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Impact of Climate on the Incidence of Acute Coronary Syndrome

— Differences Between Japan and Thailand —

Takashi Yamano, MD, PhD; Katkanit Thammakumpee, MD; Chanudda Nabkasorn, PhD; Arisara Ritngam, PhD; Nisakorn Krungkraipetch, PhD; Lalita Kaewwilai, PhD; San Suwanmanee, PhD; Arthit Phosri, PhD; Orawan Kaewboonchoo, PhD; Shin Murakami, MD; Rikuya Tanaka, MD; Nanami Murata, MD; Yosuke Katayama, MD, PhD; Akira Taruya, MD, PhD; Masahiro Takahata, MD, PhD; Teruaki Wada, MD, PhD; Shingo Ota, MD, PhD; Keisuke Satogami, MD, PhD; Yuichi Ozaki, MD, PhD; Manabu Kashiwagi, MD, PhD; Yasutsugu Shiono, MD, PhD; Akio Kuroi, MD, PhD; Takashi Tanimoto, MD, PhD; Hironori Kitabata, MD, PhD; Atsushi Tanaka, MD, PhD

Background: Although there are many reports of temperature being associated with the onset of acute coronary syndrome (ACS), few studies have examined differences in ACS due to climatic differences between Japan and Thailand. The aim of this joint Japan–Thailand study was to compare patients with myocardial infarction in Japanese and Thai hospitals in different climates.

Methods and Results: We estimated the climate data in 2021 for the Wakayama Prefecture and Chonburi Province, two medium-sized cities in Japan and Thailand, respectively, and ACS patients who were treated at the Wakayama Medical University (WMU) and Burapha University Hospital (BUH), the two main hospitals in these provinces (ACS patient numbers: WMU, n=177; BUH, n=93), respectively. In the Chonburi Province, although the average temperature was above 25°C, the number of ACS cases in BUH varied up to threefold between months (minimum: July, 4 cases; maximum: October, 14 cases). In Japan and Thailand, there was a mild to moderate negative correlation between temperature-atmospheric pressure at the onset of ACS, but different patterns for temperature-humidity (temperature-atmospheric pressure, temperature-humidity, and atmospheric pressure-humidity: correlation index; r=–0.561, 0.196, and –0.296 in WMU vs. r=–0.356, –0.606, and –0.502 in BUH).

Conclusions: The present study suggests that other climatic conditions and factors, not just temperature, might be involved in the mechanism of ACS.

Key Words: Acute coronary syndrome; Climate index; Japan; Thailand

Annual fluctuations of seasons influence the incidence of cardiovascular diseases.[1] In Japan and many other cities in the Northern Hemisphere, which has four seasons, the peak seasonal incidence of acute coronary syndrome (ACS) is winter.[2,3] In a previous study examining the relationship between temperature and mortality using data from 384 sites worldwide, including Bangkok and Tokyo, temperature-related mortality was higher in all countries during the 'moderately cold' period.[4] However, the mean temperatures in Tokyo during the 'moderately cold' period ranged widely from 4°C to 26°C, and in Bangkok from 25°C to 30°C, with significant differences between countries with four seasons and cities in the tropics.

In contrast, a recent large cohort study on temperature in Japan showed a bimodal distribution of the number of acute myocardial infarction (AMI) cases, with mean ambient temperatures with a trough at 20°C.[5]

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Department of Cardiovascular Medicine, Wakayama Medical University, Wakayama (T.Y., S.M., R.T., N.M., Y.K., A. Taruya, M.T., T.W., S.O., K.S., Y.O., M.K., Y.S., A.K., T.T., H.K., A. Tanaka), Japan; Faculty of Medicine (K.T.), Faculty of Nursing (C.N., A.R., N.K.), Burapha University, Chonburi; and Faculty of Public Health, Mahidol University, Bangkok (L.K., S.S., A.P., O.K.), Thailand

Mailing address: Takashi Yamano, MD, PhD, Department of Cardiovascular Medicine, Wakayama Medical University, 811-1 Kimiidera, Wakayama 641-8510, Japan. email: ymntks@wakayama-med.ac.jp

