METS-IR, a novel score to evaluate insulin sensitivity, is associated with the urinary albumin–creatinine ratio in Chinese adults: A cross-sectional REACTION study

Wanlu Su

Nankai University <https://orcid.org/0000-0003-0811-9957>

Jie Wang

Chinese PLA General Hospital

Songyan Yu

Beijing Tiantan Hospital

Kang Chen

Chinese PLA General Hospital

Wenhua Yan

Chinese PLA General Hospital

Zhengnan Gao

Dalian Municipal Central Hospital Affiliated of Dalian Medical University

Xuelei Tang

The First Hospital of Lanzhou University

Qin Wan

Affiliated Hospital of Luzhou Medical College

Zuojie Luo

The First Affiliated Hospital of Guangxi Medical University

Guang Ning

Shanghai Jiaotong University

Yiming Mu (✉ muyiming@301hospital.com.cn)

Chinese People's Liberation Army General Hospital <https://orcid.org/0000-0002-3344-3540>

Research

Keywords: urinary albumin–creatinine ratio, metabolic score for insulin resistance, cardiovascular disease, age, sex

Posted Date: August 4th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-731268/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Version of Record: A version of this preprint was published at Journal of Diabetes Investigation on February 26th, 2022. See the published version at <https://doi.org/10.1111/jdi.13782>.

Abstract

Background

The metabolic score for insulin resistance (METS-IR) is a novel noninsulin-based metabolic index used as a substitution marker of insulin resistance. However, whether METS-IR is associated with the urinary albumin–creatinine ratio (UACR) is not well known. Therefore, we explored the associations between METS-IR and UACR and compared the discriminative ability of METS-IR and its components for elevated UACR.

Methods

This study included 37,290 subjects. METS-IR was calculated as follows: $(\ln [2 \times \text{fasting blood glucose (FBG)} + \text{fasting triglyceride level (TG)}]) \times \text{body mass index (BMI)} / [\ln (\text{high-density lipoprotein cholesterol (HDL-C)})]$. Participants were divided into four groups on the basis of METS-IR: <25%, 25%–49%, 50%–74%, and $\geq 75\%$. Logistic regression analyses were conducted to determine the associations between METS-IR vs. its components (FBG, TG, BMI, and HDL-C) with UACR.

Results

Participants with the highest quartile METS-IR presented a more significant trend towards elevated UACR than towards its components (odds ratio [OR]: 1.260, 95% CI: 1.152–1.378, $P < 0.001$ in all subjects; OR: 1.321, 95% CI: 1.104–1.579, $P = 0.002$ in men; OR: 1.201, 95% CI: 1.083–1.330, $P < 0.001$ in women). There were significant associations between METS-IR and UACR in younger participants (<65 years for women and 55–64 years for men). Increased METS-IR was significantly associated with UACR in men with $\text{FBG} \geq 5.6 \text{ mmol/L}$ or postprandial blood glucose $\geq 7.8 \text{ mmol/L}$ and systolic blood pressure $\geq 120 \text{ mmHg}$ or diastolic blood pressure $\geq 80 \text{ mmHg}$. The relationships were significant in women with diabetes and hypertension.

Conclusions

Increased METS-IR was significantly associated with elevated UACR, and its discriminative power for elevated UACR was superior to that of its components. This findings support the clinical significance of METS-IR for evaluating renal function damage.

Background

Increased urinary albumin–creatinine ratio (UACR) has been regarded a marker of early kidney dysfunction and an independent factor for cardiovascular disease (CVD) risk [1]. An elevated UACR is more closely associated with increased CVD risk than with the estimated glomerular filtration rate (eGFR) in patients with diabetes [2]. In addition, elevated fasting blood glucose (FBG) level, hyperlipidaemia, and obesity are not only associated with CVD but also with chronic kidney disease (CKD) [3–6]. Compelling evidence confirmed that dyslipidaemia, including high levels of low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), and triglycerides (TG) and low levels of high-density lipoprotein cholesterol (HDL-C), is the cornerstone of arteriosclerosis and is an important risk factor for the progression of CKD and CVD [7–10]. Moreover, both diabetes and albuminuria are risk factors for CVD, and the morbidity of microalbuminuria (MAU) remarkably increased in people with diabetes [11,12].

Insulin resistance (IR) plays roles in the pathophysiology of dyslipidaemia, obesity, type 2 diabetes mellitus (T2DM), and MAU [9,13,14]. Many studies found that IR is a major risk factor for CVD events and has strong relationships with other risk factors for CVD (inflammation, dyslipidaemia, and hypertension) via various pathophysiologic mechanisms [13,14]. The routine assessment of IR may probably hold great significance in preventing a global pandemic and reducing the socioeconomic burden. The homeostatic model assessment of the IR index has been widely used for IR evaluation in clinical practice [15]. However, this index has limitations, including variability depending on the utilised technique, low practicality, and invasiveness.

Compared with other noninsulin-based IR indices, the novel surrogate of IR, namely, the metabolic score for IR (METS-IR) [3], demonstrates a higher concordance with the euglycemic–hyperinsulinemic clamp and its components, including the TG, HDL-C, and FBG levels and body mass index (BMI), and has strong predictive abilities for CVD risk [3]. IR is a key factor connecting CVD and increased UACR. However, information is limited on the association of METS-IR with UACR. Therefore, the current study

evaluated the association between METS-IR and UACR and compared it with the associations between FBG level, BMI, and HDL-C level with UACR in the Chinese population.

Material And Methods

Participants

This study was a sub-study of the REACTION study ("Risk Evaluation of cAncers in Chinese diabeTic Individuals: a lONgitudinal" study), which was designed to investigate the association of prediabetes and T2DM with the risk of cancer among Chinese adults [16]. The REACTION study was conducted on individuals aged over 40 years in centres across mainland China from 2011 to 2012. A total of 47,808 participants from seven regional centres (Guangzhou, Zhengzhou, Dalian, Luzhou, Lanzhou, Shanghai, and Wuhan) were included in this study. We excluded participants (1) diagnosed with primary kidney disease at baseline (n = 4,050), (2) who used lipid-lowering drugs or angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (n = 2,174), (3) had incomplete clinical or demographic data (n = 873), or (4) used hypoglycaemic drugs and insulin (n = 3,421). Finally, 37,290 subjects were included in the present study.

Social, clinical, and biological parameters

All participants were administered a detailed questionnaire on their lifestyle, medical history, and medication use and subsequently underwent anthropometric assessments according to standardised procedures. Medical history included history of T2DM, hypertension, kidney disease, CVD (including stroke, myocardial infarction, and coronary artery disease), and drug use. Smoking habits were categorised as a history of never smoking, currently smoking (frequently: smoking one or more cigarettes daily; occasionally: smoking less than seven cigarettes weekly), or formerly smoking (had already quit smoking for at least half a year). Drinking habits were categorised as a history of never drinking, currently drinking (frequently: drinking more than once a week; occasionally: drinking less than once a week), or formerly drinking (had already quit drinking for at least half a year).

Height (cm), weight (kg), and waist circumference (WC; cm) were measured by trained nurses. Subjects were required to take off their shoes during height measurements. WC was measured between the inferior margin of the 12th rib and the top of the iliac crest in the horizontal plane. BMI was calculated as the ratio of the body weight in kilograms and the squared body height in meters (kg/m²). Blood pressure (BP) and resting heart rate (RHR) were measured sequentially three times with 1 min intervals each. The three measurement results of diastolic BP (DBP) and systolic BP (SBP) were averaged for analysis.

