Introduction

It has been reported that meteorological conditions are environmental risk factors for acute myocardial infarction (AMI)\(^1,2\). Human physical conditions are maintained relatively constant, independent of surrounding environmental changes, because of “homeostasis”\(^3\). This property may fail if the magnitude of environmental change exceeds the limit of controllability. Diseases affected by changes in daily weather conditions are called meteorotropic. AMI is one such disease\(^4\).

Japan is in a temperate zone and has four distinctive seasons. Thus, meteorological conditions have great seasonal change. Low atmospheric pressure systems frequently traverse the country and residents must adapt to their changes\(^5\). Therefore, meteorotropic diseases are of major concern in Japan. AMI is one of the most important meteorotropic diseases, because of its frequency and lethality.

There are many studies on the relationship between AMI onset and meteorological conditions. However, these studies mainly address the relationship with seasonal variation\(^6-9\) or temperature\(^10-15\). There has been very little investigation of other meteorological conditions. Some studies that considered the effect of atmospheric pressure suggest that mean daily atmospheric pressure does not have a significant effect on the AMI onset\(^14,16-18\). In contrast, other works indicate that AMI is frequent with a rapid decline of atmospheric pressure\(^1,19-21\). However, there has been no clear evidence of the effect of atmospheric pressure.
In Hiroshima Prefecture, warnings of high-risk days of AMI are announced via the mass media\textsuperscript{22}. An alert for stroke is now provided in the same way (Fig. 1). The AMI warning has three risk levels, namely, “caution,” “attention,” and “small risk.” “Caution” carries the highest risk, the criterion for which is that average temperature and pressure are low (less than 6°C and and 1013 hPa, respectively)\textsuperscript{30}. The present criterion does not use information on decline of atmospheric pressure, leaving room for improvement. The purpose of the present study is to clarify the impact of pressure decline on AMI incidence, for improving the AMI alert system.

Model construction

Probability distributions of AMI incidence and model selection

When a response variable in the model is count data like numbers of occurrence, the variable has non-negative integer values. Therefore, it is inappropriate to assume that error has a normal distribution, as in an ordinary multiple regression model. We used a Poisson regression model, assuming that the response variable has a Poisson distribution, for which the logarithmic transformation of the Poisson parameter (mean value, $\lambda$) is expressed by linear combination of explanatory variables.

The risk prediction model for AMI is

$$\log (\lambda) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 \cdots$$

$\lambda$ : Daily average events of AMI  
$X_1$ : Atmospheric pressure  
$X_2$ : Atmospheric temperature  
$X_3$ : Other meteorological condition

Coefficients of the linear model are estimated by the maximum likelihood method. To evaluate the aptness of the Poisson distribution, we examined observed and predicted values from January and June separately, when daily average AMI events were greatest or smallest, respectively.

Criterion of decline in atmospheric pressure

Decline in daily atmospheric pressure may take various forms; there is considerable variation of steepness and duration. We need a criterion for defining the decline, to detect the specific type related to AMI occurrence\textsuperscript{15,19,20,24-26}. Consequently, we created five types (Type 1 - Type 5) of variables defining specific pressure declines (Table 1). Next, we analyzed the relationship between AMI onset and these decline variables using the Poisson regression models. We explored which type of declines are most related to the
cardiac diseases such as heart failure. The data were collected independent of any history of heart failure. Meteorological data were provided by the Japan Weather Association. The data included daily mean atmospheric temperature, daily mean atmospheric pressure, weather type, hourly atmospheric temperature and pressure, relative humidity, rainfall, and snowfall.

Materials and Methods

Materials

The data used were records of conveyance by ambulances in the city of Hiroshima during the 10-year period from January 1993 to December 2002, along with corresponding meteorological data in the area. The ambulance data were provided by the Hiroshima Municipal Fire Department. The data were completely anonymous and included no personal information, so no ethical review was required. The data contained the date and time for each conveyance. Daily numbers of AMI incidence were calculated from the data. AMI for each patient was diagnosed by physicians in the emergency department to which patients were conveyed. AMI diagnosis does not include similar but distinct
Table 1. Definition of variables used in models

