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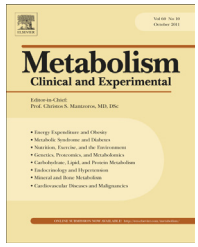

An examination of sex and racial/ethnic differences in the metabolic syndrome among adults: A confirmatory factor analysis and a resulting continuous severity score

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ABSTRACT

Objective. The metabolic syndrome (MetS) is typically diagnosed based on abnormalities in specific clustered clinical measures that are associated with increased risk for coronary heart disease (CHD) and Type 2 diabetes mellitus (T2DM). However, current MetS criteria result in racial/ethnic discrepancies. Our goals were to use confirmatory factor analysis (CFA) to delineate differential contributions to MetS by sub-group, and if contributions were discovered, develop sex and racial/ethnic-specific equations to calculate MetS severity.

Research Design and Methods. Using data on adults from the National Health and Nutrition Examination Survey 1999–2010, we performed a CFA of a single MetS factor that allowed differential loadings across groups, resulting in a sex and race/ethnicity-specific continuous MetS severity score.

Results. Loadings to the single MetS factor differed by sub-group for each MetS component ($p < 0.001$), with lower factor loadings among non-Hispanic-blacks for triglycerides and among Hispanics for waist circumference. Systolic blood pressure exhibited low factor loadings among all groups. MetS severity scores were correlated with biomarkers of future disease (high-sensitivity C-reactive-protein, uric acid, insulin resistance). Non-Hispanic-black-males with diabetics had a low prevalence of MetS but high MetS severity scores that were not significantly different from other racial/ethnic groups.

Conclusions. This analysis among adults uniquely demonstrated differences between sexes and racial/ethnic groups regarding contributions of traditional MetS components to an assumed single factor. The resulting equations provide a clinically-accessible and interpretable continuous measure of MetS for potential use in identifying adults at higher risk for MetS-related diseases and following changes within individuals over time. These

Abbreviations: AIC, Akaike's Information Criteria; ATP-III, Adult Treatment Panel III; AUC, Area under the curve; CDC, Centers for Disease Control; CFA, Confirmatory Factor Analysis; CHD, Coronary heart disease; CHF, Congestive heart failure; CVD, Cardiovascular disease; GFI, Goodness of Fit Index; Hisp, Hispanic; HOMA-IR, Homeostasis model of insulin resistance; hsCRP, High-sensitivity C-reactive protein; MetS, Metabolic syndrome; MI, Myocardial infarction; NFI, Bentler–Bonett Normed Fit Index; NHANES, National Health and Nutrition Examination Survey; NHB, Non-Hispanic Black; NHW, Non-Hispanic White; RMSEA, Root Mean Square Error of Approximation; ROC, Receiver operating characteristic; SBP, Systolic blood pressure; SRMR, Standardized Root Mean Square Residual; T2DM, Type 2 diabetes mellitus; WC, Waist circumference.

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equations hold potential to be a powerful new outcome for use in MetS-focused research and interventions.

1. Introduction

With rising rates of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM), there has been significant focus on risk prediction. One way clinicians can identify individuals at higher risk for disease progression is by assessing for the metabolic syndrome (MetS)[1,2], a cluster of cardiovascular risk factors that is associated with insulin resistance [1,3] and that correlates with underlying inflammation [4–7] and oxidative stress [7–11]—additional risk factors for CVD and T2DM. Compared to those without MetS, individuals who are classified as having MetS and followed for 10 years have an odds ratio of 1.2–1.8 for progressing to CVD [12,13] and 4.1 for progressing to T2DM [14], demonstrating its utility as a clinical tool.

