



## Clinical Research

# The Effects of Acute Atmospheric Pressure Changes on the Occurrence of ST-Elevation Myocardial Infarction: A Case-Crossover Study

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### ABSTRACT

**Background:** Few studies have explored the influence of short-term exposure to atmospheric pressure changes on the abrupt onset of ST-elevation myocardial infarction (STEMI). We sought to evaluate the association between acute atmospheric pressure changes and the occurrence of STEMI.

**Methods:** We studied STEMI patients from the Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH) from March 1, 2002 to December 31, 2016 in a case-crossover study design. Each case was matched with control intervals according to the same day of week, month, and year. All STEMI patients were linked with the nearest weather station within a 40-km radius according to residential postal code. The effect of exposure to air pressure changes, rate of air pressure changes, acute air pressure increase, and acute air pressure decrease 1 day to 7 days earlier on

### RÉSUMÉ

**Contexte :** Rares sont les études qui ont exploré l'influence d'une exposition à court terme à des changements de pression atmosphérique sur la survenue soudaine d'un infarctus du myocarde avec élévation du segment ST (STEMI). Nous avons cherché à évaluer l'association entre des changements de pression atmosphérique aigus et la survenue du STEMI.

**Méthodologie :** Nous avons étudié des patients ayant subi un STEMI inscrits dans la base de données Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH) entre le 1<sup>er</sup> mars 2002 et le 31 décembre 2016 en utilisant un plan d'étude cas-croisé. Chaque cas était apparié à des périodes témoins correspondant au même jour de la semaine, au même mois et à la même année. Tous les patients ayant subi un STEMI ont été associés à la station météorologique la plus proche dans un rayon de 40 km en

Acute myocardial infarction (AMI), causes more than 2.4 million deaths in the United States, and more than 4 million deaths in Europe and northern Asia, which accounts for more than a third of all deaths in developed nations annually.<sup>1</sup> AMI is traditionally classified into ST-elevation myocardial infarction (STEMI) and non-STEMI.<sup>2</sup> STEMI, constituting nearly 25%–40% of all AMI cases, is a medical emergency that requires prompt recognition and treatment.<sup>3</sup>

Atmospheric pressure, also termed barometric pressure or air pressure, is the force per unit area exerted against a surface by the weight of the air above that surface.<sup>4</sup> Several previous studies have shown that atmospheric pressure might have a significant effect on the morbidity and the mortality of AMI.<sup>5,6</sup> Bijelović et al. have reported that lower air pressure (< 100.9 kPa), adjusted for temperature and relative humidity, was associated with lower AMI incidence among adults and elderly people.<sup>7</sup> A 10-year survey spanning 1985 to 1994 has revealed a U shape association between atmospheric pressure and AMI, showing that increases and decreases in atmospheric pressure from 101.6 kPa were both associated with an increase in daily myocardial infarction event rates.<sup>8</sup> Moreover, in a study among 1.64 million German-Swiss residents living at an altitude between 259 and 1960 m, the investigators reported a relative risk reduction of 22% per 1000 m of altitude above sea level for myocardial infarction.<sup>9</sup> Because altitude is inversely related with atmospheric pressure, we suspected that atmospheric pressure

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See page 759 for disclosure information.

the onset of STEMI were analyzed with conditional logistic regression. All models were adjusted with daily average temperature, relative humidity, and average levels of 5 air pollutants.

**Results:** In 11,379 STEMI patients, positive associations with the onset of STEMI were only found at 7 days after exposure to acute air pressure decrease (odds ratio, 1.12; 95% confidence interval, 1.03-1.21), which was consistent in sensitivity and subgroup analyses. All the other models showed no evidence of statistically significant associations.

**Conclusions:** Acute air pressure decrease is associated with higher odds of a STEMI event 7 days after exposure. Weather advisories might be issued when atmospheric pressure decrease occurs.

might be one of the mechanisms to explain the protective effect of living at high altitude. However, few studies have explored the effects of short-term exposure to atmospheric pressure changes on the abrupt onset of STEMI. Therefore, the objective of this study was to investigate the relationship between acute air pressure changes and the occurrence of STEMI.

## Methods

### Study design

We used a case-crossover study design, which is a variant of a case-control design and is widely used to study the association between a transient exposure and an acute event.<sup>10</sup> Because STEMI generally has an abrupt onset and a short latency period for diagnosis, we used this design to explore the effects of acute atmospheric pressure changes on the onset of STEMI. This design is advantageous because it minimizes confounding from time-independent risk factors such as age, sex, the family history, and comorbidities.<sup>11</sup> In the case-crossover study, each case serves as its own control. The exposure of the case interval was compared with the exposure of the control interval.

