

# Risk of hypertension and treatment on out-of-hospital cardiac arrest incidence

## A case-control study

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### Abstract

Hypertension (HTN) is a high risk factor for major cardiovascular adverse events. This study aimed to investigate the effect of HTN risk on out-of-hospital cardiac arrest (OHCA) incidence and determine whether the effect of HTN on OHCA incidence differs according to antihypertensive medication.

This case-control study used the Korean Cardiac Arrest Resuscitation Consortium and Korean Community Health Survey (CHS). Cases were defined as emergency medical service-treated adult OHCA patients presumed to have a cardiac etiology from 2015 to 2017. Patients without information on HTN diagnosis were excluded from the study. The Korean CHS database's controls were matched at a 1:2 ratio with strata, including age, gender, and county of residence. Multivariable conditional logistic regression analysis was conducted to estimate HTN risk and antihypertensive treatment on OHCA incidence.

A total of 2633 OHCA patients and 5266 community-based controls were enrolled in this study. Among them, 1176 (44.7%) patients and 2049 (38.9%) controls were diagnosed with HTN. HTN was associated with an increased risk of OHCA (adjusted odds ratio [AOR]: 1.19 [1.07–1.32]). On comparing HTN with or without the antihypertensive treatment group with the non-HTN-diagnosed group (as a reference), the HTN without treatment group had the highest AOR (95% confidence interval) (3.41 [2.74–4.24]). The AOR in the HTN treatment group was reduced to that in the non-HTN-diagnosed group (0.96 [0.86–1.08]).

HTN increased OHCA risk, and the HTN without treatment group had the highest OHCA risk. Conversely, OHCA risk decreased to the non-HTN-diagnosed group level with HTN treatment.

**Abbreviations:** AOR = adjusted odds ratio, BP = blood pressure, CHS = Community Health Survey, CI = confidence interval, CVD = cardiovascular disease, DM = diabetes mellitus, ED = emergency department, EMS = emergency medical service, HTN = hypertension, IRB = Institutional Review Boards, KoCARC = Korean Cardiac Arrest Research Consortium, OHCA = out-of-hospital cardiac arrest, SCD = sudden cardiac death.

**Keywords:** antihypertensive agent, hypertension, out-of-hospital cardiac arrest, prevention

## 1. Introduction

Out-of-hospital cardiac arrest (OHCA) is a global health burden.<sup>[1,2]</sup> In Korea, the OHCA incidence rate is 46.8 per

100,000 person-years for emergency medical service (EMS)-assessed OHCA, and the survival rate is 3.6%.<sup>[3]</sup> Despite the development of various strategies in prehospital cardiopulmo-

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The KoCARC dataset used and analyzed during the current study are available from the authors. The Korean CDC has authority for the Korean CHS dataset; permission is required to use the Korean CHS. Requests can be sent for access permission to the Korean CHS dataset (Office Tel: +82-43-719-7399, website: <http://chs.cdc.go.kr/chs/index/do>).

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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nary resuscitation and postresuscitation care, the survival rate remains low, and patients still experience severe neurologic deficits.<sup>[3,4]</sup> Therefore, the optimal management of OHCA patients after the event occurs, the evaluation of high-risk groups of cardiac arrest, and the development of strategies of prevention methods in our community are of great importance in reducing the burden of OHCA.

