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Abstract

Patients with Diabetes Have Decreased Survivability with Good Neurological Outcomes After Out of Hospital Cardiac Arrest

By Dayea Beatrice Jang

Out of hospital cardiac arrest strikes as a fatal public health concern in South Korea as the estimated survivability is around 3%. While previous studies have identified health conditions that increase the risk for OHCA, there is limited understanding in predicting OHCA survivability with good neurological outcomes. This study aims to provide a scientific evidence of the association between diabetes and the probability of OHCA survival with good neurological outcomes.
Methods: This study is a retrospective cross-sectional observational study based on a nationwide cohort in South Korea. The study population includes 5,936 emergency medical services-assessed non-traumatic OHCA cases with known diabetes statuses from 2009 to 2012. Association was evaluated using a multivariate logistic regression model adjusting for age, gender, history of heart disease, and hypothermia.
Results: A total of 186 out of 1,940 (9.59%) diabetic patients survived to discharge with good neurological outcomes. Overall, we observed that having diabetes led to decreased probability of surviving OHCA with good neurological outcomes with distinctive difference in the magnitude of how diabetes plays a role between men and women as well as with history of heart disease. The adjusted OR measuring the effect of diabetes on survival with good neurological outcomes for male with history of heart disease was 0.32 (0.22-0.48, p-value <0.0001), for male without history of heart disease was 0.55 (0.34-0.89, p-value <0.0001), for female with history of heart disease was 0.60 (0.48-0.76, p-value 0.0152), and for female without history of heart disease was 1.03 (0.71-1.47, p-value 0.8919).
Conclusion: This study provides evidence of significant associations of diabetes and decreased OHCA survivability with good neurological outcomes where the association is greater in male and patients with heart disease. Given the findings, further epidemiologic research is required to better understand the association between pre-existing health conditions with neurological recovery after OHCA.

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“It only seems impossible until it’s done.” – Nelson Mandela

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Introduction

Burden of Disease

An out-of-hospital cardiac arrest (OHCAs) is defined as “cessation of cardiac mechanical activity that is confirmed by the absence of signs of circulation and that occurs outside of a hospital setting [1].” OHCA reportedly affects approximately 300,000 persons each year in the United States [1] and 275,000 persons in Europe [2]. The survival rate of patients with OHCA is estimated to be less than 7% and strikes as a significant health concern globally [3]. The survival rate is estimated to be even lower in the Republic of Korea compared to the global average, marking around 3% for emergency medical services (EMS)-assessed OHCA [4]. While the total number of OHCA cases captured by the national registry is projected to be increasing every year by 3-5%, the survival rate has not been improving [5].

Sudden Cardiac Arrest Risk Factors and Survivability

There have been many studies that reported on the chances of OHCA survival as well as that investigated the risk factors associated with the sudden cardiac arrest (SCA) incidence. Enhancing survival is often referred to the “chain of survival,” as termed by the American Heart Association (AHA), which describes a sequence of events in responding to SCA including early EMS access and activation, early initiation of basic cardiopulmonary resuscitation (CPR), early defibrillation, and early access to advanced medical care such as emergency departments (EDs) [6]. Improving SCA survival not only requires systematic interventions from different agents such as ambulatory dispatch, EMS, and hospitals as indicated, but clinical characteristics of the individual patient also hold corresponding importance. The clinical criteria that are most commonly associated with increased chance of survival include bystander witnessed arrest, EMS-witnessed arrest, provision of bystander CPR, shockable cardiac rhythm, and return of spontaneous circulation (ROSC) in the field [7]. Additionally, clinical factors such as coronary heart diseases, myocardial infarction, diabetes, and hypertension have been studied to be most closely linked to SCA [8, 9] . As described, the current understanding of survival predictability primarily relies on basic or advanced life support; however, there is little known about the variability of survival by each risk factor, which creates a challenge in developing an effective prevention or treatment strategy that can target a population with specific symptoms.

Furthermore, there are insufficient findings in predicting OHCA survival with good neurological outcomes. A retrospective study has observed that patients with early awakening time after receiving therapeutic hypothermia were associated with better neurologic status at discharge [10]. However, related findings in regard to OHCA survival with good neurological outcomes are limited to post-arrest care.

Diabetes

Diabetes has been associated with various cardiac complications including sudden cardiac death [11]. Furthermore, a prospective study have shown that impaired fasting plasma glucose (FPG) levels without diagnosed type 2 diabetes was also a comparable risk factor for SCD [12]. With increasing prevalence of approximately one in ten Korean adults ≥30 years of age having diabetes [13], identifying clinical manifestations of diabetes would be of great importance.

The direct mechanism between diabetes and how it contributes to SCA or post-resuscitation variations is unclear. However, diabetes has been extensively studied in regard to its complex manifestations to brain damage [14], where several modalities have been suggested including insulin resistance, hypoglycemia, and hyperglycemia [15].