Blood samples were collected by venepuncture after a 10 h overnight fast. A 75 g oral glucose tolerance test was then performed. Biochemical parameters included FBG, 2 h post-load blood glucose (PBG), TC, LDL-C, HDL-C, TG, aspartate transaminase (AST), gamma-glutamyl transferase (GGT), alanine transaminase (ALT), serum creatinine, and glycosylated haemoglobin (HbA1c). The biological parameters were assayed by quality control procedures. The eGFR (mL/min/1.73 m²) was calculated according to the following formula: $eGFR = 186 \times (\text{serum creatinine} \times 0.011)^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ if female}) \times 1.233$, where serum creatinine was presented in $\mu\text{mol/L}$. The procedure used the Modification of Diet in Renal Disease, which was recalibrated for the Chinese population [17].

Definition of variables

According to the self-reported questionnaires, history of hypertension and history of diabetes were defined as documented hypertension at baseline and documented diabetes at baseline, respectively. Urinary albumin and creatinine concentrations were determined in the first-void sterile urine specimens collected early in the morning. UACR was defined as the ratio of the urinary albumin concentration to the urinary creatinine concentration, which was divided into two groups: $UACR \geq 30 \text{ mg/g}$ or $UACR < 30 \text{ mg/g}$. METS-IR was calculated using the following formula: $(\ln [2 \times \text{FBG} \{ \text{mg/dL} \} + \text{TG0} \{ \text{mg/dL} \}] \times \text{BMI}) / (\ln [\text{HDL-C} \{ \text{mg/dL} \}])$ [3]. The METS-IR index was divided by quartiles.

Statistical analysis

All statistical analyses were performed using SPSS 24.0 (IBM, Chicago, IL, USA). We used one-way analysis of variance to compare the distinctions among the continuous variables of the four groups. The least significant distinction was compared using the multiple comparison test, and continuous variables were expressed as means $\pm$ standard deviations. Continuous variables with non-normal distributions were expressed as medians (interquartile range [IQR]). Categorical variables were described as percentages (%). The odds ratios (ORs) and 95% confidence intervals (CIs) were estimated to explore the associations between METS-IR and UACR via logistic regression analyses. Model 1 was a non-adjusted model. Model 2 was adjusted for centre, age, and sex. Model 3 was further adjusted for education status, smoking habits, drinking habits, and previous diagnosis of CVD. Model 4 was further adjusted for history of diabetes and hypertension and use of hypotensive drugs. Model 5 was further adjusted for eGFR, WC, SBP, DBP, LDL-C, TC, AST, ALT, GGT, HbA1c, and RHR. The relationships between METS-IR and UACR were also explored in subgroups that were stratified by age (<55, 55–64, and ≥ 65 years), eGFR (<60, 60–90, and ≥ 90 mL/min/1.73 m²), blood glucose (BG) status (normal: FBG < 5.6 and PBG < 7.8 mmol/L; prediabetes: $5.6 \leq \text{FBG} < 7.0$ or $7.8 \leq \text{PBG} < 11.1$ mmol/L; and diabetes: $\text{FBG} \geq 7.0$ or $\text{PBG} \geq 11.1$ mmol/L), and BP status (normal BP: $\text{SBP} < 120$ and $\text{DBP} < 80$ mmHg; prehypertension: $80 \leq \text{DBP} < 90$ or $120 \leq \text{SBP} < 140$ mmHg; and hypertension: $\text{DBP} \geq 90$ or $\text{SBP} \geq 140$ mmHg). This study also investigated the interactions between METS-IR and the stratified variables among subjects with increased risk of UACR. Two-tailed $P < 0.05$ was considered statistically significant.

Results

Clinical characteristics of the participants

Among the 37,290 subjects included in this study, 10,909 were men, and 26,381 were women. Table 1 shows the characteristics of the study subjects, who were divided into four groups on the basis of the quartiles of the METS-IR index. The mean age of the Q4 group was 58.72 ± 9.13 years. The mean age of the Q1, Q2, and Q3 groups were 56.77 ± 9.29 , 57.49 ± 8.01 , and 58.30 ± 9.13 years. The proportions of men and women were the highest in the highest and lowest quartile METS-IR groups, respectively (men: Q1, 19.3%; Q2, 21.4%; Q3, 26.8%; Q4, 32.5%; women: Q1, 27.3%; Q2, 26.5%; Q3, 24.3%; Q4, 21.9%). The highest quartile METS-IR group was characterised by significantly higher WC, BMI, UACR, SBP, DBP, RHR, and TC, TG, ALT, AST, GGT, FBG, and HbA1c levels. Moreover, the eGFR and HDL-C levels were lower because METS-IR was higher.

Association between UACR and METS-IR quartiles

Logistic regression analyses were performed to examine the association between the METS-IR quartiles and UACR. As presented in Table 2, only the highest quartile METS-IR group had a positive relationship with UACR after adjusting for confounding factors among all subjects (OR: 1.260, 95% CI: 1.152–1.378, $P < 0.001$).

As shown in Table 3, in the non-adjusted model, Q1–Q4 were all associated with UACR; however, after adjusting for various confounding factors, only the highest quartile of METS-IR was associated with UACR in both men and women in Model 5 (for men: OR: 1.321, 95% CI: 1.104–1.579, $P = 0.002$; for women: OR: 1.201, 95% CI: 1.083–1.330, $P < 0.001$). The association in men was more significant than that in women.

Association between METS-IR and UACR according to different levels of age, BG, BP, and eGFR

Stratified analyses were performed for the subgroups of age, BG level, BP, and eGFR to further investigate whether the relationships between METS-IR and UACR were still significant (Tables 4 and 5). Moreover, to better discuss the sex hormone-related associations between METS-IR and UACR, we divided women into two groups, namely, the postmenopausal women group and premenopausal women group (Additional Table 1). Significant interactions were found in the BP and age subgroups (all subjects: age [P for interaction = 0.136] and BP [P for interaction = 0.016]; men: age [P for interaction = 0.593] and BP [P for interaction = 0.336]; women: age [P for interaction = 0.028] and BP [P for interaction = 0.035]; postmenopausal women: age [P for interaction = 0.028] and BP [P for interaction = 0.024]). Significant associations between the fourth METS-IR quartile and UACR were found among all subjects and women younger than 65 years. The relationship between the third METS-IR quartile and UACR was also significant in women (55–64 years subgroup). However, among men, a significant association was only observed in men aged 55–64 years (OR: 1.494, 95% CI: 1.114–2.004, $P = 0.007$). Moreover, we also analysed the association between UACR

and METS-IR in BG subgroup. A significant association was found in all subjects and men with critical BG levels and diabetes, whereas a significant association was only observed in women with diabetes (Tables 4 and 5). In addition, similar results were found according to BP, the risk of elevated UACR occurrence in the Q4 METS-IR group was increased in the prehypertension and hypertension groups among all subjects and men. Among women, this risk was only increased in the hypertension group. We also explored the subgroup associations in postmenopausal and premenopausal women (Additional file 1), and the findings for postmenopausal women were similar to those for men.