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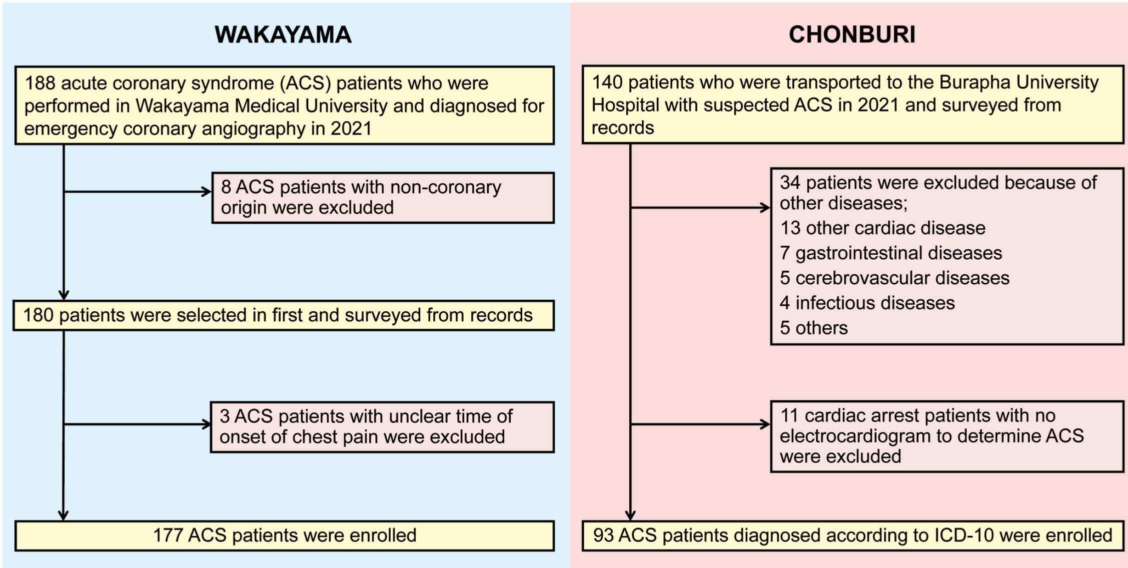

Figure 1. Patient enrolment flowchart for Wakayama Medical University and Burapha University Hospital. In the present study, acute coronary syndrome (ACS) patients were retrospectively identified from catheterized patients at Wakayama Medical University, and those at Burapha University Hospital were identified from emergency patients. The data were individually examined and extracted from medical records.

Furthermore, a report from our institution in Japan showed the same bimodal distribution as that cohort study,[6] and suggested that plaque rupture in the coronary artery might be involved in myocardial infarction at low temperatures. However, the underlying mechanism remains unclear, and the involvement of other climatic factors such as atmospheric pressure and humidity is unknown.

As a future social issue, previous studies have found that the incidence of AMI has increased in the Asia-Pacific region, including tropical regions.[7] However, climatic conditions differ between Japan, with four seasons, and Southeast Asian countries. There is a report of increased hospital admissions for ACS when the temperature is below 26.2°C in Taipei,[8] which is relatively warm, but few studies have examined the relationship between the climate index and ACS in Thailand, which is a tropical region.

The purpose of this collaborative study between Japan and Thailand was to investigate the differences in the incidence of myocardial infarction due to climatic variations by comparing patients with myocardial infarction between a Japanese hospital and a Thai hospital with different climates.

Methods

Study Population (Japanese Side)

The present study included 188 patients with ACS (ST-elevation myocardial infarction [STEMI], non-STEMI [NSTEMI], or unstable angina pectoris [UAP]) at the Wakayama Medical University (WMU) who were eligible for emergency coronary angiography from January 2021 to December 2021 and were excluded according to current guidelines criteria.[9]

Of the 188 patients, 11 were excluded because the ACS occurred in non-coronary arteries (n=8), and an unknown time of ACS onset due to poorly recognized symptoms (n=3). Thus, data from 177 patients were analyzed. A patient enrollment flowchart is shown in **Figure 1**. The onset of chest pain was defined as the time of ACS.[10] All demographic data, including axillary temperatures measured in our emergency department, were obtained from patient records.

The study protocols were reviewed by the local ethics committee of WMU (number 3780). The study was conducted in accordance with the World Medical Association Declaration of Helsinki and Good Clinical Practice Guidelines.

Study Population (Thailand Side)

A total of 140 patients who were transported to the Burapha University Hospital (BUH) from January 2021 to December 2021 with suspected ACS were included (**Figure 1**). Based on the emergency physician's diagnosis, 34 patients with diagnoses other than ACS (cardiac diseases such as heart failure and atrial fibrillation [13 patients]; gastrointestinal diseases such as gallstones and acute gastritis [7 patients]; cerebrovascular diseases such as cerebral hemorrhage [5 patients]; infectious diseases such as coronavirus disease 2019 (COVID-19) [4 patients]; and others [5 patients]) were excluded. Among the patients who died of cardiac arrest in the emergency room, those who were diagnosed with AMI based on the remaining electrocardiogram were included in the present study. As a result, 93 patients were diagnosed with ACS based on the International Classification of Diseases, Tenth Edition (ICD-10 code: I249). Of the surviving patients, those with STEMI were transferred urgently, and those with NSTEMI and UAP were transferred to the Chonburi Hospital on a standby basis for catheterization.