<table>
<thead>
<tr>
<th>Variable</th>
<th>Type</th>
<th>Definition of values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Response variable</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMI</td>
<td>Events of AMI</td>
<td>discrete (count)</td>
</tr>
<tr>
<td><strong>Explanatory variables: temperature and pressure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T</td>
<td>Daily mean atmospheric temperature</td>
<td>continuous</td>
</tr>
<tr>
<td></td>
<td></td>
<td>discrete (trinary)</td>
</tr>
<tr>
<td>P</td>
<td>Daily mean atmospheric pressure</td>
<td>continuous</td>
</tr>
<tr>
<td></td>
<td></td>
<td>discrete (trinary)</td>
</tr>
<tr>
<td><strong>Explanatory variables: decline of atmospheric pressure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1 (= the sum of the hourly declines in a 24-hour period)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>dec</td>
<td>The decline of atmospheric pressure</td>
<td>continuous</td>
</tr>
<tr>
<td></td>
<td></td>
<td>discrete (binary)</td>
</tr>
<tr>
<td>Type 2 (= the variables representing 21 different weather patterns)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tnk1-tnk21</td>
<td>Weather pattern</td>
<td>discrete (binary)</td>
</tr>
<tr>
<td>lagtnk1-lagtnk21</td>
<td>(previous day, the day)</td>
<td></td>
</tr>
<tr>
<td>Type 3 (= the rate of change per hour from maximum atmospheric pressure to minimum atmospheric pressure within 24 hours)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>slope</td>
<td>The rate of change per hour of the atmospheric pressure*</td>
<td>continuous</td>
</tr>
<tr>
<td></td>
<td></td>
<td>discrete (binary)</td>
</tr>
<tr>
<td>Type 4 (= binary variables representing whether or not continuous decline of atmospheric pressure occurred between 0-6, 0-8, 0-12, 0-18, or 0-24)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>deck1-deck5</td>
<td>Continued atmospheric pressure decline</td>
<td>discrete (binary)</td>
</tr>
<tr>
<td>(lagdeck1-lagdeck5)</td>
<td>(previous day, day, next day)</td>
<td></td>
</tr>
<tr>
<td>Type 5 (= variables representing the sum of decline of atmospheric pressure within a definite time intervals)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>lagdeck 1-5</td>
<td>Atmospheric pressure decline of definite period of time interval</td>
<td>continuous</td>
</tr>
</tbody>
</table>

\[\text{The rate of change per hour of the atmospheric pressure} = \frac{\text{difference of pressure in 24 hours}}{\text{continued time of pressure decline}}\]
onset. The decline variables of atmospheric pressure were selected in the model when the risk ratio of onset was larger than 1.0 and \( p < 0.10 \).

**Selection of the optimal model**

The selection of the models was performed based on the Akaike Information Criterion (AIC)\(^{(27)}\). AIC can evaluate goodness of fit of a model with consideration of its complexity. Models with smaller AIC values are deemed superior to others. We established the baseline model as one containing only temperature as an explanatory variable, because temperature is known as the most influential factor in AMI onset. Next, we comprehensively evaluated goodness of fit for candidate models with various atmospheric pressure declines, and determined which had optimum goodness of fit using AIC. Finally, we checked model consistency using fundamental knowledge of AMI risk factors. We performed statistical analyses using PASW Statistics 18 (SPSS Japan Inc.). We considered a P-value less than 0.05 as statistically significant.

**Results**

**Descriptive statistics of data used**

The study period spanned 3652 days, during which 3755 AMI events occurred on 2312 days (63.33\% of total days), with an average of 1.03 events per day (range 0–6).

The monthly distribution of AMI events and meteorological conditions from 1993 to 2002 in Hiroshima are shown in Fig. 2. There were more daily events with statistical significance from October through April, relative to those in June. Daily mean temperature was highest in August (28.4 ± 1.8°C) and lowest in January (5.6 ± 2.3°C). Daily mean atmospheric pressure was highest in December (1016.0 ± 4.4 hPa) and lowest in July (1001.9 ± 3.9 hPa). These daily means had strong negative correlation \( r = -0.676; p < 0.001 \). There were only a few days in winter when the daily mean atmospheric pressure was lower than that in summer. In contrast, the sum of all hourly atmospheric pressure declines in a 24-hour period was largest in March (5.4 ± 3.6 hPa) and smallest in July (3.4 ± 1.7 hPa).

**Fit of observed AMI incidence to Poisson distribution**

We statistically tested whether the observed values at AMI onset in January and June would fit the Poisson distribution. Figure 3 shows that those values conformed to the distribution (daily incidence was 1.24 in January and 0.86 in June).

**Atmospheric pressure decline affecting AMI onset**

Among the variables of atmospheric pressure decline, Type 1 sum of hourly declines in a 24-hour period was selected as influential if its value was ≥ 16 hPa (risk ratio = 1.44 (\( p = 0.05 \)), 95% CI = (0.99, 2.08)).

![Fig. 2. Relative risk of AMI incidence by month, with monthly variation of atmospheric temperature and pressure.](image)

Relative risk (risk ratio) was estimated by Poisson regression model (reference was set as June).