To better explore the relationship between UACR and METS-IR according to the kidney function level, we divided the participants into three groups on the basis of eGFR (<60 , $60-90$, and ≥ 90 mL/min/1.73 m²). When eGFR ≥ 90 mL/min/1.73 m², the positive relationships between the fourth METS-IR quartile and UACR were significant regardless of sex (all subjects: OR: 1.289, 95% CI: 1.172–1.417, $P < 0.001$; men: OR: 1.316, 95% CI: 1.089–1.589, $P = 0.004$; women: OR: 1.268, 95% CI: 1.135–1.417, $P < 0.001$).

Discussion

To the best of our knowledge, this study is the first to explore the association between the METS-IR and UACR among a nationwide community-based population of Chinese adults. The main findings of our study were as follows: (1) UACR was significantly associated with the METS-IR index after controlling for confounding factors, and the association was more significant for the METS-IR index than for its components (FBG, TG, BMI, and HDL-C). (2) Differences among the subgroups were observed on the basis of sex. Among men, the association between METS-IR and UACR was significant in those aged 55–64 years with prediabetes or diabetes, prehypertension or hypertension, and eGFR ≥ 90 mL/min/1.73 m². Among women, the association between METS-IR and UACR was significant among those aged < 65 years with diabetes, hypertension, and eGFR ≥ 90 mL/min/1.73 m². Thus, early monitoring and treatment are essential for increased UACR, and alleviation of IR perhaps conduce to the early prevention and intervention of negative consequences, particularly in populations with higher blood glucose and BP abnormalities.

Although previous studies found that the components of METS-IR, including BMI, TG, FBG, and HDL-C, could be treated as predictors of CVD and hypertension [3,4], our study showed that BMI, FBG, and TG in men and HDL-C in women were not significantly associated with UACR. However, METS-IR remained strongly associated with UACR among all subjects and both sexes. Moreover, the assessment of these METS-IR components has potential limitations. An increased FBG level is a less competent indicator of cardiovascular outcomes [18]. The role of BMI is debatable since different studies have presented conflicting results [19,20]. Moreover, lower HDL-C and higher TG levels were significantly associated with a risk of elevated UACR among the conventional parameters of dyslipidaemia [21]. This study indicated that METS-IR may be regarded as a better vigilant value for albuminuria detection than BMI or TG, FBG, and HDL-C levels.

Few studies have investigated sex- or age-stratified associations between UACR and METS-IR. In our study, we found age- and sex-based differences. In this population-based study of middle-aged and older participants, the results showed that an elevated UACR was significantly associated with an increased METS-IR index among men (55–64 years) and women (<65 years). And in all subjects, the relationships were found in younger people (<65 years). A previous study has found that BMI, which is a component of METS-IR, is significantly associated with CKD, and this association becomes weaker with increasing age (particularly among women) [22]. Similar findings of another study showed that the influence of lipid variability on unfavourable outcomes was greater in younger adults [23]. Our findings support the fact that younger adults exhibit greater sensitivity to increasing the variability of cholesterol than older adults. UACR has been reported to be predictive of CVD [2]. It has a negative association with the risk of CVD and is independent of sex and age [24]. Likewise, mortality risk ratios for coronary artery disease among men were halved between the age of 55–64 years and 65–74 years [25]. The findings of our study were not fully consistent with those of the abovementioned studies. In our study, there are some elderly people in retirement to a certain extent; we speculated that such people have possibly more time to exercise to reduce inflammation which could lead to renal dysfunction [26]. Therefore, the early detection and intervention are vital for people with risk factors.

In the subgroup analyses, it was noticeable that the different associations were significant in men with diabetes and prediabetes, prehypertension, and hypertension and in women with hypertension and diabetes. However, we found that the interaction between BP and METS-IR was only significant among women, particularly premenopausal women. Therefore, our findings indicated that

the independent association of METS-IR with UACR were more significant in men and postmenopausal women. Moreover, the proportion of men was higher in the highest METS-IR quartile group, and the OR for elevated UACR was higher in men than in women. Our findings disagree with those of some previous studies that indicated that being female seems to intensify the progression of diabetic renal disease [27] or that being male could be considered a risk for the disease [28]. The possible reasons for the conflicting findings are unclear. However, data from a review study confirmed that the risk of incidence of nondiabetic renal disease was higher among men than among age-matched women without diabetes. It suggested that a possible mechanism for the deficiency of the distinct sex discrepancy in the status of diabetes may be due to the imbalance of sex hormone levels with diabetes [30]. This finding was consistent with that of the current study. A sex-stratified study had similar conclusions and showed that the components of METS-IR in men were more impaired than that in women and that the values of TG or TG/HDL ratios were higher in men [30]. Further evidence could come out in support of the role of endogenous oestrogen in the metabolic homeostasis and the decrease of visceral lipid accumulation [31]. Our results may be due to the latent lipid distribution differential based on sex and the different levels of steroid hormone. An animal study showed that oestrogen therapy may have a beneficial impact on proteinuria [32]. Therefore, further analysis among postmenopausal and premenopausal women is essential. Similar results to those in men were found in the population of postmenopausal women. Simultaneously, the results of premenopausal women were distinct from those of men, which provided evidence for the hypothetic mechanism and indicated the higher accumulation of risk factors with gradual elevation of UACR in postmenopausal women and men. The present study provided new insights to support that age and sex should be an essential consideration when referring to albuminuria.

The underlying pathophysiological mechanism linking UACR to METS-IR and its constituents are not fully established. The possible reason may be attributed to visceral obesity. The relationship between IR and visceral adipose tissue (VAT) has long been recognised [33]. Given that METS-IR has a particularly stronger association with visceral adiposity than insulin-based indexes [3], it could be a predictor for ectopic lipid accumulation and visceral fat, which were confirmed risk factors for hypertension and CVD [34,35]. Furthermore, recent studies have proposed that visceral adiposity may be pivotally involved in UACR excretion and albuminuria may be a manifestation of VAT [36,37]. It is presumptive that adiponectin's role in renal dysfunction may be an underlying factor of the association between albuminuria and VAT [38]. Elevated VAT and increased albuminuria have both been reported to have inverse associations with adiponectin [39,40]. Adiponectin had a positive correlation with age, and the concentration levels of adiponectin were different based on sex. Intra-abdominal fat was less in women than in men. These findings are concordant with our findings. An adiponectin-deficient animal-based model showed that glomerular damage was promoted by lower levels of adiponectin [41]. Furthermore, the adipocytokines of VAT, such as IL-6 and TNF- α , could exacerbate renal vascular damage via inflammation and lead to the development of albuminuria owing to increased eGFR [42-45]. The findings of these studies are consistent with our findings. Taken together, the above findings confirm that the relationship between UACR with METS-IR could be explained by the increased VAT associated with both adiponectin and IR.

Study Strengths And Limitations

The major strength of this study was that the study benefited from a relatively large multicentre investigation of the Chinese population. However, a few limitations should be considered. First, no inference of causality can be drawn owing to the cross-sectional design; a follow-up analysis should be performed to determine whether METS-IR is a predictor of elevated UACR. Second, the measurement of UACR was based on a single morning spot urine specimen. Despite its recommendation as a reliable method in large epidemiological studies, misestimations of urinary albumin excretion owing to intra-individual variance cannot be eliminated. Third, although the population who used lipid-lowering drugs or angiotensin-converting enzyme inhibitors/angiotensin receptor blockers was excluded, the use of other medications that were not investigated might have influenced the findings of this study. Finally, despite regulating a series of confounding factors, some remnants or unmeasured confounders could not be excluded.

