‖原 著‖

Seasonal variations and the effect of atmospheric temperature on the incidence of coronary heart disease in Hiroshima, Japan

Hongli Wang[1*], Makoto Matsumura[2], Masayuki Kakehashi[1] and Akira Eboshida[3]

Key words：1. coronary heart disease 2. season 3. temperature

Background : Seasonal variations in the incidence of Coronary Heart Disease (CHD) have rarely been studied qualitatively and quantitatively, although it is often pointed out that CHD is more likely to happen in winter.

Methods and Results : We analyzed the 10 year population-based data by using Logistic Regression and Poisson Regression Models to examine seasonal variations and the effect of atmospheric temperature on the incidence of CHD in Hiroshima City, Japan.

There were 3755 incident events, 63.33% days on which CHD events occurred and 1.03 events per day. Relative Risk (RR) for winter, spring and autumn in comparison with summer was 1.53, 1.25 and 1.24 respectively, and there were 30.0%, 19.4% and 19.2% more events than in summer. In contrast with September, there was a higher risk in January (RR=1.99, $p<0.001$), November (RR=1.65, $p=0.003$) and December (RR=1.58, $p=0.006$), whereas the risk in June (RR=1.06, $p>0.05$) and July (RR=1.00, $p>0.05$) was as low as September.

Atmospheric temperature had a statistically significant effect on CHD incidence. Odds ratios and risk ratios estimated by Logistic Regression Model and Poisson Regression Model were all higher when the daily mean atmospheric temperature was lower than 18℃, the highest risk occurring below 4℃. Lower risks were observed from 18 to 30℃ and the lowest risk was found at 28-30℃.

Conclusions : The incidence of CHD shows a more than 50% higher value in winter than in summer. There exists a higher risk on cold days, especially when the daily mean temperature is below 4℃.

Introduction

Seasonal variations were reported in coronary heart disease (CHD) in the 1930s[1, 2]. Since these initial observations, a higher rate of CHD in winter has been reported by numerous studies in countries both north and south of the equator[3-11]. Kunst et al. showed that coronary mortality was largely attributable to the direct effect of exposure to cold temperature, taking into account the effects of influenza, air pollution and season[12].

The relationship between CHD and atmospheric temperature reported by different studies were inconsistent. Some researchers reported that only low temperature had a deleterious effect on the heart and that rates of CHD events increased linearly with decreasing atmospheric temperature[13]. In contrast, some researchers found a U-shaped relationship between outdoor temperature and cardiovascular disease mortality, which suggested that atmospheric temperature had a dual impact on CHD[14]. Meanwhile, one study performed in countries with extremely cold temperatures demonstrated that atmospheric temperature was not significantly correlated with the incidence of myocardial infarction[15].

The influence of temperature on CHD may not be universal in different geographic areas. Although Hiroshima City has a favorable climate, the indoor temperature is difficult to maintain both in the winter and

・Seasonal variations and the effect of atmospheric temperature on the incidence of coronary heart disease in Hiroshima, Japan
・1）Graduate School of Health Sciences, Hiroshima University 2）Hiroshima City Medical Association
3）Department of Public Health and Health Policy, Graduate School of Biomedical Sciences, Hiroshima University
・＊Tel：082-257-5350, E-mail：wanghl@hiroshima-u.ac.jp
・広島大学保健学ジャーナル Vol. 4 (2)：82～89, 2005

summer due to the typical Japanese building structure which does not insulate from cold and hot temperatures. In addition, the proportion of elderly people (≧65-year-old), who are usually regarded as high risk group for CHD, is high (16.2%, in 2004). Therefore it is important to reveal what influence temperature has on CHD incidence in this area.

Furthermore, it was not clear whether seasonal variations in CHD mortality reflect variations in incidence or survival[16]. Results from mortality based studies may be biased by the increase in case fatality rates observed in winter. Hospital admission based studies related only to people admitted alive to hospital and do not cover all coronary events. Community based studies covering all cases are relatively few[15].

Our study used as data the population of Hiroshima City from 1993 to 2002. The purpose of the present study was to evaluate seasonal variations in the incidence of CHD qualitatively and quantitatively. We also aimed to clarify the impact of atmospheric temperature on the incidence of CHD and to ascertain dangerous and safe temperature ranges in order for primary and secondary prevention.

