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ORIGINAL RESEARCH

Sex-Specific Associations Between Metabolic Patterns and Renal Function Decline: A Retrospective Cohort Study in Southeastern China

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Purpose: To construct sex-specific metabolic patterns and investigate their effect on renal function decline among individuals without chronic kidney disease (CKD).

Patients and Methods: The subjects were from a community-based health survey in China from 2012 to 2018. 8511 eligible participants with at least three times of investigations were included. Metabolic patterns were constructed by Latent Profile Analysis based on total cholesterol, blood pressure, and fasting glucose. Renal function decline was defined as eGFR < 90 mL/[min•1.73m^2]. The effect of metabolic patterns on renal function decline over time was evaluated using Generalized Estimating Equations (GEE).

Results: Women were classified into No Metabolic Abnormalities (NMA), Hypertension-Impaired Fasting Glucose-Borderline Dyslipidemia (HIB), and Hypertension-Hyperglycemia-Borderline Dyslipidemia (HHB). Men were classified into NMA, Hypertension-Impaired Fasting Glucose-Normal Total Cholesterol (HIN), and Hypertension-Hyperglycemia-Normal Total Cholesterol (HHN). Compared to NMA, the risk of renal function decline over time was approximately 1.33 times higher in the HIB group and 1.41 times higher in the HHB group (95% CIs: 1.29–1.37 and 1.25–1.59, respectively). Consistently, these groups showed a faster eGFR decline over time than NMA. For men, the risks of renal function decline increased by 26% per year in the HIN group compared to NMA (95% CI = 1.19–1.33). No such time-dependent association was observed in the HHN group. Both HIN and HHN groups showed no significant effect on accelerated eGFR decline.

Conclusion: Women with HIB and HHB, and men with HIN, have an accelerated risk of renal function decline. Earlier management of metabolic abnormalities is critical for kidney protection.

Keywords: metabolic abnormality, estimated glomerular filtration rate, renal function decline, gender difference, latent profile analysis

Introduction

Chronic kidney disease (CKD) has an insidious onset and a poor prognosis. Patients with CKD are more likely to develop end-stage kidney disease.[1] In China, CKD has become a major public health concern, with a prevalence of 6.6% in individuals aged 40–49, 9.3% in those aged 50–59, 14.0% in those aged 60–69, and 31.1% in those aged 70 and older during 2018–2019.[2] Additionally, the prevalence of CKD is higher in women than in men among individuals aged 45 and above, with rates of 10.63% in men and 12% in women.[3] Therefore, investigating risk factors of renal function decline and considering their gender-specific effects are necessary to prevent renal function deterioration.

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Hyperglycemia, hyperlipidemia, and hypertension are major risk factors for renal function decline. Chronic hyperglycemia could induce multiple metabolic disturbances, such as activation of the polyol pathway and formation of advanced glycation end products (AGEs). These processes promote redox imbalance, oxidative stress, and cellular injury, ultimately contributing to structural damage and renal function decline.[4–7] Both cross-sectional and longitudinal studies have consistently supported the evidence that abnormal blood glucose levels are a risk factor for renal function decline. For example, prediabetic female kidney donors showed significantly worse renal outcomes five years post-donation compared to normoglycemic donors.[8,9] In addition, using national health check-up data, a recent study reported that the age-standardized prevalence of prediabetes had reached 19.7%, underscoring a substantial at-risk population.[10] Meanwhile, dyslipidemia, particularly impaired cholesterol efflux, could lead to lipid accumulation in renal cells, triggering inflammation, mitochondrial damage, and progressive kidney injury.[11] Many studies have demonstrated the association between dyslipidemia and the decline of renal function.[12,13] A cohort study from Zhejiang province, China, reported that elevated triglycerides and total cholesterol levels were significantly associated with an increased risk of renal function decline.[14] Elevated blood pressure can also cause glomerular hyperfiltration and vascular remodeling, then lead to renal function impairment. These processes are partly mediated by activation of the renin-angiotensin-aldosterone system (RAAS), increased oxidative stress, and endothelial dysfunction.[15] Epidemiological studies have also supported the relationship between higher blood pressure and renal function decline.[16]

