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Strategies to Enhance Survival of Out-of-hospital Cardiac Arrest: From Individual to Systems-of-care perspectives

심정지 생존율 향상을 위한 전략:
개인부터 치료시스템까지의 관점

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Ph.D. Dissertation of Public Health

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Abstract

Strategies to Enhance Survival of Out-of-hospital Cardiac Arrest: From Individual to Systems-of-care perspectives

Background

Out-of-hospital cardiac arrest (OHCA) is a sudden, unexpected happening with high incidence and poor neurologic intact survival, which makes it a major public health challenge to overcome. Efforts in various fields, including public health, emergency medicine and in-hospital critical care are essential for decreasing burden of OHCA. The first goal of this study is to estimate the effect of hypertension, which is the most prevalent cardiovascular risk factor, and treatment on incidence of emergency medical service (EMS)-assessed OHCA in Korea. The second goal of this study is to estimate the effect of mechanical chest compression device during transportation of patients with OHCA according to patient transport interval. Although mechanical chest compression device itself did not show significant survival benefit compared with manual compression, in an EMS system where all EMS-treated OHCA patients

are transported to hospitals, CPR quality at moving ambulance may affect the survival. The third goal of this study was to evaluate the outcome of patients with OHCA who are transported to cardiac resuscitation centers (CRC) compared with non-tertiary centers.

Method

For the first study goal, case-control analysis was conducted using Korean Cardiac Arrest Research Consortium (KoCARC) database, a multicenter OHCA registry database as a case and community-based controls using Community Health Survey (CHS) conducted by the Korean Centers for Disease Control and Prevention (KCDC) as a control. Cases were defined as ES-treated adult OHCA patients presumed to have cardiac etiology from 2015 to 2017. Controls were matched at a 1:2 ratios with strata, including age, gender and county of residence. Multivariable conditional logistic regression was conducted after adjusting for diabetes, smoking and alcohol consumption habit.

For the second study goal, KoCARC database from year 2015 to 2020 was used for the analysis. KoCARC database includes information such as patient demographics, prehospital and hospital factors based on Utstein criteria, and survival outcomes. Primary outcome was survival to admission. Multivariable logistic regression was conducted to analyze the effect of mechanical chest compression device (MCPRD) compared with that of manual CPR and calculated adjusted odds ratios (AORs) with 95% confidence intervals (CIs) after adjusting for potential confounders: age, sex, medical histories, initial electrocardiography, witness status, provision of bystander

CPR, place pf arrest, provision of advanced airways, EMS response time interval and scene resuscitation time interval. The interaction effect of MCPRD according to patient transport interval (PTI) was evaluated. PTI was categorized into three groups: short PTI for 0–5 minutes, intermediate for 6–10 minutes, and long PTI for 11 min and longer. To control for selection bias and confounding factors, two methods of propensity score analysis was performed.

For the third study gold, Hospital Assessment Survey and national OHCA databased was used. Hospital Assessment Survey was conducted through Gyeonggi Emergency Medical Support Center to all OHCA receiving EDs in Gyeonggi province at 2015. The data of prehospital and hospital factors of OHCA patients transported to hospitals in Gyeonggi province at 2012-2014 was collected using the national OHCA database constructed by KCDC. The hospitals were classified as definite cardiac resuscitation center (D-CRC) if they had a standard resuscitation protocol at the ED; had the device, manpower, and standard protocol for TTM; if PCI was available 24/7; if they had an OHCA registry system; if they could confirm brain death, had an available rehabilitation program for post-resuscitated patients, and provided community-based CPR programs. Otherwise, hospitals were classified as primary cardiac resuscitation center (P-CRC). The primary outcome was favorable neurologic outcome defined as cerebral performance category 1 or 2. Multivariable logistic regression was conducted to calculate adjusted odds ratios (AORs) with 95% confidence intervals (CIs) of D-CRCs and P-CRCs after adjusting for potential confounders.

Results

From the first study goal, a total 2,633 cases of OHCA patients and 5,266 cases of community controls were matched for the analysis after excluding pediatric patients (N=177) and patients with unknown information of hypertension (N=504). After adjusting for diabetes, smoking and alcohol consumption habits, hypertension was significantly associated with OHCA risk; the AOR (95% CI) for OHCA was 1.19 (1.07-1.32). In terms of hypertension treatment, the without hypertension treatment group was significantly associated with increased OHCA risk (3.41 [2.72-4.24]), whereas the hypertension treatment group was not significantly associated with OHCA risk (0.96 [0.86-1.08]) compared with the without hypertension group.

For the second study goal, among 9,861 patients with OHCA after excluding pediatric patients (N=232), those who achieved prehospital return of spontaneous circulation (N=1,281), those without information of MCPRD or PTI (N=4,818), total 3,530 patients were eligible for the analysis. The AOR for survival to admission and hospital ROSC was significant compared to manual CPR (AOR 1.36, 95% CI 1.07-1.77 and AOR 1.47, 95% CI 1.20-1.79). Interaction effect of long PTI on the effect of MCPRD was significant for both survival to admission (AOR 1.49, 95% CI 1.05-2.12) and hospital ROSC (AOR 1.70, 95% CI 1.26-2,29). Optimal and Greedy PS matched cohorts were extracted. From both propensity-matched cohort, interaction effect of long PTI on the effect of MCPR was both significant; AOR 1.60 (95% CI 1.06-2.24) and AOR 1.60 (95% CI 1.06-2.42), respectively.

In third study, among the 90 cardiac receiving hospitals in Gyeonggi province, total 77 hospitals responded to the survey. According to the result of the survey, 15 hospitals were categorized as D-CRCs. Among 9,912 OHCA patients who were transported to cardiac arrest receiving hospitals, 4,036 patients (40.7%) were initially transported D-CRCs. After adjusting to potential confounders, patients transported to D-CRCs were significantly associated with good neurologic outcome (AOR 2.10, 95% CI 1.51-2.93) compared to those transported to P-CRCs. For patients who survived to admission, D-CRC was significantly associated with better neurologic outcome (AOR 1.48, 95% CI 1.02-2.14).

Conclusion

In this multicenter population-based OHCA study, individual, prehospital and hospital strategies to enhance survival were evaluated.

HTN was an independent risk factor for OHCA presumed of cardiac etiology. The most high-risk population was the HTN diagnosed but without treatment group, and the magnitude of risk was observed to be reduced to the non-HTN-diagnosed population level when anti-hypertensive treatment was taken. Individualized and appropriate risk control management should be emphasized to reduce the burden of cardiovascular complications by HTN

In EMS perspective, the use of mechanical chest compression device showed a significant survival benefit when patient transportation interval is prolonged. In systems-of-care perspective, regional CRC system significantly affected the neurologic outcome of patients with OHCA. Establishing an appropriate, optimal patient transport protocol for improving outcome considering EMS performance, prehospital special situations and regional hospital resources is necessary.

Keyword: Out-of-hospital cardiac arrest, prevention, survival

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Chapter 1. Introduction

1.1. Overview of out-of-hospital cardiac arrest

Out-of-hospital cardiac arrest (OHCA) is a leading cause of global mortality. Although regional variation exists, the incidence of OHCA is estimated 40-60 cases per 100 000 of the population [1]. Approximately 350,000 cardiac arrests occur in the United States, 100,000 in Japan and 30,000 in Korea annually and the incidence is increasing [1–3]. Despite the various efforts to increase the survival rate, including emphasizing elements of chain of survival such as immediate bystander cardiopulmonary resuscitation (CPR), development of a public access defibrillation system and post-resuscitation care, OHCA survival is dismal [4,5]. Although some cities have achieved survival of 20-40%, globally, it is estimated that on average, less than 10% of all patients with OHCA survives [1,6]. Only a small fraction of patients are discharged from the hospital with minimal neurologic impairment and consequently, most OHCA victims die or survive with severe disability [2,3,7].

The primary focus of cardiac arrest management is to optimization of all critical steps required to improve outcomes according to chain of survival. A slight loosening of the link critically affects the outcome of OHCA victims. The OHCA is a sudden, unexpected happening with high incidence and poor neurologic intact survival, which makes it a major public health challenge to overcome. Various medical fields, including public health, community, emergency medical service and hospitals are making their at most efforts to solve this problem.

1.2. Cardiovascular risk factors and Out-of-hospital Cardiac Arrest

OHCA shares risk factors with SCD, and thus most previous studies have focused on the risk of SCD. The major risk factors for SCD are established coronary artery disease (CAD) or high risk for CAD, previous myocardial infarction (MI), decreased ejection fraction of the heart, and a history of ventricular arrhythmias [8]. These are potential risk factors that increases the relative risk of SCD, but the contribution of SCA in those with such risk factors to the cumulative rate of SCD is relatively low [9]. Most cases of SCD occur in the general population, typically without a known history of heart disease.

Classic cardiovascular risk factors have been found to be associated with SCD. In around 50% of cases, SCD is the first clinical manifestation of heart disease [10]. Although coronary artery disease (CHD) is the most common underlying cause of SCD, risk factors for CHD such as hypertension, diabetes, and dyslipidemia can be predictive of SCD in both men and women [11].

Diabetes mellitus (DM) is a well-established risk factor of cardiovascular disease including CHD and ischemic stroke [12]. Both macro- and microvascular complications of DM explain the close link between DM and fatal cardiovascular disease. Previous studies reported that DM increased the risk of sudden cardiac arrest, including OHCA. When compared DM group with non-DM group, the odds ratio (OR) for SCD was 1.73 (1.28-2.34) and when compared DM with microvascular complications group with non-DM group, OR increased to 2.66 1.84-3.85) after adjusting potential confounders [13]. In a meta-analysis of comparing DM with non-DM, the risk of SCD was 2.18 (95% CI 1.289-2.52) in overall which did not differ according to the definitions of SCD or DM [14]. The risk of DM depending on the therapeutic methods on OHCA incidence has be reported as well [15]. DM without treatment group was associated with increased risk of OHCA with OR 4.17 (2.91-5.96) and when treated with insulin OR decreased to 2.69 (1.82-3.96) and with oral hypoglycemic agent OR was 1.55 (1.31-1.85), respectively [15].

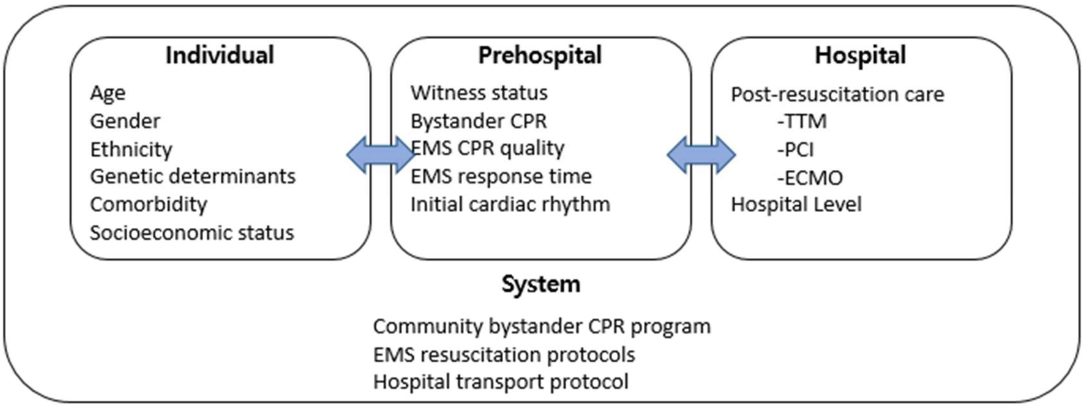
As abnormal lipid profile is a significant risk factor for atherosclerotic disease, studies have been conducted to evaluate its association with OHCA [16–20]. Some of these studies reported of no significant association with serum lipid profile and risk of SCD [16,17]. Other studies showed that serum cholesterol appears to be strongly associated to SCD below age 65, and the total cholesterol (TC)/high density lipoprotein (LDL) ratio predisposes both men and post-menopausal women to acute plaque rupture [18–20]. Some studies have found that not only low high-density lipoprotein (HDL) but also low LDL or triglyceride (TG) may be a risk factor for the occurrence of cardiac arrest [21,22]. This inconsistency of study results are possibly due to different functions of lipids. Hypercholesterolemia is a significant risk factor for atherosclerotic disease, and but also cholesterol is an essential nutrient in the human body that plays a positive role in signal transduction and hormone synthesis. The athero- and cardio-protective effects of high-density lipoprotein (HDL) cholesterol are well known.

Hypertension is the single largest contributor to the global burden of disease, accounting for two-thirds of strokes, half of CHD cases and a total of 9.4 million global deaths per year [23]. Several cohort studies have been published on the association between hypertension and the risk of SCD [24–26]. HTN increased the risk of SCD by 1.46 (1.11-1.93) in post-menopausal women and by 1.52 (1.05-2.19) [24,25] in Asian men. HTN significantly increases the lifetime risk of sudden cardiac arrest/SCD at 30 years of age by 30% and per 20-mmHg increase in systolic blood pressure (BP) was associated with a 28% increased risk of SCD [27,28].

The beneficial effects of blood-pressure lowering treatments on the risks of major cardiovascular events are also well established [29,30]. Compared with those untreated, there was treatment benefit for stroke and for major cardiovascular events [29] and ACE inhibitor and calcium antagonists were the most beneficial blood-lowering agent compared with placebo [30]. Most of these studies evaluating risk of HTN treatment on the risk of OHCA were conducted on population with HTN or with high blood pressure. Currently, there are few studies investigating association between antihypertensive treatment and the risk of OHCA with non-HTN patients as a reference.

1.3 Prehospital high quality cardiopulmonary resuscitation and out-of-hospital cardiac arrest survival

Although prevention is a key strategy in reducing the incidence of OHCA, many events occur among those without clinical heart disease or warning symptoms, making prevention an incomplete strategy to address this public health challenge. Therefore to reduce overall morbidity and mortality after OHCA, scientific advances in providing high quality cardiopulmonary resuscitation (CPR) are essential. But despite the efforts, the survival rate was unchanged over 3 decades [4]. Several studies are pointing to factors that affect the chances of survival with favorable neurologic outcome. Predictors of survival after OHCA can be categorized into patient factors, prehospital and hospital therapeutic factors and system related factors, which mainly indicates coordination and interaction between CPR providers (Figure 1-1).



Figure오류! 여기에 표시할 텍스트에 0을(를) 적용하려면 홈 탭을 사용하세요.**1-1. Predictors of survival after out-of-hospital cardiac arrest**

CPR, cardiopulmonary resuscitation; EMS, emergency medical service; TTM, target temperature management; PCI, percutaneous coronary intervention; ECMO, extracorporeal membrane oxygenation.

The key factor in enhancing survival after occurrence of cardiac arrest is high quality CPR. Quality of CPR is increasingly emphasized to CPR providers, both layperson and EMS providers. Appropriate compression depth, rate and recoil with minimal interruptions during CPR are basic components for high quality CPR [31].Current 2020 Resuscitation guidelines for CPR suggests a compression rate between 100-120/min, a compression depth between 5-6 cm, a complete recoil between compressions and minimizing interruptions. Compliance with these quality measures has been associated with improved survival in cases of OHCA with prolonged time to return of spontaneous circulation (ROSC) [32].

Numerous studies have reported results on prehospital interventions based on randomized controlled and observational studies. To encourage layperson to recognized and initiate CPR, compression to breathing ratio 30:2 has been changed to compression only CPR. Mouth-to-mouth rescue breathing was one of the most known barriers in checking the patient and initiating CPR. Bobrow et al. showed improved survival using compression only CPR compared to traditional CPR [33] and in a study of meta-analysis, compression only CPR increased the survival by risk ratio 1.22 (1.01-1.46) [34].

Various practices, not only adhering to CPR measures, also real-time feed-back device on CPR, team-based training, structured resuscitation choreography and scene leader ship has been emphasized to EMS provider to decrease the variation between providers and increase the survival of OHCA [35,36]. But the most crucial component in providing high quality CPR is that sustaining uniform high quality of chest compression during whole resuscitation period, which is physically demanding. Mechanical chest compression devices automate the process and deliver consistent, high-quality chest compression. However, three large randomized-controlled studies found improved rates of survival at hospital discharge or after 30 days or favorable neurologic outcome [37–39]. These findings led the International Liaison Committee on Resuscitation to no recommend the routine use of mechanical chest compression devices [40]. Despite the absence of benefit, mechanical chest compression device has been considered to use in special situations where patient transport is prolonged or manual chest compression is hazardous. A few animal studies and simulation studies using manikins observed better performance with mechanical chest compression devices use during cardiac arrest transportation [41–43]. Due to differences in EMS system, the effect of mechanical chest compression device while on transportation has been rarely been evaluated. A meta-analysis conducted in 2021 reported that pre-hospital use of mechanical chest compression device showed a positive effect in achieving return of spontaneous circulation (ROSC) and survival to admission [44].

For prehospital interventions, such as advanced airway management and intravenous drug administration, for high quality resuscitation, there are controversies. Observational studies have produced conflicting results when comparing basic (eg, bag-valve-mask) with advanced airways (eg, intubation or supraglottic airways) [45–47]. The training and experience of the provider undertaking airway management would be an important contributing factor [48]. Medication, such as adrenaline, was considered as part of cardiac arrest algorithm since their inception. However, two representative studies found no evidence that drugs improved outcomes [49,50].

1.4 Systems-of-care to enhance OHCA survival

Post-cardiac arrest syndrome, a consequence of whole-body ischemia-perfusion injury with devastating multigrain involvement, is a significant contributor to poor outcomes among OHCA survivors, for which complex multidisciplinary approach is required [51–53]. Post-resuscitation care has been suggested to be fifth link in the chain of survival concepts, and a component of an integrated emergency care network comprising community first responders, EMS, and hospitals aiming to provide quality care to patients with OHCA. It is an urgent question how to best organize hospitals and emergency care systems to improve access to quality care and clinical outcomes [54].