Hypertension (HTN) is a well-recognized risk factor for sudden cardiac death (SCD) and cardiovascular disease (CVD). HTN triggers cardiac remodeling and development of left ventricular hypertrophy, causing subendocardial ischemia, myocardial fibrosis, ion channel remodeling, and gap junction remodeling that results in complex ventricular arrhythmias, subclinical organ damage, and eventually leads to major complications, cardiovascular events, and SCDs.<sup>[5,6]</sup> Several cohort studies have reported the association of HTN and the risk of SCD. HTN significantly increases the lifetime risk of sudden cardiac arrest/SCD at 30 years of age by 30%<sup>[7]</sup> and per 20-mm Hg increase in systolic blood pressure (BP) was associated with a 28% increased risk of SCD.<sup>[8]</sup> Also there are evidences demonstrating the risk of untreated HTN on CVD events compared to normotensive subjects.<sup>[9]</sup> One meta-analysis study concluded that antihypertensive medication reduced the cardiovascular events.<sup>[10]</sup> Another study showed that the larger reduction in BP produced larger reduction in cardiovascular risk.<sup>[11]</sup>

In 2010, the global age-standardized prevalence of HTN was 31.1%, and in 2013 to 2016, the estimated prevalence of HTN was 32.0% in the United States.<sup>[12]</sup> Because of the aging population and increased exposure to unhealthy lifestyle risk factors, including unhealthy diet and lack of physical activities, the prevalence of HTN has increased.<sup>[13]</sup> According to several studies, the prevalence of pre-HTN ranged from 25.2% to 46.0%, accounting for almost 50% to 70% of the adult population with higher than normal BP.<sup>[14]</sup> In Korea, the prevalence of HTN was 29.1% in 2016, and with an increasing population with pre-HTN, 55% of Koreans aged 30 years or older have higher than normal BP.<sup>[15]</sup> Given the high prevalence of HTN and because HTN is a well-known risk factor for OHCA, understanding whether and how it affects OHCA incidence is challenging.

Therefore, this study aimed to determine the effect of HTN risk on OHCA incidence and investigate whether the effect of HTN on OHCA incidence differs according to antihypertensive medication.

## 2. Materials and methods

### 2.1. Study design and data source

This case-control study used data from the Korean Cardiac Arrest Research Consortium (KoCARC) database in Korea. The KoCARC is a multicenter collaborative research network of hospitals<sup>[16]</sup> and was established to evaluate missing links and provide evidence to strengthen the chain of survival. The KoCARC enrolled OHCA patients transported to the emergency department (ED) by the EMS with resuscitation efforts (EMS-treated OHCA) and patients with a presumed cardiac etiology identified by emergency physicians in each ED. The KoCARC registry excluded OHCA patients with a terminal illness documented in medical records, patients under hospice care, pregnant patients, and patients with previously documented

“Do No Resuscitation” cards. In addition, OHCA patients with definite noncardiac etiology, including trauma, drowning, poisoning, burn, asphyxia, or hanging, were excluded.

The KoCARC registry collects data of OHCA patients' demographic information, health behavior, past medical history, information of the community, EMS and ED resuscitation using Utstein template, ED laboratory test results, cardiac evaluation results, and short and long-term outcomes. Each participating ED collects data using a standardized form and enters it into a web-based electronic database registry. The study coordinator at each site ensures the accuracy of the data, fills up the laboratory and cardiac evaluation results through medical record review, and contacts family members of the patients to survey outcomes after 6 months. A total 32 of 62 hospitals are currently collecting and entering data.

The quality management committee comprising emergency physicians, statistical experts, and local research coordinators was organized and trained for data collection protocol before actual data collection. Quality management committee meetings were held every 3 months to provide feedback on quality management and clarify a coding element's definition. The KoCARC registry was registered at [clinicaltrials.gov](http://clinicaltrials.gov) as protocol NCT03222999.

Community-based controls were identified based on data from the Community Health Survey (CHS) conducted by the Korean Centers for Disease Control and Prevention. The Korean CHS is a cross-sectional national health survey conducted annually in accordance with the Community Health Act, with the target population of adults aged 19 years or older. It assesses health conditions, health care utilization, health behaviors, quality of life, and sociodemographic information of responders. Responders are members of representatively selected households from 253 counties who were sampled using multistage, stratified, and random sampling methods. An average of 920 individuals from each local county participated in the survey. All surveys were conducted by trained surveyors using computer-assisted personal interviewing methods.

