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Original Contribution

The seasonality of acute coronary syndrome and its relations with climatic parameters

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Abstract

Background: Most research on the seasonality of acute coronary syndrome (ACS) has been were reported from hospital-based data. We aimed to investigate the seasonal distribution of ACS in Beijing and to elucidate the relations between ACS occurrence and climatic parameters in a prehospital setting.

Methods: We retrospectively reviewed the electronic prehospital medical records from the Beijing's emergency medical service system spanning August 1, 2005, to July 31, 2007. Case data were analyzed by month and season with χ^2 test. The effects of climatic factors on the occurrence of ACS were analyzed by Poisson regression with generalized linear model.

Results: During the 2-year study period, a total of 7037 ACS events were identified, including 4135 male patients (58.8%) and 2902 female patients (41.2%). Significant variations were observed in the monthly ($P < .001$) and seasonal ($P < .001$) distribution of ACS. The highest seasonal incidence occurred in winter and lowest in autumn. Significant negative correlations were noticed between the number of ACS events and daily mean temperature ($P < .001$) and between the number of ACS events and barometric pressure ($P < .001$). Comparing to the baseline level (temperature of 25°C to approximately 31°C; barometric pressure of 1026 to approximately 1048 hectopascal (hPa)), an increase of 41.3% of daily ACS incidence was associated with temperature lower than 2°C (−10.0°C to approximately 2.0°C), and an increase of 19.8% was associated with barometric pressure under 1006 hPa (991.0 to approximately 1006 hPa).

Conclusions: There are clear monthly and seasonal rhythms of ACS in Beijing metropolitan area. Temperature and barometric pressure are negatively related with the occurrence of ACS.

1. Introduction

Acute coronary syndrome (ACS) usually presents in the late stages of coronary heart disease (CHD) and is one of the leading causes of death in the world. Many risk factors

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such as the diet, hypertension, smoking, and obesity for ACS have been identified [1]. Previous studies suggest there is significant seasonality with respect to the incidence of ACS [2-6]. A few small studies have addressed the effect of barometric pressure on ACS [7-10]. In this study, we examined data from the emergency medical service system (EMSS) in Beijing. Four climatic parameters' effects on the occurrence of ACS were analyzed: temperature, barometric pressure, humidity, and wind speed. Understanding of the seasonal pattern of ACS and the climatic parameters' influence on its occurrence might aid in the preventive strategies for prehospital planning.

2. Methods

2.1. Study population

The EMSS ambulances in Beijing are staffed by physicians with training in emergency medicine diagnosis and procedures appropriate for the prehospital evaluation and treatment of ACS. The EMSS physicians enter clinical data on standardized forms, including the patients' general information, chief complaint, medical history, bedside physical examination, and a preliminary diagnosis. In this study, the electronic prehospital medical records from the Beijing's EMSS spanning August 1, 2005, to July 31, 2007, were reviewed by 2 emergency attending physicians. Acute coronary syndrome was diagnosed by EMSS physicians in the prehospital setting, based on symptoms, medical history, physical examination, and the patient's prehospital 12-lead electrocardiogram. In this study, we used the diagnosis of the EMSS physician. All protocols and procedures were approved by the human studies research committee of Peking Union Medical College (Beijing, China) before the advent of the study.

The World Health Organization multinational MONItoring of trends and determinants in CArdiovascular disease (MONICA) project monitors the prevalence of acute cardiac events in 21 countries, including China [11]. On the basis the MONICA project and the high incidence of ACS in the aged population in Beijing, we chose to study ACS events in individuals older than 20 years. Data from all case records including age, sex, date, time of onset of ACS, and the diagnosis were extracted for the present study. Cases were grouped in intervals by decade from the age of 20 to 89, with one group including all patients older than 89 years. Demographic data (in the year 2006) population ratios of age groups and sex groups were obtained from the Beijing Statistical Information Net [12]. Adjusted frequency, corresponding to relative ACS frequency in unit population of the age group, was calculated by the following equation: adjusted frequency = cases of the age group/ratio of the age group in Beijing population (%)/100.

