

Long-Term Survival of Discharged Patients Admitted to Intensive Coronary Care Unit after Out-of-Hospital Cardiac Arrest

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ABSTRACT: **Background:** Survival of patients who were discharged from the hospital following out-of-hospital cardiac arrest (OHCA) has not been well defined. **Objective:** To verify predictor variables for prognosis of patients following OHCA who survived hospitalization. **Methods:** We retrospectively reviewed clinical, demographic, and outcome data of consecutive patients who were hospitalized from January 1, 2009, through December 31, 2014, into the intensive coronary care unit (ICCU) after aborted OHCA and discharged alive. The patients were followed until December 31, 2015. **Results:** Of the 180 patients who were admitted into ICCU after OHCA, 64 were discharged alive (59.3%): 55 were male (85.9%), 14 died 16.5 ± 18 months after their discharge. During 1 year follow-up, nine patients (14.1%) died after a median period of 5.5 months and 55 patients (85.9 %) survived. Diabetes mellitus and chronic renal failure (CRF) were more frequent in patients who died within 1 year after their hospital discharge than those who survived. Ventricular fibrillation, such as initial arrhythmia, and opening of occluded infarct related artery were more frequent in survivors. **Conclusions:** Most of the patients who were discharged after OHCA were alive at the 1 year follow-up. The risk of death of cardiac arrest survivors is greatest during the first year after discharge. CRF remains a poor long-term prognostic factor beyond the patients' discharge. Ventricular fibrillation, as initial arrhythmia, and opening of occluded infarct related artery have a positive impact on long-term survival.

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KEY WORDS: long-term survival, out-of-hospital cardiac arrest (OHCA), cardiopulmonary resuscitation (CPR)

Cardiac arrest is the abrupt loss of heart function of a person with or without known heart disease. It usually results from an abnormal heart rhythm and the time and mode of events are unexpected.

The most common arrhythmia that causes sudden cardiac arrest is ventricular fibrillation (VF), followed by asystole and pulseless ventricular tachycardia [1].

Causes of fatal arrhythmias include cardiomyopathies, inherited defects in the conduction system (as long QT syndrome, Brugada syndrome, Wolf-Parkinson-White syndrome), heart medications, and ischemic injury from acute myocardial infarction or previous infarcts. The most common causes of sudden cardiac arrest, which are not initiated by the heart, include electrocution, commotio-cordis, and recreational drug user.

A decline of death-on-arrival situations and an increased trend of out-of-hospital cardiac arrest (OHCA) have been reported [2]. Despite efforts to improve patient management and therapy, the survival outcome for OHCA is poor [3]. The chain-of-survival concept has been proposed to increase survival among patients after OHCA. It suggests recognition and activation of the emergency response system, immediate high quality cardiopulmonary resuscitation, early defibrillation, basic and advanced emergency medical services, advanced life support, and post-arrest care [4].

The survival rate at discharge from the hospital among OHCA survivors increased from the beginning of the millennium compared to reports in previous years. The better outcome most probably is due to the new therapies and therapeutic procedures during hospital care.

The long-term survival of patients discharged from the intensive coronary care unit (ICCU) is not well known. Our aim was to characterize those patients and to define the predictor variables for their prognosis.

PATIENTS AND METHODS

The approval for the study was obtained from the ethics review committee on human research, Emek Medical Center, Afula (Nr. 0153-15-EMC).

Emek Medical Center is a secondary hospital that serves a population of about 400,000 people. Patients who present with OHCA are treated by the local emergency medical services and brought to our emergency room. We retrospectively analyzed data of consecutive patients resuscitated from OHCA and admitted to the ICCU of our institution from January 1, 2009 to December 31, 2014. These patients were followed until December 12, 2015.

All of the medical data were computerized and archived in the hospital database.

All of the patients with acute or suspected myocardial infarction underwent emergency catheterization and intervention as needed.

Therapeutic hypothermia in our department was available from December 2010.

Left ventricular ejection fraction (LVEF) was calculated by echocardiogram at hospital admission.

We analyzed the demographics, previous and current clinical data, in-hospital treatment, and initial documented rhythm reported by the rescue treating teams. The group of patients who were discharged alive from our institution comprised our study population.

