



Impact of Age on Gender Differences in the Acute Myocardial Infarction Onset–Weather Association

— Oita AMI Registry —

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Background: The onset of acute myocardial infarction (AMI) is related to weather conditions, but the impact of age on gender differences in the AMI onset–weather association has not been elucidated.

Methods and Results: We analyzed the Oita AMI Registry and obtained data for 403 enrolled patients. To examine the impact of age, we categorized the patients into 4 groups: young (age ≤ 65 years) women ($n=20$); young men ($n=123$); elderly (age >65 years) women ($n=84$); and elderly men ($n=176$). The analyzed meteorological factors were maximum and minimum temperature, intraday temperature difference, average humidity, and average atmospheric pressure. The young women group had a higher minimum temperature ($17.7\pm 5.7^\circ\text{C}$ vs. $13.8\pm 8.2^\circ\text{C}$, $P=0.04$), lower intraday temperature difference ($7.0\pm 2.6^\circ\text{C}$ vs. $8.4\pm 2.9^\circ\text{C}$, $P=0.03$), higher average humidity ($74.5\pm 12.1\%$ vs. $68.1\pm 12.0\%$, $P=0.03$), and lower average atmospheric pressure ($1,009.5\pm 5.0\text{hPa}$ vs. $1,012.9\pm 5.8\text{hPa}$, $P=0.01$) than the young men group on the onset day. In the elderly groups, there was no significant difference in meteorological variables except for the intraday temperature difference 2 days before AMI onset.

Conclusions: AMI onset appears to be more sensitive to weather conditions (i.e., minimum temperature, average atmospheric pressure, and average humidity) in young patients than in elderly patients. In particular, young women had AMI on days with low intraday temperature difference and high humidity relative to men.

Key Words: Acute myocardial infarction; Aging; Elderly; Sex

Acute myocardial infarction (AMI) is generally caused by lifestyle-related diseases such as hypertension, dyslipidemia, and diabetes. Weather conditions are considered promoting factors for AMI onset. AMI onset has been shown to be associated with seasonal variations, with the highest rate observed in winter and the lowest rate in summer.^{1–5} Based on the data from the Oita AMI Registry, we recently reported that AMI onset in summer was associated with the maximum temperature 2 days before AMI onset.⁶ Moreover, women were found to develop coronary artery disease (CAD) approximately 10 years after men; thus, menopausal women are considered at high risk of developing CAD.⁷ In Korea, the fatality risk in women has been reported to be high in months with low

temperature; in contrast, the fatality risk in men is high in August.⁸ The aim of the present study was therefore to investigate the impact of age on gender differences in the AMI onset–weather association.

Methods

AMI data were obtained from the Oita AMI Registry.⁶ The present subjects consisted of a total of 403 patients enrolled in the Oita AMI Registry who were admitted with AMI to 20 institutions between April 2012 and September 2013. Mean patient age was 71 ± 12 years, and 104 patients (26%) were women. To examine the impact of age and gender on the relationship between AMI onset and meteorological

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Table 1. Weather Conditions in Oita Prefecture

	2011	2012	2013	Observation period (April 2012–September 2013)
Maximum temperature (°C)	20.9±8.0	20.5±8.2	21.4±8.3	23.1±8.0
Minimum temperature (°C)	12.8±8.7	12.6±8.3	12.9±8.6	14.9±8.3
Intraday temperature difference (°C)	8.2±1.3	7.9±0.9	8.5±1.2	8.2±3.0
Humidity (%)	65.8±8.6	67.3±6.4	68.8±6.0	69.2±11.8
Atmospheric pressure (hPa)	1,014.0±5.7	1,013.4±4.9	1,013.7±5.1	1,012.1±16.3

Data given as mean±SD.