The study protocol was reviewed by the local ethics committee of the Burapha University (HS065). This study

Table 1. Clinical Characteristics of ACS Patients Between WMU and BUH

	WMU (n=177)	BUH (n=93)	P value
Age (years)	71.3±11.3	65.6±14.0	0.002
Male (%)	142 (80)	59 (62)	0.003
Body mass index (kg/m²)	22.9±4.0	24.3±4.3	0.010
Systolic blood pressure at ER (mmHg)	137±35	136±27	0.866
Diastolic blood pressure (mmHg)	81±21	80±17	0.621
Heart rate at ER (beats/min)	87±24	91±25	0.164
Body temperature at ER (°C)	36.3±0.7	36.5±0.4	0.004
WBC count (/μL)	9,218±3,436	10,384±4,187	0.022
Hemoglobin (g/dL)	13.3±2.4	12.6±2.5	0.025
Platelet count (×10³/uL)	221±76	265±72	<0.001
Maximum creatinine kinase (IU/L)	1,653±2,927	–	–
Maximum troponin T (ng/L)	–	28.8±61.9	–
Hypertension (%)	146 (82)	42 (45)	0.004
Diabetes mellitus (%)	72 (40)	27 (29)	<0.001
Chronic kidney disease (%)	50 (28)	6 (6)	<0.001
ACS categories			<0.001
STEMI (%)	117 (66)	22 (21)	
NSTEMI (%)	47 (27)	58 (64)	
UAP (%)	13 (7)	13 (14)	
Target coronary arteries			–
LAD or LMCA (%)	80 (45)	–	
RCA (%)	67 (38)	–	
LCX (%)	30 (17)	–	
ACS onset time			0.069
0:00–5:59 (%)	28 (16)	9 (10)	
6:00–11:59 (%)	70 (40)	37 (38)	
12:00–17:59 (%)	38 (21)	32 (33)	
18:00–23:59 (%)	41 (23)	15 (16)	
Climate index on ACS onset			
Temperature (°C)	17.4±7.6	29.4±1.8	<0.001
Atmospheric pressure (hPa)	1,013.5±6.5	1,008.9±2.6	<0.001
Humidity (%)	69.5±16.7	75.8±9.6	0.048
Death within 30 days of ACS onset (%)	8 (4.5)	6 (6.5)	0.497

Values are presented as n (%), or mean±SD. ACS, acute coronary syndrome; BUH, Burapha University Hospital; ER, emergency room; LAD, left anterior descending artery; LCX, left circumflex artery; LMCA, left main coronary artery; NSTEMI, non-ST-elevation myocardial infarction; RCA, right coronary artery; STEMI, ST-elevation myocardial infarction; UAP, unstable angina pectoris; WBC, white blood cell; WMU, Wakayama Medical University.

was conducted in accordance with the World Medical Association Declaration of Helsinki and Good Clinical Practice Guidelines.

Ambient Temperature, Atmospheric Pressure, and Humidity (Japanese Side)

The temperature, atmospheric pressure, and humidity data were obtained from the Japan Meteorological Agency (JMA). From the JMA website, data for every 10 min at the time of AMI in Wakayama City, as well as the monthly average temperature, atmospheric pressure, and humidity, can be obtained. We determined the time of onset from the hospital medical records and calculated the meteorological data at that time.

Ambient Temperature, Atmospheric Pressure, and Humidity (Thailand Side)

On the Thailand side as well as the Japanese side, the time of onset was determined from the hospital medical records. As no Thai weather data were available on the website, we asked the Meteorological Department of Thailand to provide us with weather data for Chonburi City, Chonburi Province. A co-author (C.N.) negotiated with the Meteorological Department, but the Meteorological Department had just three-hourly meteorological data for Chonburi City. We obtained the three-hourly temperature, atmospheric pressure, and humidity data for Chonburi City, Chonburi Province, and applied them to the time closest to the onset time.

