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ORIGINAL RESEARCH

Ambient Temperature Effect on Acute Myocardial Infarction by Risk Factors

Daily Data From 2000 to 2017, Taiwan

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ABSTRACT

BACKGROUND A U-shaped relationship between temperature and acute myocardial infarction (AMI) was observed, but the risk factors were rarely included.

OBJECTIVES The authors sought to examine AMI's cold and heat exposure after considering their risk groups.

METHODS Daily data on ambient temperature, newly diagnosed AMI, and 6 known risk factors of AMI for the Taiwan population from 2000 to 2017 were created by linking 3 Taiwan national databases. Hierarchical clustering analysis was performed. Poisson regression was performed on the AMI rate with the clusters along with the daily minimum temperature in cold months (November-March) and the daily maximum temperature in hot months (April-October).

RESULTS There were 319,737 patients with new-onset AMI over 109.13 billion person-days, corresponding to the incidence rate of 107.02 per 100,000 person-years (95% CI: 106.64-107.39 person-years). Hierarchical clustering analysis identified 3 distinct clusters (1: age <50 years, 2: age ≥50 years without hypertension, and 3: mainly age ≥50 years with hypertension) with AMI incidence rates of 16.04, 105.13, and 388.17 per 100,000 person-years, respectively. Poisson regression revealed that below 15 °C, cluster 3 had the highest risk of AMI per 1°C reduce in temperature (slope = 1.011) compared with clusters 1 (slope = 0.974) and 2 (slope = 1.009). However, above the 32 °C thresholds, cluster 1 had the highest risk of AMI per 1 °C increase in temperature (slope = 1.036) compared with clusters 2 (slope = 1.02) and 3 (slope = 1.025). Cross validation showed a good fit for the model.

CONCLUSIONS People ≥50 years of age with hypertension are more susceptible to cold-related AMI. However, heat-related AMI is more prominent in individuals <50 years of age. (JACC: Asia 2023;3:228–238) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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Acute myocardial infarction (AMI) is caused by the rupture of atherosclerotic plaque, resulting in thrombotic vessel occlusion and ischemic events. Environmental factors, such as atmospheric temperature, are associated with myocardial infarction (MI).[1] A U-shaped relationship between ambient temperature and MI[2,3] has been reported, including an increased risk at cold[4,5] and high temperatures above a threshold of 20 °C.[6] However, some important risk factors for AMI, such as age, sex, hypertension, hyperlipidemia, diabetes, and chronic kidney disease (CKD), were rarely considered in the relevant studies. Therefore, it remains unknown how the effect of ambient temperature on new-onset AMI varies with different underlying risk factors.

To address these knowledge gaps, we used the 3 national Taiwan databases from 2000 to 2017 to create daily data for the entire Taiwan population. Next, we used hierarchical clustering to identify risk clusters based on 6 important risk factors of AMI. Poisson regression models with various temperature variables, especially looking for inflection points, were applied to examine cold exposure and heat exposure on AMI after considering their risk groups. Cross validation was performed to test the robustness of the main results.

MATERIALS AND METHODS

STUDY DESIGN. We linked the Taiwan National Health Insurance Research Database (NHIRD), Taiwan Death Registry (TDR), and Taiwan Air Quality Monitoring Network (AQMN) to create daily data on ambient temperature, newly diagnosed AMI, and 6 important risk factors for AMI for the entire Taiwan population during 2000 to 2017. First, the NHIRD and the TDR were linked by a unique encrypted ID for each individual. Next, we excluded people with missing information on sex and the insured area on the offshore island to avoid sparse data bias[7] and unreasonable records, such as death before the new onset of AMI. Next, we merged these records with the daily temperature data based on the hospital visit date and the county of seeking treatment/insured county. We also excluded the daily data if the individual's age was <20 years at the study date because of the low AMI rate (**Figure 1**). There were 28.62 million people during 2000 to 2017 and 319,737 patients with new-onset AMI over 109.13 billion person-days (= 298.78 million person-years). This study was approved by the Chang Gung Institutional Review Board (202000435B1).

DATA SOURCE. The NHIRD was derived from the single-payer national health insurance (NHI) program and covered almost 99% of the total population in Taiwan.[8] There were 910 hospitals (27 medical centers, 107 regional hospitals, and 776 district hospitals) during 2000 to 2017. The NHIRD has many subsets, including beneficiary registry (birth year, sex, residence area, and date in and out of the NHI program) and ambulatory or inpatient claims (dates of clinical visits, medical diagnoses, lists of prescriptions, examinations, and procedures). The TDR included the date and cause of death, which have been validated.[9] The AQMN included the hourly climatic data in Taiwan.

