Environmental factors in out-of-hospital cardiac arrests

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Out-of-hospital cardiac arrest (OHCA) is a condition characterized by unexpected cardiovascular collapse due to an underlying cardiac cause. The most common cause of cardiac arrest is coronary artery disease. Survival rate after an incident of OHCA is as low as 8% so that it is often used as a surrogate for sudden cardiac death, a leading cause of death in the world.[1] Emerging evidence supports a relationship between OHCA and environmental factors such as extreme weather conditions and air pollution.

Sudden cardiac deaths occur more often during morning hours, on Mondays, and during winter months.[2] The winter peak in sudden cardiac death could be explained by cold temperature in the winter.[3] Extreme weather conditions associated OHCA have also been examined.[4–6] A study conducted in six large Chinese cities[4] and a nationwide study in 47 prefectures of Japan[5] suggested that both extremely cold and hot temperatures are associated with an increased risk of OHCA. The association of heat waves with an increased risk of OHCA has also been confirmed by a multi-city study in Korea.[6]

Air pollution, especially by $PM_{2.5}$ and ozone, is another risk factor for OHCA, as summarized in recent systematic reviews.[7,8] A time-stratified case-crossover design using 11 677 emergency medical service-logged OHCA events between 2004 and 2011 in Houston, Texas reported an increased risk of OHCA (OR=1.046; 95% confidence interval (CI), 1.012-1.082) for each increment of $PM_{2.5}$ pollution by 6 $\mu g/m^3$ in the two days prior to an OHCA event , and an increased risk of OHCA (OR=1.039; 95% CI, 1.005-1.073) for each increment of ozone pollution by 20 ppb on the same day as an OHCA event.[9] Another case-crossover study in Stockholm, Sweden found ambient ozone was associated with an increased risk of OHCA for the time windows of 0-2, 0-24, and 0-72 hours before an OHCA event, with odds ratios (OR) of 1.02 (1.01-1.05), 1.04 (1.01-1.07), and 1.05 (1.01-1.09), respectively, per 10 $\mu g/m^3$ increment in ozone concentration.[10] Exposure to forest fire smoke (particulate matter and carbon monoxide) was also linked to an increased risk of OHCA in Australia.[11]

Interestingly, sunshine exposure was also linked to risk of OHCA, as reported by Onozuka and Hagihara in an ecological study in Japan.[12] The authors followed Antonio Gasparrini's method [13] to calculate the fraction and number of OHCA events attributable to sunshine exposure. The distributed lag nonlinear models integrated in quasi-Poisson regression and the second stage random-effect meta-analysis were acceptable and standard. The sample size was large, with a total of 658,742 cases from 47 Japanese prefectures. A total of 5.78% OHCA cases were attributed to non-optimal durations of daily sunlight exposure, among which 4.18% and 1.59% to short and long sunshine duration, respectively.

Is sunshine good for our heart? Reduced sunshine exposure may result in vitamin D deficiency, which is associated with incident cardiovascular disease and even sudden cardiac death. Avoidance of sun exposure has been indicated as a risk factor for major causes of death in women with a similar magnitude as smoking in a large Sweden cohort with 20-year's follow-up.[14] The beneficial effects of sunlight on cardiovascular health has also been hypothesized to be mediated by mechanisms that are independent of melatonin, vitamin D, and exposure to ultraviolet B. It is suggested that the skin maintains a significant store of nitric oxide (NO)-related species which can be mobilized by sunlight and delivered to the systemic circulation to exert coronary vasodilator and cardio-protective as well as antihypertensive effects.[15]

Although the relationship between sunshine exposure and heart health may be biological plausible, we need to interpret the human epidemiologic data with caution. The sunshine and OHCA study by Onozuka and Hagihara was strengthened by its comprehensive nationwide data and sufficient covariate adjustment in a standard statistical model. On the other hand, the authors acknowledged the limitations of potential exposure misclassification and the heterogeneous relationships in different seasons. The daily sunshine duration and intensity may vary with season, and the health effects of reduced sunlight exposure are distinct in cold and warm seasons. According to the stratified analysis by season that the authors provided in the supplementary materials, [12] the OHCA risk attributable to non-optimal sunshine exposure was much higher in winter than that in summer (37.1% vs. 10.7%). Another question to be explored in the future is whether the association between sunshine exposure and OHCA represents a direct effect or an indirect effect mediated by other environmental factors such as ambient temperature and air pollution.