2.2. Meteorologic data

Beijing is characterized by warm temperate subhumid continental monsoon climatic zone with 4 distinct seasons. Seasons are defined as spring (March to May), summer (June to August), autumn (from September to November), and winter (from December to February). To investigate the relations between the occurrence of ACS and climatic parameters, meteorologic data of every 3 hours during the study period were obtained from the Beijing Meteorological Bureau, including temperature (°C), barometric pressure (hPa), relative humidity (%), and wind speed (m/s).

2.3. Statistical analysis

The incidence of ACS was summarized as the count of daily cases during the study period. Case data were analyzed by month and season with χ^2 test. Daily means of the climatic parameters were calculated and related with the number of ACS cases on the given day. To evaluate the relative risk of different meteorological conditions, the number of events and related climatic parameters were analyzed using Poisson regression with generalized linear model. Because of a wide annual variance of climatic parameters in Beijing (temperature, −10°C to approximately 31°C; barometric pressure, 991 to approximately 1048 hPa; relative humidity, 7%-97%; and wind speed, 0.5 to approximately 6.5 m/s), the mean values of daily temperature and barometric pressure were categorized into 5 levels (Table 1). To evaluate the value of relative risk, the highest levels of temperature (25°C to approximately 31°C) and barometric pressure (1026 to approximately 1048 hPa) were set as the baseline for each factor in the present study. Because of the strong correlations between climatic parameters, the levels of humidity and wind speed were adjusted by Poisson regression. All analyses were carried out with the software SPSS (Statistical package for Social

Table 1 The 5 categories of temperature and barometric pressure

	Variation range	n (%)
Daily mean temperature (°C)		
−10.0 to 2.0	12.0	152 (20.8%)
2.0 to 11.0	9.0	143 (19.6%)
11.0 to 20.0	9.0	147 (20.1%)
20.0 to 25.0	5.0	135 (18.5%)
25.0 to 31.0	6.0	153 (21.0%)
		Total records: 730 (100%)
Daily mean barometric pressure (hPa)		
991.0 to 1006.0	15.0	144 (19.7%)
1006.0 to 1012.5	6.5	146 (20.0%)
1012.5 to 1019.0	6.5	143 (19.6%)
1019.0 to 1026.0	7.0	144 (19.7%)
1026.0 to 1048.0	22.0	153 (21.0%)
		Total records: 730 (100%)

Sciences) 11.5 (SPSS Inc, Chicago, Ill). $P < .05$ was considered as statistically significant for all results.

3. Results

3.1. Age distribution

There were a total of 355,418 electronic medical records in Beijing's EMSS during the study period. Among them, a total of 7037 cases of ACS were identified during the 2-year study period. Of these cases, there were 536 cases of acute ST-elevation acute myocardial infarction. Of the 7037 ACS cases, there were 4135 male patients (58.8%) and 2902 female patients (41.2%). The mean age was 64.5 ± 14.4 years old. More than two thirds (69.8%) of cases occurred in patients older than 55 years. There was a small but statistically significant difference in age for males (63.0 ± 14.7) vs females (66.0 ± 13.7) ($P < .001$).

Peak incidence was observed at the seventh decade. When the frequency of ACS was adjusted by the percentage of the decade to the total population, a definite increment of episodes was noticed as age increased (Fig. 1). The variation of the frequency of ACS in each decade showed a curve approximating exponential growth ($R^2 = 0.999$; $P < .001$), with a sharp takeoff after the sixth decade. People in eighth decade had a higher risk ratio, about 50-fold, compared to individuals in their thirties.

3.2. The monthly and seasonal patterns of ACS

Significant variations were observed in the monthly ($\chi^2 = 77.359$; $P < .001$) and seasonal ($\chi^2 = 57.448$; $P < .001$) distribution. The highest seasonal incidence occurred in winter and decreased as the seasons changed from winter to autumn (Fig. 2A). Monthly cases reached the peak and the nadir in March and in September, respectively. The second highest and lowest month during which cases occurred was in January and in October, respectively (Fig. 2B).

Paralleling the monthly variation of total cases, similar variations were observed in the incidence of cases occurring in females ($r = 0.942$; $P < .001$) and in males ($r = 0.952$; $P < .001$). The monthly peak of ACS cases in females occurred in March and the nadir in October. For males, the highest ACS incidence was in February and the lowest was in September.

