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The association between the cardiac metabolic index and rapid kidney function decline and CKD in individuals with different glucose metabolism statuses: results from the China health and retirement longitudinal study

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Abstract

Background The Cardiometabolic Index (CMI) is a new measure that combines fat distribution and lipid profiles. However, its relationship with rapid decline in renal function and the chronic kidney disease (CKD), especially in individuals with varying glucose metabolism, is still unclear.

Method This study included 3,485 participants aged 45 and above from the China Longitudinal Study on Health and Retirement (CHARLS), with baseline assessments in 2011–2012 and follow-ups in 2015 and 2018. Participants were grouped into four categories (Q1-Q4) based on baseline CMI levels. The primary outcome was rapid decline in renal function, with CKD events also observed. Multivariable logistic models and restricted cubic spline (RCS) analysis were used to explore the relationship between baseline CMI levels and the risk of kidney disease in individuals with different glucose metabolism statuses. Nine machine learning models were developed using baseline CMI to validate its predictive ability for kidney disease risk. Finally, mediation causal analysis was conducted to examine whether the development of diabetes in the non-diabetic population serves as an important mediator in the relationship between CMI and kidney disease.

Results During the follow-up period, a total of 173 participants (4.96%) experienced rapid decline in renal function, and 87 participants (2.50%) developed CKD. With increasing baseline CMI levels, the risk of rapid decline in renal function and CKD significantly increased. Among the various machine learning models for predicting kidney disease, logistic regression performed excellently, with AUCs exceeding 0.6, indicating the strong predictive ability of baseline CMI. For the primary outcome, multivariable logistic regression analysis showed that, in all participants, as well as in

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the normal glucose regulation (NGR) group and the prediabetes (Pre-DM) group, the incidence of rapid decline in renal function significantly increased across different CMI groups ($P < 0.05$), with trend RR values of 1.285(1.076,1.536), 1.308 (1.015, 1.685) and 1.566 (1.207, 2.031), respectively. However, this association was not observed in patients with diabetes (P for trend > 0.05). RCS analysis further indicated that higher baseline CMI levels were associated with a greater risk of rapid decline in renal function in all participants and in the non-diabetic population. A similar trend was observed for CKD. Finally, mediation causal analysis showed that the development of new-onset diabetes in the non-diabetic population may not be an important mediator in the relationship between CMI and kidney disease.

Conclusion Higher baseline CMI levels were significantly linked to rapid decline in renal function and CKD in middle-aged and elderly individuals, with the relationship varying by glucose metabolism status. CMI may serve as a useful indicator for predicting kidney disease risk, especially in non-diabetic population.

Keywords Cardiometabolic index, CHARLS, Rapid kidney function decline, CKD, Glucose metabolism

Introduction

CKD has gradually become a major global public health issue affecting human health [1]. The ultimate outcome of CKD is renal failure, which not only severely impacts quality of life but also significantly increases morbidity and mortality [2]. Multiple factors contribute to kidney function decline, including glomerulonephritis, diabetes, hypertension, and nephrotoxic drugs. Since 2011, diabetes has replaced glomerulonephritis as the leading cause of CKD. Despite numerous efforts, effective treatments for its devastating renal consequences remain a significant challenge [3]. Therefore, identifying modifiable risk factors and strengthening risk stratification for kidney disease is urgent.

Previous studies have confirmed a significant relationship between dyslipidemia, obesity, and the deterioration of kidney function [4, 5]. In patients with CKD, alterations in lipid profiles typically manifest as decreased high-density lipoprotein cholesterol (HDL-C) levels and elevated triglyceride (TG) levels [6]. Additionally, studies have shown that the TG/HDL-C ratio (an index that considers both risk and protective factors) is positively correlated with CKD and is more strongly associated with CKD than TG levels alone [7–9]. Obesity plays a key role in the onset and progression of CKD. Traditional obesity indicators, such as body mass index (BMI), are associated with CKD, but the correlation is not entirely clear, possibly due to BMI's inability to accurately identify abdominal obesity [10]. One study found that the CKD risk in normal-weight individuals with obesity was approximately three times higher than that of non-obese individuals [11]. Another study showed that the visceral fat volume assessed by abdominal CT was associated with CKD risk, while BMI did not demonstrate such a correlation [12]. Waist-to-height ratio (WHtR) is an indicator of visceral fat, but the WHtR alone does not comprehensively estimate visceral fat content. Therefore, it is recommended to combine lipid abnormality parameters with WHtR for more accurate assessment [12].

Recently, a new index called the CMI has been proposed. Studies have shown that CMI is significantly correlated with conventional cardiovascular risk factors, including hypertension, diabetes, metabolic syndrome, and hyperuricemia [13–16]. As an emerging index related to obesity and metabolism, CMI combines height and waist circumference and is superior to BMI in reflecting visceral obesity. Furthermore, CMI integrates lipid parameters, and lipids are key factors in the pathogenesis of kidney disease [17]. In cross-sectional studies, CMI has been reported to be associated with kidney-related diseases. For example, Xu et al. found a positive correlation between CMI and albuminuria, which is the most sensitive and accurate diagnostic indicator of early kidney disease [17]. Additionally, Yu et al. reported an independent positive correlation between CMI and CKD risk in elderly adults with hypertension [18]. However, several critical gaps remain in the current literature. First, longitudinal evidence linking CMI to kidney disease risk in the general middle-aged and elderly population is limited. Second, no clear causal relationship between CMI and kidney disease has been established. Additionally, given the significant impact of glucose metabolism on kidney disease development [19], the interaction between CMI and kidney outcomes across different glucose metabolism statuses has not been adequately explored.

To address these gaps, this study aims to investigate the association between CMI and kidney disease risk in a large-scale prospective cohort of middle-aged and elderly individuals. Specifically, we will examine whether CMI predicts rapid kidney function decline and CKD progression, and how this relationship may vary based on individual glucose metabolism status. This research is essential for advancing our understanding of kidney disease mechanisms and identifying potential biomarkers for early intervention.

Methods

Study participants and design

The data for this study were sourced from the CHARLS conducted from 2011 to 2015. CHARLS is a nationally representative longitudinal survey covering adults aged 45 and above in China, encompassing demographic, economic, lifestyle, and health information [20]. Participants were from different living areas across 28 provinces (including autonomous regions and municipalities) and had varying educational levels. The baseline survey was conducted from June 2011 to March 2012, enrolling a total of 17,708 participants. The sample was subsequently updated through three face-to-face interviews and questionnaires in 2013, 2015, and 2018. Fasting blood samples were collected only in 2011 and 2015 through a standardized process which was detailly described elsewhere (http://charls.pku.edu.cn/index/en.html) and were properly stored and sent to a professional testing institution (Capital Medical University You'anmen Clinical Testing Center).

The study used data from three waves of the CHARLS survey in 2011, 2013, and 2015. Initially, the baseline survey included 17,708 participants. We further excluded the following groups: individuals aged under 45 or with missing age information, those with missing data on high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), and waist-to-height ratio (WHtR), as well as those with missing covariate data. Participants without data on fasting plasma glucose (FPG) or glycated hemoglobin (HbA1c), those missing information on smoking or alcohol consumption, and individuals without kidney outcomes (creatinine and cystatin C) at baseline and follow-up visits, as well as those with impaired kidney function (eGFR < 60 ml/min/1.73 m^2) at baseline were also excluded. Ultimately, 3,485 participants were included in the final analysis. The detailed screening process is shown in Fig. 1.

Data collection

Trained interviewers collected participants' demographic information (such as age, sex, and marital status), health status, and functional data (such as smoking, alcohol consumption, hypertension, and diabetes) using standardized questionnaires. All participants, except those with arm injuries, were asked to rest for 15 min before undergoing three blood pressure measurements on the left arm, with a 45-second interval between each measurement. The final blood pressure value was reported as the average of the three measurements. Participants were instructed to remove their shoes and heavy clothing before measuring their weight and height. Weight and height were measured using standardized scales, accurate to 0.1 kg and 0.1 cm, respectively. Medically trained staff collected venous blood samples from each participant according to standardized blood collection protocols for biochemical testing. Fasting blood glucose levels and serum lipid parameters were measured using enzyme-linked colorimetric assays, while hemoglobin A1c (HbA1c) was determined using boronate affinity high-performance liquid chromatography. Serum creatinine and cystatin C were measured using the Jaffe rate-blank compensation method and particle-enhanced turbidimetric immunoassay, respectively. It is worth mentioning that in the CHARLS, blood samples were collected in 2011 and 2015, respectively. Therefore, our study only evaluated serum creatinine and cystatin C levels at baseline (2011) and endpoint (2015). Consequently, the definitions of rapid kidney function decline and CKD outcomes are consistent with those used in most CHARLS studies [21, 22].