Conclusions

METS-IR was significantly associated with an elevated UACR among Chinese adults and was superior to its components. Moreover, men or postmenopausal women with diabetes and hypertension, particularly those aged below 65, needed specific supervision when screening for the METS-IR index. In practice, clinicians should detect the potential risk factors timely to alleviate

the prevalence of kidney dysfunction and CVD based on the novel perceptions of METS-IR which may be regarded as a convenient tool to identify the patients. Our study also provided proof to support that age and sex should be an essential consideration when referring to the albuminuria.

Abbreviations

AST, aspartate transaminase; ALT, alanine transaminase; BMI, body mass index; BP, blood pressure; BG, blood glucose; CI, confidence interval; CKD, chronic kidney disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; GGT, gamma-glutamyl transferase; GH, glomerular hyperfiltration; HbA1c, glycosylated haemoglobin; HDL-C, high-density lipoprotein cholesterol; IQR, interquartile range; IR, insulin resistance; LDL-C, low-density lipoprotein cholesterol; MAU, microalbuminuria; METS-IR, metabolic score for insulin resistance; OR, odds ratio; PBG, 2 h post-load blood glucose; RHR, resting heart rate; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; T2DM, type 2 diabetes mellitus; UACR, urinary albumin–creatinine ratio; VAT, visceral adipose tissue; WC, waist circumference.

Declarations

Data Availability

The datasets used to support this study are not freely available to protect the privacy of participants.

Funding

The study is supported by the Chinese Society of Endocrinology, the Key Laboratory for Endocrine and Metabolic Diseases of Ministry of Health (1994DP131044), the National Key New Drug Creation and Manufacturing Program of Ministry of Science and Technology (2012ZX09303006-001), the National High Technology Research and Development Program of China (863 Program, 2011AA020107), National Science Foundation of China (81300717), the Beijing Municipal Science and Technology Commission (No. D141107005314004); National Science and Technology Major Project 288 (2011ZX09307-001-08), the REACTION Study.

Acknowledgements

We would like to thank the participants in this study.

Competing interests

The authors declare no competing interests.

Consent for publication

Not applicable

Ethics approval and consent to participate

The study protocol was approved by the Committee on Human Research at Rui-Jin Hospital affiliated with the School of Medicine, Shanghai Jiao Tong University. Written informed consents were obtained from all participants before data collection.

Authors' contributions

Wanlu Su and Jie Wang contributed equally to this article. Wanlu Su and Yiming Mu designed the conception of the manuscript. Wanlu Su performed the statistical analysis, interpreted the data, and drafted and revised the manuscript. Jie Wang interpreted the data and drafted and revised the manuscript. Yiming Mu assisted in data collection and acquisition and revised the manuscript. Songyan Yu, Kang Chen, Wenhua Yan revised the manuscript and recruited the subjects. Zhengnan Gao, Xuelei Tang, Qin Wan, and Zuojie Luo offered advice and assistance, recruited the subjects, and supervised the study. Each author contributed to the final approval of the version to be published and ensured that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Casmir E Amad, Amam C Mbakwem, Oyewole A Kushimo, Jayne N Ajuluchukwu, Michael Akinkunmi. Prevalence of positive chronic kidney Disease screening in professional male long haul drivers at risk of cardiovascular Disease in Lagos, Nigeria: a cross-section study. *BMC Public Health*. 2019; 19(1): 1032.
2. Wada T, Haneda M, Furuichi K, Tetsuya Babazono, Hiroki Yokoyama, Kunitoshi Iseki. Clinical impact of albuminuria and glomerular filtration rate on renal and cardiovascular events, and all-cause mortality in Japanese patients with type 2 diabetes. *Clin Exp Nephrol*. 2014; 18(4): 613-620.
3. Omar Yaxmehen Bello-Chavolla , Paloma Almeda-Valdes, Donaji Gomez-Velasco, Tannia Viveros-Ruiz , Ivette Cruz-Bautista , Alonso Romo-Romo. et al. METS-IR, a novel score to evaluate insulin sensitivity, is predictive of visceral adiposity and incident type 2 diabetes. *Eur J Endocrinol*. 2018; 178(5): 533-544.
4. Katarina Eeg-Olofsson, Soffia Gudbjörnsdottir, Björn Eliasson, Björn Zethelius , Jan Cederholm, NDR. The triglycerides-to-HDL-cholesterol ratio and cardiovascular disease risk in obese patients with type 2 diabetes: an observational study from the Swedish National Diabetes Register (NDR). *Diabetes Res Clin Pract*. 2014; 106(1): 136-144.
5. Kurella M, Lo JC, Chertow GM.(2005) Metabolic syndrome and the risk for chronic kidney disease among nondiabetic adults. *J Am Soc Nephrol*. 2005; 16(7): 2134-2140
6. Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration. Cardiovascular Disease, Chronic Kidney Disease, and Diabetes Mortality Burden of Cardiometabolic Risk Factors From 1980 to 2010: A Comparative Risk Assessment. *Lancet Diabetes Endocrinol*. 2014; 2(8): 634-647.
7. Expert Panel on Detection E, Treatment of High Blood Cholesterol in A. Executive summary of the third report of the national cholesterol education program (ncep) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). *JAMA*. 2001; 285(19): 2486-2497.
8. Jamal S Rana, Jennifer Y Liu, Howard H Moffet, Matthew D Solomon, Alan S Go, Marc G Jaffe, et al. Metabolic dyslipidemia and risk of coronary heart disease in 28,318 adults with diabetes mellitus and low-density lipoprotein cholesterol < 100 mg/dl. *Am J Cardiol*. 2015; 116 (11): 1700-1704.
9. Muntner P, Coresh J, Smith JC, Eckfeldt J, Klag MJ. Plasma lipids and risk of developing renal dysfunction: the atherosclerosis risk in communities study. *Kidney Int*. 2000 58(1): 293-301.
10. Nordestgaard, B. G., and A. Varbo. 2014. Triglycerides and cardiovascular disease. *The Lancet*. 2014; 384 (9943): 626-635.
11. Mann JF, Yi QL, Gerstein HC et al. Albuminuria as a predictor of cardiovascular and renal outcomes in people with known atherosclerotic cardiovascular disease. *Kidney Int Suppl*. 2004; 92: S59-62.
12. Ferrannini E, Cushman WC. Diabetes and hypertension: the bad companions. *Lancet*. 2012; 380 (9841):601.
13. L Mykkanen, D J Zaccaro, L E Wagenknecht, D C Robbins, M Gabriel, S M Haffner. Microalbuminuria is associated with insulin resistance in nondiabetic subjects: the insulin resistance atherosclerosis study. *Diabetes*. 1998; 47 (5): 793-800.
14. Enzo Bonora , Gianni Formentini, Francesco Calcaterra, Simonetta Lombardi, Franco Marini, Luciano Zenari, Francesca Saggiani, Maurizio Poli, Sandro Perbellini, Andrea Raffaelli, et al. HOMA-estimated insulin resistance is an independent predictor of cardiovascular disease in type 2 diabetic subjects: prospective data from the Verona Diabetes Complications Study. *Diabetes Care*. 2002; 25 (7): 1135–1141.
15. D.J.Rader. Effect of insulinresistance,dyslipidemia,andintra-abdominal adiposity on the development of cardiovascular disease and diabetes mellitus. *American Journal of Medicine*. 2007;120: S12-18.
16. Borai A, Livingstone C & Ferns GA. The biochemical assessment of insulin resistance. *Annals of Clinical Biochemistry*. 2007; 44 (pt4): 324–342..
17. Ning G. Risk Evaluation of cAncers in Chinese diabeTic Individuals: a lONgitudinal (REACTION) study. *Journal of diabetes*. 2012; 4 (2): 172-173.
18. Ying-Chun Ma, Li Zuo, Jiang-Hua Chen, Qiong Luo, Xue-Qing Yu, Ying Li, et al. Modified glomerular filtration rate estimating equation for Chinese patients with chronic kidney disease. *J Am Soc Nephrol*. 2006; 17 (10): 2937–2944

