RESEARCH REPORT

Myocardial infarction deaths after high level exposure to particulate matter

Yoshitaka Murakami, Masaji Ono

J Epidemiol Community Health 2006;**60**:262–266. doi: 10.1136/jech.2005.038315

See end of article for authors' affiliations

Correspondence to: Dr Y Murakami, Department of Health Science, Shiga University of Medical Science. Seta Tsukinowa-cho, Otsu City, Shiga, 520-2192, Japan; ymura@belle.shiga-med.ac.jp

Accepted for publication 26 September 2005

Study objective: To examine the short term effects of raised concentrations of air pollutants on myocardial infarction deaths, the authors measured if incidence rate ratios increased after the concentration of suspended particulate matter (SPM) reached various critical values and were sustained for various periods of time.

Design: Retrospective analysis of a database, which contained hourly SPM concentrations and myocardial infarction deaths.

Methods: The rate of death (events/1000 hours) attributable to myocardial infarction was compared among SPM categories. SPM categories were classified by five different critical values that measured high SPM levels, and by the hours of exposure (exposure window) after reaching the critical SPM level.

Main outcome measures: The adjusted incidence rate ratios in the various SPM categories were compared with the reference category (0–99 $\mu g/m^3$) to determine the incidence rate ratio.

Setting: Tokyo Metropolitan area, Japan.

Patients/participants: 14 950 people who died of myocardial infarction in the Tokyo Metropolitan area from 1990 to 1994.

Main results: When the exposure window was one hour, the adjusted incidence rate ratio in each category were 1.13 (95% CI: 1.07 to 1.20) in the 100–149 $\mu g/m^3$ category, 1.17–1.24 in the intermediate categories, and 1.40 (1.00 to 1.97) in the highest (300 $\mu g/m^3$ over) category. When the exposure window was one to six hours, increased rate ratios were seen in the highest category (1.17 (four hours) to 1.40 (one hour)). Gradual increases in the incidence rate ratio were seen as the SPM category increased when the exposure window was less than six hours.

Conclusion: An increased rate ratio of myocardial infarction deaths was seen within a few hours after reaching a high concentration of SPM. When the exposure window was less than six hours, there was a gradual increase in the incidence rate ratio as the SPM concentration increased.

A vast number of papers have shown both the short term[1 2] and long term[3 4] adverse health effects of air pollutants. Public health policy makers have paid attention to the potential deleterious effects of air pollutants, and the focus has now shifted to disease specific issues, such as cardiovascular disease.[5 6] Daily mortality in cardiovascular disease increases when the daily average of air pollutants increases. This acute effect might arise from an increase in the mortality of myocardial infarction. For myocardial infarction, the temporal relation between acute onset and transient increase in the level of air pollutants was examined previously in a case-crossover approach.[7 8] Another approach is to focus on the occurrence of high level concentrations of pollutants and to examine whether there is an increase in mortality during the subsequent hours after such high levels. However, few studies have focused on the short term exposure to high levels of air pollutants and mortality in the subsequent hours.

In Japan, both air pollutant levels and time of death from death certificates are available on an hourly basis. This allowed us to analyse the temporal relation between air pollutants and adverse health events in an hourly scaled measure. Therefore, we examined whether an increase of myocardial infarction deaths occurred after a transient increase in air pollutant levels.

METHODS

Description of data

Tokyo has an area of 2187 km^2, and about 11.8 million people lived there in the year 1994. Thirty four districts (19 in the urban area and 15 in the suburban area) of the Tokyo Metropolitan area were selected for the study, where 60 ambient air pollution monitoring stations were evenly distributed by the Tokyo Metropolitan government.

The number of myocardial infarction deaths (*International Classification of Disease 9th Revision: 410*) for each hour was calculated from the Vital Statistics of Japan from 1 January 1990 to 31 December 1994.

In Japan, the criterion used for air pollution is the concentration of suspended particulate matter (SPM)—particles with diameters less than 10 μm, intermediate between and $PM_{2.5}$ and PM_{10}. The diameters of SPM are mainly PM_7. The SPM concentrations and temperature are measured every hour at ambient air pollution monitoring stations. These data were obtained from the National Institutes for Environmental Studies and linked with mortality data by district, year, month, day, and hour. When there was more than one ambient air pollution monitoring station in the same district, the average values at these stations were used for the analysis.

