Out-of-Hospital Death in Israel — Should We Blame the Weather?

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In the last two decades, reperfusion (pharmacological or mechanical) and other therapies (anti-platelets, antithrombin, β-blockers, ACE-I) have dramatically changed the in-hospital prognosis of patients with acute myocardial infarction and other coronary syndromes. As a result cardiac mortality has declined substantially [1–5], but still remains the leading cause of death in adults in most western countries [6]. Moreover, cardiac death is increasing in newly developed countries and particularly in Eastern Europe [7]. It should be emphasized that cardiovascular diseases will remain the leading cause of disability and mortality in most parts of the world in the next 20 years.

Despite the recent progress in the management and outcome of patients with coronary artery disease, out-of-hospital sudden cardiac death still remains the "Achilles heel" of medicine in general and of cardiology in particular. Seventy-five percent of out-of-hospital natural deaths are due to cardiac causes. Furthermore, out-of-hospital SCD accounts for more than 50% of all coronary deaths. The rates of SCD in the USA and Israel are usually estimated at 300,000 and 6,000 SCDs per year respectively (1–1.5/1000 population) [8,9]. While the characteristics, management and outcome of hospitalized patients with AMI and other coronary syndromes have been extensively assessed, prevention and successful management of out-of-hospital death remain largely unexplored. Prediction of candidates for SCD is presently vague and largely imprecise. Thus, a major challenge in cardiology in the next century will be the prevention and successful management of SCD.

Among the commonly recognized triggering and risk factors for SCD — namely smoking, emotional stress, alcohol consumption, overweight, and physical inactivity or over-activity — circadian, seasonal and climatic variations have also been explored. Interestingly, Pope Clement XII, impressed by the high number of sudden deaths that occurred in the winter of 1705–1706, asked his physician, Lancini, to explore the influence of the cold weather on mortality [10]. Most of the recent papers on this topic have concluded that a peak of SCD, AMI and other cardiovascular conditions is usually observed in low temperature weather during winter [11–16], although other studies reported a peak of cardiovascular events in summer [17–19]. A recent publication from the Second National Registry of Myocardial Infarction [20] reported an excess (>50%) of AMI in winter compared with summer in this very large MI population cohort.

"The heat is killing me," a ubiquitous complaint of Israeli citizens during summer, intrigued Katz and co-workers and prompted them to conduct a study on the subject. In this issue of the Journal [21], these researchers address the issue of seasonal variations in out-of-hospital sudden death in the Negev (the desert region of southern Israel), which is considered to have the highest temperature in the country. In this region 300,000 citizens live in a semi-desert climate with temperatures ranging from 10°C in short winters to up to 42°C in long summers. Their study population comprised 243 consecutive cases of out-of-hospital deaths (excluding fatal cases due to accidents, violence or unnatural causes). As expected, the majority of cases were men and elderly, with 50% of patients having a previous history of cardiac disease. Interesting was the finding that despite the fact that temperatures in summer often exceeded 30°C, while in winter temperatures are relatively moderate and did not drop below 10°C, a trend for a higher number of out-of-hospital sudden deaths was noted in winter rather than summer. The same was true when data were analyzed according to heat stress with a hazard ratio of 1.57 in low heat stress versus 1.01 and 0.28 for days with moderate and high heat stress respectively ($P=0.05$). Relative humidity and barometric pressure were not associated with the incidence of out-of-hospital sudden death. These findings are in line with most previous studies and are reassuring for populations living in hot countries. In a previous publication from Israel, Green et al. [22] showed that between 1976 and 1985, mortality from cardiovascular disease was higher by 50% in mid-winter than in mid-summer, both in men and women and in different age groups.

The excessive prevalence of fatal and non-fatal cardiovascular events during cold weather was explained by different physiopathological mechanisms such as alteration of the hemodynamic, sympathetic and coagulation systems. In a recent editorial on this topic, Zipes [23] emphasized the importance of the short days in winter, which interfere with the body's internal clock for triggering excessive cardiovascular events, in addition to temperature variations. Other

SCD = sudden cardiac death
AMI = acute myocardial infarction

authors have suggested that the excess of cardiovascular events in winter could also be related to the peak of respiratory infections occurring in cold weather [24]. The data of Katz et al. indicate a peak of out-of-hospital sudden death in winter in a country where the temperatures in winter are moderate. However, Green et al. concluded that respiratory infectious disease, although more common in winter in Israel, did not play a major role in triggering cardiovascular disease [22].

In a recent large community study, Kloner and coworkers [25] observed a striking seasonal variation in the development of coronary death, with a 33% excess of deaths in December and January in comparison with June–September. The study, conducted in Los Angeles county, comprised more than 220,000 case fatalities during 12 consecutive years. This pattern was consistent from 1985 to 1996, although cardiac mortality declined progressively through the years. Since cardiac death peaked on 1 January and could not be explained solely on the basis of temperature change, and since others have noted a clustering of SCD during winter holidays, the authors suggest that stress factors (behavioral, emotional, psychological) related to the holidays could also be triggers for sudden death in winter.

In general, our understanding of the mechanisms and risk factors for SCD remains poor. As shown by this and previous studies, out-of-hospital SCD is irreversible in the majority of cases, and combined efforts of the health authorities and the public are necessary to reverse this trend in the future. Hopefully, the emergence of new risk factors, such as endothelial dysfunction, inflammatory and thrombogenic states, are promising and will help to combat coronary artery disease more efficiently. Parallel to the progress achieved in basic and clinical research for the prevention and management of coronary artery disease, more clinical and epidemiological data on SCD should be collected systematically all around the world. Israel is fortunate in having a unique rescue service of mobile intensive care units that cover the entire country under the same umbrella (*Magen David Adom*). It is imperative that periodic national surveys be conducted on the incidence, causes, management and outcome of out-of-hospital death, which may lead to improving the management of patients who suffer a critical heart problem but did not have the "chance" to reach the hospital alive. Such a survey is currently being planned and will be conducted in the near future.

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I'm a slow walker, but I never walk back.

Abraham Lincoln