Meteorological Parameters and the Onset of Chest Pain in Subjects with Acute ST-Elevation Myocardial Infarction: an Eight-Year, Single-Center Study in China

En-Zhi Jia a, Zhe Liu a, Ai-Jun Chen b, Yan Gu a, Zhao-Yang Li a, Tie-Bing Zhu a, Chun-Jian Li a, Lian-Sheng Wang a, Wen-Zhu Ma a, Zhi-Jian Yang a

a Department of Cardiovascular Medicine, First Affiliated Hospital of Nanjing Medical University, Nanjing, China; b School of Atmosphere Physics, Nanjing University of Information Science and Technology, Nanjing, China

Key Words
Acute ST-elevation myocardial infarction • Atmospheric pressure variation • Temperature

Abstract
Objective: The purpose of this study was to investigate the influence of weather on the occurrence of acute ST-elevation myocardial infarction in Chinese subjects. Methods: Weather and climate data, as well as the occurrence of STEMI, were monitored at 2 am, 8 am, 2 pm, and 8 pm between 2003 and 2010. Generalized additive Poisson models were utilized to plot the numbers of patients with STEMI within 6 hour intervals against climatological variations, after accounting for the effects of the hour and season. Results: The inclusion of meteorological conditions, including observed atmospheric pressure (hPa, hectopascal) variations during the previous three hours and temperature (°C, degrees Celsius), significantly affected the occurrence of STEMI, as measured every six hours. Compared with the 50th percentile of atmospheric pressure variations, the RRs (95% CI) for the first percentile, 10th percentile, 25th percentile, 75th percentile, 90th percentile, and 99th percentile of atmospheric pressure variation over lag 0 were 1.66 (1.36~2.03), 1.47 (1.30~1.67), 1.22 (1.12~1.33), 1.16 (1.07~1.25), 1.27 (1.13~1.43), and 1.16 (0.92~1.46), respectively. Compared to the 50th percentile of temperature, the RRs (95% CI) for the first percentile, 10th percentile, 25th percentile, 75th percentile, 90th percentile, and 99th percentile of temperature over lag 0 were 0.58 (0.40~0.83), 0.60 (0.46~0.78), 0.69 (0.57~0.83), 1.33 (1.14~1.56), 1.39 (1.13~1.71), and 1.17 (0.84~1.63), respectively. Conclusions: Based on the eight-year, single-center study, significant relationships were observed among the occurrence of STEMI and atmospheric pressure variations during the previous three hours and temperature after account for long-term time trends.

Z. Liu and E.-Z. Jia contributed equally to this article.
Introduction

Acute ST-elevation myocardial infarction (STEMI), a clinical syndrome defined by characteristic symptoms of myocardial ischemia in association with persistent electrocardiographic (ECG) ST elevation and the subsequent release of biomarkers of myocardial necrosis [1], is a major cause of mortality and morbidity worldwide [2]. Recently, investigators have focused on the relationship between meteorological parameters and the occurrence of acute myocardial infarction (MI). A case-crossover study performed in the United States indicated that exposure to cold increased the risk of acute MI, and exposure to heat increased the risk of dying after an acute MI [3]. A Korean AMI Registry study found that the occurrence of AMI demonstrates seasonal and monthly variations and that meteorological parameters have a significant influence on the occurrence of AMI, particularly in females and in younger patients [4]. Additionally, a study performed in southern China indicated that cool temperatures and higher NO\textsubscript{2} levels substantially increased the risk of AMI in these normally warm-climate cities: the sizes of the observed effects were larger than those noted in previous studies [5]. However, most of the studies in question have primarily examined the association between mortality or hospitalization due to acute myocardial infarction and meteorological parameters. Due to periodic variations in the time distribution patterns of the onset of chest pain in subjects with acute ST-elevation myocardial infarction [6], an exploration of the association between meteorological parameters and the time distribution patterns of the onset of chest pain in subjects with acute ST-elevation myocardial infarction is necessary.

