An innovative non-invasive model for screening reduced estimated glomerular filtration rate in a working population

Running title: Screening for reduced eGFR

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Abstract

Background. Most of the existing risk scores for identifying people with reduced estimated glomerular filtration rate (eGFR) involve laboratory-based factors, which are not convenient and cost-effective to use in large population-based screening program. We aimed at using non-invasive variables to identify subjects with reduced eGFR in a Chinese working population.

Methods. Two study populations were recruited in 2012 and 2015, respectively. The 2012 study population (n=14,374) was randomly separated as the training dataset (n=9,621) or the internal testing dataset (n=4,753) at a ratio of 2:1, and the 2015 study population (n=4,371) was used as the external testing dataset. Stepwise logistic regression analysis with age, gender, hypertension and body mass index (BMI) status were first performed in the training dataset and then validated in both internal and external testing dataset. A nomogram was further developed based on the final model.

Results. Results showed that older females with higher BMI status were more likely to have reduced eGFR. The model had excellent discrimination (AUC: 0.887 [95%CI: 0.865, 0.909] in the internal validation and 0.880 [95%CI: 0.829, 0.931] in the external validation) and calibration (Hosmer-Lemeshow test, P=0.798 and 0.397 for internal and external dataset, respectively). The probability of having reduced eGFR increased gradually from <0.1% at a total score of 0 to 26% at a total score of 58 shown in the nomogram.

Conclusion. Non-invasive variables could help identify individuals at high risk of reduced eGFR for further kidney function testing or intervention, aiding in decision-making and resource allocation in large population screening.

In this study conducted in selected ethnic working class Uighur Chinese population, the authors show that advanced age, female sex and higher body mass index are associated with the likelihood of having reduced eGFR

Keywords:

Innovative model, nomogram, non-invasive variables, reduced eGFR, working population

Introduction

Chronic kidney disease (CKD) is a major public health issue that has been linked to ageing, hypertension, diabetes and unhealthy lifestyle.[1] As a key factor for the diagnosis, classification and staging of CKD, glomerular filtration rate (GFR) measures the flow rate of filtered fluid through the kidney.[2] It is considered the best indicator of the overall kidney function and an important clinical tool for health and disease in the daily care.[2] However, GFR is not readily assessable directly. Several different formula, as a result, have been developed using clinical available parameters.[3, 4] Nowadays, the estimated GFR (eGFR) is widely used in the clinical decision-making process for renal dysfunction and renal dialysis.[2]

Reduced eGFR (<60 mL/min/1.73 m^2) is categorized as stage 3 – 5 CKD according to the Kidney Disease – Improving Global Outcomes (KDIGO) guidelines, indicating a substantial reduction in kidney function.[2] Reduced eGFR is also associated with increased risk of cardiovascular disease (CVD) and all-cause mortality,[5] it is therefore urgent and important to identify individuals with reduced eGFR at an early stage and execute appropriate management, in order to prevent or delay the onset of the adverse outcomes. However, a cost-effectiveness study showed that screening reduced eGFR in the general population is not as cost-effective as targeting subgroups, such as diabetes patients.[6] Nevertheless, there is a substantial proportion of patients with diabetes are undiagnosed, and this figure is up to 60.7% in China.[7] Thus, it is not feasible to screen reduced eGFR among the high-risk groups, in considering the high rate of undiagnosed diabetes.

Several risk scores were developed to identify individuals with high risk of reduced eGFR.[8-17] However, most of these studies involved laboratory tests, which may be cumbersome to be

used in population-based screening program. Thus, in this study, we aimed at estimating the prevalence of reduced eGFR and establishing a model using non-invasive variables in a working population, in order to identify subjects with reduced eGFR for further kidney function testing or intervention for preventing adverse outcomes.

