Twenty Year Trends of Survival after In-Hospital Cardiac Arrest

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ABSTRACT: **Background:** In 2006, the Israeli Ministry of Health distributed guidelines for improving cardiopulmonary resuscitation (CPR) knowledge among hospital staff. The impact of these guidelines on survival after in-hospital cardiac arrest (IHCA) is unclear.

Objectives: To compare rates of incidence and survival to discharge after IHCA, preceding and subsequent to issuance of the guidelines: 1995–2005 and 2006–2015.

Methods: Data were retrieved from the computerized records of patients who had an IHCA and underwent CPR. In addition, we retrieved data available from the hospital's resuscitation committee that included number, type, methods of training in CPR refresher courses, type and number of audits carried out during the past 10 years, and type of CPR quality assessments.

Results: From 1995 to 2015, IHCA incidence increased from 0.7 to 1.7 per 1000 admissions ($P < 0.001$), while survival rate did not increase ($P = 0.37$). Survival for shockable rhythms increased from 15.4 to 30.2% ($P = 0.05$) between the two time periods. The ratio of non-shockable to shockable rhythms increased from 2.4 to 4.6 ($P = 0.01$) between the two time periods.

Conclusions: Overall IHCA survival did not improve following the issuance of guidelines requiring CPR refresher courses, although survival improved for patients with initial shockable dysrhythmia. A decrease of events with initial shockable dysrhythmia, an increase with acute renal failure, and a decrease occurring in intensive care units contributed to understanding the findings. We found that CPR refresher courses were helpful, although an objective measure of their effectiveness is lacking.

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KEY WORDS: cardiac dysrhythmia, in-hospital cardiac arrest (IHCA), cardiopulmonary resuscitation (CPR), medical education

A number of studies have investigated changes in survival rates for in-hospital cardiac arrest (IHCA) following the issuance of new guidelines or the implementation of a quality improvement program. In a single hospital in Denmark, systematic training in cardiopulmonary resuscitation (CPR) did not improve survival from IHCA [1]. Nor did IHCA survival improve in one Australian hospital following implementation of the Australian Resuscitation Council 2006 guidelines [2]. Moreover, the implementation of rapid response teams [3] and the utilization of remote intensive care unit monitoring did not yield improved rates of IHCA survival [4]. A recently published meta-analysis reported no improvement in the survival to discharge rate between studies performed before issuance of the 2010 cardiopulmonary resuscitation (CPR) guidelines and those performed subsequently, 15% and 14% for the respective mean pooled rates [5]. In contrast, a large nationwide study reported increased risk adjusted rates of survival to discharge, from 13.7% in 2000 to 22.3% in 2009 in U.S. hospitals participating in the Get with the Guidelines (GWTG)–Resuscitation registry [6]. However, some of the studies that investigated the impact of new guidelines and programs examined short periods of time, ranging from a few months [1] to a few years [2]. Moreover, in the GWTG study, the occurrence of nearly 60% of IHCA events in the intensive care unit (ICU) [6] raises the question as to whether the observations reflect general hospital populations.

In 2006, the Israeli Ministry of Health distributed guidelines requesting hospitals to implement a program for improving theoretical and practical knowledge in CPR among medical staff. According to these guidelines, each hospital designated a resuscitation committee to ensure that medical staff undergo a biennial 2 hour refresher CPR course, and document and scrutinize every CPR for monitoring and learning purposes.

In the current study we reviewed the survival to discharge of adult patients who had IHCA and underwent CPR during a 20 year period (1995–2015). We compared rates of incidence and of survival to discharge between the period preceding and subsequent to the issuance of the guidelines: 1995–2005 and 2006–2015.

PATIENTS AND METHODS

Data were retrieved from the medical records of patients hospitalized at Emek Medical Center in Afula, Israel, during the years 1995–2015. Computerized records were available from the year 1995. We included records of adult patients (≥ 18 years) who suffered from IHCA and underwent CPR during hospitalization. Events occurring in the ICU, the intensive cardiac care unit (ICCU), the emergency department (ER), and inpatient wards were included. Patients who suffered from primary ventricular fibrillation or periprocedural cardiac arrests (during coronary angiogram or electrophysiological studies) were excluded since these patients have particular clinical characteristics.

