American Journal of Emergency Medicine 37 (2019) 608–614

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Original Contribution

Effect of hypertension across the age group on survival outcomes in out-of-hospital cardiac arrest☆

Eujene Jung, MD [a], Jeong Ho Park, MD [b], Young Sun Ro, MD, DrPH [c], Kyoung Jun Song, MD, PhD [b], Hyun Ho Ryu, MD, PhD [a,*], Seung Chul Lee, MD, PhD [d], Sang Do Shin, MD, PhD [b]

[a] Department of Emergency Medicine, Chonnam National University Hospital, Gwang-ju, Republic of Korea
[b] Department of Emergency Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea
[c] Laboratory of Emergency Medical Services, Seoul National University Hospital Biomedical Institute, Seoul, Republic of Korea
[d] Department of Emergency Medicine, Dongkuk University Ilsan Hospital, Goyang, Republic of Korea

ARTICLE INFO

Article history:
Received 10 March 2018
Received in revised form 6 May 2018
Accepted 19 June 2018

Keywords:
Out-of-hospital cardiac arrest
Hypertension
Age

ABSTRACT

Objective: There are few studies on the effects hypertension has on survival outcomes in out-of-hospital-cardiac arrest (OHCA) patients, although hypertension is a major risk factor for the incidence of cardiac arrest. This study aims to investigate whether hypertension is associated with survival outcomes in cardiac arrest patients across age groups.

Methods: This study was conducted using the national cardiac arrest registry of OHCA patients who survived to hospital admission from 2012 to 2016. The clinical histories of hypertension were obtained from patients' medical records. The endpoint was cerebral performance category (CPC) 1 and 2 (good CPC) and survival to discharge. Multivariable logistic regression analysis was performed on the data collected. The final model with an interaction term was evaluated to compare the effects of hypertension across age groups.

Results: A total 11,610 patients (61.0% hypertensive patients and 39.0% non-hypertensive patients) were included. The group over 80 years old with hypertension were more likely to have good neurologic recovery (AOR 2.53 [1.43–4.50]) and those under 65 years old with hypertension were more likely to survive to hospital discharge with statistical significance (AOR 1.19 [1.04–1.35]).

Conclusions: Hypertension does not imply poor survival outcomes independently for all ages, as those over 80 years of age can have rather good neurological outcomes.

1. Background

Out-of-hospital cardiac arrest (OHCA) is a serious public health problem worldwide with a low survival. Survival rates reported varied from community to community, generally ranges between 5% and 10% [1-3]. In patients aged >70 years, the survival rate drops to approximately 4% [4].

Survival after cardiac arrest is dependent on several pre-hospital resuscitation factors. Several Utstein elements are well-established predictors of survival outcomes among emergency medical service (EMS)-treated arrests including age, gender, location of arrest, witnessed status, bystander cardiopulmonary resuscitation (CPR), initial rhythms at scene, attempts at defibrillation and EMS response times [5, 6]. These variables have been shown to predict about 72% of the variation in survival [5, 6]. However, a portion of the variation remains unaccounted for, suggesting that there are unknown patients' variables that would present an opportunity to reduce the public health burden of OHCA [6].

The most common co-morbidity directly associated with cardiac arrest is heart disease which includes myocardial infarction, coronary artery disease and heart failure [7]. Hypertension is a risk factor for all these diseases and heart disease has been shown to be associated with a 2–3 fold increase in the risk of cardiac arrest [7, 8]. Also, primary hypertension is a well-recognized risk factor for renal diseases and slightly elevated blood pressure (BP) levels lead to increased risk in diabetes or stroke [9, 10]. Although, there were some differences depending on population, about 40% of OHCA patients have hypertension (HTN). The rate of diagnosis and the prevalence of HTN in adolescents appear to show a steady upward trend. In Korea, the prevalence of hypertension in adults over 30 years old is about 30%, with the trend increasing with age, with a prevalence of about 60% in those over 60 years old.

Advanced age is reported to be associated with reduced survival rates after OHCA [11-13]. Also, the presence of comorbidities, such as

☆ The manuscript is not under consideration for publication and has not been published elsewhere in any medium including electronic journals and computer databases of a public nature.

* Corresponding author at: 42 Jebong-ro, Dong-gu, Gwangju 61469, Republic of Korea.
E-mail addresses: oriryu@hanmail.net (H.H. Ryu), shinsangdo@medimail.co.kr (S.D. Shin).

https://doi.org/10.1016/j.ajem.2018.06.049
0735-6757/

hypertension, diabetes, heart disease, stroke, renal disease is known to increase with age [14] There is a general belief that survival outcomes after CPR for OHCA may be poor in older patients, especially in patients with multiple co-morbidities [14-16].

There are many studies on OHCA that were done independently of heart disease, especially myocardial infarction, coronary artery disease and heart failure. Stroke, kidney disease and diabetes worsen the prognosis in OHCA patients [17, 18] and previous studies have shown that hypertension directly or indirectly is a risk factor for OHCA, but, studies on the survival outcomes of OHCA patients with hypertension are rare and there has been no report to compare the effects of hypertension with OHCA patients across ages.