However, most previous population-based studies have primarily focused on the impact of a single metabolic abnormality on renal function. It has been suggested that their combination may represent distinct risks for renal function decline. Findings indicated that the coexistence of central obesity, hypertension, and hyperglycemia was associated with a 3.02-fold increased risk of renal function decline compared to the general population, while the combination of hyperglycemia and dyslipidemia resulted in a 2.296-fold higher risk.[17–19] Moreover, the impact of hypertension, hyperglycemia, and hyperlipidemia on renal function decline varies by sex. For example, blood pressure has a stronger effect on the risk of renal function decline in males than in females,[20,21] while hyperglycemia causes more significant renal damage in females than in males.[22,23] In addition, dyslipidemia is associated with the risk of renal function decline in males but not in females.[24] Therefore, sex-specific analyses are essential because biological differences, particularly the influence of sex hormones, can alter metabolic regulation and renal vulnerability.[25] Recognizing these differences allows for more accurate risk stratification and support of the development of targeted prevention strategies.

Latent profile analysis (LPA) is a clustering method that classifies a population into distinct subgroups based on individuals' responses to multiple observed variables.[26] It has been widely used to reveal hidden patterns in complex data and to better understand population heterogeneity.[26] While traditional clustering methods such as K-means are commonly used to identify subgroups, they often require pre-specifying the number of clusters, are sensitive to initial conditions, and assign individuals to fixed groups without accounting for uncertainty.[27] In contrast, by using probabilistic classification, providing statistical criteria (eg, BIC, AIC) to guide model selection, LPA shows greater model interpretability.[26] Therefore, utilizing LPA to identify metabolic abnormality patterns/subtypes and exploring their effects on renal function decline could facilitate the identification of high-risk populations of CKD and enable its personalized, early management. In this study, we aim to outline the sex-stratified metabolic patterns using the LPA method and further investigate their longitudinal impact on the risk of renal function decline over time.

Materials and Methods

The study protocol was approved by the Ethics Committee of Hangzhou Normal University (Ethics Approval Number: 20220009) and conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was formally waived by the Ethics Committee because the study used anonymized retrospective data. We confirm that all data accessed complied with relevant data protection and privacy regulations.

Study Participants

The study participants were recruited from a National Basic Public Health Services Program in China, which aims to gain insights into the health of the population, to monitor and manage patients with chronic diseases. In this national program, participants who have local residency or have lived in the community for more than six months were invited

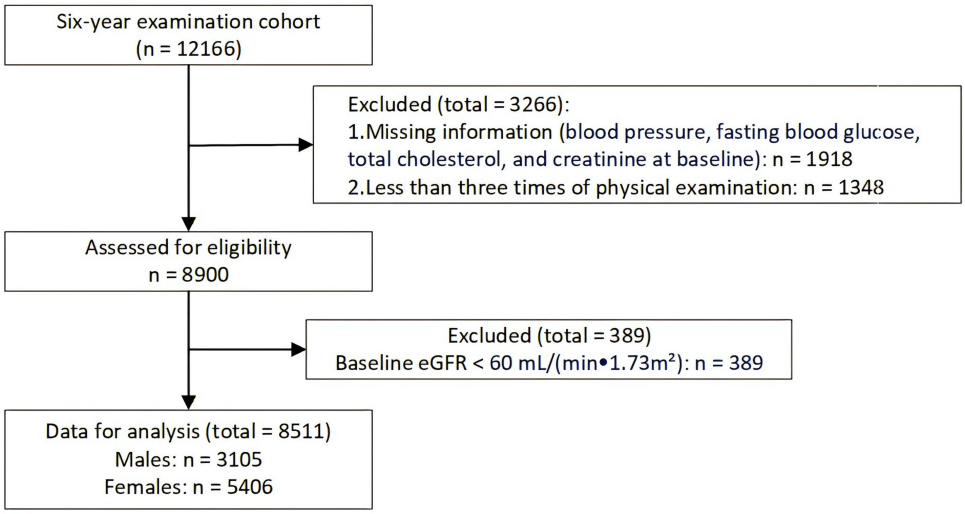

Figure 1 Flowchart of participant inclusion.
Abbreviation: eGFR, estimated glomerular filtration rate.

to conduct a health check every two years, including questionnaire investigation, physical examination, and biochemical tests. The primary study population comprised 12166 individuals aged 40 and older. All participants underwent at least one health examination from January 2012 to December 2018. Participants with less than 3 physical examinations (N = 1348), with missing data on blood pressure (BP), fasting blood glucose (FBG), total cholesterol (TC), and creatinine at baseline (N = 1918), and those with CKD at baseline (eGFR < 60 mL/[min•1.73m^2]) (N = 389) were excluded. Ultimately, a total of 8511 participants, including 5406 females and 3105 males, were included in the study (Figure 1).