3.3. Relations between meteorologic parameters and the occurrence of ACS

The daily number of ACS cases fluctuates with seasons in Beijing, indicating a possible association with climatic

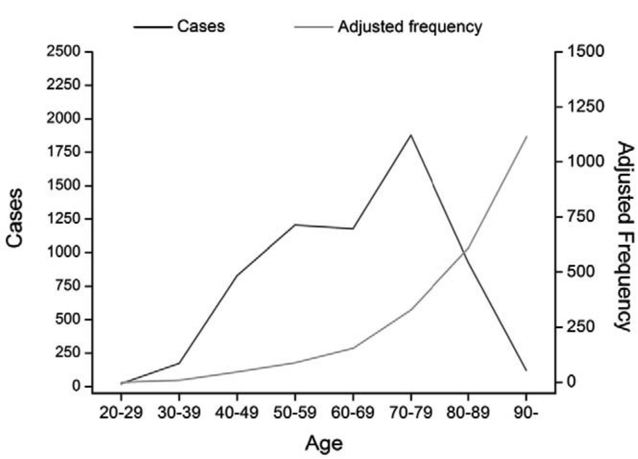

Fig. 1 The age distribution of the total 7037 cases of ACS and the increasing tendency of adjusted frequency of ACS in each decade. Adjusted frequency = cases of the age group/population ratio of the age group, corresponding to relative ACS frequency in unit population of the age group.

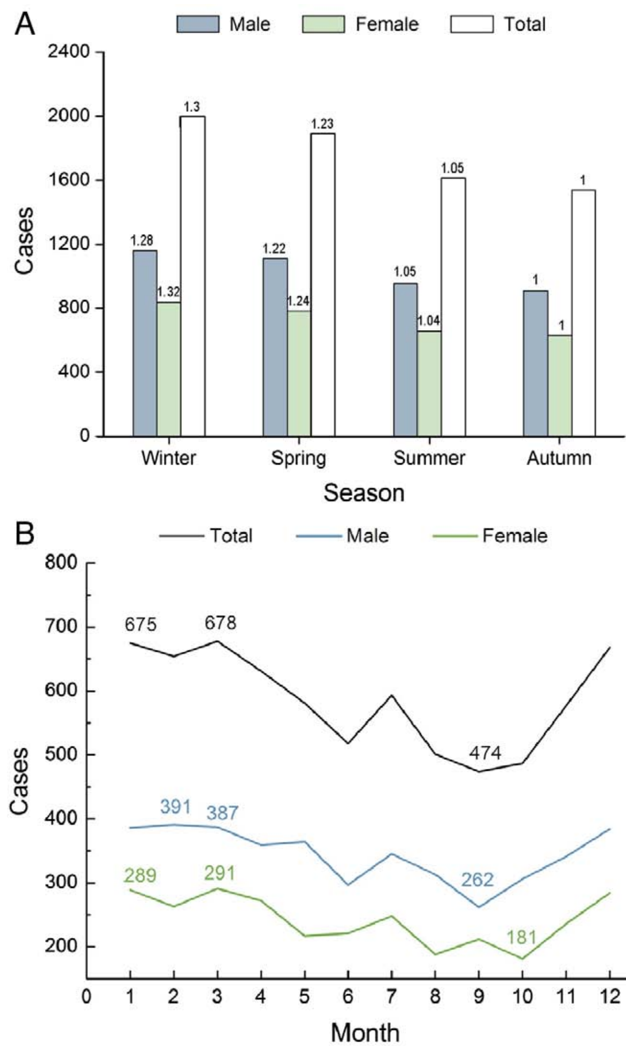

Fig. 2 (A) Seasonal variation of ACS incidence. The ratios to autumn were indicated on each column. (B) Monthly variation of ACS incidence. The highest, the second highest, and the lowest monthly cases were indicated with numbers.

parameters. The results of Poisson regression analysis showed significant negative correlations between daily events and daily mean temperature ($\beta = -.018$; $P < .001$) and between daily events and daily mean barometric pressure ($\beta = -.011$; $P < .001$). No relation was found between the daily occurrence of ACS and wind speed or relative humidity (Table 2). An overall increasing of relative risk was noticed with the decrease of the daily mean temperature and with that of barometric pressure. Comparing to the baseline level, an increase of 41.3% of daily ACS incidence was associated with temperature lower than 2°C (−10.0°C to approximately 2.0°C), and an increase of 19.8% was associated with barometric pressure under 1006 hPa (991.0 to approximately 1006 hPa) (Fig. 3). The influence of temperature was slightly stronger than that of barometric pressure.