The purpose of this study was to investigate the influence of weather on the occurrence of acute ST-elevation myocardial infarction in Chinese subjects and to use this information to develop a means of forecasting acute ST-elevation myocardial infarction occurrence in the future.

Patients and Methods

The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Nanjing Medical University (Nanjing, China). Written informed consent was provided by each patient.

Study subjects

This study was a prospective, observational single-center study that investigated the association between meteorological parameters and time distribution patterns in patients with STEMI, in China. Adult patients with acute STEMI who presented to the First Affiliated Hospital of Nanjing Medical University from 1 January 2003 to 31 December 2010 were consecutively enrolled in and included in the study. The diagnosis of acute STEMI was defined as ≥30 min of continuous chest pain, ST-segment elevation >2.0 mm on ≥2 contiguous electrocardiographic leads, and a two-fold elevation or more in creatine kinase-MB (CKMB) levels [7]. Exclusion criteria included cardiac shock, severe liver or renal dysfunction, drug allergy, and severe hypovolemia. The rationale for the use of these criteria was that subjects suffering from the above complications may not have been able to accurately report the time of acute STEMI onset, which was determined by self-reported chest pain. Overall, 1467 subjects were included in this study.

Climatological data

Meteorological data are based on observations by the Meteorological Information Comprehensive Analysis and Process System (MICAPS) of China and were provided by the School of Atmosphere Physics, Nanjing University of Information Science and Technology.

Nanjing city is located at a latitude of 118°46’ East and longitude of 32°03’ North. The weather and climate data, including sea level pressure (hPa, hectopascal), atmospheric pressure variations during the previous three hours (hPa, hectopascal), six hour precipitation (mm, millimeter), dew-point temperature (°C, degrees Celsius), visibility (km, kilometer), and temperature (°C, degrees Celsius), were monitored at 2 am, 8 am, 2 pm, and 8 pm. Meteorological data for November and December of 2007 and July of 2008 were not included.
Statistical analyses

This was a time series study. Generalized additive Poisson models were utilized to plot numbers of patients with STEMI within 6 hour intervals against climatological variations after accounting for the effects of the hour and season [8]. All analyses were performed using R version 3.0.2 (http://www.R-project.org). The R package, mgcv, was used to fit the GAMs in conjunction with the dlnm package, which was used for distributed lag modeling. Long-term time trends were controlled using a smooth function for each 6 hour interval of study, and seasonality was controlled using a smooth function for the day of the year, with a maximum of 4 df. Meteorological parameters were initially modeled using non-linear polynomial-constrained distributed lag models, with a maximum lag of 30. The df for the lag structure was 4, and the df for each smooth term describing the association between the predictor and the response was 4. The `quasipoisson' option was used to account for the possibility of overdispersion (variance greater than the mean) of outcome variables. These choices were based on the results of previous studies [5]. The meteorological variables were included in the model simultaneously; however, two of the variables, dew point temperature and temperature, appeared to be strongly correlated and were not included in the model together; therefore, the variable of temperature was included in the model to allow comparisons with other studies.

After the core model was built, we plotted the relationship between meteorological conditions and the onset of STEMI. Because a unit change in meteorological conditions above or below a particular threshold would have led to different effect estimates with the DLNMs, we calculated each meteorological parameter's risk using a cutoff (percentile) value and compared this value to another cutoff value over lags 0–30. Therefore, the relative risks (RRs) and 95% confidence intervals (CIs) for the onset of STEMI at the first percentile, 10th percentile, 25th percentile, 75th percentile, 90th percentile, and 99th percentile of meteorological conditions were calculated and compared with the 50th percentile of meteorological conditions. The selection of these cutoffs for calculating the RRs and 95% CIs was made based on a previous study [9].
Results

Meteorological conditions and numbers of patients with STEMI within 6 hour intervals

