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Acute effects of ambient temperature on hypotension hospital visits: A time-series analysis in seven metropolitan cities of Korea from 2011 to 2015

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ABSTRACT

Background: Although blood pressure decreases in response to high ambient temperature, little is known about whether the ambient temperature can induce clinical hypotension events. Therefore, we conducted a time-series analysis to evaluate the association between hypotension hospital visits and ambient temperature in seven metropolitan cities of Korea.

Methods: We used the National Health Insurance Database, which contains the complete hospital visit data of the entire Korean population. We collected hospital visit data of seven metropolitan cities and linked the number of daily hypotension hospital visits to city-level ambient temperature, relative humidity, and air pollution levels from 2011 to 2015. Time-series analysis using the Poisson generalized additive model was conducted for each metropolitan city and we meta-analyzed the time-series results using the random effect model.

Results: There were 132,097 hospital visits for hypotension during our study period. A 1 degree Celsius (°C) increase in ambient temperature was associated with 1.1% increase in hospital visits for hypotension on lag day 0. Effects of ambient temperature lasted for 7 days, showing greater effects in shorter lag days. Subgroup analysis by sex and income groups showed similar results, but effects of ambient temperature on hypotension hospital visits was higher in the younger age group compared to older age group (aged over 65 years old). The results were unchanged when we applied cumulative lags, different case definitions, degrees of freedom per year, and multi-pollutant model adjusting for air pollutants.

Conclusions: Hospital visits for hypotension were positively associated with ambient temperature. Increased hypotension events in response to increased ambient temperature might explain the high cardiovascular mortality on hot days.

1. Introduction

Many epidemiologic studies have revealed the V- or U-shaped relationship between ambient temperature and risk of cardiovascular disease mortality and morbidity, showing increased risk in both low and high temperature range (Bai et al., 2018; Lee et al., 2017; Yang et al., 2015). One of the suggested mechanisms for the association in low temperature is increased blood pressure in response to low ambient temperature (Hanna, 1999; Hong et al., 2012). If external temperature decreases, the body maintains its optimal temperature by increasing the sympathetic tone and vasoconstriction mechanisms, in order to decrease the external dissipation of heat, which might increase blood pressure (Charach et al., 2013; Koeppen and Stanton, 2017). Because increased blood pressure may lead to damage and rupture of the blood vessels, increase in blood pressure in response to decreased ambient temperature may cause cardiovascular events (Halonen et al., 2011).

On the other hand, the variations in blood pressure may also explain the increased cardiovascular disease mortality and morbidity in the high ambient temperature range. If external temperature increases, the body attempts to dissipate heat by decreasing the thyroid gland activity, increasing sweating, and increasing peripheral blood circulation (Charach et al., 2013; Koeppen and Stanton, 2017). Consequently, systemic vasodilation, blood volume redistribution, and hypovolemia after exposure to high ambient temperature may result in decreased blood pressure. A recent meta-analysis showed that a 1 degree Celsius (°C) increase in ambient temperature was associated with 0.26 and 0.13 mmHg decrease in systolic and diastolic blood pressure, respectively (Wang et al., 2017). Rapid decrease in blood pressure may lead to

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decreased coronary or cerebral blood flow (Chou et al., 2015; Xin et al., 2016); therefore, hypotension in response to ambient temperature may cause cardiovascular disease via myocardial ischemia and cerebral hypo-perfusion mechanisms.

In summary, changes in blood pressure in response to ambient temperature may cause cardiovascular events. However, even with the plausible biological mechanisms, little is known about whether ambient temperature is associated with hypotension-related hospital visits. As shown in the recent meta-analysis, previous studies focused on the effects of ambient temperature on blood pressure level itself, instead of hypotension events (Wang et al., 2017). Although the incidence of orthostatic hypotension (defined as a reduction of blood pressure after standing) increases in summer (Charach et al., 2013; Medow et al., 2008; Naschitz and Rosner, 2007), the association between hypotension hospital visits and ambient temperature has been poorly quantified. In addition, studies evaluating possible association between ambient temperature and hypotension-related symptoms such as fainting, dizziness, and syncope are also limited. (Ganzeboom et al., 2003; Graham and Kenny, 2001; Hensel et al., 2017; McGeehin and Mirabelli, 2001).

Therefore, in this study, we conducted a time-series analysis to evaluate the possible association between ambient temperature and hypotension hospital visits using the Korea health insurance data. Our primary hypothesis was that an increase in ambient temperature may lead to signs and symptoms related to hypotension, which may result in increased hospital visits.