The assessed neurological status at discharge from the hospital was based on the Glasgow–Pittsburgh cerebral performance categories (GP-CPC) [5]. Significant neurologic deficits were considered when the CPC score was ≥ 3 . Long-term follow-up was recorded using the OFEK computer program, which is connected directly to the Internal Ministry of Israel database. Data of patients who died at home were collected during telephone calls with family members.

Long-term survival was defined as survival longer than 1 year after hospital discharge.

STATISTICAL ANALYSIS

Categorical variables were presented using frequencies and percentages. Continuous variables were presented using mean \pm standard deviation. The association between the studies groups and categorical variables was examined using the chi-square test (or Fishers' exact test). For continuous variables the Wilcoxon two-sample test was used. Survival analysis was presented with Kaplan–Meier curves, and a log-rank test was used for the survival curve comparison. A multivariate Cox regression model was used and the adjusted hazard ratios, along with 95% confidence intervals (CI) were presented. The statistical analyses were performed using SAS software, version 9.2 (SAS Institute Inc., Cary, NC, USA). Significant result was considered if $P < 0.05$.

RESULTS

Our study sample included 180 patients who had been admitted to the ICCU after OHCA. Of these, 64 patients (59.3%) were discharged. Initial arrhythmia ventricular fibrillation was present in 70 patients (64.8%) and asystole in 38 (35.2%). The baseline characteristics of patients who did not survive (group 1) were compared to those of patients who survived and were discharged (group 2). These data are reported in Table 1.

Multivariate Cox regression showed that severe neurologic deficit, temporary pacemaker implantation, and dura-

Table 1. Univariate analysis: baseline characteristics of patients who underwent OHCA and were admitted to the intensive coronary care unit

Baseline characteristics	Group 1 44 patients	Group 2 64 patients	P value
Age (years), mean \pm SD	64.2 \pm 11.7	56.6 \pm 13.4	0.0037
Male gender, n (%)	35 (79.5)	55 (85.9)	NS
Ischemic heart disease, n (%)	25 (56.8)	27 (42.2)	NS
Congestive heart failure, n (%)	17 (38.6)	21 (32.8)	NS
Cardiomyopathy, n (%)	5 (11.4)	11 (17.2)	NS
Hypertension, n (%)	35 (79.5)	37 (57.8)	0.0186
Diabetes mellitus, n (%)	24 (54.5)	17 (26.6)	0.0032
Hyperlipidemia, n (%)	30 (68.2)	40 (62.5)	NS
Chronic renal failure, n (%)	9 (20.4)	7 (10.9)	0.0032
Smoker, n (%)	28 (63.6)	39 (60.9)	NS
Valvular heart disease, n (%)	3 (6.8)	6 (9.4)	NS
Obesity, n (%)	18 (40.9)	11 (17.2)	0.0063
LVEF, mean \pm SD	39 \pm 8	40 \pm 11	NS
Ventricular fibrillation, n (%)	16 (36.4)	54 (84.4)	< 0.0001
Acute ischemic events, n (%)	23 (52.3)	38 (59.4)	NS
Severe neurologic deficit, n (%)	33 (75)	20 (31.5)	< 0.0001
Primary percutaneous, coronary intervention, n (%)	20 (45.4)	40 (62.5)	NS
Opening IRA successful, n (%)	15 (34.1)	31 (48.4)	NS
Therapeutic hypothermia, n (%)	12 (27.3)	17 (26.6)	NS
Temporary pacemaker implantation, n (%)	6 (13.6)	1 (1.6)	0.0176
Duration of hospitalization (days), n (%)	9.5 (12.9)	15.2 (14.7)	0.0011

OHCA = out-of-hospital cardiac arrest, LVEF = left ventricular ejection fraction, IRA = infarct related artery, SD = standard deviation, NS = non-significant

tion of hospitalization were independent predictors of more adverse outcomes, while patients with ventricular fibrillation as the initial arrhythmia had a favorable outcome [Table 2]. Kaplan–Meier curves for survival of patients admitted into ICCU are reported in Figure 1A.

Fourteen patients died 16.5 ± 18 months (range 1–50 months) after their hospital discharge.

