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CVD hospitalization risks associated with temperature change between neighboring days in South Korea (2002 ~ 2019)

Pehlivan, Nazife* · Kim, Ejin** · Song, Insung* and Kim, Ho***†

*Ph. D. Student, Dept. of Public Health Sciences, Graduate School of Public Health, Seoul National University, Seoul, Korea
**Research Professor, Institute of Health and Environment, Graduate School of Public Health, Seoul National University, Seoul, Korea
***Professor, Dept. of Public Health Sciences, Graduate School of Public Health, Seoul National University, Seoul, Korea

ABSTRACT

There is a growing literature on the impacts of temperature change between neighboring days (TCN) on human health; however, the direction and magnitude of such impacts remain unclear. TCN is defined as the previous day's mean temperature subtracted from the current day's mean temperature. We investigated year-round and season-stratified associations between TCN and total, sex-specific, and age-specific cardiovascular disease (CVD) hospital admissions. We performed two-stage analysis utilizing nationwide CVD hospital admission data (N=4,859,112) from 2002 to 2019 using distributed lag non-linear model, DLNM, in the first stage and meta-regression in the second stage. A positive TCN was associated with elevated CVD hospital admission risk accounting for 192,117 (182,781; 197,192) hospitalizations during the study period. Season-stratified analyses revealed increased risk associated with positive TCN in both cold (November to April) and hot (May to October) seasons. Risk was more pronounced in the cold season (total relative risk [RR]: 1.70 [1.56, 1.86]) with no significant sex-related differences (RR: 1.81 [1.60, 2.06] vs. 1.59 [1.43, 1.78], respectively). Age-specific risk in the cold season was significantly higher among those aged 65 and older (RR: 2.52 [2.25, 2.81]) compared to those aged under 65 (RR: 0.95 [0.84, 1.08]). This study obtained the total, sex-specific, and age-specific CVD hospitalization risk associated with TCN year-round as well as specific to the hot and cold seasons. People over the age of 65 years were the most vulnerable to day-to-day temperature rise in the cold season. Season-specific policies targeting vulnerable populations may prevent adverse health outcomes of temperature fluctuations. This concern will become increasingly important as climate change proceeds.

Key words: Temperature Change between Neighboring Days, Cardiovascular Disease, Hospitalization, Sex-Specific, Age-Specific, Season-Stratified

1. Introduction

Climate change is causing increasingly extreme weather events that can lead to severe health problems especially among people with underlying health issues. Short-term temperature fluctuations, indicator of unstable weather, have been receiving growing attention as a public health risk factor (IPCC, 2023), however; there is still a smaller literature about such fluctuations compared to the effects of absolute non-optimum temperatures (Guo et al., 2021; Lei et al., 2021; Vicedo-Cabrera et al., 2016; Yang et al., 2021).

Temperature change between neighboring days (TCN) which captures the difference between mean temperature of two neighboring days is a commonly used index of short-term temperature change (Wu et al., 2022; Zhan et al., 2017). Although studies have investigated the

Lead authors : Pehlivan, Nazife and Kim, Ejin
†Corresponding author : hokim@snu.ac.kr (Seoul National University, 1 Kwanak-ro Kwanak-gu, Seoul 08826, Korea. Tel. +82-2-880-2702)
ORCID Pehlivan, Nazife 0009-0005-6718-1883 Song, Insung 0000-0003-3394-8829 Kim, Ejin 0000-0001-6293-785X Kim, Ho 0000-0001-7472-3752

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relationship between increased disease burden and a wider diurnal temperature change or increased temperature variability at regional, national, and global levels (Byun et al., 2020; Cheng et al., 2019; Wu et al., 2022), the current evidence about the health effects of TCN is inconsistent (Guo et al., 2011; Huang et al., 2023; Lin et al., 2013; Ma et al., 2020; Zha et al., 2022; Zhan et al., 2017). For instance, while a nationwide study in the United States suggested that positive TCN (a temperature rise between 2 adjacent days) increased the risk of death from respiratory and cardiovascular diseases in each season (Zhan et al., 2017), a study in Qingyang city located in Northwest China found the opposite (Zha et al., 2022). Therefore, there is a need to conduct additional studies on the associations between TCN and human health to better understand this issue.