2. Materials and methods

2.1. Study population and hypotension hospital visit case definition

We used the customized National Health Insurance Database (NHID), which is a healthcare utilization database constructed based on the health insurance claims data. Because Korea has been using a single-payer medical insurance system since 2002, the National Health Insurance Service (NHIS) archives the entire Korean population's medical use data. To utilize the NHIS data for political and academic research purposes, the NHIS provides service to customize the NHID according to the researchers' requests. The customized NHID contains hospital utilization information (diagnostic codes, date of each hospital visit, admission days, and types of medicine used), general characteristics (age, sex, household income, types of insurance, and residential location), and health examination results of the Korean population.

To evaluate association between ambient temperature and hypotension events, we requested for the hospital utilization information, if one's primary or secondary diagnoses were coded as hypotension (*International Classification of Disease (ICD), 10th revision* codes; I95: hypotension, I95.0: idiopathic hypotension, I95.1: orthostatic hypotension, I95.8: other hypotension, and I95.9: hypotension, unspecified). We did not include I95.2: hypotension due to drugs as our hypotension cases with the hypothesis that use of antihypertensive drugs or physician prescription may not be associated with ambient temperature. We additionally conducted sensitivity analysis focusing on orthostatic hypotension, defined as a reduction in systolic blood pressure by at least 20 mmHg or diastolic blood pressure by at least 10 mmHg within 3 min of standing, due to the suggested association with ambient temperature in previous studies. To count the daily hospital visits due to hypotension and to avoid multiple hospital visits due to a single episode of disease, we regarded consecutive hypotension hospital visits in < 7 days as a single disease episode.

Our study participants were those who resided in the metropolitan cities (Seoul, Busan, Incheon, Daegu, Daejeon, Gwangju, and Ulsan) of Korea from 2011 to 2015 (Supplementary Fig. S1). Korea has seven metropolitan cities which works as the centers for politics, economy, and culture of the local regions. The size, population, economical indexes, and medical assessment indexes of the seven metropolitan cities are summarized in Supplementary Table S1. The economic and medical convenience indicators of each city showed similar pattern during our study period. The institutional review board of the Seoul National University Hospital, Republic of Korea, exempted this study from review because the data were de-identified (IRB no. 1708-056-876).

2.2. Weather and air pollution data

Hourly mean temperature and relative humidity data were obtained from the Korean Meteorological Administration. There is one meteorological monitoring station for each metropolitan city. We calculated the daily mean temperature and humidity using the hourly monitored data. For the sensitivity analysis using the multi-pollutant model, the hourly concentration of particulate matter < 10 μm in diameter (PM_{10}), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and ozone (O_3) were obtained from the National Institute of Environmental Research, Republic of Korea. There were 96 air pollution monitoring stations in year 2015 (Seoul: 25; Busan: 16; Incheon: 15; Daegu: 11; Daejeon: 8; Gwangju: 7; and Ulsan: 14). We calculated the daily mean concentration for each metropolitan city by averaging the daily mean values of monitoring stations located within the same metropolitan city. The descriptive statistics of ambient temperature, relative humidity, and air pollutants are summarized in Supplementary Table S2.

2.3. Statistical analysis

We conducted a time-series analysis using the Poisson generalized additive model and a meta-analysis, using the random effect models, to evaluate the association between daily ambient temperature and the number of daily hospital visits. The generalized additive model is a semi-parametric model that has been widely used in environmental epidemiology to evaluate association between short-term exposure and disease-specific hospital visits (Barnett and Dobson, 2010; Dominici et al., 2002; Han et al., 2017). To confirm a linear association between temperature and hypotension hospital visits, we visualized the association using a generalized additive model (GAM) in each metropolitan city at lag day 0 (Fig. 1 and Supplementary Fig. S2). After assuming linearity, we conducted a time-series analysis for each metropolitan city

