



UNIVERSITÀ
DEGLI STUDI
FIRENZE

FLORE

Repository istituzionale dell'Università degli Studi di Firenze

Relationships between weather and myocardial infarction: a biometeorological approach.

Questa è la Versione finale referata (Post print/Accepted manuscript) della seguente pubblicazione:

Original Citation:

Relationships between weather and myocardial infarction: a biometeorological approach / Morabito M; Modesti PA; Cecchi L; Crisci A; Orlandini S; Maracchi G; Gensini GF.. - In: INTERNATIONAL JOURNAL OF CARDIOLOGY. - ISSN 0167-5273. - STAMPA. - 7:(2005), pp. 288-293. [10.1016/j.ijcard.2004.12.047]

Availability:

The webpage <https://hdl.handle.net/2158/780914> of the repository was last updated on

Published version:

DOI: 10.1016/j.ijcard.2004.12.047

Terms of use:

Open Access

La pubblicazione è resa disponibile sotto le norme e i termini della licenza di deposito, secondo quanto stabilito dalla Policy per l'accesso aperto dell'Università degli Studi di Firenze (<https://www.sba.unifi.it/upload/policy-oa-2016-1.pdf>)

Publisher copyright claim:

La data sopra indicata si riferisce all'ultimo aggiornamento della scheda del Repository FloRe - The above-mentioned date refers to the last update of the record in the Institutional Repository FloRe

(Article begins on next page)

Relationships between weather and myocardial infarction: A biometeorological approach

Marco Morabito^{a,*}, Pietro Amedeo Modesti^a, Lorenzo Cecchi^a, Alfonso Crisci^b,
Simone Orlandini^a, Giampiero Maracchi^b, Gian Franco Gensini^a

^aInterdepartmental Centre of Bioclimatology- University of Florence, Piazzale delle Cascine 18, 50144, Florence, Italy

^bInstitute of Biometeorology- National Research Council, Via Caproni 8, 50145, Florence, Italy

Received 27 September 2004; accepted 31 December 2004

Available online 8 March 2005

Abstract

Objectives: To calculate threshold values of weather discomfort which increase the risk of hospital admissions for myocardial infarction in winter and summer.

Background: Notwithstanding heat waves were reported to acutely increase hospital admissions for cardiovascular diseases, large surveys failed to reveal any increase of event rates with increasing air temperature. However, the assessment of air temperature does not allow evaluation of the actual discomfort perception caused by the combination of different meteorological parameters.

Methods: Hospital admissions for myocardial infarction for the period 1998–2002 in Florence, Italy, were considered. The percentages of variation of daily event rates according to daily mean air temperature variations were preliminarily derived by using a regression analysis. An alternative biometeorological approach, considering the Apparent Temperature Index (ATI) in summer, and the New U.S./Canada Wind Chill Temperature Index (NWCTI) in winter, which combine air temperature, relative humidity and wind velocity, was then used.

Results: The traditional approach showed that daily event rates significantly increased with daily mean air temperature decrease (10 °C decrease were associated with 19% increase in daily event rates for people older than 65 years), but failed to show any negative effect caused by hot climatic conditions. Conversely the biometeorological approach allowed to show that at least 9 h per day of severe discomfort caused by hot conditions significantly increased the rate of admission ($P < 0.01$).

Conclusions: This approach might be useful for the development of an operative weather watch/warning system for population and for hospital professional care.

© 2005 Elsevier Ireland Ltd. All rights reserved.

Keywords: Biometeorological indices; Myocardial infarction; Hospital admissions; Weather

1. Introduction

Cardiovascular diseases, in particular myocardial infarction (MI), have been consistently reported to be more frequent during winter [1–4]. Studies performed to evaluate the effects of weather conditions investigated the influence of a single meteorological parameter [5–8]

and revealed that the increase in hospital admission rates for MI in winter was related with low temperature [9,10]. Indeed Marchant et al. [11] found that MI was more common on colder days, independently of the season. More recently, a large 10-year longitudinal survey [12] and a study performed in the Athens area [13], confirmed the effects of low temperature showing a linear increase in event rates with decreasing mean daily air temperature [12].

All these studies observed no effects on hospitalizations caused by high air temperatures. Conversely,

* Corresponding author. Tel.: +39 055 3033701; fax: +39 055 308910.