Cardiac arrest centers (CACs) are specialized facilities that provide comprehensive, evidence-based post-cardiac arrest care, including emergency cardiac catheterization, target temperature management, hemodynamic support, and neurologic expertise [55]. CACs may also have protocols and quality improvement programs to ensure guideline-compliant care. Although the evidence of CACs are mostly observational studies and their results are non-consistent [56–58], recent guidelines from the International Liaison Committee on Resuscitation recommend with low certainty that patients with OHCA should be transported to CACs [55]. Especially for those with initially shockable rhythm and did not achieve ROSC at field, the treatment effect of CAC showed to be significantly better [59]. Patients may be transported directly to CAC by EMS either during CPR or after ROSC, or they could be transferred from another hospital to a CAC after ROSC. There are only two studies evaluating outcomes for patients directly transported to a CAC versus transferred to a CAC from another hospital and both reported that there were no significant differences in survival or neurologic outcomes [57,60]. Currently, the evidence of official criteria for designation of CAC is lacking. The American Heart Association proposed two levels of cardiac arrest centers and suggested the criteria for each level of CACs [61]. Arizona implemented a statewide system of cardiac receiving centers and resulted in the improvement of survival of OHCA patients [62].

Evidences of CACs and their use in communities are currently lacking. On the other hands, not all hospitals have same level of resources and infrastructures. In terms of efficient use of limited resources, appropriate transport protocol established appropriate for their own community is important.

1.4. Purpose of this study

From this study, I focused on how to decrease the burden of OHCA in three perspectives, individual, prehospital and systems-of-care, from prevention and survival based on chain of survival. Multifaceted efforts, through communities to hospitals, for enhancing OHCA survival outcomes are essential.

The first goal of this study was to estimate the effect of hypertension and treatment on incidence of EMS-assessed OHCA in Korea. It focused not only hypertension diagnosis but also on the effect of antihypertension medication on incidence of OHCA. The second goal of this study was to estimate the effect of mechanical chest compression device during transportation of patients with OHCA according to patient transport interval. Although mechanical chest compression device itself did not show significant survival benefit compared with manual compression, in an EMS system where termination of resuscitation is limited, CPR quality at moving ambulance may affect the survival. I thought mechanical chest compression device could be effective in prolonged transportation of patients with OHCA. The third goal of this study was to designate cardiac arrest centers according to the result of hospital assessment survey at whole province and evaluate the outcome of patients with OHCA who are transported to cardiac arrest centers compared with non-cardiac arrest centers. OHCA receiving hospitals in Gyeonggi-province were categorized by hospital resources and evaluated the neurologic outcome between the groups. A comprehensive approach to enhance the survival of OHCA might lead to evidence-based strengthening of the chain of survival.

Chapter 2. Method

This study used multicenter OHCA database, Korea Cardiac Arrest Research Consortium (KoCARC), for the first and second subtitles. Community Health Survey was used as controls for the first subtitle. For the third subtitle, provincial survey data on hospital resources conducted by Gyoneggi Emergency Support Center and population-based EMS-assessed OHCA database from the Korean Centers for Disease Control and Prevention (KCDC) was used after their approval. This study was approved by the Institutional Board of Review at Korea University Ansan Hospital.

2.1. Data Source

The KoCARC is a multicenter collaborative research network of hospitals and was established to evaluate the missing links and provide evidence to strengthen then chain of survival [63]. The KoCARC database enrolls patient with OHCA transported to the emergency department (ED) by EMS with resuscitation efforts (EMS-treated OHCA) and patients with presumed cardiac etiology identified by emergency physicians in each ED. The registry excludes OHCA patients with a terminal illness documented by medical records, patients under hospice care, pregnant patients, and patients with a previously documented ‘Do No Resuscitate’ record. OHCA of definite non-medical etiology, including trauma, drowning, poisoning, burn, asphyxia, or hanging, were also excluded. The KoCARC registry collects data of OHCA patients’ epidemiologic data, such as demographic information, health behavior, medical history, cardiac arrest data such as community, EMS and ED resuscitation information and outcome data of survival to discharge and neurologic status at hospital discharge using cerebral performance category (CPC) based on Utstein template [64]. Epidemiologic, community and EMS information is collected by interviewing family members and ambulance crews. Information not obtained via interview is collected from the Emergency Medical Service run sheet provided through Fire Department web site. Research coordinators at each participating ED gather laboratory test, cardiac intervention results and hospital outcome via medical record view. They also ensure the accuracy of the data and enters it into a web-based electronic database registry. Currently, a total of 32 hospitals are collecting and entering the data.

Community-based controls were identified based on data from the Community Health Survey (CHS) conducted by the KCDC. 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. Tong Ban/Lee is defined as the primary sampling unit of housing types in Dong/Eup Myeon through probability proportionate sampling. After the number of households in the sampling point of Tong Ban/Lee was counted and the household list was completed, the survey households are sampled by systematic sampling. In the sampling point, five households on average were selected as samples, and all household members aged $\geq$ 19 years in the sample household are interviewed. According to the stratification of the surveyed population, which shows the characteristics of the surveyed contents, the first stratum is Dong/Eun Myeon where 253 community health centers are located across the country. Responders are members of representatively selected households from 253 communities. The survey assesses sociodemographic information of responders, vaccination status, contraction of disease, medical care utilizations, accidents experience, addition status, and quality of life. An average of 920 individuals from each local community participates the survey and all surveys were conducted by trained surveyors.

For the third subtitle, Hospital Assessment Survey and national OHCA database was used. Hospital Assessment Survey was conducted through Gyeonggi Emergency Medical Support Center which is a regional center under the National Emergency Medical Center. It was a spot survey collecting data on the availability of resources, number of personnel, and physical infrastructures of each emergency medical center in the Gyeonggi province performed at 2015. The survey was conducted primarily via the National Emergency Department Information System (NEDIS) and additively by email to all EDs that provided care to at least on OHCA patients between 2013 and 2014. The result of the survey was used to categorize the EDs into cardiac resuscitation center.

The data of OHCA patients transported to hospitals in Gyeonggi province was collected using the nationwide OHCA registry database (2013-2014) in Korea. The nationwide OHCA registry database captures all incidence cases of OHCA in the country using the EMS run sheet for basic ambulance operation information. The Korean OHCA registry is retrieved from the following four sources: the EMS run sheet, the in-depth EMS CPR registry, the dispatcher CPR registry, and the hospital medical review registry. All EMS registries for each patient are linked, using ambulance dispatch numbers in the national fire departments' electronic database server and are integrated as a single episode. Hospital care data and survival outcomes are collected via trained medical reviewers from the KCDC. They visit all the hospital where patients are transported and review the medical record to complete the information related to the risks and outcomes based on Utstein guidelines for reporting cardiac arrest and resuscitation data. Ultimately, The Korean OHCA registry contains demographic finding, cardiac arrest situation, community and EMS resuscitation, and hospital care information of Korean population. To ensure the quality of the medical record review process, a quality management committee of emergency physicians, epidemiologists, statistical experts, and medical record review experts analyse the data every month while providing feedback to each medical record reviewer. For this study, the neurologic outcome according to the categorization of cardiac arrest center was analyzed.

2.2. Study Setting

2.2.1 Community

Korea is comprised of 248 counties, the boundaries of which are defined by statute for geographical administrative purposes. The incidence of OHCA per 100,000 patients increased steadily from 48.2 in 2008 to 53.8 in 2011 and 66.7 in 2017.

An education and training program for bystander CPR was started by several organizations, including hospitals, fire departments, and non-governmental organizations, in the early 2000s. Annually 600,000-700,000 bystanders participate in this education program according to the annual report of the National Emergency Medical Center. Contents on public access defibrillation is immersed in bystander CPR training program, which started in early 2010s. Currently, 50,429 AEDs are disseminated in whole country; however, one third are located in community health centers. Therefore, most defibrillators are performed by the ambulance crew during the prehospital resuscitation.

Gyeonggi province has an area of 10,175 km^2, which is seventeen times larger than the Seoul Metropolitan area and nine times larger than Hong Kong. It occupies 10.1% of the national territory and is the 5th largest province in Korea. The population in Gyeonggi almost reached a total of 12.5 million, which is almost a quarter of the total Korean population.

2.2.2 Emergency Medical Service

The Korean EMS is a government-based system managed and operated by 17 provincial headquarters of the fire department. Korea started providing a multi-tier dispatch system in 2016 when severely ill patients, including patients with OHCA or severe trauma, were recognized by the dispatch center. EMS providers are composed of level 1 or level 2 emergency medical technicians (EMTs), where level 1 is comparable to EMT intermediate and level 2 to EMT basic in the United States, respectively. Ambulance EMT teams are composed of three members in most metropolitan provinces and two members in most rural areas with at least one level 1 EMT in an ambulance. EMS providers provide CPR at the scene and during transport according to the EMS CPR protocol based on the 2015 American Heart Association (AHA) guidelines. They can perform intravenous fluid administration and apply advanced airway management techniques such as supraglottic airway or endotracheal intubation under direct medical guidance by a physician.[19] All EMS-assessed patients were transported to hospitals. Notably, ambulances in Korea have been equipped with a mechanical compression device (MCPRD) since 2014. Each fire station provides its own educational program for the use of MCPRD; additionally, ambulance crews are allowed to apply MCPRD without medical direction in case of transporting patients with cardiac arrest. Generally, after 5 min of CPR at the scene, EMS providers attach MCPRD and transport patients with OHCA to hospitals. After ED arrival, the patients are provided with CPR based on the recommendations of the 2015 AHA guidelines for advanced cardiovascular life support.

2.2.3 Hospital

All EDs are formally designated as levels 1-3 by the government. Currently, there are 38 regional medical centers, designated as level 1, 129 local medical centers, which designated as level 2, and 236 local small EDs, which were designated as level 3. The designation is based on human resources, essential instruments and equipments, and service levels, such as the availability of certain specialists. Remoted rural areas and isolated islands usually have no designated ED; therefore, most patients with OHCA are transported to the nearest non-emergency hospitals (level 4, non-ED facilities).

2.3. Study population and data collection

The eligible patients were patients with OHCA presumed of cardiac etiology with a final outcome on record during each study period for each subtitles. The collected information included age; gender; medical history of hypertension and diabetes; smoking and alcohol habit; arrest place; initial recorded ECG, such as ventricular fibrillation, pulseless ventricular tachycardia, pulseless electrical activity and asystole; witnessed status; provision of bystander CPR; response interval (time from call to ambulance arrival at the scene); scene resuscitation interval; patient transport interval; prehospital defibrillation; prehospital EMS intervention, such as advanced airway or intravenous fluid; hospital interventions, such as target temperature manage (TTM) or percutaneous coronary intervention (PCI). Outcome variables were collected whether prehospital return of spontaneous circulation (ROSC) was achieved, survival to admission, survival to discharge was abled. For those survival to discharge patients, neurologic performance was collected also according to cerebral performance category (CPC) score. CPC 1 is defined when conscious and alert, able to work with normal neurological function. CPC 2 is defined when discharge with moderate cerebral disability; able to function for independent activities of daily life and work in sheltered environment.

Community based controls for the first subtitle were selected from the Korean Community Health Survey (CHS) from 2015-2017. Information of gender, age, hypertension, diabetes, smoking and alcohol habit were collected from the CHS and were matched by 1:2 according to age, gender and county of resident.

Chapter 3. Risk of hypertension and treatment on out-of-hospital cardiac arrest incidence: A case-control study

3.1. Introduction

Out-of-hospital cardiac arrest (OHCA) is a global health burden [1,65]. In Korea, the OHCA incidence rate is 46.8 per 100,000 person-years for emergency medical service (EMS)-assessed OHCAs, and the survival rate is 3.6% [2]. Despite the development of various strategies in prehospital cardiopulmonary resuscitation (CPR) and post-resuscitation care, the survival rate remains low, and patients still experience severe neurologic deficits [2,66]. Therefore not only establishing optimal strategies after the event occurs but also 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.

The major risk factors for OHCA are established coronary artery disease (CAD) or high risk for CAD, and for prevention strategies, easily identifiable classic cardiovascular risk factors are an appropriate target. Several risk factors such as older age, male sex, cigarette smoking, hypertension, hypercholesterolemia and obesity has been associated with an increased risk of sudden cardiac death. In the means of prevention, not only health behavior change, such as cessation of cigarette, maintaining physical activity and avoiding obesity, but also pharmacological prevention through medications is considered. Moreover, the prevention would be more effective if the target disease is of highly prevalent, high risk factor, such as diabetes or hypertension.

As for diabetes, Ro et al. reported that diabetes increased the risk of OHCA highest in non-pharmacotherapy group and the risk decreased in magnitude with pharmacotherapy [15]. Hypertension is also highly prevalent with known high risk factor for CVD. In 2010, the global age-standardized prevalence of HTN was 31.1%, and in in Korea, the prevalence of HTN was 29.1[67]. HTN significantly increases the lifetime risk of sudden cardiac arrest/SCD at 30 years of age by 30% [27] and per 20-mmHg increase in systolic blood pressure (BP) was associated with a 28% increased risk of SCD [28].

Up to now, there are studies evaluating high blood pressure and CVD risk but association of HTN treatment and OHCA is not yet completed evaluated. 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.

3.2. Methods

3.2.1 Study population

Cases were defined as OHCA patients aged 19–80 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 ratios with age by 5 years, gender, and county of residence.

3.2.2 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 this study we defined ‘HTN treatment’ only to taking medication in both cases and controls.

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.

3.2.3 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=1,745) and alcohol consumption (N=3,136).

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, USA).

3.2.4 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.

3.3. Results

3.3.1 Demographic findings

Among 4,274 EMS-treated OHCA patients during the study period, 3,653 were assigned to a case group after excluding pediatric patients (N=117) and patients with unknown information about HTN (N=504). For the community control group, 5,266 participants were selected within strata from the 2015–2017 Korean CHS database with a case-to-control ratio of 1:2. A total of 7,899 case-control matched sets were analyzed in the study (Figure 3-1).

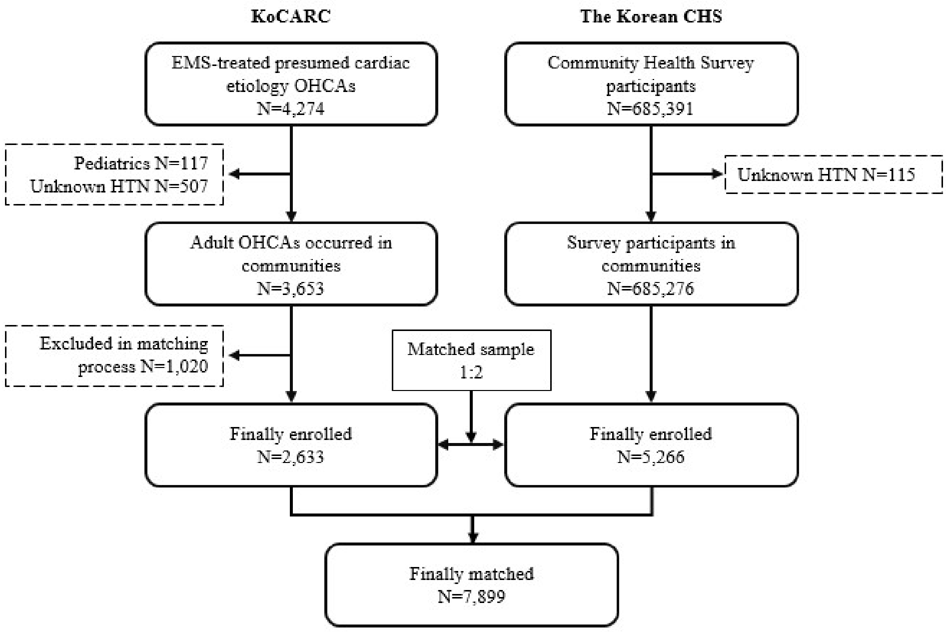


Figure 3-1. Eligible study population flow

KoCARC, Korean Cardiac Arrest Research Consortium; CHS, community health survey; EMS, emergency medical service; OHCA, out-of-hospital cardiac arrest; HTN, hypertension;

The characteristics of OHCA cases and community controls of the original and imputed datasets are shown in Table 1 and supplement Table 1. Among 2,633 EMS-treated OHCA patients with presumed cardiac etiology, 1,174 (44.7%) were diagnosed with HTN, and among them, 297 (11.3%) patients did not receive medical treatment. Among 5,266 community controls, 2,049 (38.9%) were diagnosed with HTN, and 158 participants (3.0%) did not receive medical treatment. DM was diagnosed3 in 28.7% of OHCA cases and 17.4% of community controls (Table 3-1).