Insulin resistance is a distinctive characteristic in diabetic populations. Insulin resistance has been closely associated with peripheral autonomic neuropathy as promoted by elevated free fatty acids [16] that leads to peripheral neuron injury [17]. Additionally, studies have observed attenuated insulin receptor activity in neurons in the brain that contributed to neuronal stress and injury in high-fat diet induced rats [18]. Diabetic neuropathy was estimated to affect more than 66% of diabetic patients in a prospective longitudinal study [19], and remains as a critical condition leading to severe autonomic deficits and even death.

The multifactorial nature of underlying causes of diabetic neuropathy complicates the identification process of its pathogenesis [20, 21], but hyperglycemia has been studied to be closely associated with the initiation of neuropathy development [22]. The molecular mechanism occurs via multiple pathways including upregulated oxidative stress mediators such as nicotinamide adenine dinucleotide phosphate oxidase (NADPH) that promotes excessive production of reactive oxygen species (ROS) as confirmed in both laboratory and clinical settings [23-25]. Additionally, a retrospective analysis has found significantly worsened neurological outcomes for severe traumatic brain injury patients with hyperglycemia [26], suggesting that unregulated hyperglycemia in diabetic patients can have detrimental effects on the brain.

Hypoglycemia is a serious condition that affects both type 1 and type 2 diabetics that can lead to critical neuronal damage by limiting neuronal metabolism with falling blood glucose level [27]. Past studies have found hypoglycemia-induced brain damage in laboratory settings [28] as well as in clinical settings where damage in the cortex and the hippocampus was observed [29, 30], which may lead to impaired cognitive performance [31].

As described, diabetes can trigger multiple adverse pathways leading to brain damage and diminished cognitive function. Therefore, identifying the association between diabetes and OHCA survival with good neurological outcomes will set the ground for facilitating future researches in therapeutic methods to alleviate brain damage in diabetic OHCA patients such as intense glucose control.

Study goal

This study aims to provide a scientific evidence of the association between pre-arrest risk factor and the probability of OHCA survival. Specifically, we investigated OHCA cases with known diabetes statuses and whether the exposure was related to a change in OHCA survival with good neurological outcomes.

Methods

Study Design

This study is a retrospective cross-sectional observational study based on a nationwide, population-based database in South Korea involving all patients who experienced SCA and were transported to the hospitals by EMS with resuscitation efforts.

Participants

A total of 8486 EMS-assessed OHCA cases survived to admission in South Korea during the period of January 1, 2009 to December 31, 2012 were pulled from the cardiovascular disease surveillance (CAVAS) database for this study. Out of 8486 OHCA cases, 2550 cases were missing information on diabetes status and were excluded from the analysis. Further exclusion criteria included patients with non-cardiac etiologies, a terminal illness, “Do Not Resuscitate” card, in hospice care, pregnant, living alone, or homeless. All other study variables with standard definitions were retrospectively reviewed and collected from the EMS run sheets and hospital medical records.

Data sources and measurement

The cardiovascular disease surveillance (CAVAS) database is a nationwide, population-based database of EMS-assessed OHCA patients in South Korea. The registry utilizes standardized definitions and reporting templates as known as Utstein-style, and are comprised of data collected from EMS runs sheets and hospital medical records.

EMS run sheets are completed by EMS personnel and include patient information including demographic, event demographic, ambulance operation information (time of call, departure time, arrival time, return time), patient clinical information, treatment such as defibrillation or CPR, and transport information such as to which hospital the patient was transported. They are coded and filed electronically in each provincial EMS headquarters.

Hospital medical records are obtained from the emergency departments the patient was transported to and include patient clinical information, treatment information, operation information (time to admission, time to discharge), and outcomes. Medical records were collected by trained medical record reviewers who visited the hospitals to evaluate chart records and document hospital outcomes electronically.

Variables

The primary exposure variable of interest was diabetes. Diabetes status includes both type 1 and type 2 diabetes mellitus and was abstracted from the hospital medical records as a dichotomized variable by a trained medical record reviewer. Diabetes types are not considered as different group in this study. When the patients were diagnosed or treated by physicians, we defined the patients as having with diabetes.

Other covariates that were examined are listed as follows. The type of electrocardiogram (ECG) was categorized to ventricular fibrillation (VF) or ventricular tachycardia (VT), pulseless electrical activity (PEA), and asystole. EMS defibrillation indicates whether the EMS provider performed a defibrillation on the patient at the field or during transport using the automated external defibrillators (AEDs); defibrillation is usually limited to patients with shockable rhythms such as VF or VT. Prehospital return of spontaneous circulation (ROSC) indicates a presence of palpable pulse for longer than 20 minutes after documented asystole. Bystander witness status indicates whether the OHCA occurrence was witnessed. The place of OHCA was categorized to public, private, or other. The level of ED where the patient was transported to was categorized as level 1, level 2, and level 3 as formally designated by the government where level 1 is the highest and is characterized by human resources, medical instruments and equipment, and service availability; level 2 is equipped with ability to provide 24-7 services by certified emergency physicians; and level 3 is usually served by general physicians.