Table 1 depicts the meteorological conditions and the numbers of subjects with STEMI during each 6 hour interval during the study period (from 1 January 2003 to 31 December 2010). A total of 1407 subjects with STEMI were included in our study population, and 0.12 subjects suffered a STEMI every 6 hours. During the study period, the median levels of meteorological conditions were 165.00, 2.00, 0.00, 11.80, 7.00 and 18.10 for sea level pressure (hPa, hectopascal), atmospheric pressure variations during the previous three hours (hPa, hectopascal), six hour precipitation (mm, millimeter), dew-point temperature (°C, degrees Celsius), visibility (km, kilometer), and temperature (°C, degrees Celsius), respectively.

Table 2. Relative risks and corresponding 95% confidence intervals of sea level pressure (hPa) for each 6 hour interval of STEMI over multiple lags, during the study period (from 1 January 2003 to 31 December 2010)

Table 3. Relative risks and corresponding 95% confidence intervals of atmospheric pressure variations during the previous three hours (hPa) for each 6 hour interval of STEMI over multiple lags, during the study period (from 1 January 2003 to 31 December 2010)

Table 4. Relative risks and corresponding 95% confidence intervals of dew-point temperature (°C) for each 6 hour interval of STEMI over multiple lags, during the study period (from 1 January 2003 to 31 December 2010)
Generalized additive Poisson models were utilized to plot the results of the time series following adjustments for long-term trends: the results are included in Table 2-6, and the cumulative effects of meteorological conditions on the onset of STEMI for each 6 hour period at lag 0 are presented in Figure 1-6. A relationship between meteorological conditions, including sea level pressure (hPa, hectopascal), six hour precipitation (mm, millimeter), dew-point temperature (°C, degrees Celsius), and visibility (mm, kilometer), and the onset of STEMI was not observed in this study; however, atmospheric pressure (hPa, hectopascal) variations during the previous three hours and temperature (°C, degrees Celsius) were each significantly associated with the occurrence of STEMI within each 6 hour period.

### Table 5. Relative risks and corresponding 95% confidence intervals of visibility (km) for each 6 hour interval of STEMI over multiple lags, during the study period (from 1 January 2003 to 31 December 2010)

| Lag | 1st percentile (0.05) vs. 99th percentile (0.95) | 5th percentile (0.05) vs. 95th percentile (0.95) | 25th percentile (0.25) vs. 75th percentile (0.75) | 75th percentile (0.75) vs. 95th percentile (0.95) | 90th percentile (0.90) vs. 100th percentile (1.00) |
|-----|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| 0   | 0.89 (0.077–1.16)               | 1.00 (0.089–1.33)               | 1.00 (0.091–1.19)               | 0.95 (0.065–1.03)               | 0.94 (0.052–1.07)               |
| 0.1 | 1.16 (0.092–1.47)               | 1.10 (0.094–1.23)               | 1.07 (0.092–1.23)               | 0.97 (0.085–1.10)               | 0.98 (0.082–1.18)               |
| 0.3 | 1.06 (0.078–1.14)               | 0.99 (0.074–1.11)               | 0.99 (0.074–1.09)               | 0.94 (0.060–1.11)               | 0.98 (0.078–1.23)               |
| 0.7 | 0.89 (0.062–1.14)               | 0.85 (0.065–1.11)               | 0.86 (0.067–1.13)               | 0.80 (0.064–0.99)               | 0.82 (0.061–1.10)               |
| 0.14 | 1.18 (0.072–1.91)                | 0.86 (0.061–1.23)               | 0.84 (0.059–1.18)               | 0.85 (0.064–1.13)               | 0.89 (0.061–1.32)               |
| 0.21 | 1.06 (0.059–1.90)                | 0.87 (0.054–1.33)               | 0.87 (0.057–1.31)               | 0.89 (0.056–1.10)               | 0.82 (0.051–1.39)               |
| 0.30 | 0.89 (0.049–1.57)                | 0.89 (0.054–1.46)               | 0.90 (0.055–1.46)               | 0.78 (0.052–1.17)               | 0.80 (0.046–1.57)               |