Table 3-1. Characteristics of out-of-hospital cardiac arrest cases and community controls

Characteristics	Total		OHCA cases		Community controls	
	N	%	N	%	N	%
Total	7,899	100	2,633	100	5,266	100
Gender						
Female	2,307	29.2	769	29.2	1,538	29.2
Male	5,592	70.8	1,864	70.8	3,728	70.8
Age, years						
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	1,509	19.1	503	19.1	1,006	19.1
60–69	1,908	24.2	636	24.2	1,272	24.2
70–80	3,039	38.5	1,013	38.5	2,026	38.5
Median (IQR)	65	(53–73)	65	(54–74)	64	(53–73)
Past Medical History						
Hypertension						
No HTN	4,674	59.2	1,457	55.3	3,217	61.1
HTN without treatment	455	5.8	297	11.3	158	3.0
HTN with treatment	2,770	35.1	879	33.4	1891	35.9
Diabetes Mellitus						
No DM	6,225	78.8	1,877	71.3	4,348	82.6
DM without treatment	305	3.9	210	8.0	95	1.8
DM with treatment	1,369	17.3	546	20.7	823	15.6
Health Behaviors						
Smoking						
Current smoker	1,781	22.6	655	24.9	1,126	21.4
Ex-smoker	2,419	30.6	650	24.7	1,769	33.6
Never smoker	3,699	46.8	1,328	50.4	2,371	45.0
Alcohol consumption						
Frequent	2,564	32.5	727	27.6	1,837	34.9
Occasional	2,043	25.9	653	24.8	1,390	26.4

Characteristics	Total		OHCA cases		Community controls	
	N	%	N	%	N	%
Total	7,899	100	2,633	100	5,266	100
Alcohol consumption						
Frequent	2,564	32.5	727	27.6	1,837	34.9
Occasional	2,043	25.9	653	24.8	1,390	26.4
Never	3,292	41.7	1,253	47.6	2,039	38.7

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

The demographics according to antihypertensive treatment are reported in Table 3-2. Among HTN patients, those without medical treatment were more likely to be younger, have diabetes but don't receive treatment, to be current smokers and more frequent alcohol drinkers. Among all case and control subjects, those without HTN tends to be younger, don't have diabetes, to be current smokers and frequent alcohol drinkers compare with HTN patients.

Table 3-2. 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	
	N	%	N	%	N	%	N	%
Total	7,899	100	4,674	100	455	100	2,770	100
Case/Control								
OHCA cases	2,633	33.3	1,457	31.2	297	65.3	879	31.7
Community controls	5,266	66.7	3,217	68.8	158	34.7	1,891	68.3
Gender								
Female	2,307	29.2	1,331	28.5	118	25.9	858	31.0
Male	5,592	70.8	3,343	71.5	337	74.1	1,912	69.0
Age, years								
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	1,509	19.1	1,048	22.4	91	20.0	370	13.4
60-69	1,908	24.2	1,058	22.6	115	25.3	735	26.5
70-80	2,812	35.6	1,226	26.2	163	35.8	1,423	51.4
Median (IQR)	65	(53–73)	60	(49–71)	66	(56–75)	70	(62–75)
Past Medical History								
Diabetes Mellitus								

Characteristics	Total		No HTN		HTN without treatment		HTN with treatment	
	N	%	N	%	N	%	N	%
Total	7,899	100	4,674	100	455	100	2,770	100
No DM	6,225	78.8	4,082	87.3	309	67.9	1,834	66.2
DM without treatment	305	3.9	116	2.5	123	27.0	66	2.4
DM with treatment	1,369	17.3	476	10.2	23	5.1	870	31.4
Health Behaviors								
Smoking								
Current smoker	1,778	22.5	1,183	25.3	107	23.5	488	17.6
Ex-smoker	2,419	30.6	1,329	28.4	131	28.8	959	34.6
Never smoker	3,702	46.9	2,162	46.3	217	47.7	1,323	47.8
Alcohol consumption								
Frequent	2,595	32.9	1,611	34.5	171	37.6	813	29.4
Occasional	2,050	26.0	1,248	26.7	107	23.5	695	25.1
Never	3,254	41.2	1,815	38.8	177	38.9	1,262	45.6

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

3.3.2 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 3-3. 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 3-4. 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]).

Table 3-3. 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	1,457	3,217	1.00	1.00
Yes	1,176	2,049	1.31 (1.18–1.45)	1.19 (1.07–1.32)
Model 2: HTN treatment				
No HTN	1,457	3,217	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	1,891	1.04 (0.93–1.16)	0.96 (0.86–1.08)

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

Adjusted for age, diabetes, smoking habit, alcohol consumption

Table 3-4. Multivariable conditional logistic regression of out-of-hospital cardiac arrest risk by hypertension and treatment in patients with diabetes

	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)

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

Adjusted for age, smoking habit, alcohol consumption

3.4. 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 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 [26,27]. 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 [68,69]. However, the association between antihypertensive treatment and SCD is not completely known [70]. 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 community health surveys, with antihypertensive 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]) (Supplement Table 2). 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 2,000 OHCA cases were enrolled [70].

HTN is a highly prevalent risk factor, and lifestyle affects the incidence and management of HTN. For example, high sodium intake [71,72], heavy alcohol consumption [73,74], lack of physical activity [75,76], and obesity [77] 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 [78], 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 cardiovascular disease, including coronary heart disease, heart failure, and arrhythmia, was not collected in our registry. A history of different cardiovascular diseases 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, information from cases are mostly from families or guardians of the patients whereas in controls mostly are from control themselves and this measurement difference could have resulted in information bias. There are reports that agreement percentage between OHCA victims and their spouses are similar to controls and their spouse[79,80], but since this study is a retrospective study, interviewing control's family was not available. Seventh, total OHCAs by reference region (sigungu) captured by National OHCA database and KoCARC cases by reference region were compared and was relatively low. This would affect the comparability of case and controls and the result should be cautiously interpreted. Lastly, multiple imputations were applied to process missing covariables. These factors might not have been fully adjusted. Finally, this study enrolled cases and controls aged 19–80 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.

3.5. Conclusion

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.

Chapter 4. Effect of mechanical chest compression device on survival after out-of-hospital cardiac arrest according to patient transport interval: A multicenter observational study

4.1. Introduction

Out-of-hospital cardiac arrest (OHCA) is a major public health issue, with an average global incidence among adults of 55 OHCAs per 1 00,000 person-years [1]. Despite efforts to improve OHCA survival, the survival rate has not improved much over several decades [4].

Providing high-quality chest compression during cardiopulmonary resuscitation (CPR) is crucial for improving the survival of patients with OHCA. However, it is well known that effective on-going manual chest compressions, especially at the moving ambulance, are a challenge for CPR provider due to fatigue, incorrect achievement of depth, rate and recoil of the chest [81,82].

A mechanical chest compression device (MCPRD) is a reasonable alternative to maintain chest compression quality in special situations where prolonged resuscitation or ambulance transport is required [31]. MCPRD could provide consistent standard compression in terms of compression rate and depth, set hands of EMS providers free and allow them to focus on other tasks of patient care. However, the effect of mechanical CPR devices on the clinical outcomes of OHCA remains controversial and lacks evidence regarding the benefits of mechanical CPR for OHCA patients compared to manual CPR [83–86] Zhu et al. conducted a meta-analysis in 2019, including nine randomized controlled trials (RCTs) and six non-RTCs, and found no significant differences in the resuscitative effects between mechanical and manual CPR in OHCA patients [83]. Similar result was found in Liu et al. in 2019 comparing manual CPR and mechanical CPR with the Lund University Cardiac Assist System (LUCAS) device [86]. Previous meta-analyses pooled the studies with "in-hospital" and "pre-hospital" use of mechanical CPR devices. Also due to differences in EMS system, the effect of mechanical CPR device while on transporting patient has been rarely evaluated. Recently, increasing evidence including cohort and RCTs has shown the benefit of prehospital use of mechanical CPR devices [44,87,88]. Chen et al. conducted a meta-analysis in 2022 to investigate the benefit of mechanical CPR device and reported that pre-hospital use of mechanical CPR device showed a positive effect in achieving return of spontaneous circulation (ROSC) and survival to admission [89]. A few animal studies and simulation studies using manikins found better performance with MCPRD use in cardiac arrest during transportation [41–43]

In an EMS system where field termination is limited and most of EMS-treated patients are transported to hospitals, strategies to provide high-quality CPR at moving ambulance needs to be established. Whereas most previous studies investigated MCPRD use for OHCAs at field or in-hospital cardiac arrests, relatively few papers have examined the use of MCPRD in OHCA patients with prolonged transport to the hospital.

The hypothesis of this study is that the MCPRD use on patient transport to hospital had an interactive effect on survival after OHCA according to the patient transport interval. Specifically, this study hypothesized that MCPRD use on long patient transport interval (PTI) would be beneficial compared to manual CPR.

4.2. Method

4.2.1 Study population

All EMS-treated patients with OHCA aged ≥18 years with presumed cardiac etiology transported to KoCARC-participating EDs from July 2015 to December 2019 were eligible for this study. Patients who achieved ROSC at the scene and those without information on MCPRD and patient transport interval were excluded.

4.2.2 Measurement

The main exposure of interest was the application of MCPRD to patients with OHCA when transporting patients to EDs. MCPRD was considered to be used if there was information on the use of MCPRD in medical records. PTI was defined as the time interval from the departure of EMS from the scene to arrival at the ED. PTI was categorized into three groups: short PTI for 0–5 minutes, intermediate for 6–10 minutes, and long PTI for 11 min and longer.[90]

We collected data on the following demographic and prehospital factors based on Utstein variables: age, sex, witnessed status, witnessed by public, bystander CPR, arrest location (public or other), initial electrocardiography rhythm (shockable vs. non-shockable), prehospital advanced airway, prehospital EMS defibrillation, prehospital MCPRD appliance, EMS response time interval and field resuscitation time interval.. The medical history of hypertension and diabetes mellitus of the patient was collected by interviewing the patient's family or guardian on arrival at the ED.

The primary outcome was survival to admission. In this analysis, we attempted to determine the effect of MCPRD according to patient transport interval (PTI) and assess whether differences in post-resuscitation care would affect the acute effect of MCPRD.[85] Information on survival to admission was collected via a review of medical records. The secondary outcome was hospital-sustained ROSC and tertiary outcome was survival to discharge. For survival to discharge, the effect of MCPD was evaluated between short, intermediate PTI and long PTI.

4.2.3 Statistical analysis

The study population was categorized according to PTI: short (0–5 min), intermediate (6–10 min), and long (≥10 min).[21] Demographic findings, prehospital factors, and outcomes were compared based on MCPRD use for each PTI category. Continuous variables were compared using the Kruskal-Wallis test, and categorical variables were compared using the chi-square test.

Multivariable logistic regression was conducted to analyze the effect of MCPRD compared with that of manual CPR on outcomes and to calculate adjusted odds ratios (AORs) with 95% confidence intervals (CIs) after adjusting for the following potential confounders: age, sex, medical history of hypertension, diabetes mellitus, initial ECG, witness status, public witnessed, provision of bystander CPR, place of arrest, provision of advanced airways, prehospital EMS defibrillation, EMS response time interval, and scene resuscitation time interval. No collinearity was found between the co-variables in our model.

Interaction of PTI on the effect of MCPRD use on outcomes were tested to compare the effect size of MCPRD, adjusting for the same co-variables. If PTI and MCPRD use have an interactive effect, the AOR of MCPRD on outcomes would be different depending on PTI.

To control for selection bias and confounding factors, two strategies of propensity score matching method were performed; Optimal matching and Greedy nearest matching. Optimal matching selects all controls units that match each treated unit by minimizing the total absolute difference in propensity score across all matches. Greedy nearest neighbor matching selects the control unit nearest to each treated unit. Optimal matching selects all matches simultaneously and Greedy nearest neighbor matching is done sequentially for treated units. The propensity score for each patient to receive MCPRD was estimated using a multivariable logistic regression model. The model included only pre-MCPRD variables; age, sex, hypertension, diabetes, witness status, public witnessed, provision of bystander CPR, arrest place, initial ECG rhythm, EMS defibrillation, EMS response time and scene resuscitation time. To reduce the standard error of MCPRD on outcomes, a two-to-one propensity score-matched cohort was extracted. The analysis was performed using SAS software (SAS Institute, Cary, NC, USA), version 9.4 for Windows.

4.2.4 Ethics Statement

The study complies with the Declaration of Helsinki and the study protocol was approved by all Institutional Review Boards (IRBs) of 32 participating hospitals. The IRBs of all participating institutions waived the requirement for informed consent. No funding was used to support this work. The IRB No. for Korea University Ansan Hospital is 2021AS0146.

4.3. Results

4.3.1 Characteristics of the study population in an unmatched cohort and Propensity matched cohort

Among 9,861 patients with OHCA enrolled in the KoCARC registry during the study period, after excluding pediatric patients (n=232), those who achieved prehospital ROSC (n=1,281), those without information on MCPRD (n=1,364), those without information on PTI (n=3,442), and those with PTI over 30 min (n=12), a total of 3,530 patients were eligible for the study (Figure 4-1).

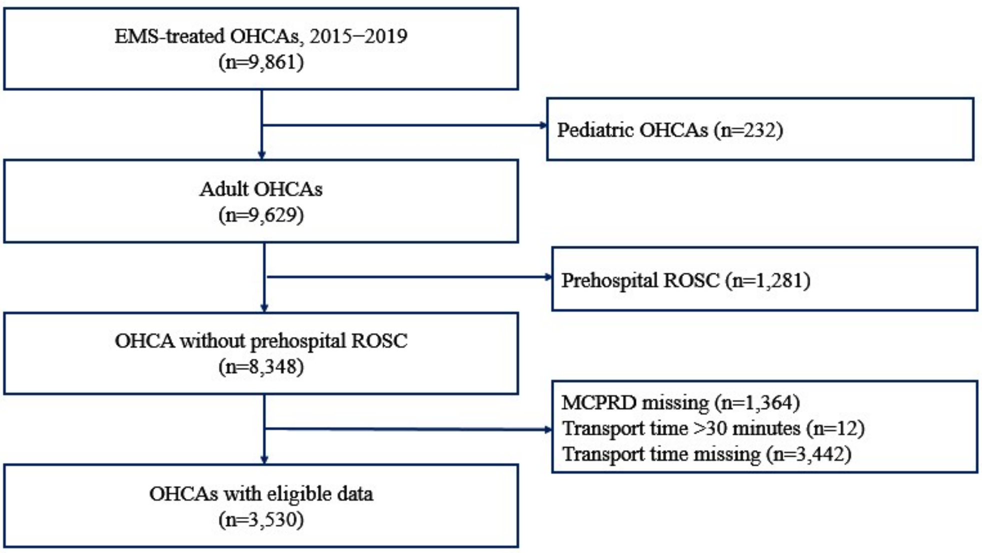


Figure 4-1. Flow chart of eligible OHCAs for analysis

EMS, emergency medical service; OHCAs, out-of-hospital cardiac arrests; ROSC, return of spontaneous circulation; MCPRD, mechanical chest compression device.

Demographic findings of study population in unmatched and propensity score matched cohorts are shown in Table 1. MCPRD was applied to 683 (19.3%) patients with OHCA during transport. The OHCA patients who were treated with MCPRD were less likely in the presence of witness, suffered OHCA in non-private places, more placed with prehospital advanced airway and more likely to be provided with bystander CPR. The rate of survival to admission and hospital ROSC was similar in both groups.

For propensity score (PS) matching, two types of matching methods was performed; Optimal matching and Greedy matching. After 1:2 PS matching, total 1,366 patients from manual CPR group and 683 patients from MCPRD group were extracted to each matched cohorts. Distribution of standardized mean differences between matched observations from each PS matched cohorts are shown in Figure 2 and 3. In Optimal PS matched cohort, survival to admission was 15.3% in manual CPR group and 18.5% in MCPRD group and in Greedy PS matched cohort, 14.6% in manual CPR group and 18.5% in MRPCD group (Table 4-1).

Table 4-1. Characteristics of the study population by transport time interval according to the mechanical compression device

	Unmatched cohort						Optimal PS matched cohort						Greedy PS matched cohort					
	Total		Manual		MCPRD		Total		Manual		MCPRD		Total		Manual		MCPRD	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
All	3,530	100.0	2,847	100.0	683	100.0	2,049	100.0	1,366	100.0	683	100.0	2,049	100.0	1,366	100.0	683	100.0
Sex																		
Male	2,256	63.9	1,801	63.3	455	66.6	1,365	66.6	910	66.6	455	66.6	1,365	66.7	910	66.7	455	66.6
Age, yrs.																		
Median(IQR)	73	60-81	73	59-81	75	61-82	74	61-81	74	60-81	75	61-82	75	61-81	74	60-81	75	61-82
18≤age<30	61	1.7	55	1.9	6	0.9	15	0.7	9	0.7	6	0.9	16	0.8	10	0.7	6	0.9
30≤age<40	96	2.7	73	2.6	23	3.4	71	3.5	48	3.5	23	3.4	69	3.4	46	3.4	23	3.4
30≤age<40	262	7.4	217	7.6	45	6.6	150	7.3	105	7.7	45	6.6	152	7.4	107	7.8	45	6.6
40≤age<50	459	13.0	379	13.3	80	11.7	245	12.0	165	12.1	80	11.7	244	11.9	164	12.0	80	11.7
50≤age<60	596	16.9	495	17.4	101	14.8	299	14.6	198	14.5	101	14.8	297	14.5	196	14.4	101	14.8
60≤age<70	1,031	29.2	828	29.1	203	29.7	616	30.1	413	30.2	203	29.7	619	30.2	416	30.5	203	29.7
70≤age<80	1,025	29.0	800	28.1	225	32.9	653	31.9	428	31.3	225	32.9	652	31.8	427	31.3	225	32.9
age≥80	61	1.7	55	1.9	6	0.9	15	0.7	9	0.7	6	0.9	16	0.8	10	0.7	6	0.9
Comorbidities																		
Hypertension	1,443	40.9	1,147	40.3	296	43.3	882	43.1	586	42.9	296	43.3	878	42.9	582	42.6	296	43.3
Diabetes	956	27.1	766	26.9	190	27.8	575	28.1	385	28.2	190	27.8	573	28.0	383	28.0	190	27.8
Witnessed	1,950	55.2	1,615	56.7	335	49.1	1,015	49.5	680	49.8	335	49.1	1,017	49.6	682	49.9	335	49.1

	Unmatched cohort						Optimal PS matched cohort						Greedy PS matched cohort					
	Total		Manual		MCPRD		Total		Manual		MCPRD		Total		Manual		MCPRD	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Public Witnessed	3105	88.0	2444	85.8	661	96.8	1,973	96.3	1312	96.1	661	96.8	1,974	96.3	1313	96.1	661	96.8
Bystander CPR	1,852	52.5	1,429	50.2	423	61.9	1,266	61.8	843	61.7	423	61.9	1,265	61.7	842	61.6	423	61.9
Arrest place																		
Public	652	18.5	548	19.3	104	15.2	297	14.5	193	14.1	104	15.2	298	14.5	194	14.2	104	15.2
Initial ECG																		
Shockable	406	11.5	328	11.5	78	11.4	234	11.4	156	11.4	78	11.4	233	11.4	155	11.4	78	11.4
Prehospital advanced airway																		
Yes	2,604	73.8	1,978	69.5	626	91.7	1,882	91.9	1,256	92.0	626	91.7	1,882	91.9	1,256	92.0	626	91.7
EMS defibrillation	604	17.1	492	17.3	112	16.4	327	16.0	215	15.7	112	16.4	328	16.0	216	15.8	112	16.4
EMS response time, median (IQR), mins.	7	5-9	7	5-10	6	5-9	7	5-9	7	5-9	6	5-9	7	5-9	7	5-9	6	5-9
Scene time, median (IQR), mins.	13	9-18	12	8-17	15	12-19	14	11-19	14	11-20	15	12-19	15	11-19	14	11-20	115	12-19

	Unmatched cohort						Optimal PS matched cohort						Greedy PS matched cohort					
	Total		Manual		MCPRD		Total		Manual		MCPRD		Total		Manual		MCPRD	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Survival to admission	656	18.6	530	18.6	126	18.5	335	16.4	209	15.3	126	18.5	325	15.9	199	14.6	126	18.5
Hospital ROSC	966	27.4	767	26.9	199	29.1	522	25.5	323	23.7	199	29.1	509	24.8	310	22.7	199	29.1

IQR: interquartile range; yrs: years; PTI: patient transport interval; CPR: cardiopulmonary resuscitation; ECG: electrocardiography; EMS: emergency medical service.
[a]$P<0.01$; [b]$P<0.05$.