Measurement of Variables

Demographic data were collected through standardized face-to-face questionnaire surveys by trained nurses. Blood pressure was assessed by community health service professionals using a mercury sphygmomanometer. Measurements were taken from the right brachial artery in a seated position, with two readings recorded at a 2-minute interval. The average of these two readings was calculated to determine the final value. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Fasting venous blood samples were obtained following an 8-hour fast. Levels of blood glucose, uric acid, blood lipids, and creatinine were analyzed using the Siemens ADVIA2400 biochemical analyzer. Weight and height were measured with calibrated scales and a stadiometer. Detailed measurement protocols are described in Text S1.

Classification of the Metabolic Patterns

In this study, metabolic patterns were constructed using the LPA method based on baseline measurements of SBP, DBP, TC, and FBG. All continuous variables used for the LPA model were standardized using z-score prior to analysis to ensure comparability and model stability. Six models were tried with class sizes ranging from 1 to 6. The optimal classification model was determined using the following fitting statistics: Akaike information criterion (AIC) and Bayesian information criterion (BIC), with lower values indicating better model fit; entropy, where higher values reflect greater model precision; and the Bootstrap-based likelihood ratio test (BLRT), where a p-value less than 0.05 suggests that the n-1 class is superior to the n class model. To ensure the stability and reliability of the subsequent analysis, each latent category was required to include at least 30 samples.[28,29]

Definition of Kidney Function Decline

According to the Guidelines for Screening, Diagnosis, Prevention, and Treatment of Chronic Kidney Disease, renal function decline was defined as eGFR < 90 mL/[min•1.73m^2].[30] EGFR was calculated using the 2010 CKD-EPI equation.[31]

Statistical Analysis

The normality of continuous variables was tested using Shapiro–Wilk tests. Variables with normal distribution were described as mean ± standard deviation (SD). Variables with non-normal distribution were expressed as median and interquartile range. Categorical variables were described as numbers (percentages). The Mann–Whitney *U*-test was utilized to compare group differences of continuous variables. The chi-square (χ^2) test was applied to compare group differences of categorical variables. Missing data on BMI and uric acid were handled using multiple imputation. All statistical analyses in this study were conducted for separate sex.

Generalized estimating equations (GEE) with a logistic regression link function were used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for renal function decline, with metabolic patterns, times (years), and interactions between metabolic patterns and times (years) as the independent variables. A linear regression link function within the GEE framework was also used to evaluate the association between different metabolic patterns and changes in eGFR over time. Regression coefficients (β) and 95% CIs for the interactions between metabolic patterns and time (years) were reported. Model 1 was unadjusted. Model 2 additionally adjusted for age, uric acid, and body mass index. Stratified analyses were conducted by age and obesity status. All statistical analyses were conducted using R software (version 4.4.0). Two-sided p-values less than 0.05 were considered statistically significant.

Results

Baseline Characteristics of the Participants Stratified by Sex

A total of 8511 participants were included in this study, with 3105 (36.48%) participants being males. The median age for the overall population was 66 years. As shown in Table 1, compared to males, females tended to have higher baseline TC and eGFR, as well as lower age, BMI, SBP, DBP, FBG, creatinine, and uric acid (P<0.05).

Baseline Metabolic Patterns of the Participants Stratified by Sex

The LPA model fitting process showed, irrespective of sex, the model 3 had the highest entropy among the fitted models (class size 1–6, Table S1). Furthermore, this model exhibited a greater reduction in AIC and BIC compared to model 2, while the AIC and BIC values for model 4 showed only marginal decreases. Therefore, this model was selected for subsequent analyses.