TCN is defined as the previous day's mean temperature subtracted from the current day's mean temperature (Huang et al., 2023; Lei et al., 2021; Lin et al., 2013; Ma et al., 2020; Zha et al., 2022; Zhan et al., 2017), therefore; negative TCN represents temperature decrease and positive TCN represents temperature increase between neighboring days.

2. Material and Methods

2.1. Data Collection

2.1.1. Hospitalization Data

Claims for hospitalization through the emergency room were identified as subjects using tailored data supplied by the National Health Insurance Corporation. Patients diagnosed with ICD-10 codes I00–I99 as either the primary or secondary condition were classified as having cardiovascular disease. To mitigate the characteristics of the claims data, daily emergency room hospitalizations were quantified by establishing hospitalization episodes that considered various intervals of non-medical treatment (within 1, 3, 7, 14, 21, and 32 days). We defined a single hospitalization episode for claims within a 14-day period, quantified daily emergency department admissions, and then aggregated daily counts by district levels.

2.1.2. Daily Temperature Data

We collected temperature data from Google Earth Engine (GEE) from hourly records of "2 m temperature" ERA-5 LAND hourly. ERA-5 "2 m temperature" is the temperature of air at 2 meters above surface of the Earth provided in units of Kelvin. 2m temperature is calculated by interpolating between the lowest model level and the Earth's surface, taking account of the atmospheric conditions (ERA5 hourly data on single levels from 1940 to present (copernicus.eu)). Daily mean temperature (tmean) is the 24-hour mean of hourly records. We converted the temperature data to degrees Celsius (°C) by subtracting 273.15. We calculated the TCN by subtracting the daily mean temperature of the previous day from the daily mean temperature of the current day.

2.2. Statistical Analysis

We performed a two-stage analysis and in the first stage a distributed lag non-linear model (DLNM) combined with quasi-Poisson generalized additive regression model (GAM) was used to explore overall and lagged effects between TCN and CVD hospitalizations (Gasparrini et al., 2010) since nonlinear and lagged relations between CVD and TCN have been found previously (Cheng et al., 2014; Huang et al., 2023; Lin et al., 2013; Shi et al., 2021; Zhan et al., 2017) and CVD daily hospital admissions are generally considered as Poisson distribution due to low probability. A TCN of 0 °C was used as a reference for calculating relative risks (RRs) (Zhan et al. 2017). The model is as follows:

$$Y_{i,t} \sim Poisson(\mu_{i,t})$$

$$Log(\mu_{i,t}) = \alpha + \beta(TCN_{i,t}, l) + ns(tmean_{i,t},\ df) + ns(time,\ \#\ years \times df) + dow_t \quad (1)$$

where t is the observation date; i is the district and $\mu_{i,t}$ is the expected daily CVD hospitalizations in district i on day t; log means the logarithmic form of ; indicates the interception; is the "cross-basis" matrix of TCN in DLNM; denotes the lag days where maximum lag is 21 days in accordance with previous literature (Cheng et al., 2014; Zhan et al., 2017), indicates the vector of the coefficients for ; *ns* is the natural cubic splines for non-linear variables; represents the degree of freedom; tmeani,t represents average temperature (full year and hot-season df = 2; cold-season df = 4); time is the variable to control the long-term trend and seasonality (df = 1) confounding; is the categorical variable indicates the day of the week. Model specifications are based on the minimum AIC values.

The reference of TCN was set to be 0°C (50^{th} percentile) which also separated the TCN to be mean temperature dropping/rising between neighboring days. Stratified analyses were performed on sex (male vs. female) and age (< 65 vs. ≥ 65).

In the second stage, we conducted meta-regression where we controlled district-specific covariates which are average of daily mean temperatures over the study period by district, range of daily mean temperatures over the study period by district and gross regional domestic product (GRDP). Finally, we calculated the attributable fractions (AF) and attributable numbers (AN) of CVD hospital admissions and their 95% empirical confidence intervals (eCI) formulated by the following method (Gasparrini et al., 2015):

$$\mathrm{AF} = 1 - \exp\left(-\sum_{l=l_0}^{L} \beta \chi_{t,l}\right) \tag{2}$$

$$\mathrm{AN} = \mathrm{AF} \times \text{the number of the hospitalizations} \tag{3}$$

3. Results

Table 1 shows that during the study period a total of 4,859,112 CVD hospital admissions were recorded with male, female, aged 65+ and aged<65 at 52.82% (2,566,702), 47.18% (2,292,410), 57.52% (2,794,854) and 42.48% (2,064,258), respectively. Mean of daily number of admissions by district were 2.96. Mean of daily maximum, mean and minimum temperatures were 16.94°C, 12.13°C, and 7.67°C, respectively. TCN ranged from -14.37°C to 11.97°C with a mean of 0°C.