Method of examining the effect of SPM on mortality rates

Figure 1 is a hypothetical example that explains the methods we used. This figure shows the SPM concentrations, the critical vale of high SPM levels, exposure windows after SPM concentration reached high levels, deaths attributable to

Abbreviations: CI, confidence interval; SPM, suspended particulate matter

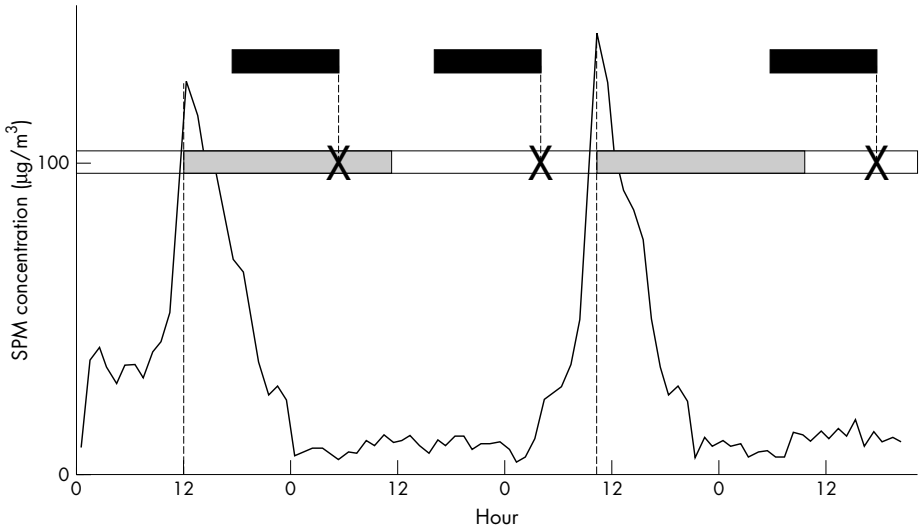

Figure 1 SPM concentrations, high levels of SPM, exposure window after SPM concentrations reached a high level, and the exposure window for averaging temperature. This is a hypothetical example to explain the method used in this paper. The straight line represents the concentration of SPM. The dotted line represents the critical value that marks the onset of the exposure window when the SPM concentration reached the critical value (in the above illustration, critical value is 100 μg/m^3). The ''X'' represents myocardial infarction deaths. Each grey band represents the exposure window after the SPM concentration reached the critical value. Those categories where bands are located stand for their SPM categories, and width stands for the duration of the exposure window (in the above illustration, the duration of the exposure window was 24 hours). The white band represents the reference exposure window. The black band represents the exposure window that was used to average the temperature (in the above illustration, this period lasted 12 hours). There were three myocardial infarction deaths, one occurred in the exposure window with an SPM category of 100 μg/m^3, and two occurred in exposure window within the reference category.

myocardial infarction, and the exposure window used for averaging the temperature values.

Five concentrations (100 μg/m^3, 150 μg/m^3, 200 μg/m^3, 250 μg/m^3, and 300 μg/m^3) of critical values were set for identifying high concentrations of SPM. Those levels were determined from the distribution of SPM concentrations in Tokyo from 1990 to 1994.

After these levels were established, we selected several window lengths (from one hour to 48 hours) to evaluate the effects of high concentrations of SPM. Each of these windows, so called ''exposure windows'', was further categorised into six SPM categories (0–99 μg/m^3, 100–149 μg/m^3, 150–199 μg/m^3, 200–249 μg/m^3, 250–299 μg/m^3, 300 μg/m^3 and over). When different SPM categories overlapped, the higher one was chosen for the analysis.

To adjust for the effect of temperature on myocardial infarction death, an average of hourly temperature before death was used for the analysis. To explore the influence of an exposure window in which hourly temperatures were averaged, several different periods were examined.

In each SPM category, the number of myocardial infarction deaths was counted throughout each period, and the incidence rate per 1000 hours was determined. The reference SPM category was set to 0–99 μg/m^3. The rate ratio (incidence rate in any SPM category divided by the reference category) was calculated to compare the different SPM categories.

Statistical analysis

A Poisson regression model was used to adjust for the effects of confounding factors. The average temperature of the period before the myocardial infarction deaths, the hour of day that the deaths occurred, and the region (urban or suburban area) were included in the model as confounders. In modelling the effect of temperature, we used a piecewise linear regression with the disjoint coding method[9] for treating cold and hot temperature effects separately. In the model, the point where the regression line turned over was set to 25℃, this was the point at which the lowest mortality was seen in the crude analysis. The hour of day that death occurred was included in the model as a dummy variable.

