

## Climatological variations in daily hospital admissions for acute coronary syndromes

Demosthenes B. Panagiotakos<sup>a,\*</sup>, Christina Chrysohoou<sup>a</sup>, Christos Pitsavos<sup>a</sup>, Panagiotis Nastos<sup>b</sup>, Aggelos Anadiotis<sup>a</sup>, Constantinos Tentolouris<sup>a</sup>, Christodoulos Stefanadis<sup>a</sup>, Pavlos Toutouzas<sup>a</sup>, Athanasios Paliatsos<sup>c</sup>

<sup>a</sup>Department of Cardiology, School of Medicine, University of Athens, 48–50 Chiou st, Glyfada, 165-61 Athens, Greece

<sup>b</sup>Department of Geology, School of Science, University of Athens, Athens, Greece

<sup>c</sup>Department of Mathematics, Technological Educational Institute of Piraeus, Piraeus, Greece

Received 13 December 2002; accepted 2 April 2003

### Abstract

**Objective:** We examined the association between climatologic parameters and daily admissions for non-fatal acute coronary syndromes (ACS) to emergency units of hospitals in the greater Athens area, from January 2001 to August 2002. **Methods:** Daily mean, maximum and minimum temperatures, relative humidity, wind speed, barometric pressure and a thermo-hydrological index (T.H.I.) were measured at the meteorological station of the Laboratory of Climatology of the Geology Department of the University of Athens. In addition, the daily number of admissions for acute myocardial infarction or unstable angina in the five major general hospitals in the greater Athens area was recorded. Generalized additive models (GAM) were applied to regress-time-series of daily numbers of outpatients with acute cardiac events against climatological variations, after controlling for possible confounders and adjustment for over dispersion and serial correlation. **Results:** Five thousand four hundred fifty-eight Athenians with non-fatal acute cardiac events were admitted to the selected hospitals during the period of the study, 4093 (75%) males and 1365 (25%) females. There was a negative correlation between hospital admissions and mean daily temperature (MDT) with a 1 °C decrease in mean air temperature yielding a 5% increase in hospital admissions ( $P < 0.05$ ). This association was stronger in females and the elderly ( $P < 0.01$ ). Relative humidity was positively correlated with hospital admissions ( $P < 0.05$ ). **Conclusion:** Despite the relatively short study period (<2 years), these findings suggest a significant association between cold weather and increased coronary heart disease incidence, especially in the elderly and females.

© 2003 Elsevier Ireland Ltd. All rights reserved.

**Keywords:** Climatologic parameters; Daily admissions; Acute coronary syndromes

### 1. Introduction

Hippocrates (430 BC), in his treatise “*Of Airs, Waters and Places*”, pointed out that environmental conditions play a role in the pathogenesis of disease. In recent years, several studies indicated that variations in ambient temperature correlated with mortality and morbidity rates [1–9]. In general, increased death rates occur principally in the elderly [1,2], with the lowest death rates occurring on days of moderate temperature and highest rates at either end of the temperature range [10]. However, the strength of the association as well as the potential mechanisms to explain the

association between climatological variations and human health is still under investigation, with both physiological and psychological mechanisms being suggested.

We examined the relationship between climatological indices (average, maximum and minimum daily temperature, relative humidity, wind speed, and barometric pressure) and admissions due to non-fatal acute coronary syndromes (ACS) in cardiology emergency units in the greater Athens area.

### 2. Methods

#### 2.1. Study population

Between 1 January 2001 and 31 August 2002 we obtained the daily counts of admissions for non-fatal ACS

\* Corresponding author. Demosthenes Panagiotakos, 46 Paleon Polemiston st, 166 74 Glyfada Greece. Tel.: +30-109-603-116; fax: +30-109-600-719.