We hypothesize that hypertension affects the prognosis in OHCA patients and may be different according to age. So, we aimed to determine whether hypertension is directly related to the prognosis in cardiac arrest patients and investigated the effects of hypertension on the prognosis of patients experiencing cardiac arrest as age increased.

2. Methods

2.1. Study design

This study is a nationwide cross-sectional observational study based on a nation-wide, population-based registry in South Korea involving all patients who experienced OHCA and were transported to hospitals by emergency medical services (EMS) with resuscitation efforts. This study was approved by the institutional review board of study areas and the Korea Center for Disease Control and Prevention (CDC).

2.2. Study setting

Korea has a population of 50 million people, with 7 metropolitan cities with populations >1 million, 10 provinces and urban, rural and wildness areas. The Korean EMS, which is a single tiered, government-based system, provides basic-to-intermediate level ambulance services from sixteen provincial headquarters of the national fire department and supports the entire population. All ambulance crews can perform cardiopulmonary resuscitation (CPR) at a scene and during transport, and can also provide care comparable to that of an intermediate-level emergency medical technical (EMT) in the United States. The current EMS CPR protocol calls for EMTs to perform CPR, using AED every 2 min, for at least 5 min on scene. Intravenous fluid administration and advanced airway management may be optionally performed by level-1 EMTs. Epinephrine and other advanced intravenous cardiac life support (ACLS) medications are not available in the field. EMTs cannot declare death in the field unless there are signs of irreversible death (rigor mortis, dependent lividity, decapitation, trans-section and decomposition) and it is confirmed by direct medical control. After delivery of >5 min of chest compressions, EMTs should transport the OHCA victim as soon as possible to the nearest emergency department (ED) while continuing CPR during transport.

The national government designated three levels to EDs according to the resources and functional requirements; level 1 (n = 20) and level 2 (n = 119) EDs have more resources and better facilities for emergency care and must be fully staffed by emergency medical physicians by law, whereas level 3 EDs (n = 293) can be staffed by general physicians. CPR guidelines from international societies are generally accepted by the academic societies and are recommended in clinical practice. In recent years, the 2015 AHA guidelines have been accepted as the standard practice by national organizations.

In Korea, generally, hypertension is diagnosed by a primary health care clinic or in a periodic health checkup by the National Health Insurance Service (NHIS). According to Joint National Committee (JNC) recommendations, hypertension can be diagnosed when the systolic blood pressure is over 140 mm Hg or diastolic blood pressure is over 90 mm Hg. The treatment of hypertension is dietary management, exercise and medication together in consideration of the accompanying diseases and risk factors. And about 60% of hypertensive patients regularly take anti-hypertensive medication.

2.3. Data source/collection

The Korean OHCA registry is a nationwide prospective clinical registry of patients with OHCA who survived to hospital admission from 2012 to 2016. The OHCA registry was established in 2006 to improve the outcome of OHCA in Korea and has been supported by the Korean CDC since 2007.

Data was obtained from both EMS records and hospital medical records. EMS records were completed by EMS providers and include EMS run sheets with information on ambulance operation and an EMS

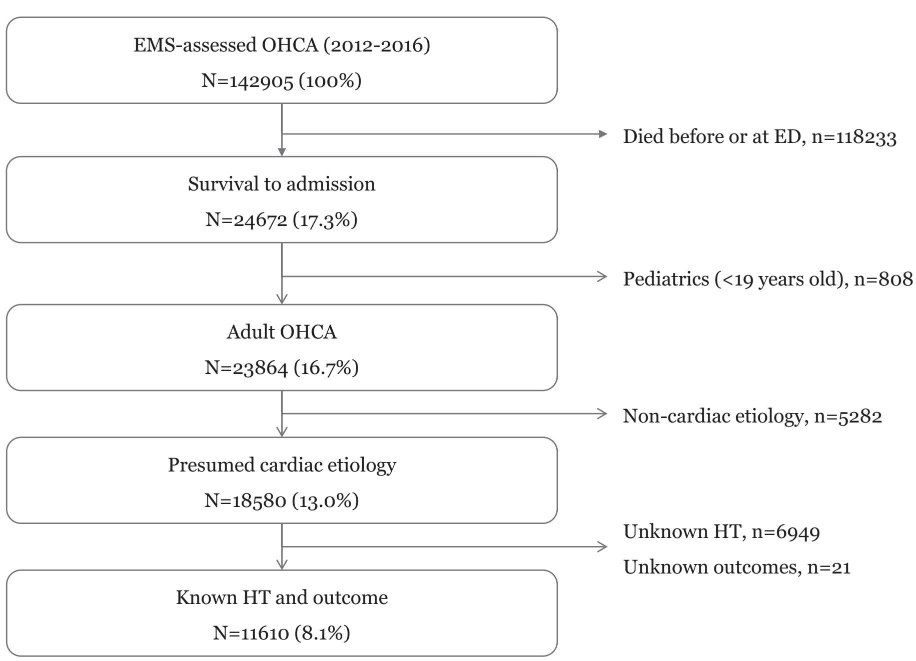

Fig. 1. Study populations.

Table 1
Demographic findings according to hypertension group.