Data and Analyses

Study area

Hiroshima City (latitude, 34 °23.7' north; longitude, 132 °27.9' east.) enjoys an oceanic, temperate climate. It has an area of approximately 741.8 km^2, with a population of about 1,138,000. Meteorological factors in Hiroshima City from 1993 to 2002 are shown in Table 1.

Data

Climatological data were provided by the Local National Meteorological Institute. Meteorological variables included daily mean, minimum and maximum atmospheric temperature (℃), atmospheric pressure (hPa), relative humidity (%), wind speed (m/s), sunshine hours (h), rainfall (mm) and snowfall (mm).

Front line ambulance crew members working in The Hiroshima Ambulance Service Center collected coronary event data since January 1, 1992. Every coronary event had its apparent symptoms and a definite diagnosis made by hospitals.

Statistical Analyses

The incidence of CHD was evaluated by the probability of days with events (percentage of days on which CHD events occurred) and daily incident events (number of events per day). Descriptive of the data were presented by plotting the number of events, probability of days with events and daily incident events according to the month.

Statistical analyses were performed with SPSS 12.0 (SPSS Institute Inc. Chicago, IL). Logistic Regression Model and Poisson Regression Model were fitted to determine the association between CHD incidence and meteorological variables. We considered a p value less than 0.05 as statistically significant.

Firstly, as meteorological variables correlated strongly, backward stepwise selection method (conditional) was employed to select significant variables by using Logistic Regression Model (enter=0.10, remove=0.15). The dependent variable was a day with or without CHD events (we set 1 if day with events≧1, and 0 if day with events=0); independent variables were meteorological variables such as atmospheric temperature, pressure, relative humidity, wind speed, sunshine hours, rainfall, snowfall and some of their

Table 1. Meteorological factors in Hiroshima City from 1993 to 2002（Mean ± SD）

Events	Daily temperature (℃)			Humidity	Pressure	Wind speed	Sunshine	Rainfall	Snowfall
(Days)	Mean	Minimum	Maximum	(%)	(hPa)	(m/s)	(h)	(mm)	(mm)
0 (1340)	17.4±8.3	13.5±8.5	22.1±8.2	68.2±10.5	1008.4±6.7	3.8±1.0	6.6±3.7	4.1±12.1	0.2±2.5
1 (1323)	16.6±8.2	12.7±8.5	21.1±8.2	68.1±10.9	1009.0±6.6	3.8±1.0	6.3±3.6	4.4±13.4	0.5±5.2
2 (642)	15.5±8.3	11.7±8.6	20.1±8.3	68.4±10.8	1009.5±6.7	3.8±1.0	6.3±3.5	4.0±12.1	0.6±6.1
3 (259)	15.1±8.3	11.0±8.5	19.7±8.3	67.8±10.6	1009.5±6.6	3.8±1.0	6.2±3.6	4.3±14.9	0.3±1.6
4 (73)	13.6±8.5	9.8±8.5	18.2±8.6	66.9±9.1	1010.7±5.8	3.9±1.0	5.8±3.1	3.0±8.8	3.3±1.6
5 (11)	13.7±6.5	9.0±6.8	18.9±6.6	62.5±5.4	1011.2±4.5	4.1±0.9	6.1±4.1	0.8±1.8	0.0±0.0
6 (4)	12.0±3.6	6.0±3.6	18.3±4.0	54.0±8.3	1012.8±1.6	4.7±0.7	8.9±2.8	0.0±0.0	0.0±0.0
Average	16.5±8.3	12.6±8.5	21.1±8.3	68.1±10.7	1008.9±6.6	3.8±1.0	6.4±3.6	4.2±12.7	0.5±5.0

Range of daily mean, minimum and maximum temperature was（−0.9 32.7），（−4.2 28.9）and（1.7 38.7）respectively.

interactions. As a result, only atmospheric temperature entered the Logistic Regression Model.

Daily mean atmospheric temperature strongly correlated with daily minimum and maximum temperature (r =0.984 and r =0.983 respectively, all of p<0.001). We only selected daily mean atmospheric temperature in order to compare with other studies and defined it as category variables for 2℃ variations from 4℃.