### 2.2. Study setting

The Korean EMS is managed by the fire department and provided by the government. It offers multitiered basic-to-intermediate level ambulance services in 17 provincial headquarters of the national fire department. Ambulance crews who are emergency medical technicians cannot declare death or discontinue cardiopulmonary resuscitation without online medical directions. Therefore, all resuscitation-attempted OHCA patients are transported to the nearest ED. The Korean EMS serves a population of approximately 50 million.

### 2.3. Study population

Cases were defined as OHCA patients aged 19 to 80 years whose data were collected using the KoCARC registry from 2015 to 2017. We excluded OHCA patients without information on the diagnosis of HTN. Community-based controls were selected from the Korean CHS from 2015 to 2017. A total of 228,558, 228,452, and 228,381 participants completed the Korean CHS in 2015, 2016, and 2017, respectively. Cases and controls were matched at a 1:2 ratio with age by 5 years, gender, and county of residence.

**2.4. Measurements**

The main exposure was physician-diagnosed HTN before study enrollment, and information on medical treatment was collected using a survey. The duration of HTN prevalence was not considered. The KoCARC registry used the same questionnaire to assess past medical history and health behaviors as the Korean CHS to ensure comparable accuracy between cases and controls. Each past medical history of both cases and control was recorded as “positive” if respondents were confirmed to be physician diagnosed. We also noted whether patients were taking HTN medication if they were diagnosed with HTN. In addition, we collected information on age; gender (male, female); date of cardiac arrest; county of residence; past medical history, including diagnosis of diabetes mellitus (DM) (whether taking medical treatment if diagnosed of DM); and health behaviors, including smoking (current smoker, ex-smoker, never a smoker, and unknown), and alcohol consumption (frequent drinker defined more than twice a week, occasional drinker, never a drinker, and unknown). Continuous variable age was categorized by 10 years.

**2.5. Statistical analysis**

We evaluated demographic findings of the OHCA case groups and community control groups. Continuous variables were compared using the Wilcoxon rank-sum test, and categorical variables were compared using the chi-square test. In addition, we conducted multiple imputations (imputation=5) using multivariable proportional logistic regression models with missing variables for smoking (N=1745) and alcohol consumption (N=3136).

Multivariable conditional logistic regression analysis was conducted for a matched case-control dataset to estimate the effect of diagnosis and medical treatment of HTN on OHCA risk. Adjusted odds ratios (AORs) and 95% confidence intervals (CIs) were calculated after controlling potential confounders. The potential confounders were age as a continuous variable, diagnosis of diabetes, alcohol consumption habit, and smoking habit. Multivariable conditional logistic regression analysis for the diabetes diagnosed population was also conducted for subgroup analysis. In addition, we analyzed collinearity and assessed if variables had conditional index >30 and variance decomposition proportion >0.5. No multicollinearity was detected in our models, and all terms were retained. All statistical analyses were performed using Statistical Analysis System (SAS) 9.4 (SAS Institute Inc., Cary, NC).