Variables	All		Hypertension				P-value
			No		Yes		
	N	%	N	%	N	%	
All	11,610	100.0	4534	100.0	7076	100.0	
Age group							<.0001
19 ≤ Age < 65	6260	53.9	3257	71.8	3003	42.4	
65 ≤ Age < 80	3838	33.1	924	20.4	2914	41.2	
Age ≥ 80	1512	13.0	353	7.8	1159	16.4	
Gender							<.0001
Female	3726	32.1	1237	27.3	2489	35.2	
Male	7884	67.9	3297	72.7	4587	64.8	
Metropolis							0.1003
No	5516	47.5	2111	46.6	3405	48.1	
Yes	6094	52.5	2423	53.4	3671	51.9	
Season							0.0007
Spring (Mar–May)	2864	24.7	1123	24.8	1741	24.6	
Summer (Jun–Aug)	2756	23.7	1152	25.4	1604	22.7	
Fall (Sep–Nov)	2975	25.6	1158	25.5	1817	25.7	
Winter (Dec–Feb)	3015	26.0	1101	24.3	1914	27.0	
Insurance							<.0001
Medical aid	845	7.3	258	5.7	587	8.3	
National Health Insurance	10,414	89.7	4106	90.6	6308	89.1	
Unknown	351	3.0	170	3.7	181	2.6	
Diabetes							
No	5566	47.9	4034	89.0	1532	21.7	
Yes	3582	30.9	488	10.8	3094	43.7	
Unknown	2462	21.2	12	0.3	2450	34.6	
Chronic heart disease							<.0001
No	3075	26.5	2616	57.7	459	6.5	
Yes	2326	20.0	489	10.8	1837	26.0	
Unknown	6209	53.5	1429	31.5	4780	67.6	
Stroke							<.0001
No	3137	27.0	2663	58.7	474	6.7	
Yes	1047	9.0	142	3.1	905	12.8	
Unknown	7426	64.0	1729	38.1	5697	80.5	
Chronic renal disease							<.0001
No	3073	26.5	2638	58.2	435	6.1	
Yes	1074	9.3	94	2.1	980	13.8	
Unknown	7463	64.3	1802	39.7	5661	80.0	
Place							<.0001
Public	2440	21.0	1082	23.9	1358	19.2	
Private	7560	65.1	2775	61.2	4785	67.6	
Unknown	1610	13.9	677	14.9	933	13.2	
Witness							.0038
No	3107	26.8	1146	25.3	1961	27.7	
Yes	8503	73.2	3388	74.7	5115	72.3	
Bystander CPR							<.0001
No	8879	76.5	3341	73.7	5538	78.3	
Yes	2731	23.5	1193	26.3	1538	21.7	
ECG							<.0001
VF/pulseless VT	3634	31.3	1740	38.4	1894	26.8	
PEA	1778	15.3	649	14.3	1129	16.0	
Asystole	6198	53.4	2145	47.3	4053	57.3	
Response time interval							.3706
0–3	748	6.4	273	6.0	475	6.7	
4–7	4750	40.9	1868	41.2	2882	40.7	
8–11	1805	15.5	693	15.3	1112	15.7	
12–15	458	3.9	169	3.7	289	4.1	
16–	3849	33.2	1531	33.8	2318	32.8	
Level of ED							<.0001
Level 1	2318	20.0	1046	23.1	1272	18.0	
Level 2	7195	62.0	2794	61.6	4401	62.2	
Level 3	2097	18.1	694	15.3	1403	19.8	
TTM							<.0001
No	10,885	93.8	4178	92.1	6707	94.8	
Yes	725	6.2	356	7.9	369	5.2	
Reperfusion							.0282
No	9589	82.6	3701	81.6	5888	83.2	
Yes	2021	17.4	833	18.4	1188	16.8	
ECMO							.0068
No	11,170	96.2	4335	95.6	6835	96.6	
Yes	440	3.8	199	4.4	241	3.4	
Outcomes							
Survival to discharge	4572	39.4	2046	45.1	2526	35.7	<.0001
Good CPC	2683	23.1	1317	29.0	1366	19.3	<.0001

CPR: cardiopulmonary resuscitation, VF/pulseless VT: ventricular fibrillation/pulseless ventricular tachycardia,
TTM: targeted temperature management, ECMO: external corporeal membrane oxygenation, CPC: cerebral performance scale.

Table 2
Demographic findings according to age group.

