Change in Metabolic Health Status Over Time and Risk of Chronic Kidney Disease: A Prospective Study

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Abstract

Objective: Metabolically healthy obesity (MHO) is a dynamic condition and is known to increase the risk for chronic kidney disease (CKD). In this study, we aimed to examine the association between metabolic health status and its change over time and CKD risk.

Methods: A total of 39463 participants from Kailuan Study were collected body mass index and metabolic health status at 2006/07 and 2010/11 examination. Metabolic abnormality was diagnosed by the presence of any 2 of 4 components (elevated blood pressure, elevated fasting blood glucose, elevated triglyceride and decreased high-density lipoprotein cholesterol). We classified participants into six groups according to metabolic health status and obesity. The changes in obesity and metabolic health status were considered from 2006/07 to 2010/11.

Results: Of the participants classified as MHNW or MHO at baseline, 17.25% and 39.64% were classified as MUNW or MUO in 2010/11, respectively. During a mean follow-up of 9.7 years, 5351 participants developed CKD from 2010/11. Compared with participants in the stable MHNW group, the stable MHO group had a significantly higher risk of incident CKD (HR: 1.16; 95% CI: 1.02-1.33), but was lower than that in individuals with MUO. Individuals with metabolic healthy at baseline who changed to metabolic abnormality during follow-up had higher risk of CKD.

Conclusions: MHO phenotype or its transition to a metabolically unhealthy phenotype were associated with increased risk of CKD. Stable metabolic health individuals had lower risk of CKD than those with metabolically unhealthy phenotype.

Introduction

Chronic kidney disease (CKD) is one of the most common chronic diseases in the world. According to the most recent GBD Chronic Kidney Disease Collaboration's report, 697.5 million people have CKD in 2017, with about 29.3% increase compared with that in 1990.[1] The prevalence of CKD in Chinese adults has reached as high as 10.8%.[2] In addition to the risk of progressing to end-stage-renal disease (ESRD), CKD plays a pathogenic role for cardiovascular diseases and all-cause mortality, and the number of deaths caused by CKD also increased continuously, which represents a major and persistent public health challenge.[3-5] However, current treatment options for patients with CKD are limited, and these options usually impose a substantial financial burden on the families.[5] Thus, it is necessary to determine the risk factors of CKD and identify the individuals who are at an increased risk of developing CKD to prevent the occurrence of CKD.

The majority of chronic disease associated with obesity is mediated through disordered glucose and lipid metabolism and elevated blood pressure, which is considered to be one of the most important causative factors. However, several studies have recently shown that not all obesity individuals were accompanied by obesity-related metabolic abnormalities, a different phenotype termed as metabolically healthy obese (MHO). [6] This phenotype was once thought to a benign condition and characterized by the absence of cardiometabolic abnormalities, including insulin resistance, dyslipidemia, and hypertension despite excessive body fat accumulation. [7-8] But a growing body of evidence shows that MHO is not an absolute healthy status for CVD and cancer. [9-11] Similar, numerous epidemiological studies supported the conclusion that MHO at baseline is associated with increased risk for CKD. [12-14] MHO is a dynamic condition that changes over time, and this transition may be at higher risk for metabolic complications, thus resulting in a higher risk for the onset of CKD. [15-18] Previous studies have reported the associations of MHO phenotype with CKD, but the sample size in these previous studies was relatively small, and disregarding the dynamic nature of MHO phenotype, and there remains uncertainty about the associations with the MHO phenotypic transitions and incident CKD.

Therefore, we investigated to determine the impact of phenotypic transitions on the risk of developing CKD by using a large study cohort from Kailuan Study.

