Unstably controlled systolic blood pressure trajectories are associated with markers for kidney damage in prediabetic population: results from the INDEED cohort study

Zi-Jun Sun†, Jin-Wei Wang†, Dong-Yuan Chang1, Shuo-Hua Chen2, Hui-Fen Zhang3, Shou-Ling Wu4, Kevin He5, Lu-Xia Zhang1, Min Chen1* and Ming-Hui Zhao1,6

Abstract

Background: The association between blood pressure change and kidney damage in patients with abnormal blood glucose remains unclear. The current study aimed to identify systolic blood pressure (SBP) trajectories among the prediabetic population and to determine their association with kidney damage after a long-term follow-up.

Methods: The incidence, development, and prognosis of diabetic kidney disease (INDEED) study is nested in the Kailuan cohort study with a focus on population with diabetes and prediabetes. We screened out people with prediabetes in 2006 and with more than three SBP records from 2006 to 2014 biennially. We used the latent mixture modeling to fit five groups of trajectories of SBP. In 2016, estimated glomerular filtration rate (eGFR), urinary albumin creatinine ratio (uACR), and urinary α1-microglobulin (α1MG), transferrin and α1-acid glycoprotein were measured, and the association between SBP trajectories and these markers was analyzed by linear regression and logistic regression models.

Results: Totally, 1451 participants with prediabetes and without kidney damage were identified in 2006. Five heterogeneous SBP trajectories were detected based on the longitudinal data from 2006 to 2014, as low-stable group (n = 323), moderate-stable group (n = 726), moderate-increasing group (n = 176), moderate-decreasing group (n = 181), and high-stable group (n = 45). Linear regression analysis showed that the moderate and high SBP groups had lower eGFR, higher uACR, higher urinary α1MG, higher transferrin, and higher α1-acid glycoprotein than the low-stable group. Multivariable analysis attenuated the association but did not change the statistical significance.

Conclusions: Prediabetic patients with persistent high-level SBP trajectory or gradually increased SBP trajectory had severer kidney damage during follow-up.

Keywords: Blood pressure, Estimated glomerular filtration rate, Kidney damage, Prediabetes, Trajectory
combination of prediabetes and hypertension is associated with a higher incidence of diabetes, CVD and chronic kidney disease (CKD) [5, 9], while the regression from prediabetes to normal glucose regulation can significantly reduce the CVD risk [10]. Besides, prediabetes might have an early renal lesion, such as the thickening of glomerular basement membrane [11], and it was an independent risk factor for glomerular hyperfiltration and could increase urinary albumin creatinine ratio (uACR), contributing to a poor kidney prognosis [8, 12, 13].

The optimal blood pressure (BP) target for patients with diabetes or prediabetes is not well defined [14, 15], and the relationship between hypertension and progression of prediabetes was unclear. Thus, to explore the influence of the longitudinal pattern of systolic blood pressure (SBP) in a population with prediabetes on the early stage of kidney damage and/or reduced kidney function is of great significance. The correlation between blood pressure merely at the baseline and the kidney disease may not adequately reflect their general and persistent association. The heterogeneity in effects may be observed for patterns of long-term blood pressure changes on the development and progression of diabetes and prediabetes. Based on the same cohort as the current study, Li et al. [16] analyzed the impact of SBP trajectories on qualitative measurements of urinary protein and reduced eGFR among diabetic patients. In the current study, we aimed to extend the research among the population with prediabetes and include the quantitatively measured spectrum of indicators, including estimated glomerular filtration rate (eGFR), uACR, and urinary α1-microglobulin (α1MG), transferrin and α1-acid glycoprotein, for early kidney injury and kidney function [17–20] after 10 years of follow-up.

**Methods**

**Study design and participants**

The incidence, development, and prognosis of diabetic kidney disease (INDEED) study is based on the participants with diabetes and prediabetes in the Kailuan study, as described previously [21]. The Kailuan study, including 101,510 participants, is an ongoing prospective cohort study, which collected health records and related questionnaires from 11 hospitals in the Kailuan Community of Tangshan, Hebei Province of China. Briefly, all participants were followed up biennially from 2006 to update information according to the standard protocol [22]. In the current study, 1771 people were identified in 2006 with prediabetes and were followed-up until 2016. Prediabetes was defined as impaired fasting glucose (IFG) (≥ 5.6 mmol/L and ≤ 6.9 mmol/L) [23]. Participants with self-reported diabetes or self-reported current use of oral hypoglycemic medication or insulin were excluded. We excluded 229 people with kidney injury in 2006, defined as eGFR < 60 ml/min/1.73 m² or urinary protein ≥ with proteinuria dipstick. The above people with more than three times of systolic blood pressure records were retained. Forty-two participants who had missing value on total cholesterol (TCHO), triglyceride, high-density lipoprotein (HDL), low-density lipoprotein (LDL), uACR or eGFR were excluded. Finally, 1451 participants were eligible and analyzed (Fig. 1). The investigation was conducted according to the Declaration of Helsinki and was approved by the Ethics Committee of Peking University First Hospital. Written informed consent was obtained from all participants.