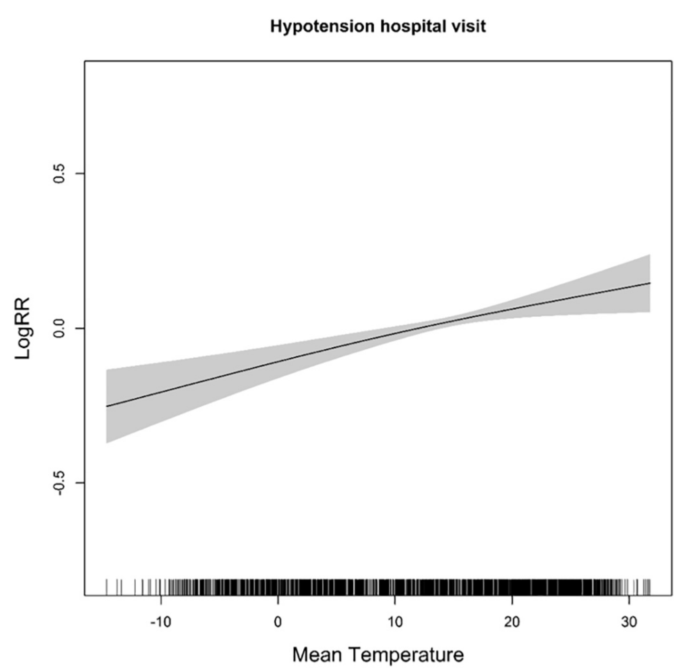

Fig. 1. Relationship between temperature and hypotension hospital visits (Seoul, Lag day 0).

and pooled the effect estimates using the random effect model meta-analysis. Detailed equations for the time series analysis are as follows:

$$\log(\textit{hypotension hospital visit}\ (lag)) = \alpha + \beta_1\,(\textit{ambient temperature}\ (lag)) + \beta_2\, s(\textit{relative humidity}\ (lag), 6\ knots) + \beta_3\, s(Time, 5\ df\ \textit{per year}) + \beta_4\,(\textit{Day of weeek}) + \beta_5\,(\textit{First day of month}) + \beta_6\,(\textit{Public holidays})$$

Blood pressure usually increase during the cold season and decrease in warm season (Modesti et al., 2018). Therefore, to adjust for seasonality and other time-varying confounders, we applied smooth function (s) of time with 5 degree of freedom per year. As measurable confounders, we adjusted for relative humidity and additionally adjusted for day of week, first day of month, and public holidays as health insurance data shows monthly or weekly claim patterns, and hospital visit patterns may be affected by holidays.

After analyzing the association between ambient temperature and daily number of hospital visits in each of the seven metropolitan cities, we conducted a random effect meta-analysis to estimate the effects of ambient temperature on hypotension hospital visits by pooling the time-series estimates of each city (exp (β_1)). Because we anticipated heterogeneity in the ambient temperature effects across each metropolitan city due to different city characteristics, we used random effect model instead of fixed effect model. The heterogeneity of effect estimates across metropolitan cities were assessed by I^2 values, and values over 50% were regarded as the estimates with significant heterogeneity.

As the effects of temperature on heart disease hospitalization are believed to occur within a few days of exposure (Schwartz et al., 2004), we examined the daily exposure to ambient temperature from lag 0 to 7 days before the hospital visits. Humidity and air pollutants in multi-pollutant models were lagged for the same number of days in our analysis. We additionally conducted subgroup analysis by sex, age groups (Age < 25, 25 ≤ Age < 45, 45 ≤ Age < 65, and 65 ≤ Age), and income groups. We used household income deciles to define low- (0–5) and high-income groups (6–10).

Several sensitivity analyses were conducted to evaluate the robustness of our study findings. First, we evaluated cumulative exposure by averaging temperature of 0 to 7 successive days preceding the hospital visits. Second, because blood pressure can be affected by air pollution levels (Hampel et al., 2011), we conducted multi-pollutant model analysis by additionally adjusting for NO_2, SO_2, CO, and PM_{10}. Third, we applied different case definitions by using only the primary diagnosis code or regarding consecutive hospital visits within 30 days as a single episode of disease. Fourth, we applied different degrees of freedom for time (4 and 6), which were used to adjust for unmeasured time varying confounders. Fifth, we conducted additional analysis by focusing on hospital visits with diagnosis of orthostatic hypotension. Finally, we conducted separate time-series analysis in each metropolitan city from lag day 0 to 30 to evaluate the delayed effects of ambient temperature on hypotension hospital visits in longer lag days.

The *gam* function of the *mgcv* package and *metagen* function of the *meta* package in the R software (R foundation for Statistical Computing, Vienna, Austria) were used to perform the time-series and meta-analyses, respectively. Results are presented as relative risks (RR) for daily hospital visits and 95% confidence intervals (CIs) per 1 °C increase in ambient temperature. All analyses were performed with SAS version 9.4 (SAS Inc., Cary, NC, USA) and R 3.4.3.