### Data sources

We obtained data from the Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH), the inpatient Discharge Abstract Database (DAD), and Environment Canada. Ethics approval was obtained from the University of Alberta of Health Research Ethics Board. The details of the data sources are addressed in the following sections.

**APPROACH.** APPROACH is an ongoing clinical data collection registry capturing data on all patients who undergo cardiac intervention and revascularization in the province of Alberta, Canada, since 1995.<sup>12</sup> The registry contains detailed clinical information including diagnosis, procedure, demographic profile, ejection fraction, smoking, and history of

fonction du code postal de leur adresse résidentielle. L'effet de l'exposition aux changements de pression de l'air, du taux de changement de pression de l'air, de l'augmentation aiguë de pression de l'air et de la diminution aiguë de pression de l'air 1 à 7 jours plus tôt sur la survenue d'un STEMI a été analysé par régression logistique conditionnelle. Tous les modèles ont été ajustés en fonction de la température moyenne journalière, de l'humidité relative et de la concentration moyenne de 5 polluants atmosphériques.

**Résultats :** Sur 11 379 patients ayant subi un STEMI, une association positive avec l'apparition du STEMI n'a été observée que 7 jours après l'exposition à une diminution aiguë de pression de l'air (rapport de cotes, 1,12; intervalle de confiance à 95 %, de 1,03 à 1,21), un résultat également observé dans les analyses de sensibilité et de sous-groupes. Pour les autres modèles, aucune association statistiquement significative n'a été mise en évidence.

**Conclusions :** La diminution aiguë de la pression atmosphérique est associée à une probabilité plus élevée de STEMI 7 jours après l'exposition. Il serait utile de diffuser des avis météorologiques lorsqu'une diminution de la pression atmosphérique est prévue.

myocardial infarction, comorbidities, and indication for revascularization, etc. Standardized information is collected in this registry on the presentation of STEMI from the only 3 cardiac catheterization laboratories in Alberta (2 located in Edmonton and 1 in Calgary), covering the entire 3.6 million population of Alberta.<sup>13</sup>

**DAD.** Patients' first admitted hospital and the admission dates were obtained from DAD, in which information on all admissions to acute inpatient care facilities is recorded and is maintained by Alberta Health Services.<sup>14</sup>

**Meteorological data.** We obtained historic climate data from Environment Canada.<sup>15</sup> Hourly atmospheric pressure, temperature, and relative humidity collected by weather stations across Alberta were used in the study. Any weather stations that did not record hourly air pressure were not considered. Air pollution data were extracted from the Environment Canada National Air Pollution Surveillance database.<sup>16</sup> Hourly records of 5 air pollutants including NO, NO<sub>2</sub>, CO, ozone, and particulate matter with an aerodynamic diameter ≤ 2.5 μm were used to calculate daily average levels of the air pollutants.

### Population

All patients admitted to the hospital from March 1, 2002 to December 31, 2016 with a primary diagnosis of STEMI, confirmed using electrocardiogram and coronary angiogram were included in this study. Patients who did not have complete data on the meteorological factors or air pollutants were excluded.

### Variables of interest

**Exposures of interest.** In this study, we investigated the effects of 4 exposures including acute atmospheric pressure changes, the rate of atmospheric pressure changes, acute atmospheric pressure increase, and acute atmospheric pressure decrease, on the onset of STEMI.

Similar definitions for acute atmospheric pressure change and the rate of air pressure change were adopted from study by Houck et al. for the convenience of subsequent comparison.<sup>17</sup> Specifically, acute atmospheric pressure change was referred to as the difference between the daily highest air pressure and the lowest air pressure from 12 AM to 11 PM. The rate of air pressure changes was defined as the acute atmospheric pressure change divided by the duration of the change. The mean and SD of daily air pressure changes over the study period were considered as the cut point to determine if acute air pressure increase or decrease was present. To be specific, acute air pressure increase was deemed present if the daily atmospheric pressure change was greater than its mean plus 1 SD and the highest air pressure was later than the lowest one. A similar definition was used for acute air pressure decrease.

**Outcome variable and covariates.** The occurrence of STEMI was the outcome variable for this study. To better describe the study population, data on demographic characteristics and comorbidities were also collected, including age, sex, heart failure, cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease, current/previous smoking, hyperlipidemia, hypertension, and diabetes mellitus.