**Questionnaire assessment**

Questionnaire information included demographic and socioeconomic data. Variables including age, gender, smoking status, alcohol consumption, physical activity, education level, history of antihypertensive medicine, lipid-lowering drugs, and antidiabetic medicine, were used in this current study. Smoking status and alcohol consumption were all classified as ‘never’, ‘former/quit’, ‘often’. Physical activity was divided as ‘never’, ‘occasionally’ and ‘often’. Education was classified as ‘illteracy/primary school’, ‘middle school’, and ‘college/university’. Diagnosis and treatment of diabetes, diabetic kidney disease (DKD), and cognitive function were also administrated.

**Anthropometric measurements**

Anthropometric indices included height and weight. Height measurement was accurate to 0.1 cm with a tape
rule and weight measurement was accurate to 0.1 kilograms with calibrated platform scales. Body mass index (BMI) was calculated as weight (kilograms) divided by height (meters) squared.

**Laboratory assessment**
Whole blood samples were drawn from all participants, generally after an overnight fast and analyzed in the Central Laboratory of Kailuan General Hospital on the same day. Plasma samples were used to measure biochemical variables. Triglyceride, TCHO, hemoglobin, HDL, LDL were measured using a Hitachi 7600 auto-analyzer (Hitachi; Tokyo, Japan). Fasting blood glucose (FBG) was tested with the Hexokinase method (BioSino Bio-Technology & Science Inc., China). High sensitivity C reactive protein (hsCRP) was measured using a high-sensitivity particle-enhanced immunonephelometry assay (Cias Latex CRP-H, Kanto Chemical Co. Inc, Japan). Laboratory urine tests including urinary creatinine, urinary albumin, and urinary α1MG, transferrin and α1-acid glycoprotein that regarded as the indices of early DKD [17] were measured in the central laboratory in Peking University First Hospital. Serum creatinine was measured using the Jaffe's method. eGFR was calculated using the CKD-EPI equation [24].

**Assessment of blood pressure**
During the biennial follow-up, BP was measured according to the JNC7 recommendation [25]. After rested in a chair for at least 5 min, BP was measured on the left arm using a mercury sphygmomanometer. SBP is the point at which the first of ≥ 2 Korotkoff sounds is heard, and the disappearance of Korotkoff sound is used to define diastolic blood pressure (DBP). Two times each of SBP and DBP were obtained at a 5-minute interval and the average value of the two measures was used for further analysis. If the two measurements differed by > 5 mm Hg, then an additional reading was taken, and the average of the three readings was used for data analysis. People with more than three records of SBP recruited in the 2006–2014 examination circles were regarded as the baseline participants in the current study.

**Statistical analysis**
Continuous variables were presented as the mean with standard deviation or median with interquartile range. Categorical variables were presented as counts with percentages. Intergroup differences were assessed using one-way ANOVA for normally distributed data. Differences of parameters that were not normally distributed were tested with the Kruskal–Wallis test. Differences of qualitative parameters were compared using the χ² test/Fisher exact test.

The SBP trajectories from 2006 to 2014 biennially were identified by latent mixture modeling (PROC TRAJ) measures which was used to identify subgroups of people sharing similar SBP patterns and the model fit was assessed using the Bayesian information criterion (BIC) [26, 27]. We launched a model with five trajectories and then compared the BIC of the model (-27173.7) to those with 4, 3, 2, and 1 trajectories, respectively. The model with five trajectories was identified with the best fit. We then compared the model in terms of functional forms. Cubic, quadratic, and linear terms were evaluated based on their statistical significance after starting with the highest polynomial. In our final model, we had two trajectories with linear order term and three trajectories with up to quadratic order terms.

Linear regression model, binary logistic regression and multinomial logistic regression model were used to assess the association between SBP trajectory groups and indicators of early kidney damage. For linear regression, uACR, urinary α1MG, transferrin, and α1-acid glycoprotein underwent a logarithmic transformation to make it normally distributed. For logistic regression, urinary albumin to creatinine ratio was divided into three groups (uACR ≤ 3 mg/mmol; 30 mg/mmol ≥ uACR ≤ 3 mg/mmol; uACR > 30 mg/mmol), eGFR was divided into two groups (eGFR ≥ 60 ml/min/1.73 m²; eGFR < 60 ml/min/1.73 m²) [28], and urinary α1MG, transferrin and α1-acid glycoprotein were all divided according to the value in 75th percentile. The variables included in multivariable regression model included age, gender in model 2; plus history of myocardial infarction (yes vs. no), stroke (yes vs. no), cancer (yes vs. no) in model 3; plus education (illiteracy/primary school vs. middle school vs. college/university), physical activity (never vs. occasionally vs. often), smoking status (never vs. former/quit vs. often), drinking status (never vs. former/quit vs. often), triglyceride (a continuous variable), total cholesterol (a continuous variable), BMI (a continuous variable), LDL (a continuous variable), HDL (a continuous variable), hsCRP (a continuous variable) in model 4; plus antihypertensive (yes vs. no), hypoglycemic (yes vs. no), lipid-lowering drug (yes vs. no) in model 5.