Methods

Settings and study population

This cross-sectional study was conducted from January to December 2012 in the People's Hospital of Xinjiang Uygur Autonomous Region, located in the northwest of the People's Republic of China. Another population was recruited from January to March 2015 at the same hospital. The two populations were working individuals coming to the health examination center at the hospital for body check arranged by their companies/institutes. Inclusion criteria included adults older than 18 years and having given consent to this study. All the eligible participants during the study recruitment periods were invited. Individuals were excluded from subsequent statistical analysis if 1). without age information or were less than 18 years old; 2). without body mass index (BMI) information; 3). without blood pressure (BP) measurement and 4). without serum creatinine test. The study design was shown in Figure 1. All the participants were provided with a written consent. The demographic and clinical data were subsequently collected anonymously. This study was approved by the hospital's ethics committee according to the 1975 Declaration of Helsinki.

Measurements

Demographic data including age and gender were self-reported by participants. BMI was calculated from participant's measured body weight and height, with overweight and obesity defined as BMI value between 23−24.9 kg/m^2 and ≥ 25 kg/m^2, respectively, based on the WHO Asian cut-off value.[18] BP was measured after at least 5 minutes of rest. Hypertension was defined as systolic BP $\geq$ 140 mmHg and/or diastolic BP $\geq$ 90 mmHg or on anti-hypertensive medication at the time of health examination. Blood samples were collected after overnight fasting to assess the levels of serum creatinine, fasting blood glucose and lipid profile (total cholesterol, triglycerides, high density lipoprotein [HDL]-cholesterol and

calculated low density lipoprotein [LDL]-cholesterol). Serum total cholesterol, triglycerides and HDL-cholesterol were measured using enzymatic techniques (Abbott Japan Co., Ltd., Tokyo, Japan).

Serum creatinine was assessed using kinetic colorimetric methods, which has been standardized against the isotope dilution mass spectrometry (IDMS) (Abbott Japan Co., Ltd., Tokyo, Japan). The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation was used to calculate eGFR based on age, gender and serum creatinine.[3] Reduced eGFR was defined as eGFR<60 mL/min/1.73 m^2 and served as the primary outcome of our study.

Statistical analysis

The 2012 study population was randomly separated into two parts, with 2/3 of the total participants as the training dataset and the remaining participants as the internal testing dataset. The 2015 study population was served as the external testing dataset. Descriptive characteristics were summarized as means ± standard deviation (SD) or numbers (percentage), as appropriate. To compare the differences between participants with reduced eGFR and those without in 2012 study population, and between training dataset and internal or external testing datasets, independent two-sample t-test was used for continuous data, and Chi-square test was used for categorical variables.

In order to identify the significant factors associated with reduced eGFR, stepwise logistic regression model was applied to the training dataset first and then validated on both internal and external testing datasets. To facilitate risk score calculation and clinical use, we categorized continuous variables as binary or categorical variables with arbitrary cut-off points. Age groups (≤40, 41−50, 51−60, 61−70, and ≥71 years), gender, hypertension and BMI status (<23 for normal, 23−24.9 for overweight and ≥25 kg/m^2 for obese) were coded and entered into the model. All the variables with a *p* value less than 0.1 were kept in the final model. The variables in the final model were used to establish a nomogram. First, each variable was assigned a score by multiplying the respective β-coefficients by 10 and rounded to the nearest integer. Second, variable axes were constructed for each variable with the length in accordance with the variable score. Last, an axe of the total score (sum of the scores

for each variable) and an axe of the corresponding estimated probability of having reduced eGFR was drawn. The area under the receiver-operating characteristic curve (AUC) was used to evaluate the model discrimination. An AUC of 0.7 – 0.8 is defined as acceptable discrimination; between 0.8 – 0.9 is defined as excellent discrimination and over 0.9 is defined as outstanding discrimination.[19] The Hosmer-Lemeshow test was used to assess the model calibration when a *p* value of test greater than 0.05 indicating no statistically significant difference between the predicted outcome in the model and the observed outcome.[19] Youden's index was used to determine the optimal cut-off score for predicting reduced eGFR.[20] We further added laboratory assessments of fasting blood glucose, triglyceride and LDL-cholesterol into the model and compared the performance with the model incorporating non-invasive variables only, in order to see whether there is any incremental AUC.

Statistical analyses were performed using STATA 13 (Stata Corp, College Station, TX, USA). All the statistical tests were two-sided and statistical significance was set at $p<0.05$.