4. Discussion

Data from our large retrospective study investigating the seasonality of ACS cases were derived from the prehospital data. Many other studies to date have examined in-patient populations. The composition of in-patient populations differs greatly from that in the prehospital setting and cannot be compared. Data from EMSS can reflect the time of disease onset and the incidence more accurately than data from the hospital admission, especially in countries with wide disparities in access to medical care [13]. Thus, our data are likely the most accurate, concurrent reflection of ACS onset time, and climatic parameters studied to date.

Beijing is a city with a population holding steady at about 16 million people during the investigative period. Most residents are the Han ethnic population accounting for about 95% of the population. During the study period, there were no significant social events (such as SARS, the Olympic Games) that could lead migration or other significant changes in the composition of the population in Beijing. In previous Sino-MONICA census on the population with age 25 to 74 years old (471 462 people in 7 districts of Beijing were surveyed in 1997), acute coronary events has a similar age distribution as the present study suggesting that we are getting a realistic sample of the population [11].

Past studies have reported differing patterns relating seasons (or temperature) and the ACS incidence. The study by Dilaveris et al indicated that as temperature increases,

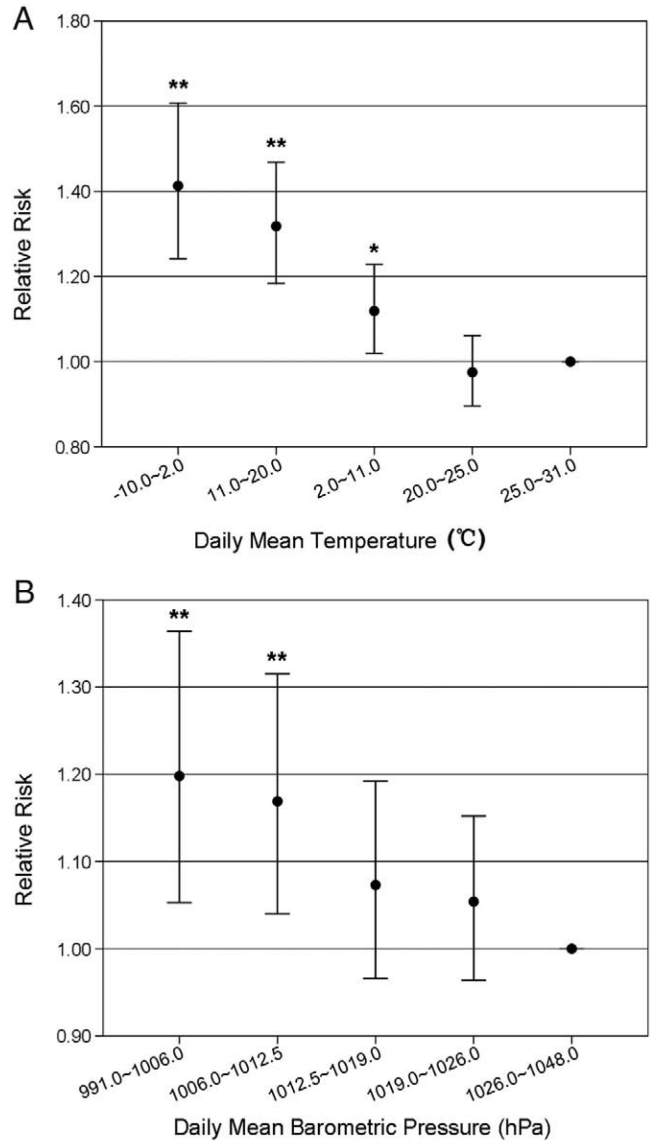

Fig. 3 (A) Relative risk of different levels of daily mean temperature comparing to 25°C to approximately 31°C as the baseline. (B) Relative risk of different levels of daily mean barometric pressure comparing to 1026 to approximately 1048 hPa as the baseline. *$P < .05$ compared with baseline; **$P < .01$ compared with baseline.