Table 1 Baseline Characteristics of the Participants by Sex

Variable	Male (N = 3105)	Female (N = 5406)	Total (N = 8511)	*P*
Age (years)	68.00 (65.00–75.00)	64.00 (59.00–71.00)	66.00 (61.00–72.00)	<0.001
BMI (kg/m^2)	24.15 (22.150–26.210)	23.64 (21.67–26.01)	23.84 (21.84–26.09)	<0.001
SBP (mmHg)	133.00 (120.00–144.00)	130.00 (120.00–140.00)	130.00 (120.00–140.00)	<0.001
DBP (mmHg)	80.00 (77.00–90.00)	80.00 (72.00–85.00)	80.00 (74.00–88.00)	<0.001
FBG (mmol/L)	5.68 (5.21–6.34)	5.46 (5.08–5.99)	5.53 (5.13–6.11)	<0.001
TC (mmol/L)	4.85 (4.29–5.47)	5.31 (4.68–5.97)	5.13 (4.50–5.82)	<0.001
Creatinine (mg/dl)	0.87 (0.77–0.97)	0.64 (0.567–0.72)	0.71 (0.60–0.84)	<0.001
eGFR [mL/(min•1.73m^2)]	86.79 (78.84–92.93)	93.77 (85.61–99.86)	90.91 (82.47–97.79)	<0.001
Uric acid (μmol/L)	352.00 (301.50–410.00)	285.00 (242.00–332.00)	307.00 (257.00–365.00)	<0.001

Notes: Data was shown as median (interquartile range). Group difference was compared using the Mann-Withney *U*-test.
Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; SBP, systolic blood pressure; TC, total cholesterol.

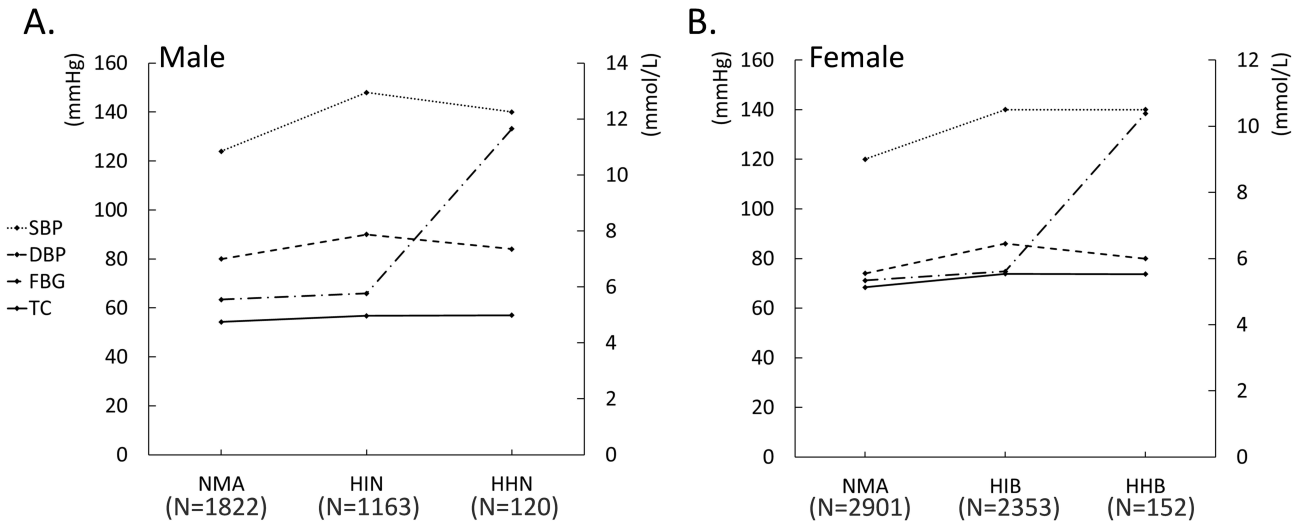

Figure 2 Baseline metabolic patterns in males (**A**) and females (**B**).
Notes: Different line types represent different metabolic indicators. The X-axis displays metabolic pattern groups, and the Y-axis shows the values of each indicator.
Abbreviations: DBP, diastolic blood pressure; FBG, fasting blood glucose; HIB, hypertension–impaired fasting glucose–borderline dyslipidemia; HIN, hypertension–impaired fasting glucose–normal total cholesterol; HHB, hypertension–hyperglycemia–borderline dyslipidemia; HHN, hypertension–hyperglycemia–normal total cholesterol; NMA, no metabolic abnormalities; SBP, systolic blood pressure; TC, total cholesterol.