E-mail address: m.morabito@ibimet.cnr.it (M. Morabito).

studies performed in tropical regions reported that also hot climate may increase the incidence of MI [14–16]. The occurrence of heat waves was repeatedly reported to be associated with an increase in cardiovascular mortality also in temperate regions [17–19]. The heat wave of summer 2003 revealed that the effects of hot conditions might be particularly relevant in Europe where, differently from USA, air conditioning systems have a low diffusion including public buildings and retirement homes [18]. During summer 2003, Italy was the second (after France) most affected European country [20]. However the effect of hot weather conditions may not be well appreciated by considering only the mean daily air temperature. Indeed the combination of air temperature, relative humidity and wind velocity, provides apparent temperature values which allow better appreciation of the increase in human discomfort perception caused by the compromised efficiency of sweating. Therefore, to obtain useful information for the development of an adequate weather/health warning system, we studied the influence of biometeorological indices on hospitalizations for MI in an Italian city characterized by a mild climate and generally without temperature extremes, Florence ($\lambda=11^{\circ}11' E$; $\Phi=43^{\circ}47' N$). Hospital discharge data for MI were considered and threshold values for the hours of severe discomfort per day (values of apparent temperature higher or lower than 90th or 10th percentile respectively for hot and cold conditions) associated with an increase of admission rate for MI were calculated.

2. Materials and methods

2.1. Meteorological data

Hourly meteorological data, for the period 1998–2002, of air temperature ($^{\circ}C$), relative humidity (%) and wind velocity ($m s^{-1}$), were obtained from the urban weather station located in the centre of Florence and managed by the Regional Office for Environmental Protection in Tuscany. Mean daily temperatures were calculated over the whole years.

Apparent temperature values for winter and summer were calculated on an hourly basis, by applying two biometeorological indices used by the main weather forecast services of United States (National Weather Service and National Oceanic and Atmospheric Administration) and Canada (Meteorological Service of Canada): 1) The Apparent Temperature Index (ATI) [21], which combines air temperature, relative humidity and wind velocity, allowing evaluation of human weather discomfort due to hot conditions; 2) The New U.S./Canada Wind Chill Temperature Index (NWCTI) [22], employed to assess human weather discomfort due to the combination of low temperatures and different intensities of wind. These indices ignore the effects of radiation and are

suitable for describing potential discomfort conditions in shade.

The 90th and the 10th percentile for ATI and NWCTI respectively for the summer and winter season were considered as threshold values for severe discomfort. Astronomical seasons were considered.

2.2. Hospital discharge data

Computerized inpatient hospital discharge data for MI, over a 5-year period, 1998–2002, was provided by the Administration of Careggi Hospital (source Azienda Ospedaliera di Careggi), the biggest and the main Regional hospital. Only data of people residents in the Florentine area were considered. Discharge diagnoses were coded by professional nosologists according to International Classification of Diseases, Ninth Revision Clinical Modification (ICD-9-CM: 410–410.92). For each patient admitted, up to five discharge diagnoses can be recorded. Only one of these is listed as the primary health condition for which the patient was hospitalized, while the remaining are secondary discharge diagnoses accounting for existing or comorbid conditions.

2.3. Statistical analyses

Statistical analyses were performed using SPSS for Windows version 9.0.

A first preliminary and exploratory statistical analysis was carried out by a traditional approach, evaluating the relationships between daily event rates and mean daily air temperatures by using a regression analysis. This examination was performed for the overall group of 2683 patients and for two different age subjects: younger than 65 and older than 65 years of age.

Chi-square test for goodness of fit for the distribution of hospital admissions for MI was performed to analyze differences between age groups, sex and seasonal fluctuations.

A second statistical analysis was concentrated in winter and in summer, the two seasons with most of the extreme weather conditions, causing discomfort for people. This analysis was carried out for the overall group of 1222 patients, as well as for sex and age groups.

To establish if the number of hours with severe discomfort conditions per day affected admissions for myocardial infarction, statistical analysis of linear regression was performed. All the “potential Discomfort Days” (pDDs) with at least 1 h of severe discomfort were evaluated in summer and winter for the 5-year period. The pDDs were divided into six classes according to the different number of hours with biometeorological discomfort: class 1 with 1–2 h; class 2 with 3–4 h; class 3 with 5–6 h; class 4 with 7–8 h; class 5 with 9–10 h; class 6 with >10 h. For the pDDs classes so obtained, patients were counted and divided by sex and age.