Secondly, Logistic Regression Model was fitted to examine monthly and seasonal variations. Meanwhile, Logistic Regression Model was also used as a qualitative method to determine the association between probability of days with events and daily mean atmospheric temperature. The qualitative analysis reflected the situation whether there was CHD incidence or not in the temperature group we defined.

Finally, in order to determine the pattern of distribution, the percentage of daily incident events of 0, 1, 2, 3, 4, 5 and 6 (totally 3652 days) was calculated and compared with Poisson distribution (Fig.1). Fig.1 shows that daily incident events of CHD were perfectly consistent with Poisson distribution, thus we use Poisson Regression Model to determine the association between daily incident events and daily mean atmospheric temperature. Poisson Regression Model served as a quantitative method in order to evaluate how many incident events occurred per day.

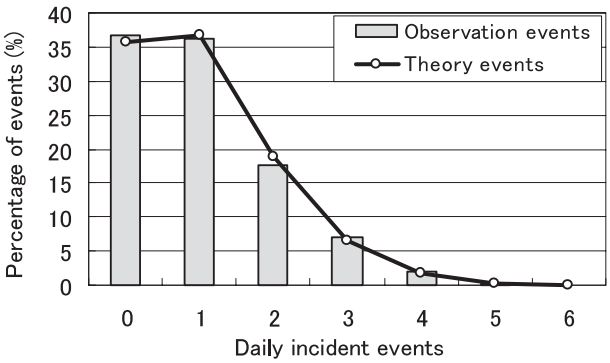

Fig.1. Comparison of daily incident events with Poisson distribution (Average daily incident events=1.03)

Results

The study period consisted of 3652 days during which there were 3755 CHD events. There were 2312 days on which CHD events occurred (63.33%) and on average 1.03 events per day.

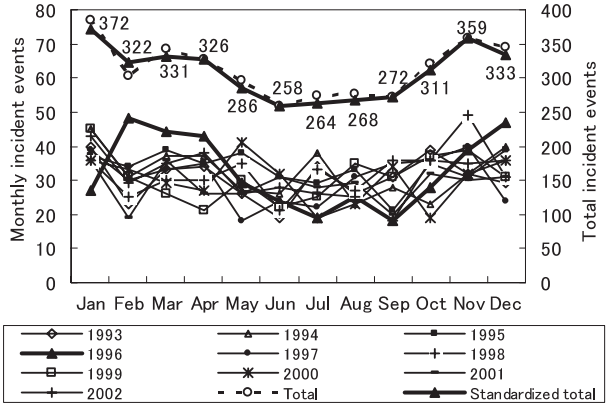

Fig.2. Incident events of CHD from 1993 to 2002 in Hiroshima City

Standardized total: monthly incident events were standardized by 30-day length

Numbers shown in the figure are standardized total events

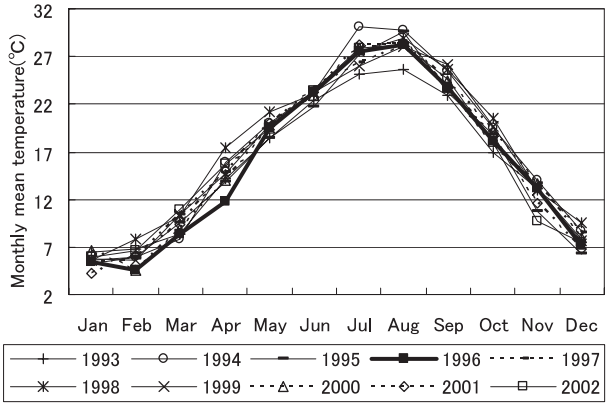

Fig.3. Monthly mean atmospheric temperature from 1993 to 2002

Seasonal Variations

Incident events of CHD and monthly mean atmospheric temperature from 1993 to 2002 in Hiroshima City are shown in Fig.2 and Fig.3. We did not find any reduction from 1993 through 2002, but U-like curves were maintained. In 1996, monthly incident events in February, March, April and December were higher than in the other years.

A plot of probability of days with events and daily incident events versus month also showed U-like curves (Fig.4). Probability of days with events and daily incident events were all higher in January, November and December and lower in June, July and September. Meanwhile, the two indexes were all higher in January, February, March, April, October, November and December, and lower in May, June, July, August, September compared with the average level of the 10 years.

