Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation

Clinical associations between metabolic syndrome and the development of microalbuminuria in Korean men

Jae-Hong Ryoo[a], *Hyejin Chun*[b], *Hong-Soo Lee*[c], *Eunkyung Suh*[d], *Joong-Myung Choi*[a], *Min-Gi Kim*[e], *HoCheol Shin*[f], *Sung Keun Park*[a,g,*], *Chang-Mo Oh*[h], *Taeg Su Ko*[i]

[a] *Department of Preventive Medicine, School of Medicine, Kyung Hee University, Seoul, Republic of Korea*
[b] *Health Promotion Center, Ewha Womans University Mokdong Hospital, Ewha Womans University School of Medicine, Seoul, Republic of Korea*
[c] *Department of Family Medicine, Ewha Womans University Mokdong Hospital, Ewha Womans University School of Medicine, Seoul, Republic of Korea*
[d] *Department of Family Medicine, CHAUM, CHA University School of Medicine, Pocheon, Republic of Korea*
[e] *Department of Occupational and Environmental Medicine, Dongguk University, Gyeongju Hospital, Seoul, Republic of Korea*
[f] *Department of Family Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University, School of Medicine, Seoul, Republic of Korea*
[g] *Total Healthcare Center, Kangbuk Samsung Hospital, Sungkyunkwan University, School of Medicine, Seoul, Republic of Korea*
[h] *Korea Institute of Drug Safety and Risk Management, Seoul, Republic of Korea*
[i] *Department of Orthopaedic Surgery, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea*

ARTICLE INFO

Article history:
Received 9 April 2014
Received in revised form
7 October 2014
Accepted 25 December 2014
Available online 15 January 2015

Keywords:
Metabolic syndrome
Microalbuminuria
Urine albumin creatinine ratio

ABSTRACT

Aims: There have been several studies on the association between metabolic syndrome (MetS) and microalbuminuria. However, none has examined whether MetS is associated with the prospective development of microalbuminuria. Accordingly, we performed a prospective study to evaluate the longitudinal effects of baseline number of MetS traits on the development of microalbuminuria in Korean men.

Methods: 1649 Korean men without microalbuminuria in 2005 were included and followed prospectively until 2010 with the endpoint being the development of microalbuminuria. MetS was defined according to the joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention. Microalbuminuria was evaluated by urine albumin creatinine ratio (UACR). Risk estimations for development of microalbuminuria were analyzed according to the number of MetS traits using multivariate adjusted Cox proportional hazards model.

* Corresponding author at: Total Healthcare Center, Kangbuk Samsung Hospital, Sungkyunkwan University, School of Medicine, 78 Saemunan-gil, Jongro-Gu, Seoul, Korea 110-746. Tel.: +82 10 3377 6314; fax: +82 2 2001 2626.
E-mail address: kkkmin7@hotmail.com (S.K. Park).

Abbreviations: UACR, urine albumin creatinine ratio; MetS, metabolic syndrome; BP, blood pressure; LDL, low-density lipoprotein; HDL, high-density lipoprotein; BMI, body mass index; HOMA-IR, homeostasis model assessment of insulin resistance; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ-glutamyltransferase; eGFR, estimated glomerular filtration rate; SCr, serum creatinine; CVD, cardiovascular disease; CKD, chronic kidney disease; CRP, C-reactive protein; ACE i, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II receptor blocker.

http://dx.doi.org/10.1016/j.diabres.2014.12.005

Results: During 5611.8 person-years of follow-up (median 3.40 ± 1.46 years), microalbuminuria developed in 91 (5.5%) participants between 2006 and 2010. After adjusting for multiple covariates, the hazard ratios (95% confidence interval) for development of microalbuminuria comparing 1, 2 and 3–5 MetS traits *vs* 0 were 2.57 (0.97–6.82), 2.94 (1.09–7.98) and 3.85 (1.37–10.86), respectively.

Conclusions: The number of MetS traits independently associated with the future development of microalbuminuria during the 5-year follow-up period, and MetS per se was an independent risk factor for microalbuminuria.