The admission rate occurring in a specific class of pDDs was determined by the following expression: Admission rate=Number of admissions/Number of pDDs.

In this way different admission rates for specific classes of pDDs were obtained.

The linear regression of admission rates versus pDDs was carried out on these values, assessing the Pearson's correlation coefficient (*r*). The statistical significance of *r* was tested using the Student *t*-test.

When a statistically significant linear regression was observed, "Discomfort Days" (DDs) were identified as those days, with threshold number of hours of severe discomfort, which increase the admission rate over the daily average rate of hospital admissions for the season. The rate of increase in event rates per hour of severe discomfort was then calculated.

Correlation between severe discomfort conditions and hospitalization for MI were investigated on that same day (lag=0) and up to three following days to detect the possible time-lag phenomenon (lag=1–3).

3. Results

3.1. Preliminary and exploratory statistical analysis

During the 5 years of the survey 2683 events were recorded, 804 (30%) occurring in patients younger than 65 years of age and 1879 (70%) in patients older than 65 years of age. Daily event rates were significantly related with daily mean air temperature in patients ≥ 65 ($P < 0.001$). For a 10 °C decrease in air temperature, the increase in event rates was 19% for patients older than 65 years of age and only 4% for the youngest age group (Fig. 1).

3.2. Seasonal distribution of hospital admissions by sex and age

Maximum peaks of hospitalization for MI were observed in autumn and winter, while the minimum value was

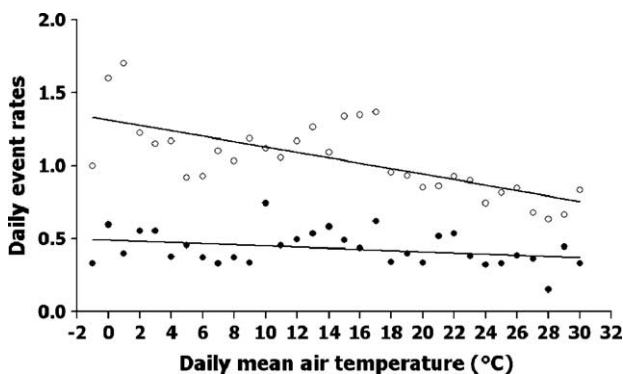


Fig. 1. Daily event rates according to daily mean air temperature by age groups. Legend: ○ indicates patients ≥ 65 years of age; ● indicates patients younger than 65 years of age; continuous line=linear regression.

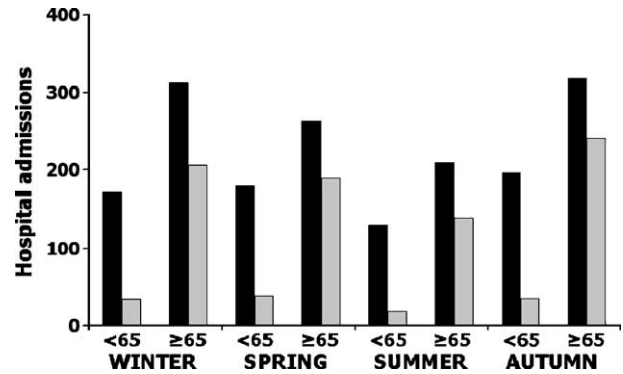


Fig. 2. Age groups, sex and seasonal fluctuation for myocardial infarction. Legend: black bar=males; grey bar=females.

reached in summer (Fig. 2). The statistical analysis of the total sample of patients showed a highly significant seasonal fluctuation ($\chi^2 = 69.9$, $P < 0.001$).

Hospital admissions for MI showed a higher prevalence in men than in women, in both age groups and in all seasons (Fig. 2). The ratio males/females, evaluated on the total sample was 2.1/1.0 and this variation was statistically significant ($\chi^2 = 286.7$, $P < 0.001$). Ratios were higher for patients < 65 than for ≥ 65 , in all seasons. The highest ratio was observed for patients < 65 during summer, with almost seven males for one female.