We performed the following sensitivity analyses to assess the robustness of our findings. We expanded the recruited population to those with more than 2 times of SBP records during the follow-up period to avoid the selection bias of the population. All P-values were calculated based on two-tailed tests of statistical significance. P < 0.05 was considered to be statistically significant. All analyses were conducted using SAS, version 9.4 (SAS Institute, CA, USA).
### Results

Altogether, 1451 patients with prediabetes and without kidney damage at the baseline were recruited in this study, with an age of 51.4 ± 8.8 years, and 81.7% (N = 1186) of males. Among the included population in our study, most people remained the status of prediabetes or progressed to diabetes during the follow-up period (259 [17.9%] and 1089 [75.0%], respectively), with only a small proportion having their fasting blood glucose level resumed to the normal range (103 [7.1%]). During the 10-year follow-up, five SBP trajectories were distinctly separated among the 1451 participants with three or more SBP measurements. The patterns of the trajectories were shown in Fig. 2. Altogether, 726 (50.03%) participants were categorized into moderate-stable group with moderate SBP increasing steadily (95% confidence intervals [CI] range from 131.67 mmHg to 133.52 mmHg), 323 (22.26%) into low-stable group (95% CI, 114.19 mmHg-116.56 mmHg), 176 (12.13%) into moderate-increasing group (95% CI 144.24 mmHg-148.57 mmHg), 181 (12.48%) into moderate-decreasing group (95% CI 157.33 mmHg-161.34 mmHg), and 45 (3.10%) into high-stable group (95% CI 165.00 mmHg-176.88 mmHg).

We used individuals in the low-stable group as the reference. People in the other four groups tend to be older, with a higher proportion of males. Compared with the low-stable group, DBP, uACR, and urinary α1MG, transferrin and α1-acid glycoprotein increased and eGFR decreased among the other four groups (all \( P \) values < 0.01). Meanwhile, compared with the low-stable group, the proportions of never alcohol intake and taking antihypertensive medicine were higher, and the education levels were lower in the other four groups (all \( P \) values ≤ 0.01). Proportions of use of lipid-lowering drugs were not significantly different among the five groups (Table 1, Additional file 1: Table S3).

Compared with the low-stable group, all the other four groups were associated with a decreased level of eGFR, with the regression coefficients of 0.85, −1.80, −1.26, and 4.99, for the moderate-stable, moderate-increasing, moderate-decreasing, and high-stable group, respectively. Higher SBP levels were associated with higher levels of kidney damage markers. For example, the regression coefficients for the logarithm transformed uACR were 0.09, 0.23, 0.25, and 0.35, respectively. The results for logarithm transformed urinary α1-microglobulin, transferrin, and α1-acid glycoprotein were similar (Table 2). In the logistic regression analysis, where eGFR and the four kidney damage markers were under categorization to represent abnormality, the other four SBP trajectories were not significantly associated with eGFR < 60 ml/min/1.73 m², but significant associations were detected between the moderate-decreasing group and uACR categories, between the high-stable group and kidney damage markers of urinary α1-acid glycoprotein > 21.27 mg/L or α1-microglobulin > 29.75 mg/L, between each of the groups (the moderate-increasing group, the moderate-decreasing group or the high-stable group) and transferrin > 3.83 mg/L, respectively, compared with the low-stable group (all \( P \) values < 0.05) (Table 3).

We did sensitivity analyses by expanding SBP records into more than twice. The results were consistent with the analysis with at least three times of SBP records. (Additional file 2: Figure S1, Additional file 1: Tables S1, and S2).

---

**Fig. 2** Systolic blood pressure was classified into five groups according to the latent mixture modeling from 2006 to 2014
Discussion

Five SBP trajectories were identified in this prospective cohort of prediabetes. Overall, higher longitudinal SBP levels based on 10 years of follow-up were associated with subsequent higher levels of markers for kidney damage including uACR, urinary a1-microglobulin, transferrin, and a1-acid glycoprotein, indicating that the current or previous uncontrolled BP was associated with kidney damage. Additional analysis revealed that SBP trajectories with higher SBP levels were associated with higher urinary albumin creatinine ratio (uACR) and urinary α1-microglobulin. These findings highlight the importance of controlling BP in individuals with prediabetes to prevent kidney damage.
damage. Therefore, long-term dynamic monitoring of BP is necessary for predicting kidney damage in the prediabetic population.