the number of daily deaths caused by acute myocardial infarction (AMI) declines, reaching a minimum corresponding to 23.3°C, then beginning to increase as the temperature rises [3]. This is a U-shaped relationship. In tropical areas, authors have reported that the higher temperature, the more ACS morbidity and mortality—a linear relationship [14]. The data by Ku et al [15] suggest no cold or hot weather impact on the incidence of AMI, which may arise from the subtropical region characteristic. The investigation by Fries et al [16] in northern Germany (Homburg/Saar) drew a conclusion that thermal stress caused by the atmospheric conditions in a consistently temperate climate are likely too weak to influence the

Table 2 Estimates of the correlation of climatic parameters with daily ACS cases by Poisson regression

Daily means	Coefficient (β) ± SE	Significance
Temperature	−0.018 ± 0.0022	<.001
Barometric pressure	−0.011 ± 0.0023	<.001
Wind speed	0.014 ± 0.0156	.372
Relative humid	7.57E−005 ± 0.0007	.917

incidence of AMI significantly. Spielberg et al [17] analyzed the incidence of 2906 AMI registered over an 8-year period in Germany and found seasonal peak occurrence of AMI in March when outside temperatures are usually moderate. Much of the difference in results can be accounted for by the markedly different physical geography of the study sites.

Beijing is a city with warm, temperate subhumid continental monsoon climate and 4 distinct seasons. Our study showed significant seasonal variation of ACS incidence, more ACS occurred in winter. This is consistent with several other studies though none of these were performed in the out-of-hospital setting [4-6,18,19]. Some investigators also found that temperature has an inverse relationship with ACS incidence. Marchant and colleagues [20] reported a significantly higher AMI rate in winter (related to lower outdoor temperatures) in 633 patients during a 4-year period in London. Similarly, Biyik et al [21] found that death arising from cardiovascular causes, especially AMI, is higher in cold winter months than in hot summer months. Ours has a similar result as Marchant and Biyik but in a significantly different setting. Another important similarity comes from the study in the southern city of Guangzhou, China [22]. In the study by Guangzhou Municipal Cardiovascular Cooperative Group, 943 acute myocardial infarction patients were studied during 5 years in 18 hospitals. Peak incidence was found in winter during January and February in their in-hospital setting. In our previous research on sudden cardiac death, in which CHD is believed the most common etiology, a similar result was noticed [23].

The significant inverse relation between temperature and ACS incidence suggests that cold may play an important role in the incidence of ACS. Several possible physiologic changes have been proposed to explain the seasonal variation of ACS incidence, including changes in clotting mechanisms, lipid levels, and blood pressure. (1) Blood pressure is a strong risk factor for AMI. Cold-induced vasoconstriction causes a significant increase in arterial pressure, sympathetic nervous output, and heart workload [24], which are balanced by coronary vasodilatation in healthy subjects, may result in myocardial ischemia in patients with coronary disease [25]. (2) The increase of fibrinogen, the platelet aggregation, and acute phase factors such a C-reactive protein during the cold months could contribute to increase the occurrence of cardiovascular diseases in winter [26-28]. Woodhouse et al [28] proposed higher fibrinogen activity in winter as a possible explanation for the seasonal variation in mortality from cardiovascular disease. Their group also proposed that part of the rise in fibrinogen concentrations in winter might be the result of seasonal respiratory tract infection. In the study by David, the cholesterol level showed a seasonal variation, 7.4 mg/dL higher on December 30 than on June 30, possibly contributing to the winter predisposition of ACS [29]. (3) There have also been studies that have related increased respiratory disease and cardiovascular disease morbidity in association with air pollution, and it was suggested that the increase in cardiovascular disease could be the result of the increased respiratory disease in winter [30-33]. (4) Recently, cold-inducible RNA binding protein has been found to play protective roles in cold-induced stroke. It has been suggested to act as a RNA chaperonin to protect and restore native RNA conformations in response to various stresses in particular cold-induced stress [34]. The role of cold-inducible RNA binding protein in cold-induced ACS needs to be studied further and may help elucidate important mechanisms leading to ACS at molecular level.