On the other hand, hospital admissions of people ≥ 65 were always higher than for people < 65 , in both males and females. A statistically significant fluctuation of the total sample of patients between different age groups was also found ($\chi^2 = 430.7$, $P < 0.001$).

3.3. Relationships between pDDs caused by hot conditions and hospital admissions during summer

A significant relationship between potential severe discomfort caused by hot conditions and hospital admissions on that same day (lag=0) was found for males < 65 ($r = 0.90$, $P < 0.01$), whereas no effect was observed in subjects ≥ 65 years. In particular the rate of hospital admission of males increased by 3% every 2 h per day increase of severe discomfort (Fig. 3) and the threshold level was reached on days with at least 9 h of severe discomfort conditions (DDs). When the whole group of subjects was considered (without difference of age and sex) a significant increase in admission rate was also showed three days after severe discomfort conditions (lag=3) ($r = 0.81$, $P < 0.05$). In this case the rate of hospital admission significantly increased by 10% every 2 h per day increase of severe discomfort conditions (Fig. 4).

3.4. Relationships between pDDs caused by cold conditions and hospital admissions during winter

Significant relationships between severe discomfort caused by cold conditions and hospitalization on that

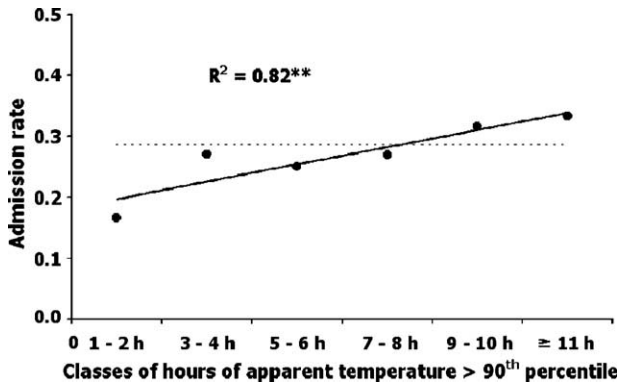


Fig. 3. Admission rates for myocardial infarction of males <65 on the same potential Discomfort Days in summer. Legend: dotted line=daily average rate of hospital admissions; continuous line=linear regression of pDD; ** $P < 0.01$ significant.

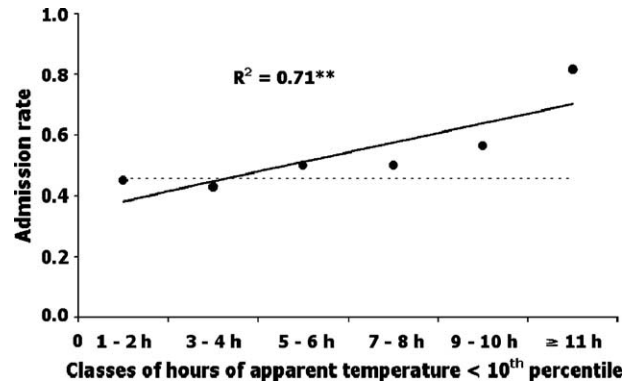


Fig. 5. Admission rates for myocardial infarction of females ≥ 65 on the same potential Discomfort Days in winter. Legend: dotted line=daily average rate of hospital admissions; continuous line=linear regression of pDD; ** $P < 0.01$ significant.

same day (lag=0) were found considering the total sample (without difference of age and sex) ($r=0.74$, $P < 0.05$) and patients ≥ 65 (without difference of sex) ($r=0.84$, $P < 0.01$). Regarding the sex of patients, males did not show any significant associations, on the other hand females showed the highest correlation coefficients in both the total sample of females (without difference of age) ($r=0.85$, $P < 0.01$) and females ≥ 65 ($r=0.84$, $P < 0.01$). During DDs with more than 4 h of severe discomfort conditions the admission rate significantly increased by 6% every 2 h per day increase of severe discomfort (Fig. 5). Statistically significant relationships were also found correlating hospitalizations occurred two days after a day with severe discomfort conditions (lag=2). These relationships concerned the total sample of patients (without differences of age and sex) ($r=0.84$, $P < 0.01$) and above all males ≥ 65 ($r=0.97$, $P < 0.001$). The maximum increase in the admission rate of males was observed two days after a day with at least 11 h of

discomfort, while, for females, days with at least 5 h were needed (figure not shown).