Monthly variations estimated by Logistic

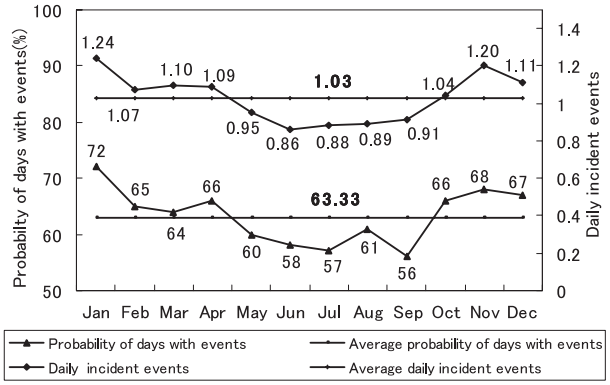

Fig.4. Probability of days with events and daily incident events versus month

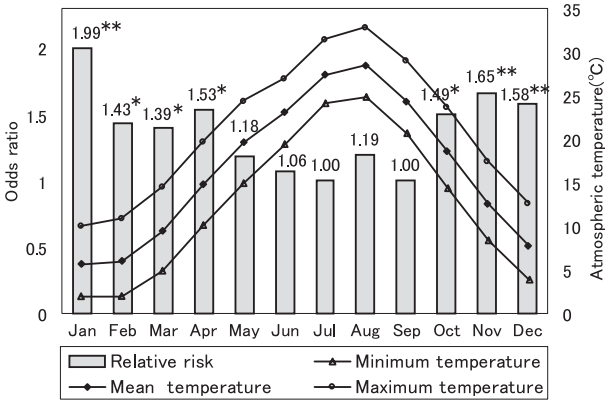

Fig.5. Relative risk for CHD incidence by months, compared to September

Relative Risk (Odds Ratio) was estimated by Logistic Regression Model (Indicator)

**:p<0.01 *:p<0.05

Regression Model are shown in Fig.5. There was a significant monthly change overall (Wald value=35.64, p<0.001). January was the month with the highest incidence risk (Relative Risk, RR=1.99; 95% confidence interval, 95%CI 1.45-2.78; p<0.001), with a 99% difference compared with September. November was the month with the second highest incidence risk (RR=1.65, 95%CI 1.18-2.30, p=0.003), with a 65% difference compared with September. The third highest incidence risk was in December (RR=1.58, 95%CI 1.14-2.10, p=0.006). There were 36.8%, 32.0% and 22.4% more events occurring respectively in January, November and December than in September. Incidence risks in June (RR=1.06, p>0.05) and July (RR=1.00, p>0.05) were both low and similar to September. The risk in August increased but showed no statistical difference compared with September (RR=1.19, p>0.05).

Seasonal variations estimated by Logistic Regression Model are shown in Fig.6. The overall seasonal variations had statistical significance (Wald

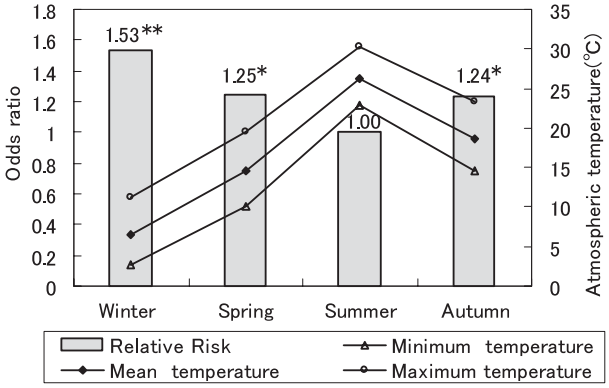

Fig.6. Relative risk for CHD incidence by seasons, compared to summer

Relative risk (Odds Ratio) was estimated by Logistic Regression Model (indicator)

Winter: Dec Jan Feb Spring: Mar Apr May

Summer: Jun Jul Aug Autumn: Sep Oct Nov

** : p<0.01 *: p<0.05

value=18.86, p<0.001). The incidence risk was highest in winter (RR=1.53, 95%CI 1.26-1.85, p<0.001) and lowest in summer with a 53% difference between the two seasons. The incidence risks in spring (RR=1.25, 95%CI 1.04-1.51 p=0.019) and autumn (RR=1.24, 95%CI 1.03-1.50 p=0.024) were close and both higher than summer, with 25% and 24% differences. In winter, spring, autumn and summer, standardized probability of CHD incidence was 27.7%, 25.5%, 25.5%, and 21.3%. Daily incident events were 1.14, 1.05, 1.05 and 0.88, respectively. There were 30.0%, 19.4% and 19.2% more events occurring in winter, spring and autumn respectively than in summer.