### Table 6. Relative risks and corresponding 95% confidence intervals of temperature (°C) for each 6 hour period of STEMI over multiple lags, during the study period (from 1 January 2003 to 31 December 2010)

| Lag | 1st percentile (0.05) vs. 99th percentile (0.95) | 5th percentile (0.05) vs. 99th percentile (0.95) | 25th percentile (0.25) vs. 99th percentile (0.95) | 75th percentile (0.75) vs. 99th percentile (0.95) | 90th percentile (0.90) vs. 100th percentile (1.00) |
|-----|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| 0   | 0.89 (0.049–0.83)               | 0.89 (0.046–0.85)               | 0.87 (0.057–0.83)               | 1.13 (1.14–1.56)               | 1.19 (1.13–1.74)               |
| 0.1 | 1.29 (0.084–1.17)               | 1.14 (0.075–1.45)               | 0.94 (0.075–1.18)               | 1.25 (1.10–1.53)               | 1.29 (1.09–1.67)               |
| 0.3 | 1.19 (0.071–1.19)               | 0.94 (0.063–1.40)               | 0.88 (0.067–1.18)               | 1.00 (0.076–1.31)               | 1.05 (0.074–1.40)               |
| 0.7 | 1.25 (0.071–1.20)               | 1.01 (0.066–1.57)               | 0.95 (0.070–1.29)               | 1.00 (0.074–1.36)               | 1.14 (0.077–1.67)               |
| 0.14 | 2.07 (1.111–3.89)               | 1.41 (0.087–2.29)               | 1.14 (0.081–1.69)               | 0.98 (0.061–1.23)               | 0.99 (0.063–1.53)               |
| 0.21 | 1.65 (0.083–3.24)               | 1.37 (0.082–2.29)               | 1.18 (0.081–1.70)               | 0.97 (0.066–1.43)               | 1.23 (0.075–2.04)               |
| 0.30 | 1.60 (0.079–3.25)               | 1.12 (0.065–1.93)               | 0.98 (0.067–1.46)               | 0.87 (0.056–1.33)               | 1.07 (0.062–1.84)               |

**Fig. 1.** The cumulative effects over lag 0 of sea level pressure (hPa, hectopascal) on the occurrence of STEMI.

**Fig. 2.** The cumulative effects over lag 0 of atmospheric pressure variations during the previous three hours (hPa, hectopascal) on the occurrence of STEMI.
The relationship between atmospheric pressure variations during the previous three hours and STEMI

Figure 2 shows the cumulative effects of atmospheric pressure variations during the previous three hours (hPa, hectopascal) on the occurrence of STEMI for each 6 hour interval at lag 0. The atmospheric pressure variation–morbidity of STEMI relationship curve was U-shaped and illustrated a higher risk of STEMI at both high and low atmospheric pressures variations. As indicated in Table 3, the effects of a decrease in atmospheric pressure lasted longer than 6 hours (Lag 0-1); however, the effects of an increase in atmosphere pressure variations were limited to the first 6 hours (Lag 0). At lag 0, the RRs (95% CI) for the first percentile, 10th percentile, 25th percentile, 75th percentile, 90th percentile, and 99th percentile for atmospheric pressure variation were 1.66 (1.36~2.03), 1.47 (1.30~1.67), 1.22 (1.12~1.33), 1.16 (1.07~1.25), 1.27 (1.13~1.43), and 1.16 (0.92~1.46), respectively, compared with the 50th percentile for atmospheric pressure variation.