\( ***p < 0.001, **p < 0.01, *p < 0.05 \)
Type 3 (the rate of change per hour from maximum to minimum pressure within a 24-hour period), Type 4 (binary variables representing whether there was continuous decline of pressure in the periods 0-6, 0-8, 0-12, 0-18, or 0-24 hours), or Type 5 (variables representing the sum of decline of pressure within a definite period, i.e., 3, 4, 6, 8, 12 hours intervals) variables contributed much to AMI onset.

Among the 21 variables for Type 2 (those representing 21 different weather patterns), only one, representing the strong winter type (strong western high and eastern low) of the previous day was statistically significant (risk ratio = 1.32 (p < 0.01), 95% CI = (1.08, 1.61)). Weather charts depicting strong winter patterns, in which there is low pressure moving east of the Japanese islands and continental high pressure emerging from the west, cause high pressure in the west and low in the east. Neither

Figure 3. Comparison of daily incidence numbers with Poisson distribution. Daily incidence was 1.24 in January and 0.86 in June.

### Table 2. Parameter estimate of baseline model and optimal models

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>Risk ratio (95%CI)</th>
<th>p-value</th>
<th>AIC</th>
<th>ΔAIC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline model</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily mean atmospheric temperature</td>
<td>-0.013</td>
<td>0.99 (0.98 - 0.99)</td>
<td>&lt;0.001***</td>
<td>9694.76</td>
<td>(-)</td>
</tr>
<tr>
<td><strong>Model 1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily mean atmospheric temperature</td>
<td>-0.013</td>
<td>0.99 (0.98 - 0.99)</td>
<td>&lt;0.001***</td>
<td>9690.31</td>
<td>-4.45</td>
</tr>
<tr>
<td>Strong winter pattern on the previous day</td>
<td>0.153</td>
<td>1.17 (1.00 - 1.35)</td>
<td>0.045*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High pressure pattern on the previous day</td>
<td>-0.073</td>
<td>0.96 (0.86 - 1.01)</td>
<td>0.069</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rear of strong low pressure pattern on the previous day</td>
<td>-0.398</td>
<td>0.67 (0.39 - 1.16)</td>
<td>0.152</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily mean atmospheric temperature</td>
<td>-0.013</td>
<td>0.99 (0.98 - 0.99)</td>
<td>&lt;0.001***</td>
<td>9693.32</td>
<td>-1.44</td>
</tr>
<tr>
<td>Low atmospheric temperature group</td>
<td>0.488</td>
<td>1.63 (1.01 - 2.63)</td>
<td>0.024*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Relative risk (risk ratio) was estimated by Poisson regression model

***p < 0.001, *p < 0.05

ΔAIC: baseline AIC — optimal model AIC
Another remarkable model that had the second lowest AIC was one using variables of atmospheric pressure decline within a 24-hour period, daily mean temperature, and an interaction term of low temperature and ≥ 16 hPa decrease in pressure (model 2 in Table 2). This model predicted a "super-risky" day for AMI (risk ratio = 2.10 (p < 0.01), 95% CI = (1.30, 3.38)) (Fig. 5). There were only 9 such days in 10 years, and these were between December and March. The probability of AMI occurrence three or more times per day was 55%. The probability was 64% after 18:00, while AMI usually takes place more frequently in the morning. We also assessed weather characteristics on these super-risky days. On such days, weather changed suddenly from the previous evening. In most cases, it changed to rain and sleet all day long and was likely to continue into the following day. In addition, there were rapid declines in atmospheric pressure from the previous night (18.7 ± 2.4 hPa decline within 24 hours). Temperature was low (6.9 ± 2.2°C daily mean) and relative humidity high (81.7 ± 4.2% daily mean).

Selection of optimal model

We first investigated how to construct the best baseline model, by considering which was more suitable for use with atmospheric temperature and pressure as continuous or discrete variables (Table 1). As shown in Table 2, the best baseline model was determined as that using only the continuous variable of daily mean temperature (AIC = 9694.76). Next, as shown in Table 2, we created candidate models using variables of pressure decline from Type 1 to Type 5, and compared them with the baseline model according to AIC. Model 1, which uses the variable of Type 2 (different weather patterns), achieved the lowest AIC (=9690.31, baseline AIC -4.45) and was therefore the best. In this model, the variable representing a strong winter weather pattern of the previous day most strongly affected the risk of AMI. Over the 10-year period, there were 143 days with such a weather pattern. The relationship between this pattern and pressure decline was further investigated. We found that more AMI patients were transported by ambulance on days with strong winter weather patterns and greater pressure declines (Fig. 4).