The Effect of Atmospheric Temperature

The association between probability of days with events and daily mean atmospheric temperature estimated by Logistic Regression Model is shown in Table 2. The temperature group of 28-30°C was set as reference. The overall effect of atmospheric temperature was statistically significant (Wald value=37.45, p=0.001). Higher incidence risks were observed when the daily mean atmospheric temperature was lower than 18°C, and the risks increased approximately above 45% compared with 28-30°C. Meanwhile, at this temperature range, the probability of days with events was higher than the average level (63.33%) during the 10-year period. The highest incidence risk of CHD occurred on days with a daily mean atmospheric temperature lower than 4°C (RR=2.14, 95%CI 1.39-3.29, p=0.001) and the probability of days with events was 72.6%. Lower incidence risks were observed from 18 to 30°C and the probability of days with events was lower than the average level. Although the

Table 2. Coefficients estimated by Logistic regression Model

	Odds ratio (95% CI)	p value	Probability of days with events (%)	Days (%)
Daily mean temperature (℃)				
	37.45 (wald)	0.001**	63.33	3652(100)
T<4	2.14 (1.39 3.29)	0.001**	72.55‡	153 (4.19)
T4-	1.52 (1.07 2.16)	0.019*	65.28‡	265 (7.26)
T6-	1.70 (1.23 2.36)	0.001**	67.77‡	363 (9.94)
T8-	1.64 (1.17 2.30)	0.004**	66.98‡	315 (8.63)
T10-	1.45 (1.01 2.07)	0.042*	64.17‡	240 (6.57)
T12-	1.75 (1.17 2.62)	0.006**	68.39‡	174 (4.76)
T14-	1.85 (1.26 2.70)	0.002**	69.52‡	210 (5.75)
T16-	1.62 (1.12 2.34)	0.010*	66.67‡	225 (6.16)
T18-	1.08 (0.77 1.52)	0.671	57.09	268 (7.34)
T20-	1.33 (0.95 1.87)	0.097	62.20	291 (7.97)
T22-	1.20 (0.86 1.69)	0.282	59.79	286 (7.83)
T24-	1.14 (0.80 1.62)	0.464	58.47	248 (6.79)
T26-	1.09 (0.77 1.54)	0.640	57.32	246 (6.74)
T28-	Reference 1.00	—	55.26	266 (7.28)
T30-	1.34 (0.83 2.15)	0.233	62.24‡	98 (2.68)
T32-	2.43 (0.25 23.65)	0.445	75.00‡	4 (0.11)

Dependent variable: Day
(1：Day with events≧1 0：Day with events =0)
Independent variable: Daily mean temperature (T)
95%CI: 95% confidence interval of odds ratio
**：p<0.01 *：p<0.05
‡：Probability of days with events was higher than 63.33%

Table 3. Coefficients estimated by Poisson Regression Model

	ß ± S.E	Risk ratio (95% CI)	p value	Daily incident events
Daily mean temperature (℃)				Average (1.03)
T<4	0.40±0.10	1.49 (1.23 1.80)	0.000**	1.27‡
T4-	0.24±0.09	1.28 (1.07 1.52)	0.006**	1.09‡
T6-	0.31±0.08	1.37 (1.16 1.61)	0.000**	1.17‡
T8-	0.27±0.09	1.31 (1.11 1.55)	0.001**	1.13‡
T10-	0.24±0.09	1.27 (1.07 1.52)	0.008**	1.09‡
T12-	0.25±0.10	1.28 (1.06 1.55)	0.011*	1.10‡
T14-	0.33±0.09	1.39 (1.16 1.66)	0.000**	1.19‡
T16-	0.28±0.09	1.32 (1.10 1.57)	0.003**	1.13‡
T18-	0.01±0.09	1.01 (0.85 1.22)	0.879	0.87
T20-	0.09±0.09	1.09 (0.23 1.30)	0.316	0.94
T22-	0.07±0.09	1.07 (0.90 1.28)	0.439	0.92
T24-	0.04±0.09	1.04 (0.87 1.26)	0.644	0.90
T26-	0.02±0.10	1.02 (0.85 1.23)	0.798	0.88
T28-	Reference	1.00	—	0.86
T30-	0.11±0.12	1.12 (0.88 1.43)	0.345	0.96
T32-	0.02±0.54	1.02 (0.35 2.93)	0.973	0.75