Patient-level data obtained from the medical files included the following variables: age, gender, ethnicity, the hospital department where the event occurred, length of stay prior to the event, date of hospitalization (index admission), hospital discharge date, outcome by the end of admission, any previous admissions within the preceding 3 months, baseline neurological depression, initial cardiac arrest rhythm (asystole, pulseless electrical activity, ventricular fibrillation, and pulseless ventricular tachycardia), time to CPR initiation, and neurological status at hospital discharge. We also retrieved the main diagnosis at admission and clinical characteristics of the acute disease: acute coronary insufficiency, heart failure, sepsis, hypotension, respiratory insufficiency, acute renal failure, hepatic insufficiency, acute stroke, and occurrence of severe metabolic acidosis (pH < 7.2) or severe electrolyte abnormality prior to the event. Data were collected regarding background diseases, including hypertension, diabetes mellitus, chronic renal failure, ischemic heart disease, congestive heart failure, chronic obstructive pulmonary disease, and a previous cerebrovascular accident. For patients who survived IHCA, mortality at 1 month, 3 months, 6 months, and 1 year were recorded.

In addition we retrieved data from the hospital's resuscitation committee that included the number of refresher courses delivered since issuance of the guidelines, the number of staff members who participated in these courses, the type and methods of training in CPR, the type and number of audits performed during the past 10 years, and the number of CPR quality assessment evaluations conducted. We also retrieved detailed data concerning time to initiation of CPR by attending staff, time to arrival of resuscitation teams, duration of CPR, drugs given during CPR, and outcome.

The study was approved by the hospital's institutional review board.

STATISTICAL ANALYSIS

We used the chi-square test (or Fisher's exact test) to investigate the association between categorical variables and death. Continuous variables were examined using the Student *t*-test (or Wilcoxon two-sample test). The effect of the independent risk factors on the odds of death was estimated with univariate and stepwise multivariate logistic regression. We used the Cochran–Armitage test to examine trends in proportions of IHCA incidence and survival rate. Data management and statistical analyses were performed using the SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

For the 1995–2005 period, there were 219 events of CPR for IHCA, of them 31 (14.2%) survived. For the 2006–2015 period, there were 483 events, of which 62 (12.8%) survived ($P = 0.6$). Six died during the month following discharge, 11 more during the first 3 months, three more during the first 6 months, and another 12 during the year following discharge. Thus, at 1 year following discharge, only 61 (8.7%) of the patients were alive.

Overall the most common initial dysrhythmias witnessed during cardiac arrest were asystole (54.1%) and pulseless electrical activity (PEA) (24.4%). For 19.1%, the dysrhythmia was ventricular fibrillation, and for 2.4%, pulseless ventricular tachycardia.

Characteristics of the patients according to the two periods of hospitalization, 1995–2005 and 2006–2015, are shown in Table 1. Survival to discharge decreased from 14.2 to 12.8% ($P = 0.3$). In parallel, the ratio of non-shockable (asystole and

Table 1. Baseline characteristics of patients with in-hospital cardiac arrest in the two periods