Clinical Data and Angiography Data of Collection and Analysis

Basic patient information, such as age, blood test results, and progress, were extracted from the medical records of each hospital after approval by the Ethics Committee. In the present study, the researchers collecting clinical data (S.M. in Japan, and K.T. in Thailand) were blinded to the meteorological data. In Japan, coronary angiography is

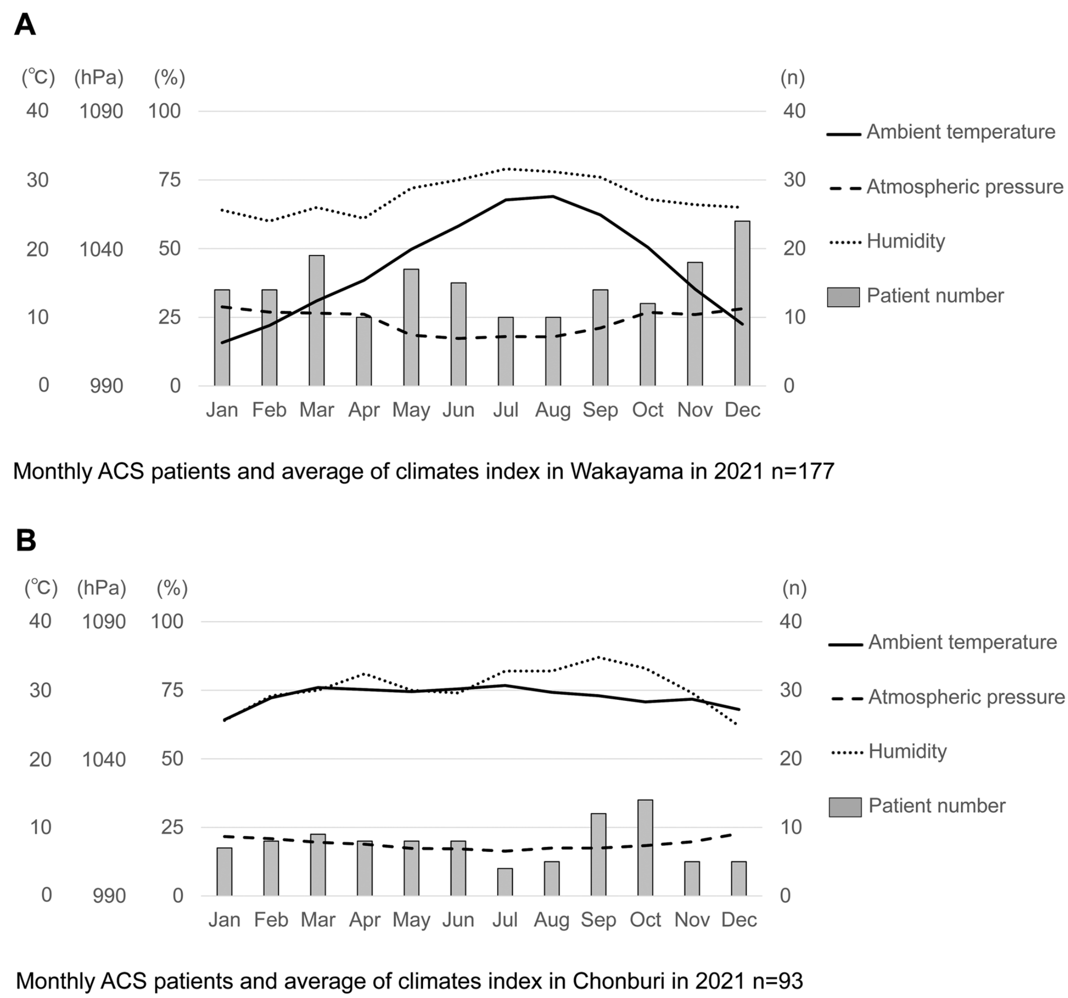

Figure 2. Monthly average climate index in Wakayama and Chonburi, and monthly number of acute coronary syndrome (ACS) patients at Wakayama Medical University (WMU) and Burapha University Hospital (BUH) in 2021. In the example from Wakayama (**A**), only summer was hot, humid, and had low pressure. In the WMU, the number of ACS cases tended to be higher in winter. In Chonburi Province (**B**), all months were hot, humid, and had low pressure, but the number of ACS patients in the BUH varied up to three times from month to month (minimum: July, 4 cases; maximum: October, 14 cases).

performed using a 5Fr Judkins-type catheter. The target coronary vessel was identified based on the coronary angiographic findings. On the Thailand side, as not all patients were catheterized, an attempt was made to identify the target vessel as far as possible from the electrocardiogram and echocardiographic findings. However, some target vessels were not evident; therefore, no analysis of these was excluded.