Methods

Study participants

The Kailuan Study is an ongoing prospective community-based cohort study conducted in Tangshan, China. All participants in the Kailuan Study are employees and retirees of the Kailuan Group. Details of the study design and procedure have been described elsewhere.[19] At baseline, 105,110 participants (81,110 males and 20,400 females; aged 18-98 years) were recruited, underwent clinical and laboratory examinations, and completed a questionnaire interview (2006/07) at 11 hospitals affiliated with the Kailuan Group. Subsequent examinations involving anthropometric, cardiometabolic risk factor measures, and self-reported questionnaires (including income, educational level, drinking and so on) occurred approximately biennially after baseline until 2017 (2008/09, 2010/11, 2012/13, 2014/15 and 2016/17). In the current analysis, participants who took physical examinations (2006/07 and 2010/11) were selected to evaluate change in metabolic health status. Participants were excluded if they had prevalent CVD, cancer, or CKD, or missing data on BMI, or missing data on metabolic health status, or BMI<18.5kg/m^2 at 2006/07 and 2010/11 examinations (Supplement figure 1).

The study was conducted in accordance with the guidelines of the Declaration of Helsinki and was approved by the Kailuan General Hospital Ethics Committee.

Definition of metabolic health status

Body weight, height and waist circumstance (WC) were reported by trained nurses according to the standard methods. BMI was calculated as weight divided by square of height(kg/m^2). The obesity was defined according to categories of BMI (kg/m^2) categorized using Chinese standards: normal weight (BMI 18.5-24 kg/m^2), overweight (BMI 24-28 kg/m^2), and obese (BMI ≥ 28 kg/m^2).[20] Blood pressure (BP) was measured in the sitting position after subjects had been in a relaxed state for at least 15 min. Blood samples were collected after at least 8 h of fasting and delivered to a central laboratory. With these samples, we assessed metabolic parameters by measuring the plasma concentration of fasting plasma glucose (FPG), total cholesterol (TC), triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C) enzymatically using a 747 Chemistry Analyzer (Hitachi 747; Hitachi).

Metabolic abnormality was defined according to the criteria of the Harmonizing the metabolic syndrome. Metabolic abnormality was diagnosed by the presence of any 2 of 4 components: (1) serum TG ≥150 mg/dL or drug treatment for elevated TG; (2) serum HDL-C <50 mg/dL in women or <40 mg/dL in men; (3) systolic blood pressure (BP) ≥130 mm Hg or diastolic BP ≥85 mm Hg or drug treatment for elevated BP; and (4) FPG ≥100 mg/dL or drug treatment for elevated FPG.[21] Participants with fewer than 2 criteria were considered metabolic healthy. Using the above criteria for obesity and metabolic abnormality, participants were categorized into six phenotypes: (1) metabolic healthy normal-weight (MHNW), (2) metabolic healthy overweight (MHOW), (3) metabolic healthy obesity (MHO), (4) metabolic unhealthy normal-weight (MUNW), (5) metabolic unhealthy overweight (MUOW), (6) metabolic unhealthy obesity (MUO).

Change in metabolic health status

Change in metabolic health status were examined during the exposure (from 2006/07 to 2010/11) in participants with information on metabolic abnormality and obese phenotypes at both time points. We defined change considered into nine groups: stable MHNW, MHNW-MUNW, MUNW, stable MHOW, MHOW-MUOW, MUOW, stable MHO, MHO-MUO, MUO.

Definition of CKD

Follow-up ended at the first record of CKD event, all-cause death or at the end of follow-up on 31 December 2018, whichever came first. In this study, CKD was defined as eGFR <60 ml/min per 1.73 m2 and/or proteinuria ≥1+ (>30 mg/dl) and/or medical records of patients with CKD.

We used the serum creatinine (Scr) level to estimate the eGFR (mL/min/1.73 m2) according to the CKD Epidemiology Collaboration Equations: eGFR = 141 × min (Scr/κ, 1) α× max (Scr/κ, 1) −1.209 × 0.993Age × 1.018 (if female), where Scr is serum creatinine, κ is 0.7 for females and 0.9 for males, α is −0.329 for females and −0.411 for males, and min and max indicate the minimum and maximum of Scr/κ or 1, respectively.[22] Using the dry chemistry method and standard urinary sediment examination, urine protein concentration in random midstream morning urine samples was measured within 2 hours using a urine analyzer (N-600; Changchun Dirui Medical Technology Co., Ltd.). The lower limit of detection was 15 mg/dl. We recorded the semiquantitative proteinuria dipstick results as negative (<15 mg/dl), trace (15-29 mg/dl), 1+ (30-300 mg/dl), 2+ (300-1000 mg/dl) or 3+ (>1000 mg/dl). The medical records were identified through the Municipal Social Insurance Institutions or the Hospital Discharge Register which have been conducted every year (ICD-10 code N18-N19).

