Risk of Out-of-Hospital Cardiac Arrest in Aged Individuals in Relation to Cold Ambient Temperature

— A Report From North Tochigi Experience —

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Background: The impact of cold ambient temperature on out-of-hospital cardiac arrest (OHCA) in aged individuals caused by cardiovascular events in indoor environments has not been investigated sufficiently.

Methods and Results: We conducted a case-crossover study. The relationship between OHCA caused by cardiovascular events and exposure to minimum temperature $<0^{\circ}\text{C}$ was analyzed. Conditional logistic regression analysis was performed to estimate the odds ratios for the relationship between exposure to minimum temperature $<0^{\circ}\text{C}$ and the risk of OHCA. Between January 1, 2011, and December 31, 2015, a total of 1,452 cases of OHCA were documented, and patients were screened for enrollment. A total of 458 individuals were enrolled in this analysis, and were divided into 2 groups of 110 (elderly group: 65–74 years old) and 348 (aged group: ≥ 75 years old). The aged individuals had a significant increased risk of OHCA after exposure to minimum temperature $<0^{\circ}\text{C}$ (odds ratio [OR]: 1.528, 95% confidence interval [CI] 1.009–2.315, $P=0.045$). Cold ambient temperature was an especially significant increased risk for OHCA occurrence for males (OR: 1.997, 95% CI 1.036–3.773, $P=0.039$) and during winter (OR: 2.391, 95% CI 1.312–4.360, $P=0.004$) in the aged group.

Conclusions: Cold ambient temperature significantly affected aged individuals (≥ 75 years old) experiencing an OHCA caused by cardiovascular events in indoor environments.

Key Words: Aged; Cardiovascular events; Minimum temperature; Out-of-hospital cardiac arrest

Annually, out-of-hospital cardiac arrest (OHCA) occurs in over 120,000 individuals in Japan, and approximately 80% of these occur indoors.¹ Moreover, in approximately 70% of OHCA the subject is an elderly individual over 70 years old, and the survival rate with favorable neurological outcome is low.¹

Recently, an association between atmospheric conditions and the occurrence of OHCA was reported.² Furthermore, previous study has reported a relationship between colder temperature and the development of myocardial infarction.³ Other studies have also shown that ischemic and hemorrhagic stroke hospital admissions are associated with extreme cold temperatures, and that the incidence of type A acute aortic dissection is associated with lower minimum temperature.^{4,5}

However, with regard to elderly individuals, the rela-

tionship between OHCA caused by cardiovascular events in indoor environments and ambient temperature has not been investigated sufficiently. The objective of this study was to investigate this relationship in elderly individuals exposed to cold ambient temperatures. If we could predict temperature-related OHCA caused by cardiovascular events, it would lead to new preventive measures against sudden cardiac arrest.

Methods

This study was a case-crossover analysis to assess the occurrence of OHCA caused by cardiovascular events in elderly or aged individuals in indoor environments after exposure to cold ambient temperature.

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Study Population

Tochigi prefecture is one of the areas where the number of deaths from heart disease and stroke is high in Japan, and this public health problem has continued for more than 20 years.⁶ In this study, North Tochigi consisted of Nasushiobara city, Otawara city, Nasukarasuyama city, Nasu town and Nakagawa town, which had 269,988 residents (2010) in an area of 1,687 km².⁷ The demographic composition of North Tochigi was 238,512 persons (88.3%) <75 years old and 31,476 persons (11.7%) ≥75 years old, which was almost the same as that of all Japan.^{7,8} North Tochigi has a humid, subtropical climate and 4 distinct seasons. Although the annual mean temperature is 12.7°C, the temperature changes considerably between seasons, ranging from 22.9°C (daily mean temperature) in the summer (June–August) to 1.8°C in the winter (December–February).⁹

The present study enrolled individuals with OHCA caused by cardiovascular events while indoors and who were then transported to medical centers in North Tochigi. Cardiovascular event was defined as an event caused by heart disease, vascular disease or stroke. Heart disease was defined as myocardial ischemia and infarction, heart failure, or cardiac arrest resulting from arrhythmia. Vascular disease was defined as ruptured aortic aneurysm, aortic dissection or pulmonary embolism. Stroke was defined as intracerebral hemorrhage, cerebral infarction or subarachnoid hemorrhage. OHCA caused by cardiovascular events outdoors were excluded, because the majority (80%) of OHCA occur indoors in Japan,¹ and the number of deaths for consecutive 5 years among those aged ≥75 years old is predicted to increase from 3,529,540 in 2010 to 6,650,448 in 2035, an 88% increase.¹⁰ Therefore, we considered OHCA occurrence in older individuals while indoors might increase.