RESULTS

Table 1 shows the summary of SPM concentrations and temperatures during the study period. The median, 90th centile, and maximum concentration of SPM (μg/m^3) were

Table 1 Median, minimum, maximum, and centile of SPM and temperature in Tokyo, 1990–1994

				Centile			
	Median	Min	Max	75	90	95	99
Urban area							
SPM (μg/m^3)	44.0	0.0	1091.3	73.5	115.0	148.3	227.2
Temperature (℃)	16.2	−4.5	39.5	22.2	26.8	29.0	32.6
Suburban area							
SPM (μg/m^3)	39.0	0.0	563.0	63.5	97.0	124.5	195.0
Temperature (℃)	15.3	−7.7	38.5	21.5	26.1	28.5	32.6

SPM, suspended particulate matter. The urban area included 15 districts in Metropolitan Tokyo. The remaining area was classified as suburban.

Table 2 Characteristics of study subjects who died of myocardial infarction in Tokyo, 1990–1994

	Men	Women
Age		
Mean	72.1	78.7
Standard deviation	12.6	10.2
Minimum	15	20
Maximum	106	103
	Number of persons	**Percentage**
Sex		
Male	8121	56.3
Female	6309	43.7
Residence		
Urban area*	11251	78.0
Suburban area	3179	22.0
Location where death occurred		
Medical institution†	11837	82.0
Home	2358	16.3
Other	235	1.7
Death by hour‡		
0 am–6 am	3090	21.4
6 am–12 am	3836	26.6
0 pm–5 pm	3779	26.2
6 pm–12 pm	3725	25.8
Months deaths occurred		
January–March	4198	29.1
April–June	3193	22.1
July–September	3141	21.8
October–December	3898	27.0
Total	14430	100.0

*The urban area includes 15 districts in Metropolitan Tokyo. The remaining area was classified as suburban. †Medical institution includes hospitals, clinics, and nursing homes. ‡0 am–6 am, 6 am–12 am, 0 pm–6 pm, and 6 pm–12 pm each represent 0:00–5:59, 6:00–11:59, 12:00–17:59, and 18:00–23:59.

44.0, 115.0, and 1091.3 in the urban areas, and 39.0, 97.0, and 563.0 in the suburban areas, respectively.

Table 2 shows characteristics of the study subjects. There were 14 430 deaths (male: 8,121, female: 6,309) from myocardial infarction during 1990–1994 in Tokyo. The average age at death was 72.1 for men and 78.7 for women. Most of the subjects lived in the urban areas (78.0%) and expired in medical institutions (82.0%).

Table 3 shows the distribution of total hours in each SPM category with six different exposure windows. When the exposure window was short (one to six hours), most of the periods fell in the lowest category (0–99 $\mu g/m^3$) (one hour: 88.4%, six hours: 77.5%). As the duration of the exposure window increased, the distribution of hours shifted to the higher categories. The proportion of overlap with multiple SPM categories was small when the exposure window was short, and increased with longer exposure windows (24 hours: 18.0%, 48 hours: 27.5%).

Table 4 shows the rate ratios of myocardial infarction deaths adjusted for temperature, the hour of day when deaths occurred, and region. In every SPM category, the rate ratios were higher than 1.00. The adjusted rate ratios in each SPM category ranged from 1.07 to 1.13 in the 100–149 $\mu g/m^3$ category, from 1.09 to 1.24 in the intermediate categories (150–199, 200–249, and 250–299 $\mu g/m^3$), and from 1.14 to 1.40 in the highest category (300 $\mu g/m^3$ and over). When the exposure window was one hour, the rate ratio was 1.40 (CI: 1.00 to 1.97) in the highest category. Although not significant, the rate ratios in the highest category still remained large when the exposure windows were short (two to six hours). As the duration of the exposure window increased, the adjusted rate ratios of the intermediate and highest categories showed similar values. For every exposure window duration, a gradual increase in the rate ratio was seen in the 100–149 and 150–199 $\mu g/m^3$ categories. When exposure window was one to six hours, an increase in the rate ratio was mainly seen as the category increased, although a slight decrease was sometimes observed in the 200–249 $\mu g/m^3$ category. There was little influence of temperature changes on the adjusted rate ratio.