Results

A total of 20,182 individuals were invited and 17,537 subjects (86.9%) were finally recruited with consent form in 2012. We excluded those aged less than 18 years (n = 28); without BP or BMI measurements (n = 271) and those without serum creatinine measurement (n = 2,864). The 2012 study population therefore included 14,374 participants with 8,154 males and 6,221 females. The mean (SD) age was 45.3 (14.3) years. No significant difference in age or gender was found between participants included and excluded from the study. Similarly, 6,016 individuals were invited in 2015 and 5,304 subjects (88.2%) were recruited with consent form. A total of 4,371 subjects were finally included as the external testing dataset (Figure 1).

In the 2012 study population, the prevalence of reduced eGFR was 2.05% (95%CI: 1.81, 2.28%). Compared to people with normal eGFR levels, those with reduced eGFR were older (68.6 ± 11.8 vs 44.8 ± 13.9 years, $p < 0.001$) and more likely to be overweight or obese (77.5% vs 64.6%, $p < 0.001$) (Table 1). Furthermore, subjects with reduced eGFR had higher systolic BP, diastolic BP, hypertension prevalence, total cholesterol, triglycerides and fasting blood glucose levels, compared to people with normal eGFR.

Around 2/3 (n = 9,621) of the total 2012 participants were randomly assigned into the training dataset, and the remaining 4,753 were entered into the internal testing dataset (Table 2). There were no statistically significant differences found in any item measured between the training dataset and the internal testing dataset. Compared to the training dataset, participants from the external testing dataset were younger and most of them were males (63.7%). Furthermore, they were more likely to be obese, but less likely to have hypertension. In terms of the kidney function, the 2015 study population had lower serum creatinine and higher eGFR levels compared to the training dataset. Only 1.01% of the 2015 study population was diagnosed as reduced eGFR.

Stepwise logistic regression was first applied in the training dataset. Age groups, BMI status and gender were kept in the final model (Table 3). This model had an AUC of 0.887 (95%CI: 0.865, 0.909) and the Hosmer-Lemeshow test had a *p* value of 0.955 (Table 4). The optimal cut-off point was score 36, with an acceptable sensitivity of 0.820 and specificity of 0.863. The logistic regression model with age groups, BMI status and gender were further applied in the internal testing dataset and the model had an AUC of 0.894 (95%CI: 0.861, 0.926) with a *p* value of 0.798 in the Hosmer-Lemeshow test. Similarly, the model in the external testing dataset had an AUC of 0.880 (95%CI: 0.829, 0.931) and a *p* value of 0.397 in the Hosmer-Lemeshow test. A nomogram incorporating age groups, BMI status and gender was further developed to estimate the probability of having reduced eGFR in the working population (Figure 2).

After including fasting blood glucose, triglyceride and LDL-cholesterol into the stepwise logistic analysis, obesity was no longer a significant factor and was ruled out from the model, while triglyceride was kept in the final model (data not shown). However, there were no significant incremental AUC of the new model compared to the model only incorporating non-invasive variables.

Discussion

The present cross-sectional study was conducted in a relatively large scale of working population, having 2.05% of subjects screened with reduced eGFR according to the CKD-EPI formula. From the model demonstrating excellent discrimination and calibration during both internal and external validations, female gender, older age and larger BMI were associated with increased risk of reduced eGFR. A nomogram incorporating these three items was further developed to estimate the probability of having reduced eGFR in the working population, which could be used as a strategy of risk stratification before any evaluation of laboratory test.