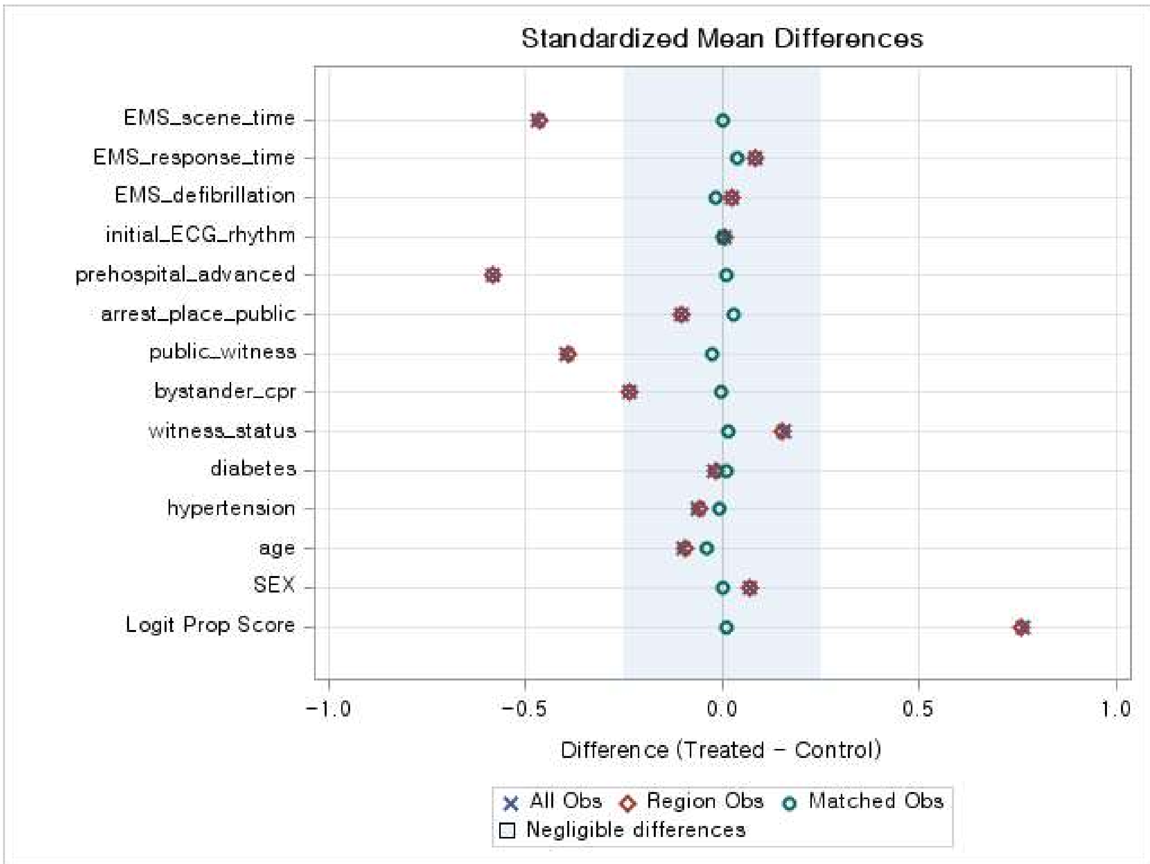


Figure 4-2. Distribution of standardized mean differences between Optimal matched observations.

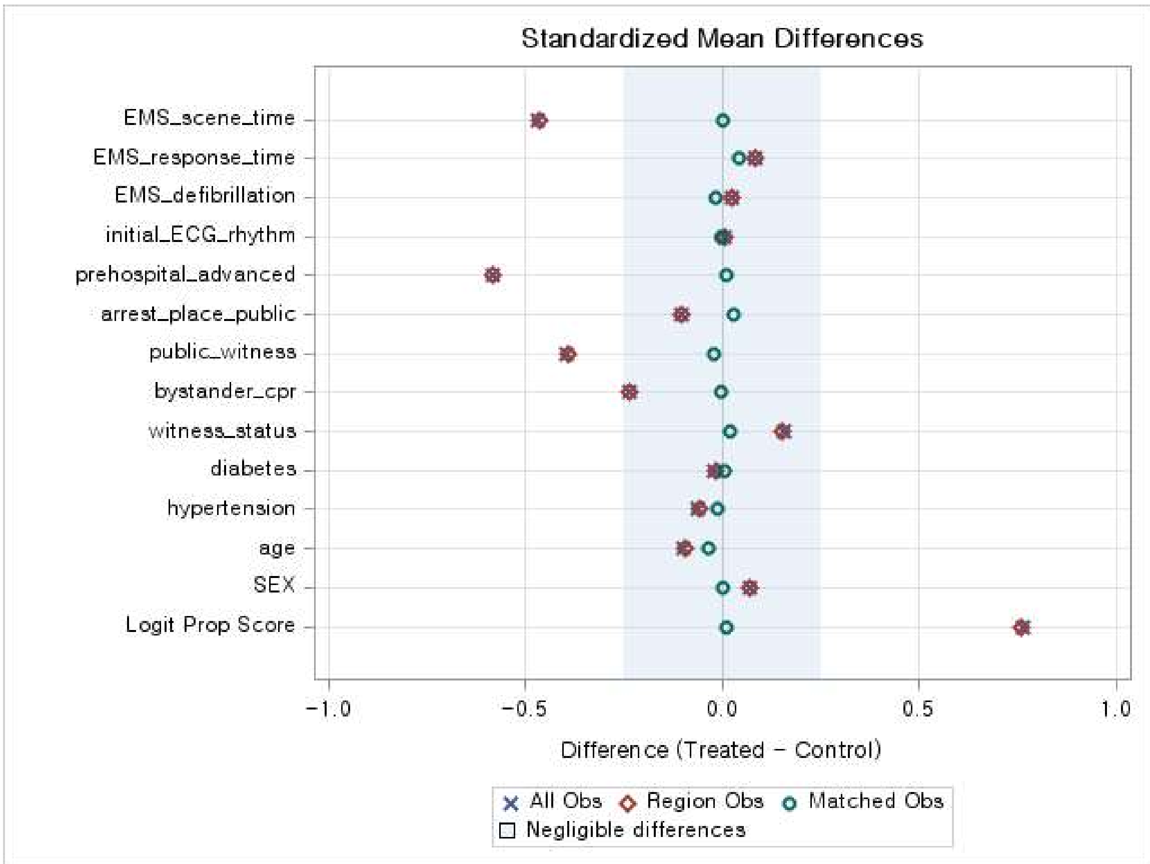


Figure 4-3. Distribution of standardized mean differences between Greedy matched observations

The outcomes of subgroups by PTI from unmatched cohort are shown in Table 4-2. In short PTI, survival to admission was 23.0% in manual CPR group and 12.2% in MCPRD group. When PTI was intermediate or long, survival to admission rate was similar or higher in MCPRD group.

The outcomes of subgroups by PTI from PS matched cohorts are shown in Table 4-3. In optimal PS matched cohort when PTI was short, survival to admission was 20.5% in manual CPR group and 12.2% in MCPRD group, whereas in intermediate PTI and long PTI subgroups, the outcome was higher in MCPRD group (Intermediate PTI, Manual CPR vs MCPRD, 16.3% vs 18.8%; Long PTI, Manual CPR vs MCPRD, 12.5% vs 19.7%). In Greedy PS matched cohort, the result was similar with Optimal matched cohort that in short PTI, the survival to admission was higher in manual CPR group (Short PTI, Manual CPR vs MCPRD, 19.6% vs 12.2%), whereas in intermediate and long PTI subgroups, the outcomes was higher in MCPRD group (Intermediate PTI, Manual CPR vs MCPRD, 15.1% vs 18.8%; Long PTI, Manual CPR vs MCPRD, 12.3% vs 19.7%).

The survival to discharge from unmatched and PS matched cohorts are shown in supplement Table 4-1. In Optimal PS matched cohort, survival to discharge in long PTI (compared with PTI 10 minutes or shorter) was 3.6% in manual CPR group and 3.8% in MCPRD group. In Greedy PS matched cohort, survival to discharge in long PTI (compared with PTI 10 minutes or shorter) was 2.9% in manual CPR group and 3.8% in MCPRD group (Supplement Table 4-1). There was no interaction of effect of MCPRD between PTI groups on both unmatched and PS matched cohorts (Supplement Table 4-2, 4-3).

Table 4-2. Outcomes of subgroups by patient transport interval from unmatched cohort

	Total		Manual CPR		MCPRD	
	N	%	N	%	N	%
Total	3,530	100.0	2,847	100.0	683	100.0
Survival to admission	656	18.6	530	18.6	126	18.4
PTI						
short PTI	88	21.1	79	23.0	9	12.2
Intermediate PTI	297	18.6	237	18.6	60	18.8
Long PTI	271	17.9	214	17.4	57	19.7
Hospital ROSC	966	27.4	767	26.9	199	29.1
PTI						
short PTI	124	29.7	103	30.0	21	28.4
Intermediate PTI	442	27.7	354	27.7	88	27.6
Long PTI	400	26.4	310	25.2	90	31.0

PTI, patient transport interval; CPR, cardiopulmonary resuscitation; MCPRD, mechanical chest compression device; ROSC, return of spontaneous circulation.

Table 4-3. Outcomes of subgroups by patient transport interval from Optimal and Greedy PS matched cohort

		Total		Manual CPR		MCPRD	
		N	%	N	%	N	%
Optimal PS matched cohort							
Total		2,049	100.0	1,366	100.0	683	100.0
Survival to admission		335	16.4	209	15.3	126	18.4
	PTI						
	short PTI	45	18.0	36	20.5	9	12.2
	Intermediate PTI	166	17.1	106	16.3	60	18.8
	Long PTI	124	15.0	67	12.5	57	19.7
Hospital ROSC		522	25.4	323	23.5	199	29.1
	PTI						
	short PTI	65	26.0	44	25.0	21	28.4
	Intermediate PTI	257	26.5	169	25.9	88	27.6
	Long PTI	200	24.2	110	20.4	90	31.0
Greedy PS matched cohort							
Total		2,049	100.0	1,366	100.0	683	100.0
Survival to admission		325	15.9	199	14.6	126	18.4
	PTI						
	short PTI	42	17.4	33	19.6	9	12.2
	Intermediate PTI	159	16.3	99	15.1	60	18.8
	Long PTI	124	14.9	67	12.3	57	19.7
Hospital ROSC		509	24.8	310	22.7	199	29.1
	PTI						
	short PTI	60	24.8	39	23.2	21	28.4
	Intermediate PTI	251	25.8	163	24.9	88	27.6
	Long PTI	198	23.7	108	19.9	90	31.0

PS, propensity score; PTI, patient transport interval; CPR, cardiopulmonary resuscitation; MCPRD, mechanical chest compression device; ROSC, return of spontaneous circulation.

4.3.2 Main analysis of an Unmatched Cohort

The logistic regression analysis examining the relation between MCPRD and outcomes from unmatched cohort is shown in Table 4-4. The crude odds ratio for MCPRD for survival to admission and hospital ROSC was 0.99 (95%CI 0.80-1.23) and 1.12 (95%CI 0.93-1.34). When the model was adjusted for potential confounders, adjusted odds ratio (AOR) for survival to admission and hospital ROSC was significant compared with manual CPR (AOR 1.36, 95%CI 1.07-1.77 and AOR 1.47, 95%CI 1.20-1.79). Analysis of interaction effect of the PTI on the effect of MCPRD on outcomes are shown in Table 5. Long PTI was associated with both survival to admission (AOR 1.49, 95%CI 1.05-2.12) and hospital ROSC (AOR 1.70, 95%CI 1.26-2.29) (Table 4-5).

Table 4-4. Multivariable logistic regression model analyzing the relationship between mechanical chest compression device use and outcomes in unmatched cohort

	Survival to admission		**Hospital ROSC**	
	Odds ratio	95% CI	Odds ratio	95% CI
Model 1	0.99	0.80-1.23	1.12	0.93-1.34
Model 2	1.36	1.07-1.72	1.47	1.20-1.79

ROSC, return of spontaneous circulation; CI, confidence interval.

Model 1: Unadjusted

Model 2: Adjusted for age, sex, hypertension, diabetes, witness status, public witnessed, bystander CPR, arrest place, initial ECG rhythm, prehospital EMS advanced airway, EMS defibrillation, EMS response time, scene resuscitation time.

Table 4-5. Model examining interactions of patients transport interval on the effect of mechanical chest compression device on outcomes in unmatched cohort

	Survival to admission		**Hospital ROSC**	
	AOR[a]	95%CI	AOR[a]	95%CI
Patient transport interval				
Short (0-5mins.)	0.55	0.24-1.26	1.33	0.70-2.51
Intermediate (6-10mins)	1.36	0.94-1.97	1.15	0.84-1.58
Long (over 11mins)	1.60	1.06-2.42	1.75	1.24-2.46

ROSC, return of spontaneous circulation; AOR, adjusted odds ratio; CI, confidence interval.

[a]Adjusted for age, gender, hypertension, diabetes, arrest place, witness, public witness, bystander CPR, initial ECG rhythm, prehospital advanced airway, EMS defibrillation. EMS response time, on scene time and interaction term (patient transport interval*mechanical chest compression device).

4.3.3 Main Analysis of Propensity Score-matched Cohorts

Multivariable logistic regression adjusted for potential confounders to examine the effect of MCPRD on outcomes was performed at each PS matched cohorts (Table 4-6). In Optimal PS matched cohort, the AOR for survival to admission was 1.29 (95%CI 0.99-1.67) whereas in Greedy PS matched cohort, the AOR was significant for the outcome (AOR 1.33, 95%CI 1.06-1.78). For hospital ROSC, the AOR was significant at both Optimal PS matched (AOR 1.37, 95%CI 1.11-1.70) and Greedy PS matched cohort (AOR 1.46, 95%CI 1.17-1.81), respectively.

In the interaction analysis, long PTI was associated with significant survival outcome in the prehospital MCPRD use in both Optimal PS matched cohort (AOR 1.60, 95%CI 1.06-2.24) and Greedy PS matched cohort (AOR 1.60, 95%CI 1.06-2.42). For hospital sustained ROSC, long PTI had significant interaction in both matched cohorts (Optimal matched cohort, AOR 1.72, 95%CI 1.24-2.46l; Greedy matched cohort, AOR 1.80, 95%CI 1.28-2.53) (Table 4-7).

Table 4-6. Multivariable logistic regression model analyzing the relationship between mechanical chest compression device and outcomes from Optimal PS matched and Greedy PS matched cohorts

		Survival to admission		Hospital ROSC	
		Odds ratio	95% CI	Odds ratio	95% CI
Optimal PS	Model 1	1.25	0.98-1.60	1.33	1.08-1.63
matched cohort	Model 2	1.29	0.99-1.67	1.37	1.11-1.70
Greedy PS	Model 1	1.33	1.04-1.70	1.40	1.14-1.72
matched cohort	Model 2	1.37	1.06-1.78	1.46	1.17-1.81

ROSC, return of spontaneous circulation; CI, confidence interval; PS, propensity score.

Model 1: Unadjusted

Model 2: Adjusted for age, sex, hypertension, diabetes, witness status, public witness, bystander CPR, arrest place, initial ECG rhythm, prehospital EMS advanced airway, EMS defibrillation, EMS response time, scene resuscitation time.