Table 2. Baseline Characteristics vs. Sex in AMI Patients

Coronary risk factor	Young women (n=20)	Young men (n=123)	P-value	Elderly women (n=84)	Elderly men (n=176)	P-value
Age (years)	59.5±5.4	57.0±7.7	0.16	81.3±6.5	76.7±6.9	<0.0001
Current smoking	45 (9)	58 (71)	0.29	7 (6)	30 (52)	<0.0001
Hypertension	65 (13)	62 (76)	0.78	80 (67)	74 (131)	0.34
Diabetes mellitus	45 (9)	35 (43)	0.39	31 (26)	36 (64)	0.39
Dyslipidemia	70 (14)	63 (77)	0.51	55 (46)	55 (96)	0.97

Data given as mean±SD or % (n). AMI, acute myocardial infarction.

variables, we performed stratified analyses by dividing the patients into 4 groups based on age and sex: young women (age ≤65 years, n=20), mean age, 59.5±5.4 years; young men (age ≤65 years, n=123), mean age, 57.0±7.7 years; elderly women (age >65 years, n=84), mean age, 81.3±6.5 years; and elderly men (age >65 years, n=176), mean age, 76.7±6.9 years.

The analyzed meteorological factors consisted of maximum and minimum temperature, intraday temperature difference, average humidity, and average atmospheric pressure on the onset day (day 0), and at 1 day (day -1) and 2 days (day -2) before AMI onset. The meteorological variables were obtained from the Japan Meteorological Agency.

Table 1 lists the weather conditions from 2011 to 2013 and the weather conditions during the observation period in Oita Prefecture.

Data Collection

Diagnosis Definitions All patients with a final diagnosis of AMI with/without ST elevation (ST-elevation myocardial infarction [STEMI]/non-STEMI) were included in the registry. We defined the diagnostic criteria for AMI according to the joint European Society of Cardiology/American College of Cardiology (ESC/ACC) criteria of 2000⁹ and the World Health Organization (WHO) criteria.¹⁰

The young group was defined as ≤65 years old, while the elderly group was defined as >65 years old, according to the WHO definition.¹¹

Ethics

In the present study involving humans, all procedures were performed in accordance with the ethics standards of each institutional research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethics standards.

Statistical Analysis

Data are presented as mean±SD. The chi-squared test was used for categorical variables, and analysis of variance

(ANOVA) was used for continuous variables. Differences between 2 groups were analyzed using Student's t-test. The impact of age on gender differences in the association between coronary risk factors and meteorological variables according to AMI-onset days was examined using multiple logistic regression analysis, calculation of odds ratios (OR) and 95% CI. Multiple logistic regression analysis was divided into 5 models involving meteorological variables according to AMI onset days and coronary risk factors (age, current smoking): model 1, maximum temperature and risk factors; model 2, minimum temperature and risk factors; model 3, intraday temperature difference and risk factors; model 4, average humidity and risk factors; and model 5, average atmospheric pressure and risk factors.

All statistical analysis was carried out with JMP version 11 (SAS, Cary, NC, USA) running under Windows 8 (Microsoft, Redmond, WA, USA).

Results

Baseline Characteristics

Table 2 lists the comparison of baseline characteristics according to age and to sex. We found no significant gender differences between the young groups in terms of age; current smoking status; or prevalence of hypertension, diabetes mellitus, and dyslipidemia. The mean age of the elderly women group was higher than that of the elderly men group (81.3±6.5 vs. 76.7±6.9 years, P<0.0001). The prevalence of smoking was higher in the elderly men group than in the elderly women group (7% vs. 30%, P<0.0001).

Impact of Age

Table 3 presents a comparison of meteorological variables on the day of AMI onset, and also for 1 day and 2 days before AMI onset, according to age and to sex. Maximum temperature on day -2 was higher in the young women group than in the young men group (25.5±5.8°C vs. 21.8±7.8°C, P=0.04, respectively). Minimum temperature and average humidity on day 0 were higher in the young