ABBREVIATIONS AND ACRONYMS

AMI = acute myocardial infarction

AQMN = Air Quality Monitoring Network

CKD = chronic kidney disease

HCA = hierarchical clustering analysis

IRR = incidence rate ratio

MI = myocardial infarction

NHI = national health insurance

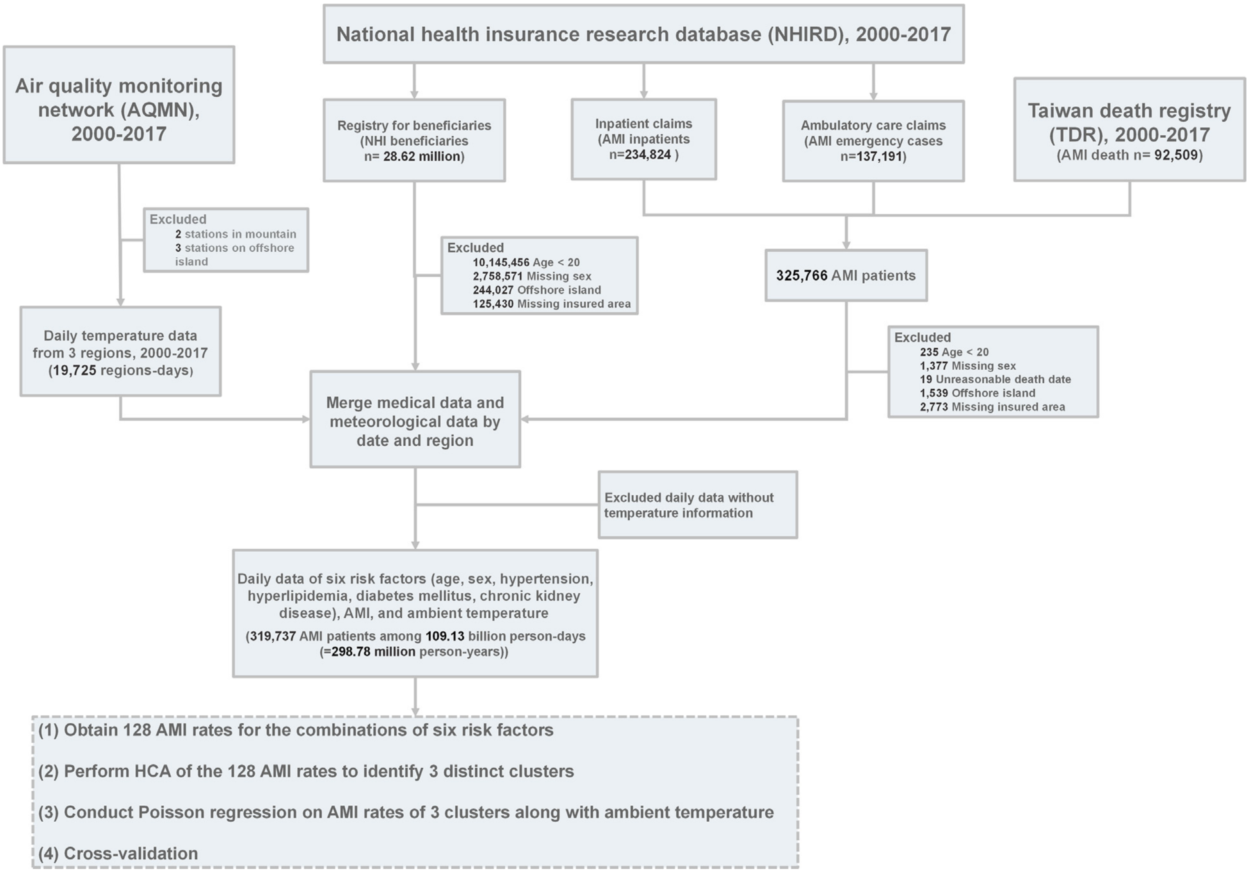
NHIRD = National Health Insurance Research Database

TDR = Taiwan Death Registry

ASCERTAINMENT OF AMI AND COMORBIDITIES. The outcome of the study was newly diagnosed AMI, which was defined as the first emergency department visit or admission caused by AMI (International Classification of Diseases-Ninth Revision-Clinical Modification code 410 before 2016 or International Classification of Diseases-Tenth Revision-Clinical Modification code I21 after 2016) in the NHIRD or AMI-related death in TDR between 2000 and 2017. Because we looked at new-onset AMI, patients with 2 AMI episodes were only counted once. Comorbidities, including hypertension, hyperlipidemia, diabetes mellitus, and CKD, were identified using diagnostic codes (Supplemental Table 1). The accuracy of the diagnoses of AMI and comorbidities in the NHIRD has been validated.[10,11]

ASCERTAINMENT OF AMBIENT TEMPERATURE. Temperature data from 75 monitoring stations of the Taiwan AQMN were analyzed, except for 2 stations in the mountain and 3 on offshore islands because of the limited number of residents in these regions. We computed the daily temperature from the hourly temperature because only the date of AMI occurrence was available in the NHIRD and TDR. The daily temperature was obtained according to the location of the hospital where the patient sought AMI treatment or the individual's residential area. The daily temperature was lowest in the north, middle in the central, and highest in the south regardless of the month. Daily temperatures were higher during the hot months (April-October) than during the cold months (November-March). The minimum and maximum daily temperature in the same area could be 4 °C to 7 °C different (Supplemental Figure 1). We used the minimum daily temperature during the cold months (November-March) and the maximum daily

FIGURE 1 **Flowchart of Creating Daily Data and Study Procedures**



This figure shows how to link the 3 national databases (National Health Insurance Research Database, Taiwan Death Registry, and Air Quality Monitoring Network) to create daily data and the study procedures to address the study aims. AMI = acute myocardial infarction; HCA = hierarchical clustering analysis.

temperature during the hot months (April-October) to reflect the effect of cold and high temperatures on AMI.[5]

STATISTICAL ANALYSIS. The incidence rate of AMI (defined as new AMI/million person-years) was calculated. It should be noted that individuals no longer contributed their daily data after having new-onset AMI, died, or withdrew from the NHI program. In other words, the million person-years involved were from either 2000 or the date they joined NHI until the date of the newly diagnosed AMI, withdrawal from the NHI, death, or December 31, 2017, whichever came first. We conducted Poisson regression to obtain AMI's incidence rate ratio (IRR) for various factors.[12] Overdispersion was examined using the chi-square value divided by the *df*. Akaike information criterion and R^2 were used to determine the best model (Supplemental Methods 1).[13] The known risk factors for AMI included age, sex, hypertension, hyperlipidemia, diabetes, and CKD. Therefore, we calculated through 109.13 billion person-days to generate the 128 AMI rates for the combination of the 6 risk factors (= 4 age groups × 2 sexes × 2 status of hypertension × 2 status of hyperlipidemia × 2 status of diabetes × 2 status of CKD). We then performed hierarchical clustering analysis (HCA) of the 128 AMI rates to identify distinct clusters (**Figure 1**). The proximity measure of the Ward linkage criteria was used to determine the optimal number of clusters (Supplemental Methods 2). We conducted an annual cross validation to examine the robustness of our final model. The advantages of annual cross validation were temperatures, from low to high, occurred throughout the year, and our daily data were of a time-variant nature. The insignificant chi-square test and the