Statistical Analysis

Statistical analyses were performed using the JMP Pro version 16 for Windows (SAS Institute, Cary, NC, USA). Results are expressed as mean±SD for approximately normally distributed variables and median (interquartile range) for skewed variables after applying the Shapiro–Wilk test. Categorical variables are presented as numerical values (percentages), and comparisons were made using the Chi-squared test or Fisher's exact test when the expected cell value was less than 5. Continuous variables are presented as mean±SD and were compared using the Student's t-test. The Wilcoxon test was used for non-parametric comparisons. Pearson's product-rate correlation coefficients were used for correlations based on summary statistics. Statistical significance was set at $P<0.05$. Statistical sample size calculations were not conducted in advance due to the survey of all cases at the facilities. However, at an average temperature of 19±8°C in Wakayama and 27±2°C in Chonburi, a sample size of 30 was calculated with a power of 0.95 and an α error of 0.05.

Results

ACS Patient Characteristics in WMU and BUH

Patient characteristics are summarized in **Table 1**. Patients with ACS in the WMU group were older and had a higher proportion of men than those in the BUH group. They also had a higher prevalence of underlying diseases and a higher proportion of STEMI. In contrast, ACS patients

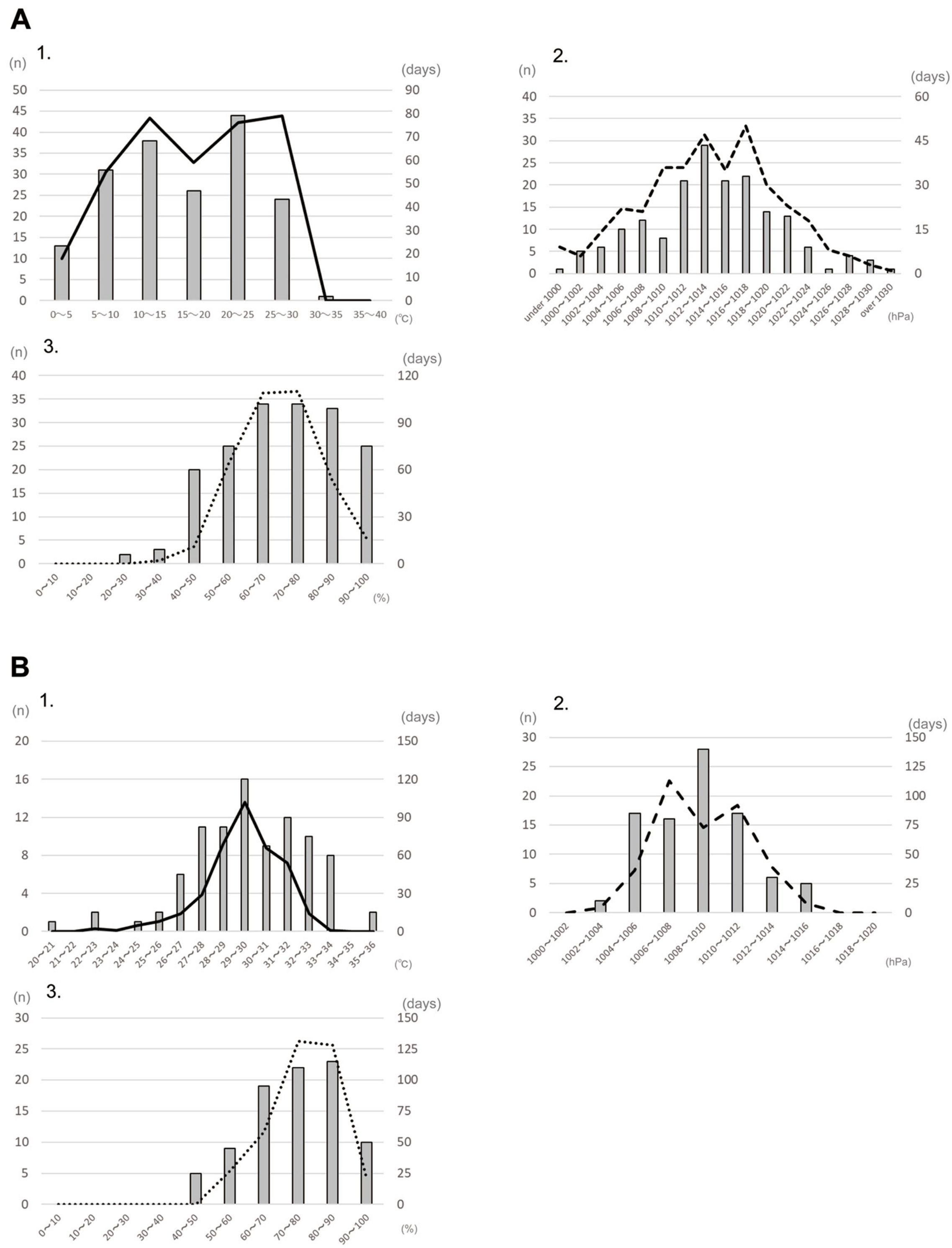

Figure 3. Number of days of daily average for climatic conditions in Wakayama and Chonburi, and the onset number of acute coronary syndrome (ACS) patients in Wakayama Medical University (WMU) and Burapha University Hospital (BUH). (**A**) Climate conditions (1, temperature; 2, atmospheric pressure; 3, humidity). Number of days of daily average value for each climatic condition in Wakayama are shown as line graphs, and numbers of ACS patients in WMU in each climatic condition on ACS onset are shown as bar graphs. Regarding temperature, both line graphs and bar graphs showed bimodal distribution with a bottom between 15°C and 20°C. Humidity and atmospheric pressure exhibited monomodal distributions. (**B**) Climate conditions (1, temperature; 2, atmospheric pressure; 3, humidity). Number of days of daily average value for each climatic condition in Chonburi are shown as line graphs, and numbers of ACS patients in BUH in each climatic condition at ACS onset are shown as bar graphs. Daily average days and ACS patient numbers for temperature and humidity were higher than those in Wakayama, whereas those for atmospheric pressure were lower.