Renal function Estimation

In this study, we primarily used the CKD-EPI creatinine-cystatin C equation developed by the Chronic Kidney Disease Epidemiology Collaboration in 2021 [23] to assess kidney function. Although numerous studies have shown that estimated glomerular filtration rate (eGFR) based on the CKD-EPI cystatin C equation can serve as a potential assessment indicator [24, 25], recent findings indicate that the eGFR estimated using the CKD-EPI equation combining creatinine and cystatin C demonstrates higher accuracy compared to the CKD-EPI cystatin C equation alone when estimating the measured glomerular filtration rate (mGFR) [26]. In this study, serum creatinine was measured using the rate-blank compensated Jaffe method, while serum cystatin C was detected using the particle-enhanced turbidimetric immunoassay.

Definitions

Hypertension was diagnosed based on self-reported physician diagnosis, and/or the use of any antihypertensive medications, and/or an average systolic/diastolic blood pressure (SBP/DBP) ≥ 140/90 mmHg [27]. Diabetes (DM) was defined as fasting plasma glucose (FPG) ≥ 126 mg/dL or HbA1c ≥ 6.5%, and/or self-reported physician diagnosis, and/or the use of antidiabetic medications [28] Pre-DM was characterized by FPG levels between 100 and 125 mg/dL or HbA1c levels between 5.7% and 6.4%. Individuals without diabetes or prediabetes were classified as normal glucose regulation (NGR). According to NCEP ATP III, dyslipidemia was diagnosed based on self-reported physician diagnosis, Dyslipidemia was diagnosed based on the following criteria: self-reported physician diagnosis, current use of lipid-lowering medication, or specific lipid profile measurements. Specifically, a fasting triglyceride level exceeding 150 mg/dl or a fasting HDL-C level below 40 mg/dl in men or 50 mg/

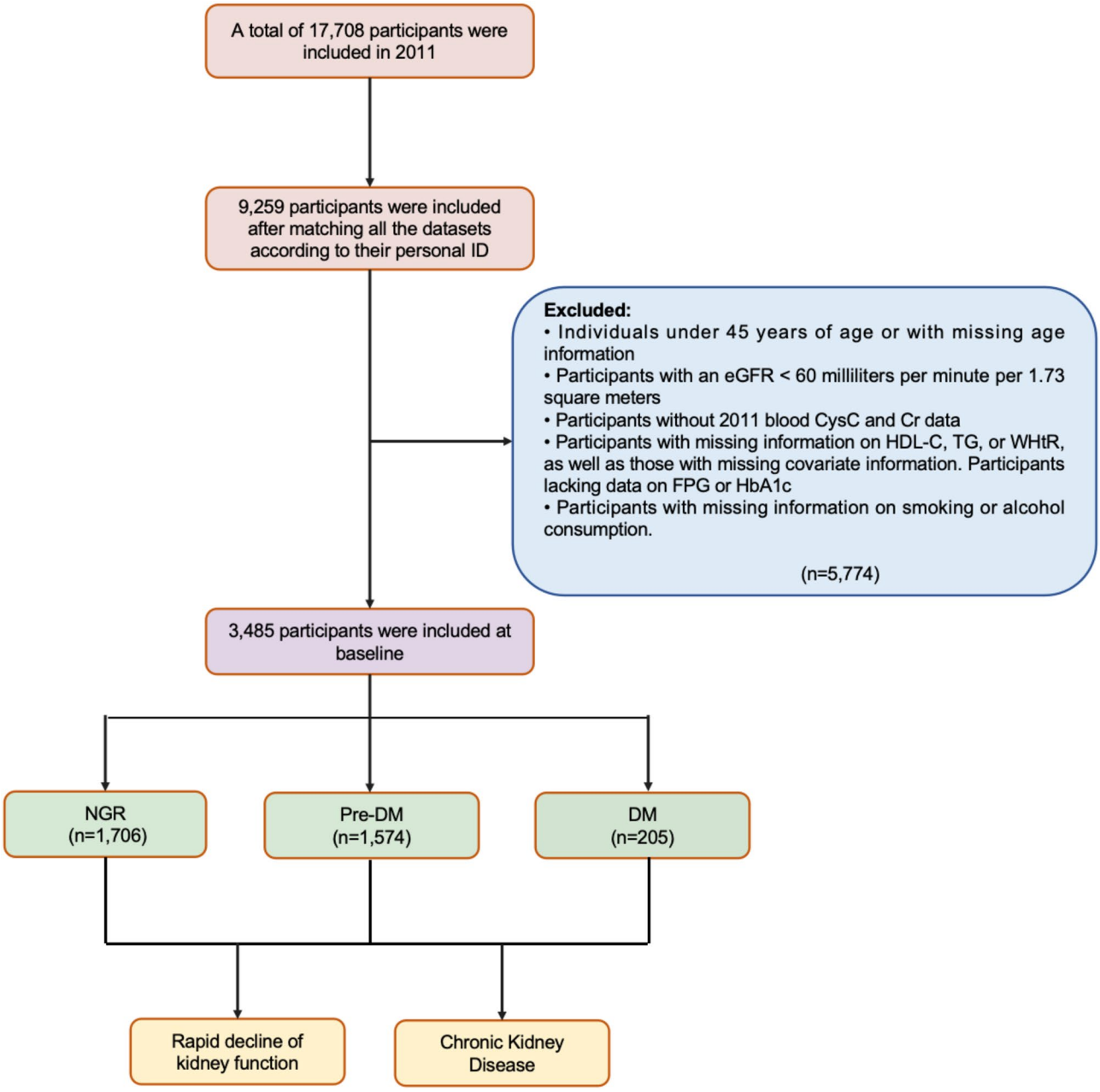

Fig. 1 Flowchart of participant selection

dl in women was considered indicative of dyslipidemia [29, 30]. The presence of heart disease was determined based on self-report by the participants. Specifically, participants were asked the following question: "Did your doctor tell you that you have been diagnosed with a heart attack, angina pectoris, coronary heart disease, heart failure, or other heart problem?" [31].

The BMI was calculated using the formula: weight/height^2 (kg/m^2). During the physical examination, measurements were taken by experienced medical personnel, and records were made by professional recorders to ensure accuracy. Waist circumference (cm) was measured at the end of normal exhalation, at the junction of the midaxillary line and the horizontal line above the outermost margin of the right iliac bone. Body weight (kg) was measured using a digital scale (Omron™ HN 286, Yangzhou Korel Technology Co., Ltd.). For weighing, participants wore examination clothes, stood barefoot in the center of the scale with their arms close to their bodies, and looked straight ahead [32, 33].

To determine smoking status (current, former, or never), participants were asked two questions. First, they were asked, "Have you ever chewed tobacco, smoked a pipe, smoked self-rolled cigarettes, or smoked cigarettes/

cigars?" If the participant answered "yes" to this question, they were then asked, "Do you still have this habit, or have you completely quit?" Participants who reported still using tobacco were classified as current smokers, while those who had quit were classified as former smokers [34]. Participants who answered "no" to the first question were classified as never smokers. For alcohol consumption, participants were classified based on their response to the question, "Did you drink any alcoholic beverages, such as beer, wine, or liquor in the past year? If yes, how often?" Those who indicated drinking more than once per month in the last year were classified as current drinkers. Participants who reported drinking less than once per month or only occasionally were classified as former drinkers. Those who answered "no" to the initial question were classified as never drinkers [35].

The outcome variables of this study were rapid kidney function decline and CKD, with the primary outcome being rapid kidney function decline, defined as a yearly eGFRcr-cys decline of 5 mL/min per 1.73 m^2 or more [21, 36]. The yearly eGFRcr-cys decline was estimated as (baseline eGFRcr-cys – exit eGFRcr-cys) / follow-up time [21]. Secondary outcome was progression to CKD, defined as an annualized decline in eGFRcr-cys of ≥ 5 ml/min per 1.73 m^2 and to a level of < 60 ml/min per 1.73 m^2 at the exit visit [22].

Assessment of CMI

CMI was calculated as (TG/HDL-c) × WHtR according to the previous literature, while WHtR was calculated as waist circumference (cm)/height (cm) [37].