DISCUSSION

This study showed an increase in the rate ratio of myocardial infarction deaths occurred once the SPM level exceeded 100 $\mu g/m^3$. A remarkably high rate ratio was seen within one hour after the SPM level exceeded 300 $\mu g/m^3$. A gradual increase in the rate ratio was found as the category of SPM concentration level increased only when the exposure window was below six hours.

With environmental quality standards in Japan, the daily average of SPM normally stays below 100 $\mu g/m^3$. This shows that the transient effects we saw were in situations with highly concentrated air pollutants. We assumed that a concentration of air pollutants during a certain hour (point exposure) caused the events in the following hours (exposure window), not merely events occurring during the same hour (point events). When using hourly scaled measures, our approach is straightforward for examining transient effects on events after exposure to high levels of air pollutants. A prior study using a case-crossover approach showed that a transient increase of air pollutants caused myocardial infarction onset during the reference period of sampling. Our approach was to examine the effect of transient rise in air pollutants using the entire reference period.

The exact duration between an exposure to air pollutants and death from myocardial infarction is difficult to estimate. In experimental studies in animals and humans, potential biological mechanisms linking air pollution and cardiovascular diseases have been investigated.[10 11] These studies show an acute response within a few hours after exposure to air pollutants, such as reduced heart rate variability, raised ST-segment elevation, and vasoconstriction. In the study using a case-crossover approach,[7] an increased rate ratio of myocardial infarction was associated with an increase in pollutants during the two hour period before the infarction onset (1.48 with an increase of 25 $\mu g/m^3$ $PM_{2.5}$), and in the 24 hour period one day before the infarction onset (1.69 with an

Table 3 Distribution of total hours in the SPM categories

Length of exposure window (hours)	Total hours in an SPM category ($\mu g/m^3$)						Hours that multiple SPM categories overlap*
	0–99	100–149	150–199	200–249	250–299	300–	
1	1317039 (88.4)	115448 (7.7)	37703 (2.5)	12897 (0.9)	4830 (0.3)	2099 (0.1)	0 (0.0)
3	1239769 (83.2)	160574 (10.8)	56640 (3.8)	20748 (1.4)	8167 (0.5)	4118 (0.3)	63840 (4.3)
6	1154252 (77.5)	208383 (14.0)	77964 (5.2)	30126 (2.0)	12439 (0.8)	6852 (0.5)	110805 (7.4)
12	1021905 (68.6)	277560 (18.6)	111977 (7.5)	46203 (3.1)	20306 (1.4)	12065 (0.8)	173402 (11.6)
24	842728 (56.6)	361419 (24.3)	161262 (10.8)	70105 (4.7)	33019 (2.2)	21483 (1.4)	268651 (18.0)
48	619841 (41.6)	447587 (30.0)	227539 (15.3)	105883 (7.1)	52020 (3.5)	37146 (2.5)	409703 (27.5)

Numbers in parentheses in each row show the percentages. *When periods were being classified into several SPM categories, and some of them overlapped, the higher one was selected.

Table 4 Adjusted rate ratio of myocardial infarction deaths

Length of exposure window (hours)	Rate ratio of myocardial infarction deaths in an SPM category (μg/m³)				
	100–149	150–199	200–249	250–299	300–
	RR 95%CI	RR 95%CI	RR 95%CI	RR 95%CI	RR 95%CI
1	1.13 (1.07 to 1.20)	1.17 (1.07 to 1.28)	1.18 (1.01 to 1.37)	1.24 (0.97 to 1.57)	1.40 (1.00 to 1.97)
2	1.09 (1.04 to 1.15)	1.17 (1.07 to 1.27)	1.10 (0.96 to 1.26)	1.20 (0.97 to 1.48)	1.25 (0.93 to 1.68)
3	1.09 (1.04 to 1.15)	1.17 (1.09 to 1.27)	1.10 (0.97 to 1.25)	1.18 (0.97 to 1.43)	1.22 (0.94 to 1.58)
4	1.09 (1.04 to 1.14)	1.18 (1.10 to 1.27)	1.09 (0.97 to 1.23)	1.18 (0.99 to 1.41)	1.17 (0.92 tp 1.49)
5	1.10 (1.05 to 1.15)	1.14 (1.06 to 1.23)	1.13 (1.01 to 1.26)	1.13 (0.96 to 1.35)	1.20 (0.96 to 1.50)
6	1.09 (1.04 to 1.14)	1.16 (1.09 to 1.24)	1.11 (1.00 to 1.24)	1.09 (0.93 to 1.29)	1.21 (0.98 to 1.49)
9	1.09 (1.04 to 1.13)	1.14 (1.08 to 1.22)	1.15 (1.05 to 1.26)	1.14 (0.99 to 1.31)	1.15 (0.96 to 1.38)
12	1.08 (1.04 to 1.13)	1.15 (1.09 to 1.22)	1.16 (1.06 to 1.26)	1.12 (0.98 to 1.27)	1.14 (0.97 to 1.34)
18	1.10 (1.05 to 1.14)	1.14 (1.08 to 1.20)	1.18 (1.09 to 1.27)	1.17 (1.04 to 1.30)	1.15 (1.00 to 1.32)
24	1.11 (1.06 to 1.15)	1.16 (1.11 to 1.23)	1.18 (1.09 to 1.26)	1.19 (1.08 to 1.32)	1.16 (1.03 to 1.32)
48	1.07 (1.03 to 1.12)	1.18 (1.13 to 1.24)	1.18 (1.10 to 1.25)	1.18 (1.08 to 1.28)	1.21 (1.10 to 1.33)