The subgroups in model 3 were interpreted according to the median values of DBP, SBP, FBG, and TC. Definitions of metabolic abnormalities for each indicator are detailed in Table S2. Among the male participants, the first group (N = 1822, 58.68%) showed normal blood pressure, fasting blood glucose, and total cholesterol, and was then named *no metabolic abnormalities* (NMA). The second group (N = 1163, 37.46%) had hypertension, impaired fasting glucose, and normal total cholesterol, then was classified as *hypertension-impaired fasting glucose-normal total cholesterol* (HIN). Participants in the third group (N =120, 3.87%) had higher blood pressure, hyperglycemia, and normal total cholesterol. So this group was labeled *hypertension-hyperglycemia-normal total cholesterol* (HHN) (Figure 2A and Table S3).

Among the female participants, the first group (N = 2901, 53.66%) displayed normal blood pressure, fasting blood glucose, and total cholesterol, so this group was named no metabolic abnormalities (NMA). The second group (N = 2353, 43.53%) exhibited higher blood pressure, impaired fasting glucose, and borderline dyslipidemia; this group was designated hypertension-impaired fasting glucose-borderline dyslipidemia (HIB). Participants in the third group (N = 152, 2.81%) had hypertension, hyperglycemia, and borderline dyslipidemia. Therefore, it was classified as Hypertension-Hyperglycemia-Borderline Dyslipidemia (HHB) (Figure 2B and Table S3).[32]

Associations of Baseline Metabolic Patterns with Renal Function Decline

Over the six-year follow-up period, 5209 participants (61.20% of the total population) experienced renal function decline. Among females, after adjusting for age, BMI, and uric acid, the groups of HIB and HHB showed progressively increased risk for renal function decline over time compared to the NMA; the OR for the interaction between HIB and HHB and years was 1.33 (95% CI = 1.29,1.37) and 1.41 (95% CI = 1.25,1.59), respectively (Table 2). In males, a significantly accelerated risk of renal function decline was observed only in the HIN compared to NMA, with an OR for the interaction between HIN and years of 1.26 (95% CI = 1.19,1.33). No significant effect was observed in the HHN group (Table 2).

Associations of Baseline Metabolic Patterns with eGFR Change

The eGFR changes over time across different metabolic patterns were shown in Figure 3. Among females, both the HIB and HHB exhibited faster declines in eGFR compared to NMA after adjustment for age, BMI, and uric acid, with the HHB having the greatest effect (Figure 3 and Table 3, $\beta_{HIB\times Years} = -0.19$, 95% CI= −0.29, −0.09; $\beta_{HHB\times Years} = -0.53$,

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Table 2 Associations Between Metabolic Patterns and the Risk of Renal Function Decline Over Time

Metabolic Pattern × Years	Model 1		Model 2	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Female				
NMA × Years	Ref		Ref	
HIB × Years	1.30(1.26,1.33)	<0.001	1.33(1.29,1.37)	<0.001
HHB × Years	1.37(1.23,1.54)	<0.001	1.41(1.25,1.59)	<0.001
Male				
NMA × Years	Ref		Ref	
HIN × Years	1.25(1.19,1.32)	<0.001	1.26(1.19,1.33)	<0.001
HHN × Years	1.12(0.98,1.27)	0.09	1.11(0.97,1.27)	0.12

Notes: Model 1 was unadjusted. Model 2 was adjusted for age, uric acid, and BMI.
Abbreviations: BMI, body mass index; HIB, hypertension-impaired fasting glucose-borderline dyslipidemia; HIN, hypertension-impaired fasting glucose-normal total cholesterol; HHB, hypertension-hyperglycemia-borderline dyslipidemia; HHN, hypertension-hyperglycemia-normal total cholesterol; NMA, no metabolic abnormalities; OR, odd ratio; CI, confidence interval.

95% CI= −0.89, −0.17). In male participants, no significant time-dependent association was identified for any metabolic patterns after similar variables adjustment (Figure 3 and Table 3, P<0.05).

Stratified Analyses by Age and BMI

In females aged 40–60, subjects in the HIB experienced a progressively increased risk of renal function decline compared to the NMA (Tables S4 and S5). However, no significant association was observed in females aged 60 and older (Tables S4 and S5). Males aged 60 and older, but not those aged 40–60, showed significant interactions between HIN/HHN and time for renal function decline risk compared to NMA (Tables S4 and S5). When eGFR was used as the outcome, a consistent association was found among females (Tables S6 and S7), while neither the HIN nor HHN showed significant time-dependent associations with renal function decline in males (Tables S6 and S7).

Among women without overweight/obese, marginal interaction effects between metabolic patterns and time were observed. In contrast, no significant interaction effects were found in overweight or obese women (Tables S8 and S9).

