Physical Activity and the Metabolic Syndrome Association With Myocardial Infarction and Stroke

To the Editor:

In a recent analysis of data from the third National Health and Nutrition Examination Study (NHANES III), Ninomiya and colleagues\(^1\) observed a significant 2-fold increase in the multivariate likelihood of prevalent myocardial infarction and stroke among individuals with the metabolic syndrome compared with individuals without the metabolic syndrome. In this study, metabolic syndrome was defined according to the criteria of the National Cholesterol Education Program’s Adult Treatment Panel III (NCEP-ATP III). The importance of the metabolic syndrome as a predictor of atherosclerotic cardiovascular disease is becoming established. As such, and because a nationally representative sample was studied, the general findings reported by Ninomiya et al\(^1\) have public health and clinical implications for global risk assessment and primary prevention.

We are, however, concerned that the authors are drawing conclusions from incomplete analysis of the relationship under study. In separate NHANES III analyses, strong and significant inverse associations were reported between physical activity and self-reported stroke,\(^2\) and angina/myocardial infarction.\(^3\) Park et al\(^4\) also showed that physical inactivity was a significant predictor of metabolic syndrome prevalence using NHANES III data. Given these established relationships, we believe the current report by Ninomiya et al\(^1\) is incomplete because it does not include physical activity as a potential confounding factor or effect modifier of the purported association. It may very well be that a major antecedent to prevalent coronary heart disease and stroke, as well as metabolic syndrome, is physical inactivity. This is an important issue and should be examined in prospective studies with careful measurement of all variables, including physical activity.

Increasing physical activity is a primary element of the NCEP-ATP III preventive and therapeutic algorithm for metabolic syndrome. Recent American Heart Association publications underscore the importance of regular physical activity in the prevention of atherosclerotic cardiovascular disease and stroke.\(^5\) The observation of a favorable association between physical activity and cardiovascular disease is robust and consistent. Therefore, exclusion of physical activity within analytic models of risk exposures and atherosclerotic cardiovascular disease outcomes is inappropriate, especially in studies where physical activity measurements are available and have been previously related with the study variables of interest.

Michael J. LaMonte, PhD, MPH
Milton Z. Nichaman, MD, ScD
Steven N. Blair, PED
The Cooper Institute
Dallas, Tex


Response

We specifically chose not to include a physical activity variable in our analyses. The possibility of reverse causality is an inherent problem with physical activity in cross-sectional data. For example, would lower current physical activity in subjects with previous myocardial infarction (MI) or stroke reflect physical inactivity leading to cardiovascular disease or vice versa? The three references\(^1–3\) cited by LaMonte et al did not investigate this ambiguity, so we have completed additional analyses. As expected, physical inactivity in multivariate analysis was an independent predictor of MI/stroke (odds ratio, 1.56; 95% CI, 1.23 to 1.99 for the combined outcome). However, subjects with a history of MI or stroke had significantly higher odds of describing themselves as less active at the time of the study than 10 years prior (odds ratio, 1.55; 95% CI, 1.28 to 1.86; with multivariate adjustment). This suggests that prior-month physical activity measures in the Third National Health and Nutrition Examination Survey as a proxy for historical activity differentially misclassified subjects with prevalent MI/stroke as (historically) inactive. Finally, analyses adjusting for physical inactivity produced no change in the risk estimate for the metabolic syndrome: 2.04 (95% CI, 1.64 to 2.54) with adjustment versus 2.05 (95% CI, 1.64 to 2.57) without, for the combined MI/stroke outcome.

We concur with LaMonte et al that physical inactivity is a strong predictor of cardiovascular events and should be a focus of preventive efforts. However, we caution them as well as other investigators to proceed carefully in evaluating problematic exposure variables in cross-sectional data.

John K. Ninomiya, MSc
Michael H. Criqui, MD, MPH
Anthony Gamst, PhD
Department of Family and Preventive Medicine
University of California
San Diego, Calif
Gilbert L’Italien, PhD
Ingenix Epidemiology
Auburndale, Mass
Joanna L. Whyte, MS, RD, MSPH
Roland S. Chen, MD
Pharmaceutical Research Institute
Bristol-Myers Squibb
Princeton, NJ

Work by Drs Criqui and Gamst and Mr Ninomiya on the original research to which this letter refers was partially funded by Bristol-Myers Squibb. Dr L’Italien and Chen and Ms Whyte are employees of Bristol-Myers Squibb.
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Circulation. 2004;109:e314
doi: 10.1161/01.CIR.0000129350.05560.EB
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/109/22/e314

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