Study Design

We used a case-crossover design to analyze the relationship between short-term exposure to cold ambient temperature and OHCA caused by a cardiovascular event. A case-crossover design is well suited for investigating the effects of transient short-term exposure on the risk of acute

events.¹¹ The hazard period was defined as 24 h preceding the OHCA (**Figure 1**). We compared cold temperature exposure on the hazard period vs. cold temperature exposure on control periods. Control periods were chosen on the same day of the week as the day of OHCA occurrence to control for a potential confounding effect by day of week. Furthermore, 3 control periods were chosen: day -1 week, day -2 weeks and day -3 weeks before the day of OHCA occurrence to control for seasonal variation. Covariates such as age, sex, smoking, socioeconomic status and other risk factors were not considered to be confounders because they remain constant when comparing hazard and control periods.

Data Collection and Quality Control

We retrospectively collected data about OHCA individuals that were summarized information by the emergency medical services (EMS) personnel in collaborating with physicians in charge, following the worldwide standardized Utstein-style reporting guidelines for cardiac arrest. Furthermore, we investigated hospital medical records of 4 centers (International University of Health and Welfare Hospital, Nasu Red Cross Hospital, Kamma Memorial Hospital and Nasu Minami Hospital) to which almost all OHCA individuals in North Tochigi were transported. Eventually, we obtained precise data such as sex, age, cause of arrest, medical condition, time of the emergency call and scene of the OHCA.

Data of the mean, minimum and maximum temperatures were obtained from the Japan Meteorological Agency.⁹

Statistical Analysis

Conditional logistic regression analysis was performed to estimate the odds ratio (OR) and 95% confidence interval (CI) of OHCA caused by cardiovascular events in indoor environments associated with exposure to cold ambient temperature.

According to the Ministry of Health, Labour and Welfare, elderly persons aged 65–74 years are defined as young-old and those aged ≥75 years are defined as old-

Figure 2. Screening and enrollment. OHCA, out-of-hospital cardiac arrest.

Figure 3. Monthly distribution of the number of occurrences of OHCA (bar graphs) and the temperatures (line graphs). Maximum temperature (●) and minimum temperature (■) indicate the average temperatures of the days when OHCA occurred. OHCA, out-of-hospital cardiac arrest.

Table 1. Characteristics of Individuals Having OHCA Caused by a Cardiovascular Event

Characteristic	All individuals n=458	Elderly group (65–74 years) n=110	Aged group (≥75 years) n=348	P value
Age (years)	81.6±8.5	70.2±3.0	85.2±6.1	
Male, n (%)	241 (52.6)	73 (66.4)	168 (48.3)	0.001
Cause of arrest, n (%)				
Heart disease	371 (81.0)	87 (79.1)	284 (81.6)	0.557
Stroke	35 (7.6)	10 (9.1)	25 (7.2)	0.512
Vascular disease	52 (11.4)	13 (11.8)	39 (11.2)	0.860
Medical condition, n (%)				
Hypertension	161 (35.2)	26 (23.6)	135 (39.0)	0.003
Diabetes mellitus	68 (14.8)	26 (23.6)	42 (12.1)	0.003
History of heart disease	115 (25.1)	21 (19.1)	94 (27.1)	0.092
History of stroke	63 (13.8)	13 (11.8)	50 (14.4)	0.492
History of vascular disease	5 (1.1)	1 (0.9)	4 (1.2)	0.831
Season, n (%)				
Spring	101 (22.0)	19 (17.3)	82 (23.6)	0.165
Summer	75 (16.4)	26 (23.6)	49 (14.1)	0.018
Autumn	109 (23.8)	33 (30.0)	76 (21.8)	0.080
Winter	173 (37.8)	32 (29.1)	141 (40.5)	0.031
Temperature on the day of OHCA, °C				
Mean temperature	10.2±8.7	11.7±8.6	9.6±8.7	0.019
Minimum temperature	5.0±9.2	7.2±9.3	4.3±9.1	0.003
Maximum temperature	15.7±9.0	16.9±8.8	15.3±9.0	0.081

OHCA, out-of-hospital cardiac arrest.

old.¹² Therefore, we divided OHCA individuals into 2 groups by age: 65–74 years (elderly group) and ≥75 years (aged group).