Table 4-7. Models examining interactions of patient transport interval on the effect of mechanical chest compression device on outcomes according to propensity matching methods.

	Survival to admission		Hospital ROSC	
	AOR	95%CI	AOR	95%CI
Optimal Matching				
Patient transport interval				
Short (0-5mins.)	0.55	0.24-1.26	1.33	0.70-2.51
Intermediate (6-10mins)	1.36	0.94-1.97	1.15	0.84-1.58
Long (over 11mins)	1.60	1.06-2.42	1.75	1.24-2.46
Greedy Matching				
Patient transport interval				
Short (0-5mins.)	0.51	0.22-1.18	1.43	0.75-2.73
Intermediate (6-10mins)	1.42	0.97-2.07	1.24	0.90-1.70
Long (over 11mins)	1.60	1.06-2.42	1.80	1.28-2.53

ROSC, return of spontaneous circulation; CI, confidence interval; AOR, adjusted odds ratio.

[a]Adjusted for age, gender, hypertension, diabetes, arrest place, witness, public witness, bystander CPR, initial ECG rhythm, prehospital advanced airway, EMS defibrillation, EMS response time, on scene time and interaction term (patient transport interval*mechanical chest compression device).

4.4. Discussion

An adequate compression rate and depth and uninterrupted chest compression are regarded as essential elements for good OHCA outcomes. When transporting patients with OHCA with on-going CPR, interruptions of compression owing to sudden changes in the speed, instability of the CPR provider during chest compression, and limited space at the back of the ambulance makes manual chest compression ineffective. Because of these limitations, several emergency medical system communities have implemented MCPRD even though their scientific evidence is weak.[91]

This study evaluated whether there was a difference between the use of MCPRD and manual compression during the transport of patients with OHCA with respect to transport interval. Based on potential advantages of MCPRD use and current research findings, we hypothesized that MCPRD use could be associated with improved survival outcomes when used in long PTI situations. This study found that the effect of MCPRD on outcomes had an interaction with PTI on patients with a presumed cardiac etiology. In both our unmatched and propensity score-matched cohorts, the benefit of MCPRDS use on survival to admission was observed in patients with PTI longer than 10 minutes. Application of MCPRD for short and intermediated PTI showed no interaction for the outcomes.

Several large RCTs of MCPRD use for patients with OHCA suggest that the device use was not superior to manual chest compression.[37–39] However, none of these studies analyzed the benefit of MCPRD on outcomes according to patient transport interval with CPR going on at ambulances. A secondary analysis from the CIRC trial investigating the effect of MCPRD for a long duration of CPR reported that MCPRD use showed significant benefits for survival in patients with OHCA when CPR duration was 16 min or longer.[92] This result supports our hypothesis that CPR quality may be affected by provider fatigue and that CPR quality may diminish with long chest compression durations.

There are a few manikin and animal studies demonstrating deterioration in manual CPR quality during patient transport.[43,93] In a manikin study, the rate of adherence to the current CPR recommendation was 67% in manual resuscitators, whereas in mechanical CPR devices, the rate was 99.96%.[93] With regard to tissue perfusion, arterial and coronary perfusion pressure and end-tidal CO_2 were significantly higher with mechanical CPR device use than with manual chest compression.[43] There are limited clinical studies comparing CPR quality during transport. In the ambulance resuscitation trial, MCPRD use on the reducible stretcher during the transport of patients with OHCA showed a higher chest compression fraction than manual CPR.[94] Although it is difficult to generalize the results of studies on CPR quality owing to small sample sizes and limited data on human patients, the direction of these results may bolster our results.

Notably, it is possible that rescuer fatigue after a certain duration of chest compression and physical effort to sustain CPR provider stability in a moving ambulance could have influenced our outcome. Manual CPR quality can degrade in less than 2 min [95,96] even in a stable environment; additionally, in several cases, CPR providers may need to perform CPR alone for more than 2 min. Performing CPR in a moving ambulance may lead to back pain,[97,98] wrist pain, and bruises in the forehead when the ambulance abruptly turns, accelerates, or decelerates. Based on our data, the effect of MCPRD was not significant when PTI was 10 min or shorter. Considering that CPR providers in our study were physically trained EMTs, manual CPR quality could have been sustained for approximately 10 min. In contrast, interruptions to chest compression owing to delayed deployment of MCPRD could have negatively affected the outcome during certain duration of CPR.[99] In the Korean EMS setting, the standard protocol for EMS providers states performing CPR at the scene for at least 5 min and MCPRD is usually deployed after 5 min of CPR before patient transport. MCPRD use may have provided high-quality CPR; however, the outcomes were not significant until PTI was 10 min or longer, during which the time loss in deployment leading to no-flow time might have affected the result. Further studies are needed to investigate the appropriate situation in which the use of MCPRD could be more effective, such as prolonged patient transport or insufficient EMS providers to perform chest compressions.

Although the evidence of the routine use of MCPRD is weak, it is now widely used in most EMS systems. To overcome the disadvantages of MCPRD, such as no-flow time when deploying the device, the effective and sufficient training of EMS providers needs to be planned. In addition, regional protocols of MCPRD use considering EMS resources, hospital resources, and average patient transport intervals need to be established.

This observational study had several limitations. First, this was an observational study and not an interventional trial; hence, there could be unmeasured potential confounders that could have affected the outcome. Second, the type of MCPRD used during the study period was not categorized; therefore, we could not compare the devices. Third, although the standard protocol for EMS provider states performing CPR for at least 5 min in the field and then deploying MCPRD, this protocol could not have been applied in the actual field depending on the situation, which might have affected the result. Fourth, this study was conducted in an EMS system where prehospital drug use or termination of resuscitation is legally prohibited. The generalization of the results may vary according to differences in the EMS system.

4.5. Conclusion

The use of MCPRD on survival to admission was different according to patient transport interval in both unmatched and PS matched cohorts. In our study, we demonstrated that for patients with OHCA with transportation duration longer than 10 min, the effect of MCPRD was significantly associated with survival compared to manual chest compression. After training for the skillful use of MCPRD, such as shortening of the time interval for deployment, MCPRD could be more effective in moving ambulances. Further studies are needed to evaluate the appropriate use of MCPRD in special situations.

Chapter 5. Effect of Transported Hospital Resources on Neurologic Outcome after Out-of-hospital Cardiac Arrest

5.1. Introduction

Out-of-hospital cardiac arrest (OHCA) is the leading cause of morbidity and mortality [100]. Although much effort has been devoted, the outcome is still poor in Korea, with an 8.0% survival rate and only 5.8% with good neurologic outcomes [101].

In 2006, integrated post-arrest care was added to the chain of survival, emphasizing the importance of comprehensive multidisciplinary post-arrest care. Currently, an increasing number of publications have reported on the beneficial effects of targeted temperature management and other forms of post-resuscitation care on neurologic outcomes [102–104].

However, not all cardiac arrest receiving facilities have the capacity to provide comprehensive post-arrest care. To overcome this issue, the concept of 'cardiac resuscitation center' or 'regionalization strategy of OHCA care' has emerged. The American Heart Association (AHA) in 2010 proposed two levels of cardiac resuscitation centers and suggested the criteria for each level of CRC [61]. The main recommended strategy is to transfer patients with spontaneous circulation after OHCA to specialized CRCs for comprehensive care [61]. Locally, in Los Angeles, OHCA patients with initial shockable rhythm were sent to ST-elevation myocardial infarction (STEMI) receiving centers, which resulted in higher rates of neurologically intact survival [105]. In Arizona, the implementation of a statewide system of cardiac receiving centers resulted in the improvement of survival in patients with intact neurologic status [62].

The appropriate transport strategy for cardiac arrest patients in a certain community could be designed and implemented after the assessment of hospital resources and performances. In this study, we aimed to categorize cardiac receiving centers (CRCs) according to the hospital resources and identified outcome differences among facilities in our community.

5.2. Method

5.2.1 Study Population

EMS-treated OHCA patients with a presumed cardiac etiology transported by Gyeonggi EMS to hospitals located in Gyeonggi province were included in this study. Among them, OHCA patients whose final outcomes are available on medical records during 2012–2014 were finally enrolled in the analysis. Patients with presumed cardiac etiology were defined if they had no definite evidence of non-cardiac causes [106]. EMS-treated OHCA patients were defined if they received at least one of the following resuscitation efforts: chest compression, rescue breathing, and defibrillation.

5.2.2 Measurement

The main exposure was the classification of CRCs, which was attained using the results of the Gyeonggi Hospital Assessment Survey. Facilities were classified as definite CRC (D-CRC) if they had a standardized resuscitation protocol in the ED, admitted OHCA patients who achieved return of spontaneous circulation (ROSC), had a standardized therapeutic temperature management (TTM) protocol, if they offered percutaneous coronary intervention (PCI) 24 hours a day and 7 days a week, if they had a cardiac arrest registry for quality assurance, could confirm brain death, had rehabilitation programs for OHCA survivors, and offered community-based resuscitation training programs. Other facilities were defined as primary CRC (P-CRC). Classification of CRC was based on the internationally accepted criteria [107,108] and consensus from expert meetings.

Data of potential confounders such as age; gender; pre-arrest medical conditions such as cardiac disease, hypertension and diabetes mellitus; initial ECG rhythm at scene; the presence of witnesses; provision of bystander CPR; EMS response interval; EMS scene resuscitation interval; patient transport interval; and pre-hospital ROSC were obtained from the national OHCA database.

The primary outcome was good neurologic recovery classified according to cerebral performance category (CPC) and defined as favorable if the CPC was 1 or 2. The secondary outcome was survival to discharge. All outcome measures were based on a review of medical records.

5.2.3 Statistical analysis

Descriptive statistics between CRCs for categorical variables are presented as frequency distributions and percentages. Continuous variables are reported as medians and interquartile ranges (IQRs). Univariate comparisons of the distributions of demographic and clinical factors were analyzed using the chi-square test for discrete variables and the Wilcoxon rank-sum test for continuous variables. We compared the outcomes between CRCs using crude and adjusted odds ratios (aORs) and 95% confidence intervals (CIs). Multivariable logistic regression was performed after adjusting for potential confounders including Utstein co-variables (age, sex, witness status, location of arrest [public vs private], bystander CPR, EMS response time, EMS transport time and pre-hospital electrocardiogram pattern [shockable vs non-shockable]), pre-existing comorbidities (hypertension, diabetes, and cardiac disease), and result of pre-hospital ROSC.

We also analyzed for collinearity and tested 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 data were analyzed using SAS 9.4 (SAS Institute Inc., NC, USA).

5.2.4 Ethics Statement

The study complies with the Declaration of Helsinki and the study was approved by Korea University Ansan Hospital Institute Review Board to be conducted with a waiver of informed consent. The IRB No. is K2018-0500-001.

5.3. Results

Among a total of 14,951 EMS-treated OHCA patients, 4,126 were definitely of non-cardiac etiology, 329 were transported to hospitals in other regions, and the final outcomes of 584 were unavailable. A total of 9,912 cases were enrolled in the study (Figure 5-1).

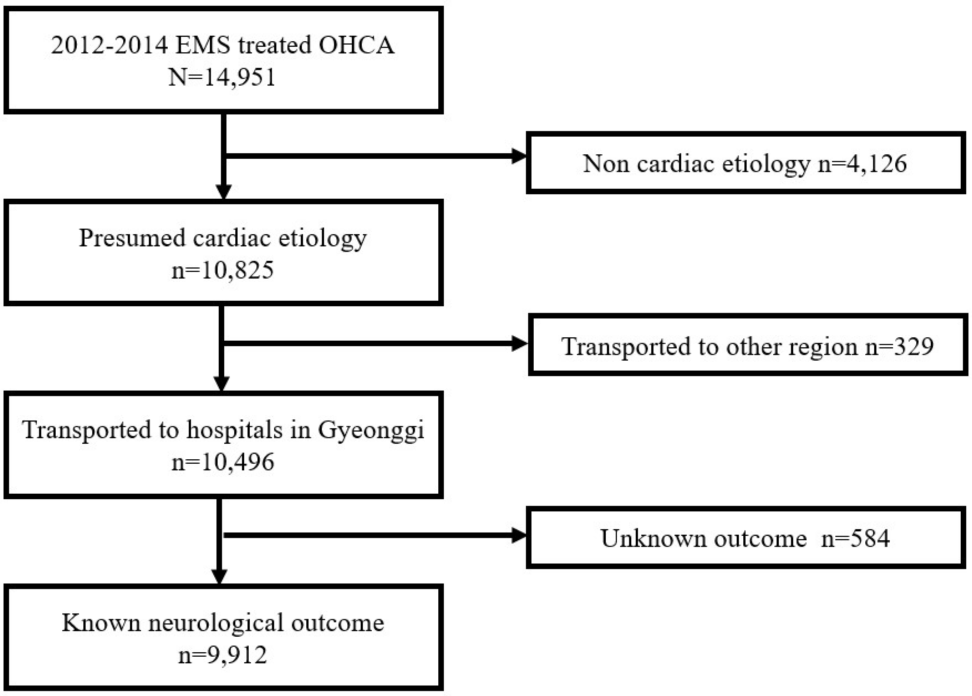


Figure 5- 1. Flow chart of study population

OHCA, out-of-cardiac arrest; EMS, emergency medical service.

5.3.1 Results of Hospital Assessment Survey

Of the 90 cardiac arrest receiving facilities, 77 facilities responded to the survey. All 13 (13.1%) facilities that did not respond to the survey were non-ED facilities. Of the 77 cardiac arrest receiving facilities, 50 facilities (64.9%) admitted post-ROSC patients and 22 facilities (28.6%) were available to provide therapeutic hypothermia. A total of 29 (37.7%) facilities offered 24/7 PCI, and 27 (35.1%) provided a quality management program on OHCA resuscitation and treatment. The facility was classified as D-CRC if they had a standard resuscitation protocol at the ED; had the device, manpower, and standard protocol for TTM; if PCI was available 24/7; if they had an OHCA registry system; if they could confirm brain death, had an available rehabilitation program for post-resuscitated patients, and provided community-based CPR programs (Table 5-1).

Table 5-1. Result of Hospital Assessment Survey and classification of Cardiac Receiving Centers by result

Hospital Assessment Survey		n	%
Questionnaire		77	100.0
1. Level of your emergency department at your medical facility?			
	Regional EMC	4	4.4
	Local EMC	26	26.3
	Local ED	33	33.4
	Non-ED facility	14	14.2
	NA	13	13.1
2. Does your medical facility usually admit or transfer post-ROSC patients?			
	Admit	50	64.9
	Transfer	27	35.1
3. Does your medical facility have a standard resuscitation protocol for OHCA at ED?			
	Yes	67	87.0
	No	10	13.0
4. Does your medical facility have a standard inter-hospital transfer protocol for post-ROSC patients?			
	Yes	48	62.3
	No	29	37.7
5. Does your medical facility have any device and manpower to provide therapeutic hypothermia to post-ROSC patients?			
	Yes	22	28.6
	No	55	71.4
6. Does your medical facility have a standard protocol for providing therapeutic hypothermia?			

Hospital Assessment Survey		n	%
Questionnaire		77	100.0
		Yes	18
		No	59
7. Is PCI available 24/7 at your medical facility?			
	Yes	29	37.7
	No	48	62.3
8. Does your medical facility have a specialized registration system for OHCA resuscitation and treatment?			
	Yes	23	29.9
	No	54	70.1
9. Does your medical facility perform quality management of OHCA resuscitation and treatment?			
	Yes	27	35.1
	No	50	64.9
10. Does your medical facility have a standard termination of resuscitation rule (or protocol)?			
	Yes	36	46.8
	No	41	53.3
11. Is EEG available to post-resuscitation patients at your medical facility?			
	Yes	35	45.5
	No	42	54.6
12. Is confirmation of brain death possible at your medical facility?			
	Yes	32	41.6
	No	45	58.4
13. Is rehabilitation program available to post-resuscitation patients at your medical facility?			

Hospital Assessment Survey	n	%	
Questionnaire	77	100.0	
	Yes	38	49.4
	No	39	50.7
14. Does your medical facility provide CPR education to the community?			
	Yes	54	70.1
	No	23	29.9

Cardiac Resuscitation Center Classification	Medical facilities	OHCA (2012–2014)
Total number of hospitals that participated in the survey	77	9,912 (100%)
D-CRC	15	4,036 (40.7%)
P-CRC	62	5,876 (59.3%)

CRC, cardiac resuscitation center; ED, emergency department; NA, no answer; EMC, emergency medical center; ROSC, return of spontaneous circulation; OHCA, out-of-hospital cardiac arrest; PCI, percutaneous coronary intervention; EEG, electroencephalography; CPR, cardiopulmonary resuscitation; D-CRC, definite cardiac resuscitation center; P-CRC, primary cardiac resuscitation center.

5.3.2 Characteristics of out-of-hospital cardiac arrest patients according to transported cardiac receiving centers

Among 9,912 OHCA, 4,036 patients (40.7%) were initially transported to D-CRC. The proportion of pre-existing comorbidities was higher among OHCA patients transported to D-CRC. OHCA patients transported to D-CRC showed better neurologic outcome (6.2% vs 1.5%, $p<0.001$) and better survival to discharge rate (11.3% vs 3.3%, $p<0.001$) than those transported P-CRC (Table 5-2).

Of the 1,681 patients who survived to admission, 1,025 (56.1%) were admitted to D-CRC. D-CRC provided higher proportions of post-resuscitation treatments, such as PCI (15.2% vs 7.5%, $p<0.001$), TTM (29.9% vs 7.6%, $p<0.001$), and extracorporeal membrane oxygenation (5.5% vs 1.4%, $p<0.001$) compared to P-CRC. Patients admitted to D-CRC showed better neurologic recovery (24.3% vs 13.1%, $p<0.001$) and survival to discharge (44.0% vs 29.7%, $p<0.001$) than those admitted to P-CRC (Table 5-3).