Variables	All		Age group						P-value
			19 ≤ Age < 65		65 ≤ Age < 80		Age ≥ 80		
	N	%	N	%	N	%	N	%	
All	11,610	100.0	6260	100.0	3838	100.0	1512	100.0	
Hypertension									<.0001
No	4534	39.1	3257	52.0	924	24.1	353	23.3	
Yes	7076	60.9	3003	48.0	2914	75.9	1159	76.7	
Gender									<.0001
Female	3726	32.1	1561	24.9	1340	34.9	825	54.6	
Male	7884	67.9	4699	75.1	2498	65.1	687	45.4	
Metropolis									.4794
No	5516	47.5	2947	47.1	1832	47.7	737	48.7	
Yes	6094	52.5	3313	52.9	2006	52.3	775	51.3	
Season									.0021
Spring (Mar–May)	2864	24.7	1535	24.5	965	25.1	364	24.1	
Summer (Jun–Aug)	2756	23.7	1574	25.1	863	22.5	319	21.1	
Fall (Sep–Nov)	2975	25.6	1594	25.5	982	25.6	399	26.4	
Winter (Dec–Feb)	3015	26.0	1557	24.9	1028	26.8	430	28.4	
Insurance									<.0001
Medical aid	845	7.3	401	6.4	291	7.6	153	10.1	
National Health Insurance	10,414	89.7	5641	90.1	3440	89.6	1333	88.2	
Unknown	351	3.0	218	3.5	107	2.8	26	1.7	
Diabetes									
No	5566	47.9	3757	60.0	1273	33.2	536	35.4	
Yes	3582	30.9	1409	22.5	1637	42.7	536	35.4	
Unknown	2462	21.2	1094	17.5	928	24.2	440	29.1	
Chronic heart disease									<.0001
No	3075	26.5	2327	37.2	521	13.6	227	15.0	
Yes	2326	20.0	961	15.4	1006	26.2	359	23.7	
Unknown	6209	53.5	2972	47.5	2311	60.2	926	61.2	
Stroke									<.0001
No	3137	27.0	2374	37.9	538	14.0	225	14.9	
Yes	1047	9.0	313	5.0	535	13.9	199	13.2	
Unknown	7426	64.0	3573	57.1	2765	72.0	1088	72.0	
Chronic renal disease									<.0001
No	3073	26.5	2329	37.2	521	13.6	223	14.7	
Yes	1074	9.3	485	7.7	463	12.1	126	8.3	
Unknown	7463	64.3	3446	55.0	2854	74.4	1163	76.9	
Place									<.0001
Public	2440	21.0	1595	25.5	681	17.7	164	10.8	
Private	7560	65.1	3713	59.3	2658	69.3	1189	78.6	
Unknown	1610	13.9	952	15.2	499	13.0	159	10.5	
Witness									<.0001
No	3107	26.8	1536	24.5	1106	28.8	465	30.8	
Yes	8503	73.2	4724	75.5	2732	71.2	1047	69.2	
Bystander CPR									<.0001
No	8879	76.5	4460	71.2	3125	81.4	1294	85.6	
Yes	2731	23.5	1800	28.8	713	18.6	218	14.4	
ECG									<.0001
VF/pulseless VT	3634	31.3	2548	40.7	908	23.7	178	11.8	
PEA	1778	15.3	857	13.7	623	16.2	298	19.7	
Asystole	6198	53.4	2855	45.6	2307	60.1	1036	68.5	
Response time interval									.2735
0–3	748	6.4	385	6.2	252	6.6	111	7.3	
4–7	4750	40.9	2600	41.5	1573	41.0	577	38.2	
8–11	1805	15.5	985	15.7	579	15.1	241	15.9	
12–15	458	3.9	242	3.9	161	4.2	55	3.6	
16–	3849	33.2	2048	32.7	1273	33.2	528	34.9	
Level of ED									<.0001
Level 1	2318	20.0	1391	22.2	679	17.7	248	16.4	
Level 2	7195	62.0	3956	63.2	2336	60.9	903	59.7	
Level 3	2097	18.1	913	14.6	823	21.4	361	23.9	
TTM									<.0001
No	10,885	93.8	5786	92.4	3632	94.6	1467	97.0	
Yes	725	6.2	474	7.6	206	5.4	45	3.0	
Reperfusion									<.0001
No	9589	82.6	4933	78.8	3260	84.9	1396	92.3	
Yes	2021	17.4	1327	21.2	578	15.1	116	7.7	
ECMO									<.0001
No	11,170	96.2	5940	94.9	3734	97.3	1496	98.9	
Yes	440	3.8	320	5.1	104	2.7	16	1.1	
Outcomes									
Survival to discharge	4572	39.4	3012	48.1	1217	31.7	343	22.7	<.0001
Good CPC	2683	23.1	2037	32.5	546	14.2	100	6.6	<.0001

CPR: cardiopulmonary resuscitation, VF/pulseless VT: ventricular fibrillation/pulseless ventricular tachycardia.
TTM: targeted temperature management, ECMO: external corporeal membrane oxygenation, CPC: cerebral performance scale.

cardiac arrest registry based on Utstein style data collection. Ambulance run sheets include age, gender, place of event (private vs. public vs. unknown), witness status, pre-hospital defibrillation, bystander CPR, time interval from call to ambulance arrival at the scene (response time), time interval from arrival to departure from the scene (scene time), time interval from departure from the scene to arrival at the ED (transport time), and initial electrocardiogram (ECG) rhythm (ventricular tachycardia/ventricular fibrillation, pulseless electrical activity and asystole). Additionally, we added the following covariates: co-morbidities including diabetes, stroke, heart disease and chronic renal disease; level of ED (levels 1–3) adjusted for ED capacity; community urbanization (rural vs. urban).