Fig. 4. Daily incidence according to decline in atmospheric pressure when strong winter pattern was observed.

**p < 0.01, *p < 0.05

D1, D2 and D3 show low, moderate and high decline groups of atmospheric pressure, respectively. Poisson regression model was used to test interaction between various meteorological groups with strong winter pattern groups. D1 and no strong winter pattern groups were set as reference. Daily events corresponding to moderate declines of atmospheric pressure groups (D2) with strong winter pattern groups were significantly greater than those with small declines of atmospheric pressure groups (D1) with no strong winter pattern groups (p < 0.05).

Daily events corresponding to strong declines in atmospheric pressure groups (D3) with strong winter pattern groups were significantly greater than those with small declines of atmospheric pressure groups (D1) with no strong winter pattern groups (risk ratio = 1.87 = 1.76/0.94 (p < 0.01), 95% CI = (1.29, 2.71)).
We also discovered that the AMI risk significantly increased in cases of low temperature and a pressure decline > 16 hPa in a 24-hour period. Previous studies of daily incidence showed that on days of low temperature and pressure, there were 37% more cases of AMI than on days of high temperature and moderate pressure\textsuperscript{15,26}. Sama et al.\textsuperscript{25} showed that in Finland, AMI increased because of conditions of low temperature and low pressure. This study showed a super-risky day of AMI with a pressure decrease > 16 hPa combined with low temperature. This result supported earlier studies and revealed more concrete meteorological conditions related to high risk. Super-risky days of AMI were all from December through March, a season with the largest pressure difference in a 24-hour period\textsuperscript{29}. Previous studies showed that all days with low temperature and low pressure had rainfall or accumulating snow, accompanied by low temperature and high relative humidity. This condition corresponded to the super-risky days. In addition to these features, it was shown that weather suddenly deteriorated from the evening of the previous day\textsuperscript{15,25}.

The present study showed that AMI is frequent under conditions of low temperature and rapid drop in pressure. However, it is not clear how such meteorological conditions affect AMI onset. One study...
reported that histamine or a similar substance in the body is released during decompression accompanying the approach of low atmospheric pressure. This triggers meteorotropic diseases because histamine can increase fluid retention within the body, contraction of smooth muscles, permeability of blood vessels, and inflammatory reaction. Sato supported this by experimentation with rats. That study showed that rats exhibited increased blood pressure and heart rate, indicating excitement of the sympathetic nervous system while acting freely under declining atmospheric temperature and pressure, which is often experienced in everyday life. Houck et al. reported that the strong influence of atmospheric pressure change damages coronary arteries by formation of plaques. In an alpine environment of low atmospheric pressure, it has been reported that the functions of breathing and blood circulation change rapidly because of oxygen and carbon dioxide partial pressures in the lung, leading to altitude sickness. However, the magnitude of this effect is unclear for changes in atmospheric pressure commonly observed near sea level. It has been shown that even a slight change of pressure may influence the condition of the human body.

Thus, the effects of atmospheric pressure decline are wide ranging. They involve direct and indirect impacts on the living body, and work independently or in conjunction with other meteorological conditions such as temperature decrease. The finding that low temperature and rapid pressure declines are important risks for AMI onset is undeniable, although the mechanism is unclear. Further study is required.

Usefulness of prediction model
AMI onset is related to multiple factors, beyond that of atmospheric pressure. Temperature change is another important risk factor for AMI onset. However, we focused only on pressure, leaving temperature to be analyzed in the future.

The prediction models analyzed herein involve weather patterns of the previous day and pressure decline to predict the risk of AMI onset. Various criteria for defining the decline were evaluated. As a result, we found that the best model was that using a weather chart indicative of a strong winter pattern on the previous day, or a decrease in pressure ≥ 16 hPa. Using these variables considerably improved the goodness of fit. We must also consider the availability of predictive variables when deciding the AMI alert level. Given this consideration, it is easy to use the strong winter pattern of the weather chart. In contrast, it is difficult to use atmospheric pressure decline over a 24-hour period, because this information is unavailable at the time of alert issuance. Use of the strong winter pattern should therefore be convenient and useful toward improving the performance of practical criteria within the alert system.

Conclusion
The goodness of fit was considerably improved by use of the weather chart showing a strong winter pattern of the previous day, or by a decrease of atmospheric pressure ≥ 16 hPa in combination with low temperature. The former usage is considered easy to execute. This suggests that the model would be useful for improving the present Hiroshima prefectural alert system.

Acknowledgments
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