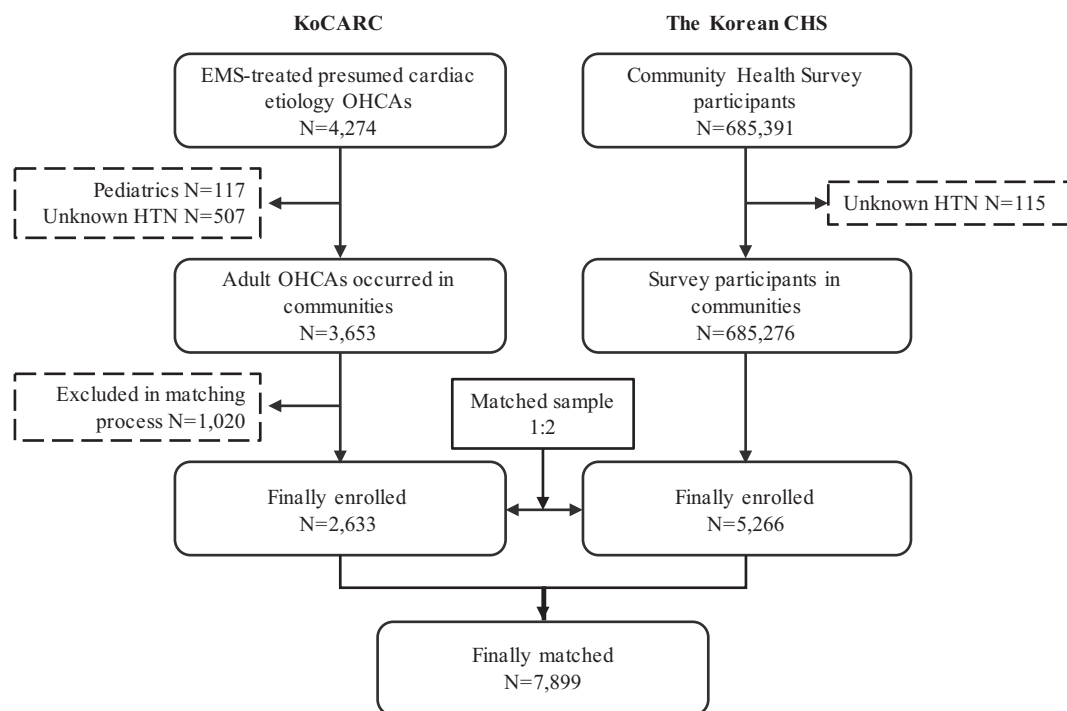
**2.6. Ethics statements**

The study complies with the Declaration of Helsinki, and the study protocol was approved by all Institutional Review Boards (IRBs) of 32 participating hospitals. In addition, the IRBs of all participating institutions waived the requirement for informed consent. No funding was used to support this work. The IRB No. for the Korea University Ansan Hospital is 2019AS0153.

**3. Result**

**3.1. Demographic findings**

Among 4274 EMS-treated OHCA patients during the study period, 3653 were assigned to a case group after excluding pediatric patients (N=117) and patients with unknown



**Figure 1.** Study population flow. CHS = Community Health Survey, EMS = emergency medical service, HTN = hypertension, KoCARC = Korean Cardiac Arrest Research Consortium, OHCA = out-of-hospital cardiac arrest.

**Table 1**  
**Characteristics of out-of-hospital cardiac arrest cases and community controls.**

Characteristics	Total		OHCA cases		Community controls		P value
	N	%	N	%	N	%	
Total	7899	100	2633	100	5266	100	
Gender							1.00
Female	2307	29.2	769	29.2	1538	29.2	
Male	5592	70.8	1864	70.8	3728	70.8	
Age, yrs							1.00
19–29	165	2.1	55	2.1	110	2.1	
30–39	366	4.6	122	4.6	244	4.6	
40–49	912	11.6	304	11.6	608	11.6	
50–59	1509	19.1	503	19.1	1006	19.1	
60–69	1908	24.2	636	24.2	1272	24.2	
70–80	3039	38.5	1013	38.5	2026	38.5	
Median (IQR)	65	(53–73)	65	(54–74)	64	(53–73)	
Past medical history							
Hypertension							<.001
No HTN	4674	59.2	1457	55.3	3217	61.1	
HTN without treatment	455	5.8	297	11.3	158	3.0	
HTN with treatment	2770	35.1	879	33.4	1891	35.9	
Diabetes mellitus							<.001
No DM	6225	78.8	1877	71.3	4348	82.6	
DM without treatment	305	3.9	210	8.0	95	1.8	
DM with treatment	1369	17.3	546	20.7	823	15.6	
Health behaviors							
Smoking							<.001
Current smoker	1781	22.6	655	24.9	1126	21.4	
Ex-smoker	2419	30.6	650	24.7	1769	33.6	
Never smoker	3699	46.8	1328	50.4	2371	45.0	
Alcohol consumption							<.001
Frequent	2564	32.5	727	27.6	1837	34.9	
Occasional	2043	25.9	653	24.8	1390	26.4	
Never	3292	41.7	1253	47.6	2039	38.7	