Trained medical record reviewers from the Korean CDC visited all hospitals receiving OHCA patients and reviewed the information for hospital care and outcomes using a structured survey form. HTN variables were obtained from medical record review. HTN was positive when the patient had a clinical history diagnosed by a physician before the arrest event.

A quality management committee (QMC) consisted of emergency medicine physicians, epidemiologists, statistical experts, cardiologists, and medical record review experts. To acquire more comprehensive knowledge and maintain supervised information procuration, the reviewers consulted an emergency medicine physician from the QMC for clarification when they were unable to objectively define a coding element.

2.4. Study population

The data was collected between January 2012 and December 2016. All adults who are older than 19 years and EMS treated OHCA of presumed cardiac etiology were included. Patients having an arrest of cardiac etiology were identified by medical record review. We presumed the cause of arrest to be of cardiac etiology if there was no clear non-cardiac cause. Patients were excluded if they had unknown neurological status at hospital discharge.

2.5. Main outcomes

The primary outcome of this study was good cerebral performance category (CPC), which was distinguished by scoring 1 (good cerebral performance), or 2 (moderate cerebral disability; able to perform daily activities independently). The CPC score was categorized by medical record reviewers on the basis of discharge summary abstracts or documentations in medical records written by inpatient care doctors. Since there was no standard for recording formality across different hospitals for coding a CPC score, the code scores were usually reviewed and revised by the Korea CDC medical record reviewers. A secondary outcome was survival to discharge.

2.6. Variables

The primary exposure variable of interest was hypertension. Hypertension information was obtained from hospital medical records. Hypertension was recorded as positive when the patient had a clinical history of hypertension with diagnosis by a physician before cardiac arrest. We collected previous health history using the Utstein recommendations, which included age, gender, co-morbidities, witness status, bystander CPR, initial heart rhythm identified at the scene (shock-able or non-shock-able), pre-hospital CPR and defibrillation, response time interval from call to ambulance arrival at the scene, time interval from EMS arrival to departure from the scene, transport time interval from the scene to arrive at the hospital, and initial electrocardiogram (ECG) at an ED (asystole, pulseless electrical activity, ventricular tachycardia/ventricular fibrillation), place of ROSC (pre-hospital vs. ED), and neurological outcome at discharge. We also collected information on insurance types (Medical aid or National Health Insurance).

We considered age, gender, year of event, season of event, residence area, insurance type (socioeconomic status) and co-morbidities as confounding variables. We did not consider treatment in an emergency department such as extracorporeal membrane oxygenation, targeted temperature management, or reperfusion therapy as confounders.

2.7. Statistical analysis

Demographic findings and outcomes by HTN and Age were described. Chi-square analysis was used for categorical variables. Continuous variables were compared using the *t*-test. In order to estimate associations between patients with or without hypertension and the study outcomes, adjusted odds ratio (OR) with 95% confidence intervals (95% CI) were calculated using multivariable logistic regression analysis. In patients without a hypertension group as a reference, the model was adjusted for potential confounders including age, gender, socioeconomic state (insurance type) and co-morbidities. To obtain an adjusted OR (95% CI) for each age group, a multivariable logistic regression model was analyzed with an interaction term (hypertension group × age group).

All statistical analysis was performed using SAS version 9.4 (SAS institute, Cary, SC, USA).

3. Results

A total of 24,672 EMS-assessed OHCA cases survived to admission in South Korea during the period of January 1, 2012 to December 31, 2016. We excluded patients who were younger than 19 years (n = 808), those who had a non-cardiac etiology (n = 5284). As well cases with missing information on hypertension (n = 6949) and survival outcomes (n = 21) were excluded from the analysis (Fig. 1).

Demographic and clinical characteristics were compared between OHCA patients with and without hypertension (Table 1). Hypertensive patients were older and more likely to have diabetes, chronic heart disease, stroke and chronic renal disease (P < .001). Hypertensive patients were more likely to be medical aid insurance patients. Survival to discharge and good neurological recovery was lower in patients with hypertension (P < .001). Demographic findings by age are demonstrated in Table 2. Patients with hypertension were 48.0% (the <65-year-old group), 75.9% (the 65–80-year-old group) and 76.7% (the >80-year-old group). A greater proportion of the under 65-year-old group (40.7%) had an initial shockable rhythm than for other groups (23.7% and 11.8%). Good neurological recovery and survival to discharge was lower in the older groups. (P < .001).

Survival outcomes are compared in Table 3. On Multivariate analysis, hypertension was associated with a low rate of favorable CPC (AOR 0.79 [0.72–0.87]) and survival to discharge in Model 1. (AOR 0.83 [0.77–0.90]). In Model 2, after adjusting preexisting diseases of patients, hypertension was associated with a high rate of favorable CPC (AOR in

Table 3
Multivariable logistic regression analysis for outcomes by hypertension group.