Insurance types were categorized into two levels including National Health Insurance, and others, which include Medical Aid (awarded to qualifying low income level households), occupation compensation insurance, non-insurance, and others. Previous health history is based on a structured medical record review form that follows the Utstein style but customized to fit the hospital settings in Korea and includes history of heart disease, lung disease, lipid disease, hypertension, and stroke.

Hypothermia refers to the medical treatment performed to lower the patient's body temperature regardless of cooling methods like external or internal cooling, which should be initiated within 12 hours after ROSC at the hospital. Reperfusion therapy indicates whether any type of reperfusion treatment to restore blood flow through blocked arteries was performed on the patient such as primary coronary intervention or intravenous thromobolysis. Both treatment variables are recorded dichotomously depending on whether the respective treatment was performed. CPR treatment was categorized to EMS CPR only, ED CPR only, both EMS CPR and ED CPR, and no CPR performed.

Variables regarding time include response time interval (RTI), scene time interval (STI), transport time interval (TTI), time from call to hospital discharge, and time from hospital admission to hospital discharge. RTI refers to the time interval from call received by the dispatcher to ambulance arrival to the scene of incidence and is measured in minutes. STI refers to the time interval from ambulance arrival to the scene to ambulance departure to appropriate emergency department and is measured in minutes. TTI refers to the time interval from ambulance departure from the scene to arrival to the emergency department and is measured in minutes.

Outcome measure

Primary endpoint is status with the outcome variable being survival to discharge with good neurological function as distinguished by scoring 1 or 2 on cerebral performance category (CPC) score as examined by a medical professional. A CPC score of 1 specifies good cerebral performance as indicated by the patient being conscious, alert, able to work, and may having mild neurologic or psychologic deficit; a CPC score of 2 indicates moderate cerebral disability as specified as the patient being conscious and having sufficient cerebral function for independent activities for daily life. A CPC score of 3, 4, and 5 respectively indicates severe cerebral disability ranging from ambulatory state to severe dementia or paralysis, coma or vegetative state, and brain death. The outcome measurement of the CPC scores is recorded on the medical record by the physician and is abstracted by the medical record reviewer.

Missing Data

Given the wide range of data sources, there were missing variables in the process of tracking previous health history. For the purpose of the study analysis, unknown values in history of heart disease, hypertension, lung disease, lipid disease, and stroke were coded as not having said health conditions. This allowed further analysis to be performed with the complete dataset.

Statistical Methods

All statistical analysis was performed via SAS 9.3. Descriptive analysis of the study variables showed an overview of the general demographics of the population and displayed what proportions of the population are exposed to known risk factors. Odds ratios (ORs) and 95% confidence intervals (CIs) are also presented to show the association of the risk factors between the exposed and unexposed groups. Crude ORs with 95% CIs were calculated to show the unadjusted association between diabetic patients and non-diabetic patients with survival outcomes including survival to discharge and survival to discharge with good neurological outcomes.

Bivariate analysis was performed to investigate the relationship between the covariates and the outcome variable by calculating ORs and 95% CIs. Stratified analysis was performed subsequently to examine the effect modification of exposure and outcome association by each variable. Unadjusted ORs and 95% CIs were calculated as well as adjusted ORs and 95% CIs. Confounding and interacting variables of interest were identified based on having values outside of 10% range of the crude OR and the Breslow-Day homogeneity test.

Multivariate logistic regression analysis was performed where the initial model included all first order variables and interaction terms with all first order terms. The initial model including interaction terms was tested to find statistically significant interaction with the reduced model only including first order terms through the "chunk test" by using likelihood ratio test. Backward elimination was performed to eliminate statistically insignificant parameter one by one, where the model was reduced to include only significant interaction terms. Confounding was assessed by comparing adjusted ORs controlling for each first order term. Confounding variables that resulted in ORs 10% outside of the range of the initial model were identified and retained in the model. The reduced model including confounding variables, interaction terms, and first order variables of the interaction terms was then assessed for collinearity to reach the final model.

Results

Of 8,486 admitted patients after survival at ED with EMS-assessed OHCAs, 5,936 cases were analyzed excluding patients with unknown diabetes statuses (n=2,550). Table 1 shows the basic demographic findings of all study participants stratified by their diabetes status and statistical significance between two groups. Diabetic patients were statistically significantly older than non-diabetic patients on average (66.31 ± 12.03 years old vs. 58.39 ± 15.95 years old, p-value <0.0001) and were more likely to have history of heart disease (OR 2.55, 95% CI 2.20-2.94), history of hypertension (6.29, 5.54-7.13), and history of stroke (2.59, 2.16-3.10).