We found that participants in trajectories of moderately or high increased SBP had an adverse spectrum of markers for kidney damage and reduced eGFR. The association was independent of other risk factors for CKD. The results extended the previous findings by providing evidence for the longitudinal pattern of SBP instead of just focusing on the point measure. Derakhshan et al. [9] found that hypertension among prediabetes was associated with abnormal levels for markers of CKD after adjusting for other risk factors for CKD. A recent study in a Chinese cohort showed that the development of hypertension in middle age could increase the risk of CVD [29]. Another study also suggested that higher BP trajectories were correlated with higher uACR [30]. Our results were in accordance with some studies to explain the association between hypertension and kidney damage among patients with prediabetes. Insulin resistance (IR) and decreased beta-cell function have already presented in the stage of prediabetes [31]. IR is associated with hyperfiltration and proteinuria, which links prediabetes and CKD. Otherwise, IR could promote blood pressure contributing to the incidence of CKD [32]. Persistent hyperglycemia promotes proximal tubular reabsorption via type 2 sodium-glucose co-transporter, which induces the decrease of sodium in macula densa with the deactivation of tubuloglomerular feedback and finally increases the glomerular pressure and filtration [12, 13].

DKD is a common complication of diabetes, which manifested as albuminuria and/or decline of eGFR. eGFR indicates the kidney function, and hyperfiltration of glomeruli is responsible for the excretion of urinary albumin. Thus, although albuminuria is considered as a marker for

| Table 2 Linear regression analysis between SBP trajectory groups and indicators of kidney disease in 2016 |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                | Group 1 | Group 2 | Group 3 | Group 4 | Group 5 |
| N (%)          |        |        |        |        |        |
| eGFR (n = 1451) |        |        |        |        |        |
| Model 1        |        |        |        |        |        |
| Model 2        |        |        |        |        |        |
| Model 3        |        |        |        |        |        |
| Model 4        |        |        |        |        |        |
| Model 5        |        |        |        |        |        |
| Log (uACR) (n = 1451) |        |        |        |        |        |
| Model 1        |        |        |        |        |        |
| Model 2        |        |        |        |        |        |
| Model 3        |        |        |        |        |        |
| Model 4        |        |        |        |        |        |
| Model 5        |        |        |        |        |        |
| Log (Orm) (n = 1444) |        |        |        |        |        |
| Model 1        |        |        |        |        |        |
| Model 2        |        |        |        |        |        |
| Model 3        |        |        |        |        |        |
| Model 4        |        |        |        |        |        |
| Model 5        |        |        |        |        |        |
| Log (α1MG) (n = 1446) |        |        |        |        |        |
| Model 1        |        |        |        |        |        |
| Model 2        |        |        |        |        |        |
| Model 3        |        |        |        |        |        |
| Model 4        |        |        |        |        |        |
| Model 5        |        |        |        |        |        |
| Log (TRF) (n = 1445) |        |        |        |        |        |
| Model 1        |        |        |        |        |        |
| Model 2        |        |        |        |        |        |
| Model 3        |        |        |        |        |        |
| Model 4        |        |        |        |        |        |
| Model 5        |        |        |        |        |        |

Table 2 (continued)

| Group 1 | Group 2 | Group 3 | Group 4 | Group 5 |
|---------|---------|---------|---------|---------|
| eGFR    | 0.02    | 1.00    | 0.10†  | 0.14‡  | 0.22‡  |
| α1MG    |         |         |         |         |         |
| ORM     |         |         |         |         |         |
| TRF     |         |         |         |         |         |
Table 3 Logistic regression analysis between SBP trajectory groups and abnormality for indicators of kidney disease in 2016