### Statistical analysis

The admission dates were treated as the case intervals. We used a time-stratified referent selection strategy to select the control intervals, which were matched with the cases according to the same day of week from the same calendar month and year. This strategy has been proven to be able to limit time-trend bias.<sup>18</sup>

Patients' first admission to hospital and the admission dates from DAD were first linked with the demographic data from the APPROACH registry using the personal health number. Next, the records of all of the STEMI cases as well as their self-controls were linked with the meteorological and air pollutants' data from the nearest weather station according to the postal code and the date of exposure. We restricted our analysis to patients who live within a 40-km radius of the nearest weather stations. A series of lag periods, from 1 to 7 days was explored. For example, if the patient was admitted to the hospital on January 15, January 14 was considered as the time window for all of the meteorological variables for a 1-day lag period. In addition, to avoid the autocorrelation that might lead to unreliable coefficient estimates, we did not use the average or distributed lag models.

The characteristics of the STEMI patients and the distribution of STEMI events in different seasons are described. Statistics including mean, SD, and 25th, 50th, and 75th percentiles of continuous predictors are presented.

Unadjusted and adjusted conditional logistic regression was used to evaluate the relationship between the occurrence of STEMI and 4 exposures of interest. A *P* value of < 0.05 was considered to be statistically significant for all statistical tests. The effects of association were reported as odds ratios (ORs) with corresponding 95% confidence interval (CI). Daily average temperature, relative humidity, and daily

average levels of 5 air pollutants were adjusted in the regression models.

Prespecified subgroup analyses were performed to determine if there were different effects of air pressure changes on the onset of STEMI in each subgroup. A sensitivity analysis restricting the STEMI population to those who live within a 20-km radius of the nearest weather station was conducted to examine if the results would be affected by the choice of the distance.

Data management was implemented using Python 3.6.1 (Python Software Foundation, Beaverton, OR). The geodesic distances between patients and weather stations were calculated using the GeoPy 1.11.0 package (GeoPy Contributors 2006-2018, MIT). Statistical analyses were implemented in STATA (version 13.1; StataCorp LP, College Station, TX).

### Results

The characteristics of the STEMI patients are shown in Table 1. In a total of 11,379 STEMI patients, the largest percentage (54.1%, *n* = 6158) of individuals was between 45 and 65 years old, and 77.6% (*n* = 8830) of all of the STEMI patients were male. Hypertension (55.8%; *n* = 6349), hyperlipidemia (56.2%; *n* = 6393), and smoking history (53.4%; *n* = 6083) were the most common comorbidities in this population. STEMI events were basically equally distributed in 4 seasons (26.0%, 24.2%, 24.9%, 24.9% from spring to winter). The percentages of patients exposed to acute air pressure increase and air pressure decrease were 7.2% (*n* = 818) and 7.1% (*n* = 808), respectively.

The statistics of continuous predictors are shown in Table 2. The mean of the daily air pressure change and the rate of air pressure change were 0.66 (SD = 0.41) kPa and 0.40 (SD = 0.20) hPa/h. The reason for using hPa/h as the unit for the rate of air pressure change was for the convenience of interpreting 1-unit changes for the OR in the regression

**Table 1. Characteristics of the STEMI patients (N = 11,379)**

Characteristic	n	%
Age, years		
< 45	1023	9.0
45-65	6158	54.1
> 65	4198	36.9
Sex		
Male	8830	77.6
Female	2549	22.4
Season		
Spring (March to May)	2956	26.0
Summer (June to August)	2749	24.2
Autumn (September to November)	2838	24.9
Winter (December to February)	2836	24.9
Comorbidity		
COPD	1088	9.6
Heart failure	1012	8.9
Cerebrovascular disease	457	4.0
Diabetes	2298	20.2
Hypertension	6349	55.8
Hyperlipidemia	6393	56.2
Smoking history	6083	53.4
PAD	837	7.36
Dichotomous exposure		
Acute air pressure increase	818	7.2%
Acute air pressure decrease	808	7.1%

COPD, chronic obstructive pulmonary disease; PAD, peripheral artery disease; STEMI, ST-elevation myocardial infarction.