19. R Borg, J C Kuenen, B Carstensen, H Zheng, D M Nathan, R J Heine, et al. HbA1(c) and mean blood glucose show stronger associations with cardiovascular disease risk factors than do postprandial glycaemia or glucose variability in persons with diabetes: the A1C-Derived Average Glucose (ADAG) study. *Diabetologia*. 2011; 54 (1): 69-72.
20. Kathleen Dittmann, Anke Hannemann, Henri Wallaschofski, Rainer Rettig, Sylvia Stracke, Henry Völzke, Matthias Nauck, and Nele Friedrich. U-shaped association between central body fat and the urinary albumin-to-creatinine ratio and microalbuminuria. *BMC Nephrol*. 2013; 17: 87
21. Chih-Hsueh Lin, Che-Yi Chou, Cheng-Chieh Lin, Chiu-Ching Huang, Chiu-Shong Liu, Shih-Wei Lai. Waist-to-height ratio is the best index of obesity in association with chronic kidney disease. *Nutrition*. 2007; 23 (11-12): 788-793.
22. Ga Eun Nam, Kyungdo Han, Do Hoon Kim, Yong Gyu Park, Yeo Joon Yoon, Young Eun Kim, et al. Relationship Between Dyslipidemia and Albuminuria in Prediabetic Adults: The Korea National Health and Nutrition Examination Survey 2011-2012. *Endocrine*. 2015; 48 (2): 557-565.
23. Richard J Silverwood, Mary Pierce, Claudia Thomas, Rebecca Hardy, Charles Ferro, Naveed Sattar, et al. Association between Younger Age When First Overweight and Increased Risk for CKD. *J Am Soc Nephrol*. 2013; 24 (5): 813–821.
24. Eric Y F Wan, Esther Y T Yu, Weng Y Chin, Jessica K Barrett, Anna H Y Mok, Christie S T Lau, et al. Greater variability in lipid measurements associated with cardiovascular disease and mortality: 10-year diabetes cohort study. *Diabetes Obes Metab*. 2020; 22 (10): 1777-1788.
25. Ane Cecilie Dale, Lars J Vatten, Tom Ivar Nilsen, Kristian Midthjell, Rune Wiseth, et al. Secular decline in mortality from coronary heart disease in adults with diabetes mellitus: cohort study. *BMJ*. 2008; 337 (7661): a236.
26. Gu K, Cowie CC, Harris MI. Diabetes and decline in heart disease mortality in US adults. *JAMA*. 1999 (14); 281: 1291-1297.
27. Dana E King, Peter Carek, Arch G Mainous 3rd, William S Pearson, et al. Inflammatory markers and exercise: differences related to exercise type. *Medicine & Science in Sports & Exercise*. 2003; 35 (4): 575–581.
28. Holl RW, Grabert M, Thon A, E Heinze. Urinary excretion of albumin in adolescents with type 1 diabetes: persistent versus intermittent microalbuminuria and relationship to duration of diabetes, sex, and metabolic control. *Diabetes Care*. 1999; 22 (9): 1555–1560.
29. Camille A Jones, Andrzej S Krolewski, John Rogus, Jay L Xue, Allan Collins, James H Warram. Epidemic of end-stage renal disease in people with diabetes in the United States population: do we know the cause? *Kidney Int*. 2005; 67 (5): 1684–1691.
30. Christine Maric. Sex, diabetes and the kidney. *Am J Physiol Renal Physiol*. 2009; 296 (4) :F680–688..
31. Dong-Hyuk Cho, Hyung Joon Joo, Mi-Na Kim, Do-Sun Lim, Wan Joo Shim, Seong-Mi Park. Association between epicardial adipose tissue, high-sensitivity C-reactive protein and myocardial dysfunction in middle-aged men with suspected metabolic syndrome. *Cardiovasc Diabetol*. 2018; 17 (1): 95.
32. Barros RP, Gustafsson JA. Estrogen receptors and the metabolic network. *Cell Metab*. 2011; 14 (3): 289–299.
33. Sandberg K. Mechanisms underlying sex differences in progressive renal disease. *Gend Med*. 2008; 5 (1): 10–23.
34. Shulman GI. Ectopic fat in insulin resistance, dyslipidemia, and cardiometabolic disease. *N Engl J Med*. 2014; 371 (23): 1131-1141.
35. Dariush Mozaffarian, Emelia J Benjamin, Alan S Go, Donna K Arnett, Michael J Blaha, Mary Cushman, Sarah de Ferranti, Jean-Pierre Després, Heather J Fullerton, Virginia J Howard, et al. Heart disease and stroke statistics—2015 update: A report from the American Heart Association. *Circulation*. 2015; 131 (4): e29–e322.
36. Abraham TM, Pedley A, Massaro JM, et al. Association between visceral and subcutaneous adipose depots and incident cardiovascular disease risk factors. *Circulation*. 2015; 132 (17): 1639-1647.
37. Ko Hanai, Tetsuya Babazono, Izumi Nyumura, Kiwako Toya, Mari Ohta, Ryotaro Bouchi, Kumi Suzuki, Aiko Inoue, Yasuhiko Iwamoto. Involvement of visceral fat in the pathogenesis of albuminuria in patients with type 2 diabetes with early stage of nephropathy. *Clin Exp*. 2010; 14 (2): 132-136.
38. M Cnop, P J Havel, K M Utzschneider, D B Carr, M K Sinha, E J Boyko, B M Retzlaff, R H Knopp, J D Brunzell, S E Kahn. Relationship of adiponectin to body fat distribution, insulin sensitivity and plasma lipoproteins: evidence for independent roles of age and sex. *Diabetologia*. 2003; 46 (4): 459–469.