TABLE 1 The Univariate and Multivariate Analysis of AMI Incidence Among Taiwan Adults, 2000-2017

	Total PY (Million)	Events (%)[a]	Incidence Rate (per 100,000 PY)	Crude IRR (95% CI)	Adjusted IRR (95% CI)
Total	298.78	319,737 (100)	107.02 (106.64-107.39)		
Age, y					
20-39	122.02	9,875 (3.09)	8.09 (7.93-8.25)	Reference	Reference
40-49	63.48	29,535 (9.24)	46.52 (45.99-47.05)	5.75 (5.62-5.88)	4.56 (4.45-4.66)
50-64	70.13	89,219 (27.90)	127.21 (126.38-128.05)	15.72 (15.4-16.05)	8.65 (8.47-8.84)
≥65	43.14	191,108 (59.77)	443.03 (441.05-445.02)	54.74 (53.65-55.86)	19.92 (19.5-20.35)
Sex					
Female	152.60	98,420 (30.78)	64.5 (64.09-64.9)	Reference	Reference
Male	146.18	221,317 (69.22)	151.4 (150.77-152.03)	2.35 (2.33-2.37)	2.43 (2.41-2.45)
Hypertension					
No	233.06	85,294 (26.68)	36.6 (36.35-36.84)	Reference	Reference
Yes	65.72	234,443 (73.32)	356.73 (355.28-358.17)	9.75 (9.67-9.82)	2.6 (2.57-2.62)
Hyperlipidemia					
No	244.75	169,428 (52.99)	69.23 (68.9-69.56)	Reference	Reference
Yes	54.03	150,309 (47.01)	278.19 (276.79-279.6)	4.02 (3.99-4.05)	1.06 (1.05-1.07)
Diabetes mellitus					
No	265.33	187,578 (58.67)	70.7 (70.38-71.02)	Reference	Reference
Yes	33.45	132,159 (41.33)	395.1 (392.97-397.23)	5.59 (5.55-5.63)	1.57 (1.56-1.59)
Chronic kidney disease					
No	284.23	242,605 (75.88)	85.36 (85.02-85.7)	Reference	Reference
Yes	14.55	77,132 (24.12)	530.22 (526.48-533.96)	6.21 (6.16-6.26)	1.77 (1.75-1.78)
Temperature				0.9901 (0.9896-0.9905)	0.9891 (0.9887-0.9896)
R^2, %					58.65

Values are n (%) unless otherwise indicated. The crude and adjusted IRR was estimated using Poisson regression. The ambient temperature was the minimum daily temperature from November to March and the maximum from April to October. [a]The column percentages of the categories for each risk factor are summed to 100%.

AMI = acute myocardial infarction; IRR = incidence rate ratio; PY = person-year.

ratio of the chi-square value to *df* <3 reflect a good fit of the test set in the final model.[14]

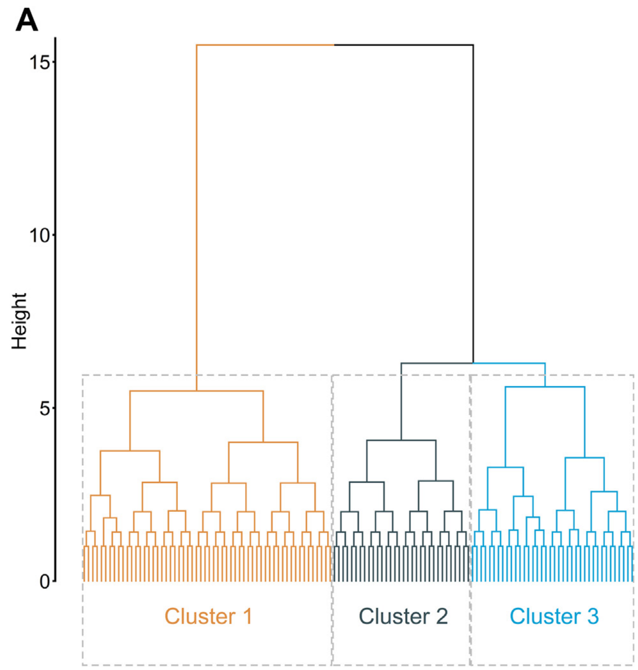
RESULTS

AMI INCIDENCE RATES FOR THE 6 RISK FACTORS PLUS TEMPERATURE. From 2000 to 2017, 319,737 patients had new-onset AMIs over 298.78 million person-years, corresponding to an incidence rate of 107.02 per 100,000 person-years (95% CI: 106.64-107.39 person-years). Of those with AMI, 55,953 (17.5%) were fatal AMI events identified by the TDR. Of 263,784 patients with nonfatal events, 124,379 (47.2%) were through emergency department visits, and the rest were from hospitalization. There were 191,108 patients (59.7%) older than 65 years of age and 9,875 patients (3.1%) younger than 40 years of age. Overall, 73.3% of the patients had hypertension, 47.0% had hyperlipidemia, 41.3% had diabetes mellitus, and 24.1% had CKD (Table 1). Univariate and multivariate analyses revealed that the 6 factors (age, sex, hypertension, hyperlipidemia, diabetes mellitus, and CKD) and the daily ambient temperature (the minimum daily temperature from November-March and the maximum from April-October) were significantly associated with AMI (Table 1). Individuals ≥65 years of age had the highest adjusted IRR (19.92; 95% CI: 19.5-20.35) of AMI compared with those 20 to 39 years of age. A history of hypertension had the second highest adjusted IRR (2.6; 95% CI: 2.57-2.62) compared with those without hypertension. The adjusted IRR of daily ambient temperature was 0.9891 (95% CI: 0.9887-0.9896).