**Table 2. Summary statistics for continuous exposures and covariates**

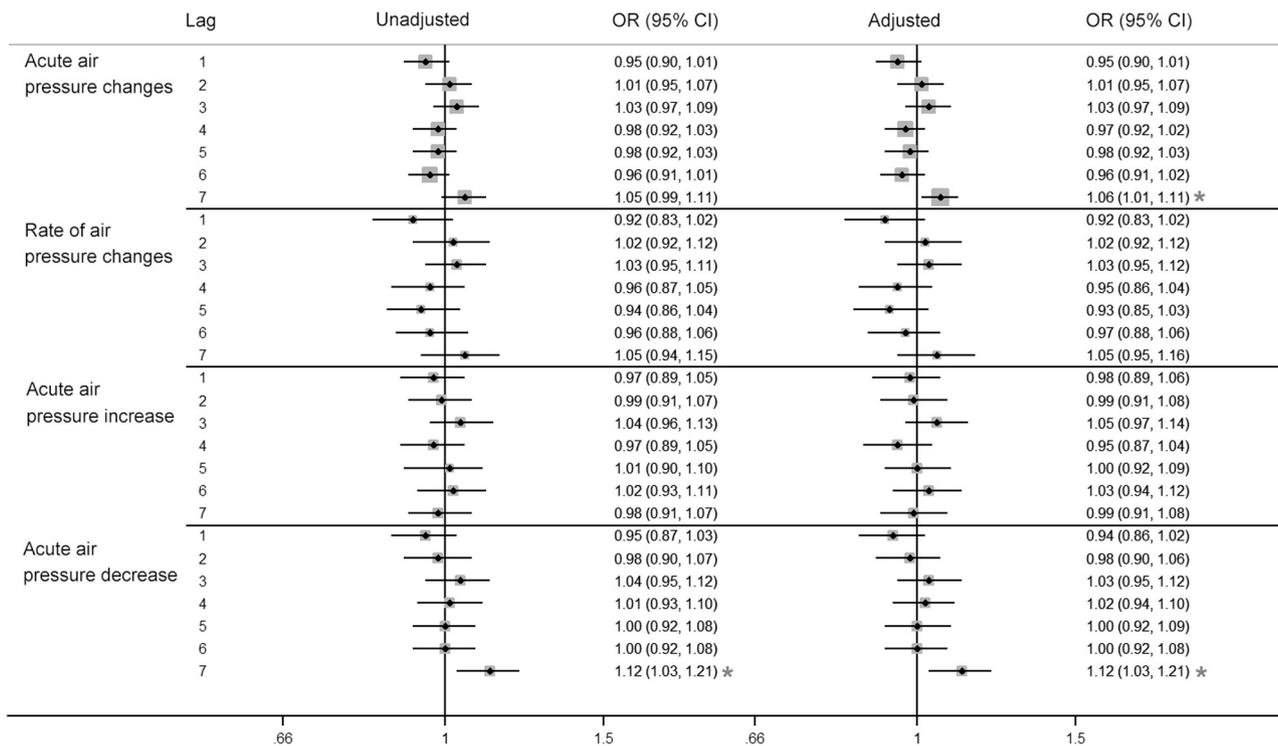
Variable	Mean	SD	25 <sup>th</sup> percentile	50 <sup>th</sup> percentile	75 <sup>th</sup> percentile
Air pressure change, kPa	0.66	0.41	0.35	0.56	0.87
Rate of air pressure change, hPa/h	0.40	0.20	0.24	0.35	0.50
Temperature, Celsius	4.33	11.0	-2.6	5.29	13.1
Relative humidity, %	64.5	14.9	53.6	64.7	75.4
CO, ppm	0.28	0.22	0.2	0.3	0.4
NO, ppb	13.08	21.1	2	6	15
NO <sub>2</sub> , ppb	15.9	10.0	8	14	22
O <sub>3</sub> , ppb	21.3	10.0	14	21	29
PM2.5, µg/m <sup>3</sup>	7.5	6.26	4	6	9

PM2.5, particulate matter with an aerodynamic diameter ≤ 2.5 µm.