During the first year after discharge nine patients (14.1%) died after a median period of 5.5 months, range 1–8 months (group A) and 55 (85.9%) survived (group B) [Figure 1B]. Five of those who died had recurrent OHCA at home 5.2 ± 3.4 months (range 1–10 months) after their discharge. Another two patients died at home (the causes of death are unknown) and two patients died at the nursing home where they were admitted after their hospital discharge because of severe neurological sequelae after 2 ± 1 months (range 1–5 months). No postmortem examinations were performed, and we could not confirm the exact diagnosis that caused recurrent OHCA.

Comparing groups A and B, we found that diabetes mellitus and chronic renal failure were more frequent in patients who died within 1 year after their hospital discharge than in

Table 2. Multivariate Cox regression model: baseline characteristics of patients who underwent OHCA and were admitted to the intensive coronary care unit

	Hazard ratio	95% confidence interval	P value
Ventricular fibrillation	3.285	7.034–1.534	0.0022
Age	1.021	1.051–0.991	0.1687
Hypertension	1.603	3.685–0.695	0.2666
Diabetes mellitus	0.832	1.796–0.385	0.6392
Obesity	1.051	2.139–0.517	0.8901
Severe neurologic deficit	6.919	15.274–3.134	< 0.0001
Temporary pacemaker implantation	3.745	11.929–1.176	0.0255
Duration of hospitalization (days)	0.918	0.961–0.877	0.0002

OHCA = out-of-hospital cardiac arrest

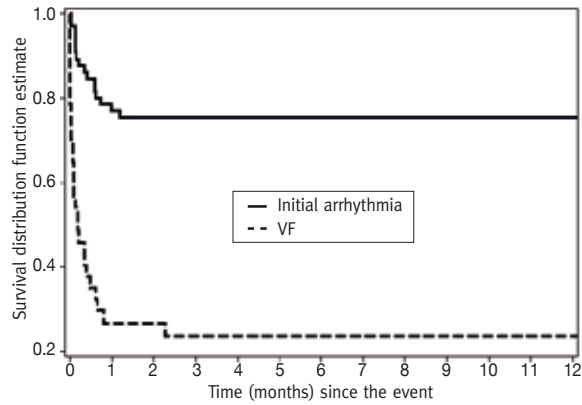
Table 3. Univariate analysis: baseline characteristics of patients who underwent OHCA and survived to hospital discharge

Baseline characteristics	Group A 9 patients	Group B 55 patients	P value
Age (years) mean ± SD	64.1 ± 16.7	55.3 ± 12.6	NS
Male gender, n (%)	8 (88.9)	47 (85.5)	NS
Ischemic heart disease, n (%)	5 (55.6)	22 (40)	NS
Congestive heart failure, n (%)	4 (44.4)	17(30.9)	NS
Cardiomyopathy, n (%)	1 (11.1)	10 (18.2)	NS
Hypertension, n (%)	8 (88.9)	29 (52.7)	NS
Diabetes mellitus, n (%)	5 (55.6)	12 (21.8)	0.0482
Hyperlipidemia, n (%)	6 (66.7)	34 (61.8)	NS
Chronic renal failure, n (%)	4 (44.4)	3 (5.4)	0.0056
Smoker, n (%)	6 (66.7)	33 (60)	NS
Valvular heart disease, n (%)	0 (0)	6 (10.9)	NS
Obesity, n (%)	3 (33.3)	8 (14.6)	NS
LVEF, mean ± SD	37.4 ± 9.9	39.8 ± 11.6	NS
Ventricular fibrillation, n (%)	5 (55.5)	49 (89.1)	0.0272
Acute ischemic events, n (%)	7 (77.8)	31 (56.4)	NS
Residual severe neurologic deficit, n (%)	3 (33.3)	14 (25.4)	NS
Primary percutaneous, coronary intervention, n (%)	6 (66.7)	34 (61.8)	NS
Opening IRA successful, n (%)	2 (22.2)	29 (52.7)	0.0304
Therapeutic hypothermia, n (%)	1 (11.1)	16 (29.1)	NS
ICD implantation, n (%)	1 (11.1)	13 (23.6)	NS

OHCA = out-of-hospital cardiac arrest, LVEF = left ventricular ejection fraction, IRA = infarct related artery, SD = standard deviation

those who survived. Ventricular fibrillation, such as initial arrhythmia, and opening of the occluded infarct related artery were more frequent in survivors [Table 3]. Multivariate Cox regression showed that ventricular fibrillation ($P = 0.0143$), chronic renal failure ($P = 0.0095$), and successful opening of the infarct related artery ($P = 0.0324$) were independent predictors of favorable outcome. Kaplan–Meier curves showed a significant difference in patient survival according to their initial arrhythmia [Figure 1C].