4. Discussion

The main findings of this study are:

1. The effect of hot weather conditions is well appreciate by considering “Discomfort Days” with at least 9 h of apparent temperature values over 90th percentile. On these days discomfort conditions should also persist during the night-time hours.
2. The effect of hot weather conditions is particularly marked considering hospitalization for MI 3 days after discomfort conditions (lag=3). This time-lag phenomenon causes more than three-fold increase in the rate of admission, in fact the rate of hospitalization significantly increased by 10% every 2 h per day increase of severe discomfort conditions against the increase of 3% observed considering the rate of hospitalization on the same day.
3. Hot weather conditions increase the rate of admission especially in young people, while cold weather conditions increase above the average rate of hospitalization of elderly.

In the present study, the analysis based on “Discomfort Days” allows to evaluate the relationship between severe discomfort, caused by both cold and hot conditions, and hospital admissions for MI better and in detail than the traditional approach based on the mean daily air temperature.

Many studies, in particular those based on mortality events, indicate that low temperatures are associated with an increase of cardiovascular events [1,4,12,23,24]. Cold conditions have different effects mediated by the activation of both the sympathetic nervous activity and the coagulation system. Cold induced vasoconstriction causes a significant

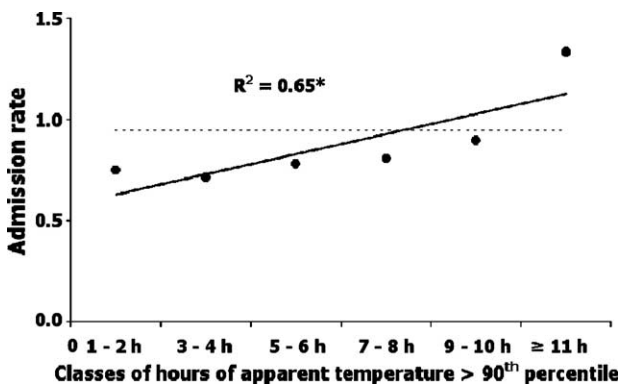


Fig. 4. Admission rates for myocardial infarction of the total sample 3 days after potential Discomfort Days in summer. Legend: dotted line=daily average rate of hospital admissions; continuous line=linear regression of pDD; * $P < 0.05$ significant.

increase in arterial pressure and heart workload [6] which are balanced by coronary vasodilatation in healthy subjects, but may result in myocardial ischemia in patients with coronary disease [25]. On the other hand the increase of fibrinogenemia during the cold months could contribute to increase the occurrence of cardiovascular diseases in winter [8,26,27].

Large epidemiological studies revealed that the effects of cold weather conditions are particularly relevant in subjects aged 55–64 when compared to the youngest groups [12]. In our study the mean daily air temperature was related to a progressive increase in hospital admissions for MI also in the elderly. In this age group the increase in the event rate for a 10 °C decrease in air temperature (19%) was similar to that observed by Danet et al. [12] in subjects aged 55–65 years (18%). In recent study carried out in another Mediterranean country (Greece), authors showed a negative correlation between hospital admissions and mean daily temperature [13]. In this case 1 °C decrease in mean air temperature was associated with a 5% increase in hospital admissions ($P < 0.05$).

On the other hand, notwithstanding heat waves are known to increase cardiovascular diseases mortality, no effects of hot conditions were observed on hospitalization for myocardial infarction. The difficulty in the evaluation of the impact of heat is particularly manifest in regions with mild climate, without temperature extremes [28,29]. This might be due to some limitations of considering only the effects of mean daily temperature. First, the effects of weather conditions on the perception of discomfort are related also to other parameters, such as relative humidity and wind velocity. Changes of relative humidity and wind velocity values can influence discomfort conditions during summer because directly affect sweat evaporation which represents the most effective physiological cooling system. Second, the use of mean daily temperature, which averages values measured during diurnal and nocturnal hours, cannot allow to consider the role of a sharp sustained increase in temperature during day time. The occurrence of MI might indeed be caused by short lasting exposition to extreme weather conditions.

The application of a biometeorological index, combining several meteorological variables simultaneously, enhances the evaluation and the comprehension of the relationships between severe discomfort conditions and hospital admissions for myocardial infarction, even in regions with mild climate, where discomfort conditions may occur also with no very high air temperatures, but with high values of relative humidity and without wind. In a recent study, which took place in Argentina, the authors found that the application of biometeorological indices well represent the prevailing meteorological conditions [16].