HIERARCHICAL CLUSTERING ANALYSIS. HCA of the 6 risk factors identified 3 distinct clusters (cluster 1: age <50 years, cluster 2: age ≥50 years without hypertension, and cluster 3: mainly age ≥50 years [84%] with hypertension) (Figure 2). The incidence rate per 100,000 person-years was 16.04 (95% CI: 15.71-16.39) for cluster 1, 105.13 (95% CI: 103.61-106.67) for cluster 2, and 388.17 (95% CI: 385.26-391.13) for cluster 3. Compared with cluster 1, individuals in clusters 2 and 3 had a 6.55 (95% CI: 6.46-6.64) and 24.19 (95% CI: 23.9-24.49) times higher risk of AMI incidence, respectively, with R^2 of 86.50% (model 1 in Supplemental Table 2).

AMI INCIDENCE RATES FOR THE 3 CLUSTERS PLUS TEMPERATURE. When running the Poisson regression of the AMI incidence rate only with the temperature

FIGURE 2 **Hierarchical Clustering Analysis of 128 (= 6 Risk Factor Combinations) Acute Myocardial Infarction Rates**



B

	Cluster1	Cluster2	Cluster3
Age, year			
20-39	32 (55.17%)	0 (0%)	0 (0%)
40-49	26 (44.83%)	0 (0%)	6 (15.79%)
50-64	0 (0%)	16 (50%)	16 (42.11%)
≥65	0 (0%)	16 (50%)	16 (42.11%)
Sex			
Female	32 (55.17%)	16 (50%)	16 (42.11%)
Male	26 (44.83%)	16 (50%)	22 (57.89%)
Hypertension			
No	32 (55.17%)	32 (100%)	0 (0%)
Yes	26 (44.83%)	0 (0%)	38 (100%)
Hyperlipidemia			
No	29 (50%)	16 (50%)	19 (50%)
Yes	29 (50%)	16 (50%)	19 (50%)
Diabetes mellitus			
No	28 (48.28%)	16 (50%)	20 (52.63%)
Yes	30 (51.72%)	16 (50%)	18 (47.37%)
Chronic kidney disease			
No	28 (48.28%)	16 (50%)	20 (52.63%)
Yes	30 (51.72%)	16 (50%)	18 (47.37%)

(A) The dendrogram of hierarchical clustering and **(B)** the frequency of different risk factors in the 3 clusters. Cluster 1 represents those <50 years of age because 100% are <50 and equally distributed in the other 5 risk factors. Cluster 2 represents those ≥50 years of age without hypertension because 100% are ≥50, 100% do not have hypertension, and are equally distributed in the other 4 risk factors. Cluster 3 represents those mainly ≥50 years of age with hypertension because 84% are ≥50, 100% have hypertension, and are equally distributed in the other 4 risk factors.

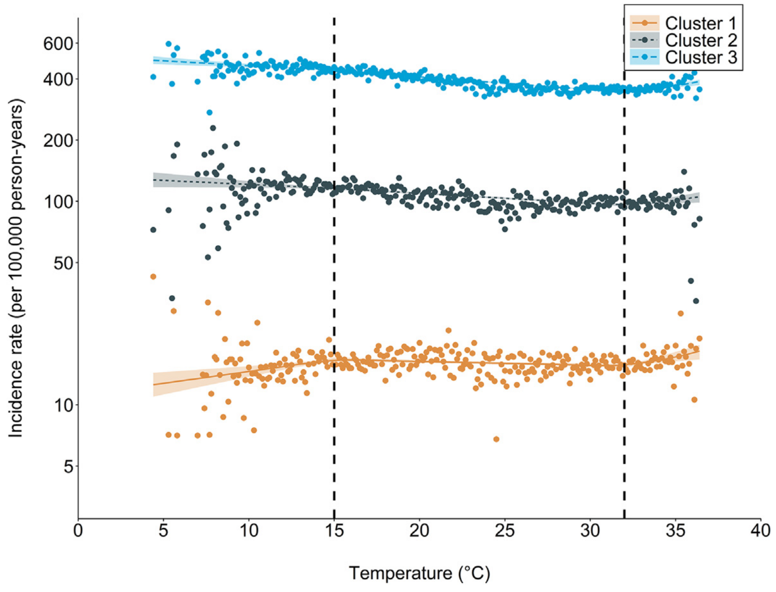
variable (minimum daily temperature in the cold months of November-March and maximum daily temperature in the hot months of April-October), R^2 was 69.74% (Supplemental Figure 2). When adding the 3 clusters plus the temperature variable in the Poisson regression, R^2 was 86.94% (model 2 in Supplemental Table 2). We located 2 temperature inflection points (15 °C and 32 °C) with the lowest Akaike information criterion (Supplemental Figure 3), and R^2 was 86.96% (model 3 in Supplemental Table 2). In other words, our final model is the 3 clusters and the daily temperature with 2 temperature inflection points at 15 °C and 32 °C (**Figure 3**, model 3). Please refer to Supplemental Methods 1 for the equation derivation of models 1 to 3 and its interpretation of regression coefficients of the final model.

Within 15 °C to 32 °C, individuals in cluster 3 had the highest risk of AMI; every 1 °C decrease was associated with a 1.4% increase in the risk of AMI (slope = 1.014, 95% CI: 1.014-1.015). It was 1.1% (slope = 1.011; 95% CI: 1.010-1.012) and 0.4% (slope = 1.004; 95% CI: 1.002-1.006) for individuals in cluster 2 and cluster 1, respectively (**Figure 4A**). Below 15 °C, every 1 °C decrease was associated with a 0.9% increase (slope = 1.009; 95% CI: 1.001-1.018) and 1.1% (slope = 1.011; 95% CI: 1.007-1.015) in the risk of AMI for clusters 2 and 3, respectively. Individuals in cluster 1 had a 0.2% reduction (slope = 0.974; 95% CI: 0.961-0.987) in the risk of AMI with every 1 °C decrease below 15 °C. Above 32 °C, there were increased risks of 3.6%, 2%, and 2.5% for every 1 °C increase in clusters 1, 2, and 3, respectively.