Statistical analysis

In our analysis, we first assessed the normality of variables using the Kolmogorov-Smirnov test. Normally distributed continuous data are presented as mean ± standard deviation and analyzed for statistical significance using one-way ANOVA. Non-normally distributed continuous data are presented as median and interquartile range, and analyzed using the Kruskal-Wallis test. Categorical data are described as frequencies and percentages, and assessed using the chi-square test. CMI was analyzed as a continuous variable using multivariable logistic regression analysis to explore the relationship between baseline CMI and the risk of rapid kidney function decline and CKD, and to calculate RRs and 95% CIs. In this analysis, CMI was log-transformed to mitigate the impact of its right-skewed distribution and better meet the statistical assumptions of the regression analysis. Three models were estimated: Model 1 was the unadjusted model estimating crude odds ratios; Model 2 adjusted for age, sex, alcohol consumption, smoking, marital status, education level, residence, retirement status, SBP, DBP, and BMI; Model 3 further adjusted for hypertension, heart disease, TC, FPG, HbA1c, Uric acid and baseline eGFRcr-cys (To eliminate the impact of baseline kidney function on subsequent kidney function changes and CKD progression, in order to more accurately assess the independent association between CMI and rapid kidney function decline and CKD) [21]. Multicollinearity between variables in each model was assessed using the variance inflation factor (VIF). The VIF values for all variables in each model were below 10, indicating no significant multicollinearity issues. Additionally, RCS analysis based on multivariable-adjusted logistic regression was conducted to visualize the linear or nonlinear relationship between baseline CMI levels and the primary outcome, the risk of rapid kidney function decline, with RR reference set at the median baseline CMI value and baseline set at Y = 1. Furthermore, the baseline CMI distribution was divided into quartiles (Q1, Q2, Q3, Q4) to examine the dose-response relationship between exposure to baseline CMI and rapid kidney function decline and CKD. Trend regression analysis was performed, using the lowest quartile (Q1) as the reference group, to assess the changing trends in outcome risk from Q1 to Q4. Subgroup analysis was performed by baseline age (< 60 years and ≥ 60 years), sex, BMI (< 24 and ≥ 24 kg/m^2), hypertension, and glucose metabolism status (NGR, Pre-DM, and DM) to evaluate whether the adverse effects of CMI on rapid kidney function decline and CKD are consistent. Nine machine learning models were developed using baseline CMI to validate its predictive ability for kidney disease risk. Additionally, to determine the prognostic value of CMI for rapid kidney function decline and CKD in different glucose metabolism statuses, participants with NGR, Pre-DM, and DM were analyzed separately. Causal mediation analysis was performed using the "mediation" package to estimate the impact of baseline CMI mediated by new-onset diabetes on rapid kidney function decline and CKD. Finally, a sensitivity analysis was conducted by excluding participants who fasted for less than eight hours to validate the relationship between baseline CMI and the risk of rapid kidney function decline and CKD across different glycemic statuses. All statistical analyses were conducted using SPSS version 26.0 and R version 4.2.3 (The R Foundation for Statistical Computing, Austria, Vienna). Statistical significance for all tests was set at a two-tailed P-value < 0.05. The principles of the mediation analysis are provided in Figure S1.

Development of ML models

Nine algorithms were used to develop and compare predictive models. Baseline CMI employed as potential predictive variables in the predictive models. The methods used to construct the predictive models included eXtreme Gradient Boosting (XGBoost), Logistic Regression, Light Gradient Boosting Machine (LightGBM),

RandomForest, Adaptive Boosting (AdaBoost), DecisionTree, K-Nearest Neighbors (KNN), Multilayer Perceptron (MLP), and GNB (Gaussian Naive Bayes). All predictive models were implemented in Python 3.7, with the package for XGBoost being "xgboost 1.2.1", for LightGBM "lightgbm 3.2.1", and for the remaining models "sklearn 0.22.1".

To construct the models, patients were randomly divided into three groups: a training set, a validation set, and a testing set. The training set, comprising 80% of the data, was used to train the predictive models, allowing them to learn patterns and relationships within the data. The validation set, consisting of 10% of the data, was used during the training process to fine-tune model hyperparameters and evaluate model performance iteratively. Finally, the testing set, which accounted for the remaining 10% of the data, was used to provide an unbiased assessment of the model's performance on previously unseen data. Ten-fold cross-validation was applied within the training phase to enhance model reliability. The models' ability to predict adverse pregnancy outcomes was evaluated using the area under the receiver operating characteristic curve (AUROC), accuracy, sensitivity, specificity, positive predictive value, negative predictive value, and F1 score.

Results

General characteristics of participants

The baseline clinical and demographic characteristics of participants grouped by CMI quartiles are shown in Table 1. At baseline, 48.90% of participants were aged 60 or older, with 1,876 (53.83%) of them being female. Compared to the lowest CMI quartile, participants in higher CMI quartiles were younger and had a higher proportion of females. Additionally, the proportion of current smokers and current drinkers was lower in higher CMI quartiles. Furthermore, the prevalence of hypertension, dyslipidemia, and heart disease was higher in the higher CMI quartiles. In terms of physiological indicators, SBP, DBP, BMI, WHtR, FPG, HbA1c, TC, TG, LDL, Uric Acid, and baseline eGFRcr-cys levels were significantly higher in the higher CMI quartiles, while HDL-C levels were lower. Notably, the proportion of individuals with NGR decreased, while the proportion of individuals with glucose metabolism abnormalities (including Pre-DM and DM) increased in the higher CMI quartiles.

The association value of baseline CMI for rapid decline in renal function and CKD

During the follow-up period, a total of 173 participants (4.96%) experienced rapid renal function decline, and 87 participants (2.50%) developed CKD. After grouping the participants into quartiles based on CMI, the incidence of rapid renal function decline was 2.86% (25 cases), 2.86% (25 cases), 3.67% (32 cases), and 10.51% (91 cases) from Q1 to Q4, respectively. For CKD, the incidence was 1.83% (16 cases), 1.72% (15 cases), 1.72% (15 cases), and 4.73% (41 cases) from Q1 to Q4, respectively. Multivariable logistic regression models were used to analyze the association between baseline CMI levels and the risk of rapid renal function decline and CKD. Baseline CMI was analyzed both as a continuous variable and as a categorical variable (quartiles). The results showed that after adjusting for potential confounders, Model 3 indicated that for each 1-unit increase in baseline CMI, the risk of rapid renal function decline increased by 35.8% (RR 1.358, 95% CI 1.106–1.676), and the risk of CKD increased by 62.7% (RR 1.627, 95% CI 1.173–2.246). Further multivariable-adjusted RCS analysis revealed a significant dose-response relationship between CMI as a continuous variable and the risk of rapid renal function decline (overall trend $P < 0.001$; non-linear $P < 0.001$; cut-off for CMI = 341.397) (Fig. 2A). In the analysis using categorical variables, Model 3 showed that for rapid renal function decline, the RR for the Q4 group was 2.115 (95% CI 1.212–3.689), with a trend RR of 1.285 (95% CI 1.076–1.536). For CKD, the RR for the Q4 group was 2.866 (95% CI 1.364–6.024), with a trend RR of 1.460 (95% CI 1.137–1.874) (Table 2).

To further investigate the relationship between baseline CMI and the primary outcome of rapid renal function decline, we performed a stratified subgroup analysis. As shown in Table S1, higher CMI levels were significantly associated with an increased incidence of rapid renal function decline, and this association was consistent across different subgroups, including age, sex, BMI, and hypertension status. Specifically, in the NGR group and the Pre-DM group, an increase in CMI levels was closely related to a higher risk of rapid renal function decline. However, this association was not observed in patients with DM.

The predictive value of baseline CMI for rapid decline in renal function and CKD

To validate the ability of baseline CMI in predicting rapid decline in renal function and CKD, the performance of several machine learning models was compared. For predicting rapid decline in renal function, nine prediction models were established: XGBoost, Logistic Regression, LightGBM, RandomForest, AdaBoost, DecisionTree, KNN, MLP, and GNB. Among these models, the Logistic Regression model demonstrated the best predictive performance (Fig. 3A and B), with an AUC of 0.667 (SD = 0.084), an optimal cutoff value of 0.047 (SD = 0.001), accuracy of 0.741 (SD = 0.035), sensitivity of 0.525 (SD = 0.108), specificity of 0.752 (SD = 0.033), positive predictive value of 0.102 (SD = 0.028), negative predictive

Table 1 Baseline characteristics according to quartiles of cardiometabolic index (CMI)