Table 3. Meteorological Parameters vs. Age and Sex in AMI Patients						
	Young women (n=20)	Young men (n=123)	P-value	Elderly women (n=84)	Elderly men (n=176)	P-value
Maximum temperature (°C)						
Day -2	25.5±5.8	21.8±7.8	0.04	22.3±7.9	23.0±7.8	0.52
Day -1	24.8±5.9	22.0±8.0	0.13	22.1±8.0	22.7±7.7	0.55
Day 0	24.7±6.6	22.3±8.0	0.12	24.7±6.6	22.8±7.6	0.76
Minimum temperature (°C)						
Day -2	17.0±7.1	13.7±8.2	0.09	14.8±8.2	14.4±8.1	0.74
Day -1	17.4±6.3	13.6±8.3	0.05	14.2±8.4	14.7±8.1	0.69
Day 0	17.7±5.7	13.8±8.2	0.04	14.5±8.4	14.7±7.9	0.84
Intraday temperature difference (°C)						
Day -2	8.5±2.8	8.2±3.2	0.61	7.6±2.8	8.6±2.5	0.004
Day -1	7.4±3.3	8.4±3.0	0.18	7.9±3.3	8.1±3.2	0.67
Day 0	7.0±2.6	8.4±2.9	0.03	8.0±3.5	8.1±3.1	0.82
Humidity (%)						
Day -2	72.7±10.9	67.5±13.0	0.09	69.5±12.8	69.1±10.4	0.80
Day -1	74.3±16.2	68.7±12.7	0.08	71.2±13.3	69.2±12.1	0.25
Day 0	74.5±12.1	68.1±12.0	0.03	71.3±11.6	69.6±11.9	0.29
Atmospheric pressure (hPa)						
Day -2	1,011.4±5.7	1,012.8±6.8	0.38	1,012.0±6.0	1,012.5±6.6	0.56
Day -1	1,010.9±4.5	1,013.0±6.2	0.14	1,012.5±6.5	1,012.4±6.0	0.81
Day 0	1,009.5±5.0	1,012.9±5.8	0.01	1,012.7±5.9	1,012.0±5.6	0.53

Data given as mean±SD. AMI, acute myocardial infarction.

women group than in the young men group (17.7±5.7°C vs. 13.8±8.2°C, $P=0.04$ and 74.5±12.1% vs. 68.1±12.0%, $P=0.03$, respectively). Intraday temperature difference and average atmospheric pressure on day 0 were significantly lower in the young women group than in the young men group (7.0±2.6°C vs. 8.4±2.9°C, $P=0.03$; and 1,009.5±5.0 hPa vs. 1,012.9±5.8 hPa, $P=0.01$, respectively). In contrast, intraday temperature difference on day -2 was the only significantly different parameter in the elderly groups, being lower in the women group than in the elderly men group (7.5±2.8°C vs. 8.6±2.5°C, $P=0.004$, respectively).

Effect of Coronary Risk Factors on Women

Table 4 presents the results of multiple logistic regression analysis to predict AMI onset in women relative to men. In the young group, maximum temperature on day -2 in model 1 (OR, 1.08; 95% CI: 1.01–1.16; $P=0.03$), intraday temperature difference on day 0 in model 3 (OR, 0.83; 95% CI: 0.70–0.99; $P=0.04$), average humidity on day 0 in model 4 (OR, 1.06; 95% CI: 1.01–1.11; $P=0.03$), and average atmospheric pressure on day 0 in model 5 (OR, 0.9; 95% CI: 0.81–0.98; $P=0.02$) independently contributed to AMI onset in women relative to men. Age and current smoking status, however, did not contribute to AMI onset in the young group. In the elderly group, intraday temperature difference on day -2 in model 3 (OR, 0.84; 95% CI: 0.75–0.94; $P=0.003$), age and current smoking status independently contributed to AMI onset in women relative to men.

Discussion

Our analysis using the data from the Oita AMI Registry demonstrated the presence of gender differences in the relationship between AMI onset and meteorological variables. The significant features observed in the young group

of women relative to men were high minimum temperature, low intraday temperature difference, high average humidity, and low average atmospheric pressure, while in the elderly group, only low intraday temperature difference was significant in elderly women relative to men.

The relationship between AMI onset and meteorological variables has been examined in a large number of studies. We recently reported that AMI onset in summer was associated with the maximum temperature 2 days before AMI onset.⁶ Hong and Kang reported that the fatality risk in women was high in months with low temperature; in contrast, the fatality risk in men is high in August.⁸

The present study confirmed that average humidity was associated with AMI onset in young women. In this regard, Panagiotakos et al found a positive correlation between relative humidity and hospital admission for acute coronary syndrome, which was stronger in women than in men.¹² It can be hypothesized that when humidity is high, perspiration and temperature homeostasis are hindered, thus increasing respiratory muscle fatigue and heart rate. Our finding is in agreement with this observation.