Time variables related to EMS transport did not differ significantly between two groups: average response time from call to ambulance arrival on scene was 6.78 ± 3.75 minutes for diabetic patients and 6.63 ± 3.65 minutes for non-diabetic patients, average scene time interval from arrival to the scene to departure was 6.81 ± 4.41 minutes for diabetic patients and 6.55 ± 4.43 minutes for non-diabetic patients, and average transport time interval from departure from scene to arrival to ED was 8.35 ± 8.77 minutes for diabetic patients and 8.32 ± 8.95 minutes for non-diabetic patients.

Table 2 presents the survival outcomes of diabetic patients. A total of 609 out of 1,940 (31.39%) diabetic patients survived to discharge and 186 patients (9.59%) survived to discharge with good neurological outcome as determined by the CPC score of 1 or 2. The unadjusted OR for diabetic patients who survived to discharge compared to all patients was 0.62 (95% CI 0.55, 0.69) and the unadjusted OR for survival to discharge with good neurological outcomes was 0.49 (0.41, 0.58).

Further analysis of the covariates was performed through bivariate association analysis and stratified analysis. Bivariate associations between the risk factors and survival to discharge with good neurological outcomes are presented in Table 3 with calculated ORs and 95% CI levels. We observed that patients who received CPR from

EMS only were highly likely to survive with good neurological outcomes (OR 14.07, 11.93-16.59) compared to patients who received CPR from ED only (0.46, 0.32-0.65) or from both EMS and ED (0.13, 0.11-0.15). Patients who received hospital level treatments including hypothermia and reperfusion were also more likely to survive with good neurological outcomes (2.00, 1.68-2.38 and 5.01, 4.21-5.97 respectively). Additionally, younger patients less than 50 years of age were more likely to have better outcomes (2.19, 1.88-2.54). Having history of hypertension, lung disease, and stroke resulted in ORs less than 1.00, indicating that such health conditions may have negative impacts on survival.

The results of stratified analysis are presented in Table 4. EMS defibrillation status (aOR 0.59, 0.49-0.70) and age (aOR 0.61, 0.51-0.73) showed adjusted ORs that are outside of 10% range of the crude OR. After performing the Breslow-Day test of homogeneity, hypothermia therapy (p-value 0.0225), gender (0.0237), history of heart disease (0.028), and history of hypertension (0.0228) resulted in statistical significance indicating heterogeneous association between the aORs and the crude OR.

In multivariate logistic regression analysis, likelihood ratio test between the model including all interaction terms and no interaction term ($28.486 \sim \chi^2$ with 24 degrees of freedom) was not statistically significant at 95% confidence level with the p-value of 0.2401. No collinearity was assessed as determined by VDP values less than 30. The chunk test suggested no statistically significant interaction term, but further examination was performed via backward elimination to assess for interaction one by one, which resulted in three significant interaction terms including gender, history of heart disease, and hypothermia therapy.

Upon assessing the number of patients in each stratum of gender, history of heart disease, and hypothermia, there was a stratum containing zero patients. Therefore, the interaction term with hypothermia therapy was eliminated from the model, but the first order term was included to be controlled for as a confounder. The model including two interaction terms (gender and history of heart disease) and all covariates was then assessed for confounding. The ORs including two interaction terms controlling for all covariates were as follows: 0.43 (0.26-0.69, p-value 0.0006) for male with history of heart disease, 0.77 (0.57-1.02, p-value 0.0695), for male with no history of heart disease, 0.73 (0.41-1.30, p-value 0.2888) for female with history of heart disease, and 1.31 (0.85-2.02, p-value 0.2184) for female with no history of heart disease.

The adjusted ORs were calculated by controlling for each covariate and variables that resulted in aORs outside of 10% range of the ORs obtained from the model controlling for all covariates were identified as confounders. History of hypertension and age were found to be confounding one or more associations and therefore were included in the final model to be controlled for as confounders. In summary, the final model included diabetes, age, history of hypertension, hypothermia, history of heart disease, gender, interaction term with diabetes and history of heart disease, and interaction term with diabetes and gender. The final OR measuring the effect of diabetes on survival with good neurological outcomes for male with history of heart disease was 0.32 (0.22-0.48, p-value <0.0001), for male without history of heart disease was 0.55 (0.34-0.89, p-value <0.0001), for female with history of heart disease was 0.60 (0.48-0.76, p-value 0.0152), and for female without history of heart disease was 1.03 (0.71-1.47, p-value 0.8919), as presented in Table 5.

Discussion

Overall, we observed that having diabetes led to decreased probability of surviving OHCA with good neurological outcomes. We also observed distinctive difference in the magnitude of how diabetes plays a role in survival with good neurological outcomes between men and women as well as with history of heart disease. The adjusted OR examining survival with good neurological outcomes comparing diabetics and non-diabetics was the lowest in male with history of heart disease at 0.32 (0.22-0.48) whereas the highest OR was for female without history of heart disease at 1.03 (0.71-1.47) but not statistically significant given the wide CI range and the p-value of 0.8919.

