The metabolic syndrome and chronic kidney disease in a Southeast Asian cohort

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US adults with metabolic syndrome, as defined by National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria, have been shown to be at increased risk of chronic kidney disease (CKD), but there is limited information in other populations. The relationship between metabolic syndrome and CKD (defined as estimated glomerular filtration rate <60 ml/min/1.73 m^2) was examined in a Southeast Asian cohort. This relationship was examined when the subjects ($n=3195$) were initially recruited in a cross-sectional analysis. The risks of developing new CKD associated with metabolic syndrome were also examined prospectively in a subgroup ($n=2067$) without CKD at entry after 12 years follow-up. Metabolic syndrome was defined according to both NCEP ATP III and the new International Diabetes Federation (IDF) criteria. The prevalence of CKD was 1.6%, and the incidence of new CKD was 6.3%. Metabolic syndrome by NCEP ATP III definition was associated with the increased risk of CKD at baseline (adjusted odds ratio (OR) 2.48 and 95% confidence interval 1.33–4.62), and of developing new CKD at follow-up (adjusted OR 1.62 and 95% confidence interval 1.00–2.61). There was a significant graded relationship between the number of metabolic syndrome components present and risk of CKD. By contrast, metabolic syndrome by IDF definition was not associated with increased risk of CKD. These results suggest the relationship between CKD and metabolic syndrome in a Southeast Asian population is highly dependent on the criteria used to define metabolic syndrome.

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Individuals with metabolic syndrome are at increased risks for developing cardiovascular diseases, stroke, and cardiovascular mortality.[1] Although the concept of metabolic syndrome is widely used, several definitions of the syndrome exist. These definitions agree on the essential components of metabolic syndrome, but differ in the criteria used in the classification. In 2001, the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) recommended the use of five variables such that individuals with any three or more out of five components are classified as having metabolic syndrome. A modified NCEP definition with a lower cutoff threshold for waist circumference has been recommended in Asian populations.[2]

More recently, the International Diabetes Federation (IDF) has proposed a new definition of metabolic syndrome.[3] The IDF definition retained four of the five NCEP ATP III criteria, but decreased the threshold for high fasting glucose.[4] In addition, the IDF definition requires the presence of obesity using an ethnic-origin-specific threshold for waist circumference plus any two or more of the other four components. Although the IDF definition aims to produce a single, universally accepted diagnostic tool to address both clinical and research needs, more information is required about its role in predicting clinical events in prospective settings.

Changes in lifestyle and diet have led to an increase in prevalence of metabolic syndrome in many parts of the world including Asia.[5] In China alone, 64 million people are currently estimated to have metabolic syndrome.[6] Globally, a rise in the incidence of chronic kidney disease (CKD) and end-stage renal disease in recent years paralleled increasing prevalence of metabolic syndrome.[1,7] Both cross-sectional[8] and prospective[9] studies of US adults have demonstrated that individuals with metabolic syndrome are at increased risk of CKD. However, there are sparse data on the risks of CKD associated with the metabolic syndrome in the non-US populations. The present report will examine the relationship between CKD and metabolic syndrome as differently defined by either NCEP or IDF in a specific Southeast Asian cohort. We will examine this relationship both cross-sectionally, with regards to the prevalence of CKD when the subjects were

initially recruited and prospectively, with regards to the incidence of new CKD after 12 years of follow-up.

RESULTS

Baseline characteristics

All subjects. Seventy-five subjects were on antihypertensive therapy. No subjects were taking HMG-Co A reductase inhibitors. Figure 1a shows the frequencies of metabolic syndrome and the number of metabolic syndrome components present among the 3195 subjects with complete baseline data in 1985. Overall, 13.2% had metabolic syndrome by NCEP ATP III criteria (METS-NCEP$_{ATP\ III}$), 19.4% had METS-NCEP$_{Mod}$, and 12.2% had METS-IDF, respectively.

New CKD subgroup. In the 1997 survey, 145 subjects had died and 301 subjects were lost to follow-up. A total of 682 subjects were excluded because they either had CKD at entry or incomplete follow-up data. Figure 1b shows the frequencies of metabolic syndrome and the numbers of metabolic syndrome components present at entry in the 2067 subjects with complete data included in the *New CKD subgroup*. In this subgroup, 11.0% had METS-NCEP$_{ATP\ III}$, 16.9% had METS-NCEP$_{Mod}$, and 10.6% had METS-IDF at baseline.

Table 1 presents the baseline characteristics of all subjects and the *New CKD subgroup* by metabolic syndrome status at entry. Subjects with METS-NCEP$_{ATP\ III}$ were older, and had higher proportion of men compared with subjects without, in all subjects and in the *New CKD subgroup*.