References:

1. McNally B, Robb R, Mehta M, Vellano K, Valderrama AL, Yoon PW, Sasson C, Crouch A, Perez AB, Merritt R, Kellermann A. Out-of-hospital cardiac arrest surveillance. Cardiac Arrest Registry to Enhance Survival (CARES), United States, October 1, 2005 - December 31, 2010. Morbidity and Mortality Weekly Report, Center for Disease Control and Prevention. Surveillance Summaries 2011; 60:1-19. https://www.cdc.gov/mmwr/pdf/ss/ss6008.pdf (Access on Nov. 14, 2016)

2. Arntz HR, Willich SN, Schreiber C, Brüggemann T, Stern R, Schultheiss HP. Diurnal, weekly and seasonal variation of sudden death. Population-based analysis of 24,061 consecutive cases. *Eur Heart J* 2000;21:315–320.

3. Gerber Y, Jacobsen SJ, Killian JM, Weston SA, Roger VL. Seasonality and Daily Weather Conditions in Relation to Myocardial Infarction and Sudden Cardiac Death in Olmsted County, Minnesota, 1979 to 2002. *J Am Coll Cardiol* 2006;48:287–292.

4. Chen R, Li T, Cai J, Yan M, Zhao Z, Kan H. Extreme temperatures and out-of-hospital coronary deaths in six large Chinese cities. *J Epidemiol Community Health* 2014;68:1119–1124.

5. Onozuka D, Hagihara A. Extreme temperature and out-of-hospital cardiac arrest in Japan: A nationwide, retrospective, observational study. *Sci Total Environ* 2017;575:258–264.

6. Kang SH, Oh IY, Heo J, Lee H, Kim J, Lim WH, Cho Y, Choi EK, Yi SM, Sang DS, Kim H, Youn TJ, Chae IH, Oh S. Heat, heat waves, and out-of-hospital cardiac arrest. *Int J Cardiol* 2016;221:232–237.

7. Zhao R, Chen S, Wang W, Huang J, Wang K, Liu L, Wei S. The impact of short-term exposure to air pollutants on the onset of out-of-hospital cardiac arrest: A systematic review and meta-analysis. *Int J Cardiol* 2016;226:110–117.

8. Teng T, Williams T, Bremner A, Tohira H, Franklin P, Tonkin A, Jacobs I, Finn J. A systematic review of air pollution and incidence of out-of-hospital cardiac arrest. *J Epidemiol Community Heal* 2014;68:37–43.

9. Ensor KB, Raun LH, Persse D. A case-crossover analysis of out-of-hospital cardiac arrest and air pollution. *Circulation* 2013;127:1192–1199.

10. Raza A, Bellander T, Bero-Bedada G, Dahlquist M, Hollenberg J, Jonsson M, Lind T, Rosenqvist M, Svensson L, Ljungman PLS. Short-term effects of air pollution on out-of-hospital cardiac arrest in Stockholm. *Eur Heart J* 2014;35:861–868.

11. Dennekamp M, Straney LD, Erbas B, Abramson MJ, Keywood M, Smith K, Sim MR, Glass DC, Monaco A Del, Haikerwal A, Tonkin AM. Forest fire smoke exposures and out-of-hospital cardiac arrests in Melbourne, Australia: A case-crossover study. *Environ Health Perspect* 2015;123:959–964.

12. Onozuka D, Hagihara A. Out-of-hospital cardiac arrest attributable to sunshine: A nationwide, retrospective, observational study. *Eur Hear J - Qual Care Clin Outcomes* 2016;in press.

13. Gasparrini A, Guo Y, Hashizume M, Lavigne E, Zanobetti A, Schwartz J, Tobias A, Tong S, Rocklöv J, Forsberg B, Leone M, Sario M De, Bell ML, Guo Y-LL, Wu C, Kan H, Yi S-M, Sousa Zanotti Stagliorio Coelh M de, Saldiva PHN, Honda Y, Kim H, Armstrong B. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. *Lancet* 2015;6736:1–7.

14. Lindqvist PG, Epstein E, Nielsen K, Landin-Olsson M, Ingvar C, Olsson H. Avoidance of sun exposure as a risk factor for major causes of death: A competing risk analysis of the Melanoma in Southern Sweden cohort. *J Intern Med* 2016;280:375–387.

15. Feelisch M, Kolb-Bachofen V, Liu D, Lundberg JO, Revelo LP, Suschek C V., Weller RB. Is sunlight good for our heart? *Eur Heart J* 2010;31:1041–1045.