Statistical analysis

Data are presented as mean±SD for continuous variables and as numbers and percentages for categorical variables. To determine the differences among groups, we used Kruskal-Wallis test for continuous values and chi-square test for categorical variables. All analyses were done with SAS (version 9.4), at a two-tailed alpha level of 0.05.

Kaplan-Meier curves of incident events across the nine groups of change in metabolic health status were compared with the log-rank test using follow-up time as the timescale. The Cox proportional hazard models were used with age as the time scale to estimate the hazard ratios (HRs) for incident CKD by metabolic health status or change, and were adjusted for baseline confounders, including sex, income (low, intermediate, high), educational level (primary school or less, middle school, and university or higher degree), drinking (never, former and current), smoking (never, former and current), physical activity (poor, moderate, active),alanine amino-transferase (ALT), low-density lipoprotein cholesterol (LDL-C) and hypersensitive C-reactive protein (Hs-CRP). The stable MHNW as the reference category. As we calculated the change in metabolic health status between 2006/07 and 2010/11, the follow-up started at 2010/11 examination. The proportional hazard assumption was examined by Schoenfeld residuals. Also, the time-dependent Cox model were used to assess the association change in metabolic health status and change in individual risk factors over the whole duration of follow-up and the risk of CKD. For these analyses, we used the baseline metabolic health status and mutually adjusted for the incident metabolic diseases (hypertension, diabetes and hyperlipidemia). In addition, to reduce the impact of competing risk bias on the result, we performed competing risk model analysis to assess the risk of CKD, with death considered as a competing event, using sub-distribution hazard model by Fine-Gray.

Missing covariates were imputed by multiple imputation using the fully conditional specification method SAS MI procedure. The results were consistent from analyses that excluded participants with missing covariates.

Sensitivity analysis

To examine the robustness of our results, we performed several sensitivity analyses. First, we excluded events occurring in the first 2 years of follow-up to minimize potential reverse causation. Second, although the BMI cut-off of ≥ 24 kg/m^2 for overweight and ≥ 28 kg/m^2 for obesity were accepted by Chinese Society for the Study Obesity, this value is lower than that in Western countries. Thus, we conducted a sensitivity analysis using an additional BMI threshold of ≥ 25kg/m^2 and ≥ 30kg/m^2. Third, we excluded participants on treatment with anti-hypertensive, glucose- and lipid-lowering. Finally, given that the incident CKD was known every 2 years on average examination, we repeated the main analysis, and the mid-point of the interval was considered the survival estimates.

And, using WC, we also defined central obesity as a WC of >90 cm in men and >80 cm in women. For WC criteria, all participants were classified into four obesity phenotypes: MHNW, MUNW, MHO, MUO. Likewise, the participants were divided into six groups (stable MHNW, MHNW-MUNW, MUNW, stable MHO, MHO-MUO, MUO) and the above analyses were repeated for change in metabolic health status.

Results

Baseline characteristics of cohort

Table 1 shows the main clinical and biological characteristics of participants stratified by metabolic health status at baseline. Among the 39463 participants, 34112 (86.44%) were men; the mean age was 51.73±11.10years. At the baseline, 3570 (9.05%) participants were defined as MHO phenotype according to BMI categories. Compared to individuals with MHNW, those with MHO were characterized by higher proportions of male and lower proportions of current smoker and drinker, university or higher degree participants. Levels of LDL-C and Hs-CRP were higher in the MHO group than in the MHNW group. In contrast, individuals with MHO exhibited more favorable risk profiles than those with MUO. FPG and TG levels were lower, and HDL-C level in the MHO group was higher than those in the MUNO group. Supplement table 1 shows the characteristics of participants in 2010/11.