1. Introduction

Metabolic syndrome (MetS) is defined as the presence of at least three of the following traits, with or without diabetes: abdominal obesity, elevated triglyceride, decreased HDL cholesterol, elevated fasting glucose (insulin resistance) and elevated blood pressure [1]. The prevalence of MetS is increasing in many countries. With an increasingly sedentary lifestyle and high rates of obesity exceeding 30% in most age and gender groups, the prevalence of MetS in Korea increased from 24.9% in 1998 to 31.3% in 2007 [2]. The central feature of MetS is insulin resistance, which results in hyperglycemia and hyperinsulinemia, and may eventually leads to the development of diabetes [3]. MetS, a cluster of several cardiovascular risk factors linked to obesity and insulin resistance, has received increasing attention as a risk factor for cardiovascular disease (CVD) and mortality [4] and maybe used as a predictive tool of future CVD risk. However, others have stated that MetS does not predict more than the sum of its traits, and a major criticism has been raised that MetS is neither associated with CVD nor all-cause mortality [5]. A recent meta-analysis concluded that the ability of currently used definitions of MetS to predict CVD and mortality may be limited [6].

The term 'microalbuminuria', which is defined as the urine albumin creatinine ratio (UACR) range within 30–300 mg/g, first appeared in a medical document written by Svendsen et al. [7]. Microalbuminuria was initially used in the evaluation and management of diabetic nephropathy [8]. Microalbuminuria is highly predictive of future overt proteinuria in diabetic patients. Recently however, studies have shown that microalbuminuria is not only a renal risk factor but is also a powerful predictor of CVD in both diabetic and non-diabetic subjects [7,8]. It has also been shown to be an indicative marker of asymptomatic cerebral ischemic lacunar infarcts observed on neuroimaging [9]. More recently microalbuminuria has been extensively regarded as a marker of generalized vascular endothelial impairment even in non-diabetic populations [10] and is reported to have a close association with CVD. The HOPE study indicated that there was no evident threshold of UACR for the risk of CVD [11] and showed a graded relationship between UACR and cardiovascular events, indicating that patients are at increased risk even before UACR reaches the currently accepted thresholds for microalbuminuria. The risk of major cardiovascular events was increased by 5.9% for each increment of 3.01 mg/g (equivalent to 0.4 mg/mmol) in microalbuminuria.

The relationship between MetS and microalbuminuria or proteinuria and chronic kidney disease (CKD) has been investigated in several cross-sectional studies [12–18]. Microalbuminuria in patients with MetS in the absence of diabetes would cause a pro-inflammatory milieu that would result in a greater prevalence of subclinical atherosclerosis and development of CVD [19]. An increasing body of evidence supports the contributory role of microalbuminuria in the prediction of CVD and all-cause mortality. Microalbuminuria represents an important intermediate endpoint of CVD risk in patients with MetS. Thus, considering the inclusion of microalbuminuria as a MetS component or testing microalbuminuria in the follow-up of MetS patients has been debated. It is still controversial whether MetS components directly influence microalbuminuria in healthy men. In other words, it is unclear whether MetS is a cause or a consequence of microalbuminuria. To our knowledge there are little data available on whether MetS traits directly influence microalbuminuria. For this reason we performed a prospective study to assess whether MetS was associated with the risk of developing microalbuminuria. We also aimed to assess whether the risk of developing microalbuminuria increase progressively with the number of MetS traits.

2. Materials and methods

2.1. Study design

A prospective cohort study was conducted in order to investigate the association baseline number of MetS traits and the development of microalbuminuria. Study participants consisted of Korean men undergoing a medical health check-up program at the Health Promotion Center of Kangbuk Samsung Hospital, Sungkyunkwan University, Seoul, Korea. The study methods have been described in detail previously [20].

The purpose of the medical health check-up program is to promote health of the employees and to enhance early detection of existing diseases. All employees participate in either annual or biennial health check-up, as required by the Industrial Safety and Health law in Korea. Most of the study population is the employees and family members of various companies from all around the country. Costs of the medical examinations are largely paid by their employers. We took advantage of this opportunity to conduct a follow-up study.

2.2. Study population

A total of 4802 men who had an UACR measurement as part of a medical check-up in 2005 participated in this study. Among