In the United States, the National Health and Nutrition Examination Surveys showed that the prevalence of reduced eGFR was around 5.6% in the 1988-1994 survey and increased to around 8.1% in the 1999-2004 survey.[21] Nevertheless, the prevalence of reduced eGFR in China is relatively low.[22-25] Two national-wide studies reported that the prevalence of reduced eGFR was 1.7% among subjects aged 18 years or older,[24] and 2.53% in another study focusing on adults aged between 34 – 74 years old.[25] Our study further showed that the prevalence of reduced eGFR was around 2.05% in the working population. Although it was relatively low compared to the United States, the situation might be aggravated in the future due to the aging population and increasing epidemic of diabetes and hypertension in China. Furthermore, substantial disparities of reduced eGFR prevalence in geographical regions were demonstrated in these studies. There were several possible explanations for such differential prevalence of reduced eGFR. First, as a developing country, the distribution of economic development, lifestyle factors, dietary habits, health literacy and access to medical care varied greatly, especially between rural and urban areas.[26] Second, there are several standardized formulas to estimate GFR.[3, 4, 27] One of the national-wide studies used the

Modification of Diet in Renal Disease (MDRD) equation to estimate GFR,[25] another study used the adopted Chinese version of the MDRD equation,[24] while our study used the CKD-EPI formula, which has been demonstrated superior accuracy than the MDRD formula.[28] Thus, it is plausible that the prevalence of reduced eGFR in our study was different from the two previous population studies in China.[24, 25]

Many available risk scores have been established to either identify the prevalent[8-10] or incident cases of reduced eGFR[11-17] in clinic settings or population-based studies. However, most of these studies required laboratory-based measures or information of previous disease diagnosis, e.g. diabetes. Only one study evaluated the risk model using age and sex, resulting a c-statistic of 0.776.[13] Better model performance in our study might be attributable to the inclusion of BMI status and a more detailed category of age. We demonstrated that ageing is a key risk factor for reduced eGFR, which might be due to the reduction in renal blood flow and renal mass.[29, 30] Hypertension was ruled out from the final model because of statistical non-significance. It might be a result of the close association between ageing and hypertension in our study population, in which hypertension was explained by ageing effect in the model.

Screening reduced eGFR among asymptomatic people is undergoing debate over the cost and the effective therapy or intervention. On one hand, there is insufficient evidence from randomized controlled trial[31] to suggest that screening for reduced eGFR can prevent or delay the adverse outcomes of end-stage renal disease or CVD at an early stage.[5] Nevertheless, we should bear in mind that insufficient evidence for screening does not imply that screening for reduced eGFR is ineffective. On the other hand, it is not cost-effective to screen for reduced eGFR in the general population. In a large scale general health survey conducted in Norway, results showed that 20.6 people needed to be screened in order to identify one case with reduced eGFR.[32] It has been proven not to be a cost-effective strategy in the general population with an estimated cost per quality adjusted life years gained of 104, 900 Canadian dollars (equal to 83,000 US dollars), compared to a figure of 22,600 Canadian dollars (equal to 17,870 US dollars) in diabetes patients,[6] which provided us with a feasible and cost-effective strategy. However, in China, around 60.7% of the diabetes patients are undiagnosed,[7] indicating a substantial gap of screening prevalent reduced eGFR in this high-risk group in developing countries.

There are several potential implications from this study. First, the score-based system allows not only the occupational health physicians but also the layman to understand the risk of having reduced eGFR, which may aid further decision-making process. Second, using non-invasive variables may broaden the application in the general population, especially in rural areas. Third, the simple and easily defined nomogram may increase the awareness of kidney disease in the general population, as it is estimated that the overall awareness rate of CKD was only 10.4% in a representative sample of the general population in China.[33] Last, we did not find any incremental AUC after including laboratory assessment. Our results suggested that in clinical practice, a two-stage process might be more efficient and cost-effective. The first step is to identify those with high risk of reduced eGFR using non-invasive variables, such as age, sex, BMI, blood pressure and other relevant information and followed by a second step of laboratory measures for serum creatinine, which would be applied only to people with high risk to further confirm the findings. Suitable interventions, such as losing weight, reducing blood pressure or changing diet habits, should be further applied to people with reduced eGFR in order to prevent adverse outcomes of severe kidney disease, CVD and mortality.[5] However, the cost-effectiveness of the two-stage strategy needs further investigation.