Table 2 shows descriptive results by cold (November to April) and hot (May to October) seasons. In cold season, the mean of daily max, mean, min temperatures were 8.95°C, 3.96°C, and -0.79°C, respectively and in hot season 24.81°C, 20.18°C, and 16.00°C. Range of TCN in cold season was -14.37°C to 11.97°C and in hot season -11.12°C to 7.85°C. Of all TCN hospitalizations 50.21% (2,439,732) was recorded in the cold season while 49.79% (2,419,380) in hot season.

Fig. 1 shows the annual time-series plots of mean of TCN over the districts from 2002 ~ 2019. Difference in seasonal patterns of TCN were observed as shorter range of TCN in hot seasons compared to wider range in cold seasons consistently over the years.

Fig. 2 shows the year-round overall associations between TCN and total, cause-specific, and age-specific CVD hospitalizations. Year-round results indicated a positive TCN was associated with increased risk of CVD hospitalizations while a negative TCN was associated with

Table 1. Full year summary statistics, 2002 ~ 2019

	N (%)	Mean	SD	Min	Median	Max
Daily temperature						
MEAN		12.13	9.72	-21.59	13.19	32.56
TCN		0	2.26	-14.37	0.19	11.97
CVD Hospitalization Counts						
All	4,859,112 (100.00)	2.96	2.93	0	2	121
Male	2,566,702 (52.82)	1.56	1.8	0	1	39
Female	2,292,410 (47.18)	1.39	1.62	0	1	88
Aged 65+	2,794,854 (57.52)	1.7	1.9	0	1	102
Aged < 65	2,064,258 (42.48)	1.26	1.56	0	1	30

Table 2. Season-stratified summary statistics (2002 ~ 2019)

	Cold season (Nov-Apr)						Hot season (May-Oct)					
	N (%)	Mean	SD	Min	Median	Max	N (%)	Mean	SD	Min	Median	Max
Daily temperature												
MEAN		3.96	6.05	-21.59	3.65	23.39		20.18	4.57	-1.86	20.69	32.56
TCN		0.02	2.75	-14.37	0.31	11.97		-0.02	1.66	-11.1	0.12	7.85
CVD Hospitalization Counts												
All	2,439,732 (50.21)	2.99	2.99	0	2	73	2,419,380 (49.79)	2.92	2.88	0	2	121
Male	1,287,798 (26.50)	1.58	1.82	0	1	39	1,278,904 (26.32)	1.54	1.77	0	1	33
Female	1,151,934 (23.71)	1.41	1.65	0	1	50	1,140,476 (23.47)	1.38	1.6	0	1	88
Aged 65+	1,415,196 (29.12)	1.74	1.95	0	1	61	1,379,658 (28.39)	1.67	1.85	0	1	102
Aged < 65	1,024,536 (21.08)	1.26	1.56	0	1	30	1,039,722 (21.40)	1.26	1.56	0	1	23

