AN ENVIRONMENTAL AND LIFE-STYLE WIDE ASSOCIATION STUDY (ELWAS) APPROACH TO AN IMPAIRED MYOCARDIAL LEFT VENTRICULAR EJECTION FRACTION

Lars Lind[1*], Samira Salihovic[2], Bert van Bavel[2], Ulf Riserus[1], P Monica Lind[4]

[1]Acute and Internal Medicine, Department of Medicine, Uppsala University, Uppsala, Sweden, [2]MTM Research Center, School of Science and Technology, Örebro University, Örebro, Sweden, [3]Department of Public Health and Caring Sciences, Clinical Nutrition and Metabolism, Uppsala University, Uppsala, Sweden, [4]Occupational and Environmental Medicine, Department of Medicine, Uppsala University, Uppsala, Sweden

Introduction

A low myocardial left ventricular ejection fraction (EF) has previously been shown to be a poor predictor for future mortality [1]. It is seen in some patients following a myocardial infarction and in most patients with heart failure [2]. We have previously shown that a poor EF is related to high levels of PCBs (unpublished). However, exposure of environmental contaminants is in part determined by a variety of life-style factors. Recently, Chirag J. Patel and co-workers presented an attractive way to present associations between multiple measured environmental contaminants and diabetes using data from the National Health and Nutrition Examination Survey (NHANES) study [1]. They used a format commonly used in genetic studies, Genetic Wide Association Study (GWAS), and then applied this format to environmental factors, Environmental Wide Association Study (EWAS). However, although these authors included a large set of environmental factors, the impact of lifestyle was not thoroughly investigated. Thus, we propose an extension of the EWAS concept to also include major lifestyle factors in order to perform an Environmental and Lifestyle Wide Association Study (ELWAS). To study this further in an integrated way, we evaluated which environmental contaminants and life-style factors that were independently related to a low EF using an "Environmental and Life-style Wide Association Study" (ELWAS) approach.

Material and Methods

1,016 subjects, all aged 70 years, were investigated in the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study. Forty-three environmental contaminants were measured in the circulation. 11 metal elements in this study were determined in whole blood. The analysis was performed using inductively coupled plasma-sector field mass spectrometry, ICP-SFMS, after microwave-assisted digestion with nitric acid. Human serum was analyzed for levels of bisphenol A (BPA) and ten phthalate metabolites (mono-[2-ethyl-5-hydroxyhexyl] phthalate [MEHHP]; mono [2-ethyl-5-oxohexyl] phthalate [MEOHP]; mono-[2-ethylhexyl] phthalate [MEHP]; monobenzyl phthalate [MBZP]; monocyclohexyl phthalate [MCHP]; monoethyl phthalate [MEP]; monoisobutyl phthalate [MIBP]; monoisononyl phthalate [MINP]; monomethyl phthalate [MMP]; and mono-n-octyl phthalate [MOP]) at ALS Canada following the general procedures presented by the Centers for Disease Control and Prevention. Analyses of POPs were performed using a Micromass Autospec Ultima (Waters, Mildford, MA, USA) high resolution chromatography coupled to high resolution mass spectrometry (HRGC/HRMS) system. A total of 24 POPs were measured: 17 PCB congeners, 5 OC pesticides, 1 octachlorodibenzo-p-dioxin (OCDD), and 1 BDE congener. Dietary records were used to evaluate 21 nutrients. Proportions of 13 fatty acids were determined in cholesterol esters to further quantify fat quality intake. Adding 5 other important life-style factors yielded together 76 environmental and life-style factors. EF was determined by echocardiography and a low EF was defined as 50% or less.

Results and Discussion

15% of the sample showed an reduced EF. Figure 1 shows the p-values for the relationships between the 76 environmental factors and a low EF. The p-values are given as –log10. The dashed line denotes the cut-off limit for the Bonferronni-corrected p-value. As could be seen, three PCBs and Co show p-values below this critical

threshold. When all 14 environmental and life-style variables with a p-value <0.05, as shown in figure 2, entered a multiple logistic regression model also including gender, only PCB105 and Co were significant (both p<0.0002).

Conclusion: Using an ELWAS approach, high levels of PCB 105 and Co were found to be independently related to an impaired myocardial left ventricular ejection fraction at echocardiography in an elderly population.

Aknowledgements
This study was financially supported by the Swedish Research Council (VR) and the Swedish Research Council for Environment, Agricultural Sciences, and Spatial Planning (Formas).

References

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Figure 1. ”Manhattan”-type of plot showing the p-values (expressed at the –log10 scale) for 76 environmental contaminants or life-style factors vs a low ejection fraction in an “Environmental and Life-style Wide Association Study”, ELWAS. The Bonferronni-adjusted p-value as a marker of significance is given as the

broken line.