We noticed that in the present study the peak of case numbers occurred in March (678 cases), which is not the coldest month in Beijing. This illustrates the importance of understanding local culture as well as local physical geography. In winter, most accommodations in Beijing have the heating systems to keep the indoor temperatures above 18°C. But in March, when outdoor temperature gets around 10°C, most heating systems are shut down, which lead to lower temperatures insides than in comparatively colder parts of winter. People experience more coldness in March than in winter months—a de facto increase in the exposure to cold. The study by Spielberg et al [17] found a similar pattern to ours, but the reasons may be very different as the heating systems and behavioral patterns of their study population likely differ from ours.

In addition to the frequently noticed correlation between temperature and ACS cases, our study also showed that the lower the barometric pressure, the higher the rate of ACS cases. Compared to more commonly studied parameters such as temperature, fewer studies have investigated the barometric effect. Briefly, Houck and colleagues [7] focused on the relative change of barometric pressure, and their results showed that there was a significant correlation between a rapid decrease in atmospheric pressure and the occurrence of AMI the day after a pressure decrease, especially during the fall and winter seasons. In a 10-year study as part of the World Health Organization-MONICA in France, Danet et al [5] detected a V-shaped relationship for atmospheric pressure, with a minimum of daily event rates at 1016 mbar. When pressure is not 1016 mbar, every 10-mbar change was associated with an approximately 11% increase in ACS rates. A study of AMI patients in Japan showed that pressure has a weaker association with mortality than does temperature [8].

Barometric pressure has not previously been shown to have a strong impact on the occurrence of ACS because studies with small sample size cannot effectively reflect the effect of barometric pressure [9]. In a study of 390 coronary cases, Adesola [10] found that the initially significant positive relationship between a rise in barometric pressure and the admission rate of patients over the age of 60 years was no longer seen when the minimum daily temperature was kept constant during the analysis. The inverse correlation between barometric pressure and ACS is an important issue regarding the safety of the people with advanced CHD during flight traveling, when barometric pressure changes could be of great magnitude.

Although our data identify a pattern relating barometric pressure to ACS incidence, the intrinsic mechanism by which barometric pressure influences ACS remains unclear. Houck et al [7] hypothesized that changes in atmospheric pressure might contribute to plaque rupture. He cited the engineering principles to support the hypothesis: a bathysphere is subject to structural failure upon ascent (decrease in pressure) rather than descent. Atmospheric pressure changes could induce structure failure of atherosclerotic plaque and rupture. The exact mechanism merits further investigation.

Limitations of this study include the assignment of patients to ACS by the EMSS physicians. No quantitative stress tests or coronary angiography were obtained to confirm the diagnosis. This may lead to over or under-counting of ACS patients; however, this should not lead to bias as a function of temperature or barometric pressure. In daily practice, most ACSs are clinically diagnosed based on the patients' medical history, physical examination, and electrocardiograms. And, this was the only unbiased way to enroll patients to this study. Oversmoothing of climatic variance using Poisson regression could potentially bring biased estimation, but this is usually seen where disease rates for geographic are unstable because of small populations. This pitfall does not seem likely in our study with a sufficiently large sample size. Another limitation is that other seasonal parameters, such as infection, were not excluded in this study. Associations of various air pollution determinants with cardiovascular mortality and morbidity have been found. For example, Biyik et al [21] found when the temperature is lower, the rate of respiratory tract infections is elevated. Infection, like other physiologic stressors, has a positive correlation with the occurrence of myocardial infarction. Previous study [35] has shown that influenza vaccination can lower the rates of pulmonary infection and acute cardiac events further supporting the patterns observed by Biyik and his colleagues. Our study did not assess atmospheric pollutants such as particulate matter thought to be associated with cardiovascular mortality [36,37]. We did not test whether knowledge of meteorologic parameters associated with ACS can be effectively translated into preventive measures or improve the efficiency and distribution of resources during anticipated increases in ACS occurrence. Our study lays the foundation for future studies addressing these important questions.

In conclusion, our large retrospective study shows that in the Beijing metropolitan area, the presentation of ACS has significant monthly and seasonal rhythms. The presentation of ACS has an inverse correlation with temperature and barometric pressure. Understanding modifiable environmental factors might decrease the incidence of ACS in those most vulnerable to this lethal disease.

Acknowledgment

None of the authors has conflicts of interest to report.

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