Reference category was set to 0–99 μg/m³. The rate ratio was estimated by adjusting for temperature, hour when deaths occurred, and region. The temperature effect used in model was averaged over 24 hours before death.

increase of 20 μg/m³ $PM_{2.5}$). Another study showed that an increase in myocardial infarction onset was seen within one hour after exposure to traffic.[12] To investigate the effect of exposure duration on myocardial infarction deaths, we studied several different exposure windows after high level exposure to SPM, from an extremely short interval (one hour) to a prolonged period (48 hours).

We selected the higher category when multiple SPM categories overlapped. From previous studies, it is obvious that the effect of air pollutants in a higher category is larger than in a lower category.[3 4] These previous results suggest that the effect of a higher SPM category is much stronger than that of a lower category during a period of overlap. In the same SPM category, the crude incidence declined slightly with an increase in the exposure window. This was presumably because the incidence was diluted when the incidence of a lower SPM category moved to a higher category. This dilution might have been less in a shorter period (one to six hours) in which the proportion of overlapping SPM categories was below 10%.

In the study with the case-crossover approach,[7] a high rate ratio of myocardial infarction onset was seen two hours and one day after there was an increased concentration of particular matter. In our study, remarkably high rate ratios in the highest SPM category were noted within one hour after reaching a high SPM concentration. Although not significant, high rate ratios were also seen in the short exposure windows (two to six hours). The adjusted rate ratios had wide confidence intervals because there were extremely few hours within the highest SPM category when the exposure window was short. For example, total hours in the highest SPM category contained only about 7000 hours (0.5%) when the exposure window was six hours. The high rate ratio in the highest SPM category during several short exposure windows suggested that deaths from myocardial infarction are likely to occur within a few hours of increased SPM concentrations. In 1994, 70% of people died within four hours after the onset of myocardial infarction in Japan.[13] The increased mortality within one to six hours after high SPM concentrations suggests that the onset of myocardial infarction occurs more frequently just after reaching a high concentration of SPM.

We searched the medical literature to identify confounding factors that strongly affected myocardial infarction deaths. We treated temperature[14–16] and the hour that myocardial infarction occurred[17 18] as confounding factors in the analysis. As there were apparent differences between urban and suburban areas, such as lifestyle and environment, we also included a regional effect as a confounding factor. As the onset of myocardial infarction has a circadian variation, it was necessary to include the hour of the day that myocardial infarctions occurred in the model. As death certificates in Japan do not include information about the time that myocardial infarction occurred, we used the hour of day when death occurred. Because most deaths from myocardial infarction occur within a few hours of myocardial infarction onset,[13] we considered it appropriate to use the hour of death instead of the hour of myocardial infarction onset. To adjust for the effect of temperature in the model, we averaged the temperature over a period of time before death. As we were not certain of the exact time period to use for the temperature averaging, we used various time periods (from three hours to 24 hours) and found that the time period had little influence on the incidence rate ratio.

We used the rate of myocardial infarction deaths per 1000 hours instead of person hours in this study, because information on person hours was not available. The range of population in the study area from 1990 to 1994 was between 11.68 million (1991) and 11.87 million (1992). We assumed that the population in the study area was stable and used the rate of myocardial infarction deaths per 1000 hours to compare the different SPM categories.

In conclusion, we examined the transient effect of SPM on myocardial infarction deaths and found an increased incidence rate ratio within a few hours after reaching high concentrations of SPM. When we focused on the effect only a few hours after SPM reached high levels, there was a gradual increase in the incidence rate ratio as the SPM concentration increased.