DM = diabetes mellitus, HTN = hypertension, IQR = interquartile range, OHCA = out-of-hospital cardiac arrest.

information about HTN (N = 504). For the community control group, 5266 participants were selected within strata from the 2015 to 2017 Korean CHS database with a case-to-control ratio of 1:2. A total of 7899 case-control matched sets were analyzed in the study (Fig. 1).

The characteristics of OHCA cases and community controls of the original and imputed datasets are shown in Table 1 and Table S1, Supplemental Digital Content, <http://links.lww.com/MD2/A987>. Among 2633 EMS-treated OHCA patients with presumed cardiac etiology, 1174 (44.7%) were diagnosed with HTN, and among them, 297 (11.3%) patients did not receive medical treatment. Among 5266 community controls, 2049 (38.9%) were diagnosed with HTN, and 158 participants (3.0%) did not receive medical treatment. DM was diagnosed in 28.7% of OHCA cases and 17.4% of community controls (Table 1).

Demographics according to antihypertensive treatment are reported in Table 2. Among patients with HTN, those without medical treatment were more likely to be younger, have diabetes but not receive treatment, be current smokers, and be more frequent alcohol drinkers. Among all case and control participants, those without HTN tend to be younger, not have diabetes, be current smokers, and be frequent alcohol drinkers compared with patients with HTN.

### 3.2. Main analysis

Results of the multivariable conditional logistic regressions after adjusting for DM, smoking, and alcohol consumption habits for OHCA risk due to HTN and treatment are shown in Table 3. HTN was significantly associated with OHCA risk; the AOR (95% CI) for OHCA was 1.19 (1.07–1.32). In terms of HTN treatment, the without HTN treatment group was significantly associated with increased OHCA risk (3.41 [2.74–4.24]), whereas the HTN treatment group was not significantly associated with OHCA risk (0.96 [0.86–1.08]) compared with the without HTN group.

Subgroup analyses of patients with DM are shown in Table 4. In DM patients, HTN significantly increased the risk for OHCA (AOR [95% CI] for OHCA was 1.46 [1.17–1.82]), and the HTN treatment group was not significantly associated with OHCA risk (AOR [95% CI] for OHCA was 1.16 [0.92–1.45]).

## 4. Discussion

This case-control study investigated HTN as a risk factor of rare patient outcome conditions such as OHCA. We found that the risk of HTN on OHCA incidence was significantly increased, and the effect of HTN risk on OHCA incidence according to treatment exhibited a different impact. Although without HTN

**Table 2**  
**Characteristics of out-of-hospital cardiac arrest cases and controls according to hypertension and treatment.**