Change in metabolic health status and risk of CKD

Among participants with MHNW at baseline, only 17.25% converted to MUNW, and 82.75% were unconverted at 2010/11 resurvey. Among participants with MHO, 39.64% converted to MUO, and 60.36% were stable MHO (Table 2).

During a mean follow-up of 7.02±2.45 years, 5351 participants developed CKD from 2010/11. The Kaplan-Meier survival curves for cumulative incidence of CKD according to the change in metabolic health status are shown in Supplement figure 2. Compared with the MHNW group, the other groups had higher probabilities of developing incident CKD (log-rank test X^2=345.72, P < 0.05).

Table 2 presents the change in metabolic health status and risk of CKD. Compared with participants in the stable MHNO group, the stable MHO group had a significantly higher risk of incident CKD (HR: 1.16; 95% CI: 1.02-1.33), but was lower than that in individuals with MUO (HR: 1.96; 95% CI: 1.74-2.12). The risk of CKD development was even much higher in people who changed to a metabolic abnormality. The risk of CKD was also higher in MHNW-MUNW (HR: 1.17; 95% CI:1.03-1.33), MHOW-MUOW (HR:1.25; 95% CI:1.12-1.39) and MHO-MUO individuals (HR: 1.36; 95% CI: 1.17-3.58).

When we stratified by age, the risk of CKD for individuals with MUO who younger than 45 years had the highest risk compared with stable MHNW (HR: 2.04; 95%CI:1.62-2.57). In each age group, participants that changed from metabolic healthy to metabolic abnormality had a higher risk of developing CKD compared with stable MHNW individuals, whereas the corresponding associations were attenuated in older than 60 years (Figure 1).

Metabolic health status as a time-dependent exposure

The results for metabolic health status, treated as a time dependent measure for risk of CKD are given in Table 3. Participants who were initially metabolic health but developed hypertension, diabetes or hyperlipidemia had a CKD risk similar but attenuated to participants who were metabolic abnormality at baseline. For these individuals with normal weight, overweight, and obesity with developed hypertension, the risk of CKD was higher compared to individuals with stable MHNW individuals without incident diabetes (normal weight, HR: 1.24; 95%CI:1.14-1.34, overweight, HR: 1.30; 95%CI:1.21-1.41, obesity, HR: 1.48; 95%CI:1.33-1.65, respectively). Similarly, initially metabolic healthy individuals with incident diabetes or hyperlipidemia had higher risk of CKD compared with stable MHNW individuals without incident diabetes or hyperlipidemia. And participants with MHO remained at an increased risk compared with those with MHNW, even if they did not develop the metabolically abnormal factors (HR: 1.19; 95%CI:1.11-1.29).

Sensitivity analysis

Sensitivity analyses did not meaningfully affect results (Supplement table 2). The results of Fine and Gray model accounting for the competing risk of death were consistent with the main analyses. In the sensitivity analyses, the associations of change in metabolic health status with risk of incident CKD categories were not materially changed after excluding participants with CKD occurring within the first two years of the follow-up, or changing the definition of overweight and obesity (overweight ≥ 25kg/m^2 and obesity≥ 30kg/m^2), or excluding participants who received medication with anti-hypertensive, glucose- and lipid-lowering, or interval censored time-to event data.

Change in metabolic health status by WC categories and risk of CKD

Baseline characteristics according to metabolic health status by wc categories are shown in Supplement Table 3. When the baseline and follow-up status of obesity was defined using WC criteria, the risk of CKD still remained higher in participants who changed to a metabolic abnormality irrespective of their obesity. However, stable MHO individuals by WC categories did not show statistically difference (Supplement Table 4).

Discussion

In the present study, we found that MHO phenotype was a dynamic condition, and the changes in metabolic health status were associated with different risks of CKD. The transition from metabolic healthy to metabolic abnormality was associated with an increased risk of CKD. Moreover, individuals with stable MHO had higher risk of CKD compared with those with stable MHNW.