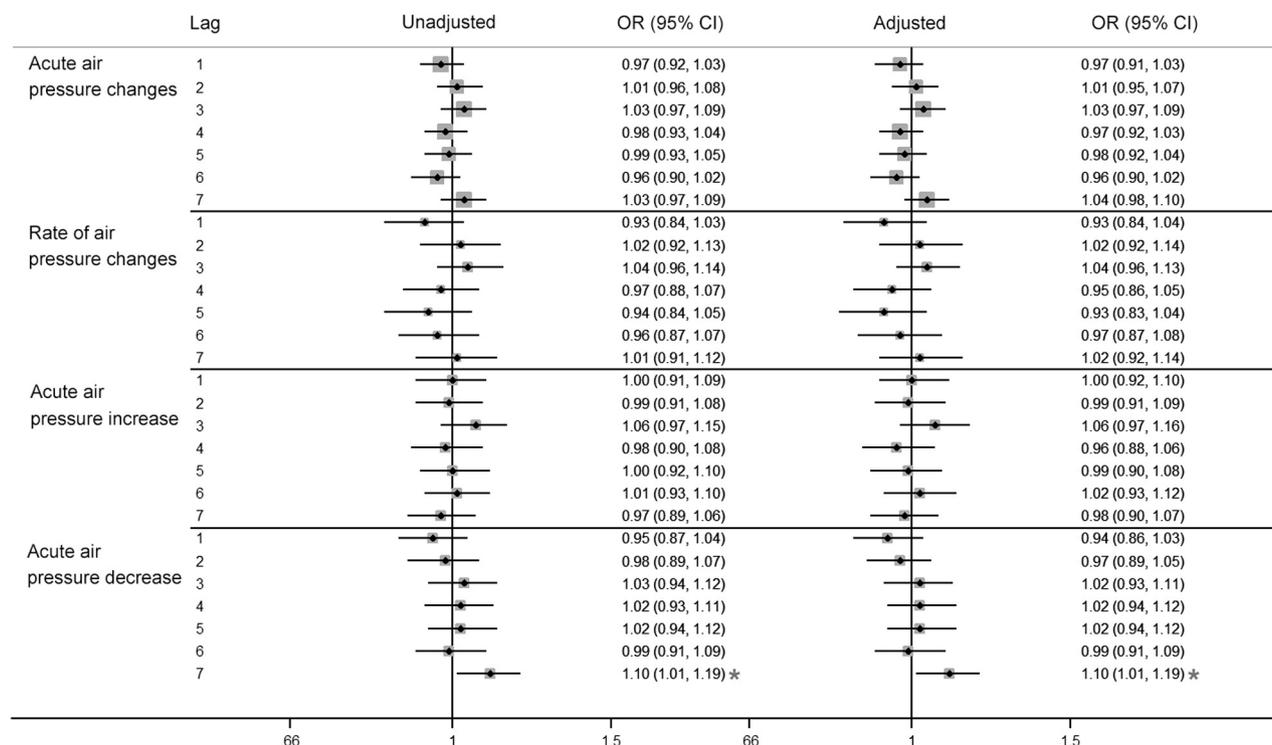
model. For the detailed statistics of other predictors, please refer to [Table 2](#).

[Figure 1](#) shows the crude and adjusted ORs of STEMI associated with 4 exposures with lag times from 1 day to 7 days for patients who were linked with the nearest weather stations within 40 km of their residences. We examined the collinearity of the independent variables in the models. No apparent correlation was observed between the primary exposures of interest and the covariates (Pearson correlation coefficients ranged from -0.16 to 0.1). Acute air pressure changes were found to have no evidence of statistically significant associations with the onset of STEMI, with and without adjustment for average temperature, relative humidity, and air pollutants in the lag periods from 1 day to 6 days. In the lag period of 7 days, this association was significant with an OR of 1.06 (95% CI, 1.01-1.11) after adjustment.

There was no evidence of a statistically significant association between the onset of STEMI and the rate of air pressure changes, with adjusted ORs ranging from 0.92 to 1.05. Similarly, acute air pressure increase had no evidence of a statistically significant effect on the onset of STEMI, with the adjusted ORs ranging from 0.98 to 1.05. However, acute air pressure decrease was associated with a higher probability of STEMI onset before and after adjustment (OR, 1.12; 95% CI, 1.03-1.21) in the lag time of 7 days, although this association was not found in the lag period from 1 day to 6 days. The ORs for all of the covariates are provided in [Supplemental Table S1](#) and [Supplemental Table S2](#). Because a significant amount of models were analyzed, only the adjusted conditional logistic regression models for acute air pressure decrease for a distance of 40 km and 20 km between patients' residence and a nearest weather station are provided.



**Figure 1.** The unadjusted and adjusted odds ratios (ORs) of ST-elevation myocardial infarction onset associated with 4 exposures of interest (< 40 km between patients' residence and the nearest weather station). One unit increase was 1 kPa for acute air pressure changes and 1 hPa/h for the rate of air pressure changes.



**Figure 2.** The unadjusted and adjusted odds ratios (ORs) of ST-elevation myocardial infarction onset associated with 4 exposures of interest (< 20 km between patients' residence and the nearest weather station). One unit increase was 1 kPa for acute air pressure changes and 1 hPa/h for the rate of air pressure changes.