The IRR of AMI for clusters 2 and 3 varied with temperatures when treating cluster 1 as a reference (**Figure 4B**). The AMI IRR for cluster 3 was highest (40.00; 95% CI: 34.52-46.35) at 4 °C, sharply reduced to 26.37 (95% CI: 25.75-27.02) at 15 °C, and slowly reduced to 21.31 (95% CI: 19.70-23.06) at 36 °C. For cluster 2, the IRR of AMI was highest (10.31; 95% CI: 8.74-12.16) at 4 °C, reduced to 6.93 (95% CI: 6.74-7.14) at 15 °C, and slowly reduced to 5.80 (95% CI: 5.29-6.36) at 36 °C.

PREDICTION OF AMI RATE AND CROSS VALIDATION. Supplemental Table 3 presents the predicted AMI rate for the 3 clusters for ambient temperatures from 4 °C

FIGURE 3 **AMI Rate vs Daily Temperatures by the 3 Clusters**



This figure shows 3 separate lines and 2 temperature inflection points (15 °C and 32 °C) for the acute myocardial infarction (AMI) incident rates in log scale for the 3 clusters. Cluster 1: <50 years of age; cluster 2: ≥50 years of age without hypertension; and cluster 3: ≥50 years of age (84%) with hypertension. The ambient temperature was the minimum daily temperature from November to March and the maximum from April to October.

to 36 °C, so it is easy to locate their predicted AMI rate according to the ambient temperature of 1 day and their cluster. For example, at the ambient temperature of 20 °C, individuals with cluster 1 characteristics (<50 years of age) have a predicted AMI rate of 16.3 per 100,000 person-years. On the other hand, at the same daily temperature of 20 °C, the AMI rate becomes 406.66 per 100,000 person-years for someone with cluster 3 characteristics (mainly ≥50 years of age and had hypertension).

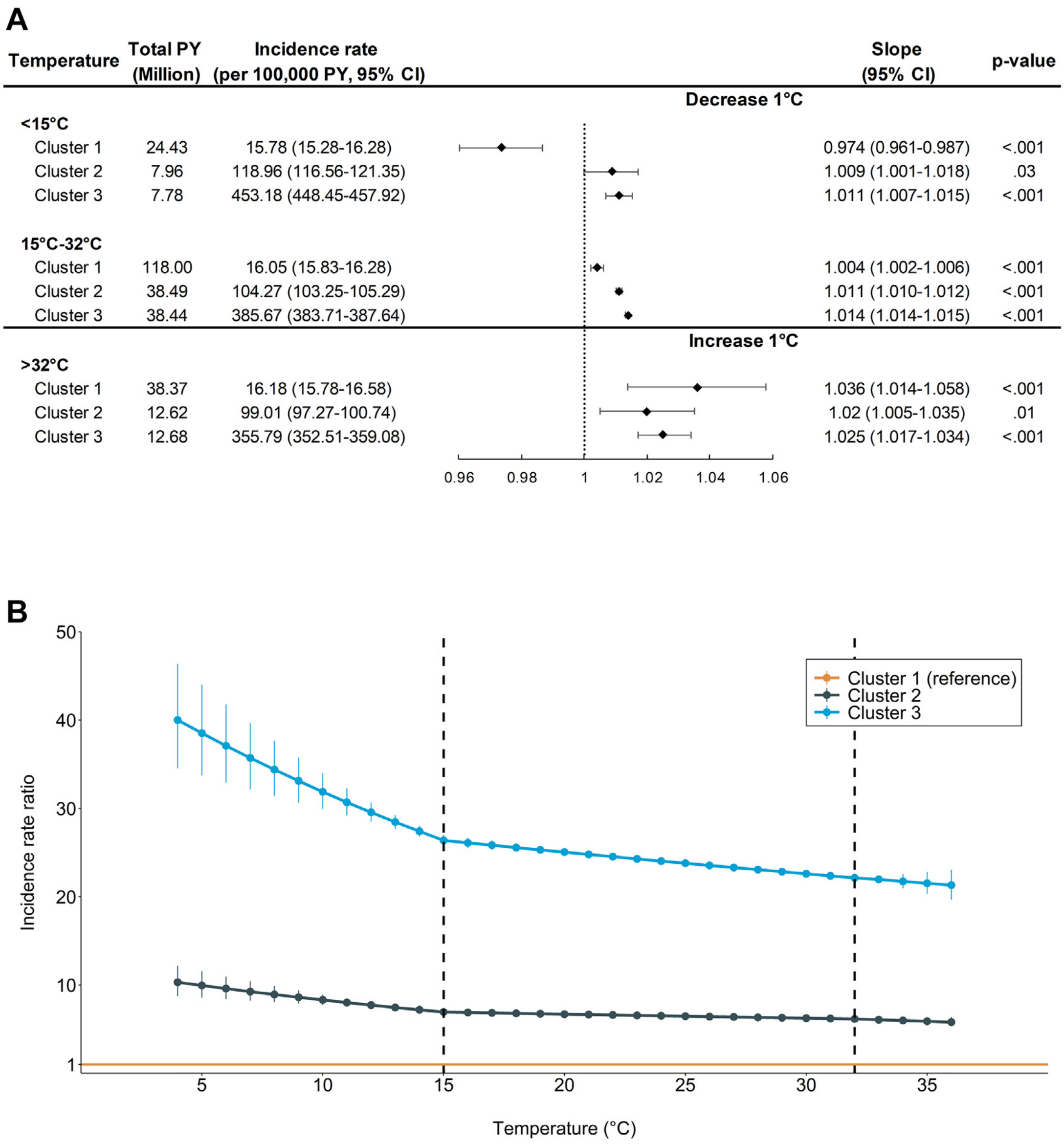
To cross validate the final model, the data of each calendar year served as the testing set, whereas the data of the rest calendar years served as the training set. All *P* values of the chi-square test and chi-square value/*df* for the 18 test sets were insignificant and <3, respectively, indicating good cross validation of the final model (Supplemental Table 4).