There is an increasing focus on the risk of chronic diseases among MHO individuals, but evidence on the risk of CKD has been lacking and inconsistent. Panwar et al. found that higher BMI was associated with lower risk of incident ESRD among those without the metabolic syndrome but not those with the metabolic syndrome.[23] In the Oike Health Survey of a large prospective cohort of 3136 Japanese employees, MHO phenotype was not associated with a higher risk of incident CKD.[14] On the contrary, more recent studies of Asian population have consistently shown a significant association between MHO phenotype and incident CKD, which is consistent with our findings.[12-13, 24-26] One possible reason for this discordant result may be the lack of a uniform clearly defined characterization of metabolic health status, particularly with regard to MHO phenotype. In this study, we used the most common definition of MHO phenotype according to American Heart Association/National Heart, Lung, and Blood Institute for Asian populations criteria and found that MHO is associated with increased risk of CKD, suggesting that MHO is not a benign condition.

However, although most findings tend to MHO is an independent risk factor for CKD, these studies were limited by their single assessment. More evidence suggests that MHO is not a permanent state, but it may be a dynamic nature. [15-18] Approximately 30% to 50% of individuals originally identified as MHO was transitioned to a metabolic abnormality over time. [27] In present study, 39.64% of the initial MHO individuals progressed to a metabolic abnormality phenotype during the 4-year period, supporting the concept that MHO phenotype is a dynamic condition. Thus, assessment of the effect of metabolic health status on the risk of CKD at a multiple-time point would facilitate the identification of the health implications of MHO.

In this background, an important finding of this study is that obese individuals were associated with an increased risk of developing CKD regardless of the change in metabolic health status. Compared with stable MHNW group, stable MHO showed increased risk of CKD, with HR of 1.16 (95% CI, 1.02-1.33). The risk of CKD development was even much higher in MHO individuals who changed to metabolic abnormality, with multivariate-adjusted HR of 1.36 (95% CI, 1.17-1.58), but was still less than MUO group (HR 1.92, 95%CI 1.74-2.12). However, little is known about the association between change in metabolic health status and risk of CKD. To our knowledge, only a few cohort studies have investigated individuals with stable MHO or changed to metabolic abnormality phenotype was associated with higher risk of CKD compared with MHNW individuals. [17-18] Similarly, we have identified the same trend in the association between changes in MHO phenotypes over time and risk of CKD. In addition, we stratified the participants into different age groups and found that changes in metabolic

health status and individual component affected CKD risk in young and middle age groups more dramatically than in the old age group. Our results show that participants who suffered MUO before the age of 40 years were at the highest risks of CKD (HR 2.29, 95%CI 1.66-3.17). Age is an important independent risk factor for both metabolic abnormality and CKD. A cohort study using data from the The Health Improvement Network (THIN) reported that compared with individuals with a MHNW, there was a higher risk of incident CKD among those who had MHOW and MHO. The association was stronger in those younger than 65 years of age. [13] One possible explanation for our findings is that individuals with metabolically abnormal younger are more likely to have lower adherence to daily treatment compared with those who were diagnosed at an older age, which in turn led to greater relative increases in CKD risk.

The time-fixed approach may lead to biased results when the proper time-dependent approach to data analysis is needed. [27-28] Dynamic changes of metabolic status could lead to misclassification of participants with initial metabolic healthy who convert to an unhealthy status during follow-up. Similarly, we also found that time-varying nature of metabolic health status with increasing age increased risk of CKD during follow-up by updating these exposures biennially. Furthermore, we considered long-term onset of single metabolic disease as well as overall metabolic health status. From the three metabolic diseases, new-onset hypertension, diabetes and hyperlipidemia during follow-up had a significant effect on CKD risk among individuals with initial metabolic healthy. Numerous previous studies confirmed that hypertension, diabetes and hyperlipidemia are strong risk factors for CKD. Our findings carry potentially important implications for population health prevention of CKD and for clinical decision-making. For the general population, maintaining BMI within the desirable range and better control of metabolic health is important for preventing the chronic diseases. However, whether the effectiveness of early anti-hypertensive, glucose- and lipid-lowering treatment or weight loss to reduce the increased risk for CKD are worth further in-depth study.