Previous findings in regard to the gender difference in the impact of diabetes have been inconsistent. A meta-analysis examining the gender difference among patients with diabetes has observed that men had more coronary heart disease deaths (CHD) attributable to diabetes than women [32]; similar finding was also observed in regard to cardiovascular risk in diabetic populations in a world-wide case control study where the authors found greater coronary risk in women with an adjusted OR of 4.3 (3.5-5.2) compared to 2.7 in men (2.4-3.0) [33]. However, a meta-analysis estimating the relative risk for coronary heart disease in diabetic men and women found greater risk reduction in women after adjusting for more adverse cardiovascular risk characteristics [34], suggesting that the gender difference may be largely mediated by more prevalent risk profiles in women.

In our findings, males were substantially less likely to survive with good neurological outcomes, which suggest that the effect may be attributable to other factors such as age. A retrospective analysis of the United States cardiac arrest registry found that even with poorer prognostic arrest characteristics such as being less likely to have a cardiac arrest in public, being witness, or being treated with defibrillation, younger females were more likely to survive an OHCA event [35]. In our study population, the mean age for men with diabetes was 70.07 years old compared to the mean age of women with diabetes of 64.26 years old. Age was controlled for in our final modeling, but such results may be indicative of gender benefits that surpass the adjustment. Similar observation in a previous study has been postulated to be related to the elevated levels of female sex hormones in younger women [36], but results have been inconclusive.

Due to limited findings in regard to neurological outcomes in OHCA survivability, only a few studies were identified to have examined the predictors for neurological recovery after OHCA. A longitudinal study has found that no history of heart disease was more frequent in patients with the CPC score of 1 or 2, and at one-year follow-up, the authors found that 96% of patients who were discharged with CPC score of 1 or 2 have survived where as 100% of patients who were discharged with CPC score greater than 3 have died [37]. Along with our study conclusion, this finding urges future investigations in OHCA survivability with good neurological outcomes to ensure quality of life in OHCA survivors beyond discharge.

This study is one of the first to examine the association of diabetes and OHCA survivability with good neurological outcomes and holds significance in its being an analysis of a nation-wide cohort, which increases generalizability. However, this study is due for several limitations. First, although the retrospective abstraction of medical records was performed by trained medical record reviewers, acquiring a complete set of variables for each patient was difficult. This poses limitations as unknown health history variables were chosen to be imputated to be not having the particular health history instead of systematically restricting the dataset and may have influenced the reported statistical analysis. Second, the study analysis was limited to patients with known diabetes status, which may restrict the generalizability of the study findings to the general OHCA patients in Korea.

Future studies should investigate associations between pre-existing health conditions with OHCA survival in order to develop specific strategies for enhanced treatment to increase survivability. Additionally, to improve the quality of life of OHCA patients after survival, more risk factors that may restrict neurological recovery should be identified to not only increase survivability, but survivability with good neurological functions.