Moreover the approach based on “Discomfort Days”, quantifying the daily number of hours with severe discomfort caused by cold and hot conditions, has greatly contributed in the evaluation of the weather impact on hospital admissions for MI. In this way it was possible to

evaluate the threshold number of hours per day with severe discomfort conditions over which the admission rate significantly increases in comparison to the daily average rate in the season.

During summer, when only admissions of younger males (age group <65) showed a statistically significant relationship on DDs with at least 9 h of severe discomfort. A possible explanation is that younger people may be more exposed to severe hot conditions, because of working outdoors and other physical activities. Furthermore, in this season, about 30% of resident inhabitants are on holiday, and the elderly people, if not alone and unhealthy, are often away from the city.

Regarding the increase of admission rate several days after a DD, this is also confirmed by other authors [16,30].

During winter, especially admissions of elderly people showed statistically significant increases in the admission rate when DDs occurred. These increases have been found on the DDs themselves or 2 days after. In this latter case a different impact on patients ≥ 65 of females and males was observed. Males seem to be more resistant to severe discomfort caused by cold conditions than females. In fact it was seen that for females, to increase the admission rate, a lesser number of hours of discomfort conditions were needed (DDs with at least 5 h) than for males (DDs with at least 11 h).

Nevertheless these results have shown that also hot weather conditions may be dangerous for people, increasing hospitalization for MI, but it is necessary that these discomfort conditions should persist during night-time hours, when generally the body needs physiological rest. The knowledge of the daily number of hours with discomfort over which significantly increase the rate of hospitalization for MI (days with at least 9 h of discomfort) will permit to inform and eventually to alert people at high risk when weather discomfort conditions are forecast. In this way it will be also possible to improve hospital assistance.

Acknowledgements

The authors wish to thank Dr F. Giovannini of ARPAT-Firenze (Agenzia Regionale per la Protezione Ambientale della Toscana) for providing meteorological data; Dr G. Pasquini and Mr S. Sinatti of A.O.C.-Firenze (Azienda Ospedaliera di Careggi) for providing hospital admission data. This study was supported by Tuscany Region “Servizio Sanitario Regionale” grant: MeteoSalute Project.

References

- [1] Mannino JA, Washburn RA. Environmental temperature and mortality from acute myocardial infarction. *Int J Biometeorol* 1989;33:32–5.
- [2] Frost DB, Aulicciems A, De Freitas C. Myocardial infarct death and temperature in Auckland, New Zealand. *Int J Biometeorol* 1992;36:14–7.