Strengths of the current study include the use of its prospective cohort design, large sample size, a long follow-up for CKD events and repeated measurements of multiple laboratory variables. However, our investigation has several limitations. First, our study population comprised participants with Kailuan Study, not covering completely Chinese. Second, GFR was not directly measured but was estimated by a serum creatinine-based equation that might have overestimated or underestimated the actual GFR. In addition, we could not consider albumin to creatinine ratio when defining CKD because the albumin to creatinine ratio was not routinely performed in health screening examinations. Last although our analysis adjusted for several potential confounders, some unmeasured possibly confounding residual factors, such as visceral fat content and family history, cannot be fully ruled out.

In the present study, we observed that MHO phenotype or its transition to a metabolically unhealthy phenotype were associated with increased risk of CKD. Moreover, stable metabolic healthy individuals had lower risk of CKD than those with metabolically unhealthy phenotype. Hence, clinicians should consider the risk of incident CKD in people with abnormal metabolically healthy status and counsel them about metabolic fitness and weight control.

Declarations

Ethics approval and consent to participate

The study was performed according to the guidelines of the Helsinki Declaration and was approved by the Ethics Committee of Kailuan General Hospital (approval number: 2006-05). All participants were agreed to take part in the study and provided informed written consent.

Consent for publication

Not Applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no potential conflict of interest.

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None

Authors' contributions

Haozhe Cui and Liu Qian wrote the main manuscript text and conceived and designed the study. Haozhe Cui analyzed the data. Liu Qian carried out literature search. Yuntao Wu and Liying Cao performed the manuscript review. All authors have read and approved the content of the manuscript.

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Tables

Table 1 Baseline characteristics of participants by metabolic health status

	MHNW	MHOW	MHO	MUNW	MUOW	MUO	*P*
N	13162	10984	3570	2703	5698	3346	-
Age, years	50.22±11.57	51.13±10.81	50.06±11.25	55.34±10.56	55.08±9.82	52.80±10.42	0.001
Male, %	9369(71.18)	8755(79.71)	2770(77.59)	2188(80.95)	4828(84.73)	2795(83.53)	0.001
BMI, kg/m^2	21.87±1.40	25.74±1.12	30.03±2.06	2.31±1.28	26.01±1.12	30.34±2.29	0.001
WC, cm	80.09±8.64	84.61±7.65	94.45±8.76	82.98±8.08	89.68±7.17	96.83±8.61	0.001
LDL-C, mmol/L	2.16(1.65-2.65)	2.30(1.80-2.75)	2.33(1.86-2.80)	2.24(1.68-2.77)	2.30(1.74-2.81)	2.37(1.80-2.85)	0.001
ATL, U/L	16.00(11.00-22.00)	19.00(13.00-26.00)	21.00(15.00-29.20)	18.00(13.00-25.00)	21.00(15.00-29.00)	23.00(16.20-30.00)	0.001
Hs-CRP, mg/L	0.48(0.20-1.40)	0.70(0.30-1.90)	1.07(0.42-2.60)	0.70(0.25-1.91)	0.90(0.37-2.31)	1.27(0.58-3.00)	0.001
Current smoker, %	4072(30.94)	3484(31.72)	1038(29.08)	925(34.22)	1914(33.59)	1066(31.86)	0.001
Current drinker, %	2249(17.09)	1949(17.74)	540(15.13)	643(23.79)	1261(22.13)	610(18.23)	0.001
Active physical exercise, %	1508(11.46)	1260(11.47)	408(11.43)	392(14.50)	849(14.90)	454(13.57)	0.001
High income, %	943(7.16)	786(7.16)	240(6.72)	181(6.70)	415(7.28)	261(7.80)	0.05
University or higher degree, %	1300(9.88)	876(7.98)	283(7.93)	151(5.59)	334(5.86)	223(6.66)	0.001

BMI, body mass index; WC, waist circumstance; MHNW, metabolically healthy normal-weight; MHOW, metabolically healthy overweight; MHO, metabolically healthy obesity; MUNW, metabolically unhealthy normal-weight; MUOW, metabolically unhealthy overweight; MUO, metabolically unhealthy obesity.