3. Results

Table 1 shows the descriptive statistics of the daily mean temperature during the study period (January 1, 2011 to December 31, 2015). The city with the highest mean temperatures were Busan (15.0 °C) and Daegu (14.7 °C) while the lowest mean temperatures were Incheon (12.4 °C) and Seoul (12.8 °C). Temperature statistics by each season is summarized in Supplementary Table S3. In summer season (from June to August), highest mean temperatures were observed in Daegu (25.8 °C) and Gwangju (25.3 °C). In winter season (from December to February), lowest mean temperatures were observed in Seoul (−1.4 °C) and Incheon (−0.9 °C).

Table 1
Descriptive data on daily mean temperature (°C) in 7 metropolitan cities of Korea during the study periods (January 1, 2011-December 31, 2015).

City	Daily mean temperature percentiles							
	Min	1st	25th	50th	75th	99th	Max	Mean
Seoul	−14.7	−9.0	3.3	14.3	22.8	29.1	31.8	12.8
Busan	−7.4	−2.3	7.8	16.3	21.9	29.1	30.3	15.0
Incheon	−12.4	−7.9	3.4	13.7	21.9	28.0	31.1	12.4
Daegu	−8.8	−4.1	5.9	15.7	23.0	31.0	32.7	14.7
Daejeon	−11.8	−7.2	4.0	14.2	22.5	29.3	31.9	13.2
Gwangju	−8.0	−4.3	5.4	15.3	22.7	29.8	31.5	14.2
Ulsan	−8.0	−3.1	6.5	15.5	21.7	30.4	33.0	14.4

Table 2 and Supplementary Table S4 summarized the number of hypotension hospital visit cases during the study period. Among 132,097 hypotension hospital visit cases, 59,208 (44.8%) and 72,889 (55.2%) occurred in men and women, respectively. By age groups, 16,588 (12.56%) and 21,014 (15.91%) cases occurred in younger age groups (Age < 25 and 25 ≤ Age < 45), respectively. In addition, 43,081 (32.61%) and 51,414 (38.92%) cases occurred in older age groups (45 ≤ Age < 65, and 65 ≤ Age), respectively. Overall, 58,353 (44.2%) and 73,744 (55.8) hospital visit cases occurred in low- (household income deciles, 0–5) and high-income (household income deciles, 6–10) groups, respectively.

The associations between temperature and hypotension hospital visits are presented in Table 3, Fig. 2 and Supplementary Fig. S3. By pooling the effect estimates across the seven metropolitan cities of Korea, a 1 °C increase in ambient temperature was associated with 1.1% increase in hypotension hospital visits in lag day 0. The effects of ambient temperature were greater in shorter lag days, showing decreasing pattern with the increase in lag days. By using cumulative lags, a 1 °C increase in mean ambient temperature during lag day 0 to 7 was associated with 1.9% increase in hypotension hospital visits.

The association was similar when we conducted stratified analysis by sex and income groups. However, temperature effects in the younger age groups were higher than the older age group (65 ≤ Age) (Table 3). In an age group under 25, a 1 °C increase in ambient temperature was associated with 2.0% increase in hypotension hospital visits in lag day 0. In a middle age group aged between 25 and 65, a 1 °C increase in ambient temperature was associated with 1.1 to 1.2% increase in hypotension hospital visits in lag day 0. However, in an elderly group (65 ≤ Age), a 1 °C increase in ambient temperature was associated with 0.6% increase in hypotension hospital visits in lag day 0.

The results were unchanged when we applied different case definitions (using primary diagnostic code for hypotension case definition or defining consecutive medical service usage within 30 days as a single episode), degrees of freedom per year (4 and 6), and in multi-pollutant model adjusted for air pollutants (Supplementary Table S5). With the individual time-series analysis for longer lag days (from lag day 0 to 30) in each metropolitan city, effects of ambient temperature on hypotension hospital visits lasted for 7 days, showing null association in longer lag days (Supplementary Fig. S4). By focusing on orthostatic hypotension diagnosed cases, we found 70,098 hospital visits during the study period. By pooling effect estimates across the seven metropolitan cities of Korea, a 1 °C increase in ambient temperature was associated with 0.9% increase in orthostatic hypotension hospital visits in lag day 0. The results with orthostatic hypotension were similar to our main analysis with the entire hypotension hospital visits (Supplementary

Table 2
Number of hypotension hospital visits during the study periods (January 1, 2011-December 31, 2015).