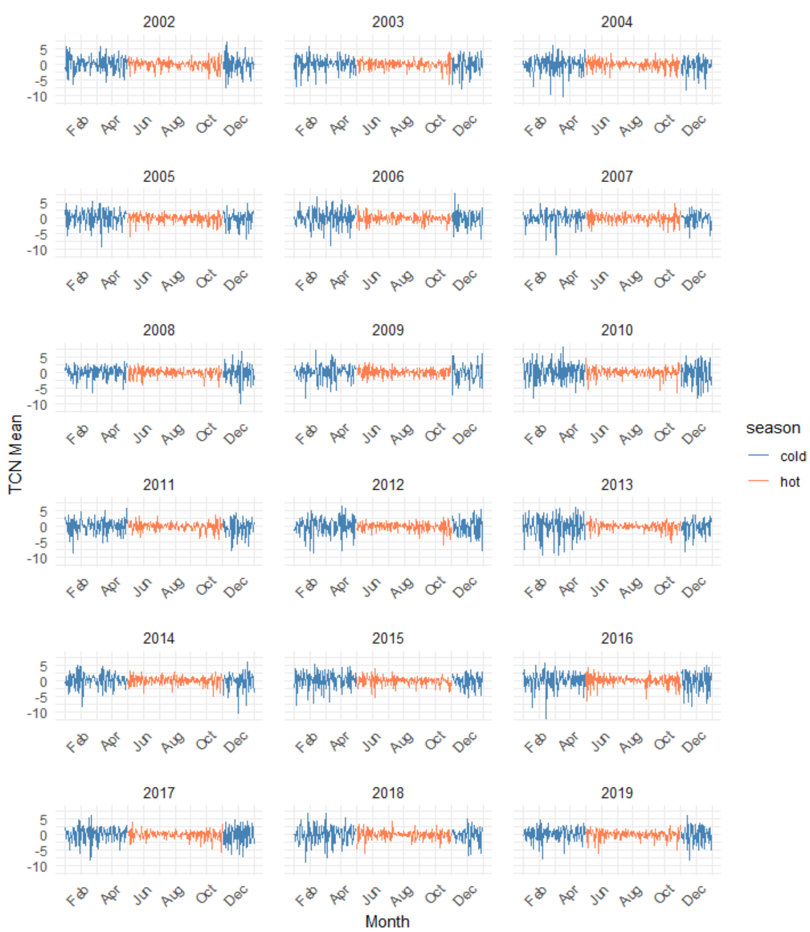

Fig. 1. Time-series plot of overall (national-level) TCN from 2002 to 2019

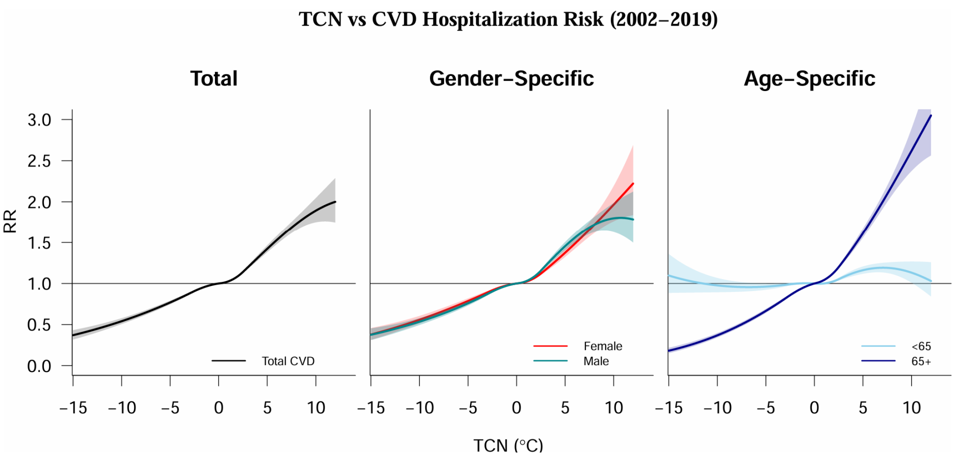

Fig. 2. Full year CVD hospitalization risks associated with TCN

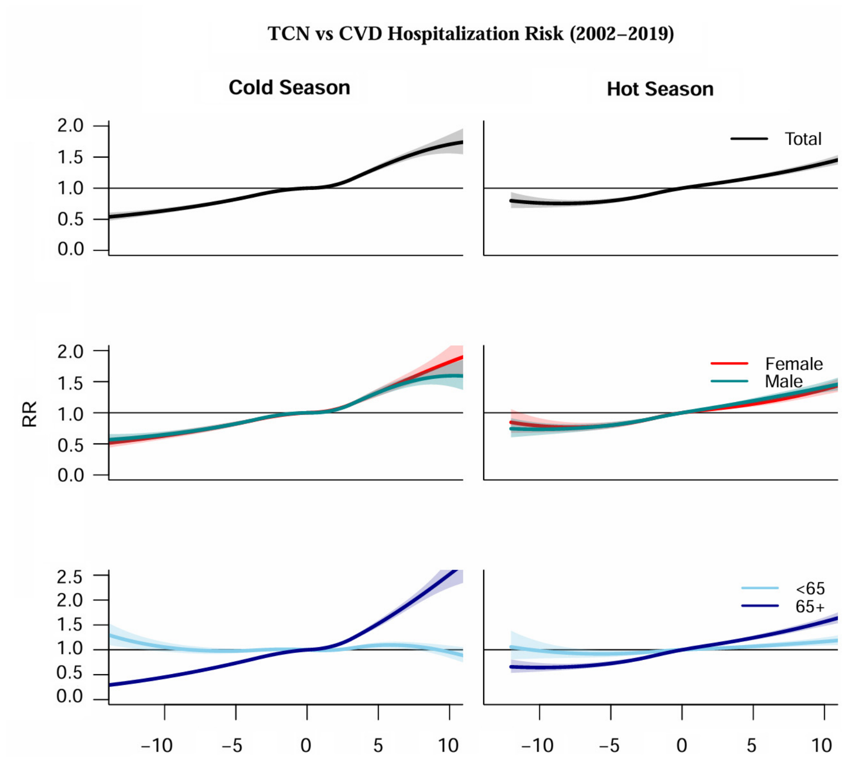

Fig. 3. Season-stratified CVD hospitalization risks associated with TCN

a decreased risk. For example, total CVD hospitalization RRs associated with positive TCN of 5°C and 10°C were 1.42 (1.38, 1.46) and 1.89 (1.75, 2.04), respectively. While sex-specific hospitalization RRs were quite distinct at lower levels of positive TCN (i.e., 1.38 (1.33, 1.43) for females vs 1.45 (1.41, 1.50) for males at TCN of 5°C) they got closer and eventually overlapped at higher levels (i.e., 1.96 (1.76, 2.19) for females and 1.80 (1.63, 1.98) for males at TCN of 10°C). Age-specific associations showed steeply increasing risks for the elderly compared to inverse u-shaped risks for the aged under 65 (i.e., at 5°C TCN 1.16 (1.12,1.21) for aged<65 vs 1.62 (1.56, 1.67) for aged 65+; at 10°C TCN 1.13 (1.01, 1.26) for aged <65 vs 2.62 (2.38, 2.89) for aged 65+).

Fig. 3 shows the season-stratified risk associations where in both seasons, positive TCN was associated with elevated RR of CVD hospitalizations and negative TCN with decreased RR similar with full year results in direction of risks. Risk associations between the extreme negative TCN and CVD hospitalization for the aged under 65 