The relationship between temperature and STEMI

Figure 6 and Table 6 each show the relationship between temperature within each 6 hour interval and the occurrence of STEMI. The cumulative effects of temperature on the
occurrence of STEMI suggest that increases in temperature are a risk factor for STEMI and that the effects of such an event last longer than 6 hours (Lag 0-1). At lag 0, the RRs (95% CI) for the first percentile, 10th percentile, and 25th percentile were 0.58 (0.40–0.83), 0.60 (0.46–0.78), 0.69 (0.57–0.83), respectively, compared to the 50th percentile for temperature. Compared to the 50th percentile for temperature, the RRs (95% CI) for the 75th percentile, 90th percentile, and 99th percentile for temperature were 1.33 (1.14–1.56), 1.39 (1.13–1.71), and 1.17 (0.84–1.63), respectively. At lag 0-7, the RR (95% CI) for the 99th percentile for temperature was 1.82 (1.01–3.27), compared to the 50th percentile for temperature. At lag 0-14, the RR (95% CI) for the 1st percentile for temperature was 2.07 (1.11–3.86), compared to the 50th percentile for temperature.

Discussion

To the best of our knowledge, this is the first study to explore the association between meteorological parameters and STEMI occurrence in China. Based on the eight-year, single-center study, significant relationships among the onset of STEMI and atmospheric pressure variations during the past three hours and temperature were observed after accounting for long-term time trends.

Recently, numerous studies have examined short-term associations between ambient temperature and acute myocardial infarction, with inconsistent results. A case-crossover study from England and the Wales Myocardial Ischaemia National Audit Project (MINAP) database suggests that with each 1°C increase in temperature above 20°C, the risk of ST elevation myocardial infarction is increased by 2.7% (0.6% to 4.9%) within one to six hours following exposure [10]. The data were based on hourly observations. After accounting for the day of the week, long-term trends and seasonal effects, a 1°C drop below a threshold temperature of 24°C was significantly (p<0.0001) associated with an AMI hospitalization-risk increase of 3.7% (average lag 0-13 temperature) in Hong Kong, 2.6% (average lag 0-15) in Taipei, and 4.0% (average lag 0-11) in Kaohsiung. No significant heat effects were observed. However, the above results were based on daily data regarding AMI hospitalizations and mean temperatures, which were collected between 2000 and 2009 in three warm-climate Asian cities [9]. In the present study, both temperature data and data regarding the occurrence of STEMI were collected at 6 hour intervals from 2003 to 2010, and the results indicated that although the immediate association between temperature and STEMI (lag 0) is consistently positive (higher temperatures are associated with a higher incidence of STEMI) long-term associations (lags 0-7, lags 0-14) appear as a U-shaped curve, as both high and low temperatures are associated with a higher risk of STEMI. The results of the present study are consistent with those of MINAP, but they were not consistent with the results of studies performed in three warm-climate Asian cities. The exact mechanism underlying the U-shaped association between temperature and STEMI requires further study.

During the past decade, various studies have noted the relationship between meteorological factors and cardiovascular mortality and morbidity. However, there are no studies exploring the relationship between atmospheric pressure variations and the occurrence of STEMI worldwide. To the best of our knowledge, this is the first study to suggest that atmospheric pressure variations, rather than the atmospheric pressure levels, increase the risk of STEMI. The exact mechanism underlying this association requires further study. In a study of diving fatalities, 947 recreational open-circuit scuba diving deaths that occurred between 1992 and 2003 were investigated, and the results indicate that cardiac incidents account for 26% of disabling injuries and 13% of deaths. The OR of disabling injury due to cardiovascular disease was 10.5 [11], and the results suggest that atmospheric pressure variations may be associated with cardiovascular disease.

Global climate change (GCC) is associated with significant changes in long-term weather characteristics and short-term weather extremes in different geographic regions [12]. The results of the present study may have important implications for the development of
strategies and policies to prevent climate change-related STEMI. However, this was a single-center study conducted in China, and the conclusions drawn based on this study's results may not be applicable to other locations. Therefore, large-scale, multi-center epidemiological studies are necessary to determine the relationship between climate changes and STEMI. Furthermore, biological mechanisms concerning the relationship among the risk of STEMI, increases in temperature, and atmospheric pressure variations must be explored via experimental studies.

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