39. Anthony J G Hanley , Donald Bowden, Lynne E Wagenknecht, Aarthi Balasubramanyam, Carl Langfeld, Mohammed F Saad, Jerome I Rotter, Xiuqing Guo, Yii-Der I Chen, Michael Bryer-Ash, Jill M Norris et al. Associations of adiponectin with body fat distribution and insulin sensitivity in nondiabetic Hispanics and African-Americans. *J Clin Endocrinol Metab.* 2007; 92 (7): 2665–2671.
40. Costas Tsioufis, Kyriakos Dimitriadis, Dimitris Chatzis, Carmen Vasiliadou, Dimitrios Tousoulis, Vasilios Papademetriou, Pavlos Toutouzas, Christodoulos Stefanadis, Ioannis Kallikazaros. Relation of microalbuminuria to adiponectin and augmented C-reactive protein levels in men with essential hypertension. *Am J Cardiol.* 2005; 96 (7): 946–951.
41. Kumar Sharma, Satish Ramachandrarao, Gang Qiu, Hitomi Kataoka Usui, Yanqing Zhu, Stephen R Dunn, Raogo Ouedraogo, Kelly Hough, Peter McCue, Lawrence Chan, Bonita Falkner, et al. Adiponectin regulates albuminuria and podocyte function in mice. *J Clin Invest.* 2008; 118 (5): 1645–1656.
42. udkin JS, Eringa E, Stehouwer CD. “Vasocrine” signalling from perivascular fat: a mechanism linking insulin resistance to vascular disease. *Lancet.* 2005; 365 (9473): 1817–1820.
43. Mallamaci F, Tripepi G. Obesity and CKD progression: hard facts on fat CKD patients. *Nephrol Dial Transplant.* 2013; 28: 105-108
44. Peter Stenvinkel, Markus Ketteler, Richard J Johnson, Bengt Lindholm, Roberto Pecoits-Filho, Miguel Riella, Olof Heimbürger, Tommy Cederholm, Matthias Girndt. IL-10, IL-6, and TNF-alpha: central factors in the altered cytokine network of uremia—the good, the bad, and the ugly. *Kidney Int.* 2005; 67 (4): 1216–1233
45. Foster MC, Hwang SJ, Massaro JM, et al. Association of Subcutaneous and Visceral Adiposity with Albuminuria: The Framingham Heart Study. *Obesity (Silver Spring).* 2011; 19 (6): 1284-1289.

Tables

Table 1. Characteristics of the study subjects by METS-IR quartiles

Variable	METS-IR				P value
	Q1 (n = 9,322)	Q2 (n = 9,323)	Q3 (n = 9,323)	Q4 (n = 9,322)	
Age, y	56.77 ± 9.29	57.49 ± 8.01	58.30 ± 9.13	58.72 ± 9.13	<0.001 ^{a,b,c,d,e}
Male sex, no. (%)	2,107 (19.3)	2,336 (21.4)	2,923 (26.8)	3,543 (32.5)	<0.001
Female sex, no. (%)	7,215 (27.3)	6,987 (26.5)	6,400 (24.3)	5,779 (21.9)	<0.001
WC, cm	76.37 ± 7.89	83.05 ± 7.13	87.77 ± 7.24	94.23 ± 8.51	<0.001 ^{a,b,c,d,e,f}
Triglycerides, mmol/L	0.96 (0.76–1.25)	1.23 (0.92–1.63)	1.51 (1.10–2.05)	1.93 (1.35–2.80)	<0.001 ^{a,b,c,d,e,f}
BMI, kg/m ²	20.62 ± 1.73	23.31 ± 1.50	25.24 ± 1.74	28.45 ± 3.74	<0.001 ^{a,b,c,d,e,f}
TC, mmol/L	4.88 ± 1.24	5.10 ± 1.13	5.06 ± 1.14	5.12 ± 1.07	<0.001 ^{b,c,d,e,f}
LDL-C, mmol/L	2.93 ± 0.87	3.06 ± 0.90	3.04 ± 0.89	2.82 ± 0.92	<0.001 ^{a,b,c,e,f}
HDL-C, mmol/L	1.60 ± 0.34	1.38 ± 0.28	1.24 ± 0.26	1.08 ± 0.26	<0.001 ^{a,b,c,d,e,f}
UACR, mg/g	8.28 (5.65–16.47)	9.39 (5.57–17.68)	10.07 (5.85–19.07)	11.56 (6.21–21.52)	<0.001 ^{c,e,f}
ALT, U/L	15.16 ± 12.62	16.34 ± 12.26	18.83 ± 13.79	21.90 ± 16.72	<0.001 ^{a,b,c,d,e,f}
AST, U/L	21.68 ± 10.57	21.28 ± 11.29	22.15 ± 12.41	23.12 ± 13.37	<0.001 ^{c,d,e,f}
SBP, mmHg	122.17 ± 19.30	128.17 ± 20.31	133.07 ± 20.95	137.51 ± 20.93	<0.001 ^{a,b,c,d,e,f}
DBP, mmHg	72.79 ± 10.68	75.89 ± 10.88	78.51 ± 11.09	81.03 ± 11.29	<0.001 ^{a,b,c,d,e,f}
RHR, (beat/min)	78.81 ± 12.60	78.45 ± 12.35	78.66 ± 12.13	79.12 ± 12.25	<0.001 ^{a,f}
HbA1c, %	5.7 (5.5–6)	5.8 (5.5–6.1)	5.9 (5.6–6.2)	6 (5.7–6.4)	<0.001 ^{a,b,c,d,e,f}
GGT, U/L	22.84 ± 35.30	25.91 ± 31.99	30.96 ± 42.74	35.38 ± 40.05	<0.001 ^{a,b,c,d,e,f}
FBG, mmol/L	5.29 ± 0.78	5.55 ± 1.07	5.82 ± 1.34	6.25 ± 1.74	<0.001 ^{a,b,c,d,e,f}
eGFR, mL/min/1.73 m ²	119.29 ± 21.73	119.84 ± 22.87	119.98 ± 24.84	122.11 ± 29.62	<0.001 ^{b,c,d,e,f}
High-school education, no. (%)	6,830 (73.3)	4,717 (50.6)	4,428 (47.5)	3,938 (42.2)	<0.001
Current smoker, no. (%)	1,110 (12.0)	1,096 (11.8)	1,325 (14.2)	1,631 (17.5)	<0.001
Former smoker, no. (%)	902 (9.68)	980 (10.51)	1,286 (13.8)	1,547 (16.6)	<0.001
Current alcohol drinker, no. (%)	2,170 (23.3)	2,195 (23.5)	2,420 (26.0)	2,513 (27.0)	<0.001
Former alcohol drinker, no. (%)	2,041 (21.9)	2,045 (22.0)	2,318 (24.9)	2,432 (26.1)	<0.001
History of hypertension, no. (%)	757 (0.08)	1,246 (13.4)	1,839 (19.7)	2,511 (27.0)	<0.001
History of diabetes, no. (%)	85 (0.91)	145 (1.56)	238 (2.55)	366 (3.93)	<0.001
Previous MI, no. (%)	6 (0.06)	16 (0.17)	25 (0.27)	56 (0.60)	<0.001
Previous stroke, no. (%)	68 (0.73)	83 (0.89)	95 (1.02)	137 (1.47)	<0.001
Previous CAD, no. (%)	201 (2.16)	223 (2.39)	332 (3.56)	431 (4.62)	<0.001
	103 (1.10)	148 (1.59)	181 (1.94)	242 (2.60)	<0.001

Taking hypertension drugs, no. (%)

Data were mean ± SD or median (IQR) for skewed variables or numbers (proportions) for categorical variables.

Statistical significant differences (P < 0.05) between two different groups separately are illustrated by a,b,c,d,e and f

a Q1 vs Q2;b Q1 vs Q3;c Q1 vs Q4;d Q2 vs Q3;e Q2 vs Q4;f Q3 vs Q4.

METS-IR, metabolic score for insulin resistance; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; UACR, urinary albumin–creatinine ratio; AST, aspartate transaminase; ALT, alanine transaminase; DBP, diastolic blood pressure; HbA1c, glycosylated haemoglobin; SBP, systolic blood pressure; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; GGT, gamma-glutamyl transferase; MI, myocardial infarction; CAD, coronary artery disease.