The subgroup analyses were conducted by age (65–74 and ≥75 years), sex (male and female), cause of arrest (heart disease, stroke or vascular disease), and season (spring, autumn, and winter). The interaction between exposure to cold ambient temperature and subgroup variables was also assessed in a conditional logistic regression model.

Categorical variables are expressed as counts (%), and differences between groups were compared by χ^2 test. Continuous variables are expressed as mean and standard deviation, and nonnormally distributed continuous variables such as temperatures at OHCA occurrence were compared by the Mann-Whitney U-test. All test were 2-tailed, and $P < 0.05$ was considered statistically significant.

All statistical analyses were performed using SPSS statistical package version 23.0 (IBM Corp, Armonk, NY, USA).

Calendar time was used to define the 4 seasons (spring, March–May; summer, June–August; autumn, September–November; winter, December–February).

Ethics

This study was approved by the institutional review boards of all participating centers. According to the Personal Information Protection Law and the National Research Ethics Guidelines of Japan, the requirement to give informed consent was waived.

Results

Between January 1, 2011, and December 31, 2015, a total of 1,452 cases of OHCA were documented in North Tochigi,

and the patients were screened for enrollment. Of these, 994 individuals were excluded for the reasons shown in **Figure 2**. A total of 458 OHCA patients were enrolled in our analysis.

The monthly distribution of the number of OHCA occurrences and daily temperatures are shown in **Figure 3**. The number of OHCA occurrences caused by cardiovascular events mainly increased in winter (December–February) when the minimum temperature was $<0^{\circ}\text{C}$, but considerably decreased in summer (June–August).

The characteristics of the study population, the season and the temperature when an OHCA caused by a cardiovascular event occurred are shown in **Table 1**. The mean age was 81.6 ± 8.5 years and the proportion of males was 52.6%. OHCA caused by a cardiovascular event occurred in 110 (24.0%) in the elderly group and in 348 (76.0%) in the aged group. The proportions of men and of diabetes mellitus in the aged group were lower than in the elderly group, whereas the proportion of hypertension in the aged group was higher than in the elderly group. Also, OHCA caused by a cardiovascular event more frequently occurred in winter in the aged group. Furthermore, mean temperatures and minimum temperatures on the days when the OHCA occurred in the aged group were lower than in the elderly group.

Table 2 presents the ORs and their 95% CIs for the elderly and aged groups by conditional logistic regression analysis. In the aged group, a total of 154 individuals (44.3%) were exposed to a minimum temperature $<0^{\circ}\text{C}$ in the hazard period, and 423 individuals (40.5%) were exposed to a minimum temperature $<0^{\circ}\text{C}$ in the control period. A significant increased risk of OHCA occurrence caused by a cardiovascular event after exposure to minimum temperature $<0^{\circ}\text{C}$ was found in the aged group (OR: 1.528, 95% CI 1.009–2.315, $P = 0.045$). However, in the elderly group, a

Table 2. Relationship Between Exposure to Minimum Temperature $<0^{\circ}\text{C}$ and the Risk of OHCA Caused by a Cardiovascular Event

	Hazard period	Control periods	OR (95% CI)	P value
Elderly group (65–74 years)				
No. of individuals with exposure to MT $<0^{\circ}\text{C}$ /total no. (%)	31/110 (28.2)	98/330 (29.8)	0.770 (0.313–1.894)	0.569
Aged group (≥ 75 years)				
No. of individuals with exposure to MT $<0^{\circ}\text{C}$ /total no. (%)	154/348 (44.3)	423/1,044 (40.5)	1.528 (1.009–2.315)	0.045

CI, confidence interval; MT, minimum temperature; OHCA, out-of-hospital cardiac arrest; OR, odds ratio.

Figure 4. Subgroup analyses of effect of exposure to minimum temperature $<0^{\circ}\text{C}$ on out-of-hospital cardiac arrest (OHCA) occurrence caused by a cardiovascular event. For each subgroup analysis, conditional logistic regression analysis was performed to estimate odds ratio (OR) and 95% confidence interval (CI). The P values are for the interaction between the 2 groups and the subgroup variable.

total of 31 individuals (28.2%) were exposed to minimum temperature $<0^{\circ}\text{C}$ in the hazard period, and 98 individuals (29.8%) were exposed to minimum temperature $<0^{\circ}\text{C}$ in the control period. No significant association was found between OHCA occurrence caused by a cardiovascular event and exposure to minimum temperature $<0^{\circ}\text{C}$ in the elderly group (OR: 0.770, 95% CI 0.313–1.894, $P=0.569$).