Table 2. Summary Statistic and Pearson's Correlation (r) of Climate Index at the Onset of ACS Patients in WMU and BUH

Variable	Model	Correlation coefficient (range)²	Covariance	P value
(A) WMU				
T vs. P	P=1,022.6811–(0.5274957×T)	−0.561 (−0.654 to −0.451)	−2.83	<0.001
T vs. H	T=10.211439+(0.0882792×H)	0.196 (0.050 to 0.333)	24.57	0.009
P vs. H	P=1,021.7886–(0.1140088×H)	−0.296 (−0.425 to −0.155)	−31.73	<0.001
(B) BUH				
T vs. P	P=1,019.6108–(0.3682758×T)	−0.356 (−0.522 to −0.164)	−2.81	<0.001
T vs. H	T=38.810962–(0.1247379×H)	−0.607 (−0.721 to −0.460)	−22.56	<0.001
P vs. H	P=1,019.1392–(0.1343973×H)	−0.502 (−0.575 to −0.421)	−12.37	<0.001

H, humidity; P, atmospheric pressure; T, temperature. Other abbreviations as in Table 1.

with BUH had a higher body mass index, and there was a higher proportion of patients with NSTEMI. There were no significant differences in blood pressure and heart rate in the emergency room or in onset time between the two groups.

Monthly Climatic Conditions (Temperature, Atmospheric Pressure, and Humidity) in Wakayama and Chonburi, and the Number of ACS Patients in WMU and BUH

Seasonal variations were observed in the number of patients with ACS at the WMU (**Figure 2A**). In addition, the summer season is hot and humid and has low pressure. As expected, the number of ACS cases tended to be higher in the winter.

In contrast, in Chonburi Province (**Figure 2B**), the average temperature was above 25°C, and there was little seasonal variation in temperature, atmospheric pressure, and humidity.

However, the number of ACS cases in BUH varied up to threefold between months (minimum: July, 4 cases; maximum: October, 14 cases).

Number of Days of Daily Average for Climatic Conditions in Wakayama and Chonburi, and the Onset Number of ACS Patients in WMU and BUH

In WMU, the number of ACS in the temperature range showed a bimodal distribution with a bottom between 15°C and 20°C (**Figure 3A**). Similarly, the mean temperature also showed a bimodal distribution in Wakayama. With regards to humidity, in Wakayama, the average was above 50% on many days. ACS tended to occur on days with high humidity. For atmospheric pressure, a peak distribution of approximately 1,014 hPa was observed for both the daily mean pressure and the time of ACS onset.

A peak distribution was observed for both mean daily temperature in Chonburi and the number of cases of ACS onset in BUH between 29°C and 30°C. Mean humidity was higher in Chonburi than in Wakayama, exceeding 60% on most days. In contrast, atmospheric pressure was lower than that in Wakayama, with a peak distribution of both daily mean atmospheric pressure and the number of ACS onset between 1,006 and 1,010 hPa.