Table 2. Association of the METS-IR index and its components with UACR in total subjects

METS-IR	Model 1		Model 2		Model 3		Model 4		Model 5	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
METS-IR	Reference		Reference		Reference		Reference		Reference	
Q1 (17.75–31.63)	1.180 (1.075–1.296)	0.001	1.168 (1.061–1.286)	0.002	1.152 (1.047–1.267)	0.004	1.106 (1.005–1.217)	0.039	1.084 (0.978–1.023)	0.124
Q2 (31.64–36.03)	1.310 (1.195–1.435)	<0.001	1.284 (1.167–1.412)	<0.001	1.175 (1.085–1.271)	<0.001	1.107 (1.022–1.199)	0.013	1.028 (0.940–1.124)	0.548
Q3 (36.04–41.03)	1.787 (1.637–1.951)		1.857 (1.693–2.037)		1.524 (1.423–1.632)		1.399 (1.304–1.500)		1.260 (1.152–1.378)	<0.001
Q4 (41.04–137.55)										
TG, mmol/L	Reference		Reference		Reference		Reference		Reference	
<1.7	1.443 (1.331–1.564)	<0.001	1.254 (1.153–1.364)	<0.001	1.239 (1.138–1.348)	<0.001	1.183 (1.086–1.289)	<0.001	1.033 (0.944–1.131)	0.476
≥1.7, <2.3		<0.001		<0.001		<0.001		<0.001		0.001
≥2.3	1.702 (1.574–1.840)		1.385 (1.276–1.503)		1.523 (1.402–1.624)		1.303 (1.198–1.417)		1.158 (1.058–1.268)	
FBG, mmol/L	Reference		Reference		Reference		Reference		Reference	
<5.6	1.235 (1.156–1.321)	<0.001	1.140 (1.079–1.182)	<0.001	1.035 (1.023–1.038)	<0.001	1.135 (0.968–1.332)	0.067	1.142 (1.032–1.265)	0.010
≥5.6, <7.0		<0.001		<0.001		<0.001		<0.001		0.287
≥7.0	1.602 (1.506–1.705)		1.225 (1.153–1.301)		1.196 (1.113–1.285)		1.148 (1.068–1.233)		1.051 (0.959–1.152)	
BMI, kg/m ²		0.887		0.059		0.687		0.916		0.094
<18.5	Reference	0.303	Reference	0.052	Reference	0.006	Reference	0.174	Reference	0.150
≥18.5, <24	0.986 (0.812–1.197)	<0.001	1.229 (0.993–1.522)	<0.001	1.042 (0.853–1.272)	<0.001	0.989 (0.808–1.211)	<0.001	0.828 (0.664–1.032)	0.493
≥24, <28	1.108 (0.912–1.345)	<0.001	1.220 (0.998–1.491)	<0.001	1.174 (1.047–1.316)	<0.001	1.083 (0.965–1.215)	<0.001	0.908 (0.796–1.035)	0.020
≥28										
HDL, mmol/L	1.447 (1.182–1.771)		1.421 (1.259–1.502)		1.513 (1.389–1.568)		1.280 (1.427–1.591)		0.912 (0.701–1.187)	
≥1										
<1	Reference		Reference		Reference		Reference		Reference	
	1.291 (1.192–1.397)		1.249 (1.146–1.360)		1.237 (1.134–1.349)		1.178 (1.079–1.286)		1.133 (1.020–1.259)	

METS-IR, metabolic score for insulin resistance; TG, triglycerides; BMI, body mass index; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; CI, confidence interval; OR, odds ratio; UACR, urinary albumin–creatinine ratio.

Model 1: Unadjusted

Model 2: Adjusted for centre, age, sex

Model 3: Further education status, smoking habits, drinking habits, CVD status

Model 4: Further diabetes history, hypertension history, hypotensive drugs

Model 5: Further eGFR, LDL-C, TC, AST, ALT, GGT, HbA1c, SBP, DBP, WC, HR

Table 4. Association of the METS-IR index with UACR for different levels of age, BG, BP, and eGFR in total subjects

Variable	METS-IR							
	Q1	Q2		Q3		Q4		P-values for
	Reference	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	interaction
All subjects								0.136
Age, year a								
<55 (n = 14,788)	1	1.099 (0.924–1.307)	0.288	0.943 (0.801–1.110)	0.483	1.313 (1.114–1.547)*	0.001	
≥55,<64 (n = 14,026)	1	0.991 (0.829–1.185)	0.920	1.118 (0.962–1.300)	0.146	1.208 (1.027–1.574)*	0.001	
≥65 (n = 7,387)	1	1.206 (0.989–1.470)	0.064	0.988 (0.838–1.164)	0.885	1.034 (0.879–1.217)	0.685	
Blood glucose, mmol/L b								0.869
FBG < 5.6 and PBG < 7.8 (n = 15,996)	1	1.029 (0.886–1.196)	0.706	0.974 (0.836–1.135)	0.736	1.082 (0.946–1.239)	0.250	
5.6 ≤ FBG < 7.0 or 7.8 ≤ PBG < 11.1 (n = 15,837)	1	1.128 (0.953–1.336)	0.160	0.955 (0.832–1.095)	0.509	1.330 (1.121–1.578)*	0.001	
FBG ≥ 7.0 or PBG ≥ 11.1 (n = 5,457)	1	1.066 (0.780–1.457)	0.688	1.084 (0.871–1.349)	0.469	1.381 (1.025–1.698)*	0.038	
BP, mmHg c								0.016
SBP < 120 and DBP < 80 (n = 11,520)	1	1.146 (0.955–1.376)	0.143	1.049 (0.865–1.272)	0.629	1.094 (0.939–1.275)	0.247	
120 ≤ SBP < 140 and/or 80 ≤ DBP < 90 (n = 14,145)	1	0.981 (0.820–1.175)	0.838	1.255 (0.686–1.565)	0.404	1.356 (1.165–1.579)*	<0.001	
SBP ≥ 140 or DBP ≥ 90 (n = 11,625)	1	1.069 (0.929–1.231)	0.351	1.127 (0.903–1.396)	0.302	1.282 (1.124–1.463)*	<0.001	
eGFR, mL/min/1.73 m ² d								0.120
eGFR ≥ 90 (n = 34,691)	1	1.088 (0.976–1.212)	0.128	1.037 (0.943–1.141)	0.449	1.289 (1.172–1.417)*	<0.001	

60 ≤ eGFR < 90 (n = 2,408)	1	1.189 (0.806–1.755) 0.384	0.959 (0.709–1.298) 0.788	1.042 (0.773–1.406) 0.785
eGFR < 60 (n = 191)	1	1.010 (0.989–1.032) 0.359	1.011 (0.960–1.065) 0.676	1.052 (0.983–1.125) 0.144

METS-IR, metabolic score for insulin resistance; UACR, urinary albumin–creatinine ratio; DBP, diastolic blood pressure; SBP, systolic blood pressure; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; PBG, 2 h postload blood glucose; CI, confidence interval; OR, odds ratio.

a Age subgroup: adjusted for sex, centres, ALT, AST, GGT, LDL-C, TC, HbA1c, SBP, DBP, eGFR, WC, smoking habits, drinking habits, CVD status, hypertension history, diabetes history, use of hypertension drugs.

b Blood glucose subgroup: adjusted for age, sex, centres, ALT, AST, GGT, LDL-C, TC, SBP, DBP, eGFR, WC, smoking habits, drinking habits, CVD status, hypertension history, use of hypertension drugs.

c BP subgroup: adjusted for age, sex, centres, ALT, AST, GGT, LDL-C, TC, HbA1c, eGFR, WC, smoking habits, drinking habits, CVD status, diabetes history.

d eGFR subgroup: adjusted for age, sex, centres, ALT, AST, GGT, LDL-C, TC, HbA1c, SBP, DBP, WC, smoking habits, drinking habits, CVD status, hypertension history, diabetes history, use of hypertension drugs.