	Total	Quartiles of CMI				*P* value
	(*n* = 3,485)	Q1	Q2	Q3	Q4	
CMI	111.73(65.85,194.46)	47.85(36.92,57.06)	86.91(76.57,98.65)	144.59(127.30,166.55)	312.03(238.40,460.10)	< 0.001*
Gender (n, %)						< 0.001*
Female	1876(53.83)	372(42.56)	478(54.69)	495(56.83)	531(61.32)	
Male	1609(46.17)	502(57.44)	396(45.31)	376(43.17)	335(38.68)	
Age (years, mean ± SD)	59.90 ± 8.92	60.46 ± 9.15	60.29 ± 8.96	59.57 ± 8.80	59.28 ± 8.70	0.016*
Age group (n, %)						0.036*
45–60	1781(51.11)	423(48.40)	431(49.31)	453(52.01)	474(54.73)	
≥ 60	1704(48.90)	451(51.60)	443(50.69)	418(47.99)	392(45.27)	
Smoking status (n, %)						< 0.001*
Never	2130(61.12)	458(52.40)	535(61.21)	565(64.87)	572(66.05)	
Former	298(8.55)	69(7.90)	68(7.78)	82(9.41)	79(9.12)	
Current	1057(30.33)	347(39.70)	271(31.01)	224(25.72)	215(24.83)	
Drinking status (n, %)						
Never	2067(59.31)	430(49.20)	534(61.10)	546(62.69)	557(64.32)	< 0.001*
Former	295(8.47)	70(8.01)	70(8.01)	84(9.64)	71(8.20)	
Current	1123(32.22)	374(42.79)	270(30.89)	241(27.67)	238(27.48)	
Marital status (n, %)						0.663
Married/cohabitating	3059(87.78)	758(86.73)	767(87.76)	766(87.95)	768(88.68)	
Divorced/separated/ widowed/never married	426(12.22)	116(13.27)	107(12.24)	105(12.06)	98(11.32)	
Education level (n, %)						0.900
Illiterate	1790(51.41)	447(51.20)	455(52.12)	457(52.53)	431(49.77)	
Primary school or below	805(23.12)	199(22.80)	211(24.17)	192(22.07)	203(23.44)	
Middle school	634(18.21)	163(18.67)	150(17.18)	153(17.59)	168(19.40)	
High school or above	253(7.266)	64(7.331)	57(6.529)	68(7.82)	64(7.39)	
Residence (n, %)						0.181
Rural	3076(88.34)	788(90.26)	772(88.33)	766(87.95)	753(87.05)	
Urban	406(11.66)	85(9.74)	107(12.24)	105(12.06)	112(12.95)	
Retired	232(6.79)	46(5.33)	57(6.63)	57(6.69)	72(8.54)	0.071
Hypertension (n, %)	887(25.53)	159(18.26)	186(21.40)	229(26.32)	313(36.23)	< 0.001*
Dyslipidemia (n, %)	1092(31.33)	38(4.35)	71(8.12)	204(23.42)	779(89.95)	< 0.001*
Heart disease (n, %)	391(11.26)	76(8.73)	76(8.75)	110(12.67)	129(14.91)	< 0.001*
SBP, mm Hg	132.00(119.00,148.00)	128.00(115.00,144.00)	130.00(116.00,145.00)	134.00(121.00,148.00)	137.00(122.00,154.00)	< 0.001*
DBP, mm Hg	77.00(69.00,86.00)	75.00(67.00,83.00)	76.00(69.00,84.00)	79.00(71.00,87.00)	80.00(71.00,89.00)	< 0.001*
BMI, Kg/m2	23.00(20.72,25.59)	21.15(19.37,22.99)	22.22(20.39,24.18)	23.71(21.41,26.06)	25.37(23.09,28.03)	< 0.001*
WHtR	53.37(49.07,58.43)	48.99(45.77,52.46)	52.50(48.60,56.50)	54.87(51.01,59.24)	58.02(53.75,62.44)	< 0.001*
TG, mg/dl	104.43(74.34,153.11)	61.95(52.22,73.46)	88.50(77.88,101.78)	123.02(106.20,141.60)	207.98(169.92,274.35)	< 0.001*
TC, mg/dl	191.37(167.40,216.11)	184.02(164.31,208.76)	189.05(165.85,213.40)	191.75(167.78,215.34)	199.87(174.74,225.39)	< 0.001*
HDL-C, mg/d	49.49(40.98,60.31)	64.18(56.44,75.00)	54.12(47.55,61.08)	46.39(40.98,52.19)	36.73(31.32,42.91)	< 0.001*
LDL-C, mg/dl	114.43(93.17,137.24)	107.09(88.15,129.12)	116.75(97.81,140.34)	120.62(99.74,142.27)	112.89(86.21,138.02)	< 0.001*
Glucose, mg/dl	102.42(94.50,112.68)	99.90(92.70,108.54)	100.26(93.24,108.36)	101.70(94.68,111.24)	109.26(99.90,128.88)	< 0.001*
HbA1c, %	5.20(4.90,5.40)	5.10(4.90,5.40)	5.10(4.90,5.40)	5.20(4.90,5.40)	5.30(5.00,5.60)	< 0.001*
Uric Acid, mg/dl	4.22(3.52;5.04)	4.14(3.42;4.88)	4.08(3.44;4.80)	4.14(3.50;5.01)	4.53(3.81;5.36)	< 0.001*
eGFRcr-cys, ml/min per 1.73 m^2	90.90(79.85,101.87)	90.42(78.80,100.99)	89.32(78.58,100.30)	90.47(80.83,101.14)	93.39(81.52,105.74)	< 0.001*
GMS, n (%)						< 0.001*
NGR	1706(48.95)	465(53.20)	460(52.63)	422(48.45)	359(41.46)	
Pre-DM	1574(45.17)	380(43.48)	375(42.91)	400(45.92)	419(48.38)	
DM	205(5.88)	29(3.32)	39(4.46)	49(5.63)	88(10.16)	

Abbreviation: Chronic Kidney Disease; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; BMI: Body Mass Index; WHtR: Waist-to-Height Ratio; CMI: Cardiometabolic Index; TG: Triglycerides; TC: Total Cholesterol; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholestero; HbA1c,: Hemoglobin A1c; eGFRcr-cys: Estimated Glomerular Filtration Rate calculated by Creatinine and Cystatin C; GMS Glucose Metabolic State; NGR: Normal Glucose Regulation; Pre-DM: Pre-Diabetes Mellitus; DM: Diabetes Mellitus.*$p < 0.05$

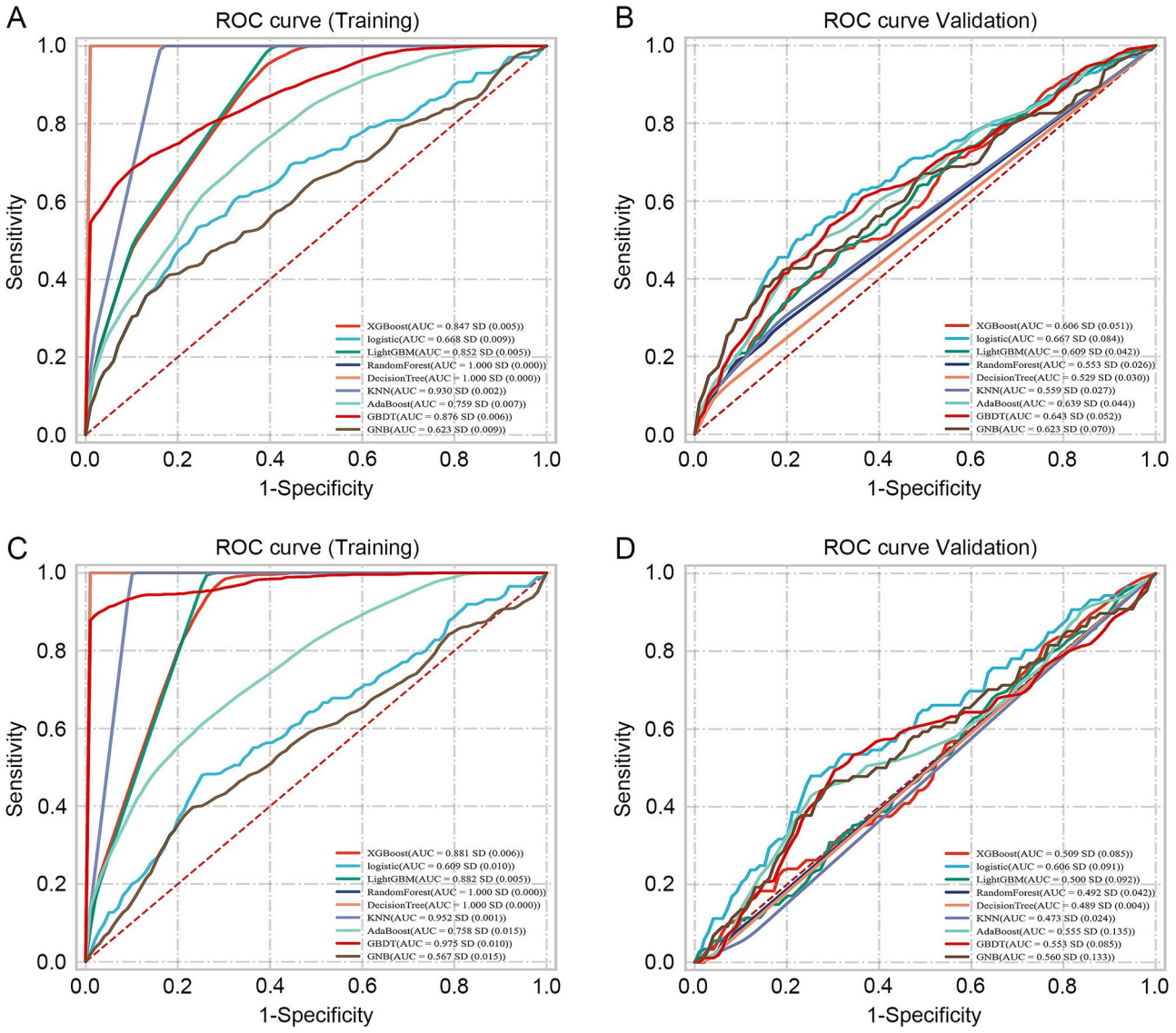

Fig. 2 Association between baseline CMI and the risk of rapid decline in kidney function: Based on a multivariable-adjusted restricted cubic spline model, we fully adjusted the model for age, gender, alcohol consumption, smoking, marital status, education level, place of residence, retirement status, systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI), hypertension, heart disease, total cholesterol (TC), fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), Uric Acid and eGFRcr-cys. The analysis results are as follows: (**A**) All participants; (**B**) Normal glucose regulation (NGR) participants; (**C**) Prediabetes (Pre-DM) participants; (**D**) Diabetes mellitus (DM) participants

value of 0.968 (SD = 0.008), F1 score of 0.170 (SD = 0.045), and Kappa coefficient of 0.095 (SD = 0.049) (Table 3).