Characteristics	Total		No HTN		HTN without treatment		HTN with treatment		P value
	N	%	N	%	N	%	N	%	
Total	7899	100	4674	100	455	100	2770	100	
Case/control									<.001
OHCA cases	2633	33.3	1457	31.2	297	65.3	879	31.7	
Community controls	5266	66.7	3217	68.8	158	34.7	1891	68.3	
Gender									.021
Female	2307	29.2	1331	28.5	118	25.9	858	31.0	
Male	5592	70.8	3343	71.5	337	74.1	1912	69.0	
Age, yrs									<.001
19–29	165	2.1	161	3.4	3	0.7	1	0.0	
30–39	366	4.6	337	7.2	13	2.9	16	0.6	
40–49	912	11.6	748	16.0	53	11.7	111	4.0	
50–59	1509	19.1	1048	22.4	91	20.0	370	13.4	
60–69	1908	24.2	1058	22.6	115	25.3	735	26.5	
70–80	2812	35.6	1226	26.2	163	35.8	1423	51.4	
Median (IQR)	65	(53–73)	60	(49–71)	66	(56–75)	70	(62–75)	<.001
Past medical history									<.001
Diabetes mellitus									<.001
No DM	6225	78.8	4082	87.3	309	67.9	1834	66.2	
DM without treatment	305	3.9	116	2.5	123	27.0	66	2.4	
DM with treatment	1369	17.3	476	10.2	23	5.1	870	31.4	
Health behaviors									<.001
Smoking									<.001
Current smoker	1778	22.5	1183	25.3	107	23.5	488	17.6	
Ex-smoker	2419	30.6	1329	28.4	131	28.8	959	34.6	
Never smoker	3702	46.9	2162	46.3	217	47.7	1323	47.8	
Alcohol consumption									<.001
Frequent	2595	32.9	1611	34.5	171	37.6	813	29.4	
Occasional	2050	26.0	1248	26.7	107	23.5	695	25.1	
Never	3254	41.2	1815	38.8	177	38.9	1262	45.6	

DM=diabetes mellitus, HTN=hypertension, IQR=interquartile range, OHCA=out-of-hospital cardiac arrest.

treatment increased the risk of OHCA by over 3 folds, when taking antihypertensive medication, OHCA risk was not significant compared with that in the without HTN group. The effect of HTN on OHCA risk was consistent in patients with DM after adjusting for health behaviors such as alcohol and smoking habits. Considering the high prevalence of HTN, BP control should be emphasized to decrease fatal adverse events of HTN.

There are mounting epidemiologic studies providing evidence for a relationship between high BP and CVD risk.<sup>[7,17]</sup> This finding is consistent with our finding that HTN increased the risk

of OHCA incidence. Therefore, it is crucial to control BP in patients with HTN to prevent major cardiovascular complications such as myocardial infarction or cerebral stroke.<sup>[11,18]</sup> However, the association between antihypertensive treatment and SCD is not completely known.<sup>[19]</sup> Previous studies addressed the diagnosis of HTN in the without HTN populations or used antihypertensive agents as an intervention in patients with HTN. In contrast, in this study, we compared HTN as a risk and assessed whether taking antihypertensive agents affected the risk of OHCA compared with the without HTN population. Based on our findings from 32 hospitals and CHSs, with antihyperten-

**Table 3**  
**Multivariable conditional logistic regression of out-of-hospital cardiac arrest risk by hypertension and treatment.**

	OHCA cases (N)	Community controls (N)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Model 1: HTN diagnosis				
No	1457	3217	1.00	1.00
Yes	1176	2049	1.31 (1.18–1.45)	1.19 (1.07–1.32)
Model 2: HTN treatment				
No HTN	1457	3217	1.00	1.00
HTN without treatment	297	158	4.21 (3.43–5.16)	3.41 (2.74–4.24)
HTN with treatment	879	1891	1.04 (0.93–1.16)	0.96 (0.86–1.08)

Adjusted for age, diabetes mellitus, smoking habit, and alcohol consumption. CI=confidence interval, HTN=hypertension, OHCA=out-of-hospital cardiac arrest, OR=odds ratio.

**Table 4**  
**Multivariable conditional logistic regression of out-of-hospital cardiac arrest risk by hypertension and treatment in patients with diabetes mellitus.**

	OHCA cases (N)	Community controls (N)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Model 1: HTN diagnosis				
No	239	353	1.00	1.00
Yes	517	565	1.47 (1.34–1.62)	1.46 (1.17–1.82)
Model 2: HTN treatment				
No HTN	239	353	1.00	1.00
HTN without treatment	121	25	7.89 (4.93–12.64)	7.92 (4.91–12.78)
HTN with treatment	396	540	1.16 (0.93–1.45)	1.16 (0.92–1.45)

Adjusted for age, smoking habit, and alcohol consumption.

