## NONLINEAR ASSOCIATION OF DIURNAL TEMPERATURE RANGE WITH OXIDATIVE AND PHYSIOLOGIC STRESS MARKERS IN THE KOREAN ELDERLY ENVIRONMENTAL PANEL STUDY (KEEPS)

Youn-Hee Lim, Department of Epidemiology and Biostatistics, School of Public Health, Seoul National University, Republic of Korea

Ho Kim, Department of Epidemiology and Biostatistics, School of Public Health, Seoul National University, Republic of Korea Jin Hee Kim, Institute of Environmental Medicine, Seoul National University Medical Research Center, Republic of Korea Sang-Hyuk Bae, Environmental Health Center, Seoul National University College of Medicine, Republic of Korea Yun-Chul Hong, Institute of Environmental Medicine, Seoul National University Medical Research Center; Department of Preventive Medicine, Seoul National University College of Medicine, Republic of Korea

**Background and Aims:** While diurnal temperature range (DTR) has been found to be a risk factor for mortality in a previous study with an assumption of linearity, some disease mortality, such as that associated with rheumatic heart disease (RHD), showed a threshold effect for DTR. To define the nonlinear relationship pathway between DTR and health effects, we investigated how physiologic and oxidative stress markers responded to DTR.

**Methods:** This study was part of the Korean Elderly Environmental Panel Study (KEEPS). Data was obtained from 569 participants who regularly attended a community elderly care center located in Seoul, Korea. The study was conducted a total of five times over a three years period beginning in August, 2008. We examined physiologic stress markers including heart rate variability (HRV) and indices such as mean heart rate, standard deviation of normal-to-normal (SDNN), normalized low frequency (LF) and high frequency (HF), and low/high frequency ratio (LF:HF). Urinary malondialdehyde (MDA) was evaluated as an oxidative stress marker. Effects of DTR below or above the median level were estimated using a generalized linear mixed model.

**Results:** Significant differences in effects of DTR above and below the median level indicated the presence of a threshold effect or a nonlinear association between DTR and HRV markers. Estimated effects for log-transformed SDNN were 0.211 (standard error [SE] 0.069, P = 0.0021) below and -0.093 (SE 0.038, P = 0.0129) above the median DTR. While the mean heart rate slope above median DTR was significant, slopes of normalized HF and LF:HF ratio below median DTR were statistically significant. In addition, log-transformed MDA showed a pattern similar to HRV indices.

**Conclusions:** The study demonstrated that physiologic and oxidative stress increased at low and high DTR with minimal stress levels around the median level of DTR indicating a physiologic comfort point.

Cao J, Cheng Y, Zhao N, Song W, Jiang C, Chen R, Kan H. Diurnal temperature range is a risk factor for coronary heart disease death. J Epidemiol 2009;19(6):328-32.

Chen G, Zhang Y, Song G, Jiang L, Zhao N, Chen B, Kan H. Is diurnal temperature range a risk factor for acute stroke death? Int J Cardiol 2007;116(3):408-9.

Kan H, London SJ, Chen H, Song G, Chen G, Jiang L, Zhao N, Zhang Y, Chen B. Diurnal temperature range and daily mortality in Shanghai, China. Environ Res 2007;103(3):424-31.

Liang WM, Liu WP, Kuo HW. Diurnal temperature range and emergency room admissions for chronic obstructive pulmonary disease in Taiwan. Int J Biometeorol 2009;53(1):17-23.

Lim Y-H, Park A, Kim H. Modifiers of diurnal temperature range and mortality association in six Korean cities. International Journal of Biometeorology 2011:1-10.

Song G, Chen G, Jiang L, Zhang Y, Zhao N, Chen B, Kan H. Diurnal temperature range as a novel risk factor for COPD death. Respirology 2008;13(7):1066-9.

Tam WW, Wong TW, Chair SY, Wong AH. Diurnal temperature range and daily cardiovascular mortalities among the elderly in Hong Kong. Arch Environ Occup Health 2009;64(3):202-6.

Okamoto-Mizuno K, Tsuzuki K, Mizuno K, Ohshiro Y. Effects of low ambient temperature on heart rate variability during sleep in humans. Eur J Appl Physiol 2009;105(2):191-7.

Park SK, O'Neill MS, Vokonas PS, Sparrow D, Schwartz J. Effects of air pollution on heart rate variability: the VA normative aging study. Environ Health Perspect 2005;113(3):304-9.

Sorensen M, Daneshvar B, Hansen M, Dragsted LO, Hertel O, Knudsen L, Loft S. Personal PM2.5 exposure and markers of oxidative stress in blood. Environ Health Perspect 2003;111(2):161-6.

Dekker JM, Schouten EG, Klootwijk P, Pool J, Swenne CA, Kromhout D. Heart rate variability from short electrocardiographic recordings predicts mortality from all causes in middle-aged and elderly men. The Zutphen Study. Am J Epidemiol 1997;145(10):899-908.

Romieu I, Castro-Giner F, Kunzli N, Sunyer J. Air pollution, oxidative stress and dietary supplementation: a review. Eur Respir J 2008;31(1):179-97.

Basu R, Samet JM. Relation between Elevated Ambient Temperature and Mortality: A Review of the Epidemiologic Evidence. Epidemiologic Reviews 2002;24(2):190-202.

McCulloch CE, Neuhaus JM. Generalized Linear Mixed Models. Encyclopedia of Biostatistics John Wiley & Sons, Ltd, 2005.

Gasparrini A, Armstrong B. The impact of heat waves on mortality. Epidemiology 2011;22(1):68-73.

Bull GM. The weather and deaths from pneumonia. Lancet 1980;1(8183):1405-8.