E-mail address: d.b.panagiotakos@usa.net (D.B. Panagiotakos).

in the emergency units from the five major Hospitals' (Hippokraton, Evangelismos, Tzaneio, Alexandras and Red Cross) in the greater Athens area. The population in the investigated area is about 3.5 million (National Statistical Services, census 2001) and the selected hospitals cover about 77–80% of hospital admissions for cardiac events (personal information provided by the Ministry of Health). Study investigators confirmed that admission diagnoses were in accordance with discharge diagnoses and cases with discordant diagnoses were excluded. Only Athens residents were included in the final study population. Acute myocardial infarction was defined by at least two of the following features: (a) electrocardiographic changes, (b) compatible clinical symptoms, and/or (c) specific diagnostic enzyme elevations. Unstable angina was defined by the occurrence of one or more angina episodes, at rest, within the preceding 48 h, corresponding to class III of the Braunwald classification. A cardiologist reviewed and confirmed each clinical evaluation. Additional information included gender and age in one of three groups: younger than 35-years-old, middle-aged (36–64-years-old) and over 65-years-old.

## 2.2. Climatological data

The studied area shows many climatological variations. The local climate is “Mediterranean” with wet, mild winters and long, hot, dry summers [11]. Daily maximum and minimum air temperatures ( $^{\circ}\text{C}$ ), wind speed (Beaufort scale), relative humidity (%) and barometric pressure (mmHg) were obtained from the Climatological Laboratory of the University campus (longitude =  $37^{\circ}58'$  North, latitude =  $23^{\circ}47'$  East). Mean daily temperature (MDT) was defined as the average of daily maximum and minimum temperature.

## 2.3. Statistical analysis

The incidence of ACS is presented as absolute and relative frequencies. The analysis of the data followed standard time-series methods. These involved the use of generalized additive models (GAM) with loess smoothers to control for seasonal patterns [12]. For the determination of the optimal amount of smoothing needed, a relatively large span was initially applied (i.e. 180 days). Afterwards, reductions in the smoothing window were made, with a reassessment of model diagnostics at each step. Thus, loess smoother, with a 90 days time window (smoothing parameter is  $90/608 = 14\%$ ), was finally used. We selected loess smoother since its local behavior picks up awkward shapes well [12]. Moreover, according to several investigators [12–14], the lag effect seems to be important. Thus, each climatological measure was averaged across lags of 0 and 2 days. Afterwards, each of these terms was included in the model if statistically significant at the 5% level. In the next step of the analysis indicator variables were used to allow for day-of-week (six “dummy” variables), season (November–March, April–October), Christmas, New Year, Easter,

strikes, bank and summer holidays (25 July to 25 August). The contribution of each variable was evaluated by the use of the  $F$ -test. Once all the aforementioned indicator variables were included in the model, as independent variables, the relationship of daily admissions with climatological parameters as well as a special environmental index [15] was finally assessed. The mathematical formulae of this thermo-hydrological-index (T.H.I.) is:  $\text{T.H.I.} = T_a - 0.55 \cdot (1 - 0.01 \text{RH}) \cdot (T_a - 14.5)$ , where  $T_a$  = mean monthly air temperature in Celsius degrees, RH = mean monthly relative humidity as a percentage. This index has been suggested as an appropriate measure for the evaluation of the effect of air temperature on health outcomes [15], since it takes into account mean air temperature after controlling for the effect of relative humidity. Goodness-of-fit of each statistical model was assessed from the residuals against time. The partial auto-correlation function was applied to determine the degree of remaining serial-correlation (non-independence of adjacent days). All analyses were carried out using the statistical software SPSS 10.1 (SPSS Inc., Chicago, IL).

## 3. Results

### 3.1. Daily hospital admissions

During the study period 5458 subjects were admitted for a non-fatal ACS in the selected hospitals, 4093 (75%) of them were males and 1365 (25%) were females. Approximately one half ( $n = 2823$ , 51%) were over 65-years-old and 55 (1%) were below 35-years-old. The mean number of daily admissions was  $9.3 \pm 3.5$  persons per day, averaging  $6.9 \pm 2.8$  male (74%) and  $2.4 \pm 1.5$  female (26%).  $55.7 \pm 2.4$  were admitted due to unstable angina (61%) and  $3.6 \pm 1.5$  due to acute myocardial infarction (39%). Fig. 1 illustrates the series of the daily number of admissions for ACS in the selected hospitals, during the 20-month study period. The mean numbers of admissions were higher in the cold compared to the warm season (Figure 1).

