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Letters to the Editor

Triggering of Cardiac Arrhythmias

The Problem of Multicollinearity Among Air Pollution and Meteorological Factors

Link et al. (1) recently suggested the influence of ambient air pollutants on the occurrence of atrial fibrillation, with a 26% increase in the risk of arrhythmic incidence for each 6-$\mu g/m^3$ increase in particulate matter <2.5 μg ($PM_{2.5}$) aerodynamic diameter. Arguably, the association of acute cardiac events with environmental influences may not be as simple because of strong correlations between the atmospheric constituents, which may also act as triggers of cardiac arrhythmias. For example, meteorological factors correlate with each other, but also substantially influence the concentration of air pollutants (2–8). A growing body of evidence has suggested a strong relationship of suspended particulate matter to wind speed, air pressure and temperature, and relative humidity (2–5). The problem of multicollinearity may be particularly important for the relationship between meteorological factors and ambient $PM_{2.5}$ (3), the particles that showed a significant association with the occurrence of atrial fibrillation in the study by Link et al. (1).

Link et al. (1) made adjustments for air temperature and dew point for 24-h periods, which could partly be the reason for nonsignificant associations between atrial fibrillation and air pollution in this analysis. Two previous studies from Poland investigated the association of the incidence of atrial fibrillation also using daily meteorological data, but without adjustments. The first study has suggested that meteorological factors such as temperature, relative humidity, and atmospheric pressure are implicated in the occurrence of atrial fibrillation in 87% of patients (9). The second study failed to confirm the influence of individual meteorological factors, but found an increased incidence of atrial fibrillation associated with the passage of a cold front and an occlusion of the cold front type (10).

The most important advantage of the study by Link et al. (1) is the 2-h time window of exposure measurements. However, using comparable time windows (i.e., 2- and 3-h periods), we reported that all 4 meteorological factors mentioned above may be involved in the triggering of both ventricular (11,12) and supraventricular arrhythmias (13,14), independently of other external triggering factors including physical activity and emotional stress. High absolute levels of atmospheric pressure and increasing air moisture were strong predictors of supraventricular tachycardia in all patient subgroups, as well as both wind speed and blowing of southeasterly and southwesterly wind directions in male patients (13). Increasing air moisture was also a strong common predictor of single supraventricular premature beats, whereas atmospheric temperature correlated with ectopy in participants younger than 65 years of age (14). In addition, we reported independent associations of atmospheric temperature and pressure, increasing relative air moisture, and wind speed and direction with the occurrence of ventricular tachyarrhythmia (11,12).

Possible mechanisms of the influence of wind speed and direction on cardiac arrhythmias, such as wind-induced turbulence and rapid atmospheric pressure oscillations (11–13,15), are highly speculative. Adverse effects of higher temperatures or increasing relative air moisture may burden and disturb the human homeostasis, particularly thermoregulatory, hemorheological, cardiovascular, and nervous systems (11,12,16). Higher absolute levels or decreasing atmospheric pressure have been associated with enhanced sympathetic activity (12,17,18). In considering their close inter-relations (2–5), one might expect that such meteorological conditions cause a more marked endogenous response and triggering burden than air pollution itself.

The main limitation of the research on environmental triggers is the lack of an adequate methodology. Link et al. (1) used a case-crossover design, comparing the risk of an incident during exposure and during control periods using conditional logistic regression (19,20). Although each patient serves as his or her own control, this design cannot control for meteorological variables and multiple correlations among environmental factors. To account for the possibility of multiple environmental triggers of cardiac arrhythmias (11–14), we applied a framework of multiple regression analysis with multiple successive measurements for each patient. We suggested that these 2 designs may be considered complementary (11). However, a more precise estimation of triggering and interaction effects of environmental factors may only be addressed through individual patient-based meta-analyses of large-scale data on air pollution and meteorological factors.

The acute effects of short-term exposure to higher pollution probably increase the myocardial vulnerability in some patients, but some concerns about the causal relationship with atrial fibrillation and other cardiac arrhythmias remain. There is a scenario in which increased air pollution is not the only or the direct culprit. Instead of a single trigger, a cluster of adverse atmospheric conditions may cause an arrhythmic incident. Further studies on interactions among all atmospheric triggers could further our understanding of the mechanisms of cardiovascular risk associated with certain atmospheric factors.

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Reply

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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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