was in the opposite direction in cold season (at -12°C 1.15 (1.02, 1.30). Hospitalization risk associated with positive TCN in cold season was higher compared to the risks in the hot season except for the aged under 65. In cold season, 10°C TCN was associated with an RR of 1.70 (1.56, 1.86) for total, 1.81 (1.60, 2.06) for female, 1.59 (1.43, 1.78) for male, 0.95 (0.84, 1.08) for aged under 65, and 2.52 (2.25, 2.81) for aged 65+ CVD hospitalizations. In hot season, TCN of 10°C was associated with an RR of 1.40 (1.34, 1.46) for total, 1.37 (1.29, 1.46) for female, 1.41 (1.33, 1.50) for male, 1.17 (1.09, 1.25) for aged under 65, and 1.56 (1.48, 1.65) for aged 65 and over CVD hospitalizations.

Table 3 presents the attributable numbers (AN) and attributable fractions (AF) of CVD hospitalizations during the period due to TCN. Global TCN means whole TCN range while positive TCN means a temperature rise and negative TCN means a temperature drop between neighboring days. Interestingly, only positive AN associated with global TCN was aged under 65 hospitalizations which was 23,140 admissions (15,673; 23,875). During the study period, AN due to positive TCN was 192,117 (182,781;197,192) total CVD hospitalizations; 81,653 (75,783; 84,735) female hospitalizations, 111,126 (105,067; 114,872) male hospitalizations; 30,598 (25,292; 33,213) aged under 65 hospitalizations; and 157,291 (150,048; 160,828) aged 65 and over hospitalizations.