### 3.2. Climatological variables and hospital admissions for ACS

Fig. 2 illustrates the daily values of mean air temperature and humidity. The application of the GAM revealed a negative correlation between daily hospital admissions and the mean air temperature, after controlling for gender, age group, season, day-of-week, number of holidays and strikes (see Table 1). A  $1^{\circ}\text{C}$  decrease in MDT was associated with a 5% increase of admissions due to an acute coronary event ( $\beta = -0.05$ , risk ratio = 1.05,  $P < 0.05$ ). This association was stronger in females ( $\beta = -0.08$ , risk ratio = 1.08,  $P = 0.058$  for females vs.  $\beta = -0.04$ , risk ratio = 1.04,  $P = 0.15$  for males) and in the elderly ( $\beta = -0.09$ , risk ratio = 1.10,  $P = 0.032$  for  $>65$ -years-old vs.  $\beta = -0.02$ , risk ratio = 1.02,  $P = 0.23$  for  $<65$ -years-old). There was also a negative

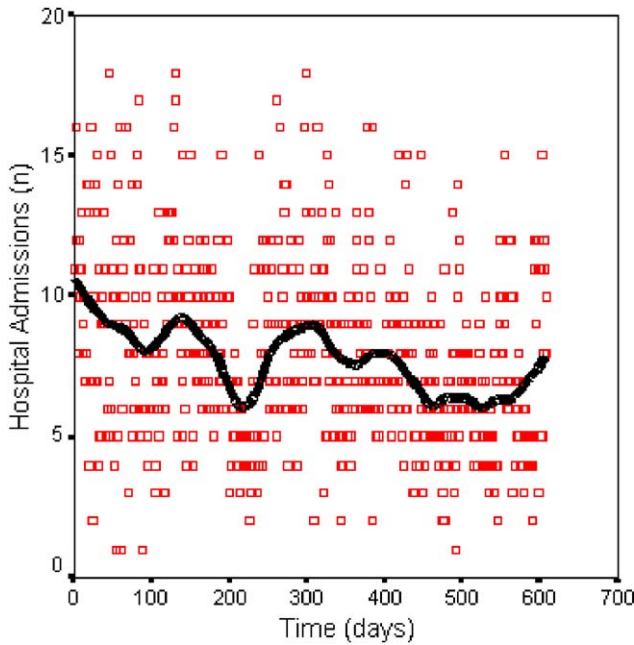


Fig. 1. Time series of observed and predicted daily number of hospital admissions for ACS, in Athens greater area. The loess smoother expresses predicted hospital admissions; the studied period is from 1 January 2001 to 31 August 2002.

correlation between hospital admissions for ACS and minimum, maximum daily temperature. A 1 °C decrease in minimum or maximum air temperature was associated with a 4% ( $\beta = -0.03$ , risk ratio = 1.04,  $P = 0.048$ ) and 5% ( $\beta = -0.05$ , risk ratio = 1.05,  $P = 0.041$ ) increase in the number of

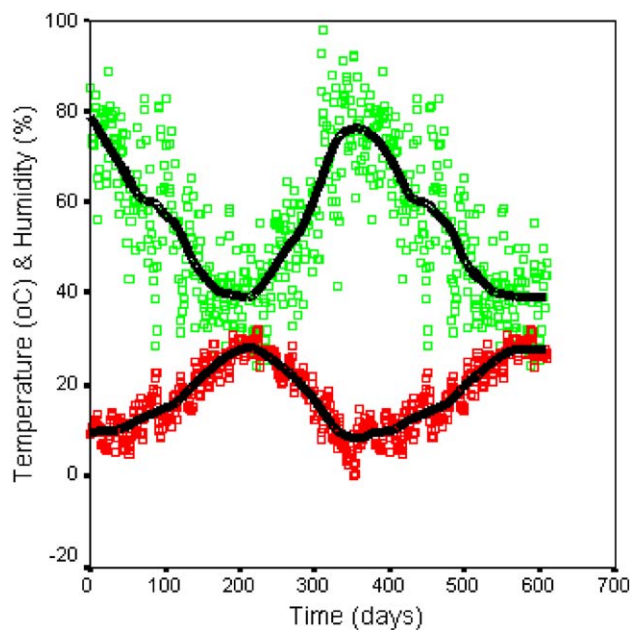


Fig. 2. Time series of observed and predicted mean air temperature and relative humidity, in Athens greater area. Mean air temperature (bottom line) is expressed in Celsius degrees and relative humidity (upper line) as a percentage; the studied period is from 1 January 2001 to 31 August 2002.