Variable	Period 1 1995–2005 n=219	Period 2 2006–2015 n=483	*P* value
Age (years), mean (range)	69.1 (18–99)	70.5 (18–106)	0.1
Male gender, n (%)	126 (57.5)	273 (56.5)	NS
Arab race, n (%)	77 (35.1)	203 (42)	0.08
Hospital stay to event (days), n (range)	4.8 (1–70)	5.4 (1–71)	0.1
Admission within prior 3 months	81 (37)	221 (45.8)	0.03
Number surviving to hospital discharge, n (%)	31 (14.2)	62 (12.8)	NS
Initial cardiac arrest rhythm, n (%)			
Asystole	106 (48.4)	274 (56.7)	0.003
Pulseless electrical activity	48 (21.9)	123 (25.5)	0.003
Ventricular fibrillation	56 (25.6)	78 (16.4)	0.003
Pulseless ventricular tachycardia	9 (4.1)	8 (1.6)	0.003
Mean time to CPR initiation (minutes)[a]	2	1.8	NS
Hospital location of arrest, n (%)			
ICU and ER	87 (39.3)	164 (33.9)	
All other inpatient wards	132 (60.3)	319 (66.1)	0.1
Coexisting conditions, n (%)			
Heart failure	85 (38.8)	167 (34.6)	0.1
Acute coronary insufficiency	78 (35.6)	122 (25.2)	0.006
Sepsis	80 (36.5)	210 (43.5)	0.08
Hypotension	90 (41.1)	191 (39.5)	NS
Respiratory insufficiency	74 (33.8)	194 (40.2)	0.1
Acute renal failure	87 (39.7)	266 (55.1)	0.002
Hepatic insufficiency	5 (2.2)	7 (1.5)	NS
Acute stroke	7 (3.2)	15 (3.1)	NS
Severe metabolic acidosis and electrolyte abnormality	56 (25.6)	156 (32.3)	0.07
Background chronic co-morbidity, n (%)			
Hypertension	147 (67.1)	365 (75.6)	0.02
Diabetes mellitus	94 (42.9)	253 (52.4)	0.02
Chronic renal failure	50 (22.8)	146 (30.2)	0.043
Ischemic heart disease	118 (53.9)	245 (50.7)	NS
Congestive heart failure	82 (37.4)	200 (41.4)	NS
Chronic obstructive pulmonary disease	34 (15.5)	101 (20.9)	0.09
Previous cerebrovascular accident	29 (13.2)	69 (14.3)	NS
Baseline decline in CNS function	18 (8.2)	47 (9.7)	NS

CPR = cardiopulmonary resuscitation, ICU = intensive care unit, ER = emergency department, CNS = central nervous system
[a]Data were available for only 38% of patients in period 1 (1995–2005)

Table 2. Rhythm-specific survival rates during the two periods

	Period 1: 1995–2005		Period 2: 2006–2015		
Arrhythmia	Number of patients	Number of survivors (%)	Number of patients	Number of survivors (%)	*P* value
Asystole	106	15 (14.1)	274	25 (9.1)	0.1
Pulse electrical activity	48	6 (12.5)	123	11 (8.9)	NS
Ventricular fibrillation	56	8 (14.2)	78	23 (29.4)	0.06
Pulseless ventricular tachycardia	9	2 (22.2)	8	3 (37.5)	NS
Non-shockable rhythm	154	21 (13.6)	397	36 (9.1)	0.08
Shockable rhythm	65	10 (15.4)	86	26 (30.2)	0.05

Table 3. Clinical and epidemiological characteristics of deceased and survivors with crude odds ratio for mortality