Fig. 4 shows the maps of geographical distribution of attributable numbers of total, sex-specific, and age-specific hospital admissions due to negative TCN and positive TCN by district. The maps did not reveal any systematic geographical pattern of AN distribution. For instance, district-specific total CVD hospitalization attributable numbers due to positive TCN which we found to be associated with elevated hospitalization risks at national level during the study period were 870 (eCI: 123, 1525) for in Seodaemungu district in Seoul city, 1085 (eCI: 254, 1876) in Sahagu district in Busan city, 1106 (eCI: 580, 1603) in Seogu district in Daegu city, and 782 (eCI: 423, 1112) in Seogwiposi district in Jeju Island.

Table 3. Attributable numbers (AN) and attributable fractions (AF) of CVD hospitalizations due to temperature change between neighboring days (TCN) during the study period (2002 ~ 2019)

	Global TCN		Negative TCN		Positive TCN	
	AN (eCI)	AF % (eCI)	AN (eCI)	AF % (eCI)	AN (eCI)	AF % (eCI)
Hospitalizations						
Total	-27,773 (-42893, -28389)	-0.57 (-0.88, -0.58)	-219,890 (-238479, -213808)	-4.53 (-4.91, -4.40)	192,117 (182781, 197192)	3.95 (3.76, 4.06)
Sex-Specific						
Female	-16,003 (-26529, -16211)	-0.70 (-1.16, -0.71)	-97656 (-109425, -93472)	-4.26 (-4.77, -4.08)	81,653 (75,783, 84735)	3.56 (3.31, 3.70)
Male	-8,949 (-17657, -9670)	-0.35 (-0.69, -0.38)	-120,075 (-130746, -115881)	-4.68 (-5.09, -4.51)	111,126 (105067, 114872)	4.33 (4.09, 4.48)
Age-Specific						
< 65	23,140 (15673, 23875)	1.21 (0.76, 1.16)	-7,458 (-14741, -4722)	-0.36 (-0.71, -0.23)	30,598 (25292, 33213)	1.48 (1.23, 1.61)
65 +	-74,881 (-91176, -74435)	-2.68 (-3.26, -2.66)	-232,172 (-249242, -228778)	-8.31 (-8.92, -8.19)	157,291 (150048, 160828)	5.63 (5.37, 5.75)