In a sensitivity analysis (Fig. 2) restricting the distances between patients and weather stations to less than 20 km, we found that the results were similar to the findings when distance between patients' residence and the weather stations was within 40 km. The exception to this was crude OR of STEMI associated with acute air pressure changes for which there was no evidence of a statistically significant effect in the lag period of 7 days (OR, 1.04; 95% CI, 0.98-1.10); however, after adjustment this finding was again significant at 1.10 (95% CI, 1.01-1.19).

Figure 3 and Figure 4 show the ORs of STEMI onset associated with 4 exposures according to sex and age, from 1 to 7 day lag periods, adjusting for daily mean temperature, relative humidity, and air pollutants. The onset of STEMI was found to have no significant association with acute air pressure changes, the rate of air pressure changes, air pressure increase, and air pressure decrease, except that air pressure changes were significantly associated with higher likelihood of STEMI onset for men (OR, 1.12; 95% CI, 1.02-1.23) and for younger patients (OR, 1.12; 95% CI, 1.02-1.24) at day 7 after the exposure. We also found a borderline significant association between the onset of STEMI and the rate of air pressure changes in a lag time of 5 days (OR, 0.88; 95% CI, 0.77-0.99).

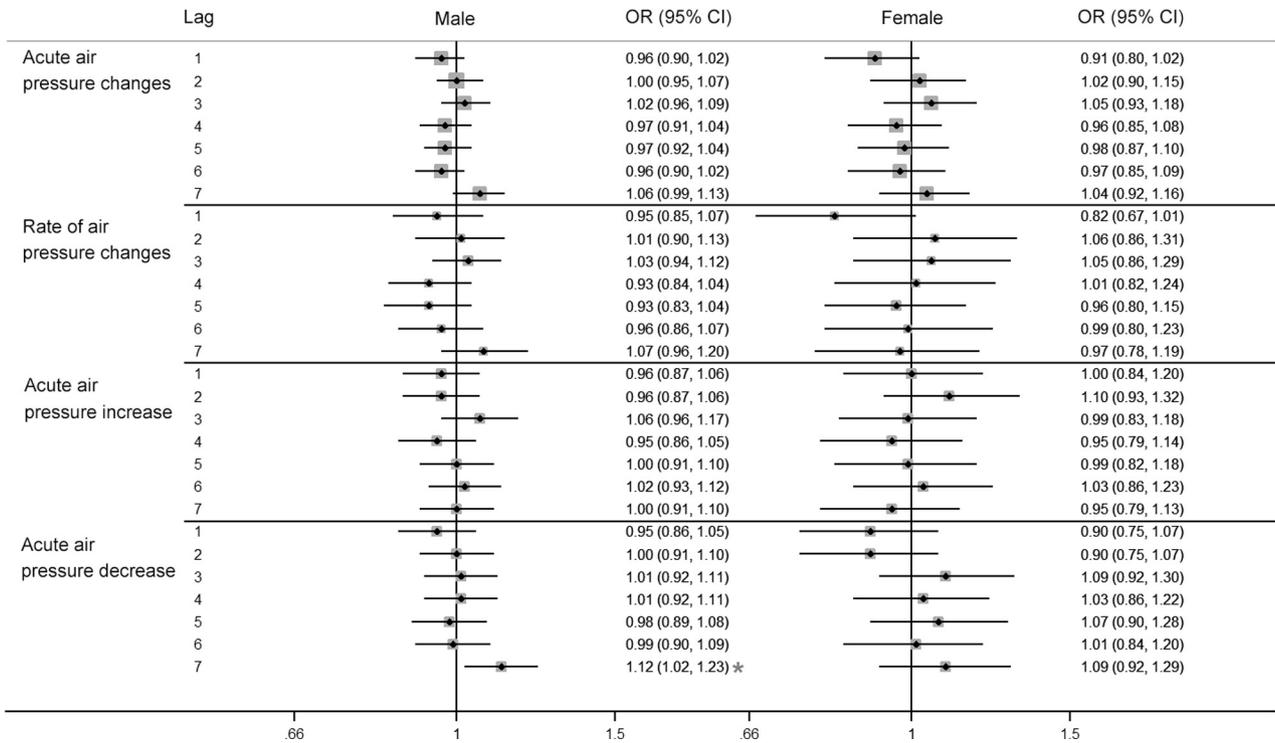
### Discussion

In the current study, we found no evidence of statistically significant associations between the occurrence of STEMI and 4 exposures including acute air pressure changes, the rate of air pressure changes, acute air pressure increase, and air pressure decrease 1-6 days after the exposure, whereas air pressure