Variable	Survivors n=93	Deceased n=609	OR (95%CI)	*P* value
Mean age, years (range)	66.3 (18-93)	70.6 (18-106)	0.98 (0.97–0.99)	0.007
Male gender, n (%)	56 (60.2)	347 (56.9)	1.14 (0.73–1.78)	NS
Jewish race, n (%)	46 (49.5)	376 (61.7)	1.65 (1.06–2.56)	0.03
Hospital stay to event (days), n (range)	4.0 (1–30)	5.5 (1–71)	0.96 (0.91–1.01)	0.06
Admission within prior 3 months, n (%)	40 (43)	262 (43)	1 (0.64–1.56)	NS
First witnessed arrhythmia during cardiac arrest, n (%)				
Asystole	40 (43)	340 (56.1)	1.67 (1.08–2.6)	0.02
Pulseless electrical activity	17 (18.3)	154 (25.3)	1.51 (0.87–2.64)	0.1
Ventricular fibrillation	31 (33.3)	103 (16.9)	0.4 (0.25–0.65)	0.003
Pulseless ventricular tachycardia	5 (5.4)	12 (1.9)	0.35 (0.12–1.02)	0.06
Hospital location of cardiac arrest, n (%)				
Intensive care unit and emergency department	45 (48.4)	206 (33.8)		
All other inpatient wards	48 (51.6)	403 (66.2)	1.83 (1.18–2.85)	0.0075
Coexisting conditions, n (%)				
Heart failure	28 (30.1)	217 (35.6)	1.29 (0.8–2.06)	NS
Acute coronary insufficiency	24 (25.8)	165 (27.1)	1.07 (0.65–1.76)	NS
Sepsis	26 (27.9)	264 (43.3)	1.97 (1.22–3.19)	0.005
Hypotension	19 (20.4)	262 (43)	2.94 (1.73–4.99)	‹ 0.0001
Respiratory insufficiency	29 (31.2)	239 (39.2)	1.43 (0.89–2.28)	0.1
Acute renal failure	29 (31.2)	324 (53.2)	2.51 (1.57–4)	0.0001
Hepatic insufficiency	1(1)	11 (1.9)		NS
Acute stroke	1 (1)	21 (3.4)		NS
Metabolite or electrolyte abnormality	20 (21.5)	192 (31.5)	1.68 (1–2.84)	0.05
Background chronic morbidity, n (%)				
Hypertension	63 (67.7)	449 (73.3)	1.34 (0.84–2.14)	NS
Diabetes mellitus	42 (45.2)	305 (50.1)	1.22 (0.79–1.890	NS
Chronic renal failure	30 (32.3)	166 (27.3)	1.27 (0.79–2.03)	NS
Ischemic heart disease	48 (51.6)	315 (51.7)	1 (0.65–1.55)	NS
Congestive heart failure	40 (43)	242 (39.7)	1.14 (0.74–1.78)	NS
Chronic obstructive pulmonary disease	17 (18.3)	118 (19.4)	1.07 (0.61–1.89)	NS
Previous cerebrovascular accident	9 (9.7)	89 (14.6)	1.6 (0.78–3.29)	NS
Baseline decline in CNS function	2 (2.1)	64 (10.5)	10.75 (1.48–76.92)	0.001

CNS = central nervous system, OR = odds ratio, CI = confidence interval, NS = not significant

PEA) to shockable rhythms (ventricular fibrillation and pulseless ventricular tachycardia) increased from 2.4 to 4.6 ($P = 0.01$). The proportion of IHCA that appeared in the presence of an acute coronary ischemic event decreased, and the proportion of cases for which cardiac arrest appeared in the presence of kidney failure increased. The proportion of events occurring in ICUs and the ER decreased from 39.7% to 34.0%, although this decrease was not statistically significant. Survival rate for shockable rhythms doubled from the first to second period, while it decreased for non-shockable rhythms [Table 2].

Of patients whose presenting rhythm was shockable, 23.8% survived to discharge; compared to 10.3% of those with initial non-shockable rhythms. Higher proportions of patients with sepsis, hypotension, and acute renal failure were observed among the deceased than among the survivors [Table 3]. Of the 66 patients with a baseline decline in neurological function, only two survived [Table 3]. In multivariate analysis, age (odds ratio [OR] = 0.98, 95% [confidence interval [CI] 0.96–0.99, P = 0.004), hypotension (OR = 3.91, 95%CI 2.17–7.04, $P < 0.001$), acute renal failure (OR = 2.16, 95%CI 1.32–3.55, $P = 0.002$), declined baseline neurological status (OR = 5.7, 95%CI 1.44–9.3, $P < 0.001$), and IHCA occurring outside ICUs (OR = 2.64, 95%CI 1.62–4.31, $P = 0.0001$), were significantly associated with increased odds for death.

Over 20 years (1995–2015) the overall number of patients hospitalized increased, as did IHCA incidence, from 0.7 events/1000 admissions (1995) to 1.7 events/1000 admissions (2015) [Figure 1]. This increase was statistically significant (Cochran–Armitage trend test P-value < 0.001), and contrasts with the lack of increase in survival rate over the same period (Cochran–Armitage trend test P-value = 0.376).