For predicting CKD, after comparing multiple machine learning models, the Logistic Regression model again showed the best predictive capability (Fig. 3C, D), with an AUC of 0.606 (SD = 0.091), an optimal cutoff value of 0.025 (SD = 0.000), accuracy of 0.743 (SD = 0.025), sensitivity of 0.468 (SD = 0.123), specificity of 0.750 (SD = 0.026), positive predictive value of 0.046 (SD = 0.014), negative predictive value of 0.982 (SD = 0.003), F1 score of 0.084 (SD = 0.026), and Kappa coefficient of 0.041 (SD = 0.025) (Table S2). The best AUCs for baseline CMI in predicting both rapid decline in renal function and CKD exceeded 0.6, indicating that baseline CMI has a relatively good predictive ability.

The relationship between CMI and the risk of rapid decline in renal function and CKD is modulated by an individual's glycemic status

During the follow-up period, there were significant differences in the incidence of rapid renal function decline and CKD among participants with different glycemic statuses. Specifically, in the NGR group, 79 participants (4.63%) experienced rapid renal function decline, and 46 participants (2.70%) developed CKD; in the Pre-DM group, 71 participants (4.51%) experienced rapid renal

Table 2 The RR and their 95% confidence intervals (CI) for the rapid decline of kidney function and CKD based on CMI in the three models

	Rapid decline of kidney function in follow-up			CKD in follow-up		
	RR (95% CI)			RR (95% CI)		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Continuous						
CMI(Ln)	2.076(1.763,2.446)	2.074(1.738,2.489)	1.358(1.106,1.676)	1.523(1.204,1.910)	1.510(1.147,1.990)	1.627(1.173,2.246)
	< 0.001*	< 0.001*	0.004*	< 0.001*	0.003*	0.003*
Quartile						
Q1	1.000 (reference)	1.000 (reference)	1.000(reference)	1.000 (reference)	1.000 (reference)	1.000(reference)
Q2	1.086(0.618,1.907)	1.094(0.621,1.928)	1.203(0.665,2.177)	0.936(0.460,1.906)	0.943(0.452,1.968)	0.935(0.438,1.993)
Q3	1.346(0.786,2.305)	1.302(0.750,2.261)	1.235(0.689,2.215)	0.936(0.460,1.906)	0.906(0.424,1.936)	1.000(0.455,2.196)
Q4	4.112(2.596,6.515)	3.982(2.450,6.474)	2.115(1.212,3.689)	2.637(1.468,4.735)	2.562(1.309,5.016)	2.866(1.364,6.024)
Trend Analysis RR Value	1.717(1.475,2.000)	1.689(1.439,1.983)	1.285(1.076,1.536)	1.442(1.180,1.762)	1.416(1.130,1.774)	1.460(1.137,1.874)

Model 1: Unadjusted

Model 2: Adjusted for age, gender, alcohol consumption, smoking, marital status, education level, place of residence, retirement status, systolic blood pressure (SBP), diastolic blood pressure (DBP), and body mass index (BMI)

Model 3: Further adjusted for hypertension, heart disease, total cholesterol (TC), fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), Uric Acid and eGFRcr-cys, in addition to the adjustments in Model 2

Abbreviation: CKD: Chronic Kidney Disease; CMI: Cardiometabolic Index

*$p < 0.05$

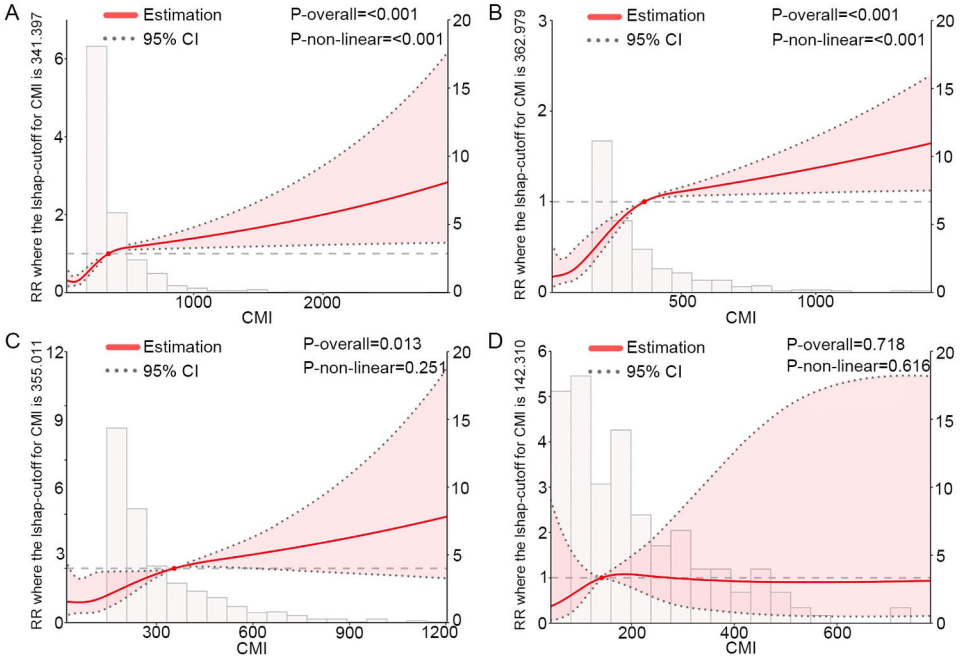

Fig. 3 Using baseline CMI to construct 9 types of machine learning models. Construction and comparison of multiple machine learning models were conducted for the prediction of rapid decline in kidney function and CKD, utilizing ROC curve analysis for the machine learning algorithms on the training set and the validation set. (**A**) Training set of rapid decline in kidney function; (**B**) Validation set of rapid decline in kidney function; (**A**) Training set of CKD; (**B**) Validation set of CKD

function decline, and 30 participants (1.91%) developed CKD; while in the DM group, 23 participants (11.22%) experienced rapid renal function decline, and 11 participants (5.37%) developed CKD. These data suggest that as glycemic status progresses from normal to prediabetes and then to diabetes, the incidence of rapid renal function decline and CKD increases, with a particularly notable rise in the diabetes group (Table S3).

The results of Table 3 show that for the primary outcome of rapid renal function decline, in Model 3, an increase in baseline CMI was significantly associated with an elevated risk in both the NGR and Pre-DM groups. Specifically, in the NGR group, after adjusting

Table 3 Using nine machine learning algorithms to evaluate the performance of CMI in predicting the rapid decline of kidney function on both training and validation datasets