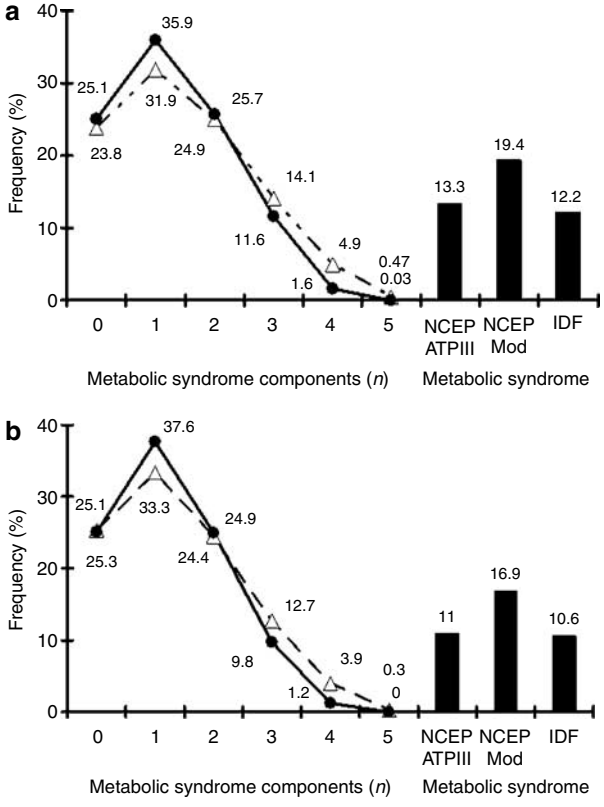

Figure 1 | Distribution of metabolic syndrome components. The proportion with metabolic syndrome and the number of metabolic syndrome components at entry among (**a**) all subjects ($n = 3195$) and (**b**) New CKD subgroup ($n = 2067$). The number of components shown according to ATP III criteria (solid line, solid circles) or modified criteria (dash line, open triangle). Filled columns denote frequency of metabolic syndrome by different definitions. NCEP$_{ATP\ III}$, metabolic syndrome by NCEP ATP III criteria; NCEP$_{Mod}$, NCEP modified criteria; IDF, IDF criteria.

Relationship between metabolic syndrome and the prevalence of CKD at baseline

Among all subjects, there was 1.6% who had CKD at baseline. Figure 2a shows the prevalence of CKD by different definitions of the metabolic syndrome. The prevalence of CKD was increased in subjects with METS-NCEP$_{ATP\ III}$ or METS-NCEP$_{Mod}$ compared with subjects without ($P < 0.01$ for each). By contrast, subjects with METS-IDF did not have increased prevalence of CKD.

Table 2 shows odds ratios (ORs) for the prevalence of CKD in all subjects at baseline associated with individual component, and with different definitions of metabolic syndrome. In the unadjusted model, high blood pressure (BP), high triglycerides (TG), and high fasting glucose (FG)-NCEP were associated with increased odds of CKD at baseline. After adjustment for age, sex, and smoking status, the prevalence of CKD at entry depended on high BP, METS-NCEP$_{ATP\ III}$, and METS-NCEP Mod. METS-IDF was not associated with increased risk for CKD. Figure 3a showed that the adjusted ORs of prevalence of CKD increased with the numbers of components of metabolic syndrome present (P for trend < 0.05 for both NCEP ATP III and NCEP Modified definitions).

Relationship between metabolic syndrome and the incidence of new CKD at follow-up

New CKD developed in 6.3% after 12 years. Figure 2b shows the incidence of new CKD at follow-up by different definitions of metabolic syndrome at entry. The incidence of new CKD was higher in subjects with METS-NCEP$_{ATP\ III}$ or METS-NCEP$_{Mod}$ compared with subjects without ($P < 0.05$ for each). By contrast, subjects with METS-IDF did not have significantly increased incidence of new CKD.

Table 3 shows ORs for the development of new CKD associated with individual component, and with different definitions of metabolic syndrome. In the unadjusted model, high TG and high FG -NCEP were associated with increased risk for new CKD. After adjustment for age, sex, and smoking status, the development of new CKD at follow-up was associated with high FG-NCEP and METS-NCEP$_{ATP\ III}$. Subjects with METS-NCEP$_{Mod}$ had 1.3-fold increased risk of new CKD, but this was not significant ($P = 0.16$). Subjects with METS-IDF had no increased risk for developing new CKD. Figure 3b showed that the adjusted ORs of new CKD incidence increased with the numbers of components of metabolic syndrome present at baseline (P for trend < 0.05 for both NCEP ATP III and NCEP Modified definitions).