ADDITIONAL ANALYSIS. Some meteorologic factors, such as atmospheric pressure and relative humidity, are associated with AMI. In this study, atmospheric pressure was highly correlated with ambient temperature ($r = -0.68$), which is consistent with the famous Gay-Lussac law of pressure temperature.[15] We did not add atmospheric pressure to our final model (model 3) to avoid the problem of unstable estimates and inaccurate variances caused by multicollinearity.[16] For humidity (not correlated with temperature), we added humidity in model 3 and did not see a significant IRR for humidity and humidity*cluster (data not shown). Therefore, we did not include humidity in our final model. We also examined an association between adjacent day temperature and AMI incidence. The significant association between temperature and AMI was observed only on the same day for each cluster but not on the previous days 1 to 7 ($P > 0.05$ for each previous day) (Supplemental Figure 4).

DISCUSSION

In this nationwide study that covered 17 years of population and weather data, we identified 3 temperature ranges (<15 °C, 15 °C-32 °C, and >32 °C) and associated them with different AMI incidences in the 3 clusters. Individuals in cluster 3 (mainly ≥50 years of age with hypertension) had the highest overall AMI incidence rate and AMI risk per 1 °C reduction in 15 °C to 32 °C and <15 °C. However, above the 32 °C

FIGURE 4 **IRR of Temperature and the 3 Clusters on AMI**

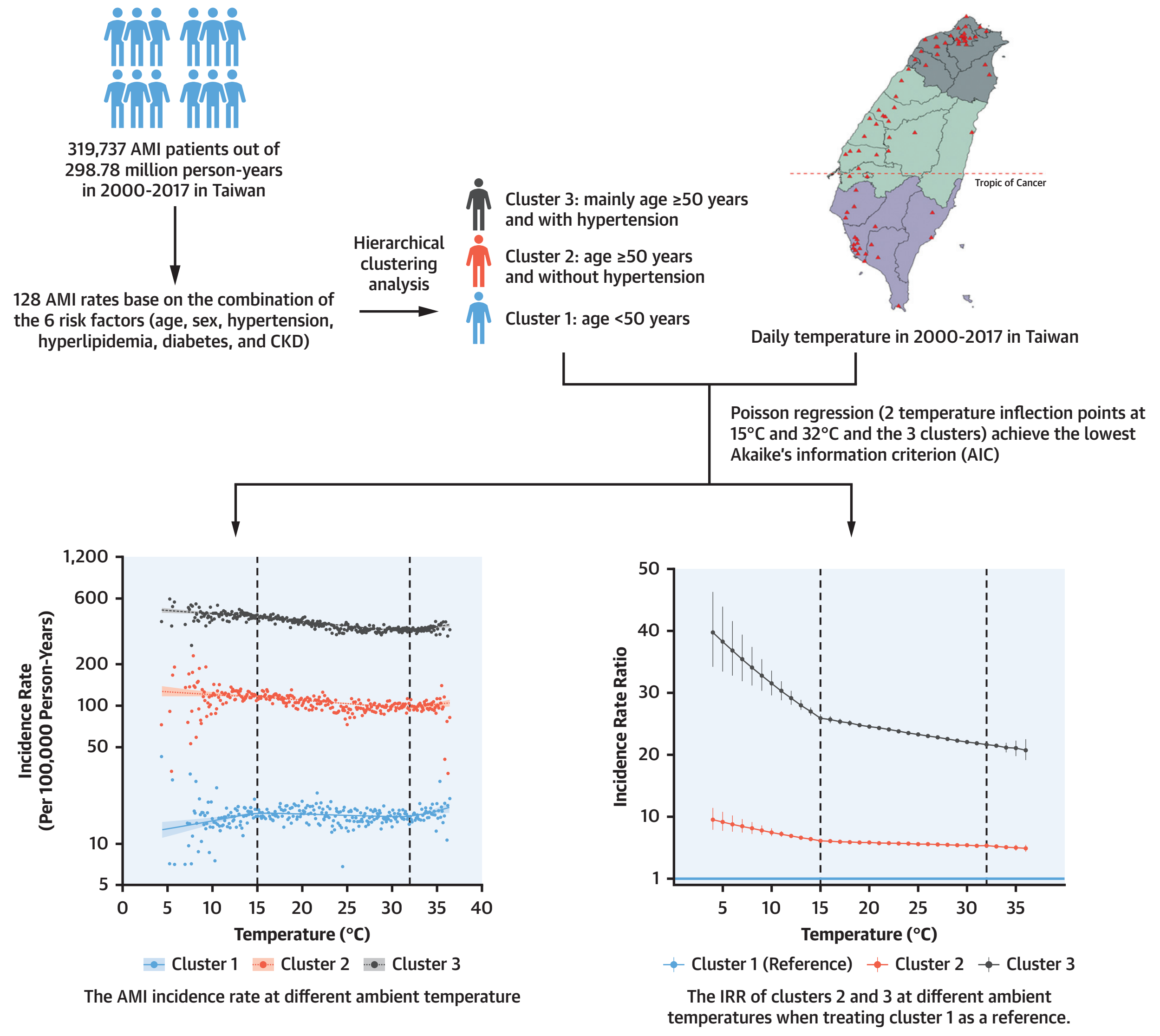


Temperature	Total PY (Million)	Incidence rate (per 100,000 PY, 95% CI)	Slope (95% CI)	p-value
<15°C				
Cluster 1	24.43	15.78 (15.28-16.28)	0.974 (0.961-0.987)	<.001
Cluster 2	7.96	118.96 (116.56-121.35)	1.009 (1.001-1.018)	.03
Cluster 3	7.78	453.18 (448.45-457.92)	1.011 (1.007-1.015)	<.001
15°C-32°C				
Cluster 1	118.00	16.05 (15.83-16.28)	1.004 (1.002-1.006)	<.001
Cluster 2	38.49	104.27 (103.25-105.29)	1.011 (1.010-1.012)	<.001
Cluster 3	38.44	385.67 (383.71-387.64)	1.014 (1.014-1.015)	<.001
>32°C				
Cluster 1	38.37	16.18 (15.78-16.58)	1.036 (1.014-1.058)	<.001
Cluster 2	12.62	99.01 (97.27-100.74)	1.02 (1.005-1.035)	.01
Cluster 3	12.68	355.79 (352.51-359.08)	1.025 (1.017-1.034)	<.001