A subgroup analysis was conducted to test for interaction among various variables for OHCA caused by a cardiovascular event after exposure to minimum temperature $<0^{\circ}\text{C}$

(Figure 4). Although a significant increased risk of OHCA occurrence was found in the aged group (Table 2), the interaction between age and OHCA occurrence was not significant ($P=0.413$), and the effect of cold ambient temperature on OHCA occurrence was consistent regardless of age. Also, none of the differences between subgroups, such as sex, cause of arrest, and season, were significant. However, in the aged group, there were significantly increased risks of OHCA occurrence for males (OR: 1.997, 95% CI 1.036–3.773, $P=0.039$) and during winter (OR:

2.391, 95% CI 1.312–4.360, $P=0.004$). Also, there was an increased risk of OHCA occurrence caused by heart disease (OR: 1.689, 95% CI 1.072–2.662, $P=0.024$) in the aged group.

Discussion

In this study, we found relationships between the occurrence of OHCA caused by cardiovascular events in indoor environments and exposure to cold ambient temperature in the aged group. We also found that the aged individuals had an increased risk of OHCA caused by heart disease after exposure to cold ambient temperature. Furthermore, this study demonstrated that in the aged group the relationship between OHCA caused by cardiovascular events and exposure to cold ambient temperature was strongest for males and during winter.

The relationship between temperatures and cardiovascular events has been well reported in previous studies.^{13–16} Another study showed that a 10°C decrease in daily mean temperature was associated with a 19% increase in hospital admissions for myocardial infarction in people older than 65 years.¹⁷ However, with respect to OHCA caused by cardiovascular events in individuals aged 75 years and older while indoors, no previous studies have clearly demonstrated that exposure to cold temperature influences the occurrence of OHCA. In our study, we demonstrated that the interaction between age and OHCA occurrence after exposure to minimum temperatures $<0^{\circ}\text{C}$ was not significant, but aged individuals who were exposed to minimum temperature $<0^{\circ}\text{C}$ had approximately 1.5-fold higher risk of OHCA caused by a cardiovascular event. Elderly individuals who were exposed to minimum temperatures $<0^{\circ}\text{C}$ did not have an increased risk of OHCA occurrence. For this reason, older individuals may have a higher risk of failure to maintain deep body temperature during exposure to a cold environment because of a higher level of skin thermal conduction.¹⁸

Several biological mechanisms may be involved in the association between cold temperature and cardiovascular events. Previous study reported that the mean systolic and diastolic blood pressures were highest during winter and lowest during summer.¹⁹ Cold temperature can induce increasing systemic vascular resistance with enhancing of the blood pressure, and consequently, myocardial oxygen supply decreases and may lead to myocardial ischemia. Also, cold temperature can induce sympathetic stimulation and increase cardiac workload, which negatively affects an individual with severe coronary stenosis and advanced heart failure beyond the point of compensation.^{3,16,20} Furthermore, cold temperature may contribute to increasing the risk of plaque rupture, thrombosis, and myocardial infarction death because of increasing sympathetic tone, blood pressure, vascular resistance, fibrinogen level, platelet count, certain clotting factors and blood viscosity.^{3,16,20}

Cold ambient temperature affected males more than females in the aged group. It may be related to males in all age groups having less adiponectin than females. Adiponectin is an adipose tissue-derived collagen-like protein that favorably affects many pathways that may have relevance to the development of atherosclerosis, inflammation, endothelial function and thrombogenesis. Previous study demonstrated that adiponectin is necessary for regulating thermogenesis, and adiponectin is required for maintaining body temperature during cold exposure.²¹ Additionally, adiponectin is associated with a lower risk of coronary

artery disease among women.²²

Study Limitations

First, we used considerably detailed data obtained from medical records investigation and the EMS inspection lists at each institutions. However, because we could not obtain data about atmospheric pressure and humidity, we could not analyze the association between atmospheric pressure and humidity and OHCA caused by cardiovascular events. Second, we did not take into consideration factors such as indoor temperatures when the OHCA occurred. Third, the number of individuals in this study might not enough, because we enrolled subjects in a limited area. Fourth, we were unable to evaluate the effect of short-term surgery related to the cardiovascular system, such as a percutaneous coronary intervention, because of the small number of OHCA patients who underwent surgery.

Conclusions

OHCA caused by cardiovascular events in aged individuals while indoors was influenced by prior exposure to cold ambient temperature.

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Conflict of Interest

None declared.

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