Hypertension	Total	Outcomes		Model 1			Model 2		
	N	n	%	COR	95% CI		AOR	95% CI	
Good CPC									
Total	11,610	2683	23.1						
No	4534	1317	29.0	1.00			1.00		
Yes	7076	1366	19.3	0.79	0.72	0.87	1.18	1.04	1.35
Survival to discharge									
Total	11,610	4572	39.4						
No	4534	2046	45.1	1.00			1.00		
Yes	7076	2526	35.7	0.83	0.77	0.90	1.13	1.01	1.27

COR: crude odds ratio, AOR: adjusted odds ratio, 95% CI: 95% confidence interval.
CPC: cerebral performance scale.
Adjusted for age group, gender, year of event, metropolis, season, and insurance type for Model 1.
Adjusted for age group, gender, year of event, metropolis, season, insurance, diabetes, chronic heart disease, stroke, and chronic renal disease for Model 2.

Table 4
Multivariable logistic regression analysis for outcomes by age group.

Age group	Total	Outcomes		Model 1			Model 2		
	N	n	%	COR	95% CI		AOR	95% CI	
Good CPC									
Total	11,610	2683	23.1						
19 ≤ Age < 65	6260	2037	32.5	1.00			1.00		
65 ≤ Age < 80	3838	546	14.2	0.35	0.32	0.39	0.39	0.35	0.44
Age ≥ 80	1512	100	6.6	0.17	0.13	0.20	0.18	0.14	0.22
Survival to discharge									
Total	11,610	4572	39.4						
19 ≤ Age < 65	6260	3012	48.1	1.00			1.00		
65 ≤ Age < 80	3838	1217	31.7	0.52	0.47	0.56	0.56	0.51	0.61
Age ≥ 80	1512	343	22.7	0.35	0.31	0.40	0.37	0.32	0.42

COR: crude odds ratio, AOR: adjusted odds ratio, 95% CI: 95% confidence interval.
CPC: cerebral performance scale.
Adjusted for gender, year of event, metropolis, season, and insurance type for Model 1.
Adjusted for gender, year of event, metropolis, season, insurance, diabetes, chronic heart disease, stroke, and chronic renal disease for Model 2.

Model 2: 1.18 [1.04–1.35]) and survival to discharge (AOR in Model 2: 1.13 [1.01–1.27]).

Age and survival rate were analyzed by multivariate analysis (Table 4). The older groups were less likely to have good neurological recovery and to survive to hospital discharge compared to younger groups.

We than added an interaction term between hypertension and age to the above adjusted model. The AORs assessing the statistical interaction on survival with good neurologic outcomes from the multivariable logistic regression which are presented in Table 5. Those over 80 years old with hypertension were more likely to have good neurologic recovery (AOR [95% CI] 2.53 [1.43–4.50]). Whereas for those under 80 years of age (age < 65 group and 65 ≤ age ≤ 80 group), there was no difference observed in neurologic outcomes between the hypertensive and non-hypertensive groups (AOR [95% CI] 1.13 [0.98–1.31] and 1.22 [0.97–1.53]). Those under 65 years old with hypertension were more likely to survive to hospital discharge with a statistical significance (AOR [95% CI] 1.19 [1.04–1.35]). But there was no difference in survival to discharge in the other groups (AOR [95% CI] 1.02 [0.86–1.22] and 1.12 [0.84–1.51]).

4. Discussion

This study evaluated the associations of hypertension with survival outcomes after cardiac arrest in adults and identified variations in the effects according to a patient's age. In multivariate analysis, hypertension was associated with good survival outcomes after adjusting for confounding factors including other co-morbidities. Then, when stratified by age, hypertension was associated with good neurological recovery for those over 80 years old and a more likely survival to discharge in those under 65 years old. These results suggest that hypertension alone may not have negative effects on the survival outcomes of patients with OHCA after adjusting for the effects of other co-morbidities, but rather may improve survival outcomes.

Our findings of an association between HTN and favorable survival outcomes are unusual. Although there are no observational studies of the association between HTN and the prognosis of OHCA patients, there are many studies that show increasing of the number of co-morbidities has an adverse effect on the prognosis in OHCA patients. On the other hand, in a study of factors affecting the prognosis of the OHCA, they suggest data that HTN does not have a negative effect on the prognosis of the OHCA, or it has rather good outcomes in univariate analysis [18-20].

Any potential explanations for the results of our study are speculative. It is possible that patients with known HTN may have had greater awareness regarding activation of emergency medical services (EMS) for ischemic symptoms. This may have resulted in a shorter duration between the onset of cardiac arrest and onset of EMS resuscitation efforts [21]. Another possibility is that the effects of hypertension medications can be considered. There are some studies that show calcium channel blockers can achieve favorable long-term outcomes in patients associated with cardiac arrest and angiotensin converting enzymes inhibitor preserved ischemic preconditioning to reduction in recurrent myocardial infarction and ischemia [22, 23]. There are some studies that b-blocker is good for survival outcomes, but there is a lot of controversy [24]. Although the mechanisms of a survival benefit are not clear, the results of this study show that hypertension alone does not adversely affect the prognosis of cardiac arrest patients.