Table 5-2. Demographics and outcomes of all OHCA patients transported to CRCs

Risk factors	All OHCA		P-CRC		D-CRC	
	n	%	n	%	n	%
All	9,912	100.0	5,876	100.0	4,036	100.0
Male	6,286	63.4	3,654	62.2	2,632	65.2
Age						
Median (IQR)	71	55–80	72	57–81	68	54–79
<15 years	179	1.8	62	1.1	117	2.9
15–64 years	3,684	37.2	2,058	35.0	1,626	40.3
Older than 65 years	6,049	61.0	3,756	63.9	2,293	56.8
Pre-arrest comorbidities						
Cardiac disease	1,338	13.5	718	12.2	620	15.4
Hypertension	3,250	32.8	1,759	29.9	1,491	36.9
Diabetes mellitus	2,191	22.1	1,209	20.6	982	24.3
Cardiac arrest location						
Public	1,579	15.9	875	14.9	704	17.4
Private	1,644	16.6	1,064	18.1	580	14.4
Unknown	6,689	67.5	3,937	67.0	2,752	68.2
Witness	4,827	48.7	2,684	45.7	2,143	53.1
Who witnessed or found						
EMT	1,139	11.5	598	10.2	541	13.4
Layperson	6,764	68.2	3,977	67.7	2,787	69.1
Unknown	2,009	20.3	1,301	22.1	708	17.5
Bystander CPR	4,743	47.9	2,703	46.0	2,040	50.6
Initial EMS ECG						

Risk factors	All OHCA		P-CRC		D-CRC	
	n	%	n	%	n	%
Shockable	1,321	13.3	639	10.9	682	16.9
Non-shockable	8,222	83.0	5,019	85.4	3,203	79.4
Unknown	369	3.7	218	3.7	151	3.7
EMS response intv.						
Median (IQR)	8	6–10.5	8	6–11	7	6–10
<4 minutes	426	4.3	241	4.1	185	4.6
4–8 minutes	4,262	43.0	2,379	40.5	1,883	46.7
Over 8 minutes	5,224	52.7	3,256	55.4	1,968	48.8
Scene resuscitation intv.						
Median (IQR)	8	5–12	8	5–11	9	6–12
<5 minutes	1,608	16.2	978	16.6	630	15.6
5–15 minutes	6,973	70.4	4,209	71.6	2,764	68.5
Over 15 minutes	1,331	13.4	689	11.7	642	15.9
Patient transport intv.						
Median (IQR)	7	5–10	6	4–10	7	5–10
<15 minutes	8,702	87.8	5,214	88.7	3,488	86.4
15–30 minutes	1,047	10.6	617	10.5	430	10.7
Over 30 minutes	163	1.6	45	0.8	118	2.9
Pre-hospital ROSC	569	5.7	163	2.8	406	10.1
Survival to admission	1,681	17.0	656	11.2	1,025	25.4
Survival to discharge	651	6.6	196	3.3	455	11.3
Good neurology	338	3.4	87	1.5	251	6.2

OHCA, out-of-hospital cardiac arrest; CRC, cardiac resuscitation center; P-CRC, primary cardiac resuscitation center; D-CRC, definite cardiac resuscitation center; IQR, interquartile range; EMT, emergency medical technician; CPR, cardiopulmonary resuscitation; EMS, emergency medical service; ECG, electrocardiography, intv., interval; ROSC, return of spontaneous circulation.

Table 5-3. Demographics and outcomes of admitted OHCA patients transported to CRCs

Risk factors	All OHCA		P-CRC		D- CRC	
	n	%	n	%	n	%
All	1,681	100.0	656	100.0	1,025	100.0
Male	1,149	68.4	432	65.9	717	70.0
Age						
Median (IQR)	61	50–74	64	51–77	60	49–73
<15 years	32	1.9	4	0.6	28	2.7
15–64 years	905	53.8	327	49.9	578	56.4
Older than 65 years	744	44.3	325	49.5	419	40.9
Pre-arrest comorbidities						
Cardiac disease	302	18.0	107	16.3	195	19.0
Hypertension	672	40.0	247	37.7	425	41.5
Diabetes mellitus	443	26.4	182	27.7	261	25.5
Location of cardiac arrest						
Public	384	22.8	124	18.9	260	25.4
Private	363	21.6	174	26.5	189	18.4
Unknown	934	55.6	358	54.6	576	56.2
Witness	1,134	67.5	432	65.9	702	68.5
Who witnessed or found						
EMT	347	20.6	137	20.9	210	20.5
Layperson	1,036	61.6	386	58.8	650	63.4
Unknown	298	17.7	133	20.3	165	16.1
Bystander CPR	937	55.7	358	54.6	579	56.5
Initial EMS ECG						

Risk factors	All OHCA		P-CRC		D- CRC	
	n	%	n	%	n	%
Shockable	509	30.3	175	26.7	334	32.6
Non-shockable	1,100	65.4	457	69.7	643	62.7
Unknown	72	4.3	24	3.7	48	4.7
EMS response intv.						
Median (IQR)	7	5–9	7	5–9.5	7	5–9
<4 minutes	90	5.4	39	6.0	51	5.0
4–8 minutes	850	50.6	323	49.2	527	51.4
Over 8 minutes	741	44.1	294	44.8	447	43.6
Patient transport intv.						
Median (IQR)	6	4–10	5	4–8	6	4–10
<15 minutes	1,465	87.2	613	93.5	852	83.1
15–30 minutes	145	8.6	40	6.1	105	10.2
Over 30 minutes	71	4.2	3	0.5	68	6.6
Post-resuscitation care						
PCI	205	12.2	49	7.5	156	15.2
TTM	356	21.2	50	7.6	306	29.9
ECMO	65	3.9	9	1.4	56	5.5
Pre-hospital ROSC	453	27.0	114	17.4	339	33.1
Survival to discharge	646	38.4	195	29.7	451	44.0
Good neurology	335	19.9	86	13.1	249	24.3

OHCA, out-of-hospital cardiac arrest; CRC, cardiac resuscitation center; P-CRC, primary cardiac resuscitation center; D-CRC; definite cardiac resuscitation center; IQR, interquartile range; EMT, emergency medical technician; CPR, cardiopulmonary resuscitation; EMS, emergency medical service; ECG, electrocardiography; intv., interval; ROSC, return of spontaneous circulation; PCI, percutaneous coronary intervention; TTM, target temperature management; ECMO, extracorporeal membrane oxygenation.

5.3.3 Outcomes of out-of-hospital cardiac arrest patients according to transported cardiac receiving centers

Among all OHCA patients, after adjusting for potential confounders, transportation to D-CRC was significantly associated with good neurologic recovery (AOR, 2.10; 95% CI, 1.51–2.93) and survival to discharge (AOR, 4.41; 95% CI, 3.45–5.65). For patients who survived to admission, D-CRC was significantly associated with better neurologic recovery than P-CRC (AOR, 1.48; 95% CI, 1.02–2.14) (Table 5-4).

Table 5-4. Effect of CRC on the neurologic outcomes and survival to discharge after OHCA

	Total n	Outcome n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]
All OHCA		Good neurology outcome		
Total	9,912	338 (3.4%)		
P-CRC	5,876	87 (1.5%)	Reference	Reference
D-CRC	4,036	251(6.2%)	4.41 (3.45–5.65)	2.10 (1.51–2.92)
		Survival to discharge		
Total	9,912	651 (6.6%)		
P-CRC	5,876	196 (3.3%)	Reference	Reference
D-CRC	4,036	455 (11.3%)	3.68 (3.10–4.38)	2.41 (1.95–2.98)
Survival to admitted OHCA		Good neurology outcome		
Total	1,681	335 (19.9%)		
P-CRC	656	86 (13.1%)	Reference	Reference
D-CRC	1,025	249 (24.3%)	2.13 (1.63–2.78)	1.48 (1.02–2.14)
		Survival to discharge		
Total	1,681	646 (38.4%)		
P-CRC	656	195 (29.7%)	Reference	Reference
D-CRC	1,025	451 (44.0%)	1.86 (1.51–2.29)	1.57 (1.22–2.03)

CRC, cardiac resuscitation center; OR, odds ratio; CI, confidential interval; OHCA, out-of-hospital cardiac arrest; P-CRC, primary cardiac resuscitation center; D-CRC, definite cardiac resuscitation center.

[a] Adjusted for age, gender, medical conditions, initial ECG rhythm at scene, the presence of witness, provision of bystander CPR, EMS response interval, EMS scene resuscitation interval, patient transport interval, pre-hospital return of circulation

Distribution of risk factors of all OHCAs and those survived to admit according to interventions of post-resuscitation care is show at Table 5-5 and Supplement Table 3. OHCA patients who are male, relatively young, arrest occurred at public and those with confirmed initially of shockable rhythm were applied with target temperature management (TTM), coronary reperfusion (CR) and intensive cardiac care (ICC). TTM, CR and ICC were more performed at D-CRC.

Effect of post-resuscitation interventions on outcomes are shown at Table 5-6 and Supplement Table 4. For all OHCA patients adjusted odds ratio (AOR) of TTM was 4.12 (95% CI, 2.63-6.46), AOR for CR was 3.46 (95% CI, 2.32-5.17) and AOR for ICC was 4.34(95% CI, 2.59-7.26) for good neurologic outcome.

Table 5-5. Distribution of post-resuscitation care by potential risk factors in all transported OHCA patients

Risk factors	All OHCA		Target Temperature Management				Coronary Reperfusion				Intensive Cardiac Care (ECMO, ICD, PM, CABG)			
			No		Yes		No		Yes		No		Yes	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
All	9,912	100.0	9,692	100.0	220	100.0	9,516	100.0	396	100.0	9,766	100.0	146	100.0
Male	6,286	63.4	6,098	62.9	188	85.5	5,996	63.0	290	73.2	6,161	63.1	125	85.6
Age														
Median(IQR)	71	55-80	71	56-80	58	50-67	71	56-80	57	48-70	71	56-80	53	44-63
<15 years	179	1.8	179	1.9	0	0.0	175	1.8	4	1.0	178	1.8	1	0.7
15-64 years	3684	37.2	3532	36.4	152	69.1	3438	36.1	246	62.1	3568	36.5	116	79.5
Over 64 years	6049	61.0	5981	61.7	68	30.9	5903	62.0	146	36.9	6020	61.6	29	19.9
Comorbidities														
Heart disease	1,338	13.5	1,291	13.3	47	21.4	1,263	13.3	75	18.9	1,305	13.4	33	22.6
Hypertension	3,250	32.8	3,149	32.5	101	45.9	3,089	32.5	161	40.7	3,198	32.8	52	35.6
Diabetes	2,191	22.1	2,148	22.2	43	19.6	2,095	22.0	96	24.2	2,162	22.1	29	19.9
Arrest place														
Public	1,579	15.9	1,483	15.3	96	43.6	1,475	15.5	104	26.3	1,523	15.6	56	38.4
Bystander CPR	4,743	47.9	4,606	47.5	137	62.3	4,537	47.7	206	52.0	4,645	47.6	98	67.1
Witness	4,827	48.7	4,653	48.0	174	79.1	4,560	47.9	267	67.4	4,712	48.3	115	78.8

Risk factors	All OHCA		Target Temperature Management				Coronary Reperfusion				Intensive Cardiac Care (ECMO, ICD, PM, CABG)			
			No		Yes		No		Yes		No		Yes	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Initial EMS ECG														
Shockable	1,321	13.3	1,164	12.0	157	71.4	1,163	12.2	158	39.9	1,212	12.4	109	74.7
EMS response intv														
Median (IQR)														
<4 mins	426	4.3	412	4.3	14	6.4	408	4.3	18	4.6	419	4.3	7	4.8
4-8 mins	4262	43.0	4160	42.9	102	46.4	4076	42.8	186	47.0	4187	42.9	75	51.4
Over 8 mins	5224	52.7	5120	52.8	104	47.3	5032	52.9	192	48.5	5160	52.8	64	43.8
Scene resuscitation intv.	8	6-10	8	6-11	8	6-12	8	6-11	8	5-12	8	6-11	8	5-12
Median (IQR)														
<5 mins	1608	16.2	1557	16.1	51	23.2	1535	16.1	73	18.4	1581	16.2	27	18.5
5-15 mins	6973	70.4	6825	70.4	148	67.3	6710	70.5	263	66.4	6877	70.4	96	65.8
Over 15 mins	1331	13.4	1310	13.5	21	9.6	1271	13.4	60	15.2	1308	13.4	23	15.8
Patient transport intv.														
Median (IQR)	8	5-12	8	6-11	8	5-11	8	5-12	8	6-12	8	5-12	9	6-12
<15 mins	8702	87.8	8517	87.9	185	84.1	8384	88.1	318	80.3	8582	87.9	120	82.2

Risk factors	All OHCA		Target Temperature Management				Coronary Reperfusion				Intensive Cardiac Care (ECMO, ICD, PM, CABG)			
			No		Yes		No		Yes		No		Yes	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
15-30 mins	1047	10.6	1024	10.6	23	10.5	1006	10.6	41	10.4	1029	10.5	18	12.3
Over 30 mins	163	1.6	151	1.6	12	5.5	126	1.3	37	9.3	155	1.6	8	5.5
Transported CRC														
P-CRC	5,876	59.3	5,821	60.1	55	25.0	5825	61.2	51	12.9	5857	60.0	19	13.0
D-CRC	4,036	40.7	3,871	39.9	165	75.0	3691	38.8	345	87.1	3909	40.0	127	87.0
Prehospital ROSC	569	5.7	460	4.8	109	49.6	437	4.6	132	33.3	502	5.1	67	45.9
Survival to discharge	651	6.6	516	5.3	135	61.4	458	4.8	193	48.7	577	5.9	74	50.7
Good neurologic outcome	338	3.4	242	2.5	96	43.6	241	2.5	97	24.5	274	2.8	64	43.8

OHCA, out-of-hospital cardiac arrest; ECMO, extracorporeal membrane oxygenation; ICD, implantable cardioverter defibrillator; PM, pacemaker; IQR, interquartile range; CPR, cardiopulmonary resuscitation; EMS, emergency medical service; ECG, electrocardiography; ROSC, return of spontaneous circulation.

Table 5-6. The effect of post-resuscitation interventions on the outcomes of OHCA with presumed of cardiac etiology (N=9,912)

	Total N	Outcome N (%)	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)[a]
All OHCA				
Target Temperature Management (TTM)				
Survival to discharge				
Non-TTM	9,692	516 (5.3%)	1	1
TTM	220	135 (61.4%)	28.24 (21.23-37.58)	6.39 (4.36-9.37)
Good neurologic outcome				
Non-TTM	9,692	242 (2.5%)	1	1
TTM	220	96 (43.6%)	30.23 (22.50-40.63)	4.12 (2.63-6.46)
Coronary Reperfusion (CR)				
Survival to discharge				
Non-CR	9,516	458 (4.8%)	1	1
CR	396	193 (48.6%)	18.80 (15.12-23.39)	12.44 (9.31-16.63)
Good neurologic outcome				
Non-CR	9,516	241 (2.5%)	1	1
CR	396	97 (24.5%)	12.49 (9.61-16.23)	3.46 (2.32-5.17)
Intensive Cardiac Care (ICC)				
Survival to discharge				
Non-ICC	9,766	577 (5.9%)	1	1
ICC	146	74 (50.7%)	16.37 (11.71-22.89)	2.76 (1.75-4.35)
Good neurologic outcome				
Non-ICC	9,766	274 (2.8%)	1	1
ICC	146	64 (43.8%)	27.04 (19.09-38.31)	4.34 (2.59-7.26)

OHCA, out-of-hospital cardiac arrest; OR, odds ratio; TTM, target temperature management; CR, coronary reperfusion; ICC, intensive cardiac care.

[a]Adjusted for age, sex, comorbidities (heart disease, hypertension, diabetes mellitus), arrest place, witness,

bystander CPR, initial ECG, EMS response interval, scene resuscitation interval, patient transport interval, prehospital ROSC.

The TTM or CR or ICC was added to be adjusted for each final counterpart model (CR and ICC for analysis of non-TTM vs. TTM group, TTM and ICC for analysis of non-CR vs, CR group, TTM and CR for analysis of non-ICC vs. ICC group).

5.4. Discussion

This is the first regional attempt to categorize cardiac arrest receiving hospitals based on their practices and resources and compare the outcomes between the two levels of cardiac arrest receiving hospitals. This population-based study demonstrated that OHCA patients transported to D-CRC had better neurologic outcome than those transported to P-CRC (Table 5-2). Patients who survived and were admitted to D-CRC showed better neurologic outcome than those admitted to P-CRC (Table 5-3). This result supports the hypothesis that comprehensive post-resuscitation care applied to successfully resuscitated patients results in a better neurologic outcome. Our result coincided with those of recent studies, which suggested that transferring OHCA patients to specialized cardiac arrest centers resulted in good neurologic recovery [62,107,109]. From this study, we were able to assess the distribution of hospital resources and OHCA results based on the distribution of our community. This result will be helpful in establishing the transport protocol of EMS and inter-hospital transfer strategy after OHCA.