Table 2 Association of change in metabolic health status and risk of CKD

	N	Events	Incidence, /1000 person-years	HR(95%CI)
Stable MHNW	10891	1147	14.62	Reference
MHNW-MUNW	2271	294	18.70	1.17(1.03-1.33)
MUNW	2703	436	24.35	1.37(1.23-1.53)
Stable MHOW	7753	884	15.80	1.06(0.97-1.16)
MHOW-MUOW	3231	438	19.18	1.25(1.12-1.39)
MUOW	5698	1002	26.22	1.54(1.41-1.68)
Stable MHO	2155	274	17.58	1.16(1.02-1.33)
MHO-MUO	1415	199	19.81	1.36(1.17-1.58)
MUO	3346	677	30.31	1.92(1.74-2.12)

Cox proportional-hazards regression models used age as the time scale, all models were adjusted for sex, income, educational level, drinking, smoking, physical activity, ALT, LDL-C, Hs-CRP. MHNW, metabolically healthy normal-weight; MHOW, metabolically healthy overweight; MHO, metabolically healthy obesity; MUNW, metabolically unhealthy normal-weight; MUOW, metabolically unhealthy overweight; MUO, metabolically unhealthy obesity.

Table 3 Association of time-varying metabolic health status with incidence of CKD

	Normal Weight at baseline			Overweight at baseline			Obese at baseline		
	MH at baseline		MU at baseline	MH at baseline		MU at baseline	MH at baseline		MU at baseline
	Stable MH	MU during follow-up		Stable MH	MU during follow-up		Stable MH	MU during follow-up	
Incident metabolic abnormality									
Reference	1.31(1.21-1.42)	1.44(1.35-1.53)		1.05(1.00-1.11)	1.36(1.27-1.46)	1.64(1.56-1.72)	1.19(1.11-1.29)	1.52(1.38-1.66)	1.88(1.77-1.99)
Incident hypertension									
Reference	1.24(1.14-1.34)	1.54(1.45-1.64)		1.16(1.08-1.25)	1.30(1.21-1.41)	1.70(1.61-1.81)	1.18(1.05-1.33)	1.48(1.33-1.65)	2.03(1.90-2.16)
Incident diabetes									
Reference	1.04(0.94-1.16)	1.40(1.30-1.51)		1.13(1.08-1.17)	1.35(1.25-1.46)	1.59(1.50-1.69)	1.36(1.29-1.43)	1.47(1.33-1.63)	1.90(1.77-2.04)
Incident hyperlipidemia									
Reference	1.21(1.12-1.31)	1.19(1.12-1.26)		1.09(1.04-1.15)	1.33(1.24-1.43)	1.40(1.34-1.48)	1.25(1.16-1.35)	1.58(1.44-1.73)	1.68(1.59-1.78)

Hazard ratios were estimated using time varying metabolic health status in Cox proportional hazards regression with age as the time-scale, adjusted for sex, income, educational level, drinking, smoking, physical activity, ALT, LDL-C, Hs-CRP, hypertension/diabetes/hyperlipidemia. Metabolic health status was updated every two years. MH, metabolic health; MU, metabolic unhealth.

Figures

Figure 1

Change in metabolic health status and risk of CKD by age groups (A. Change in metabolic health status and risk of CKD by age groups. B. Change in hypertension status and risk of CKD by age groups. C. Change in diabetes status and risk of CKD by age groups. D. Change in hyperlipidemia status and risk of CKD by age groups. MHNW, metabolically healthy normal-weight; MHOW, metabolically healthy overweight; MHO, metabolically healthy obesity; MUNW, metabolically unhealthy normal-weight; MUOW, metabolically unhealthy overweight; MUO, metabolically unhealthy obesity. Cox proportional-hazards regression models used age as the time scale, all models were adjusted for sex, income, educational level, drinking, smoking, physical activity, ALT, LDL-C, Hs-CRP.)

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