We found that atmospheric pressure was related to AMI onset in the young women group, but this relationship was not observed in the elderly women group. The mechanism by which atmospheric pressure influences AMI onset remains unclear. AMI has been shown to typically occur more frequently as the atmospheric pressure decreases.^{13–15} Wang et al reported that AMI tended to occur frequently on days with mean atmospheric pressure <1,005 hPa in Hiroshima (Japan).¹³ The present findings in young women patients are consistent with these observations.^{13–15}

Amiya et al reported that F-day (days of frequent onset, defined as days with ≥3 patients admitted for AMI) appeared to occur when intraday temperature difference was high.¹⁶ Yamaji et al reported that lower humidity

Table 4. Multivariate Predictors of AMI Onset in Women Relative to Men				
	Young group		Elderly group	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Model 1				
Maximum temperature (day –2)	1.08 (1.01–1.16)	0.03	0.99 (0.96–1.03)	0.78
Age	1.05 (0.98–1.15)	0.17	1.12 (1.06–1.16)	<0.0001
Current smoking	0.72 (0.26–2.00)	0.53	0.19 (0.07–0.46)	<0.0001
Maximum temperature (day –1)	1.05 (0.98–1.13)	0.12	1.00 (0.96–1.04)	0.96
Age	1.05 (0.98–1.15)	0.20	1.11 (1.06–1.16)	<0.0001
Current smoking	0.76 (0.27–2.09)	0.58	0.20 (0.07–0.46)	<0.001
Maximum temperature (day 0)	1.04 (0.98–1.12)	0.18	1.00 (0.97–1.04)	0.83
Age	1.05 (0.98–1.12)	0.18	1.11 (1.06–1.16)	<0.0001
Current smoking	0.73 (0.27–2.01)	0.55	0.20 (0.07–0.46)	<0.0001
Model 2				
Minimum temperature (day –2)	1.05 (0.99–1.14)	0.07	1.01 (0.98–1.05)	0.47
Age	1.06 (0.98–1.15)	0.17	1.11 (1.06–1.16)	<0.0001
Current smoking	0.75 (0.27–2.06)	0.58	0.19 (0.07–0.45)	<0.001
Minimum temperature (day –1)	1.07 (1.00–1.15)	0.06	1.00 (0.97–1.04)	0.94
Age	1.06 (0.98–1.16)	0.20	1.11 (1.06–1.16)	<0.0001
Current smoking	0.77 (0.28–2.15)	0.62	0.20 (0.07–0.46)	<0.001
Minimum temperature (day 0)	1.07 (1.00–1.16)	0.04	1.00 (0.97–1.04)	0.80
Age	1.05 (0.98–1.16)	0.15	1.11 (1.06–1.16)	<0.0001
Current smoking	0.78 (0.28–2.18)	0.64	0.19 (0.07–0.46)	<0.0001
Model 3				
Intraday temperature difference (day –2)	1.03 (0.89–1.20)	0.62	0.84 (0.75–0.94)	0.003
Age	1.05 (0.97–1.14)	0.25	1.11 (1.07–1.17)	<0.0001
Current smoking	0.70 (0.25–1.87)	0.47	0.21 (0.08–0.50)	<0.001
Intraday temperature difference (day –1)	0.90 (0.78–1.06)	0.23	1.00 (0.91–1.09)	0.93
Age	1.04 (0.97–1.14)	0.28	1.11 (1.06–1.16)	<0.0001
Current smoking	0.70 (0.26–1.90)	0.48	0.20 (0.07–0.46)	<0.001
Intraday temperature difference (day 0)	0.83 (0.70–0.99)	0.04	0.89 (0.91–1.08)	0.89
Age	1.05 (0.98–1.15)	0.19	1.11 (1.06–1.16)	<0.0001
Current smoking	0.72 (0.26–1.97)	0.52	0.20 (0.07–0.46)	<0.001
Model 4				
Average humidity (day –2)	1.03 (0.99–1.08)	0.10	1.00 (0.98–1.03)	0.79
Age	1.06 (0.98–1.16)	0.16	1.11 (1.06–1.16)	<0.0001
Current smoking	0.80 (0.28–2.21)	0.66	0.20 (0.07–0.50)	<0.0001
Average humidity (day –1)	1.04 (0.99–1.08)	0.09	1.01 (0.99–1.04)	0.27
Age	1.05 (0.98–1.15)	0.24	1.11 (1.06–1.16)	<0.0001
Current smoking	0.70 (0.25–1.90)	0.48	0.20 (0.07–0.46)	<0.001
Average humidity (day 0)	1.06 (1.01–1.11)	0.03	1.01 (0.99–1.04)	0.37
Age	1.06 (0.98–1.16)	0.17	1.11 (1.06–1.16)	<0.0001
Current smoking	0.66 (0.23–1.83)	0.43	0.20 (0.07–0.48)	<0.001
Model 5				
Average atmospheric pressure (day –2)	0.97 (0.90–1.04)	0.41	0.99 (0.94–1.03)	0.51
Age	1.05 (0.97–1.14)	0.25	1.11 (1.06–1.16)	<0.0001
Current smoking	0.70 (0.26–1.90)	0.41	0.20 (0.07–0.46)	<0.001
Average atmospheric pressure (day –1)	0.94 (0.87–1.02)	0.19	1.00 (0.95–1.05)	0.96
Age	1.05 (0.97–1.14)	0.27	1.11 (1.06–1.16)	<0.0001
Current smoking	0.73 (0.26–2.00)	0.54	0.20 (0.07–0.46)	<0.001
Average atmospheric pressure (day 0)	0.90 (0.81–0.98)	0.02	1.00 (0.96–1.06)	0.80
Age	1.05 (0.98–1.15)	0.19	1.10 (1.06–1.16)	<0.0001
Current smoking	0.78 (0.28–2.18)	0.64	0.20 (0.07–0.46)	<0.001