Table 1

Parameter estimates from Poisson autoregressive models and relative risks (RR) for daily hospital admissions, per 1 unit change in the climatological variables RR reflects a 1 °C decrease in all temperature measurements and T.H.I., and 1% increase in relative humidity, after controlling for day-of-week, season, Christmas, New Year, Easter, strikes, bank and summer holidays of the investigated period (January 2001–August 2002)

	$\beta$ -coefficient $\pm$ S.E.	RR	P-value
Mean temperature (°C)	$-0.050 \pm 0.0022$	1.05	0.030
Maximum temperature (°C)	$-0.043 \pm 0.0020$	1.04	0.031
Minimum temperature (°C)	$-0.058 \pm 0.0025$	1.06	0.020
Relative humidity (%)	$0.022 \pm 0.0010$	1.02	0.036
Barometric pressure (1 mmHg)	$0.00005 \pm 0.0002$	1.00	0.831
T.H.I. (1 °C)	$-0.056 \pm 0.0031$	1.06	0.039

hospital admissions, respectively. For relative humidity, a positive correlation was found with hospital admissions ( $\beta = +0.02$ , risk ratio per 10% change = 1.24,  $P = 0.04$ ) (Figure 2). This correlation was stronger in females ( $\beta = +0.04$ , risk ratio per 10% change = 1.49,  $P = 0.015$ ) than males ( $\beta = 0.01$ , risk ratio per 10% change = 1.11,  $P = 0.35$ ). A negative correlation was found between T.H.I. and hospital admissions, in both genders (3). A 1 °C decrease in T.H.I. yielded a 6% ( $\beta = -0.06$ , risk ratio = 1.06,  $P = 0.039$ ) increase in hospital admissions for ACS (see Table 1). This correlation was, slightly, stronger in the elderly ( $\beta = -0.09$ , risk ratio = 1.09,  $P < 0.001$ ). No differences were found when we stratified our analysis according to the type of syndrome (unstable angina or acute myocardial infarction) and no significant interactions between mean temperature and hu-

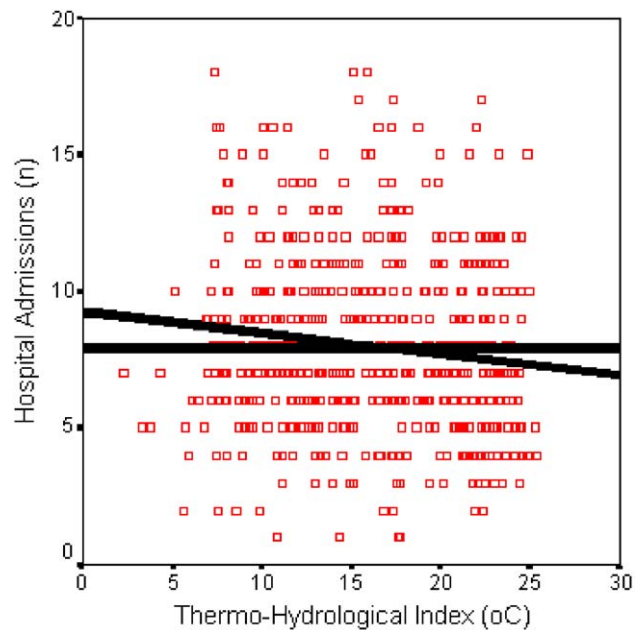


Fig. 3. Hospital admissions for ACS in the selected hospitals and the T.H.I. (°C). Horizontal line represents mean daily hospital admissions for ACS in the selected hospital, and gradient line represents linear association between log(daily hospital admissions) and T.H.I., after adjustment for several confounders.

midity or with day-of-the-week, holidays and strikes were observed with respect to hospital admissions.

Regarding the other investigated climatological parameters, wind speed was negatively correlated with hospital admissions, but this relationship was not statistically significant ( $\beta = -0.10 \pm 0.15$ , risk ratio = 1.11,  $P = 0.479$ ). Similar results were found regarding the mean barometric pressure (see Table 1).