Model 3 was used to estimate the association of temperature with 2 inflection points at 15 °C and 32 °C with the 3 clusters on acute myocardial infarction (AMI). **(A)** The slope of temperature (= incidence rate ratio [IRR] of every temperature change): a decrease for temperatures <15 °C or between 15 °C and 32 °C, and a 1 °C increase for temperatures >32 °C. **(B)** The IRR of clusters 2 and 3 at different ambient temperatures when treating cluster 1 as a reference. PY = person-year.

thresholds, individuals in cluster 1 (younger than 50 years of age) had the highest risk of AMI risk per 1 °C increase in temperature. Our study is the first to demonstrate that the effect of ambient temperature on new-onset AMI varies by different risk factors. Using the Poisson regression model on the daily data, our final model well predicted the AMI incidence rate at each temperature (from 4 °C-36 °C) of the 3 clusters. This analysis provided valuable information for potential high-risk people susceptible to the low- or high-temperature–related occurrence of AMI (**Central Illustration**).

CENTRAL ILLUSTRATION **Effect of Temperature on Acute Myocardial Infarction by Risk Factors**



319,737 AMI patients out of 298.78 million person-years in 2000-2017 in Taiwan

128 AMI rates base on the combination of the 6 risk factors (age, sex, hypertension, hyperlipidemia, diabetes, and CKD)

Hierarchical clustering analysis

Cluster 3: mainly age ≥50 years and with hypertension

Cluster 2: age ≥50 years and without hypertension

Cluster 1: age <50 years

Daily temperature in 2000-2017 in Taiwan

Poisson regression (2 temperature inflection points at 15°C and 32°C and the 3 clusters) achieve the lowest Akaike's information criterion (AIC)

The AMI incidence rate at different ambient temperature

The IRR of clusters 2 and 3 at different ambient temperatures when treating cluster 1 as a reference.

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The cold and heat exposure on acute myocardial infarction (AMI), aligning with their risk groups, was examined using 3 Taiwan national databases. HCA identified 3 distinct clusters with different AMI incidence rates. The Poisson regression using the daily ambient temperature well predicted the AMI incidence rate at each temperature (ranging from 4 °C to 36°C) of the 3 different risk groups. People ≥50 years of age with hypertension (cluster 3) are more susceptible to cold-related AMI. However, heat-related AMI is more prominent in individuals <50 years of age (cluster 1). CKD = chronic kidney disease.

Previous studies have described a U-shaped association between temperature and the risk of MI, with increased risks for both temperatures above and below the optimum temperature.[3,17,18] For cold-related increasing AMI, it has been reported that every 1 °C reduction in mean daily temperature was associated with a cumulative increase of 2.0% (95% CI: 1.1%-2.9%) in the risk of MI.[4] One meta-analysis study showed that with cold exposure, every 1 °C decrease was associated with an increased relative risk of 1.014 (95% CI: 1.004-1.024) for MI hospitalization.[2] Consistent with the previous study, we further demonstrated that the risk of AMI per 1 °C reduction was not similar at different temperature ranges and varied with different risk factors. We used HCA to determine 3 clusters characterized by different ages and underlying comorbidities, such as hypertension, that are at risk. Cluster 1 was considered a low-risk individual <50 years of age, and cluster 2 was the intermediate-risk group of those ≥50 years of age without hypertension. Cluster 3 represented the high-risk group of most individuals (84.2%) older than 50 years of age with hypertension. Within 15 °C to 32 °C, there was a progressive elevation in the risk of AMI from cluster 1 to cluster 3, and every 1 °C decrease was associated with a 4%, 11%, and 14% increase in the risk of AMI for clusters 1, 2, and 3, respectively. Below 15 °C, there was also an elevated risk of AMI per 1 °C decrease in cluster 3 (11%) compared with cluster 2 (9%). However, for cluster 1, no apparent association between cold temperature and AMI was detected below the threshold of 15 °C. Compared with cluster 1, cluster 3 had the highest IRR of AMI, which was more apparent below the threshold of 15 °C. Our study provides methods to differentiate the high-risk group and suggests that individuals in cluster 3 (≥50 years of age and had hypertension) were more vulnerable to cold weather-related acute coronary events.

Two potential physiological mechanisms explain the elevated risk of cold-induced acute coronary events in the cluster 3 population (ie, older individuals with hypertension). First, low temperatures may stimulate cold receptors on the skin leading to a rise in catecholamine levels, subsequent vasoconstriction, and increased heart rate and blood pressure.[19-21] For individuals with hypertension, cold-related fluctuations in high blood pressure could be aggravated and may precipitate myocardial ischemia and coronary plaque instability. Furthermore, the elderly showed a pronounced enhancement in the rise of blood pressure surge with cold weather, which may increase the risk of cardiovascular events.[22] Second, a decrease in temperature could increase diuresis, leading to a decrease in plasma volume with hemoconcentration and an increase in blood viscosity.[19,23] A previous study showed higher fibrinogen, tissue plasminogen activator, protein C, and protein S levels in older (≥75 years of age) compared with younger (25-30 years of age) individuals during cold weather.[24] Increased plasma concentrations of clotting factors can promote and increase the risk of atherothrombotic disease. Therefore, the proposed mechanism is more likely to be prominent in older than younger individuals and thus explains why the older population with hypertension has a pronounced effect on the risks of AMI related to cold temperature.