Model 1, maximum temperature and risk factors; model 2, minimum temperature and risk factors; model 3, intraday temperature difference and risk factors; model 4, average humidity and risk factors; model 5, average atmospheric pressure and risk factors. day 0, day of AMI onset; day –1, 1 day before AMI onset; day –2, 2 days before AMI onset. AMI, acute myocardial infarction.

correlated with the occurrence of STEMI in a Japanese nationwide percutaneous coronary intervention registry.¹⁷ Based on the present analysis, however, intraday temperature difference and humidity were important for the development of AMI.

The interaction between age and gender differences in the AMI onset–weather association has been poorly reported.^{18,19} Male subjects have been reported to be more resistant to changes in air temperature and relative humidity than female subjects.^{12,20} Grech et al reported that there is no relationship between seasonal variation and AMI onset in male subjects.¹⁹ CAD was rarely detected in women <70 years of age because of the anti-atherogenic effect of estrogen.^{21,22} Honda et al reported that women have lower muscle mass, which considerably contributes to heat production, than men; therefore, they have more difficulty in maintaining body temperature due to the additional distribution of blood flow to the uterus and ovaries.²⁰ It has been reported that the effect of cold weather on death due to AMI was greater in the elderly than in younger individuals.²³ Elderly women with AMI were reportedly more susceptible to low air temperature than their young counterparts.^{24,25} Exposure to cold reportedly increases blood pressure, sympathetic nerve output, and platelet aggregation.²⁶ Another study reported that the relationship between air temperature and hospital admission for AMI was stronger in subjects aged >65 years than in those aged ≤65 years.²⁷

Although it appears difficult to predict AMI onset in the real-world clinical setting using the present observations alone, accumulating evidence on the association between AMI onset and meteorological parameters may become useful to predict AMI onset in specific populations in the future.

Study Limitations

The present study had several important limitations. First, this study was performed in Oita Prefecture only, and, because the period of enrollment was short (1.5 years), the number of cases was small, especially in the young women group. Second, this study included both STEMI and non-STEMI patients. It was impossible to analyze these 2 different pathological conditions separately, because of the small number of patients.

Conclusions

AMI onset appears to be more sensitive to weather conditions such as minimum temperature, average atmospheric pressure, and average humidity in young patients than in elderly patients. In particular, young women had AMI on days with a low intraday temperature difference and high humidity relative to men.

Disclosures

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