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Tables and Figures

Figure 1. Selection process of the study population

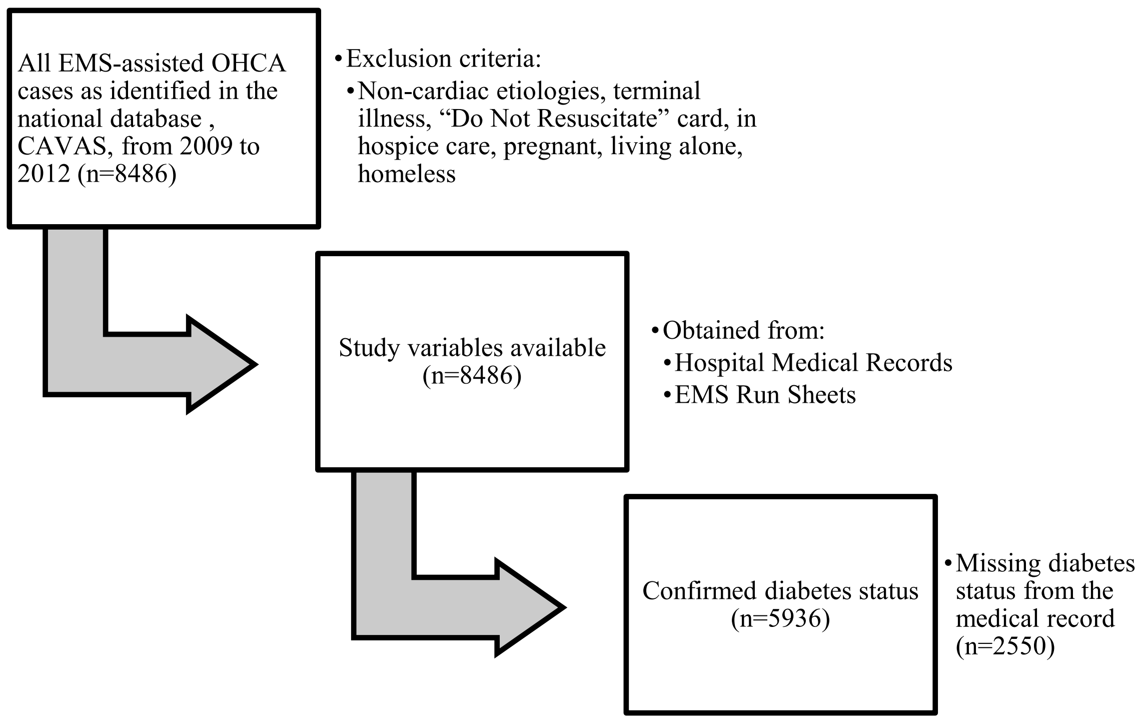

Table 1. Basic characteristics of all EMS-assessed out of hospital cardiac arrest (OHCA) patients in South Korea, 2009-2012

	Diabetes n=1940		No Diabetes n=3996		All n=5936		OR	(95% CI)	
	No.	(% or SE)	No.	(% or SE)	No.	(% or SE)			
Demographic									
Age (mean/SD)	66.31	(12.03)	58.39	(15.95)	60.98	(15.24)			
Gender									
Male	1256	(64.74)	2718	(68.02)	3974	(66.95)	0.86	(0.77,	0.97)
Female	684	(35.26)	1278	(31.98)	1962	(33.05)			
Insurance Type									
National Health Insurance	1621	(83.56)	3498	(87.54)	5119	(86.24)	1.70	(1.42,	2.03)
Other	319	(16.44)	498	(12.46)	817	(13.76)			
Metropolitan									
No	895	(46.13)	1676	(41.94)	2571	(43.31)	0.84	(0.76,	0.94)
Yes	1045	(53.87)	2320	(58.06)	3365	(56.69)			
Hospital and SCA Characteristics									
Type of ECG[1]									
VF or VT	236	(12.16)	746	(18.67)	982	(16.54)	0.60	(0.52,	0.71)
PEA	187	(9.64)	400	(10.01)	587	(9.89)	0.96	(0.80,	1.15)
Asystole	1517	(78.20)	2850	(71.32)	4367	(73.57)	1.44	(1.27,	1.64)
Place of OHCA									
Public	324	(16.70)	896	(22.42)	1220	(20.55)	0.68	(0.59,	0.78)
Private	1467	(75.62)	2746	(68.72)	4213	(70.97)	1.48	(1.28,	1.70)
Unknown	149	(7.68)	354	(8.86)	503	(8.47)	0.86	(0.70,	1.05)
Level of ED[2]									
Level 1	305	(15.72)	729	(18.24)	1034	(17.42)	0.84	(0.72,	0.97)
Level 2	1256	(64.74)	2702	(67.62)	3958	(66.68)	0.88	(0.78,	0.99)
Level 3	379	(19.54)	565	(14.14)	944	(15.90)	1.07	(1.04,	1.09)
EMS[3] Defibrillation									
No	1650	(85.05)	3012	(75.38)	4662	(78.54)	0.54	(0.47,	0.62)
Yes	290	(14.95)	984	(24.62)	1274	(21.46)			
Prehospital ROSC[4]									
No	229	(11.80)	700	(17.52)	929	(15.65)	1.59	(1.35,	1.86)
Yes	1711	(88.20)	3296	(82.48)	5007	(84.35)	0.63	(0.74,	0.54)

Table 1. (Continued)

	Diabetes n=1940		No Diabetes n=3996		All n=5936		OR	(95% CI)	
	No.	(% or SE)	No.	(% or SE)	No.	(% or SE)			
Bystander Witness									
No	607	(31.29)	1151	(28.80)	1758	(29.62)	0.89	(0.79,	1.00)
Yes	1333	(68.71)	2845	(71.20)	4178	(70.38)			
CPR[5]									
EMS CPR and ED CPR	1576	(81.24)	2988	(74.77)	4564	(76.89)	1.46	(1.28,	1.67)
EMS CPR Only	229	(11.80)	700	(17.52)	929	(15.65)	0.63	(0.54,	0.74)
ED CPR Only	135	(6.96)	308	(7.71)	443	(7.46)	0.90	(0.73,	1.10)
Reperfusion Therapy									
No	1752	(90.31)	3509	(87.81)	5261	(88.63)	0.77	(0.65,	0.92)
Yes	188	(9.69)	487	(12.19)	675	(11.37)			
Hypothermia Therapy									
No	1682	(86.70)	3379	(84.56)	5061	(85.26)	0.84	(0.72,	0.98)
Yes	258	(13.30)	617	(15.44)	875	(14.74)			
Clinical Characteristics									
History of Heart Disease									
No	801	(41.29)	2782	(69.62)	3583	(60.36)	2.55	(2.20,	2.94)
Yes	448	(23.09)	611	(15.29)	1059	(17.84)			
Unknown	691	(35.62)	603	(15.09)	1294	(21.80)			
History of Hypertension									
No	447	(23.04)	2701	(67.59)	3148	(53.03)	6.29	(5.54,	7.13)
Yes	1337	(68.92)	1285	(32.16)	2622	(44.17)			
Unknown	156	(8.04)	10	(0.25)	166	(2.80)			
History of Stroke									
No	905	(46.65)	3003	(75.15)	3908	(65.84)	2.59	(2.16,	3.10)
Yes	248	(12.78)	318	(7.96)	566	(9.54)			
Unknown	787	(40.57)	675	(16.89)	1462	(24.63)			
History of Lipid Disease									
No	1016	(52.37)	3208	(80.28)	4224	(71.16)	2.07	(1.37,	3.13)
Yes	38	(1.96)	58	(1.45)	96	(1.62)			
Unknown	886	(45.67)	730	(18.27)	1616	(27.22)			