- [3] Thompson DR, Pohl JEF, Tse YYS, Hiorns RW. Meteorological factors and the time of onset of chest pain in acute myocardial infarction. *Int J Biometeorol* 1996;39:116–20.
- [4] Stewart S, McIntyre K, Capewell S, McMurray JJV. Heart failure in a cold climate. *J Am Coll Cardiol* 2002;39:760–6.
- [5] Hall RJC, Bullock RE, Albers C. The effect of cold on patients with angina pectoris—a review. *Postgrad Med J* 1983;59:59–61 [suppl].
- [6] Keatinge WR, Coleshaw SRK, Cotter F, Mattock M, Murphy M, Chelliah R. Increases in platelet and red cell counts, blood viscosity, and arterial pressure during mild surface cooling: factors in mortality from coronary and cerebral thrombosis in winter. *Br Med J* 1984;289:1405–8.
- [7] Elwood PC, Beswick A, O'Brien JR, Renaud S, Fifield R, Limb ES, et al. Temperature and risk factors for ischaemic heart disease in the Caerphilly prospective study. *Br Heart J* 1993;70:520–3.
- [8] Neild PJ, Syndercombe-Court D, Keatinge WR, Donaldson GC, Mattock M, Caunce M. Cold-induced increases in erythrocyte count, plasma cholesterol and plasma fibrinogen of elderly people without a comparable rise in protein c or factor x. *Clin Sci* 1994;86:43–8.
- [9] Thakur CP, Anand MP, Shahi MP. Cold weather and myocardial infarction. *Int J Cardiol* 1987;16:19–27.
- [10] Lloyd EL. The role of cold in ischaemic heart disease: a review. *Public Health* 1991;105:205–15.
- [11] Marchant B, Ranjadayalan K, Stevenson R, Wilkinson P, Timmis AD. Circadian and seasonal factors in the pathogenesis of acute myocardial infarction: the influence of environmental temperature. *Br Heart J* 1993;69:385–7.
- [12] Danet S, Richard F, Montaye M, Beauchant S, Lemaire B, Graux C, 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.
- [13] Panagiotakos DB, Chrysoshoou C, Pitsavos C, Nastos P, Anadiotis A, Tentolouris C, et al. Climatological variation in daily hospital admissions for acute coronary syndromes. *Int J Cardiol* 2004;94:229–33.
- [14] Al-Yusuf AR, Kolar J, Bhatnagar SK, Hudak A, Smid J. Seasonal variation in unstable angina and acute myocardial infarction: effect of hot dry climate on the occurrence of complications following acute myocardial infarction. *J Trop Med Hyg* 1986;89:157–61.
- [15] Lecha E. Biometeorological classification of daily weather types for the humid tropics. *Int J Biometeorol* 1998;42:77–83.
- [16] Rusticucci M, Bettolli ML, Harris de los Angeles M. Association between weather conditions and the number of patients at the emergency room in an Argentine hospital. *Int J Biometeorol* 2002;46:42–51.
- [17] Semenza JC, Rubin CH, Falter KH, Selanikio JD, Flanders WD, Howe HL, et al. Heat-related deaths during the July 1995 heat wave in Chicago. *N Engl J Med* 1996;335:84–90.
- [18] Grynszpan D. Lessons from the French heatwave. *Lancet* 2003;362:1169–70.
- [19] Smoyer-Tomic KE, Kuhn R, Hudson A. Heat wave hazard: an overview of heat wave impacts in Canada. *Natural Hazard* 2003;28:463–85.
- [20] BBC News. Italy killed “4,000”. Sept 11, 2003: <http://news.bbc.co.uk/1/hi/world/europe/3099878.stm> [accessed May, 2004].
- [21] Steadman RG. A universal scale of apparent temperature. *J Appl Meteor* 1984;23:1674–87.
- [22] OFCM. Report on wind chill temperature and extreme heat indices: evaluation and improvement projects. FCM-R19-2003 Washington, DC Jan 2003: <http://www.ofcm.gov/jagti/r19-ti-plan/r19-ti-plan.htm> [accessed May, 2004].
- [23] Wilmsmurst P. Temperature and cardiovascular mortality. Excess deaths from heart disease and stroke in northern Europe are due in part to the cold. *Br Med J* 1994;309:1029–30.
- [24] Donaldson GC, Ermakov SP, Komarov YM, McDonald CP, Keatinge WR. Cold related mortalities and protection against cold in Yakutsk, eastern Siberia: observation and interview study. *Br Med J* 1998;317:978–82.
- [25] Dubois-Rande JL, Dupouy P, Aptecar E, Bhatia A, Teiger E, Hittinger L, et al. Comparison of the effects of exercise and cold pressor test on the vasomotor response of normal and atherosclerotic coronary arteries and their relation to the flow-mediated mechanism. *Am J Cardiol* 1995;76:467–73.
- [26] Stout RW, Crawford V. Seasonal variations in fibrinogen concentrations among elderly people. *Lancet* 1991;338:9–13.
- [27] Woodhouse PR, Khaw KT, Plummer M, Foley A, Meade TW. Seasonal variations of plasma fibrinogen and factor VII activity in the elderly: winter infections and deaths from cardiovascular disease. *Lancet* 1994;343:435–9.
- [28] Gnechchi Ruscone T, Crosignani P, Micheletti T, Sala L, Santomauro D. Meteorological influences on myocardial infarction in the metropolitan area of Milan. *Int J Cardiol* 1985;9:75–80.
- [29] Ku CS, Yang CY, Lee WJ, Chiang HT, Liu CP, Lin SL. Absence of a seasonal variation in myocardial infarction onset in a region without temperatures extremes. *Cardiology* 1998;89:277–82.
- [30] Miric D, Rumboldt Z. The impact of meteorological factors on the onset of myocardial infarction in the coastal region of middle Dalmatia. *G Ital Cardiol* 1993;23:655–60.