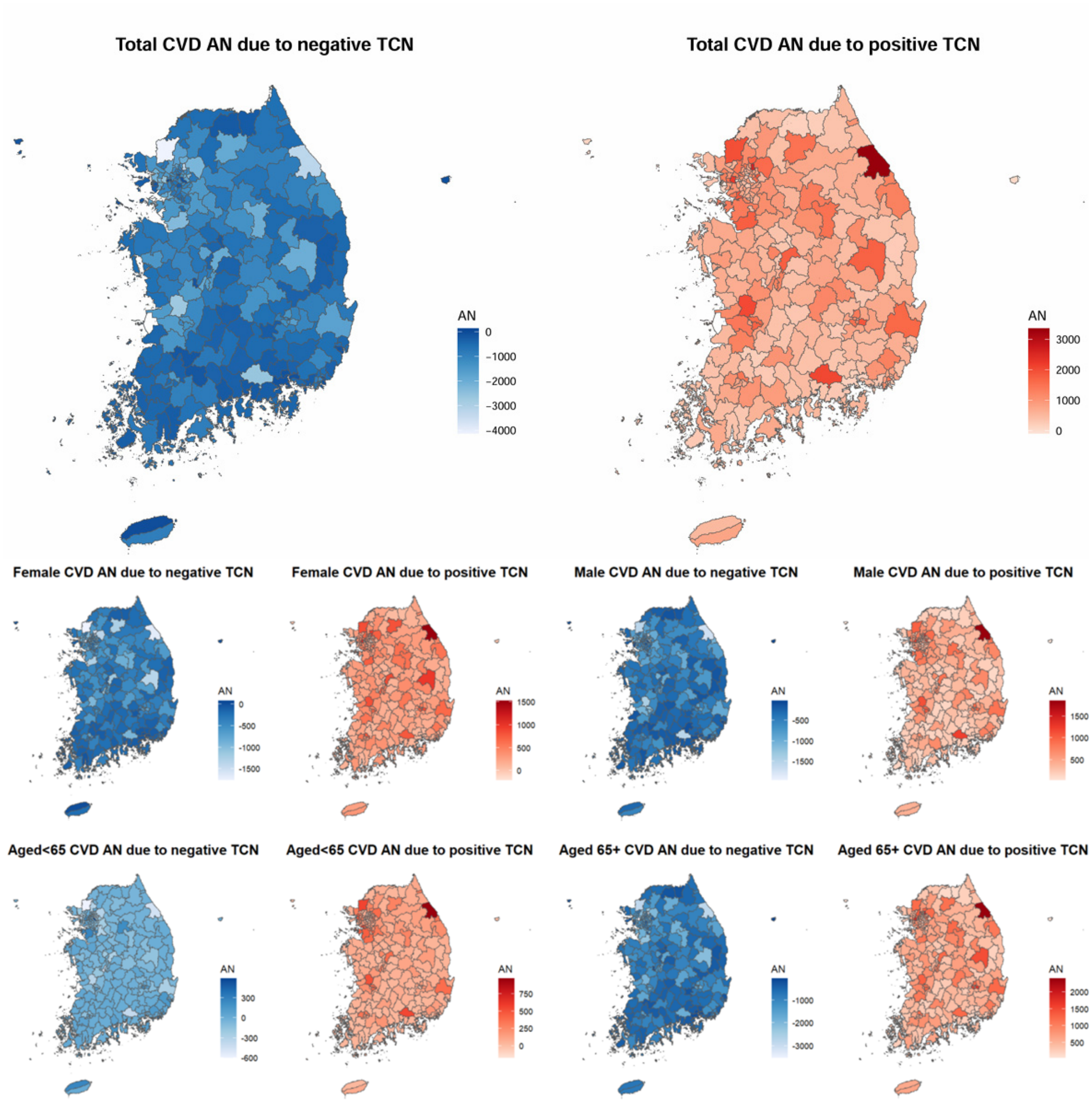

Fig. 4. Geographical distribution of attributable number of total, sex-specific, and age-specific CVD hospital admissions due to TCN by district

4. Discussion

To the best of our knowledge, this study, covering over 4.8 million hospital admissions nationwide from the year 2002 to 2019, is the first study to evaluate impacts of TCN on CVD hospital admissions in South Korea. Full-year and season-specific results show that rising temperature was generally associated with increased risk of CVD hospital admissions. Interestingly, among individuals aged under 65 associations between TCN and

CVD hospitalizations were null except for low positive TCN values in cold season and high positive TCN values in hot season where we obtained positive RR. Another implication of our results was that age could be a potential effect modifier of the impact of TCN on CVD hospitalizations which is in line with the previous literature (Cheng et al., 2014; Shi et al., 2021), while we observed no significant difference in risk associations among males vs. females. Our analysis revealed a non-linear association between TCN and CVD hospitalization which is in line with the previous literature that investigates the associations between TCN and human health with the consistent direction of associations in full-year and season-stratified analysis. Also, the magnitude of risks was different by season where we observed higher hospitalization risks associated with TCN in cold season in comparison with the risk associations in hot season. This can be expected given the range of TCN was wider in cold season compared to hot throughout the study period as reported in Fig. 1. In cold season, in all stratifications, an increase in temperature from day to day was associated with a high risk of CVD hospitalization with the highest risks observed among elderly aged over 65.

There are several studies that reported no significant sex-difference while there are also others that reported significant sex-differences (Cheng et al., 2014; Lin et al., 2013; Shi et al., 2021; Yang et al., 2018; Zhao et al., 2019) which makes the effect of sex as a potential modifier on association between temperature fluctuations and human health inconclusive. When there is significant sex-difference in hospitalization risks it may be attributed to physiological differences of the thermoregulation processes in human body by sex (Kaciuba-Uscilko and Grucza, 2001; Karjalainen, 2012). Another reason for sex differences in risk of hospitalization associated with TCN could be disparities in time spent outdoors between females and males (Huang et al., 2023; Zeng et al., 2024). Our full-year and season-stratified results suggest no significant sex-specific risk difference due to TCN.