Dependent variable: Daily incident events
Independent variable: Daily mean temperature (T)
Risk ratio was the risk of daily incident events in different temperature groups compared with T28- (from 28 to 30℃).
**：p<0.01 *：p<0.05
‡：Daily incident events was higher than 1.03

incidence risk increased with atmospheric temperatures higher than 30℃, we failed to find a statistical significance due to the smaller sample size of hot days.

The association between daily incident events and daily mean atmospheric temperature estimated by Poisson Regression Model is presented in Table 3. We also set 28-30℃ as reference. Risk ratio was defined as the risk of daily incident events in different temperature groups compared with reference. Compared to 28-30℃, risk ratios were statistically higher when the daily mean atmospheric temperature was lower than 18℃, and daily incident events were all higher than the average level (1.03). The risk ratio was highest with a daily mean atmospheric temperature lower than 4℃ (Risk ratio=1.49, 95%CI 1.23-1.80, p<0.001). Risk ratios were all lower at the range of 18-30℃, and daily incident events were all lower than the average level. Risk ratio increased with atmospheric temperatures higher than 30℃ but did not show significant difference.

Daily mean, minimum and maximum temperature in the T<4, T18- and T28- groups are shown in Table 4.

Table 4. Daily temperature in T<4, T18- and T28- group (℃) (Mean±SD)

group	Mean temperature (Range)	Minimum temperature (Range)	Maximum temperature (Range)
T<4	2.7±1.1	−0.3±1.4	7.0±1.8
	(−0.9 3.9)	(−4.2 2.0)	(1.7 11.0)
T18-	19.0±0.6	14.7±1.8	23.7±1.8
	(18.0 19.9)	(11.1 18.9)	(18.8 28.2)
T28-	28.9±0.6	25.3±1.1	33.3±1.1
	(28.0 29.9)	(22.1 27.9)	(29.6 36.7)

Discussion

In this 10-year period population based study, we observed obvious seasonal variations in the incidence of CHD with a winter peak and summer trough. Atmospheric temperature had a stronger effect than other meteorological factors. Higher risks were found when daily mean atmospheric temperatures were below 18℃ and the highest risk occurred when temperatures were below 4℃; risks were lower with daily mean atmospheric temperatures at the range of 18-30℃ and the lowest risk was found at 28-30℃.

Cold temperatures cause a high CHD incidence risk. This conclusion was reinforced when we found that there were more CHD events in February, March, April and December in 1996. The reason was that the monthly mean atmospheric temperature was the lowest compared with corresponding months in the other years (Fig.3). In fact, we actually found that monthly incident events correlated negatively with monthly mean atmospheric temperatures ($r= -0.449$, $p<0.001$).

In contrast with previous studies based on hospital admission rates[3, 4] or mortality data[5-10], we found that there were also obvious seasonal variations in CHD incidence. U-like curves between the probability of days with events, daily incident events and month were observed; incidence risks of CHD in winter, spring and autumn were statistically higher than in summer; the highest incidence risk occurred in January with the coldest temperatures throughout the year. Our results showed that the influence of season or month on CHD incidence presented the same pattern as mortality or hospital admission rates.

Although the mechanisms of seasonal variations in CHD mortality or incidence were unclear, some risk factors have been proposed by many investigators. These risk factors included environmental factors such as temperature and ultraviolet radiation; lifestyle risk factors such as diet, obesity, exercise and smoking; physiological risk factors such as blood pressure, serum cholesterol level, coagulation factors and glucose tolerance; and respiratory infections[16].