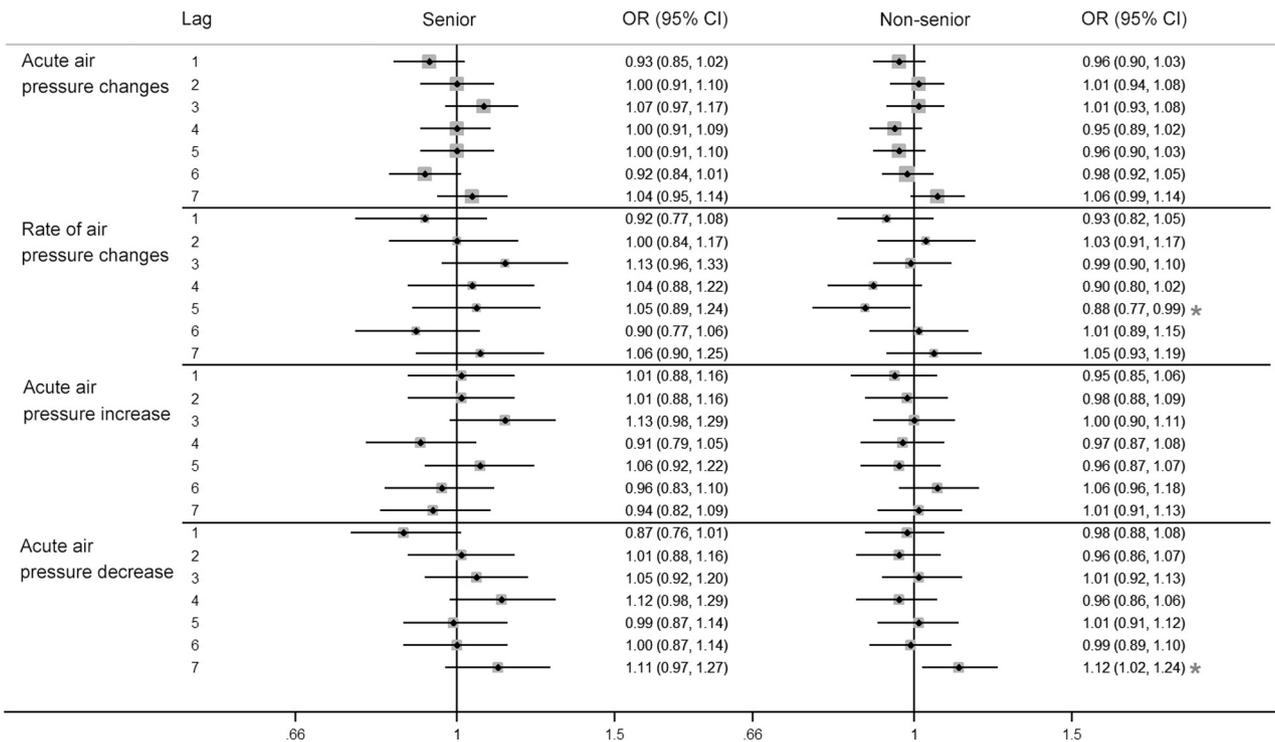
decrease was significantly associated with higher odds of STEMI onset 7 days after the exposure. Although acute air pressure changes were significantly associated with higher odds of STEMI events in the adjusted model 7 days after the exposure, this association is likely a false positive error, which was not consistently found in the subsequent sensitivity analysis and subgroup analysis.

There is a growing body of literature reporting that meteorological factors such as air pollutants,<sup>19</sup> temperature,<sup>8,20</sup> atmospheric pressure, and relative humidity<sup>21</sup> might trigger AMI, which is often induced by a ruptured or eroded atherosclerotic plaque that leads to a sudden and critical reduction in blood flow.<sup>22</sup> Although the effect of climate triggers to any single person is relatively small compared with the effect of traditional risk factors (eg, smoking), the public health relevance is considerable, because environmental factors affect hundreds of millions of individuals on a continuous and involuntary basis.<sup>23</sup>

Several studies have indicated that acute air pressure change might have an effect on the onset of myocardial infarction. AMI is one of the common medical emergencies during a commercial flight.<sup>24</sup> During air travel, passengers experience a reduced ambient air pressure equivalent to the air pressure at an altitude of 6000-8000 feet.<sup>25</sup> In an *in vitro* study, Ikeyama et al. have shown that subtle changes of atmospheric pressure (5-20 hPa) can induce elevation of intracellular calcium level in cultured human keratinocytes,<sup>26</sup> suggesting that keratinocytes might act as the sensors of atmospheric pressure changes in our bodies. It has also been shown that an air pressure changes as small as 5 hPa could have an effect on the body. The authors also reported



**Figure 3.** The adjusted odds ratios (ORs) of ST-elevation myocardial infarction onset associated with 4 exposures of interest according to sex (< 40 km between patients' residence and the nearest weather station). One unit increase was 1 kPa for acute air pressure changes and 1 hPa/h for the rate of air pressure changes.