Figure 1A. Kaplan–Maier survival curves stratified by initial arrhythmia of patients admitted to the intensive coronary care unit after being resuscitated from out-of-hospital cardiac arrest (OHCA)



Log rank test $P \leq 0.0001$

Figure 1B. Kaplan–Maier survival curve of patients resuscitated from out-of-hospital cardiac arrest (OHCA) and discharged alive from hospital during 6 year follow-up

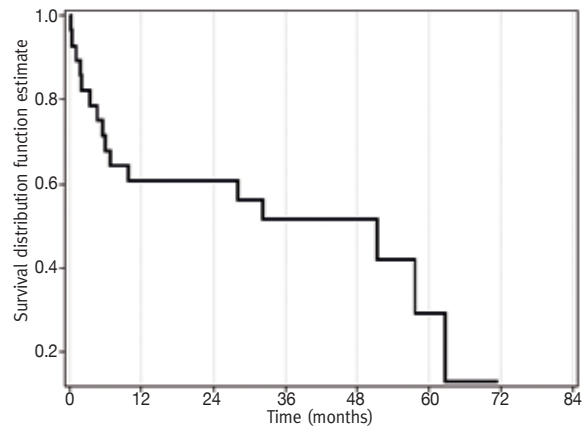
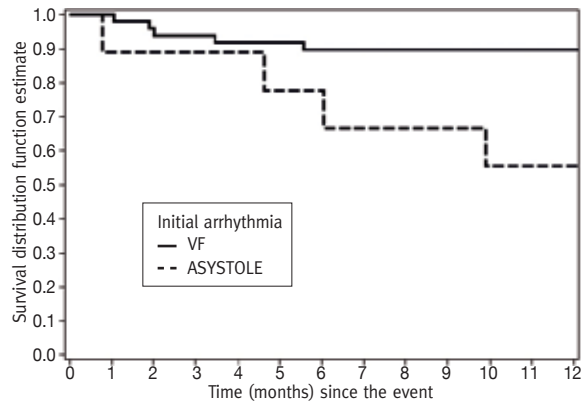


Figure 1C. Kaplan–Maier survival curves stratified by initial arrhythmia of patients discharged alive from hospital after being resuscitated from out-of-hospital cardiac arrest (OHCA)



Log rank test $P = 0.01$

DISCUSSION

During a 20 year period (1980–2000) live discharge from the hospital among OHCA patients was about 36%, without any improvement during this period [4]. Our data showed an improvement in survival rate of 60%. This finding is in accordance with recent data [6,7]. Improved survival in OHCA patients upon discharge from hospital could be due to new therapies, therapeutic procedures such as emergency percutaneous coronary intervention [8,9], and therapeutic hypothermia [7].

Published data on long-term survival of patients after OHCA and discharged from the hospital are rare and the conclusions are conflicting. Engdahl and colleagues [10] showed that survival rate after OHCA from years 1980 to 1998 did not change. On the contrary, Rea and co-authors [11] and Pell et al. [12] reported that long-term survival increased consistently and constantly over the time.

At the 1 year follow-up, 80% of our patients were alive, but most of the deaths among OHCA survivors occurred in the first year after discharge (69%). Similar results have been reported by others [13,14]. Increased mortality rates at 1 year after discharge have been reported also among in-hospital cardiac arrest survivors [15].

As might be expected, age is a contributing factor to survival outcome. Patients who died were older at the time of OHCA than those who survived at hospital discharge. Similar findings have been reported by others [6,9]. However, data about the age of patients who were discharged and who survived compared with those of patients who did not survive at long-term follow-up are contradictory. We found no significant age difference in the two groups of patients, as reported also by Pleskot and collaborators [14], in contrast to the findings of Reinhard et al. [13].

An implantable cardioverter-defibrillator (ICD) has been reported to reduce cardiac death [16,17]. Our study showed no significant difference in the outcome of patients with ICD compared to patients without ICD implantation, most probably significance was not reached because of the low number of implanted ICD.