Among the above risk factors, temperature changes could account for practically all of the seasonal variations observed in CHD. This point of view was supported by the evidence of changing CHD mortality by insulating from cold or hot atmospheric temperatures. Some investigators in the United States demonstrated that CHD mortality showed a decreasing time trend, the decline being attributed to improvements in indoor and vehicular heating and air-conditioning[5, 17]. Meanwhile, CHD mortality was independently associated with a low living room temperature, limited bedroom heating, inactivity and less use of protective clothing[18]. The mechanisms of temperature on the cardiovascular system have been reported by some studies which indicated that cold temperature was associated with both higher systolic and diastolic blood pressure[19-22]. Furthermore, low temperature results in an increase in fibrinogen, platelets, erythrocytes, plasma viscosity and a reduction in plasma volume. This effect was related to thrombosis, which could also account for a large part of the winter excess in incidence and mortality from CHD[23, 24].

We estimated the CHD incidence by two indexes in our study. The one was the probability of days with events, which as the qualitative index reflected the CHD incident condition; the other was daily incident events, which as the quantitative index reflected the number of events per day. By using the two indexes and fitting our data with Logistic Regression Model and Poisson Regression Model, we could exactly estimate the association between atmospheric temperature and CHD incidence. In our study, the two indexes showed exactly the same risk tendencies even when different statistical models were used. This confirmed that our results were not causal.

Incidence risk had a increasing tendency when mean temperature was higher than 30℃, but we did not find any higher significant risk. It may be that the climate in Hiroshima City was not hot enough to reveal the hot temperature effect. Some studies have demonstrated that both cold and hot temperatures increase CHD mortality. Pan et al. in Taiwan, with a mean atmospheric temperature range from 9 to 32℃, reported a U-shaped relationship. The lowest risk of CHD mortality was found at 26-29℃; the risk increased by 2.8% per 1℃ reduction below 26-29℃; the risk of CHD at 32℃ was 22% higher than at 26-29℃[14].

An association between CHD and atmospheric temperature has been reported by several investigators, whereas the results showed a lack of consistency owing to the different geographical areas and type of data they were based on. One population-based study performed in France, with a mean atmospheric temperature range from −14 to 28℃, found a decreasing linear relationship, a 10℃ decrease in mean temperature being associated with an

11% increase in incident and coronary heart death rates[13]. Similar to this result, Panagiotakos et al. in Athens, located at latitude of 23 °47' north, reported that a 1°C decrease in mean temperature yielded a 5% increase in hospital admissions[25]. Brage et al. analyzed the effect of weather on respiratory and cardiovascular death in 12 U.S. Cities. They found that both high and low temperatures were associated with the increased number of cardiovascular deaths in cold cities, whereas neither hot nor cold temperatures had much effect in hot cities[26]. One study performed at a high latitude with an average temperature range from −19.7 to 21.2°C failed to observe any association between cold temperatures and CHD deaths[15]. These discrepancies may be due to the peculiar physiological responses of different people acclimating to different atmospheric temperatures. We also believe that analysis of the impact of climate should take cold protective measures into account, as regions with ambient cold weather usually have stricter building regulations and better indoor heating systems.

We found the lowest CHD incidence risk was at daily mean temperatures of 28-30°C. This range was similar to the result of Pan et al., which indicated that the lowest risk of CHD mortality was at 26-29°C[14]. However, our result was different from that of Huynen et al., which demonstrated that the optimum temperature value for cardiovascular mortality was 16.5°C[27]. We were not clear whether the influence of atmospheric temperature on CHD incidence and mortality was the same or different. Further studies based on population are needed to confirm our results.

Excess CHD incident events can be preventable through controlling indoor temperature. Based on our results, we suggest that indoor temperature should be maintained at least 18°C. Our suggestion is supported by Kunst et al., who showed that all-cause mortality increased rapidly when temperatures were below 16.5°C[12]. Furthermore, a number of simple precautions such as wearing protective clothing, hats and gloves, and outdoor protection of the face should be taken in winter.

Our study suggested that cold environment temperature may play a major role in the triggering of CHD. The results also indicated that CHD incident events can be predicted by Logistic or Poisson Regression Models according to atmospheric temperature. A prediction system for CHD has a practical public health significance: it can warn the public to pay more attention or to take preventive measures for patients on cold days, especially when the daily mean temperature is lower than 4°C.

Study Limitation

We only take atmospheric temperature into account to explain seasonal variations of CHD. Other risk factors such as lifestyle risk factors, respiratory infections and air pollution were neglected owing to lacking of data.

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