Models	AUC(SD)	cutoff(SD)	Accuracy(SD)	Sensitivity(SD)	Specificity(SD)	PPV(SD)	NPV(SD)	F1 score(SD)	Kappa(SD)
Training set									
XGBoost	0.847(0.005)	0.040(0.003)	0.628(0.020)	0.952(0.017)	0.611(0.021)	0.114(0.004)	0.996(0.001)	0.203(0.006)	0.125(0.007)
Logistic Regression	0.668(0.009)	0.047(0.001)	0.744(0.025)	0.541(0.033)	0.754(0.028)	0.104(0.005)	0.969(0.001)	0.174(0.006)	0.098(0.008)
LightGBM	0.852(0.005)	0.046(0.003)	0.620(0.009)	0.998(0.003)	0.600(0.009)	0.115(0.002)	1.000(0.000)	0.207(0.004)	0.129(0.004)
RandomForest	1.000(0.000)	0.365(0.032)	0.992(0.003)	1.000(0.000)	0.992(0.003)	0.862(0.044)	1.000(0.000)	0.926(0.025)	0.921(0.027)
AdaBoost	1.000(0.000)	1.000(0.000)	1.000(0.000)	1.000(0.000)	1.000(0.000)	1.000(0.000)	1.000(0.000)	1.000(0.000)	1.000(0.000)
DecisionTree	0.930(0.002)	0.200(0.000)	0.846(0.004)	1.000(0.000)	0.838(0.004)	0.244(0.004)	1.000(0.000)	0.392(0.006)	0.340(0.007)
KNN	0.759(0.007)	0.485(0.001)	0.680(0.083)	0.705(0.097)	0.679(0.092)	0.106(0.013)	0.978(0.005)	0.183(0.017)	0.107(0.021)
MLP	0.876(0.006)	0.075(0.008)	0.881(0.037)	0.707(0.034)	0.890(0.041)	0.269(0.065)	0.983(0.001)	0.383(0.064)	0.335(0.073)
GNB	0.623(0.009)	0.016(0.001)	0.811(0.013)	0.404(0.023)	0.832(0.015)	0.112(0.007)	0.964(0.001)	0.175(0.009)	0.106(0.011)
Validation set									
XGBoost	0.606(0.051)	0.040(0.003)	0.582(0.031)	0.532(0.103)	0.584(0.034)	0.063(0.011)	0.960(0.008)	0.112(0.020)	0.025(0.022)
Logistic Regression	0.667(0.084)	0.047(0.001)	0.741(0.035)	0.525(0.108)	0.752(0.033)	0.102(0.028)	0.968(0.008)	0.170(0.045)	0.095(0.049)
LightGBM	0.609(0.042)	0.046(0.003)	0.581(0.036)	0.539(0.085)	0.584(0.039)	0.063(0.009)	0.960(0.008)	0.113(0.016)	0.027(0.018)
RandomForest	0.553(0.026)	0.365(0.032)	0.903(0.014)	0.116(0.064)	0.944(0.015)	0.099(0.054)	0.953(0.004)	0.105(0.057)	0.055(0.060)
AdaBoost	0.529(0.030)	1.000(0.000)	0.911(0.014)	0.104(0.063)	0.954(0.015)	0.105(0.053)	0.953(0.003)	0.102(0.056)	0.057(0.057)
DecisionTree	0.559(0.027)	0.200(0.000)	0.783(0.022)	0.301(0.053)	0.808(0.024)	0.076(0.013)	0.957(0.004)	0.121(0.021)	0.046(0.023)
KNN	0.639(0.044)	0.485(0.001)	0.661(0.078)	0.525(0.117)	0.668(0.086)	0.078(0.014)	0.964(0.006)	0.135(0.023)	0.053(0.026)
MLP	0.643(0.052)	0.075(0.008)	0.835(0.040)	0.310(0.129)	0.862(0.045)	0.108(0.046)	0.960(0.006)	0.157(0.062)	0.091(0.066)
GNB	0.623(0.070)	0.016(0.001)	0.807(0.026)	0.375(0.147)	0.830(0.028)	0.103(0.037)	0.962(0.008)	0.161(0.058)	0.091(0.062)

Abbreviation: AUC, area under the curve; PPV, positive predictive value; NPV, negative predictive value; XGBoost, extreme gradient boosting; LR, logistic regression; LightGBM, light gradient boosting machine; RF, random forest; AdaBoost, Adaptive Boosting; KNN, k-nearest neighbor; MLP, multilayer perceptron; GNB: Gaussian Naive Bayes; PPV: Positive Predictive Value; NPV: Negative Predictive Value

for potential confounders, for each 1-unit increase in baseline CMI, the risk of rapid renal function decline increased by 55.1% (RR 1.551, 95% CI 1.150–2.100). Compared to the lowest quartile (Q1), the RR for the highest quartile (Q4) was 2.434 (95% CI 1.032–5.741), with a trend RR of 1.308 (95% CI 1.015–1.685). In the Pre-DM group, for each 1-unit increase in baseline CMI, the risk of rapid renal function decline increased by 104.2% (RR 2.042, 95% CI 1.473–2.844). Compared to Q1, the RR for Q4 was 3.097 (95% CI 1.480–6.479), with a trend RR of 1.566 (95% CI 1.207–2.031).

However, in the diabetic group, after adjustment, no significant association between increasing CMI and rapid renal function decline was found (RR 1.504, 95% CI 0.892–2.610), and the trend analysis by quartile also showed no significant difference, with a trend RR of 1.027 (95% CI 0.625–1.688). Further RCS analysis revealed a dose-response relationship between baseline CMI and the risk of rapid renal function decline under different glycemic statuses. The results showed that with increasing baseline CMI, the risk of rapid renal function decline significantly increased in the NGR and Pre-DM groups (NGR: P-overall trend $P<0.001$; Pre-DM: P -overall trend $P=0.013$). In the prediabetic group, a linear relationship was observed (non-linear $P=0.251$; Cutoff for CMI = 355.011), whereas in the NGR group, a non-linear relationship was found (non-linear $P<0.001$; Cutoff for CMI = 362.979) (Fig. 2B-C). In contrast, no significant dose-response relationship between CMI and the risk of rapid renal function decline was observed in the DM group (Fig. 2D), although the 95% CIs were wide, indicating potential uncertainty.

For CKD, in Model 3, after adjusting for potential confounders, in the NGR group, each 1-unit increase in baseline CMI was associated with a 70.3% increase in CKD risk (RR 1.703, 95% CI 1.072–2.683), although the trend RR did not reach statistical significance. In the Pre-DM, Model 3 showed a trend RR of 1.595 (95% CI 1.036–2.453), suggesting a significant trend toward an association between CMI and CKD risk. Finally, after adjustment, no significant association was found between increasing CMI and CKD in the diabetic group, and the trend analysis by quartile also showed no significant difference, with a trend RR of 3.307 (95% CI 0.889–12.305). This indicates that in diabetic patients, the relationship between CMI and CKD risk was not significant (Table 4).

Mediation analysis

Finally, to further explore whether incident new-onset diabetes mediates the relationship between CMI and rapid renal function decline in the non-diabetic population, we conducted a mediation analysis. In the

Table 4 The relationship between CMI and the risk of rapid decline in kidney function and CKD under different glucose metabolism States

	Rapid decline of kidney function in follow-up			CKD in follow-up		
	RR (95% CI)			RR (95% CI)		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
NGR						
Continuous						
CMI(Ln)	2.224(1.755,2.822)	2.187(1.693,2.844)	1.551(1.150,2.100)	1.504(1.085,2.044)	1.510(1.007,2.245)	1.703(1.072,2.683)
	< 0.001*	< 0.001*	0.004*	0.011*	0.045*	0.023*
Quartile						
Q1	1.000 (reference)	1.000 (reference)	1.000 (reference)	1.000 (reference)	1.000 (reference)	1.000 (reference)
Q2	1.645(0.675,4.010)	1.532(0.621,3.776)	1.615(0.638,4.086)	1.128(0.431,2.951)	1.033(0.384,2.778)	1.064(0.379,2.985)
Q3	2.439(1.056,5.635)	2.083(0.884,4.908)	1.913(0.784,4.670)	1.385(0.551,3.478)	1.157(0.436,3.068)	1.218(0.445,3.333)
Q4	5.252(2.424,11.379)	4.489(2.026,9.948)	2.434(1.032,5.741)	2.300(0.989,5.347)	1.940(0.768,4.898)	2.239(0.818,6.132)
Trend Analysis RR Value	1.765(1.406,2.216)	1.681(1.328,2.128)	1.308(1.015,1.685)	1.339(1.021,1.756)	1.264(0.937,1.704)	1.315(0.950,1.821)
Pre-DM						
Continuous						
CMI(Ln)	1.797(1.366,2.360)	1.995(1.465,2.717)	2.042(1.473,2.844)	1.394(0.908,2.105)	1.481(0.899,2.412)	1.543(0.873,2.711)
	< 0.001*	< 0.001*	< 0.001*	0.121	0.117	0.132
Quartile						
Q1	1.000 (reference)	1.000 (reference)	1.000 (reference)	1.000 (reference)	1.000 (reference)	1.000 (reference)
Q2	0.589(0.255,1.362)	0.625(0.268,1.458)	0.673(0.285,1.591)	0.709(0.223,2.252)	0.786(0.232,2.664)	0.665(0.185,2.386)
Q3	0.862(0.405,1.836)	1.028(0.465,2.271)	1.095(0.488,2.459)	0.567(0.165,1.953)	0.732(0.195,2.754)	0.887(0.221,3.560)
Q4	2.380(1.275,4.444)	2.896(1.425,5.884)	3.097(1.480,6.479)	2.032(0.811,5.089)	2.526(0.827,7.714)	3.209(0.945,10.898)
Trend Analysis RR Value	1.451(1.159,1.817)	1.540(1.197,1.981)	1.566(1.207,2.031)	1.319(0.945,1.841)	1.421(0.962,2.100)	1.595(1.036,2.453)
DM						
Continuous						
CMI(Ln)	1.951(1.265,3.065)	1.751(1.082,2.932)	1.504(0.892,2.610)	1.603(0.876,2.815)	3.347(1.176,11.937)	4.420(0.583,76.278)
	0.003*	0.026*	0.133	0.108	0.036*	0.197
Quartile						
Q1	1.000 (reference)	1.000 (reference)	1.000 (reference)	1.000 (reference)	1.000 (reference)	1.000 (reference)
Q2	0.480(0.084,2.743)	0.449(0.071,2.837)	0.701(0.078,6.303)	NA	NA	NA
Q3	2.518(0.722,8.781)	3.464(0.883,13.586)	5.000(0.922,27.109)	NA	NA	NA
Q4	2.136(0.601,7.597)	1.612(0.401,6.477)	0.655(0.109,3.925)	NA	NA	NA
Trend Analysis RR Value	1.458(0.970,2.191)	1.348(0.881,2.064)	1.027(0.625,1.688)	1.869(0.999,3.499)	2.309(0.990,5.385)	3.307(0.889,12.305)