In this study, we also observed a significant heat-related increased risk of new-onset AMI events above the temperature threshold of 32 °C. Heat-related MI was described by a previous study in Germany that revealed a significant association between heat (23.5 °C) and MI occurrence between 2001 and 2014.[3] Another study in England and Wales showed that higher ambient temperature above a threshold of 20 °C was associated with an increased risk of MI.[6] In contrast to the previous study, the temperature threshold of heat-related AMI was 32 °C in this study. Taiwan is located in Southeast Asia and has tropical to subtropical areas. The climate is relatively warm, with a mean daily maximum temperature of 30.3 °C in the hot months and a mean minimum temperature of 16.5 °C in the cold months. The higher threshold for heart-related AMI in our study is consistent with 2 previous studies: 1 study in Vietnam[25] that found an increase in the risk of hospitalization for AMI above the temperature of 29.9 °C and another study in Hong Kong revealing increasing AMI hospitalization among patients with diabetes mellitus when the temperature reached above 28.8 °C during the hot season.[26] Taken together, exposure to heat may be an important environmental trigger for new-onset AMI, and the threshold of heat temperature can differ in various latitude countries, with a higher threshold in tropical or subtropical areas.

Potential pathophysiological mechanisms related to a high ambient temperature that trigger incident coronary events have been suggested, including the increased surface blood circulation and sweating induced by hot temperature followed by dehydration and salt depletion, leading to elevated blood viscosity, plasma cholesterol, and a “thrombosis promoting” state of hemoconcentration.[27] Furthermore, heat stress has been shown to induce the release of interleukin-1 and interleukin-6, resulting in inflammatory responses of damage and hyperactivation of endothelial cells.[27] Finally, increased temperature was associated with the increased cardiac workload as a compensatory circulation reaction to maintain the volume of heart minute volume and falling blood pressure.[27] Our study demonstrated that different underlying risk factors affect new-onset heat-related AMI by ambient temperature. The previous meta-analysis of 23 studies has shown that the relationship between temperature and the relative risk of MI hospitalization was 1.016 (95% CI: 1.004-1.028) for every 1°C increase.[2] In our study, above the 32 °C temperature threshold, the relative risk of new-onset MI for every 1°C increase was 1.036 (95% CI: 1.014-1.058), 1.021 (95% CI: 1.005-1.035), and 1.025 (95% CI: 1.017-1.034) in clusters 1, 2, and 3, respectively. Furthermore, these are equivalent to an increased risk of 3.6%, 2.0%, and 2.5% for every 1 °C increase. Similar to cold-related AMI, we observed a higher risk of AMI per 1°C increase in cluster 3 than in cluster 2 (2.5% vs 2%) above the threshold of 32 °C. This finding is supported by a previous study showing that hot temperature is associated with increased systolic pressure at night in treated elderly hypertensive patients.[22] Interestingly, individuals in cluster 1 (ie, those <50 years of age) have the highest heat-related AMI. One potential explanation is that younger people may be more exposed to severe hot conditions from working outdoors and doing other physical activities.[28] Further research is needed to elucidate the mechanisms.

The strengths of the present study include its large and representative sample obtained using nationwide claim-based data of 18 years to obtain daily data for the entire country of Taiwan. Taiwan's population was 23.6 million people in 2018, and the total area of Taiwan is 36,197 km^2. Additionally, Taiwan's routinely collected nationwide databases (including health insurance claims, death registry, and detailed climatic data) provided good resources for analyzing this issue in Asian populations. Unlike previous studies based only on hospital admissions, which may have underestimated actual temperature effects, our study provided an accurate incidence rate of AMI, including patients who had AMI admission or had MI deaths in the emergency room.[18] We are the first to identify the 3 different groups at risk and demonstrate that the effect of heat or cold temperature on new-onset AMI varies by different underlying risk factors. The Poisson regression model well predicted the incidence rate across the 3 clusters at each temperature (ranging from 4 °C to 36 °C). We hope this information helps high-risk people foresee their cardiovascular problems at different ambient temperatures and react appropriately to reduce the incidence of cardiovascular diseases. As the global population ages, the burden of temperature-related AMI in extreme global climate change becomes more apparent.[27] Finally, our study's higher threshold of heat-related AMI is consistent with 2 previous studies in Southeast Asia. Taiwan is an island country with 4 distinct tropical and subtropical seasons. Therefore, our findings may be generalized to other Asian populations with similar latitudes.

STUDY LIMITATIONS. First, Taiwan lies in the Tropic of Cancer, and its general climate is tropical marine, with a temperature range between 4 °C and 36 °C. Therefore, we saw a higher variation in the AMI rate in cold and high temperatures. Second, the NHIRD database lacks data on lifestyle factors, cardiac troponin measures, body mass index, smoking, and alcohol consumption, which might confound our results. Third, we cannot examine the hourly temperature's impact on AMI occurrence because the hourly visit time to the hospital is unavailable in the NHIRD. Indoor temperature is unavailable also. Fourth, cluster analysis results are challenging to validate because the groups are not known a priori. The evaluation of clustering results is as tough as the clustering itself. More research is needed to validate our HCA results. Finally, we could not differentiate the type of AMI (ST-segment elevation MI or non-ST-segment elevation MI) because of the limitation of the NHIRD.

CONCLUSIONS

The effect of ambient temperature on new-onset AMI varies with different underlying risk factors. People ≥50 years of age and with hypertension are more susceptible to cold-related AMI. However, heat-related AMI is more prominent in young individuals <50 years of age. Heat and cold weather pose a high risk to AMI, especially in high-risk populations.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: The effect of ambient temperature on new-onset AMI varies with different underlying risk factors. People ≥50 years of age with hypertension are more susceptible to cold-related AMI. However, heat-related AMI is more prominent in individuals <50 years of age.

TRANSLATIONAL OUTLOOK: Heat and cold weather pose a high risk to AMI, especially in high-risk individuals. This information helps high-risk people to foresee their cardiovascular problems at different ambient temperatures.

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APPENDIX For an expanded Methods section and supplemental tables and figures, please see the online version of this paper.