	Seoul	Busan	Incheon	Daegu	Daejeon	Gwangju	Ulsan	Total
Number of hospital visits	58,887	24,709	15,310	15,391	6132	8118	3550	132,097
By sex								
Men (%)	24,338 (41.33)	11,619 (47.02)	6764 (44.18)	8174 (53.11)	2926 (47.72)	3857 (47.51)	1530 (43.10)	59,208 (44.82)
Women (%)	34,549 (58.67)	13,090 (52.98)	8546 (55.82)	7217 (46.89)	3206 (52.28)	4261 (52.49)	2020 (56.90)	72,889 (55.18)
By age group								
Age < 25 (%)	7650 (12.99)	2472 (10.00)	1983 (12.95)	1514 (9.84)	946 (15.43)	1540 (18.97)	483 (13.61)	16,588 (12.56)
25 ≤ Age < 45 (%)	11,472 (19.48)	3035 (12.28)	2194 (14.33)	1774 (11.53)	950 (15.49)	1070 (13.18)	519 (14.62)	21,014 (15.91)
45 ≤ Age < 65 (%)	18,509 (31.43)	9201 (37.24)	4987 (32.57)	4681 (30.41)	2016 (32.88)	2523 (31.08)	1164 (32.79)	43,081 (32.61)
65 ≤ Age (%)	21,256 (36.10)	10,001 (40.48)	6146 (40.14)	7422 (48.22)	2220 (36.20)	2985 (36.77)	1384 (38.99)	51,414 (38.92)
By income group								
Low-income (%)	24,683 (41.92)	11,635 (47.09)	7331 (47.88)	6923 (44.98)	2802 (45.69)	3626 (44.67)	1353 (38.11)	58,353 (44.17)
High-income (%)	34,204 (58.08)	13,074 (52.91)	7979 (52.12)	8468 (55.02)	3330 (54.31)	4492 (55.33)	2197 (61.89)	73,744 (55.83)

Table S6).

4. Discussion

In this time series study, we found an association between ambient temperature and hospital visits for hypotension. By using the complete hospital visit data of the entire population residing in seven metropolitan cities of Korea (from 2011 to 2015), a 1 °C increase in ambient temperature in lag day 0 was associated with 1.1% increase in hypotension hospital visits. By using cumulative lags, a 1 °C increase in mean ambient temperature during lag day 0 to 7 was associated with 1.9% increase in hypotension hospital visits. Effects of ambient temperature lasted for around 7 days, showing greater effects in shorter lag days. Diverse subgroup and sensitivity analyses showed the robustness of our study findings.

Hypotension refers to a state when blood pressure is lower than the normal expected value for the individual. Hypotension usually arises as a result of hypovolemia, impaired cardiac output, and impaired peripheral vasoconstriction. Because we extracted hypotension cases using primary and secondary diagnostic codes, it is difficult to speculate that cardiogenic causes such as acute coronary syndrome, heart failure, and obstruction to cardiac filling were primarily diagnosed and coded as hypotension instead of the disease itself. Therefore, rather than cardiogenic origin, hypovolemia and impaired vasoconstriction which arises from loss of fluid and vasodilation in response to increase in ambient temperature might be the reasonable mechanism to explain the association between ambient temperature and hospital visits for hypotension (Proppe, 1987; Rosenthal, 2004).

In our study, the majority of hypotension cases were coded as orthostatic or unspecified hypotension. Orthostatic hypotension patients experience increased events in summer and are instructed to avoid hot environment which may cause peripheral vasodilation (Lahrmann et al., 2006). In addition, vasodilation during heat stress may also reduce sensitivity of baroreflex response (Charach et al., 2013). Dizziness and syncope, the characteristic symptoms of orthostatic hypotension (Lahrmann et al., 2006), were also associated with ambient temperature. Patients with nausea, dizziness, and fainting increased during the heat wave days and nearly 30% of patients with prior syncope experience mentioned warm environment as one of the triggers for their syncope event (Ganzeboom et al., 2003; Graham and Kenny, 2001; McGeehin and Mirabelli, 2001). Seasonality of orthostatic hypotension events and increased hospital visits for nausea, dizziness, and fainting during the hot days supports our study findings.

In addition, many epidemiological studies have shown negative associations between ambient temperature and blood pressure. By analyzing 1897 patients referred to the hypertension unit in Italy, a 1 °C increase in personal level air temperature was associated with 0.14 mmHg decrease in systolic blood pressure (Modesti et al., 2013). With the repeated measurement of 55,567 adults who visited a health care clinic in Korea, a 1 °C increase in ambient temperature was associated with 0.19 and 0.12 mmHg decrease in systolic and diastolic blood pressure (Hong et al., 2012). By analyzing 11,434 participants from 24 populations in 16 countries with different climate conditions, a 1 °C increase in ambient temperature was associated with 0.19 mmHg decrease in systolic blood pressure (Barnett et al., 2007). Recent meta-analysis with 6 longitudinal studies and 8 cross-sectional studies, a 1 °C increase in temperature was associated with 0.26 and 0.13 mmHg decrease in systolic and diastolic blood pressure (Wang et al., 2017). Findings from our study additionally suggest that increase in ambient temperature is associated with not only decrease in blood pressure, but also the clinical symptoms, which leads to hospital visits and diagnosis with hypotension.