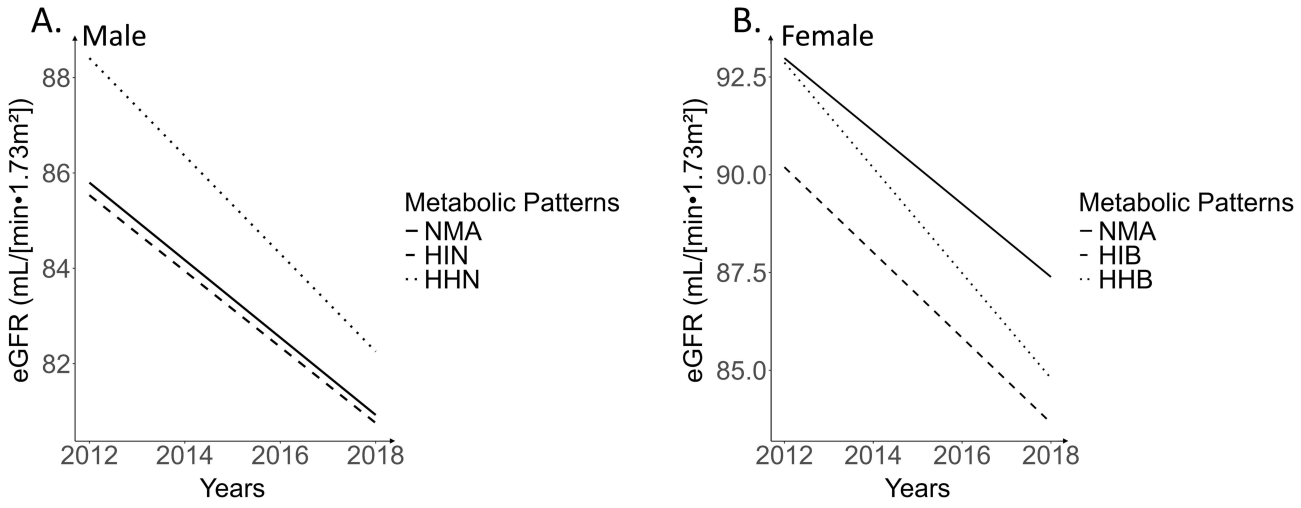

Figure 3 eGFR trajectories from 2012 to 2018 across baseline metabolic patterns in males (**A**) and females (**B**).
Notes: Trajectories were estimated using linear regression models. The X-axis represents time, and the Y-axis represents age-, BMI-, and uric acid–adjusted eGFR values.
Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; HIB, hypertension–impaired fasting glucose–borderline dyslipidemia; HIN, hypertension–impaired fasting glucose–normal total cholesterol; HHB, hypertension–hyperglycemia–borderline dyslipidemia; HHN, hypertension–hyperglycemia–normal total cholesterol; NMA, no metabolic abnormalities.

Table 3 Associations Between Metabolic Patterns and the eGFR Change

Metabolic pattern × Years	Model 1		Model 2	
	β (95% CI)	*P*	β (95% CI)	*P*
Female				
NMA × Years	Ref		Ref	
HIB × Years	−0.18(−0.28, −0.08)	<0.001	−0.19(−0.29, −0.09)	<0.001
HHB × Years	−0.56(−0.92, −0.20)	0.002	−0.53(−0.89, −0.17)	0.004
Male				
NMA × Years	Ref		Ref	
HIN × Years	−0.03(−0.32,0.25)	0.82	−0.05(−0.33,0.24)	0.75
HHN × Years	−0.44(−1.40,0.53)	0.37	−0.41(−1.36,0.55)	0.41

Notes: Model 1 was unadjusted. Model 2 was adjusted for age, uric acid, and BMI.
Abbreviations: BMI, body mass index; HIB, hypertension-impaired fasting glucose-borderline dyslipidemia; HIN, hypertension-impaired fasting glucose-normal total cholesterol; HHB, hypertension-hyperglycemia-borderline dyslipidemia; HHN, hypertension-hyperglycemia-normal total cholesterol; NMA, no metabolic abnormalities; CI, confidence interval.

Regardless of BMI status, males in the HIN exhibited a progressively higher risk of renal function decline (Tables S8 and S9). When eGFR was analyzed as the outcome, women without overweight/obese showed significant interaction effects between HIB/HHB and time on accelerated eGFR declines (Tables S10 and S11). No significant interaction effects between any metabolic patterns and time were found in males regardless of BMI status (Tables S10 and S11).