CI = confidence interval, HTN = hypertension, OHCA = out-of-hospital cardiac arrest, OR = odds ratio.

sive medication, HTN could be a controllable risk factor in reducing OHCA incidence. However, by taking antihypertensive medication, the risk of OHCA was not significantly different compared with that in those without HTN. Moreover, unlike other studies, treatment with antihypertensive medication lowered the risk of OHCA incidence compared with that in the without HTN-treatment group among patients with HTN (AOR [95% CI] for OHCA was 0.27 [0.21–0.34]) (Table S2, Supplemental Digital Content, <http://links.lww.com/MD2/A988>). This difference may be due to the high volume of cases enrolled from the OHCA cohort, because in other studies, SCD cases are limited. For example, in a meta-analysis of antihypertensive treatment and SCD, the total cases of SCD enrolled were less than 500, whereas in our study, over 2000 OHCA cases were enrolled.<sup>[19]</sup>

HTN is a highly prevalent risk factor, and lifestyle affects the incidence and management of HTN. For example, high sodium intake,<sup>[20,21]</sup> heavy alcohol consumption,<sup>[22,23]</sup> lack of physical activity,<sup>[24,25]</sup> and obesity<sup>[26]</sup> increase the risk of HTN. In our study, the rate of current smoking status and heavy drinking was not high in the HTN group, which was inconsistent with findings of other studies, and this could be due to more number of older people being present in the HTN group.

This study is significant because the findings would encourage the HTN population to receive appropriate management and the without HTN population to receive regular health check-ups from perceiving HTN. With an increase in the prevalence of HTN and awareness varying among countries or populations within communities,<sup>[27]</sup> it is crucial to identify high-risk populations to target appropriate antihypertensive management. In our study, HTN was an independent risk factor for OHCA, and patients with HTN without antihypertensive treatment were at the highest risk for OHCA.

It is crucial to emphasize recommendations such as individualized BP management regarding risk control of HTN to decrease the incidence and burden of cardiac arrest among patients with HTN.

This study had several limitations to acknowledge. First, the study design was a case-control study and not an intervention trial; thus, significant potential biases may not be controlled. We selected controls from the same community residents to satisfy the “population at risk,” the most preferable controls. However, there is a possibility of misclassification for matching variables. Second, information on HTN was collected using survey, and we did not objectively measure BP to confirm. Responders could have interpreted the survey questionnaire differently, and HTN

could have been under- or over-diagnosed, resulting in data bias. Third, information on HTN was collected as a single dichotomous variable. The prevalence duration of HTN, stages of HTN, compliance of antihypertensive treatment, and how well HTN was controlled were not considered. Those details not collected in our registry could have affected the effect size in our study outcome. Fourth, patients’ past medical history of CVD, including coronary heart disease, heart failure, and arrhythmia, was not collected in our registry. A history of different CVDs could have affected OHCA occurrence, which could not be controlled in this study. Fifth, to minimize biases, we used the same survey questionnaire to obtain history about HTN, DM, and health behaviors from both cases and controls. However, most survey responders of cases were family members and presumably collected information of controls from the control themselves; hence, there was an inherent source of bias. Sixth, multiple imputations were applied to process missing covariables. These factors might not have been fully adjusted. Finally, this study enrolled cases and controls aged 19 to 80 years. We did not enroll participants aged over 80 years due to data incompleteness. The effect of sample size for OHCA risk could have been different if all aged populations were enrolled.

## 5. Conclusions

HTN was an independent risk factor for OHCA. The most high-risk population was the HTN without treatment group, and the magnitude of risk was observed to be reduced to the non-HTN-diagnosed population level when antihypertensive treatment was taken. Therefore, individualized and appropriate risk control should be emphasized to reduce the burden of cardiovascular complications by HTN.

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### Author contributions

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