| Indicator                  | Group 1     | Group 2     | Group 3     | Group 4     | Group 5     |
|----------------------------|-------------|-------------|-------------|-------------|-------------|
| N (%)                      | 726 (50.3%) | 323 (22.3%) | 176 (12.1%) | 181 (12.5%) | 45 (2.8%)   |
| eGFR < 60 ml/min/1.73 m²    |             |             |             |             |             |
| Model 1                    | 0.66 (0.11, 4.01) | 0.92 (0.08, 10.19) | 2.71 (0.45, 16.34) | 3.65 (0.32, 41.06) |
| Model 2                    | 0.41 (0.06, 2.51) | 0.41 (0.04, 4.75) | 1.18 (0.18, 7.71) | 1.33 (0.11, 16.04) |
| Model 3                    | 0.41 (0.07, 2.54) | 0.42 (0.04, 4.88) | 1.17 (0.18, 7.66) | 1.30 (0.11, 15.87) |
| Model 4                    | 0.32 (0.04, 2.30) | 0.23 (0.02, 3.07) | 0.78 (0.10, 5.99) | 0.86 (0.06, 11.36) |
| Model 5                    | 0.32 (0.04, 2.35) | 0.18 (0.01, 2.71) | 0.61 (0.07, 5.74) | 0.73 (0.05, 10.24) |
| 3 mg/mmol ≤ uACR ≤ 30 mg/mmol |             |             |             |             |             |
| Model 1                    | 0.99 (0.64, 1.52) | 1.00         | 0.92 (0.08, 10.19) | 2.71 (0.45, 16.34) | 3.65 (0.32, 41.06) |
| Model 2                    | 0.97 (0.63, 1.51) | 0.97 (0.09, 2.69) | 2.26 (1.45, 3.52) | 1.14 (0.39, 3.33) |
| Model 3                    | 0.97 (0.62, 1.51) | 0.97 (0.09, 2.69) | 2.27 (1.46, 3.54) | 1.13 (0.39, 3.32) |
| Model 4                    | 0.90 (0.57, 1.42) | 0.90 (0.57, 1.42) | 2.22 (1.38, 3.57) | 1.23 (0.41, 3.71) |
| Model 5                    | 0.90 (0.57, 1.43) | 0.90 (0.57, 1.43) | 2.29 (1.40, 3.77) | 1.27 (0.42, 3.88) |
| uACR ≥ 30 mg/mmol          |             |             |             |             |             |
| Model 1                    | 0.79 (0.51, 1.24) | 0.99 (0.61, 1.69) | 1.68 (1.06, 2.64) | 0.59 (0.20, 1.71) |
| Model 2                    | 0.76 (0.48, 1.20) | 0.95 (0.56, 1.60) | 1.58 (0.98, 2.52) | 0.54 (0.18, 1.59) |
| Model 3                    | 0.76 (0.48, 1.20) | 0.95 (0.56, 1.61) | 1.58 (0.99, 2.54) | 0.53 (0.18, 1.58) |
| Model 4                    | 0.72 (0.45, 1.17) | 0.90 (0.52, 1.58) | 1.65 (0.99, 2.73) | 0.58 (0.19, 1.75) |
| Model 5                    | 0.73 (0.45, 1.18) | 0.93 (0.53, 1.64) | 1.74 (1.03, 2.93) | 0.61 (0.20, 1.86) |
| Orm > P75 (Orm = 21.27 mg/L)|             |             |             |             |             |
| Model 1                    | 1.28 (0.93, 2.25) | 1.79 (1.18, 2.73) | 1.63 (1.07, 2.49) | 3.63 (2.17, 6.08) |
| Model 2                    | 1.31 (0.94, 1.83) | 1.94 (1.25, 3.01) | 1.76 (1.14, 2.73) | 3.02 (1.53, 5.95) |
| Model 3                    | 1.31 (0.94, 1.83) | 1.94 (1.25, 3.02) | 1.76 (1.14, 2.73) | 3.05 (1.54, 6.01) |
| Model 4                    | 1.29 (0.92, 1.82) | 1.97 (1.25, 3.10) | 1.61 (1.02, 2.54) | 3.13 (1.56, 6.27) |
| Model 5                    | 1.27 (0.90, 1.80) | 1.92 (1.21, 3.05) | 1.53 (0.95, 2.46) | 2.92 (1.44, 5.94) |
| a 1MG > P75 (a 1MG = 29.75 mg/L) |             |             |             |             |             |
| Model 1                    | 1.40 (1.02, 1.93) | 1.64 (1.07, 2.51) | 1.45 (0.94, 2.23) | 3.02 (1.57, 5.97) |
| Model 2                    | 1.33 (0.95, 1.85) | 1.56 (0.99, 2.44) | 1.40 (0.89, 2.20) | 2.95 (1.48, 5.84) |
| Model 3                    | 1.33 (0.95, 1.85) | 1.56 (0.99, 2.44) | 1.39 (0.89, 2.19) | 2.92 (1.47, 5.79) |
| Model 4                    | 1.31 (0.93, 1.85) | 1.52 (0.96, 2.43) | 1.31 (0.83, 2.09) | 2.96 (1.47, 5.95) |
| Model 5                    | 1.31 (0.92, 1.85) | 1.53 (0.96, 2.45) | 1.31 (0.81, 2.13) | 2.91 (1.43, 5.94) |
| TRF > P75 (TRF = 3.83 mg/L) |             |             |             |             |             |
| Model 1                    | 1.39 (0.99, 1.95) | 2.28 (1.49, 3.50) | 2.61 (1.72, 3.97) | 4.56 (2.37, 8.75) |
| Model 2                    | 1.43 (1.02, 2.02) | 2.46 (1.58, 3.84) | 2.80 (1.82, 4.32) | 5.04 (2.58, 9.86) |
| Model 3                    | 1.44 (1.02, 2.02) | 2.47 (1.58, 3.86) | 2.80 (1.81, 4.32) | 5.09 (2.60, 9.96) |
| Model 4                    | 1.34 (0.94, 1.91) | 2.48 (1.57, 3.93) | 2.50 (1.60, 3.92) | 5.28 (2.65, 10.55) |
| Model 5                    | 1.33 (0.93, 1.89) | 2.46 (1.54, 3.92) | 2.42 (1.51, 3.87) | 5.08 (2.51, 10.27) |

