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Risk of coronary heart disease associated with metabolic syndrome and its individual components in Iranian subjects: A matched cohort study

Alireza Esteghamati, MD*, Nima Hafezi-Nejad, MPH, MD, Sara Sheikhbahaei, MPH, MD, Behnam Heidari, MPH, MD, Ali Zandieh, MPH, MD, Maryam Ebadi, MD, Manouchehr Nakhjavani, MD

Endocrinology and Metabolism Research Center, Vali–Asr Hospital, School of Medicine, Tehran University of Medical Sciences, PO Box 13145–784, Tehran, Iran

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BACKGROUND AND OBJECTIVES: To evaluate the risk of coronary heart disease (CHD) associated with metabolic syndrome (MetS) and its individual components in a representative sample of diabetic and nondiabetic Iranians. Moreover, we aimed to define the most hazardous MetS components.

METHODS: Two cohorts consisting of 1737 nondiabetic and 2385 diabetic participants were followed for the first CHD event during 8.5 years (until December 2013).

RESULTS: MetS is defined as having 3 individual components associated with increased risk of CHD (hazard ratio [HR] for MetS: in the unadjusted were 2.85 [2.27–3.57] and in the fully adjusted model 1.80 [1.42–2.28]). MetS was associated with lower hazard of CHD in subjects older than 65 (HR: 1.50 vs. 3.47; P for interaction $< .05$) and in men (HR: 1.68 vs. 4.87; P for interaction $< .05$). Presence of 4 of 5 individual MetS components increased the risk of CHD associated with MetS as a constellation. The value of MetS is augmented in the presence of low high-density lipoprotein-cholesterol (HR: 5.74 [2.52–13.08]) versus its absence (HR 1.91 [1.33–2.75]), high triglycerides (HR: 3.39 [1.38–8.34] vs. 1.99 [1.40–2.82] in its absence) and elevated blood pressure (HR: 2.61 [1.43–4.76] vs. 1.80 [1.26–2.58] in its absence).

CONCLUSIONS: We address the value of MetS components in the prediction of CHD and in the absence of traditional risk factors. This study provides evidence for the synergistic effect of MetS components on the incidence of CHD.

Metabolic syndrome (MetS) is recognized as clustering of a number of components including hypertension, hypertriglyceridemia, low serum high-density lipoprotein cholesterol (HDL-C), impaired glucose metabolism (IGM), and abdominal obesity. It has been tightly linked to thrombotic vascular events including coronary heart disease (CHD).[1] Worldwide prevalence of MetS is on the rise.[2] MetS is responsible for up to one fourth of the CHD events[2,3]; however, early management of MetS is an effective strategy in the prevention of CHD.[4]

Knowledge of region-specific cardiometabolic risk factors is essential for health care decision-making.[2,5,6] Numerous studies have evaluated the MetS-CHD association worldwide.[1,3,7,8] However, literature is contentious

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* Corresponding author.
E-mail address: esteghamati@tums.ac.ir

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regarding the issue in developing countries, specifically among West Asian populations. Interestingly, Asian populations have been reported to manifest greater susceptibility to the adverse effects of MetS.[9–11] Calls for studies revealing the epidemiology of cardiometabolic risk factors in the region have been made in recent years.[2,6]

Iran's epidemiology of disease has changed in recent years. Noncommunicable diseases and their risk factors are emerging.[12] MetS-related disorders are on the rise.[9] Nevertheless, only a limited number of studies, with shortcomings in their evaluations, have assessed the prospective impact of MetS on CHD in the region.[13,14] Importantly, no previous longitudinal study has examined the issue in diabetic subjects. Moreover, the differential clustering of the MetS components and its relation with CHD is not clearly understood, and the population who bears the highest hazard for CHD development in the presence of MetS has not been fully recognized.

The objective of this study was to evaluate the risk of CHD associated with MetS and its individual components in a representative sample of Iranians. We aimed to investigate the risk of CHD according to the MetS definition, in both the presence and absence of traditional risk factors and of individual MetS components to reveal the characteristics that modify the impact of MetS on CHD.

Methods

Study population

This study is part of an ongoing Iranian prospective cohort. The primary goal of the survey was to reveal the determinants and the outcomes of the cardiometabolic syndrome in a representative population of Tehran (the capital of Iran). Systematic subject recruitment for research purposes started in January 2005 with the aid of 4 health surveillance centers located in the center, east, west, and south of Tehran. The surveyed population comprised residents who were under the coverage of 1 of the 4 health surveillance centers, and thus were participating in the health surveys of the corresponding health centers. Multiple cross-sectional studies demonstrated the characteristics of a selected sample of the original cohort, during years of follow-up.[10,15–17] The current study only includes subjects who were at least 40 years old and the follow-up end point was set as the end of 2013. Details on the sampling and extrapolation of the data to the general population are described elsewhere.[10,15] The original cohort consisted of 2 subcohorts of diabetic and nondiabetic community-dwelling participants. Subjects with newly diagnosed diabetes in the entry examination comprised the diabetic subcohort. The rest of the participants were included in the nondiabetic subcohort. Subjects with type 1 diabetes, pancreatitis-related diabetes, and malignant conditions (including diabetes in the setting of pancreatic cancer) were not included in the diabetic cohort. Diabetic subjects began their treatment by lifestyle modification, glibenclamide, and/or metformin. Details on the baseline investigations and the characteristics of the included participants have been described previously.[10,15] Overall, 5893 subjects had available follow-ups until the end of 2013. Less than 0.5% (0.005) of all variables was missing, and baseline characteristics of those with missed values were not different from the baseline cohort. Finally, data from 4122 subjects (who were at least 40 years old) consisting of 1737 nondiabetic and 2385 diabetic subjects were analyzed. The mean follow-up period was 8.5 years, which accounted for a maximum follow-up of approximately 35,000 person-years. The study protocol was approved by the review board of the Endocrinology and Metabolism Research Center, Tehran University of Medical Sciences, according to the Declaration of Helsinki.

Data collection and laboratory investigation

Demographic data including age, gender, and medication were obtained through interviews. Weight and height were measured in light clothing without shoes for each participant. Waist circumference was measured at the midpoint between iliac crest and the lower rib with the patient in the standing position and after normal expiration. The obtained values were then rounded to the nearest 0.1 cm. Systolic and diastolic blood pressures were measured using standard mercury sphygmomanometers after 10 minutes of resting in supine position. After at least 12 hours' overnight fasting, venous blood samples were collected for biochemical measurements. Fasting plasma glucose was determined using glucose oxidase method. Lipid profile including total cholesterol, triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and HDL-C were measured by the direct enzymatic method (Parsazmun, Karaj, Iran). Radioimmunoassay was used to measure plasma insulin with no cross-reactivity for the employed antibody, pro-insulin, and C-peptide (Immunotech, Prague, Czech Republic). Hemoglobin A1c was determined by high-performance liquid chromatography (DS5 Pink kit; Drew, Marseille, France). C-peptide and creatinine were measured using radioimmunoassay (Immunotech) and the Jaffe method (Parsazmun), respectively.

Outcome measures and definitions

For the current study, the first CHD event was set as the outcome. Outcome ascertainment was performed in accordance with the established protocols[18] and similar to our previous experiences.[16,17] A CHD event was defined as episodes of recognized or unrecognized myocardial infarction, angina pectoris, coronary insufficiency, or CHD death. For subjects with events, the date of the event was recorded as the end point, whereas the date of the last visit was set as the end point for nonevents and censored cases. In our study, all of the included subjects were under health surveillance of our associated health centers. Included