Both hot- and cold-season results showed clearly differentiated associations by age where elderly CVD hospitalization risk was significantly higher compared to risk of younger hospitalizations in the case of temperature rise and protective impact of temperature drop was more pronounced for the elderly. The protective effect of negative TCN may be a result of protective behaviors such as going out less when possible or wearing thicker clothing. Even though people aged 65 years and over are considered to be highly vulnerable to temperature effects as aging is associated with a deteriorated ability of thermoregulation of body (Bunker et al., 2016; Schneider et al., 2017) the reason why protective effect of negative TCN was more pronounced for the elderly may be a result of differential behavioral patterns by the elderly to compensate for their deteriorated thermoregulation by seeking higher ambient temperatures (Van Someren, 2007), therefore; we may carefully infer that the elderly might prefer to stay indoors altogether when there is a high drop in outside temperature, especially if they have underlying health conditions, which may lead to a seemingly higher protective effect of negative TCN on CVD hospitalization risk. A positive TCN in both hot and cold seasons was associated with higher risks of hospitalizations in both age groups and the risks were higher for people aged 65 and over. This finding was supported by previous findings by Cheng who attributed this result to lower ability of the elderly to regulate body temperature compared to the younger people (Cheng et al., 2014). In addition to that, we think the elderly may regard warming days in cold season as an opportunity to engage in outdoor activities. Despite being slightly warmer compared to the previous day, the absolute temperature may still be too cold to be tolerated by thermoregulation ability of the elderly which, in turn, may lead to increased hospitalization risk.

4.1. Limitations

Our study has several limitations. Firstly, we did not control air pollutants and relative humidity due to lack of data. Even though relative humidity may affect the results to some extend depending on the season and should be controlled when data is available, we do not expect the results differ substantially whether or not air pollutants are controlled. Secondly, even though we conducted stratified analyses by age and sex which were reported to be significant modifiers of TCN on mortality and morbidity in several studies we could not consider further individual characteristics such as education level, socioeconomic status or pre-existing medical conditions which can have significant modification effect due to lack of data. Thirdly, measurement error may be present since we used regional data of temperature and TCN instead of personal exposure, however we expect it to be random and lead to an underestimation of risks. Also, use of indoor heating and air-conditioning and individual behaviors such as a preference to stay indoors instead of engaging in outdoor activities may modify the impact of TCN on human health (Zhan et al., 2017). Additionally, The use of insurance claims data has limitations, but we attempted to reduce these limitations in the following ways. Research utilizing insurance claim data must delineate participants and cases prior to analysis, given the objective of gathering claims data. Specifically, the administrative processing, including the medical service claim term, varies by medical service institution, therefore utilizing the raw data in its original form influences the research outcomes. As a result, an examination of previous studies employing claims data reveals that several definitional methodologies have been attempted. Numerous prior researches utilizing claim data often employ the approach for defining diseases, specifically with the inclusion of both primary and secondary disease codes. Consequently, this study defined the disease by taking into account both the primary and secondary disease codes. The reason for utilizing the primary or secondary diagnosis code is that if only the primary diagnosis code is used to define the case, there is a concern that the number of cases may be excessively reduced for the purpose of the billing data. For cardiovascular disease, excluding patients diagnosed with a secondary diagnosis code is unreasonable, as it is a serious condition often requiring hospitalization, regardless of coding priority. Secondly, episodes must be developed in alignment with the study objective. A hospitalization episode that encompassed hospitalization services utilized by the same patient at various nursing institutions, including treatment episodes that took into account the period of no treatment, was defined as a disease exacerbation associated with a specific environmental exposure factor in this study. And this study does not permit an exclusive focus on the treatment episode due to disease exacerbation linked to a particular environmental exposure factor, thus, instances of hospitalizations for cardiovascular disease that involved a transfer from the emergency room within a two-week timeframe were treated as a single case and aggregated into the daily total.

5. Conclusion

This study obtained the total, sex-specific, age-specific CVD hospitalization risks associated with day-to-day temperature fluctuations year-round as well as in hot and cold seasons, and evaluated the disease burden attributable to TCN in South Korea from 2002 to 2019. The results showed that the people over the age of 65 years were most vulnerable to temperature rise between consecutive days in cold season. Season-specific policies targeting vulnerable populations may minimize the adverse health outcomes of temperature fluctuations. This matter becomes increasingly important as climate change proceeds.

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