Table 5. Association of the METS-IR index with UACR for different levels of age, BG, BP, and eGFR by sex

METS-IR								
Variable	Q1	Q2		Q3		Q4		P-values for
	Reference	OR (95% CI) value	P	OR (95% CI) value	P	OR (95% CI) value	P	interaction
Men								0.593
Age, year a								
<55 (n = 3,477)	1	0.862 (0.504–1.475)	0.589	0.862 (0.571–1.300)	0.478	1.078 (0.748–1.555)	0.686	
≥55,<64 (n = 4,361)	1	0.933 (0.631–1.381)	0.730	0.898 (0.652–1.236)	0.508	1.494 (1.114–2.004)*	0.007	
≥65 (n = 3,071)	1	1.053 (0.719–1.543)	0.791	1.111 (0.820–1.505)	0.496	1.113 (0.820–1.511)	0.494	
Blood glucose, mmol/L b								
FBG < 5.6 and PBG < 7.8 (n = 3,995)	1	0.846 (0.582–1.231)	0.382	0.738 (0.521–1.045)	0.087	1.020 (0.709–1.469)	0.914	0.564
5.6 ≤ FBG < 7.0 or 7.8 ≤ PBG < 11.1 (n = 4,797)	1	1.040 (0.711–1.523)	0.839	0.816 (0.606–1.098)	0.179	1.231 (1.011–1.498)*	0.001	
FBG ≥ 7.0 or PBG ≥ 11.1 (n = 2,117)	1	1.040 (0.579–1.868)	0.896	1.380 (0.933–2.041)	0.107	1.511 (1.070–2.134)*	0.019	
BP, mmHg c								0.336
SBP < 120 and DBP < 80 (n = 2,612)	1	0.617 (0.410–1.128)	0.206	0.845 (0.602–1.186)	0.330	1.190 (0.865–1.639)	0.285	
120 ≤ SBP < 140 and/or 80 ≤ DBP < 90 (n = 4,256)	1	1.500 (0.915–2.460)	0.108	1.069 (0.663–1.724)	0.784	1.635 (1.020–2.622)*	0.041	
SBP ≥ 140 or DBP ≥ 90 (n = 4,041)	1	1.451 (0.984–2.140)	0.060	1.114 (0.848–1.464)	0.439	1.368 (1.070–1.750)*	0.012	
eGFR, mL/min per 1.73 m ² d								0.116
eGFR ≥ 90 (n = 10,057)	1	0.991 (0.772–1.273)	0.943	0.939 (0.766–1.151)	0.544	1.316 (1.089–1.589)*	0.004	

60 ≤ eGFR < 90 (n = 792)	1	1.496 (0.588–3.804) 0.398	1.282 (0.690–2.384) 0.432	1.128 (0.620–2.051) 0.693	
eGFR < 60 (n = 60)	1	1.001 (0.788–1.379) 0.688	0.941 (0.849–1.044) 0.254	1.005 (0.998–1.012) 0.168	
Women					
Age, year a					0.198
<55 (n = 11,814)	1	1.159 (0.964–1.394) 0.117	0.977 (0.816–1.169) 0.799	1.378 (1.144–1.662)* 0.001	
≥55,<64 (n = 10,048)	1	0.998 (0.816–1.220) 0.981	1.203 (1.014–1.429)* 0.034	1.319 (1.105–1.574)* 0.002	
≥65 (n = 4,519)	1	1.250 (0.989–1.579) 0.061	0.921 (0.756–1.122) 0.414	0.991 (0.816–1.203) 0.927	
Blood glucose, mmol/L b					0.872
FBG < 5.6 and PBG < 7.8 (n = 12,837)	1	1.083 (0.746–1.572) 0.674	0.973 (0.745–1.270) 0.838	1.127 (0.884–1.436) 0.334	
5.6 ≤ FBG < 7.0 or 7.8 ≤ PBG < 11.1 (n = 9,368)	1	1.162 (0.962–1.403) 0.119	1.003 (0.858–1.171) 0.975	1.118 (0.853–1.465) 0.420	
FBG ≥ 7.0 or PBG ≥ 11.1 (n = 4,176)	1	1.162 (0.962–1.403) 0.119	1.003 (0.858–1.171) 0.975	1.630 (1.398–1.845)* 0.004	
BP, mmHg c					0.035
SBP < 120 and DBP < 80 (n = 8,908)	1	1.102 (0.905–1.342) 0.335	1.058 (0.856–1.308) 0.603	1.170 (0.907–1.509) 0.227	
120 ≤ SBP < 140 and/or 80 ≤ DBP < 90 (n = 9,889)	1	1.096 (0.897–1.340) 0.370	1.170 (0.985–1.390) 0.073	1.279 (0.999–1.638) 0.051	
SBP ≥ 140 or DBP ≥ 90 (n = 7,584)	1	1.055 (0.894–1.246) 0.524	1.182 (0.073–1.284) 0.220	1.242 (1.060–1.456)* 0.007	
eGFR, mL/min per 1.73 m ² d					0.225
eGFR ≥ 90 (n = 24,634)	1	1.115 (0.989–1.258) 0.076	1.073 (0.963–1.026) 0.199	1.268 (1.135–1.417)* <0.001	

60 ≤ eGFR < 90 (n = 1,616)	1	1.236 (0.799– 1.914) 0.341	0.889 (0.620– 1.275) 0.524	1.152 (0.806– 1.646) 0.437
eGFR < 60 (n = 131)	1	1.051 (0.952– 1.162) 0.325	1.294 (0.916– 1.294) 0.143	1.258 (0.395– 2.167) 0.468

METS-IR, metabolic score for insulin resistance; UACR, urinary albumin-to-creatinine ratio; DBP, diastolic blood pressure; SBP, systolic blood pressure; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; PBG, 2 h postload blood glucose; CI, confidence interval; OR, odds ratio.

a Age subgroup: adjusted for centres, ALT, AST, GGT, LDL-C, TC, HbA1c, SBP, DBP, eGFR, WC, smoking habits, drinking habits, CVD status, hypertension history, diabetes history, use of hypertension drugs.

b BG subgroup: adjusted for age, centres, ALT, AST, GGT, LDL-C, TC, SBP, DBP, eGFR, WC, smoking habits, drinking habits, CVD status, hypertension history, use of hypertension drugs.

c BP subgroup: adjusted for age, centres, ALT, AST, GGT, LDL-C, TC, HbA1c, eGFR, WC, smoking habits, drinking habits, CVD status, diabetes history.

d eGFR subgroup: adjusted for age, centres, ALT, AST, GGT, LDL-C, TC, HbA1c, SBP, DBP, WC, smoking habits, drinking habits, CVD status, hypertension history, diabetes history, use of hypertension drugs.

Supplementary

Due to technical limitations, Table 3 is only available as a download in the Supplemental Files section.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Table3.docx](#)
- [AdditionalTable1.docx](#)