Several studies showed increase in blood pressure in winter and decrease in summer, suggesting seasonal patterns (Charach et al., 2013; Modesti et al., 2018). By inserting both temperature and seasonal factors (daylight hours) in the model, one study suggested that blood pressure is independently affected by the personal-level environmental temperature and seasonality (Modesti et al., 2013). Because lifestyle factors such as dietary habits and exercise may change with season, seasonal effects should be adjusted in studies evaluating the possible association between temperature and blood pressure. Therefore, we used smoothing function of time in our time-series models to adjust for seasonal patterns and unmeasured time-varying confounders, thereby focusing on the acute effects of temperature on hospital visits for hypotension.

Many epidemiological studies suggested the V- or U-shaped relationship between ambient temperature and adverse health outcomes, showing increased risk in both low and high temperature range. Most of the cardiovascular disease mortality increases in high ambient temperature due to the loss of thermoregulation and fluid and electrolyte balance (Gasparrini et al., 2015; Keatinge et al., 1986). In case of cold ambient temperature, excessive cardiovascular stress and disrupted immune mechanisms may cause cold-related cardiovascular and respiratory disease mortalities (Eccles, 2002; Keatinge et al., 1984). The piecewise linear regression with flexion point may be applicable for analysis of the non-linear relationship. However, we assumed that a linear relationship exist between ambient temperature and risk of hypotension hospital visits based on the biological mechanism.

Hypotension is associated with blood pressure level itself, which decreases in hot ambient temperature and increases in cold ambient temperature. Therefore, although the risk of hypotension hospital visits increases in hot environment, the risk may not increase in cold environment. Because blood pressure actually increases in cold environment, risk of hypotension hospital visits may decrease in cold ambient temperature. Therefore, we assumed linear relationship between ambient temperature and risk of hypotension hospital visits and confirmed the pattern using GAM plot (Fig. 1 and Supplementary Fig. S2), before conducting our main analysis.

In subgroup analysis, the effect of ambient temperature on hypotension hospital visits was higher in younger age (Age < 25,

Table 3
Association between daily mean temperature and hypotension hospital visits based on lag days [Pooled RR (95%CI) per 1 °C increase in ambient temperature].

Lag	Total	Men	Women	Age < 25	25 ≤ Age < 45	45 ≤ Age < 65	65 ≤ Age	Low-income	High-income
0	1.011 (1.007-1.014)	1.010 (1.007-1.013)	1.011 (1.007-1.016)	1.020 (1.014-1.026)	1.012 (1.006-1.017)	1.011 (1.006-1.017)	1.006 (1.003-1.010)	1.009 (1.006-1.013)	1.011 (1.007-1.016) [b]
1	1.010 (1.006-1.014) [b]	1.009 (1.005-1.014)	1.011 (1.005-1.017) [b]	1.020 (1.013-1.027)	1.007 (1.001-1.012)	1.010 (1.005-1.016)	1.005 (1.001-1.008)	1.011 (1.005-1.017) [b]	1.009 (1.005-1.014)
2	1.009 (1.005-1.013) [b]	1.007 (1.001-1.014) [b]	1.010 (1.004-1.016) [b]	1.020 (1.014-1.027)	1.002 (0.996-1.007)	1.010 (1.004-1.017) [b]	1.002 (0.999-1.006)	1.008 (1.003-1.014) [b]	1.008 (1.003-1.013) [b]
3	1.007 (1.004-1.010)	1.005 (1.001-1.009)	1.008 (1.005-1.01)	1.014 (1.007-1.02)	1.004 (0.999-1.009)	1.008 (1.004-1.012)	1.003 (0.999-1.007)	1.007 (1.003-1.011)	1.008 (1.003-1.012)
4	1.006 (1.004-1.008)	1.005 (1.001-1.009)	1.008 (1.005-1.011)	1.011 (1.004-1.018)	1.007 (1.002-1.012)	1.008 (1.004-1.011)	1.003 (0.998-1.009)	1.007 (1.004-1.010)	1.006 (1.003-1.008)
5	1.006 (1.003-1.008)	1.007 (1.002-1.012)	1.005 (1.002-1.008)	1.016 (1.005-1.028) [b]	1.003 (0.998-1.008)	1.006 (1.001-1.012)	1.004 (0.999-1.010)	1.005 (1.002-1.008)	1.007 (1.003-1.010)
6	1.004 (1.000-1.008) [b]	1.005 (1.000-1.009)	1.003 (0.998-1.007)	1.011 (1.002-1.019)	1.001 (0.996-1.006)	1.003 (0.996-1.010) [b]	1.001 (0.997-1.006)	1.002 (0.999-1.005)	1.005 (0.999-1.010) [b]
7	1.002 (0.999-1.005)	1.002 (0.998-1.007)	1.002 (0.999-1.005)	1.010 (1.003-1.018)	1.000 (0.992-1.008)	1.003 (0.999-1.007)	0.999 (0.995-1.003)	1.000 (0.997-1.003)	1.004 (1.000-1.008)
0-7[a][b]	1.019 (1.012-1.026) [b]	1.017 (1.007-1.028) [b]	1.018 (1.011-1.026)	1.044 (1.026-1.062) [b]	1.012 (1.003-1.020)	1.018 (1.011-1.025)	1.009 (1.001-1.018)	1.016 (1.009-1.023)	1.019 (1.010-1.029) [b]