**Figure 4.** The adjusted odds ratios (ORs) of ST-elevation myocardial infarction onset associated with 4 exposures of interest according to senior/nonsenior (< 40 km between patients' residence and the nearest weather station). One unit increase was 1 kPa for acute air pressure changes and 1 hPa/h for the rate of air pressure changes.

neurotransmitters and hormones that influence multiple systems (nervous, cardiovascular, endocrine, and immune systems) were generated and released from epidermal keratinocytes after exposure to acute atmospheric pressure changes.<sup>27</sup> Their findings suggest that atmospheric pressure change might be sensed by epidermal keratinocytes, causing the synthesis and release of NO, which might subsequently influence the blood vessels.<sup>27</sup> In our study, we found that acute air pressure decrease (> 10.7 hPa) increased the odds of STEMI occurrence (OR ranged from 1.10 to 1.12) in a lag time of 7 days with and without adjustment of the confounders, with consistent findings in sensitivity analyses. In the subgroup analysis, this positive association was also observed in male and in younger patients. Primarily, our results indicate that the short-term exposure to daily air pressure decrease might require an induction period of 7 days before the occurrence of STEMI. The mechanism of why the effect of acute air pressure decrease on STEMI event occurred on 7 day lag instead of earlier latent period is unclear. Generally, there is an inverse association between exposure dose and latent period. In other words, a low dose means long latent period. Therefore, we speculate that because air pressure change is relatively a small exposure, it might take longer for the patients to develop the symptom. Our results are partially congruent with those of Houck and colleagues,<sup>17</sup> who showed no relation between the daily occurrence of AMI and the maximum air pressure changes for a lag period of 1-3 days. However, they<sup>17</sup> did not investigate a longer latency period. Therefore, further investigations are required to confirm the positive association between acute air pressure decrease and STEMI occurrence at a 7-day lag period.

Our study has several strengths. First, to our best knowledge, this is the first study to evaluate the relationship between acute atmospheric pressure changes and the onset of STEMI using a case-crossover study design, which intrinsically adjusts for all measured and unmeasured time-invariant individual-level confounders, such as age, sex, social economic status, lifestyle, body mass index, and comorbidities. Second, we used the resident postal code of each patient to locate the nearest weather station for personalized atmospheric pressure data, which makes our study more precise than the studies using the city-wide averaged atmospheric pressure. Third, this study has a large sample size, which includes all STEMI patients who underwent cardiac angiogram in a province, which reduces the selection bias arising from the selection of patients from a single research site. Finally, the time-stratified referent selection strategy adopted in this study controlled the time-trend bias.

There are some limitations in our study. Because the outcome definitions of STEMI were defined according to hospital admissions; major events leading to out-of-hospital mortality were not included in the study. There is a potential misclassification of timing of onset of STEMI. To ensure the exposure preceded the admission, same-day exposure was not appropriate to be assessed in our study, which could limit the ability to observe an association. Another limitation is a potential selection bias induced by excluding weather stations that did not record hourly atmospheric pressure. Approximately 90% of our cohort lives in an urban area, therefore our findings might not be applicable to those who live in more rural areas of the province. Moreover, we were unable to adjust for other plausible triggers, such as physical exertion or

psychological stress. However, it is unlikely that all of these rare triggers happened at the same time. Last, some measurement error might exist that would bias the estimate toward the null, because individual-level exposure can only be measured by the nearest weather station to the patients' residence.

In conclusion, there is no evidence of a statistically significant association between acute air pressure changes and the onset of STEMI in a lag time of 1-6 days, whereas acute air pressure decrease is associated with higher odds of a STEMI event 7 days after exposure. Weather advisories might be issued when atmospheric pressure decrease occurs.

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### Disclosures

The authors have no conflicts of interest to disclose.

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### Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at [www.onlinecjc.ca](http://www.onlinecjc.ca) and at <https://doi.org/10.1016/j.cjca.2019.02.015>.