Numerous studies have shown that presenting cardiac rhythms have an important prognostic factor during OHCA: asystole had worse impact than VF on survival at hospital discharge [18,19,20]. We observed that most of our survivors had VF as the initial heart rhythm, and VF continues to be a good prognostic index beyond patient discharge.

OHCA was associated with higher incidence of diabetes mellitus and CRF compared to the remaining admission [21]. Diabetes mellitus was found to be an adverse prognostic factor on hospital survival in patients admitted in a coronary care unit after resuscitating from OHCA [22]; according to our findings CRF is an independent predictor of poor prognosis on survival, even beyond hospital discharge.

Successful immediate percutaneous coronary angioplasty (PCI) has been found to improve hospital survival in patients with ST-segment elevation myocardial infarction (STEMI) and resuscitated from OHCA [8,9]. We did not see any similar finding, most probably because STEMI was present in only about half of our patients. Discordant results were seen in long-term survival. Garot et al. [23] reported a similar early successful PCI rate both in patients who died and in patients who survived during a 6 month follow-up. Bendz and colleagues [24] found that early PCI may have contributed to a long-term survival benefit in patients with STEMI and after OHCA similar to that of patients without OHCA. Our results confirmed that opening the occluded infarct related artery had a positive impact on long-term survival.

Therapeutic hypothermia was not associated with improved hospital survival in our patients after OHCA as also reported by others [6,23], but in contrast to the result of Loma-Osorio and colleagues [7] and Dumas et al. [9]. Data on long-term survival are lacking [25]. Our study did not show a different survival in long-term follow-up of patients who had therapeutic hypothermia versus those who had not.

Severe neurological deficits were more frequent in patients who died than in patients who survived hospitalization, but not in patients discharged from the hospital, independent of whether they died or were alive at the 1 year follow-up. This result may be due to the fact that most of the patients with serious neurological deficit were too ill to survive hospitalization.

LVEF at hospital admission was found to be neither a short-term nor a long-term prognostic sign. In our patients it was not significantly different in those who survived or died during hospitalization and during follow-up. Only LVEF failure to improve within 48 hours from OHCA has been found to be an adverse short-term sign and low LVEF at hospital discharge is an adverse long-term prognostic sign [1].

LIMITATIONS

This study was retrospective and thus some data for analysis were not available. Specifically, information regarding pre-hospital details about the cardiopulmonary resuscitation were insufficient and were not considered. Postmortem examinations were not performed; therefore, the exact diagnosis is unknown.

The number of patients in our study was low and subset analysis could have been influenced by the limited power of the study.

Other factors that we did not consider may have influenced patient outcome.

CONCLUSIONS

Most of the patients who were discharged after OHCA were alive at the 1 year follow-up. The risk of death of cardiac arrest survivors is greatest during the first year after discharge. CRF remains a poor long-term prognostic factor beyond patient

discharge. Opening of the occluded infarct related artery and VF may have a positive impact on long-term survival.

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Capsule

Risk of hypersensitivity to biologic agents among Medicare patients with rheumatoid arthritis

Hypersensitivity reactions (HSRs) can occur with any of the available biologic agents used to treat rheumatoid arthritis (RA). Yun et al. compared drug-specific risks for HSRs among RA patients enrolled in the U.S. Medicare program. The authors identified 725,591 biologic agent administrations and 248 HSRs among 80,587 new users of biologic agents. Of these, 26.9% occurred in users of intravenous abatacept, 4.6% in rituximab, 5.8% in intravenous tocilizumab, 22.9% in infliximab, and 39.7% in injectable anti-tumor necrosis factor inhibitors (anti-TNFi). The cumulative incidence of HSRs over 6 months for all biologic agents was low (< 1%). The incidence rates (IRs) for HSRs ranged from 2.4 (abatacept) to 239.5

(rituximab) per 10⁶ person-days. After adjustment, and using injectable anti-TNFi over 0–30 days as the referent, rituximab, infliximab, abatacept, and tocilizumab infusions were associated with a statistically significant higher risk of HSR. The sensitivity analysis yielded similar results. The authors conclude that among RA patients taking biologic agents, rituximab and infliximab were most strongly associated with HSRs. The absolute IRs of HSR events for all biologic agent exposures were low.

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