The result of this study suggests that it is desirable for the prognosis of OHCA patients to be transported to D-CRC. However, in a large district like Gyeonggi province, direct transfer of OHCA patients to D-CRC may result in long-distance transportation with resuscitation performed at the back of the moving ambulance. Many studies have demonstrated that the quality of CPR is suboptimal during ambulance transportation. Korean EMTs are legally restricted from performing advanced skills such as endotracheal intubation or intravenous drug infusion. The ambulance crew is composed of not more than three members. Therefore, to overcome these legal and resource barriers, instead of transporting OHCA patients to D-CRC regardless of transport interval, it is important to provide high-quality resuscitation at P-CRC and transfer patients safely to D-CRC as soon as they achieve ROSC. The American Heart Association proposed 2 levels of CRCs and provided the criteria for each center. Arizona established a statewide network of hospitals classified by the government as 'cardiac receiving centers' or 'cardiac referral centers' [62,107]. Although the criteria should be re-evaluated periodically, the basic concept of a regional system of care is focused on providing specialized post-resuscitation care in selected hospitals and transferring post-ROSC patients to these hospitals as appropriate [61].

A safe inter-hospital transfer protocol between P-CRC and D-CRC is also essential to the regionalization of OHCA care. A previous study reported that therapeutic hypothermia had a less beneficial effect on the neurologic recovery of patients who arrived via inter-hospital transfer than those who were directly transported to the hospital [110]. Other literature reported that good neurologic recovery was less frequently observed among patients who experienced any events during the transfer [111]. To date, a successful inter-hospital transfer protocol for post-resuscitation care has been integrated into an existing regional system of care for STEMI[112]. No study was able to define the role of secondary transfer to a regional center after initial care at primary care hospitals. Nevertheless, inter-hospital transfer is an inevitable procedure in operating a regionalization strategy especially with the EMS system at an intermediate level. Considering that this is the first study that attempts to suggest a regionalization model in Korea, developing a safe inter-hospital transfer protocol based on the current resources would be necessary.

Lastly, optimization of a regionalization strategy in communities must be implemented. The interval between EMS arrival on the scene and transport to a D-CRC is unduly long in rural and suburban areas of the Gyeonggi province. Although observational studies suggested that the duration of transport to the hospital was not associated with patient outcomes, this negative association was only observed among OHCA patients successfully resuscitated on-scene [113,114]. To date, no study has been able to provide a safe transport interval for OHCA patients who failed to achieve ROSC in the field. A priori categorization, verification, and designation of CRCs based on their actual practice performances should be done within the community. High-quality resuscitation at P-CRCs followed by a safe transfer to D-CRCs to provide multidisciplinary post-resuscitation care would enhance the survival of OHCA patients.

This study had several limitations. First, all patients with unknown final outcome were excluded from the study. Second, the year of survey (2015) and OHCA occurrence (2012–2014) differed. However, the list of facilities for the survey was selected if they received an OHCA patient during 2013–2014; thus, it would not have affected the result. Third, post-resuscitation care, such as PCI timing or TTM protocol, was not standardized among the CRCs. Although patient care policy may differ between CRCs, this would increase the generalizability of our study findings. Fourth, similar to other observational studies, the unmeasured bias would have influenced the study. Lastly, the result of this study can only be implemented in an EMS system where field termination of OHCA is legally not allowed.

5.5. Conclusion

Through this study, we were able to categorize CRCs according to hospital resources in our region. After adjusting for potential confounders, D-CRC was independently associated with better neurologic outcome compared to P-CRC. This finding highlights an important opportunity to implement the regionalization strategy for OHCA in Gyeonggi province.

Chapter 6. Discussion

6.1. Overall discussion from public health perspective

This study aimed to strengthen evidence based prevention and cement up the missing links of chain of survival in patients of OHCA. Based on multicenter OHCA and community population data, the incidence of OHCA decreased when one of the most prevalent cardiovascular risk factor, hypertension, was controlled. The untreated HTN patients were the most at-risk population. Effect of prehospital MCPRD was assessed according to patient transport interval, which could be considered as a special situation. Finally, the differences in-hospital resources significantly showed differences in the outcomes of OHCA, which could provide evidence to emphasize the importance of the systems-of-care.

These strategies to decrease the incidence and enhance survival of OHCA could be used to provide a framework to potentially improve resuscitation care and outcome through EMS resource planning, targeted community-based interventions, which are more cost-effective than a general population level intervention. Searching at-risk population throughout the communities, find out the cause of risk and provide appropriate individualized treatment modalities are the role of community public health authorities. Also cardiac arrest researches could incorporate this result into various intervention and trials to broaden the scope and strength of the evidence. The routine use of MCPRD lacks evidence but EMS providers are asking for use in actual field. In moving ambulance, the MCPRD could take a role as a chest compressor leaving EMS provider to do other procedures. It is the role of researchers from public health and from clinical fields to evaluate the usage and efficiency of MCPRD to enhance survival. This study in that sense, suggest the evidence for conducting trials and interventions.

Furthermore, an in-depth understanding of essential elements of post-ROSC care could guide the optimized regional OHCA transport protocol that are used in some communities but have not been implemented in others. The model of cardiac arrest centers are conceived from ST-elevation myocardial infarction (STEMI) centers or trauma centers which is currently functioning. Theses acute diseases needs personnel, infrastructure and expertise to diagnose and treat patients who require intensive medical and survival care, specialized tests, or interventional therapies. Post-cardiac arrest care is similar in that specialized personnel and infrastructures are needed and that systems in communities could provide appropriate care to appropriate patients.

The aim of this work was to provide evidence to complement strategies to improve OHCA outcome, including community support, equitable access to high quality prehospital emergency care and to utilize regional hospital resources systematically.

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6.2. Decrease the incidence of OHCA by controlling cardiovascular risk factor

In this study, diagnosis of HTN increased the incidence of OHCA and when not treated, the incidence increased to at least 3 times comparing with those not diagnosed with HTN. On the contrary, those with HTN with treatment, the incidence decreased to the level of those without HTN.

There are numerous of studies assessing association between HTN and CVD risk [26,27]. Considering that OHCA share majority of risk factors with CVD, the result is consistent with previous papers. However, the association with anti-hypertensive treatment and SCD is not completely known [70] especially comparing those with non-HTN diagnosed population. From this case-control study, we successfully assessed the effect of HTN treatment on incidence of OHCA and the incidence decrement was to the level of those of non-HTN diagnosed population.

One of reasonable explanation is that hypertension accounts for an estimated 54% of all strokes and 47% of all ischemic heart disease event, globally [115]. Therefor by controlling blood pressure could have reduced the mortality cause by major CVDs. Another is that HTN patients have more CVD risk factors to control. It is well known fact that non-adherence to medications is common and is associated with adverse outcomes [116]. Those who are in good adherence with anti-hypertension treatment are more likely to be adherent to other medications. This compliance could have reduced the overall risk of OHCA.

Ro et al. compared OHCA incidence risk by diabetes treatment [15]. Diabetes is another high prevalent cardiovascular risk factor which is known to end up with macro- and micro-complications. From Ro et al. study, the OHCA incidence was reduced when treated with oral hypoglycemic agent and this result supports this study in that by pharmacological treatment, the OHCA incidence is reduced. But not like my study, OHCA risk from Ro et al. study did not significantly reduced to non-diagnosed status. Difference of risks between diabetes and HTN needs further research.

Studies on blood cholesterol and cardiovascular risk showed similar results in that with lipid-lowering medications, 22% reduction of major cardiovascular events [117]. But the phenotypes of low-density lipoproteins or types of lipoprotein showed different results in cardiovascular risk that the interpretation of lipid profile and cardiac arrest risk is currently needs to be unveiled [118].

Further studies are needed to develop effective and individualized public interventions to identify and control not only HTN but also other CVD risk factors.

6.3. Strategies to increase the survival outcome of OHCA by modifiable determinants

The outcomes of OHCA are strongly related to the sequential performances of community, EMS and hospital care. In the perspective of prehospital efforts, early response by the public and the EMS should be delivered to patients to achieve increased survival and good neurologic outcome after OHCA [119]. In this study, EMS performing high quality CPR during patient transport and the importance of providing optimal care for post-ROSC patients were discussed. Mechanical chest compression device has been an attractive alternative for providing high quality CPR given the fatigue and safety of the provider during patient transport. In this study, the analysis based on hypothesis showed significant difference that if patient transport interval (PTI) was prolonged, the effect of MCPRD was significant compared with manual CPR. This result was not consistent with other major studies that showed no significant survival benefit of MCPRD.

The most explainable factor is the safety and fatigue issue for the EMS providers [95–98]. Where EMS system that termination of resuscitation is limited and all EMS-treated OHCAs are transported to hospitals, providing high-quality resuscitation during transportation is an issue. It is not easy to maintain an appropriate chest compression posture in a moving ambulance, while it accelerates, decelerated and abruptly stops. Also space at the back of the ambulance is too small for enough crews to participate in resuscitation and chest compression. In most Korean ambulances, at most two EMS providers can ride at the back during transport of OHCA patients, one manipulating the airway and one chest compressing.

The outcome of survival to admission did not significantly differ when PTI was 10 minutes or shorter. The key risk associated with the use of mechanical chest compression devices is the pause in chest compression associated with their deployment [120]. In the LINC randomized controlled trial of the use of mechanical chest compression devices in OHCA, a sub-study found that the median chest compression pause associated with device deployment was 36.0s (IQR 19.5-45.5) [121]. Such pauses are associated with a reduction in coronary pressure during the early part of a cardiac arrest and may therefor offset the potential benefit of improved chest compression delivery associated with devices [122]. In this study, the offset effect of mechanical chest compression device could have affect the survival until PTI 10 minutes. Until now in Korea, the EMS providers had the choice to use or not to use the mechanical chest compression device depending on the user's propensity. Appropriate and effective strategies in using mechanical chest compression devices should be implemented to maximize the outcome with available EMS resources.

6.4. Development of system-of-care to enhance survival outcome of OHCA

The management of patients following OHCA is more diverse as the patient frequently presents with multi-organ involvements [52]. Although various therapies provides evidence for survival after OHCA, these are often used insufficiently because of lack of resources, staff, infrastructure, experience and knowledge in the responsible medical systems [123]. The 5th link in the chain of survival after OHCA is increasingly being seen as the next real opportunity to improve long-term survival. In 2010, the American Heart Association published a policy statement supporting the idea of regional systems of care for OHCA [61]. Previous studies reported that admission of patients resuscitated after OHCA to tertiary centers is associated with lower mortality than in non-tertiary hospitals [124,125]. The recent 2020 guidelines from International Liaison Committee on Resuscitation recommended with low certainty that patients with OHCA should be transported to cardiac arrest centers [126,127].

This study categorized cardiac receiving centers in Gyeonggi province into two levels (Cardiac Resuscitation Center (CRC) vs others) according to the hospital resources and system. As a result, the neurologic outcome was significantly higher in when patients was initially transported to CRCs (AOR 2.41 (1.95-2.98)). As for those survived to admission, still the neurologic outcome was significantly higher in CRCs (AOR 1.57 (1.22-2.03)).

There are two main reasons for this outcome difference to consider. First, hospitals designated as CRCs receive more high volume of OHCA patients at ED. OHCA is a condition that requires a comprehensive, high quality and team-approach-based treatment. EDs with high CPR volumes showed a significant better outcomes for OHCA patients than those with low volumes [128,129]. Therefore, patients with OHCAs initially transported to CRCs are likely to receive comprehensive high quality CPR at ED.

Second, multidisciplinary optimal approach after ROSC enhances neurologic outcome after OHCA. The most common cause of OHCA in adults with ROSC is cardiovascular disease and especially coronary heart disease. Therefore, in patients with ROSC, assessment with 12-lead electrocardiography, echocardiography and acute coronary angiography should be done as soon as possible, regardless of ST-segment elevation [130]. Targeted temperature management has been the cornerstone for neuroprotection in patients resuscitated but comatose after OHCA for the past 15 years. It should be applied to all indicated patients after ROSC with each hospital's evidence based protocols. This study categorized CRC if coronary angiography is performed 24/7, if target temperature manage is provided with standard protocol and post-ROSC prognostication is measured. In this study, patients who received target temperature management, coronary perfusion or intensive cardiac care showed significant neurologic outcome benefit compared with those who did not received post-ROSC interventions. And moreover, each post-ROSC interventions were performed mostly at D-CRCs

In Korea, the EMS standard protocol is to transport patients with OHCA to the nearest CRC after at least 5 minutes of scene resuscitation. This protocol is being applied to all OHCA patients regardless of patient's resuscitative condition and regional hospital resources. The 2020 International Liaison Committee on Resuscitation statement noted that the evidence for CRCs among subgroups of patients remains inconclusive [131]. Although transport to a CRC improves outcomes, it remains unclear if EMS should bypass the nearest EDs in favor of CRCs [132,133]. Survival benefit caused by increase in the transport time by bypassing the nearest hospital should be evaluated. Also regional system-of-care including initial transport to a non-CRC with eventual inter-hospital transfer to a CRC could be considered. In means of considering optimal OHCA systems-of-care, the result of this study could be provided as one of evidences. Further studies are needed to establish regionalized cardiac arrest system-of-care that including designating CRCs considering regional EMS and hospital resources.

6.4. Limitations

This study has several limitations. One major limitation is that this study was not a controlled trial but a retrospective multicenter observational study, and no strict procedure for quality control was applied. The potential that a confounding issue might have exerted an impact is significant, as is the case with any retrospective evaluation of a data set. In addition, a rather large number of records were excluded. The characteristics of these excluded cases are unknown, which could have influenced the reported data.

Second, the EMS setting in Korea is under rapid development. The EMS system and post-cardiac arrest care is also evolving. This study is performed on the basic-to-intermediate EMS service level, and the rate of prehospital ROSC is extremely low. Therefore, this study cannot be generalized to advanced EMS systems. Third, the in-hospital OHCA management differs between the facilities and there is no national standard protocol. Although most EDs and hospitals would adhere to globally representative guidelines, such as American Heart Association CPR guideline, the heterogeneity on OHCA management could have affected the overall result.

Lastly, this study used two different OHCA registry data collected differently. Data from Korean Cardiac Arrest Resuscitation OHCA registry is prospectively collected data from over 30 hospitals, mostly tertiary hospitals. Data from Korean Centers for Disease Control and Prevention is a national data collected retrospectively based on medical record review. Although the analysis was performed on similar study population, OHCA presumed of cardiac etiology, the basic characteristics could differ between the data.

6.5. Conclusion

In this multicenter population-based OHCA study, individual, prehospital and hospital strategies to enhance survival were evaluated.

One of major cardiovascular risk factor, HTN, was an independent risk factor for OHCA presumed of cardiac etiology. The most high-risk population was the HTN diagnosed but without treatment group, and the magnitude of risk was observed to be reduced to the non-HTN-diagnosed population level when anti-hypertensive treatment was taken. Individualized and appropriate risk control management should be emphasized to reduce the burden of cardiovascular complications by HTN.

In EMS perspective, the use of mechanical chest compression device showed a significant survival benefit when patient transportation interval is prolonged. This study suggested that the use of mechanical chest compression device is assumed to be effective for providing high quality CPR and for enhancing safety of CPR providers during patient transport. Evaluation of optimal approach in training for the skillful use of MCPRD, such as shortening of the time interval for deployment, is needed to further implement this result.

In hospital perspective, regional CRC system significantly affected the neurologic outcome of patients with OHCA. Establishing an appropriate, suitable patient transport protocol for improving outcome considering regional hospital resources and EMS performance is necessary.

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Supplement Table 3-1. Demographic characteristics of OHCA cases and Community controls (before multiple imputation)

	Total		OHCA cases		Community controls		p
	N	%	N	%	N	%	
Total	7,899	100	2,633	100	5,266	100	
Gender							1.00
Female	2,307	29.2	769	29.2	1,538	29.2	
Male	5,592	70.8	1,864	70.8	3,728	70.8	
Age							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	1,509	19.1	503	19.1	1,006	19.1	
60-69	1,908	24.2	636	24.2	1,272	24.2	
70-80	3,039	38.5	1,013	38.5	2,026	38.5	
Median(IQR)	65	(53-73)	65	(54-74)	64	(53-73)	
Past Medical History							
Hypertension							<0.001
No HTN	4,674	59.2	1,457	55.3	3,217	61.1	
Diagnosed but no treatment	455	5.8	297	11.3	158	3.0	
Diagnosed and treatment	2,770	35.1	879	33.4	1891	35.9	
Diabetes Mellitus							<0.001
No DM	6,225	78.8	1,877	71.3	4,348	82.6	
Diagnosed but no treatment	305	3.9	210	8.0	95	1.8	
Diagnosed and treatment	1,369	17.3	546	20.7	823	15.6	
Health Behaviors							
Smoking							<0.001
Current smoker	1,525	19.3	399	15.2	1,126	21.4	
Ex-smoker	2,050	26.0	281	10.7	1,769	33.6	
Never smoker	3,169	40.1	798	30.3	2,371	45.0	
Unknown	1,155	14.6	1,155	43.9	0	0.0	
Alcohol consumption							<0.001

	Total		OHCA cases		Community controls		p
	N	%	N	%		N	%
Frequent	1,814	23.0	350	13.3	1,464	27.8	
Occasional	1,473	18.7	371	14.1	1,102	20.9	
Never	2,398	30.4	742	28.2	1,656	31.5	
Unknown	2,214	28.0	1,170	44.4	1,044	19.8	

HTN: hypertension; OHCA: out-of-hospital cardiac arrest; IQR: interquartile range; DM: diabetes mellitus;

Supplement Table 3-2. Effect of hypertension treatment for out-of-hospital cardiac arrest incidence in hypertension diagnosed patients

	OHCA cases (N)	Community controls (N)	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)
HTN treatment				
HTN without medication	297	202	1.00	1.00
HTN with medication	879	2,150	0.26 (0.21-0.31)	0.27 (0.21-0.34)

[a]Adjusted for DM diagnosis, smoking habit, alcohol consumption, age

OHCA: out-of-hospital cardiac arrest; HTN: hypertension; OR: odds ratio; CI: confidence interval

Supplement Table 4-1. Survival to discharge of subgroups by patient transport interval from unmatched cohort and PS matched cohorts

		Total		Manual CPR		MCPRD	
		N	%	N	%	N	%
Unmatched cohort		3,530	100.0	2,847	100.0	683	100.0
Survival to discharge	Patient transport interval	177	5.0	158	5.5	126	2.8
	0≤PTI≤10 mins.	96	4.8	79	5.4	9	2.0
	PTI over 10 mins.	81	5.3	237	5.7	60	3.8
Optimal PS cohort		2,049	100.0	1,366	100.0	683	100.0
Survival to discharge	Patient transport interval	70	3.4	51	3.7	19	2.8
	0≤PTI≤10 mins.	39	3.3	31	3.9	8	2.0
	PTI over 10 mins.	31	3.6	20	3.6	11	3.8
Greedy PS cohort		2,049	100.0	1,366	100.0	683	100.0
Survival to discharge	Patient transport interval	57	2.8	38	2.8	19	2.8
	0≤PTI≤10 mins.	39	2.5	22	2.7	8	2.0
	PTI over 10 mins.	31	3.2	16	2.9	11	3.8

Supplement Table 4-2. Multivariable logistic regression model analyzing the relationship between mechanical chest compression device and outcomes

		Survival to admission	
		Odds ratio	95% CI
Unmatched cohort	Model 1	0.49	0.30-0.79
	Model 2	0.81	0.48-1.36
Optimal PS cohort	Model 1	0.74	0.43-1.26
	Model 2	0.86	0.49-1.53
Greedy PS cohort	Model 1	1.00	0.57-1.75
	Model 2	0.98	0.55-1.75

Model 1: Unadjusted

Model 2: Adjusted for age, sex, hypertension, diabetes, witness status, public witnessed, bystander CPR, arrest place, initial ECG rhythm, prehospital EMS advanced airway, EMS defibrillation, EMS response time, scene resuscitation time.