[a] Cumulative exposure by averaging temperature of 0–7 successive days preceding the hospital visits.
[b] I^2 values over than 50%.

25 ≤ Age < 45, and 45 ≤ Age < 65) groups compared to elderly group (65 ≤ Age). This was an unexpected result regarding the fact that elderlies are more vulnerable to heat stress (Donaldson et al., 2003). However, cutaneous vasodilation and vasoconstriction functions in response to external temperature are impaired with aging (Holowatz and Kenney, 2010). Therefore, diminished skin blood flow under the heat stress in elderly population may be the one reason for elderlies to maintain constant blood pressure level in the hot ambient temperature. In addition, blood pressure continuously increases with age due to the structural changes of large arteries (Pinto, 2007). Therefore, baseline blood pressure of the elderlies tend to be higher than younger population, which gives more reservoir capacity till the hypotension related symptoms to be developed by the effects of high ambient temperature.

In our study, over 60% of the entire hypotension cases occurred in the young population (< 65 years). It is also plausible that older population might have shown more severe clinical symptoms in response to elevated temperature and decreased blood pressure, and been diagnosed as other diseases or symptoms instead of hypotension. However, further analysis with refined age group categories with diverse past medical history or underlying chronic diseases are needed to evaluate the vulnerable population regarding ambient temperature effects on hypotension hospital visits.

Several limitations need to be indicated for this study. First, potential misclassification might have arisen from the use of fixed monitoring station values. We assigned daily temperature to each participant using the monitoring results from the monitoring station within each metropolitan city. However, this non-differential misclassification might have shifted our estimates toward the null. Secondly, due to the methodological approach and the dataset used in our analysis, we were unable to adjust for personal characteristics such as body mass index, smoking, and drinking status, which might have affected our study findings. Although the distribution of these individual factors may not change from day to day and cannot be regarded as confounders in the time series study (Bhaskaran et al., 2013), future longitudinal studies with repeated measurements are needed to confirm our study findings. Thirdly, because our study was conducted in seven metropolitan cities of Korea, our findings need to be validated in other environmental settings (rural) or countries with different economic and health status. In addition, as presented in Supplementary Table S1, different city characteristics may result in heterogeneous effect estimates of ambient temperature on hypotension hospital visits. To partially solve this problem, we used random effects model meta-analysis allowing for heterogeneity of the effect estimates. However, caution in the interpretation is needed for the pooled estimates, which showed significant heterogeneities (I^2 value over 50%). Fourth, because we extracted hospital use data from the NHID using hypotension ICD-10 code, we were unable to assess hospital use data for other disease outcomes. Population with chronic disease such as cardiovascular disease or diabetes might be more sensitive to the ambient temperature, but we were unable to confirm past medical history of each hypotension patient. Lastly, we were only able to focus on ambient temperature because information on indoor temperature was not available. Because many people use air conditioning nowadays, ambient temperature itself may not sufficiently explain the actual temperature that individuals are exposed to. Therefore, studies using personalized monitoring devices for temperature are needed in the future.