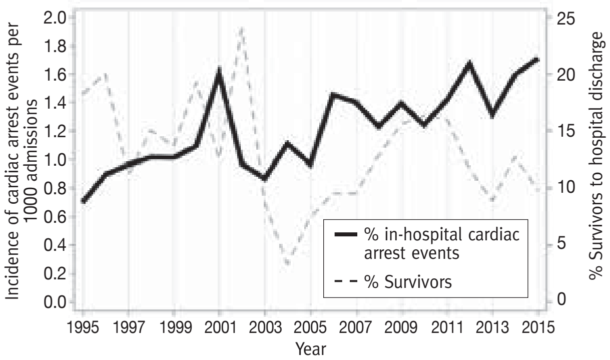
CPR REFRESHER COURSES: TRAINING, AUDITS AND EVALUATIONS

Since issuance of the guidelines in 2006, and until 2016, three refresher courses were conducted. Despite a growing trend, only 66.8% of doctors participated in these courses, compared with nearly 88% of the nursing staff. The 2 hour refresher courses included a 1 hour theoretical session and a 1 hour practical session with face-to-face training while practicing CPR on manikins. Since 2006 only one audit, in 2015, was conducted. It tested theoretical and practical knowledge of the medical staff by simulating scenarios of cardiac arrest with various initial rhythms. The audit was conducted in medical and surgical departments without advanced notice and tested the adequacy of response to a possible IHCA event, including initial approach, adequacy of chest compressions, and treatment of possible dysrhythmias. The overall staff performance of each department was evaluated as poor, good, and very good without reference to specific individuals. Quality assessment of CPR treatment was carried out retrospectively based on electrocardiogram recordings retrieved from defibrillators. Written reports prepared by staff included time to CPR initiation after IHCA event, description of the clinical setting, initial witnessed rhythm, drugs given during CPR, length of CPR, and time to restoration of spontaneous circulation.

DISCUSSION

Overall, no improvement in survival following IHCA was observed during the 10 year period after distribution of nation-

Figure 1. Annual rates of in-hospital cardiac arrest events and survival to discharge, 1995–2015



% in-hospital cardiac arrest events: Cochran–Armitage trend test *P* value < 0.0001
% survivors: Cochran–Armitage trend test *P* value = 0.3796

wide regulations calling for CPR refresher course (2006–2015), compared to the 10 year period preceding (1995–2005). The data on survival rates concur with other studies that did not show improvement over time in IHCA survival [1-5,7] and contrasts with a study that reported improvement [6].

In the current study, differences in the characteristics of the ICHA events in the later period may explain the lack of improvement in overall IHCA survival, primarily, an increased proportion of non-shockable rhythms; an increased proportion of patients with acute renal failure, sepsis, background comorbidities (hypertension, diabetes mellitus, and chronic renal failure); and a decreased proportion of patients with coronary ischemia. Survival nearly doubled for shockable dysrhythmias but decreased for non-shockable rhythms. Other studies have also demonstrated better survival for cardiac arrest when the presenting dysrhythmia was shockable [1-6,8-10]. In the GWTG-Resuscitation registry, survival was better for shockable rhythms, yet improvement in survival was similar for the two rhythm groups [6]. A recently published systematic review of IHCAs in Australia and New Zealand showed a relatively high rate of initial cardiac rhythms that were shockable (31%) as well as a high rate of survival to discharge (25%) [11]. Better management of heart failure and acute myocardial infarction would be expected to reduce both the incidence of IHCAs due to shockable rhythms and the overall rate of IHCA survival. While the meta-analysis by Zhu and Zhang [5] showed a lack of improvement in IHCA survival, they reported significant heterogeneity among studies and did not analyze data according to first dysrhythmia.

The increased survival rate for shockable dysrhythmias is gratifying. Based on a single audit it is hard to draw any conclusions concerning the impact of CPR training on staff performance and to what extent the increased survival for shockable dysrhythmias is attributed to CPR training. We think that these CPR refresher courses were beneficial and may have reduced time to CPR initiation by attending staff. However, due to poor documentation of time to CPR initiation during the first period (1995–2005) (available only in 38% of cases), we cannot determine if the improved survival was indeed secondary to shorter CPR initiation times.