Discussion

This study explored the relationships between metabolic patterns and renal function decline among participants without chronic kidney disease. We found metabolic patterns differed across sexes, with females showing borderline dyslipidemia while males did not. Compared with normal metabolic patterns, the metabolic patterns of HIB and HHB in females were associated with an accelerated, higher risk of renal function decline and a greater eGFR reduction over time. In males, the HIN, but not the HHN, was linked to a progressively higher risk of renal function decline. However, in the analysis for eGFR as the outcome, no significant time-dependent relationships between metabolic patterns and eGFR decline were identified.

Through LPA, we identified distinct subgroups characterized by varying metabolic profiles. Female participants were classified into NMA, HIB, and HHB, whereas male participants were classified into NMA, HIN, and HHN. As the degree of metabolic pattern abnormality increased, the participants showed an increasing trend in blood pressure, fasting blood glucose, and lipid levels. Females in the HIB and HHB exhibited borderline elevated lipid levels, whereas males maintained normal lipid levels. The gender differences in metabolic patterns may be attributed to the effects of sex hormones on females over 40 years old. Studies have suggested that since the loss of estrogen's protective effects, menopause is associated with body composition changes. Endogenous hormones may affect lipid levels and fat metabolism in females.[33–35] In this study, reduced estrogen protection likely contributed to higher lipid levels in females compared to males of the same age. Therefore, gender differences should be taken into account when addressing metabolic abnormalities in middle-aged and elderly populations.

The eGFR levels decline over time due to reduced protein intake, decreased muscle mass, and lower basal metabolism in older individuals, which lessen the metabolic demands of glomerular function. Aging also leads to a reduction of kidney weight, glomerular number, and glomerular volume, further leading to a decline in glomerular filtration rate.[36,37] Metabolic abnormalities may accelerate these structural and functional changes in the kidney, serving as independent risk factors for renal function decline. Experimental studies have shown that altered activity of key metabolic enzymes (eg, aldose reductase), lipotoxicity, oxidative stress, inflammation, and apoptosis are potential mechanisms.[38,39] Hypertension, a key risk factor for CKD, causes prolonged hyperperfusion, leading to glomerular damage and impaired renal function. These processes involve elevated oxidative stress and vascular remodeling.[15,40,41] Previous studies have demonstrated

that paraoxonase-1 (PON1), an HDL-associated enzyme with protective roles against lipid oxidation and vascular dysfunction, was significantly lower in hypertensive patients than in controls.[42]

Metabolic abnormalities, when combined with the effect of time, can significantly accelerate renal function decline. Studies suggested that as the follow-up time increased, some participants might develop CKD due to elevated blood pressure, indicating an interaction effect between time and blood pressure on the renal function decline risk.[43] The interaction between baseline lipid levels and time significantly influences renal function decline risk.[44] Rising blood glucose levels over time have been indicated to be associated with an increased risk of renal function decline.[45] Beyond their individual effects, hyperglycemia and hyperlipidemia also interact metabolically. Insulin resistance, a common feature of metabolic disorders, promotes renal lipid deposition and amplifies lipotoxic injury. Meanwhile, both conditions share downstream mechanisms such as oxidative stress, inflammation, and endothelial dysfunction, which collectively contribute to microvascular remodeling and podocyte damage, accelerating renal function decline.[46,47] In parallel, sex hormone dynamics may further influence renal deterioration, particularly in aging populations. Estrogen has been shown to protect against oxidative stress, inflammation, and fibrosis in the kidney.[48,49] After menopause, declining estrogen levels may weaken these protective mechanisms, increasing susceptibility to glomerular and tubular injury. Prior epidemiological studies have also shown that women who experience menopause before the age of 45 have a higher risk of renal function decline.[49] However, as menopause status was not available in the present dataset, it limited our ability to examine how menopausal transition modifies the impact of metabolic abnormalities on renal outcomes.