Model 1: Unadjusted

Model 2: Adjusted for age, gender, alcohol consumption, smoking, marital status, education level, place of residence, retirement status, systolic blood pressure (SBP), diastolic blood pressure (DBP), and body mass index (BMI)

Model 3: Further adjusted for hypertension, heart disease, total cholesterol (TC), fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), Uric Acid, and eGFRcr-cys, in addition to the adjustments in Model 2

Abbreviation: CKD: Chronic Kidney Disease; CMI: Cardiometabolic Index; NGR: Normal Glucose Regulation; Pre-DM: Pre-Diabetes Mellitus; DM: Diabetes Mellitus

*$p < 0.05$

overall non-diabetic population, the mediation analysis of the association between CMI and rapid renal function decline showed that CMI had a significant positive effect on incident diabetes (coefficient = 0.398, $p < 0.001$), while the effect of incident new-onset diabetes on rapid renal function decline was not significant (coefficient = -0.012, $p = 0.506$). This suggests that incident new-onset diabetes is not a major mediator in the relationship between CMI and rapid renal function decline. Furthermore, the total effect (coefficient = 0.022, $p < 0.001$) and the direct effect (coefficient = 0.023, $p < 0.001$) of CMI on rapid renal function decline were both significant, while the indirect effect was not significant (coefficient = -0.009, $p = 0.208$) (Table S4).

Specifically, in the NGR group, CMI had a significant positive effect on incident new-onset diabetes (coefficient = 0.904, $p < 0.001$), but the effect of incident new-onset diabetes on rapid renal function decline was not significant (coefficient = 0.012, $p = 0.670$), suggesting that incident new-onset diabetes may not be an important mediator between CMI and rapid renal function decline in this group. In the Pre-DM group, CMI had no significant effect on incident new-onset diabetes (coefficient = -0.060, $p = 0.604$), and the effect of incident diabetes on rapid renal function decline was also not significant

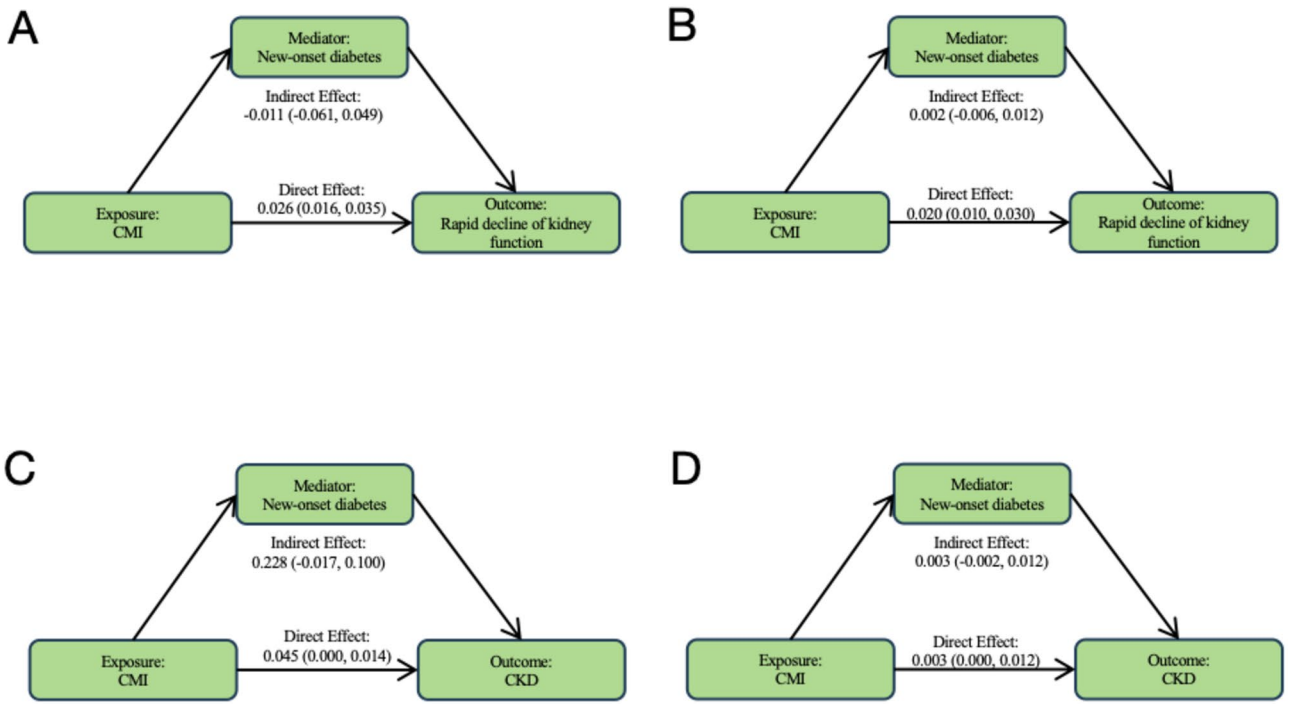

Fig. 4 The mediating role of new-onset diabetes in the association between CMI and Kidney diseases: (**A**) Rapid decline in kidney function investigated within NGR group; (**B**) Rapid decline in kidney function investigated within Pre-DM group; (**C**) CKD investigated within NGR group; (**D**) CKD investigated within Pre-DM group

(coefficient = -0.032, $p = 0.210$). These results indicate that in the non-diabetic population, incident new-onset diabetes may not be a key mediator in the relationship between CMI and rapid renal function decline, suggesting that the impact of CMI on renal function may operate through other mechanisms (Fig. 4, Table S5, S6).

For the secondary outcome of CKD, the mediation analysis results similarly indicate that, in non-diabetic populations including those with NGR and pre-DM, new-onset diabetes is not an important mediator of the relationship between baseline CMI and CKD. Detailed data can be found in Fig. 4 and Tables S7-S9.

Sensitivity analysis

Since 293 participants (8.41%) fasted for less than eight hours, which could potentially affect the classification of their glycemic status, a sensitivity analysis was conducted by excluding these participants to reassess the relationship between baseline CMI and the risk of rapid kidney function decline and CKD across different glycemic statuses. The results remained robust after this adjustment. In the NGR group, for every unit increase in baseline CMI, the risks of rapid kidney function decline and CKD increased by 100.9% (RR 2.009, 95% CI 1.472–2.750) and 49.3% (HR 1.493, 95% CI 1.013–2.150), respectively. In the Pre-DM group, the trend regression analysis showed that baseline CMI was significantly associated with kidney disease outcomes, with relative risks of 1.459 (95% CI 1.115–1.908) for rapid kidney function decline and 1.474 (95% CI 1.010–2.151) for CKD. However, in patients with diabetes, both continuous variable and trend regression analyses revealed no significant association between baseline CMI and kidney disease risk after adjustment (Table S10).

Discussion

In this nationwide longitudinal cohort study of middle-aged and elderly individuals, a significant association was revealed between higher baseline CMI levels and an increased risk of rapid renal function decline and CKD. The moderate AUC values obtained in this study suggest that while baseline CMI is a useful predictor, further research incorporating additional biomarkers and larger datasets is needed to enhance predictive accuracy. Future studies should also explore the integration of longitudinal data and advanced machine learning techniques to improve the discriminatory ability of predictive models. This association was particularly prominent in individuals without diabetes, including those in the NGR and Pre-DM groups. The study suggests that baseline CMI levels may serve as a reliable biomarker for stratifying kidney disease risk, and maintaining lower CMI levels could be beneficial for primary prevention of kidney disease in individuals without diabetes.