Model 1: no adjustment;
Model 2: adjusted for age, gender;
Model 3: further adjusted for history of myocardial infarction, stroke, cancer;
Model 4: further adjusted for education, physics, smoking status, drinking status, salt habit, triglyceride, total cholesterol, body mass index, LDL, HDL, hsCRP;
Model 5: further adjusted for antihypertensive, hypoglycemic, lipid-lowering drug;

eGFR estimated glomerular filtration rate, a1MG Urinary a1-microglobulin, TRF Transferrinuria, Orm Urinary a1-acid glycoprotein, uACR urinary albumin creatinine ratio
glomerular damage and is an independent risk factor for the progression of CKD, some individuals could only present decreased eGFR and have a normal level of uACR [33, 34]. In the current study, a more comprehensive spectrum of markers were used, including those indicating glomerular injury (transferrinuria), tubular injury (urinary α1MG) and inflammation (urinary α1-acid glycoprotein) [18–20]. These markers can be complementary to the routinely used eGFR and uACR [20, 35, 36]. Part of normoalbuminuric type 2 diabetic patients had transferrinuria and it could be a more sensitive marker of glomerular function [18, 37]. The role of tubular damage and inflammation in kidney disease for patients with prediabetes and diabetes is well known. Studies have shown that urinary α1MG and urinary α1-acid glycoprotein are useful markers of early renal damage among people with abnormally controlled glucose [19, 20]. Our results provided new evidence for the relationship between hypertension and kidney disease by investigating markers of early damage of the kidney.

The current study has some strengths and limitations. Strengths included the large sample size and long-term follow-up. Also, we used longitudinal SBP trajectories and included a spectrum of markers for kidney injury. However, some limitations should be mentioned. First, our study was based on a population with a majority of men and that may limit the generalizability of the study findings to women. Besides, for women, we don’t have records of menopause, so we cannot evaluate the effects of estrogen on blood glucose. Second, patients with isolated impaired glucose tolerance are more than those with isolated abnormal fasting glucose [38], and our study only used the fasting blood glucose to recruit our target population with prediabetes. Thus, some prediabetes people might be excluded by our current criterion. Besides, the records of glycated albumin were lacking, and this parameter may serve as a better indicator for screening prediabetes [39–41]. Third, prediabetes can be induced by lipid-lowering drugs, and change of dose or stop of treatment for such drugs may have introduced bias for the recruited population. However, since the proportion of using lipid-lowering therapy is low and most of patients did not experience remission of prediabetes during the follow-up period, the influence of the bias may be negligible in the current study.

Conclusions

In summary, patients with persistent high-level SBP or gradually increased SBP could lead to lower level of eGFR and higher levels of markers of kidney damage than those with persistent low SBP. Performing long-term dynamic monitoring for trajectories of blood pressure may be a reliable approach to identify the prediabetic population with a higher risk of DKD.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s12967-020-02361-5.

Additional file 1: Table S1. Linear regression analysis between SBP trajectory groups and indicators of kidney disease in 2016 among participants with two or more records of SBP. Table S2. Logistic regression analysis between SBP trajectory groups and abnormality for indicators of kidney disease in 2016 among participants with two or more records of SBP. Table S3. Concomitant therapies between SBP trajectory groups from 2006 to 2012.

Additional file 2: Figure S1. Systolic blood pressure was classified into five groups according to the latent mixture modeling from 2006 to 2014 among participants with two or more records of SBP.

Abbreviations

α1MG: α1-microglobulin; BIC: Bayesian information criterion; BMI: Body mass index; BP: Blood pressure; CI: Confidence interval; CKD: Chronic kidney disease; CVD: Cardiovascular disease; DBP: Diastolic blood pressure; DKD: Diabetic kidney disease; eGFR: Estimated glomerular filtration rate; FBG: Fasting blood glucose; HDL: High-density lipoprotein; hsCRP: High sensitivity C reactive protein; IFG: Impaired fasting glucose; INDEED: The incidence, development, and prognosis of diabetic kidney disease; IR: Insulin resistance; LDL: Low-density lipoprotein; ORM: Urinary α1-acid glycoprotein; SBP: Systolic blood pressure; TCHO: Total cholesterol; TRF: Transferrinuria; uACR: Urinary albumin creatinine ratio.

Acknowledgements

Not applicable.

Authors’ contributions

ZJS analyzed statistics and drafted the manuscript. JWVW provided methods of testing and revised the manuscript. SHC, HFZ, and SLW provided the data of the Kailuan cohort and revised the manuscript. DYC, KH, LXZ, MC, and MHZ designed the study, participated interpretation of data and revised the manuscript. MC had full access to all of the data and provided final approval of the submitted manuscript. All authors read and approved the final manuscript.

Funding

This study was supported by the grants from the National Key Research and Development Program (No. 2016YFC1305405), the grant from Peking University Medicine Seed Fund for Interdisciplinary Research (No. BMU2018MX025), the grant by Peking University Health Science Center (No. BMU2017CY002), the grant from the University of Michigan Health System and Peking University Health Sciences Center Joint Institute for Translational and Clinical Research, and a grant from the Peking University Medicine Fund of Fostering Young Scholars (Scientific and Technological Innovation) (No. BMU2018PYB005).

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate

Informed consent was signed by each participant. This research was in compliance with the Declaration of Helsinki and approved by the ethics committee of Peking University First Hospital.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.
References

1. Wang L, Gao P, Zhang M, Huang Z, Zhang D, Deng Q, Li Y, Zhao Z, Qin X, Jin D, et al. Prevalence and ethnic pattern of diabetes and prediabetes in China in 2013. JAMA. 2017;317:2515–23.

