2	0.6 (0.4–0.9)	
Hypothermia	19 (8.5–45.4)	2.8	30 (11.5–78.0)	

CPR, cardiopulmonary resuscitation; AED, automated external defibrillator.
[a] This Nagelkerke R^2 represents the % of variance in the survival outcome that is explained by each factor in a univariate logistic regression model. Therefore the individual variances may add up to more than that of the full model using multivariate analysis.
[b] This Nagelkerke R^2 represents the total % of variance in the survival outcome that is explained by all the factors in the full multivariate logistic regression model.

multivariate model, bystander CPR was not associated with survival, unlike previous studies.[7] Perhaps the proportion of people trained in the population is still not large enough to appreciably increase the chance of a trained bystander being on scene when a cardiac arrest happens. Other unknown factors include the quality of CPR administered, or delay of the bystanders attempting CPR after the crucial first 4 min of a collapse.[14] Remaining barriers could be cultural, fear of mouth-to-mouth contact and even being sued for performing CPR incorrectly.[15] Since 2012, EMS dispatchers are now trained to teach callers to recognize the symptoms of cardiac arrest and provide instructions on CPR. This new intervention will hopefully increase bystander CPR rates and decrease CPR administration delay.[16]

Bystander defibrillation was found to be significant in improving survival, as consistent with past literature.[17] In Singapore, AEDs have been introduced at the airport, community sports facilities, casinos, government buildings, dialysis centres, hotels and selected shopping centres. AEDs seem to be underutilized, perhaps due to persistent public fear of doing harm, and misconception that AED's are difficult to use. There are plans for a nationwide AED registry linked to emergency dispatch to enable them to match a first responder with the nearest available AED.

Response times (defined as call received at dispatch to arrival of EMS at scene) were found to decrease over the period of the study. This is most likely due to deployment of more ambulances on the road and a more efficient dispatching and routing process. The improvement is also likely due to the use of motorcycle-based FRP equipped with AEDs, dispatched for all likely cardiac arrests (e.g. primary complaint of unconsciousness, chest pain or breathlessness). The FRPs arrived 3 min earlier on average than the ambulances – demonstrating their utility in congested traffic, narrower roads or limited access buildings.

Response times were significantly related to survival in our study. This is similar to other recent literature.[7,18] Ambulance response times are important, especially in locations where bystander CPR and AEDs are still low, as EMS personnel become the first point of contact for CPR and AED administration.

The median scene time (EMS arrival at patient side to leave scene) increased by 2.1 min, between 2001–2004 and 2010–2012, which might be due to more procedures being performed by EMS on scene for OHCA. We note that our scene times are relatively short compared to North American and European systems, as ambulance crews will initiate transport after a maximum of 3 shocks at scene or 3 rounds of CPR (scoop and run model). They do not have a termination of resuscitation protocol in the field.

Epinephrine utility in the field of cardiac arrest is still controversial. The most recent study conducted in Singapore showed that epinephrine in combination with vasopressin did not improve long term survival but seemed to improve survival to admission in patients with prolonged cardiac arrests.[19] Survival bias could be a reason for these observations, as patients with rapid return of circulation in the field would be less likely to receive epinephrine or advanced airways compared to patients with prolonged resuscitation. Alternatively, this could point to a need for closer quality supervision and refresher airway training for the paramedics locally. Previous reports on the effect of supraglottic airways on cardiac arrest survival have also had conflicting results.[20–24] Another possibility is that these additional procedures may have contributed to a delay in transport, and thus seem to have a negative effect on survival.

In this study, we also did not see an association of the use of mechanical CPR with increased survival. This parallels several large trials comparing mechanical and manual CPR published recently which failed to demonstrate increased survival with the devices.[25–27]

Possible explanations of why our VT/VF rates were found to be low as compared to some other studies could be due to a variety of reasons, including a different patient profile, longer response times and later activation of EMS. Other studies have reported a higher proportion of bystander witnessed arrests and usage of automated external defibrillators before EMS arrival. In this scenario, shockable rhythms such as VT and VF would be more likely to be captured.[28]

One limitation of this study is that we did not have data on post resuscitation PCI. Previous studies have shown that post resuscitation PCI was associated with a lower risk of death (hazard ratio (HR): 0.46; 95% CI 0.34–0.61).[29] In the CHEER trial[30] where patients were treated with mechanical CPR, hypothermia, ECMO and early PCI, full neurological recovery was achieved in 54% of their patients.

Other limitations include the inability to ascertain the impact of secular trends and any changes in the training of the EMS personnel or dispatch algorithm that could have resulted in more efficient ambulance dispatch processes. We are also unable to collect pre-hospital timings in cases where private transportation or private ambulances were employed (~2% of all cardiac arrests cases at the 7 hospitals). The pre-hospital timings are mainly from SCDF emergency ambulance records.

There were other potential cofounders in the study that were not addressed. For example, from 2001 to 2004, EMS providers were following the International Liaison Committee on Resuscitation (ILCOR) 2000 guidelines, while from 2010 to 2012, they followed the ILCOR 2010 guidelines. It is difficult to distinguish the impact of the change in CPR guidelines from the other changes in interventions. Without accounting for confounding effects due to resuscitation guideline changes, the demographic and resuscitation factors investigated in our multivariate analysis accounted for a modest but still substantial 25% of the variance in the outcome of survival to discharge.

Timings recorded by our study were derived from official system times of the EMS system, or from resuscitation equipment. Efforts were made to synchronize all timings, but human, systematic, measurement, and random errors are difficult to eliminate entirely. It is also difficult and impossible (for unwitnessed arrests) to record the true time interval between when cardiac arrest event happened and the exact time interval of when bystander CPR, bystander AED, and other interventions were administered.

5. Conclusions

The Utstein survival to discharge rate increased significantly from 2.5% to 11% and overall survival to discharge rate also increased from 1.6% to 3.2% over the past 10 years. Our results suggest that changes in Singapore's pre-hospital and in-hospital system were associated with improved outcomes for OHCA patients.

Specifically, improvement in response time, public AEDs and post-resuscitation hypothermia was associated with the increase in survival in the multivariate model. Singapore's experience might suggest that developing EMS systems should focus on reducing times to basic life support, including bystander defibrillation and post resuscitation care.

Conflict of interest statement

A/Prof Ong has licensing agreement and patent filing (Application no: 13/047,348) with ZOLL Medical Corporation for a study titled 'Method of predicting acute cardiopulmonary events and survivability of a patient'. No further conflict of interests for other authors.

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