Previous studies have shown that excessive fat accumulation and abdominal obesity lead to renal inflammation

and oxidative stress, promote the onset of proteinuria, and accelerate the progression of kidney disease [38]. Lifestyle interventions are considered an important strategy for alleviating the burden of kidney disease [39]. Recent research has emphasized the benefits of adopting a healthy lifestyle, including dietary modifications, weight management, and regular physical activity, in reducing mortality and cardiovascular risk in patients with CKD [40–43]. However, due to the heterogeneity of individual behaviors, differences in reference populations, and the complexity of CKD progression classifications, the implementation of lifestyle interventions remains challenging [44]. Therefore, it is crucial to develop effective predictive biomarkers to identify individuals at high risk during the preclinical stage of kidney disease. Since CMI integrates information on body fat distribution and lipid metabolism abnormalities, it provides a more comprehensive assessment of metabolic dysfunction [45, 46]. Our findings highlight the close relationship between CMI and the risk of rapid renal function decline and CKD, underscoring its potential utility in identifying high-risk kidney disease populations and aiding in early screening and preventive efforts.

According to research, subcutaneous fat is considered benign or protective, while visceral fat accumulation is the primary pathological state of obesity [47, 48]. BMI and WC are easily measured and have been widely used to define obesity and abdominal obesity [49]. However, BMI and WC cannot distinguish between visceral fat and subcutaneous fat [50], despite the significant functional differences between the two. Therefore, reliance on anthropometric measurements alone is insufficient for accurately assessing obesity-related risks [51]. As a result, imaging-based body fat assessment provides a faster diagnosis of obesity. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) can accurately measure visceral fat area, generate high-resolution images, and have high reproducibility [52, 53]. However, CT is expensive and involves radiation exposure, and there is currently a lack of research on technologies assessing visceral fat. CMI, a newly developed evaluation tool (a model combining anthropometric measurements and blood metabolic data), is being studied in various fields, particularly in relation to metabolic diseases. In this study, we found a strong association between CMI and rapid decline in renal function and CKD in the general elderly population, although its underlying mechanism remains unclear. Previous studies suggest that CMI, as a more suitable obesity assessment marker, may explain this association. First, when fat generation exceeds the storage capacity, fat accumulates in tissues and organs, including the kidneys [54]. Fat accumulation can trigger inflammation, oxidative stress, and autophagy via various signaling pathways, leading to extensive proliferation of glomerular basement membrane cells, exacerbating glomerulosclerosis and tubulointerstitial injury, which promotes proteinuria and accelerates the progression of kidney damage [55–57]. Secondly, fat distribution also plays a crucial role in kidney function impairment. Studies have shown that individuals with central fat distribution, whether lean, overweight, or obese, have a higher risk of decreased glomerular filtration rate [58]. Central fat distribution is associated with changes in renal hemodynamic characteristics, as an imbalance between afferent and efferent arterioles leads to impaired glomerular filtration, which may contribute to the susceptibility and progression of chronic kidney injury. CMI, as an integrated indicator considering both lipid and fat distribution, may predict kidney disease progression through the mechanisms outlined above and serve as an excellent early predictor of kidney disease.

This study is the first to find that higher baseline CMI levels are associated with the onset of kidney disease in non-diabetic populations, including those with normal glucose levels and prediabetes. This suggests that an increase in CMI may serve as an early marker for kidney disease risk in non-diabetic individuals, and that elevated CMI may indirectly increase the risk of developing new-onset diabetes, thereby further raising the risk of kidney disease [14, 37, 46]. However, CMI is less effective in predicting rapid kidney function decline or the occurrence of CKD in diabetic patients. This may be related to the dominant role of hyperglycemia in diabetes. Glucotoxicity induced by diabetes directly damages the kidneys through multiple mechanisms, such as the accumulation of advanced glycation end-products (AGEs) and the activation of pro-inflammatory and pro-fibrotic pathways [59–61]. Therefore, in diabetic patients, the impact of hyperglycemia may outweigh the metabolic abnormalities reflected by CMI. Moreover, diabetic patients often have metabolic comorbidities such as hypertension and hyperlipidemia, which contribute to further renal injury through mechanisms like increased vascular resistance, endothelial dysfunction, and oxidative stress [62, 63]. These multiple metabolic risk factors may reduce the predictive value of CMI for kidney disease in diabetic patients. Our mediation analysis suggests that new-onset diabetes is not a key mediating factor in the relationship between CMI and kidney disease. In the non-diabetic population, CMI may more directly reflect the relationship between metabolic burden and kidney function decline, while in diabetic patients, the effects of hyperglycemia and metabolic comorbidities may dominate this process. Therefore, CMI holds more clinical significance in non-diabetic middle-aged and elderly populations. In these groups, where diabetes and its related factors are less prevalent, CMI is more likely to serve as an early predictor of kidney function decline. Given the rising global

prevalence of metabolic diseases and CKD, early identification of high-risk populations is critical for slowing the progression of kidney disease. In conclusion, while CMI may be associated with kidney disease risk in diabetic patients, its role is likely overshadowed by the effects of hyperglycemia and comorbidities. In non-diabetic populations, however, CMI appears to have greater predictive value. Future research should further explore the specific predictive thresholds of CMI, particularly in non-diabetic populations, to enable early detection of kidney disease.

Strengths and limitations

This is the largest population-based longitudinal study to date investigating the relationship between CMI and kidney disease under different glucose metabolism conditions in middle-aged and elderly populations. The data comes from a high-quality, nationally representative longitudinal survey that covers elderly populations across various regions in China, including both urban and rural areas. To obtain robust results, we included potential confounders in the analysis to eliminate any bias that could affect the outcomes. Our analysis demonstrates that baseline CMI is a reliable predictor of kidney disease in the non-diabetic middle-aged and elderly population. Furthermore, since standard tests for TG and HDL-C are widely used in clinical practice, and CMI can be easily calculated using TG, HDL-C, waist circumference, and height, it is reasonable to recommend CMI as an efficient and convenient indicator for assessing kidney disease risk.

However, there are several limitations of this study that need to be considered. First, the Logistic model did not account for medications such as antihypertensive, lipid-lowering, and antidiabetic drugs, which may influence renal function and metabolic markers. This omission was due to substantial missing data on medication use, which precluded their inclusion in the analysis. Second, although the diagnostic criteria for glucose metabolism status have been clearly defined, there may still be slight misclassification for participants at the glucose threshold. Third, due to strict exclusion criteria, some participants from the CHARLS were excluded from this study, resulting in a limited number of participants, which may introduce selection bias. Fourth, this study was conducted on middle-aged and elderly Chinese individuals, and the findings need further validation in other racial and age groups to determine their generalizability. Fifth, this study only focused on the baseline CMI level's impact, without investigating longitudinal changes in CMI during follow-up, which may limit a comprehensive understanding of the dynamic effects of CMI. Sixth, due to the lack of albuminuria measurements in the CHARLS database, albuminuria was not included in the assessment of CKD, which may have led to the omission of relevant data from some CKD populations. However, most CHARLS studies currently use the definition method adopted in this study, making it relatively reliable [21]. Additionally, the small sample size of CKD cases in this study may have limited statistical power and hindered further analysis of CKD stages, thereby obstructing a deeper understanding of the relationship between CMI and CKD severity. This should be addressed in future research. Finally, kidney function was assessed only at baseline and exit visits, with no more frequent measurements, which may affect the accurate capture of kidney function changes over time. The inability to restrict treatment during the study period could further impact the interpretation of the results. Therefore, further validation of our findings in other large cohort studies is required.

Conclusion

This study highlights the significant association between higher baseline CMI levels and an increased risk of rapid decline in renal function and CKD in middle-aged and elderly individuals. The relationship between CMI and kidney disease risk was influenced by glucose metabolism status, with stronger associations observed in individuals with NGR and Pre-DM, while no significant link was found in those with diabetes. These findings suggest that CMI, as a composite indicator of fat distribution and lipid profiles, may serve as a valuable tool for predicting kidney disease risk, particularly in non-diabetic individuals. Additionally, mediation analysis revealed that incident new-onset diabetes does not mediate the relationship between CMI and kidney disease, indicating that other mechanisms may be at play in CMI's effect on renal function. Overall, CMI could be a useful marker for early detection and risk stratification of kidney disease, particularly in clinical settings targeting prevention and early intervention.

Supplementary Information

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Supplementary Material 1

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Author contributions

Wei-Zhen Tang: Conceptualization, Methology, Software, Formal analysis, Writing - Original Draft; Resources, Supervision, Writing - Review & Editing; Qin-Yu Cai: Conceptualization, Methology, Software; Tai-Hang Liu: Cnceptualization, Writing - Original Draft, Wrting– Review & Editing, Visualization; Tao-Ting Li: Resources, Data curation; Gao-hui Zhu: Writing - Original Draft, Wrting– Review & Editing; Jia-cheng Li: Software, Validation; Kang-Jin Huang: Writing - Original Draft, Supervison; Hong-Yu Xu: Investigation; He-Zhe Hua: Investigation; Rong Li: Software, Validation, Resources, Supervision, Writing - Review & Editing.

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Data availability
The data underlying this article will be provided by the corresponding author on reasonable request.

Declarations

Consent for publication
Not applicable.

Competing interests
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