2. Menke A, Casagrande S, Geiss L, Cowie CC. Prevalence of and trends in diabetes among adults in the United States, 1988–2012. JAMA. 2015;314(1):91–9.

3. Schmidt MI, Duncan BB, Bang H, Pankow JS, Ballantyne CM, Golden SH, Folsom AR, Chambless LE. Identifying individuals at high risk for diabetes: the Atherosclerosis Risk in Communities study. Diabetes Care. 2005;28:213–8.

4. Levitzky YS, Pencina MJ, D’Agostino RB, Meigs JB, Murabito JM, Vasan RS, Fox CS. Impact of impaired fasting glucose on cardiovascular disease: the Framingham Heart Study. J Am Coll Cardiol. 2008;51:264–70.

5. Qiu M, Shen W, Song X, Ju L, Tong W, Wang H, Zheng S, Jin Y, Wu Y, Wang W, Tian J. Effects of prediabetes mellitus alone or plus hypertension on subsequent occurrence of cardiovascular disease and diabetes mellitus: longitudinal study. Hypertension. 2015;65:525–30.

6. Tabak AG, Herder C, Rathmann W, Brunner EJ, Vasan RS, D’Agostino RB, Meigs JB, Murabito JM, Vasan RS, Fox CS. Impact of impaired fasting glucose on cardiovascular disease: the Framingham Heart Study. J Am Coll Cardiol. 2008;51:264–70.

7. Tsimihodimos V, Gonzalez-Villalpando C, Meigs JB, Ferrannini E. Hypertension and diabetes mellitus: coprediction and time trajectories. Hypertension. 2018;71:1422–8.

8. Ali MK, Bullard KM, Saydah S, Imperatore G, Gregg EW. Cardiovascular and renal burdens of prediabetes in the USA: analysis of data from serial cross-sectional surveys, 1988–2014. Lancet Diabetes Endocrinol. 2018;6:392–403.

9. Derakhshan A, Bagherzadeh-Khbandari F, Arshi B, Ramezankhani A, Azizi F, Hadaegh F. Different combinations of glucose tolerance and blood pressure status and incident diabetes, hypertension, and chronic kidney disease. J Am Heart Assoc. 2016;5:e003917.

10. Perreault L, Temprosa M, Mathur KJ, Horton E, Pittock SJ, Glazier M, Thayer D, Orchard TJ, Hamman RF, Goldberg RB. Regression from prediabetes to normal glucose regulation is associated with reduction in cardiovascular risk: results from the Diabetes Prevention Program outcomes study. Diabetes Care. 2014;37:2622–31.

11. Mac-Moune Lai F, Szezo CC, Choi PC, Ho KK, Tang NL, Chow KM, Li PK, To KF. Isolate diffuse thickening of glomerular capillary basement membrane: a renal lesion in prediabetes? Med Pediatr. 2004;17:1506–12.

12. Melsom T, Schei J, Stefansson VT, Solbu MD, Jenssen TG, Mathiesen UD, Wilsgaard T, Erkens BO. Prediabetes and risk of glomerular hyperfiltration and albuminuria in the general nondiabetic population: a prospective cohort study. Am J Kidney Dis. 2016;67:841–50.

13. De Nicola L, Conte G, Minutolo R. Prediabetes as a precursor to diabetic kidney disease. Am J Kidney Dis. 2016;67:817–9.

14. Cushman WC, Evans GW, Byington RP, Goff DC Jr, Grimm RH Jr, Cutler JA, Simons-Morton DG, Basile JN, Conlin PR, Foley RN, et al. Effects of intensive blood-pressure control in type 2 diabetes patients with abnormalities of albumin excretion rate. Diabetes. 2000;49:476–84.

15. Kazumi T, Hozumi T, Ishida Y, Ikeda Y, Kishi K, Hayakawa M, Yoshino G. Increased urinary serum excretion excretion predicts microalbuminuria in patients with type 2 diabetes. Diabetes Care. 2004;27:195–200.

16. Li JC, Tian J, Wu SL, Wang ZJ, Zhang XF, Jia D, Ding RJ, Xiao XF, Fan YB, Hu DY. Effect of long-term systolic blood pressure trajectory on kidney damage in the diabetic population: a prospective study in a community-based Chinese cohort. Chin Med J (Engl). 2018;131:1199–205.

17. Gluhovschi C, Gluhovschi G, Petrica L, Timar R, Vekiov S, Ionita I, Kaycsa A, Timar B. Urinary biomarkers in the assessment of early diabetic nephropathy. J Diabetes Res. 2016;2016:4626125.

18. Nair T, Hosoba M, Kakei M, Ito S. Increased urinary excretion of immunoglobulin g, ceruloplasmin, and transferrin predict development of microalbuminuria in patients with type 2 diabetes. Diabetes Care. 2006;29:142–4.

19. Christiansen MS, Hommel E, Friberg L, Mogplug J, Magid E, Feldt-Rasmussen B. Increased urinary crossmucoid excretion is not related to impaired renal function in patients with type 2 diabetes. J Diabetes Compl. 2010;24:28–36.