#### 4. Discussion

We evaluated the association between several climatologic parameters (temperature, humidity, wind speed and barometric pressure) and hospital admissions for non-fatal ACS (unstable angina or acute myocardial infarction) in the greater Athens area. Time-series analysis revealed a statistically significant association between ambient temperature and relative humidity and hospital admissions for ACS. This relationship was more marked in females and the elderly.

Several observational studies reported a relationship between air temperature and mortality, with most of the excess mortality due to respiratory and cardiovascular disease [16–22]. For example, in the United Kingdom a 2% increase in mortality has been estimated for every 1 °C fall in temperature from 18 °C [23]. Other studies examined the correlation between temperature and humidity and increased cardio-respiratory morbidity; they reached a variety of conclusions [24–27]. In general, studies show that increased death rates occur principally in the elderly, and that this relationship with temperature takes the form of a ‘V’ or a ‘U’ shape [20,28].

In contrast to the aforementioned studies, our study revealed a linear association between air temperature and hospital admissions for ACS, with a 1 °C decrease in MDT resulting in a 5% increase in hospital admissions. These findings were reinforced when we included in the analysis a T.H.I., suggesting that the ambient temperature is inversely related to the investigated cardiac events, when taking into account the effect of relative humidity. Also, the association between air temperature and hospital admissions was stronger in females (+8%) and the elderly (+9%). A potential pathophysiological mechanism is that low air temperatures produce vasoconstriction, which increases the arterial pressure [21]. Furthermore, an increase in the circulating levels of catecholamines can increase heart rate and cardiac work (a similar reaction to bathing in cold water) [21,22]. The combination of increased cardiac work and peripheral resistance might lead to a greater oxygen demand and a potentially ischemic reaction in the vulnerable myocardium. Furthermore, the higher cardiovascular mortality during periods of cold weather might be associated with an increase in blood pressure variability [27].

However, other investigators report a positive association between air temperature and cardio-respiratory mortality

and morbidity. In particular, a 35% increase in mortality has been reported in New York during a heat wave in June 1984, mainly due to an increase in mortality of the elderly living in poorly air-conditioned residences [2]. High temperatures during heat waves in 1976, 1995 and 1998 in London were also associated with a 15% increase in total mortality [8,10]. The increased temperature during July 1987, in Athens was also associated with 2000 additional deaths, a 97% increase in daily mortality [4]. Finally, a recent study involving 44 cities in USA has shown an association between high variability of daily temperature during summer and increased mortality [9].

The data studied in this survey consisted only of people admitted alive in the emergency units of the selected hospitals and, consequently, do not cover all the major coronary events. We have not investigated concomitant air pollution variations and the relatively short duration of the study period also limits somewhat our confidence in a cause–effect relationship for the meteorological variables. Nevertheless, the findings suggest a strong association between mean air temperature and hospital admissions due to ACS. Due to the large burden of acute cardiac disease and its sequelae, this is a matter of some public health importance. Further studies are needed in order to confirm or refute our findings and the suggested pathophysiological mechanisms.

#### 5. Competing interests

None.

#### 6. Authors' contributions

Demosthenes B. Panagiotakos, design of the study, statistical analysis and drafted the manuscript; Christina Chrysohoou, drafted the manuscript; Christos Pitsavos, design of the study and drafted the manuscript; Athanasios Paliatsos, editing; Panagiotis Nastos, climatological evaluation; Aggelos Anadiotis, design of the study and data collection; Constatninos Tentolouris, editing; Christodoulos Stefanadis, editing; and Pavlos Toutouzias, editing.

#### Acknowledgements

We thank the Hellenic Heart Foundation for financial support (research grant 11/2002).

#### References

- [1] Lye M, Kamal A. Effects of a heat-wave on mortality-rates in elderly inpatients. *Lancet* 1977;5;1(8010):529–31.
- [2] Fish PD, Bennett GC, Millard PH. Heat wave morbidity and mortality in old age. *Age Ageing* 1985;14(4):243–5.