Also, there are several observational studies evaluating the relationship between blood pressure and survival outcomes in cardiac arrest patients. Observational studies found that systolic blood pressure <90 mm Hg or >100 mm Hg was associated with higher mortality and diminished neurologic recovery. One observational study found that mean arterial pressure (MAP) >100 mm Hg during the 2 h after a return of spontaneous circulation (ROSC) was associated with better neurologic recovery at hospital discharge. Another study with a goal MAP >65 mm Hg within 6 h found no change in hospital mortality or functional recovery at hospital discharge. Based on these generally consistent studies, published protocols targeted MAP goals of >65 mm Hg to >80 mm Hg. But, there is no study on whether hypertensive patients have high blood pressure even after ROSC, so it is difficult to confirm the association with this study [25-29].

We found that HTN, which is commonly considered to be a risk factor for cardiac arrest, does not adversely affect the survival outcomes in OHCA patients, or rather it is a good prognostic factor. There is no clear basis for whether this study's outcomes are due to the pathophysiology of HTN itself, whether it is related to changes in the lifestyle and drug use after the patient's awareness of HTN.

In the future, it is necessary to study the factors related to HTN which improve the survival outcomes of OHCA patients.

5. Limitation

This study has some limitations. First, although the retrospective abstraction of medical records was performed by trained medical record reviewers, it was difficult to obtain a complete set of variables for each

Table 5
Interaction analysis for outcomes by hypertension and age group.

Outcomes	Hypertension	Age group								
		19 ≤ Age < 65			65 ≤ Age < 80			Age ≥ 80		
		AOR	95% CI		AOR	95% CI		AOR	95% CI	
Good CPC	No	1.00			1.00			1.00		
	Yes	1.13	0.98	1.31	1.22	0.97	1.53	2.53	1.43	4.50
Survival to discharge	No	1.00			1.00			1.00		
	Yes	1.19	1.04	1.35	1.02	0.86	1.22	1.12	0.84	1.51

AOR: adjusted odds ratio, 95% CI: 95% confidence interval.
CPC: cerebral performance scale.
Adjusted for gender, year of event, metropolis, season, insurance, diabetes, chronic heart disease, stroke, and chronic renal disease.

patient, the HTN patients in this study may have been underestimated. Patient selection in our study may be subject to a selection bias as it is possible that some patients with HTN were unaware of their status or did not have adequate resources to be examined for clinical diagnosis before cardiac arrest. Second, among adult OHCA patients of cardiac etiology, 37.4% (n = 6949) of patients do not have a record showing HTN, so patients who are excluded may have an effect on the survival outcomes.

Third, the study analysis was limited to patients with known HTN, which may restrict the generalizability of the study findings to OHCA patients in general. Also, our data on HTN was limited to doctors' medical records. The data set did not include laboratory results on the severity, duration and treatment of HTN. Fourth, the main outcome, CPC score, was measured by medical record reviewers without any being blind to previous medical history. Also, no validation or reliability studies were performed prior to the study. Measurement bias might contribute to the study findings, although the QMC had tried to give advice for controversial cases. Finally, we could not adjust for unmeasured bias.

6. Conclusion

Hypertension does not adversely affect the survival outcomes of OHCA patients across all age groups of this study. In the group over 80 years old, HTN is significantly associated with survival with favorable neurologic recovery.

Author contributions

Dr. Jung and Ryu has full access to all the data in the study and the responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Jung, Ryu, Shin.

Acquisition, analysis, or interpretation of data: Jung, Ryu, Shin, Ro, Song.

Drafting of the manuscript: Jung, Ryu, Ro, Lee.

Critical revision of the manuscript for important intellectual content: Jung, Ryu, Ro.

Statistical analysis: Jung, Ryu, Ro, Song, Park.

Administrative, technical, or material support: Ryu, Shin, Ro,

Study supervision: Ryu, Ro, Park,

Manuscript approval: all authors.

Funding

This study was supported by the National Emergency Management Agency of Korea and the Korea CDC (2012-E33010-00, 2013-E33015-00, 2014-E33011-00, 2016-E33012-00).

Conflict of interest statement

None.