The interactive effect of time and multiple metabolic abnormalities influences the risk of renal function decline. This study shows that over time, individuals with hypertension, hyperglycemia, and elevated blood lipids experience a greater decline in eGFR and a higher renal function decline risk in females. These findings align with Kathleen E. Adair's research, which linked metabolic syndrome to an increased likelihood of CKD.[50] In the male participants, the interaction between the HIN and time significantly affects the risk of renal function decline when using a categorical variable as the outcome. However, when the outcome is eGFR, a continuous scale, the associations between metabolic patterns and the degree of eGFR decline are not significant. This may be due to two main factors. First, the relatively small sample size of the HHN group may have limited statistical power. Second, the differences in the rate of renal function decline between the HIN and NMA groups may not have been large enough to reach significance for the continuous outcome of eGFR. Additionally, sex-specific metabolic profiles may have contributed to this discrepancy, as male subgroups lacked broadly elevated TC, a factor that has been associated with renal dysfunction.[51] Overall, the study emphasizes the significant impact of blood lipid abnormalities, particularly in women, on renal function decline, suggesting that managing lipid levels may protect renal function in individuals with multiple metabolic abnormalities.

In summary, although the effect of time on renal function is irreversible, actively managing metabolic health may reduce the risk of renal function decline. Special attention should be given to the impact of multiple metabolic abnormalities on renal function in middle-aged and elderly populations, with a particular focus on the combined effects of blood lipid abnormalities and other metabolic factors in females. Clinically, incorporating comprehensive metabolic assessments—including blood pressure, glucose, and lipid profiles—into routine evaluations may help identify individuals at elevated risk for renal function decline. Moreover, sex-specific risk stratification based on metabolic profiles may improve early detection and facilitate timely interventions to reduce the development of CKD. From a public health perspective, targeted prevention and screening programs that address metabolic abnormalities while accounting for sex differences are also warranted. For example, early screening in postmenopausal women with dyslipidemia or close monitoring in prediabetic men with hypertension may help mitigate kidney function decline. Although this study was based on a community-dwelling population in Southeastern China, the identified metabolic patterns and sex-specific associations may be relevant to broader populations. Future studies in diverse geographic and clinical settings are needed to validate these findings.

Strengths and Limitations

The strengths of this study include its large sample size, long-term follow-up, and prospective design. The use of LPA enhances the accuracy of the classification of metabolic patterns. This study provides valuable insights into the relationship between metabolic patterns and renal function decline in a specific population and highlights significant

gender differences. Further investigation in this area could improve our understanding of the pathogenesis of CKD and may inform the development of preventive and therapeutic strategies.

There are some limitations that should be noted. First, some lifestyle factors (eg, smoking, alcohol consumption, physical activity, and diet) were not measured in this study, which may introduce residual confounding and lead to overestimation of the observed associations. Second, the present study was a single-center survey that included only community-dwelling middle-aged and older populations aged 40 years and above, which may limit the generalizability of the findings. Third, the lack of medication history may bias the results, since medication could affect blood pressure, blood glucose, lipids, and may also modify kidney function. More comprehensive adjustment for potential confounders should be prioritized in future studies. Finally, metabolic profiles were assessed at baseline and were treated as time-invariant, which may not fully capture temporal fluctuations in metabolic status. Future research using repeated measures and longitudinal modeling of metabolic patterns is warranted.

Conclusion

This retrospective cohort study revealed the associations between metabolic patterns and decline in renal function in separate sexes. The findings of this study highlight the gender differences in the effects of metabolic patterns on renal function decline. Women with HIB and HHB, and men with HIN have an accelerated risk of renal function decline. Earlier management of metabolic abnormalities is critical for kidney protection. Early and integrated metabolic management, including control of blood pressure, glucose, and lipids, is essential for slowing kidney function decline. Moreover, our findings provide a rationale for developing future strategies that incorporate sex-specific risk profiles into CKD prevention and management.

Abbreviations

AIC, akaike information criterion; BIC, bayesian information criterion; BLRT, the bootstrap-based likelihood ratio test; BMI, body mass index; BP, blood pressure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; GEE, Generalized Estimating Equations; HHB, hypertension-hyperglycemia-borderline dyslipidemia; HHN, hypertension-hyperglycemia-normal Total Cholesterol; HIB, hypertension-impaired fasting glucose-borderline dyslipidemia; HIN, hypertension-iImpaired fasting glucose-normal total cholesterol; LPA, latent profile analysis; NMA, metabolic abnormalities; TC, total cholesterol.

Ethics Declarations

The study protocol was approved by the Ethics Committee of Hangzhou Normal University (Ethics Approval Number: 20220009) and conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was formally waived by the Ethics Committee because the study used anonymized retrospective data. We confirm that all data accessed complied with relevant data protection and privacy regulations.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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