Relationship Between Temperature, Atmospheric Pressure, and Humidity at the Time of ACS Occurrence in WMU and BUH

As expressed in the 'Climate index on ACS onset' entry in **Table 1**, there were significantly lower temperatures, higher air pressure, and lower humidity at the onset of ACS in the WMU compared with the BUH. Therefore, we investigated the relevancies of temperature-atmospheric pressure, temperature-humidity, and atmospheric pressure-humidity at the onset of ACS in each of the facilities (**Table 2**). We found that the correlation between temperature and atmospheric pressure using summary statistics showed a moderate negative correlation (r=−0.561) in the WMU (**Table 2A**). However, there was little correlation (r=0.196) between temperature and humidity. We also found that there was little correlation between atmospheric pressure and humidity (r=−0.296).

Next, we investigated the relevancies of the temperature-atmospheric pressure, temperature-humidity, and atmospheric pressure-humidity at the onset of ACS in the BUH (**Table 2B**). The correlation between temperature and atmospheric pressure using summary statistics indicated a mild negative correlation (r=−0.356) between temperature and atmospheric pressure, as with WMU. However, unlike WMU, there was a moderate negative correlation (r=−0.606) between temperature and humidity. Also, we found that there was a mild negative correlation between atmospheric pressure and humidity (r=−0.502).

Discussion

This retrospective study was conducted in Japan and Thailand to investigate the association between the incidence of ACS and climate. Similar to previous studies, Japan showed a bimodal distribution of the incidence of ACS; however, the mean temperature was also bimodal. This was not the case in Thailand. In Japan and Thailand, there was a negative correlation between temperature and atmospheric pressure at the onset of ACS, but different patterns for temperature and humidity.

Ambient Temperature, and the Onset of ACS

In countries with four distinct seasons, such as Japan, ACS is known to follow a bimodal distribution, with a higher frequency when the temperature is below 10°C and above 20°C.[5,11] The incidence of ACS is higher in summer and winter, but in areas such as northern China, where temperatures do not rise much, even in summer, the incidence of ACS is not high.[12] However, unlike morbidity, mortality has been reported to be higher in winter than in other seasons.[2,3,13] Another study of major cities around the world concluded that most of the temperature-related mortality burden is due to the contribution of the cold.[4]

Differences in ACS etiology (plaque rupture and non-plaque rupture) in the coronary artery might explain why mortality is higher in winter. Plaque rupture occurs when the lipid core in the plaque grows, ruptures, and adheres to a fibrin-rich thrombus, resulting in acute occlusion of the coronary artery.[14] In addition to plaque rupture, the primary etiology of ACS is plaque erosion. This erosion is caused by the fragility of the plaque, such as endothelial cell damage, which leads to ACS due to platelet-rich thrombi. Moreover, one report stated that the maximum creatinine kinase (CK) value for plaque rupture is higher than that for non-plaque rupture, and that plaque rupture is more likely to be severe.[15] Our group focused on the differences in ACS etiology and reported that plaque rupture is more common in winter and erosion is more common in summer, based on data from optical coherence tomography, a coronary artery imaging device.[6] Although the mechanism by which erosion is the most common cause of ACS in summer has not been clarified, we believe that this difference in etiology is the reason why the mortality rate is the same as that in other seasons, despite the high morbidity rate. It is generally accepted that patients with NSTEMI have a milder disease than those with STEMI,[16] and this mechanism of plaque erosion might be involved in the higher incidence of NSTEMI in the Thailand facilities in the present study, which are warm all year round. However, we were unable to determine the cause because intravascular imaging, such as optical coherence tomography, is not performed in general hospitals in Thailand.

Another Climate Barometer, and the Onset of ACS

First, because air becomes lighter at higher temperatures, a meteorological relationship exists between higher temperatures and lower atmospheric pressure. Although there are various reports on the effect of atmospheric pressure on the incidence of AMI, Danet et al[17] reported that the mean daily incidence was lowest at 1,016 hPa and that a V-shaped relationship between the incidence of myocardial infarction and atmospheric pressure was established. The results from Japan in the present study also showed the same trend, but it is interesting to note that the atmospheric pressure was unimodal, while the temperature was bimodal, at the time of the ACS. It is also reported in cold regions that AMI and stroke are more likely to occur due to low atmospheric pressure as well as low temperatures,[18] and it is very interesting that the present study found an association between atmospheric pressure and temperature in Thailand as tropics for the onset of ACS.

