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Reply

Triggering of Cardiac Arrhythmias

The Problem of Multicollinearity Among Air Pollution and Meteorological Factors

Dr. Čulić suggests that the associations that we reported (1) between particulate air pollution ($PM_{2.5}$) and atrial fibrillation (AF) may be confounded by inadequate control of meteorology. There is a well-developed body of literature suggesting that acute particulate air pollution exposures can trigger cardiac events and arrhythmias (2,3). There is, however, more limited evidence that temperature and other meteorological variables can trigger such events (4).

Dr. Čulić acknowledges that the evidence of these meteorological associations is inconsistent and, in some cases, speculative, but suggests that uncontrolled meteorological variables may be the true causative actors. As evidence, Dr. Čulić cites 4 analyses (5–8) of Holter monitoring for a single 24-h period in up to 457 patients over 1 period (January to April) in 2001. Čulić et al. (5–8) examined the frequency of arrhythmias in each hour in different patients versus individual characteristics plus level and change in 8 meteorological parameters using multiple linear regression.

In our study, 176 patients were followed for an average of 1.9 years with continuous monitoring for atrial fibrillation (AF) by implanted dual-chamber monitors. The risk of AF events associated with air pollution and meteorology were estimated using case-crossover methods, in which the risk in the same patient is estimated over time using multiple regression.

We controlled for 2 of the meteorological factors that Čulić et al. (5–8) identify as important risk factors: atmospheric temperature and moisture (dew point). In their analyses, 16 meteorological factors were considered, but no measures of air pollution. Although examination of additional meteorological factors may be marginally informative in our study, we would suggest that assessment of air pollution in the Čulić study may be even more informative.

In terms of clinical implications, understanding the role of meteorology in triggering acute cardiac events may help in providing guidance on activities in vulnerable patients during extreme weather events. Understanding the cardiac risks of air pollution exposures independent of meteorology would inform not only vulnerable patients but also public policy in reducing population risk (9).

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Should We Forget About Low-Density Lipoprotein Cholesterol?

The U.S. National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults recommendations (1) have had a huge impact on the treatment of hypercholesterolemia around the world and have had a decisive influence on all recommendations worldwide. Until now, the recommendations were based on lowering low-density lipoprotein cholesterol (LDL-C) as the treatment goal. The accumulated information for more than 100 years built the "lipid theory of atherosclerosis" (2), and the recommendations fit well with that scientific knowledge: lowering LDL-C reduces cardiovascular risk by reducing atherosclerosis, and LDL-C lowering is, therefore, the objective. Over the years, as the evidence from clinical trials has emerged, LDL-C goal levels have been reduced and the population subsidiaries of reduction benefit have been expanding. The results have been dramatic and the reduction of cardiovascular disease in many countries reflects this (3).

The recently published "2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults" (4) has substantially changed the message. What is important, according to the new guideline, is to prescribe statins, and cholesterol reduction is a consequence, not the goal, of treatment. The guidelines have gone from a low-density lipoprotein–focused vision to a vision focused only on statins. They forget lipid goals, the concentration of cholesterol in the monitoring of patients, and, ultimately, all evidence of the pathogenesis of atherosclerosis. The document concentrates only on 1 type of evidence, which comes from randomized clinical trials. It should be remembered that not all scientific evidence comes from randomized clinical trials, and that we will never be able to have solid evidence for many patients excluded from the trials. What are we to do with a diabetic patient of age 60 years, with a personal history of coronary disease and with LDL-C 130 mg/dl after maximally-tolerated doses of statins? The document tells us to do nothing to further reduce his LDL-C. We believe that the scientific knowledge is misinterpreted, and a large group of patients is being unreasonably discriminated against. In contrast, the document indicates that we should prescribe high-intensity statin treatment in an otherwise healthy woman of 21 years, with LDL-C 190 mg/dl and, for example, high-density lipoprotein cholesterol 90 mg/dl. Even the document supports the use of a second or third nonstatin lipid-lowering drug to further lower her LDL-C; however, it refuses this approach to our diabetic patient.

The document has, according to the Spanish Atherosclerosis Society, many positive aspects: the systematic review of the literature, the definition of the groups susceptible to treatment, the classification of the statins' effects, and the new calculation of cardiovascular risk. However, the uncertainty and nihilism in many important issues is worrisome and may harm many patients; leaving behind the concept of intensive reduction of LDL-C will confuse many doctors; and focusing on statins will be detrimental to the investigation and development of other lipid-lowering drugs. For these reasons, the Spanish Society of Arteriosclerosis does not support this document and better recommends the guidelines from the European Society of Cardiology/European Atherosclerosis Society (5).

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