Parallel to the lack of improvement in survival, the incidence of IHCA increased during the 20 year period of the current study. Possible reasons may be that the population in the later period was of higher risk or that IHCA prevention declined. We report a higher proportion of acute renal failure in the later period; which was associated with poorer survival. A study based on a large U.S. registry showed lower survival rates in hospitals with higher cardiac arrest incidence after adjusting for patient characteristics [12]. A hospital's nurse-to-bed ratio was found to attenuate this relationship. At our medical center, as well as at most hospitals in Israel, the nurse-to-bed ratio decreased during the study period [13]. This trend may have contributed to the increased IHCA incidence and the decreased survival, despite the implementation of refreshing courses.

In the later period, the proportion of events that occurred in ICUs and the ER was lower than in other inpatient units. However, survival to discharge was greater for events occurring in the former than latter locations. Other studies reported higher survival rates in the ER than in other medical units [14]. In addition, it is possible that more events were prevented in ICUs than in other units during the later period.

The increased number of IHCA events may also reflect an increased attempt to perform CPR. Of note, while no improvement was observed in IHCA survival following CPR training in Denmark, more CPR attempts were initiated after the intervention, which resulted in more patients surviving cardiac arrest [1]. Such observation supports the proposition that survival may not be the best outcome measure for cardiac arrest, and that high survival rates may in fact be due to poor prevention [15]. Return of spontaneous circulation or 24-hour survival may be more meaningful measures of CPR success and of the effect of new CPR guidelines than the outcome, survival to discharge. Albeit, both IHCA incidence and CPR initiation involve many factors, and their retrospective interpretation is problematic. Requests from patients and families not to resuscitate reduce the proportion of IHCAs for which CPR is initiated. Relevant to this point is the initiation in June 2012 of an intervention to improve communication skills with patients and families regarding end-of-life issues. Emek Medical Center is one of 10 hospitals within the Clalit Health Services, the largest health maintenance organization in Israel, that was included in this intervention. Nevertheless, we do not have any information as to whether this intervention affected the numbers of patients for whom CPR was initiated.

This study has a number of limitations. As with all before-and-after studies, unexamined processes occurring during the 20 year study period may have affected the findings. We would expect positive results from processes due to technological advances and international publications of guidelines and research. However, changes in hospital factors, such as decreases in the nurse-to-bed ratio and fewer beds for admission to the intensive care unit could lead to decreases in survival rates. Furthermore, information was not fully available for measures that may have affected IHCA survival, especially in the first period (1995–2005). In addition, the investigation of a single center enables in-depth examination of processes. The extent that the findings are generalizable to other medical centers is unknown. Nonetheless, due to the considerable heterogeneity that has been reported among hospitals in IHCA incidence and survival [5,12,16-19], studies from different geographic areas and populations are important.

CONCLUSIONS

This study did not find improvement in IHCA survival following the issuance of national guidelines requiring CPR refresher training. We found an increased survival rate of patients with initial shockable dysrhythmia. A decreased proportion of events with this dysrhythmia, an increased proportion with acute renal failure, and a decreased proportion occurring in intensive care units are clearly part of the explanations for these findings. We believe that CPR refresher courses were helpful, although an objective measurement of their effectiveness is lacking.

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Capsule

Type III interferons prime neutrophils

Type I interferons (IFNs) have a well-established role in antiviral immunity. **Espinosa** and co-authors found that type III IFNs (IFN-λs) play an essential role in driving antifungal responses. They studied immune responses to *Aspergillus fumigatus* in mice lacking receptors for type I or type III IFNs. Monocyte-derived type I IFNs were key drivers of IFN-λ production. Although the authors could not pin down the sources of IFN-λs, they identified neutrophils as the functional target of IFN-λs. Selective deletion of IFN-λ receptor in neutrophils caused mice to succumb to *Aspergillus fumigatus* infection.

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Eitan Israeli

"We need diversity of thought in the world to face the new challenges"

Tim Berners-Lee, (born 1955), also known as TimBL, English engineer and computer scientist, best known as the inventor of the World Wide Web