What this paper adds

The rate ratio of myocardial infarction death was high in subsequent hours after the detection of a high concentration of SPM. Gradual increases in the rate ratio were seen as the category of SPM concentration increased.

Authors' affiliations
Y Murakami, Department of Health Science, Shiga University of Medical Science, Japan
M Ono, Epidemiology and International Health Research Section, Environmental Health Sciences Division, National Institute for Environmental Studies, Japan

Funding: this study was partially supported by the Ministry of Education, Culture, Sports, Science and Technology's Grant-in-Aid for Young Scientists (B), 15790290, 2003–2004.

Conflicts of interest: none declared.

REFERENCES

1 **Samet JM**, Dominici F, Curriero FC, *et al*. Fine particulate air pollution and mortality in 20 US cities, 1987–1994. *N Engl J Med* 2000;**343**:1742–9.
2 **Omori T**, Fujimoto G, Yoshimura I, *et al*. Effects of particulate matter on daily mortality in 13 Japanese cities. *J Epidemiol* 2003;**13**:314–22.
3 **Dockey DW**, Pope III AC, Xiping X, *et al*. An association between air pollution and mortality in six U.S. cities. *N Engl J Med* 1993;**329**:1753–9.
4 **Pope III CA**, Burnett RT, Thun MJ, *et al*. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *JAMA* 2002;**287**:1132–41.
5 **Dockery DW**. Epidemiologic evidence of cardiovascular effects of particulate air pollution. *Environ Health Perspect* 2001;**109**(suppl 4):483–6.
6 **Morris RD**. Airborne particulates and hospital admissions for cardiovascular disease: a quantitative review of the evidence. *Environ Health Perspect* 2001;**109**(suppl 4):495–500.
7 **Peters A**, Dockery DW, Muller JE, *et al*. Increased particulate air pollution and the triggering of myocardial infarction. *Circulation* 2001;**103**:2810–15.
8 **D'Ippoliti D**, Forastiere F, Ancona C, *et al*. Air pollution and myocardial infarction in Rome—a case-crossover analysis. *Epidemiology* 2003;**14**:528–35.
9 **Rothman KJ**, Greenland S. *Modern epidemiology*. 2nd ed. Philadelphia: Lippencott-Raven, 1998:359–99.
10 **Pope III CA**, Burnett RT, Thurston GD, *et al*. Cardiovascular mortality and long-term exposure to particulate air pollution—epidemiological evidence of general pathophysiological pathways of disease. *Circulation* 2004;**109**:71–7.
11 **Brook RD**, Franklin B, Cascio W, *et al*. Air pollution and cardiovascular disease—a statement for healthcare professionals from the expert panel on population and prevention science of the American Heart Association. *Circulation* 2004;**109**:2655–71.
12 **Peters A**, von Klot S, Heier M, *et al*. Exposure to traffic and the onset of myocardial infarction. *N Engl J Med* 2004;**351**:1721–30.
13 **Matsumoto K**, Matsubara S, Tamakoshi A, *et al*. Investigation of death certificate in Aichi prefecture. (In Japanese). *Jpn J Public Health* 2003;**50**:540–6.
14 **Marchant B**, Ranjadayalan K, Stevenson R, *et al*. Circadian and seasonal factors in the pathogenesis of acute myocardial infarction: the influence of environmental temperature. *Br Heart J* 1993;**69**:385–7.
15 **Danet S**, Richard F, Montaye M, *et al*. Unhealthy effects of atmospheric temperature and pressure on the occurrence of myocardial infarction and coronary deaths—a 10-year survey: the Lille-World Health Organization MONICA project (Monitoring trends and determinants in cardiovascular disease. *Circulation* 1999;**100**:e1–7.
16 **Yamasaki F**, Seo H, Furuno T, *et al*. Effect of age on chronological variation of acute myocardial infarction onset: study in Japan. *Clin Exp Hypertens* 2002;**24**:1–9.
17 **Muller JE**, Stone PH, Turi ZG, *et al*. Circadian variation in the frequency of onset of acute myocardial infarction. *N Engl J Med* 1985;**13**:1315–22.
18 **Kinjo K**, Sato H, Sato H, *et al*. Circadian variation of the onset of acute myocardial infarction in the Osaka area, 1998–1999 -characterization of morning and nighttime peaks. *Jpn Circ J* 2001;**5**:617–20.