Table 1. (Continued)

	Diabetes n=1940		No Diabetes n=3996		All n=5936		OR	(95% CI)	
	No.	(% or SE)	No.	(% or SE)	No.	(% or SE)			
History of Lung Disease									
No	962	(49.59)	3019	(75.55)	3981	(67.07)	1.30	(1.02,	1.65)
Yes	104	(5.36)	252	(6.31)	356	(6.00)			
Unknown	874	(45.05)	725	(18.14)	1599	(26.94)			
Time									
Response Time[5] (min)	6.78	(3.75)	6.63	(3.65)	6.68	(3.68)			
Scene Time Interval[6] (min)	6.81	(4.41)	6.55	(4.43)	6.64	(4.43)			
Transport Time Interval[7] (min)	8.35	(8.77)	8.32	(8.95)	8.33	(8.89)			
Time from Call to Survival to Discharge (hr)	291.90	(616.99)	341.71	(691.12)	325.43	(668.15)			
Time from Admission to Discharge (hr)	289.05	(618.71)	340.32	(694.35)	323.51	(670.86)			

1. Electrocardiogram where VF stands for ventricular fibrillation, VT stands for ventricular tachycardia, and PEA stands for pulseless electrical activity
2. Emergency Department where level 1 indicates the highest level
3. Emergency Medical Services
4. Return of Spontaneous Circulation
5. Cardiopulmonary Resuscitation
6. Response Time refers to the time in minutes from the time of call to arrival on scene by EMS dispatcher
7. Scene Time Interval refers to the time in minutes from the arrival on scene to departure to emergency department by EMS dispatcher
8. Transport Time Interval refers to the time in minutes from the departure to emergency department to arrival to emergency department by EMS dispatcher

Table 2. Unadjusted survival outcomes for all EMS-assessed out of hospital cardiac arrest (OHCA) patients in South Korea, 2009-2012

	Survival to Discharge		Survival to Discharge with Good Neurological Outcome	
	% (n/N)	Crude OR (95% CI)	% (n/N)	Crude OR (95% CI)
Diabetes	31.39 (609/1940)	0.62 (0.55, 0.69)	9.59 (186/1940)	0.49 (0.41, 0.58)
All	38.92 (2310/5936)		15.18 (901/5936)	

EMS: Emergency Medical Services

Table 3. Bivariate analysis between potential confounders and survivability with good neurological outcomes

	OR (95% CI)		
Gender	2.06	(1.74,	2.45)
Age			
<50 years	2.19	(1.88,	2.54)
50 years to 60 years	1.70	(1.45,	1.98)
61 years to 72 years	0.69	(0.58,	0.82)
>72 years	0.23	(0.18,	0.29)
Metropolitan	1.13	(0.98,	1.30)
National Health Insurance	0.61	(0.46,	0.81)
ED[1] Level			
Level 1	2.08	(1.77,	2.45)
Level 2	0.92	(0.80,	1.07)
Level 3	0.36	(0.28,	0.47)
EMS[2] Defibrillation	7.38	(6.34,	8.60)
ECG[3]			
VF or VT	5.30	(4.53,	6.21)
PEA	0.54	(0.40,	0.72)
Asystole	0.54	(0.40,	0.72)
Place of OHCA			
Public	1.79	(1.52,	2.11)
Private	0.56	(0.47,	0.66)
Other	1.58	(1.26,	1.98)
Witness	2.53	(2.09,	3.05)
Pre-hospital ROSC[4]	0.07	(0.06,	0.08)
EMS/ED CPR[5]			
EMS and ED	0.13	(0.11,	0.15)
EMS only	14.07	(11.93,	16.59)
ED Only	0.46	(0.32,	0.65)

Table 3. (Continued)

	OR (95% CI)		
Hypothermia	2.00	(1.68,	2.38)
Reperfusion	5.01	(4.21,	5.97)
History of Heart Disease	1.23	(1.03,	1.47)
History of Hypertension	0.76	(0.66,	0.88)
History of Lipid Disease	2.72	(1.77,	4.20)
History of Lung Disease	0.63	(0.45,	0.90)
History of Stroke	0.46	(0.33,	0.62)