- [3] Tanaka M, Ohnaka T, Yamazaki S, Tochihara Y. The effects of different vertical air temperatures on mental performance. *Am Ind Hyg Assoc J* 1987;48(5):494–8.
- [4] Katsouyanni K, Trichopoulos D, Zavitsanos X, Touloumi G. The 1987 Athens heat wave. *Lancet* 1988;3:573.
- [5] Glantz SA. Heart disease and the environment. *J Am Coll Cardiol* 1993;21:1473–4.
- [6] Kay RW. Geomagnetic storms: association with incidence of depression as measured by hospital admission. *Br J Psychiatry* 1994;164:403–9.
- [7] Colwell RR, Epstein PR, Gubler D, Maynard N, McMichael AJ, Patz JA, et al. Climate change and human health. *Science* 1998;13:279(5353):968–9.
- [8] Rooney C, McMichael AJ, Kovats RS, Coleman MP. Excess mortality in England and Wales, and in Greater London, during the 1995 heat wave. *J Epidemiol Community Health* 1998;52(8):482–6.
- [9] McMichael AJ. The urban environment and health in a world of increasing globalization: issues for developing countries. *Bull Who* 2000;78(9):1117–26.
- [10] Hajat S, Kovats RS, Atkinson RW, Haines A. Impact of hot temperatures on death in London: a time series approach. *J Epidemiol Community Health* 2002;56(5):367–72.
- [11] Touloumi G, Samoli E, Katsouyanni K. Daily mortality and winter type air pollution in Athens, Greece—a time series analysis within the APHEA project. *J Epidemiol Community Health* 1996;50:s47–51.
- [12] Hastie T, Tibshirani R. *Generalized additive models*. 50. London: Chapman and Hall, 1990.
- [13] Braga AL, Zanobetti A, Schwartz J. The effect of weather on respiratory and cardiovascular deaths in 12 US cities. *Environ Health Perspect* 2002;110(9):859–63.
- [14] Brockwell PJ, Davis RA. *Time series: theory and methods*. 2nd ed. New York: Springer, 1991.
- [15] Thom E. The discomfort index. *Weatherwise* 1959;12:57–60.
- [16] Tanaka H, Shinjo M, Tsukuma H, Kawazuma Y, Shimoji S, Kinoshita N, et al. Seasonal variation in mortality from ischemic heart disease and cerebrovascular disease in Okinawa and Osaka: the possible role of air temperature. *J Epidemiol* 2000;10(6):392–8.
- [17] Huynen M, Martens P, Schram D, Weijnenberg M, Kunst AE. The impact of cold spells and heat-waves on mortality rates in the Dutch population. *Environ Health Perspect* 2001;109:463–70.
- [18] Keatinge WR, Donaldson GC. Mortality related to cold and air pollution in London after allowance for effects of associated weather patterns. *Environ Res* 2001;86:209–16.
- [19] Kunst AE, Looman CWN, Mackenbach JP. Outdoor air temperature and mortality in the Netherlands: a time-series analysis. *Am J Epidemiol* 1993;137:331–41.
- [20] Donaldson GC, Keatinge WR. Early increases in ischaemic heart disease mortality dissociated from and later changes associated with respiratory mortality after cold weather in southeast England. *J Epidemiol Community Health* 1997;51:643–8.
- [21] Opie L. *The heart*. 51. Philadelphia: Lippincott-Raven Publishers, 1998.
- [22] Sheth T, Nair C, Muller J, Yusuf S. Increased winter mortality from acute myocardial infarction and stroke: the effect of age. *J Am Coll Cardiol* 1999;33:1916–9.
- [23] Alderson MR. Season and mortality. *Health Trends* 1985;17: 87–95.
- [24] Thakur CP, Anand MP, Shahi MP. Cold weather and myocardial infarction. *Int J Cardiol* 1987;16:19–25.
- [25] Barer D, Ebrahim S, Smith C. Factors affecting day to day incidence of stroke in Nottingham. *Br Med J* 1984;289(6446):662.
- [26] Messner T, Lundberg V, Wikstrom B. A temperature rise is associated with an increase in the number of acute myocardial infarctions in the subarctic area. *Int J Circumpolar Health* 2002;61(3):201–7.
- [27] DASH Collaborative Research Group, Jehn M, Appel LJ, Sacks FM, Miller ER III. The effect of ambient temperature and barometric pressure on ambulatory blood pressure variability. *Am J Hypertens* 2002;15(11):941–5.
- [28] Landsberg HE. The assessment of human bioclimate: a limited review of physical parameters. Geneva, WHO Technical Note No 123, 1972.