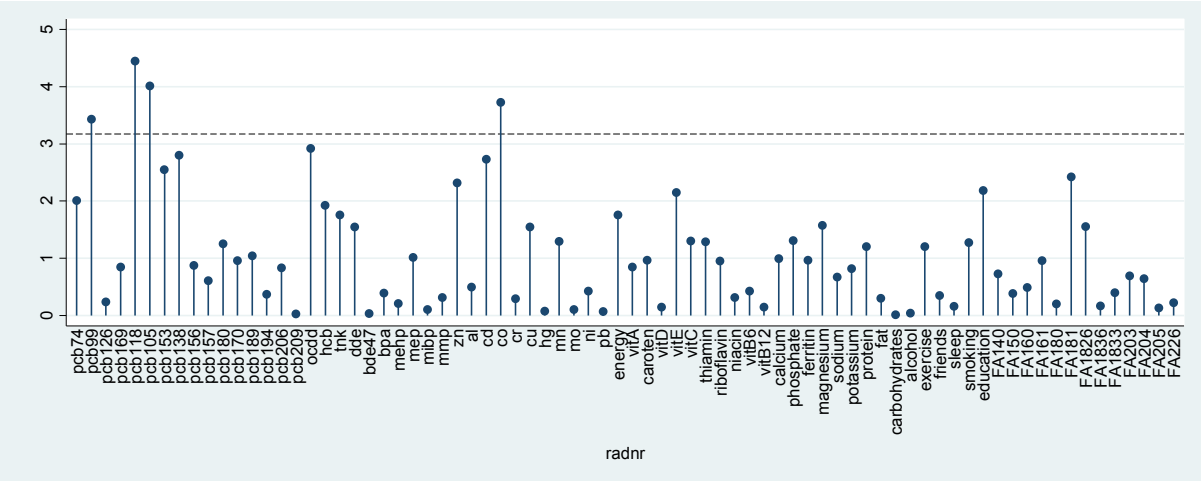
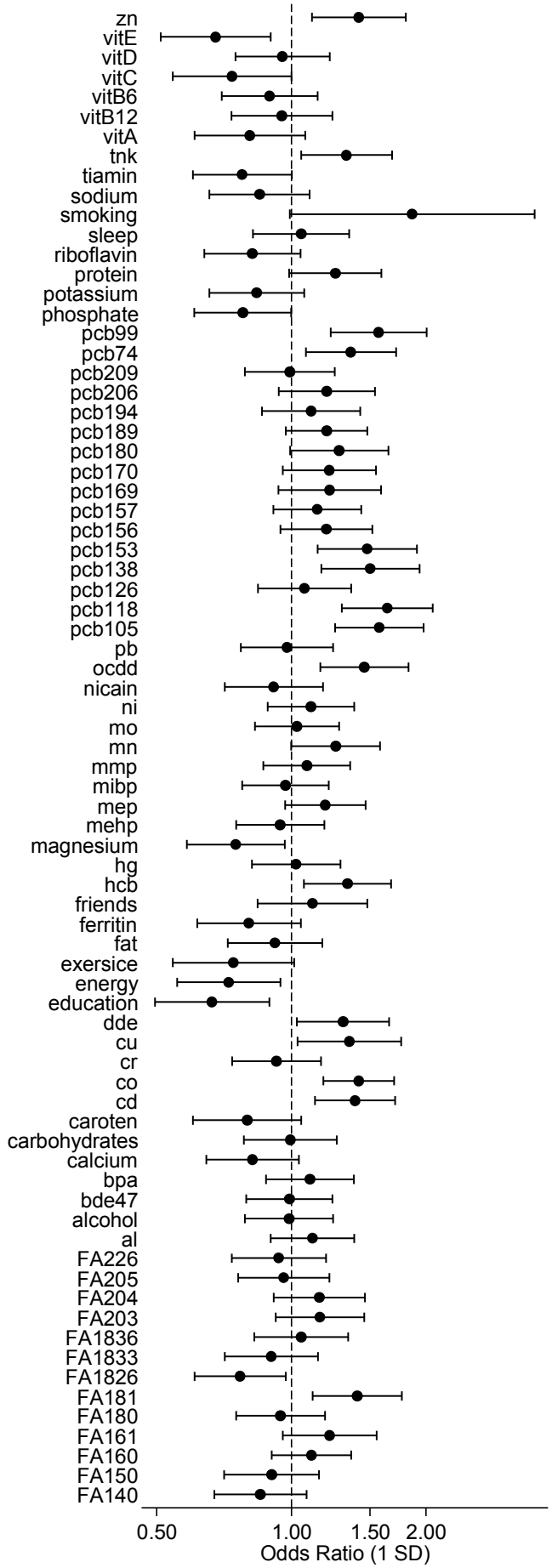


Figure 2. Forest plot showing the odds ratios (OR) and 95%CI for 1 SD change in the different environmental contaminants and the life-style factors investigated.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Odds Ratio (1 SD)