There are even fewer reports on the relationship between temperature and humidity in relation to coronary artery disease. One study on AMI patients admitted to an acute-care hospital in Japan reported that lower temperatures and low humidity were associated with increased hospital admissions due to AMI.[19] However, the present study found a moderate negative correlation between humidity and temperature in both Japan and Thailand, so we believe the mechanism of humidity-mediated ACS pathogenesis requires further research.

A retrospective study in Iran reported that ACS events were most frequent from March to May and that daily relative humidity and daily minimum temperature showed negative correlations.[20] Another national hope study in Slovenia explored the short-term association between meteorological parameters and the incidence of ACS by using emergency coronary catheter intervention.[21] The mean daily temperature, humidity, and atmospheric pressure were associated with the incidence of ACS in that study; however, the results showed a large variability in atmospheric pressure and humidity. The present study also found temperature-humidity and temperature-atmospheric pressure relationships in Thailand; however, we were unable to derive a direct relationship between humidity and pressure in the ACS.

Recent studies have used artificial intelligence (AI) to predict the number of ACS cases.[22] We hope that future developments in AI will help to solve the mechanism of ACS.

Differences Between Thailand and Japan in the Incidence of ACS

As mentioned earlier, it has been reported that ACS-associated mobility is high but mortality is low when temperatures are above 20°C. However, previous reports indicate that age-standardized death rates per 100,000 people for cardiovascular diseases in Thailand are higher than that in Japan.[23] This result might be due not only to differences in the quality of medical care in Japan and Thailand but also to differences in the environment.

What was most surprising in the present study was the variation in the number of ACS cases per month, even in Thailand, which experiences high temperatures throughout the year. Because the average temperature in Chonburi Province is above 20°C on all days, all days are on the hot peak when applied to Japan, which has a bimodal climate. However, in the present study, the peak for ACS patients was in October, a relatively cool month with temperatures ranging from 20°C to 25°C.

Among previous studies in which cold weather increased ACS mortality,[4] the impact was weaker in Brazil and Thailand than in the rest of the world. This is similar to the findings of the present study, and unlike in other tropical regions, factors other than temperature might be significantly related.

Study Limitations

WMU is a major core hospital for treating ACS located in Wakayama Prefecture, with a population of approximately 900,000; it is also located in Chonburi Province, with a population of approximately 1.4 million. Although the two hospitals share similarities in terms of distance from major cities, the Japanese and Thai people differ in many ways, including race, average life expectancy, eating habits, and exposure to air pollution. For example, long-term exposure to air pollution such as particulate matter <2.5 μm (PM2.5) is one of risk factors for cardiovascular disease,[24] and such air pollution is more severe in Thailand than in Japan.[25,26] In contrast, smoking rates in both Japan and Thailand were approximately 20%, with no significant difference between them.[27] Therefore, we could not perform a simple comparison. In addition, because both results were obtained from a single site, they might contain bias.

The present study is a comparison between a single hospital in two countries and has a limited number of cases. In addition, the proportion of STEMI and NSTEMI in the two groups is different, and there is the possibility of selection bias due to differences in population sampling. Therefore, direct comparisons in climatic conditions could not be performed. We researched the historical temperature, atmospheric pressure, and humidity in Wakayama City in 10-min increments from the JMA website. The temperature, atmospheric pressure, and humidity at the time of onset were calculated from the estimated time of onset. However, because we were not able to correct for indoor/outdoor conditions or exact location, we were not able to investigate the exact conditions. In addition, we were unable to obtain accurate hourly information on climatic conditions in Thailand. Although some previous studies have investigated the rate of change in temperature within 24h or 48h, only the temperature at onset was used in the present study.

Last, as the present study only investigated the onset of ACS, long-term outcomes were not examined.

Conclusions

There were seasonal differences and bimodal changes with temperature in ACS incidents and days per year in Japan but not in Thailand. The temperature at the onset of ACS was found to correlate only with atmospheric pressure in Japan, and with atmospheric pressure and humidity in Thailand. The present study suggests that other climatic conditions and factors, not just temperature, might be relevant to the mechanism of ACS.

Acknowledgment

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Disclosures

All authors report that they have no relationships relevant to the content of this paper.

IRB Information

The study protocols were reviewed by the local ethics committee of Wakayama Medical University (number 3780) and Burapha University (HS065).

Data Availability

The deidentified participant data will not be shared.

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