Nevertheless, there are significant racial/ethnic differences in MetS that limit its use over time [15–18]. Non-Hispanic blacks have a low prevalence of MetS despite having more insulin resistance, more T2DM and more death from CVD than non-Hispanic whites [17–23]. The binary nature of MetS may contribute to these observed racial/ethnic differences, as it requires extreme values (e.g., triglycerides greater than 150 mg/dL or HDL less than 40 mg/dL for males) that may not be appropriate for all groups, particularly if certain groups have on average lower values of any of the components of MetS (e.g., lower triglyceride levels among non-Hispanic blacks)[24]. Furthermore, a binary MetS classification makes it difficult to follow for a worsening condition over time. Because of this, some have advocated for continuous scores for MetS [25]. The majority of these scores have been composed of a sum of z-scores of the various components of MetS (blood pressure, waist circumference [WC], etc.)[26–28]. This approach does not take into account weighting of how these components correlate together as a manifestation of the processes underlying MetS, nor do they take into account that such weighting may vary by sex or race/ethnicity [29–31].

Our goal was to examine the differences between sexes and among racial/ethnic groups with respect to how the traditional MetS components correlate with a single MetS "factor" via a confirmatory factor analysis, utilizing data from adults in the National Health and Nutrition Examination Survey (NHANES). Rather than explore whether or not there are multiple factors or examine whether additional components should be added to MetS, we instead operated under the framework that a single metabolic syndrome exists and is made up of the components utilized in common definitions such as the Adult Treatment Panel III (ATP-III)[1,32]—namely WC, systolic blood pressure (SBP), triglycerides, HDL-cholesterol, and fasting blood glucose. Such a statistical exploration then would not only allow for an examination of sex- and racial/ethnic differences in how these components correlate with the hypothesized single MetS factor, but it also would take into account any observed differences in producing a continuous MetS score from this analysis — thus providing in essence a sex- and race/ethnicity-specific risk or severity score that can be followed over time in individuals either clinically or in research settings. Our hypothesis was that the contribution of MetS components to such a factor would vary by sex and race/ethnicity in a way that could improve on correlations between MetS and clinically-relevant measures related to insulin resistance, CVD risk and disease diagnosis.

2. Methods

Data were obtained from NHANES (1999–2010), a complex, multistage probability sample of the US population [33]. These annual cross-sectional surveys are conducted by the National Center for Health Statistics (NCHS) of the Centers for Disease Control (CDC), with randomly-selected subjects undergoing anthropometric and blood pressure measurements, answering questionnaires and undergoing phlebotomy. The NCHS ethics review board reviewed and approved the survey and participants gave informed consent prior to participation. WC, SBP, and laboratory measures of triglycerides, HDL-cholesterol, and fasting glucose were obtained using standardized protocols and calibrated equipment [33]. For SBP, the mean of up to four readings taken on each individual was used. All blood samples used for analyses were obtained following a fast $\geq$8 h prior to the blood draw.

Data from non-Hispanic-white, non-Hispanic-black, or Hispanic (Mexican-American/other Hispanic) participants 20–64 years old were analyzed. For the initial confirmatory factor analysis described below, participants were excluded if they were pregnant, had known diabetes or unknown diabetes (fasting plasma glucose >125 mg/dL), or were taking anti-hyperlipidemic or anti-diabetic medications all of these situations all likely to alter lipid and insulin levels. For the confirmatory factor analysis, individuals who reported having congestive heart failure (CHF) or coronary heart disease (CHD), or ever having had a myocardial infarction (MI) or a stroke, were also excluded.

We combined all data sets from the 6 two-year cycles (1999–2010) for statistical analyses to increase sample size. Prevalence rates of MetS were calculated by sex, race/ethnicity, and age group, according to ATP III criteria [1], and mean levels (95% CIs) of the MetS components of interest (WC, SBP, HDL, triglycerides, and glucose) as well as the surrogate outcomes (hsCRP, uric acid, homeostasis model of insulin resistance [HOMA-IR] [3]) were calculated by sex, race/ethnicity, and age group.

The general methods for the formulation of this score have been reported previously [29]. The previous study [29] found racial/ethnic as well as sex differences in the how traditional components are correlated with MetS, among adolescents ages 12–19. We felt it essential to validate these findings and examine if similar differences were found among adults, when MetS and its ability to predict future disease are more