1. Emergency Department where level 1 indicates the highest level
2. Emergency Medical Services
3. Electrocardiogram where VF stands for ventricular fibrillation, VT stands for ventricular tachycardia, and PEA stands for pulseless electrical activity
4. Return of Spontaneous Circulation
5. Cardiopulmonary Resuscitation

Table 4. Stratified analysis of diabetes status and survival with good neurological outcomes controlling for potential confounders

		Unadjusted OR (95% CI)			Adjusted OR (95% CI)			P-value*
Gender	Male	0.69	(0.49,	0.96)	0.49	(0.42,	0.59)	0.0237
	Female	0.44	(0.36,	0.54)				
Age	<50 years	0.69	(0.47,	1.01)	0.61	(0.51,	0.73)	0.3357
	50 to 60 years	0.54	(0.40,	0.74)				
	61 to 72 years	0.56	(0.40,	0.77)				
	>72 years	0.87	(0.54,	1.41)				
Metropolitan	No	0.51	(0.39,	0.66)	0.49	(0.41,	0.58)	0.6977
	Yes	0.47	(0.38,	0.60)				
Insurance	National Health Insurance	0.47	(0.39	0.56)	0.49	0.41	0.59	0.0596
	Other	0.82	(0.47	1.43)				
ED[1] Level	Level 1	0.37	(0.26,	0.54)	0.51	(0.43,	0.60)	0.1067
	Level 2	0.54	(0.43,	0.66)				
	Level 3	0.71	(0.42,	1.22)				
EMS[2] Defibrillation	No	0.62	(0.49,	0.78)	0.59	(0.49,	0.70)	0.4840
	Yes	0.54	(0.41,	0.72)				
ECG[3]	VF or VT	0.50	(0.36,	0.69)	0.54	0.45	0.64	0.7520
	PEA	0.65	(0.34,	1.25)				
	Asystole	0.54	(0.43,	0.68)				
Place of OHCA	Public	0.60	(0.43,	0.85)	0.50	(0.42,	0.60)	0.1825
	Private	0.45	(0.36,	0.56)				
	Other	0.67	(0.41,	1.10)				
Witness	No	0.55	(0.37,	0.82)	0.49	(0.41,	0.58)	0.5455
	Yes	0.48	(0.40,	0.58)				
Pre-hospital ROSC[4]	No	0.55	(0.44,	0.71)	0.53	(0.44,	0.64)	0.5673
	Yes	0.50	(0.37,	0.67)				

Table 4. (Continued)

		Unadjusted OR (95% CI)			Adjusted OR (95% CI)			P-value*
EMS/ED CPR[5]	EMS and ED	0.54	(0.42,	0.69)	0.53	(0.44,	0.64)	0.5762
	EMS only	0.50	(0.37,	0.67)				
	ED Only	0.77	(0.35,	1.70)				
Hypothermia	No	0.54	(0.45,	0.66)	0.49	(0.42,	0.59)	0.0225
	Yes	0.32	(0.21,	0.49)				
Reperfusion	No	0.45	(0.37,	0.56)	0.49	(0.41,	0.59)	0.0934
	Yes	0.64	(0.45,	0.92)				
History of Heart Disease	No	0.53	(0.41,	0.69)	0.46	(0.37,	0.56)	0.0340
	Yes	0.33	(0.23,	0.47)				
History of Hypertension	No	0.38	(0.27,	0.55)	0.51	(0.42,	0.61)	0.0431
	Yes	0.59	(0.47,	0.74)				
History of Lipid Disease	No	0.50	(0.40,	0.63)	0.50	(0.40,	0.63)	0.9775
	Yes	0.51	(0.20,	1.27)				
History of Lung Disease	No	0.47	(0.37,	0.59)	0.47	(0.37,	0.59)	0.7653
	Yes	0.53	(0.23,	1.26)				
History of Stroke	No	0.47	(0.37,	0.60)	0.48	(0.39,	0.60)	0.4275
	Yes	0.62	(0.32,	1.18)				

*. P-value is obtained from performing Breslow-Day Test of Homogeneity
1. Emergency Department where level 1 indicates the highest level
2. Emergency Medical Services
3. Electrocardiogram where VF stands for ventricular fibrillation, VT stands for ventricular tachycardia, and PEA stands for pulseless electrical activity
4. Return of Spontaneous Circulation
5. Cardiopulmonary Resuscitation

Table 5. The effect of diabetes on survival to discharge with good neurological outcomes in EMS-assessed out of hospital cardiac arrest patients in South Korea, 2009-2012: multivariate logistic regression analysis

		Male			Female		
		OR	95% CI	P-value	OR	95% CI	P-value
Heart Disease	Yes	0.32	(0.22, 0.48)	<0.0001	0.60	(0.48, 0.76)	0.0152
	No	0.55	(0.34, 0.89)	<0.0001	1.03	(0.71, 1.47)	0.8919

EMS: Emergency Medical Services