References

[1] Atwood C, Eisenberg MS, Herlitz J, Rea TD. Incidence of EMS-treated out-of-hospital cardiac arrest in Europe. Resuscitation 2005;67(1):75–80.
[2] Nichol G, Thomas E, Callaway CW, Hedges J, Powell JL, Aufderheide TP, et al. Regional variation in out-of-hospital cardiac arrest incidence and outcome. JAMA 2008;300(12):1423–31.
[3] Rea TD, Eisenberg MS, Sinibaldi G, White RD. Incidence of EMS-treated out-of-hospital cardiac arrest in the United States. Resuscitation 2004;63(1):17–24.
[4] van de Glind EM, van Munster BC, van de Wetering FT, van Delden JJ, Scholten RJ, Hooft L. Pre-arrest predictors of survival after resuscitation from out-of-hospital cardiac arrest in the elderly a systematic review. BMC Geriatr 2013;13:68.
[5] Perkins GD, Jacobs IG, Nadkarni VM, Berg RA, Bhanji F, Biarent D, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update of the Utstein resuscitation registry templates for out-of-hospital cardiac arrest: a statement for healthcare professionals from a task force of the international liaison committee on resuscitation (American Heart Association, European Resuscitation Council, Australian and New Zealand Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia); and the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. Resuscitation 2015;96:328–40.
[6] Rea TD, Cook AJ, Stiell IG, Powell J, Bigham B, Callaway CW, et al. Predicting survival after out-of-hospital cardiac arrest: role of the Utstein data elements. Ann Emerg Med 2010;55(3):249–57.
[7] Bergner DW, Goldberger JJ. Diabetes mellitus and sudden cardiac death: what are the data? Cardiol J 2010;17(2):117–29.
[8] Yusuf S, Hawken S, Ôunpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004;364(9438):937–52.
[9] He J, Whelton PK. Elevated systolic blood pressure as a risk factor for cardiovascular and renal disease. J Hypertens Suppl 1999;17(2):S7–13.
[10] Kannel WB. Elevated systolic blood pressure as a cardiovascular risk factor. Am J Cardiol 2000;85(2):251–5.
[11] Deasy C, Bray JE, Smith K, Harriss LR, Bernard SA, Cameron P. Out-of-hospital cardiac arrests in the older age groups in Melbourne, Australia. Resuscitation 2011;82(4):398–403.
[12] Herlitz J, Eek M, Engdahl J, Holmberg M, Holmberg S. Factors at resuscitation and outcome among patients suffering from out of hospital cardiac arrest in relation to age. Resuscitation 2003;58(3):309–17.
[13] Swor RA, Jackson RE, Tintinalli JE, Pirrallo RG. Does advanced age matter in outcomes after out-of-hospital cardiac arrest in community-dwelling adults? Acad Emerg Med 2000;7(7):762–8.
[14] Gijsen R, Hoeymans N, Schellevis FG, Ruwaard D, Satariano WA, van den Bos GA. Causes and consequences of comorbidity: a review. J Clin Epidemiol 2001;54(7):661–74.
[15] Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. J Gerontol A Biol Sci Med Sci 2004;59(3):255–63.
[16] Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: a systematic review of the literature. Ageing Res Rev 2011;10(4):430–9.
[17] Fukuda T, Ohashi-Fukuda N, Kondo Y, Sera T, Doi K, Yahagi N. Epidemiology, risk factors, and outcomes of out-of-hospital cardiac arrest caused by stroke: a population-based study. Medicine 2016;95(14):e3107.
[18] Parry M, Danielson K, Brennenstuhl S, Drennan IR, Morrison LJ. The association between diabetes status and survival following an out-of-hospital cardiac arrest: a retrospective cohort study. Resuscitation 2017;113:21–6.
[19] Sasson C, Rogers MA, Dahl J, Kellermann AL. Predictors of survival from out-of-hospital cardiac arrest: a systematic review and meta-analysis. Circ Cardiovasc Qual Outcomes 2010;3(1):63–81.
[20] Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet (Lond Engl) 2004;364(9438):937–52.
[21] Lee MH, Fook-Chong S, Wah W, Shin SD, Nishiuchi T, Ko PC, et al. Effect of known history of heart disease on survival outcomes after out-of-hospital cardiac arrests. Emerg Med Australas 2018;30(1):67–76.
[22] Domanski MJ, Exner DV, Borkowf CB, Geller NL, Rosenberg Y, Pfeffer MA. Effect of angiotensin converting enzyme inhibition on sudden cardiac death in patients following acute myocardial infarction. A meta-analysis of randomized clinical trials. J Am Coll Cardiol 1999;33(3):598–604.
[23] Stecker EC, Teodorescu C, Reinier K, Uy-Evanado A, Mariani R, Chugh H, et al. Ischemic heart disease diagnosed before sudden cardiac arrest is independently associated with improved survival. J Am Heart Assoc 2014;3(5):e001160.
[24] Czarnecki A, Morrison LJ, Qiu F, Cheskes S, Koh M, Wijeysundera HC, et al. Association of prior beta-blocker use and the outcomes of patients with out-of-hospital cardiac arrest. Am Heart J 2015;170(5) [1018–24.e2].
[25] Mullner M, Sterz F, Binder M, Hellwagner K, Meron G, Herkner H, et al. Arterial blood pressure after human cardiac arrest and neurological recovery. Stroke 1996;27(1):59–62.
[26] Walters EL, Morawski K, Dorotta I, Ramsingh D, Lumen K, Bland D, et al. Implementation of a post-cardiac arrest care bundle including therapeutic hypothermia and hemodynamic optimization in comatose patients with return of spontaneous circulation after out-of-hospital cardiac arrest: a feasibility study. Shock 2011;35(4):360–6.
[27] Kilgannon JH, Roberts BW, Reihl LR, Chansky ME, Jones AE, Dellinger RP, et al. Early arterial hypotension is common in the post-cardiac arrest syndrome and associated with increased in-hospital mortality. Resuscitation 2008;79(3):410–6.
[28] Gaieski DF, Band RA, Abella BS, Neumar RW, Fuchs BD, Kolansky DM, et al. Early goal-directed hemodynamic optimization combined with therapeutic hypothermia in comatose survivors of out-of-hospital cardiac arrest. Resuscitation 2009;80(4):418–24.
[29] Sunde K, Pytte M, Jacobsen D, Mangschau A, Jensen LP, Smedsrud C, et al. Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. Resuscitation 2007;73(1):29–39.