Supplement Table 4-3. Model examining interactions of patient transport interval on the effect of mechanical chest compression device on outcomes

	Survival to admission	
	AOR[a]	95%CI
Unmatched cohort		
Patient transport interval		
0≤PTI≤10 mins.	0.67	0.31-1.42
PTI over 10 mins.	1.00	0.50-1.99
Optimal PS cohort		
Patient transport interval		
0≤PTI≤10 mins.	0.68	0.30-1.53
PTI over 10 mins.	1.16	0.52-2.58
Greedy PS cohort		
Patient transport interval		
0≤PTI≤10 mins.	0.87	0.37-2.02
PTI over 10 mins.	1.13	0.50-2.54

PTI, patient transport interval; PS, propensity score; AOR, adjusted odds ratio; CI, confidence interval; mins., minutes.

[a]Adjusted for age, gender, hypertension, diabetes, arrest place, witness, public witness, bystander CPR, initial ECG rhythm, prehospital advanced airway, EMS defibrillation. EMS response time, on scene time and interaction term (patient transport interval*mechanical chest compression device).

Supplement Table 5-1. Distribution of post-resuscitation care by potential risk factors in admitted OHCA patients

Risk factors	All OHCA		Target Temperature Management				Coronary Reperfusion				Intensive Cardiac Care (ECMO, ICD, PM, CABG)			
			No		Yes		No		Yes		No		Yes	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
All	1,681	100.0	1,476	100.0	205	100.0	1,325	100.0	356	100.0	1,554	100.0	127	100.0
Male	1,149	68.4	975	66.1	174	84.9	885	66.8	264	74.2	1,039	66.9	110	86.6
Age														
Median(IQR)	61	50-74	62	50-75	58	50-66	63	51-76	56	46-68	62	51-75	53	43-63
<15 years	32	1.9	32	2.2	0	0.0	28	2.1	4	1.1	31	2.0	1	0.8
15-64 years	905	53.8	761	51.6	144	70.2	674	50.9	231	64.9	804	51.7	101	79.5
Over 64 years	744	44.3	683	46.3	61	29.8	623	47.0	121	34.0	719	46.3	25	19.7
Comorbidities														
Heart disease	302	18.0	257	17.4	45	22.0	235	17.7	67	18.8	272	17.5	30	23.6
Hypertension	672	40.0	577	39.1	95	46.3	529	39.9	143	40.2	625	40.2	47	37.0
Diabetes Mellitus	443	26.4	400	27.1	43	21.0	356	26.9	87	24.4	418	26.9	25	19.7
Arrest place														
Public	384	22.8	294	19.9	90	43.9	287	21.7	97	27.3	334	21.5	50	39.4
Bystander CPR	937	55.7	805	54.5	132	64.4	751	56.7	186	52.3	849	54.6	88	69.3

Risk factors	All OHCA		Target Temperature Management				Coronary Reperfusion				Intensive Cardiac Care (ECMO, ICD, PM, CABG)			
			No		Yes		No		Yes		No		Yes	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Witness	1,134	67.5	971	65.8	163	79.5	891	67.3	243	68.3	1,033	66.5	101	79.5
Initial EMS ECG														
Shockable	509	30.3	358	24.3	151	73.7	359	27.1	150	42.1	410	26.4	99	78.0
EMS response intv														
Median (IQR)	7	5-9	7	5-9	8	5-11	7	5-9	7	6-10	7	5-10	7	6-9
<4 mins	90	5.4	77	5.2	13	6.3	74	5.6	16	4.5	84	5.4	6	4.7
4-8 mins	850	50.6	754	51.1	96	46.8	678	51.2	172	48.3	785	50.5	65	51.2
Over 8 mins	741	44.1	645	43.7	96	46.8	573	43.3	168	47.2	685	44.1	56	44.1
Scene resuscitation intv.														
Median (IQR)	8	5-11	8	5-11	8	5-11	8	5-11	8	6-12	8	5-11	9	6-12
<5 mins	327	19.5	279	18.9	48	23.4	260	19.6	67	18.8	303	19.5	24	18.9
5-15 mins	1,164	69.2	1,026	69.5	138	67.3	931	70.3	233	65.5	1,082	69.6	82	64.6
Over 15 mins	190	11.3	171	11.6	19	9.3	134	10.1	56	15.7	169	10.9	21	16.5
Patient transport intv.														

Risk factors	All OHCA		Target Temperature Management				Coronary Reperfusion				Intensive Cardiac Care (ECMO, ICD, PM, CABG)			
			No		Yes		No		Yes		No		Yes	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Median (IQR)														
<15 mins	1,465	87.2	1,295	87.7	170	82.9	1,179	89.0	286	80.3	1,363	87.7	102	80.3
15-30 mins	145	8.6	122	8.3	23	11.2	108	8.2	37	10.4	128	8.2	17	13.4
Over 30 mins	71	4.2	59	4.0	12	5.9	38	2.9	33	9.3	63	4.1	8	6.3
Admitted CRC														
P-CRC	656	39.0	607	41.1	49	23.9	606	45.7	50	14.0	637	41.0	19	15.0
D-CRC	1,025	61.0	869	58.9	156	76.1	719	54.3	306	86.0	917	59.0	108	85.0
Prehospital ROSC	453	27.0	345	23.4	108	52.7	329	24.8	124	34.8	388	25.0	65	51.2
Survival to discharge	646	38.4	511	34.6	135	65.9	453	34.2	193	54.2	572	36.8	74	58.3
Good neurologic outcome	335	19.9	239	16.2	96	46.8	238	18.0	97	27.3	271	17.4	64	50.4

OHCA, out-of-hospital cardiac arrest; ECMO, extracorporeal membrane oxygenation; ICD, implantable cardioverter defibrillator; PM, pacemaker; IQR, interquartile range; CPR, cardiopulmonary resuscitation; EMS, emergency medical service; ECG, electrocardiography; ROSC, return of spontaneous circulation.

Supplement Table 5-2. The effect of post-resuscitation interventions on the outcomes of OHCA with presumed of cardiac etiology of admitted patients (N=1,681)

	Total N	Outcome N (%)	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)[a]
All OHCA				
Target Temperature Management (TTM)				
Survival to discharge				
Non-TTM	1,476	511 (34.6%)	1	1
TTM	205	135 (65.9%)	3.64 (2.68-4.96)	1.50 (1.03-2.18)
Good neurologic outcome				
Non-TTM	1,476	239 (16.2%)	1	1
TTM	205	96 (46.8%)	4.56 (3.35-6.20)	1.71 (1.11-2.61)
Coronary Reperfusion (CR)				
Survival to discharge				
Non-CR	1,325	453 (34.2%)	1	1
CR	356	193 (54.2%)	2.28 (1.80-2.89)	2.37 (1.77-3.16)
Good neurologic outcome				
Non-CR	1,325	238 (18.0%)	1	1
CR	356	97 (27.3%)	1.71 (1.30-2.25)	1.41 (0.96-2.07)
Intensive Cardiac Care (ICC)				
Survival to discharge				
Non-ICC	1,554	572 (36.8%)	1	1
ICC	127	74 (58.3%)	2.40 (1.66-3.46)	0.82 (0.52-1.29)
Good neurologic outcome				
Non-ICC	1,554	271 (17.4%)	1	1
ICC	127	64 (50.4%)	4.81 (3.32-6.98)	2.00 (1.22-3.27)

ROCS, return of spontaneous circulation; OHCA, out-of-hospital cardiac arrest; OR, odds ratio; 95%CI, confidence interval.

[a]Adjusted for age, sex, comorbidities (heart disease, hypertension, diabetes mellitus), arrest place,

witness, bystander CPR, initial ECG, EMS response interval, scene resuscitation interval, patient transport interval, prehospital ROSC.

The TTM or CR or ICC was added to be adjusted for each final counterpart model (CR and ICC for analysis of non-TTM vs. TTM group, TTM and ICC for analysis of non-CR vs, CR group, TTM and CR for analysis of non-ICC vs. ICC group).

국문초록

심정지 생존율 향상을 위한 전략:
개인부터 치료시스템까지의 관점

배경

병원 밖 심정지는 갑작스럽게 심장박동이 중지되는 상태로 발생률이 높고 사망률이 높아 전세계적인 보건학적 문제로 대두되고 있다. 병원 밖 심정지의 질병 부담을 줄이기 위해서는 공중보건학, 응급의학 그리고 중환자 의학 등 여러 다양한 분야에서의 노력이 필수적이다. 이 연구의 목적은 1) 가장 흔히 발생하는 심혈관질환 위험인자인 고혈압과 그것의 치료가 병원 밖 심정지 발생에 미치는 영향을 확인하고, 2) 병원 밖 심정지 환자에게 적용된 기계식 가슴 압박 장치와 생존율과의 관계를 환자 이송 시간에 따라 분석하며, 마지막으로 3) 심정지 치료 센터가 병원 밖 심정지 환자의 신경학적인 예후에 미치는 영향을 파악하고자 하였다.

방법

본 연구는 연구 대상은 병원 밖 심정지 환자로 2015-2019까지의 한국 심정지 연구 컨소시움 데이터베이스를 활용하였다. 한국 심정지 연구 컨소시움 데이터베이스는 다기관에서 수집하는 심인성 병원 밖 심정지 데이터로 환자들의 일반적 특성, Utstein 가이드 라인에 근거한 정보, 병원 전 단계와 병원 단계 정보를 수집하여 구축된 자료이다.

첫번째 연구 목적을 위해서는 환자-대조군 분석을 시행하였으며 환자군은 한국 심정지 연구 컨소시움 데이터베이스에 2015-2017년까지 등록된 병원 밖 심정지 환자이며 대조군은 같은 기간 성별, 연령, 거주지역을 1:2로 매칭하여 지역사회 건강조사 데이터에서 추출하였다. 고혈압 진단받지 않은 군과 비교하여 고혈압 진단 및 치료여부에 따른 병원 밖 심정지 발생의 오즈비 산출을 하였으며 당뇨, 흡연 그리고 알코올 소비 행태 등을 보정한 다변수 조건부 로지스틱 회귀 분석을 시행하였다.

두번째 연구 목적은 2015-2019까지 수집된 한국 심정지 연구 컨소시움 데이터베이스를 이용하여 현장에서 환자 이송거리에 따른 기계식 흉부 압박 장치의 효과를 분석하였다. 노출변수는 기계식 압박장치 사용여부와 환자 이송거리이며 결과변수는 생존 입원이다. 성별, 연령, 병력, 초기 심전도 리듬, 목격여부, 일반인 심폐소생술 제공 여부, 발생 장소, 구급대 처치 및 반응 시간 등을 보정한 다변수 로지스틱 회귀 분석을 통하여 보정 오즈비와 95% 신뢰구간을 산출하였다. 환자 이송거리에 따른 기계식 압박장치 효과는 교호분석을 하였다. 환자 이송시간은 기존 논문에 근거하여 0-5분, 6-10분, 10분 이상으로 분류하였다. 선택 편향과 혼란 변수를 보정하기 위

해서 2가지 방법의 성향 점수 매칭을 시행하였다.

마지막 연구 목적은 경기도를 기반으로 시행되었으며 결과 산출을 위하여 질병관리청의 국가 급성 심장정지 데이터를 이용하였다. 경기응급의료지원센터에서 2015년 병원 밖 심정지 환자를 수용하는 병원 전체를 대상으로 병원 내 자원, 인력, 소생 후 치료 및 예후 평가 여부 그리고 시스템과 관련된 문항의 설문을 시행하였고 그 결과를 바탕으로 병원 밖 심정지 수용 병원을 최종 심정지 치료 병원과 초기 심정지 치료 병원으로 분류하였다. 노출 변수는 최종 심정지 치료 병원 여부 이며 결과 변수는 좋은 신경학적 결과로 뇌 기능 분류 척도 1 또는 2로 정의하였다. 최종 심정지 치료 병원과 초기 심정지 치료 병원의 좋은 신경학적인 결과는 다변수 로지스틱 회귀 분석을 통하여 보정된 오즈비와 95% 신뢰 구간으로 산출되었다.

결과

첫 번째 연구 목적을 위해서는 총 2,633건의 병원 밖 심정지 환자와 5,266건의 지역사회 대조군 매칭이 되었으며 당뇨, 흡연 그리고 음주 행태를 보정한 결과 고혈압 진단으로 인한 병원 밖 심정지 발생의 오즈비는 1.19 (1.07-1.32)이었다. 고혈압 치료를 받지 않은 군의 병원 밖 심정지 발생 오즈비는 3.41(2.72-4.24)이었으며 고혈압 치료를 받는 군의 병원 밖 심정지 발생 오즈비는 0.96 (0.86-1.08)이었다.

두번째 연구 목적을 위해 2015-2019년 구급대가 소생을 시도한 총 3,530명의 병원 밖 심정지 환자를 분석하였다. 환자 이송거리가 10분 초과인 경우 기계식 압박 장치 이용 생존 효과의 교호 작용의 오즈비가 1.49 (1.05-2.21)로 유의했다.

Optimal과 Greedy 성향 점수 매칭으로 각각 2,049건의 코호트가 추출되었다. 두 성향 점수 매칭된 코호트 모두 환자 이송거리가 10분 초과인 경우 기계식 흉부압박장치 사용에 의한 생존 효과의 교호 작용이 각각 오즈비 1.72 (1.24−2.46), 1.80 (1.28−2.53)으로 유의했다.

최종 심정지 치료 병원 분류를 위한 병원 자원 조사를 총 90개 병원 대상으로 실시하였으며 77개의 병원이 응답을 하였다. 병원 자원 조사 결과를 바탕으로 15개 병원을 최종 심정지 치료 병원으로 분류가 가능하였으며 그 외 병원을 초기 심정지 치료 병원으로 분류하였다. 2012−2014년 경기도 소개 병원으로 이송된 9,912건의 병원 밖 심정지 환자 중 4,036명의 환자가 병원 전에서 최종 심정지 치료 병원으로 이송되었다. 초기 심정지 치료 병원과 비교하여 최종 심정지 치료병원으로 이송된 환자들의 좋은 신경학적인 예후 오즈비는 2.10 (1.51−2.93)이었다. 생존 입원한 환자들만 추가 분석하였으며 최종 심정지 치료병원에 입원한 환자들의 좋은 신경학적인 예후 오즈비는 1.48 (1.02−2.14)로 분석되었다.

결론

본 연구는 다기관 병원 밖 심정지 환자를 대상으로 심정지 발생을 줄이고 생존률을 향상시키기 위한 개인수준, 병원 전 단계 그리고 치료시스템에서의 전략을 분석했다. 고혈압은 심인성 병원 전 심정지 발생에 독립적인 위험 요인이였으며 가장 높은 위험 인구군은 고혈압을 진단받았으나 치료를 받지 않은 군이었다. 기계식 압박 장치

의 사용은 현재까지 근거가 미약하지만 환자 이송 거리가 긴 경우 등의 특별한 상황에서는 생존 효과는 수기 압박보다 높았다. 최종 심정지 치료병원의 지정과 효과적인 병원 환자 이송 및 병원 간 이송 프로토콜 수립, 적용한다면 병원 밖 심정지 환자의 생존율을 높일 수 있을 것이다.

병원 밖 심정지 환자의 질병 부담을 줄이기 위해서는 심정지 발생 예방 및 환자의 생존율 향상을 위한 전략 개발 및 자원 배분이 매우 중요하다. 따라서 심정지 발생 및 생존을 위한 여러 단계에서의 위험요인 및 고위험군을 파악하여 예방 전략을 수립하고 현재 가용중인 자원을 효과적으로 사용할 수 있는 전략 수립 및 적용이 필수적이다.

주요어: 급성심정지, 예방, 생존율

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