20. Hong CY, Hughes K, Chia KS, Ng V, Ling SL. Urinary alfa1-microglobulin as a marker of nephropathy in 2 type 2 diabetic Asian subjects in Singapore. Diabetes Care. 2003;26:338–42.

21. Yang YZ, Wang JW, Wang F, Wu YT, Zhao HY, Chen M, Zhang LX, Wu SL, Zha MH. Incidence, development, and prognosis of diabetic kidney disease in China: design and methods. Chin Med J (Engl). 2017;130:199–202.

22. Wu S, Huang Z, Yang Z, Zhou Y, Wang A, Chen L, Zhao H, Ruan C, Wu Y, Xin A, et al. Prevalence of ideal cardiovascular health and its relationship with the 4-year cardiovascular disease events in a northern Chinese industrial city. Circ Cardiovasc Qual Outcomes. 2012;5:487–93.

23. Standards of medical care in diabetes–2013. Diabetes Care 2013, 36 Suppl 1:S1–114.

24. Levey AS, Stevens LA, Schmid CH, Fox CH, Isakova T, Lash JP, Peralta CA, Kurella Tamura M, Feldman NH. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. Am J Kidney Dis. 2013;62:2560–72.

25. Jones BL, Nagon DS, Roeder K. A SAS procedure based on mixture models for estimating developmental trajectories. Social Methods Res. 2001;29:374–93.

26. Allen NB, Siddique J, Wilkins JT, Shay C, Lewis CE, Goff DC, Jacobs DR Jr, Liu K, Lloyd-Jones D. Blood pressure trajectories in early adulthood and subclinical atherosclerosis in middle age. JAMA. 2014;311:490–7.

27. Inker LA, Astor BC, Fox CH, Isakova T, Lash JP, Parkata CA, Kurella Tamura M, Feldman NH. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. Am J Kidney Dis. 2014;63:713–35.

28. Fan JH, Wang JB, Wang SM, Abnet CC, Qiao YL, Taylor PR. Longitudinal change in blood pressure is associated with cardiovascular disease mortality in a Chinese cohort. Heart. 2018;104:1764–71.

29. Zheng W, Mu J, Chu C, Hu J, Yan Y, Ma Q, Lv Y, Xu X, Wang K, Wang Y, et al. Association of blood pressure trajectories in early life with subclinical renal damage in middle age. J Am Soc Nephrol. 2018;29:2835–46.

30. Gastaldelli A, Ferrannini E, Miyazaki Y, Matsuda M, DeFronzo RA. Beta-cell dysfunction and glucose intolerance: results from the San Antonio metabolic (SAM) study. Diabetologia. 2004;47:31–9.

31. Ritze E, Kolegavanova N, Piecha G. Is there an obesity-metabolic syndrome related glomerulopathy? Curr Opin Nephrol Hypertens. 2011;20:444–9.

32. Maclsaic RJ, Tsalamandris C, Panagiotopoulos S, Smith TJ, McNeil KJ, Jeeres G. Nonalbuminuric renal insufficiency in type 2 diabetes. JAMA. 2004;27:195–200.

33. Nosadini R, Velussi M, Brocco E, Bruseghin M, Abaterusso C, Saller A, Dalla Vesta M, Carriero A, Bontollose E, Sambataro M, et al. Course of renal function in type 2 diabetic patients with abnormalities of albumin excretion rate. Diabetes. 2000;49:476–84.

34. Kazumi T, Hozumi T, Ishida Y, Ikeda Y, Kishi K, Hayakawa M, Yoshino G. Increased urinary serum excretion excretion predicts microalbuminuria in patients with type 2 diabetes. Diabetes Care. 1999;22:1176–80.

35. Jiang H, Guan G, Zhang R, Liu G, Liu H, Hou X, Cheng J. Increased urinary excretion of crossmucoid is a risk predictor of diabetic nephropathy. Nephrology (Carlton). 2009;14:332–7.
37. Kanauchi M, Nishioka H, Hashimoto T, Dohi K. Diagnostic significance of urinary transferrin in diabetic nephropathy. Nihon Jinzo Gakkai Shi. 1995;37:649–54.

38. Yang W, Lu J, Weng J, Jia W, Ji L, Xiao J, Shan Z, Liu J, Tian H, Ji Q, et al. Prevalence of diabetes among men and women in China. N Engl J Med. 2010;362:1090–101.

39. Zendjabil M. Glycated albumin. Clin Chim Acta. 2020;502:240–4.

40. Bellia C, Cosma C, Lo Sasso B, Bivona G, Agnello L, Zaninotto M, Ciaccio M. Glycated albumin as a glycaemic marker in patients with advanced chronic kidney disease and anaemia: a preliminary report. Scand J Clin Lab Invest. 2019;79:293–7.

41. Bellia C, Zaninotto M, Cosma C, Agnello L, Lo Sasso B, Bivona G, Plebani M, Ciaccio M. Definition of the upper reference limit of glycated albumin in blood donors from Italy. Clin Chem Lab Med. 2017;56:120–5.

**Publisher’s Note**
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.