5. Conclusion

Although many studies showed negative association between temperature and blood pressure, our study is the first to show the association between ambient temperature and hypotension hospital visits in a large population.

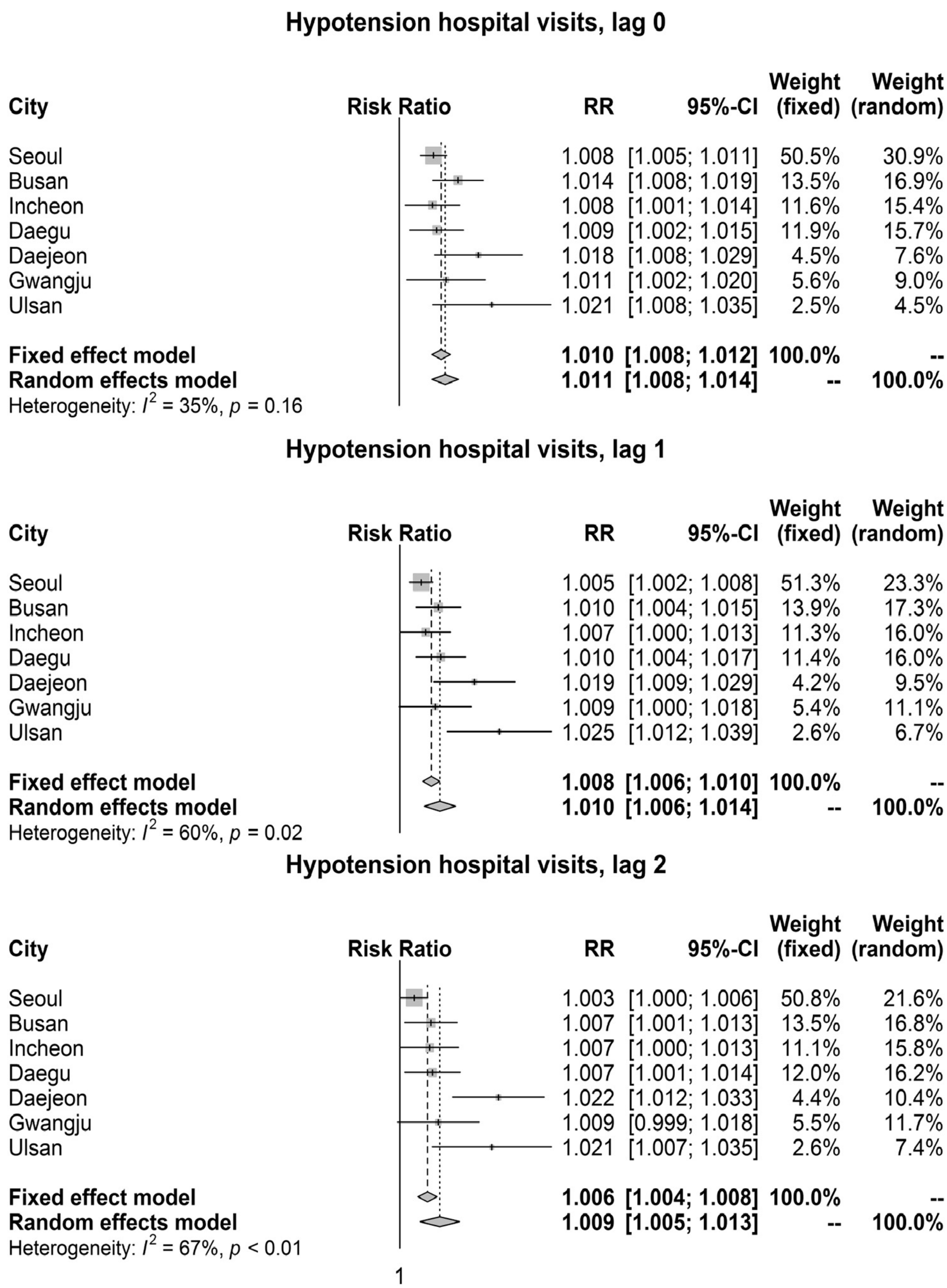

Fig. 2. Pooled association between ambient temperature and hypotension hospital visits in 7 metropolitan cities of Korea (Lag day 0 to 2) [Pooled RR (95%CI) per 1 °C increase in ambient temperature].

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Declaration of Competing Interest

None.

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This study used the customized Health Insurance Data based on health insurance claims data in Korea. The aim and conclusion of this study are irrelevant to the National Health Insurance Service, Republic of Korea. The research number of this study is NHIS-2017-1-256.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2019.104941.

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