Strengths and limitations

There are several strengths of this study. Firstly, we included a large study population. Secondly, all the assessments were conducted in the same assessment center, which minimize the measurement errors and confounding effects of various tests. Thirdly, the model developed in our study was further validated both internally and externally, revealing excellent discriminations and calibration. Lastly, we developed a nomogram, which would be used as a risk-stratification tool to identify those at high risk of reduced eGFR in the working population and general population at large.

The limitations of this study deserved discussion. First, the cross-sectional nature of these data precludes us from exploring the casual relationship between these non-invasive variables and reduced eGFR. However, several previous cohort studies have already well-documented that older age, female and obesity were related to reduced eGFR,[34, 35] which supported the findings in our study. Second, we have arbitrarily converted continuous variables into categorical data to facilitate risk score calculation and nomogram establishment, although

most risk factors were continuous data. Third, the generalizability of our study to other populations needs further investigation. Fourth, we cannot rule out the influence of other unmeasured confounders. For example, cigarette smoking[34] and sedentary behaviors[36] have been linked to increased risk of reduced eGFR. However, in this study, we were unable to address this association. Last, urine albumin to creatinine ratio is also an important aspect of CKD, linking with end-stage renal disease and CVD. Nevertheless, due to the lack of information on urine albumin and creatinine measures, we were unable to predict CKD as the study outcome.

Conclusion

In conclusion, age, gender and BMI status were associated with detection of reduced eGFR in a working population. The validated model incorporating these three variables would be integrated as a simple tool to identify those with high risk of reduced eGFR and allocate appropriate resources to them accordingly. Although people with reduced eGFR without progressing receive little treatment or intervention by urologists, it should be recognized that most of these people die from CVD, rather than progressing to end-stage renal disease,[37] which signifies the importance of identifying these people from the general population. However, even though the prevalence of reduced eGFR is relatively low in China when compared to other countries, the absolute burden is substantial in considering the large population size. The nomogram developed in our study thus would be used to efficiently allocate resources to screen and intervene high risk individuals.

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CONFLICT OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest.

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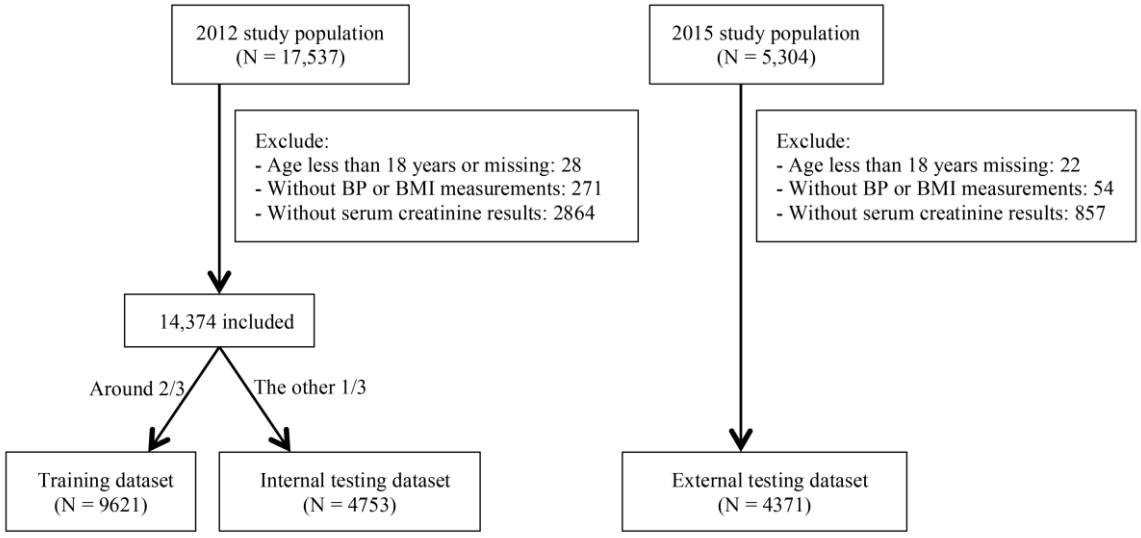

Figure 1. Design and participants flow of this study, 2012 and 2015. Abbreviation: BP, blood pressure; BMI, body mass index.

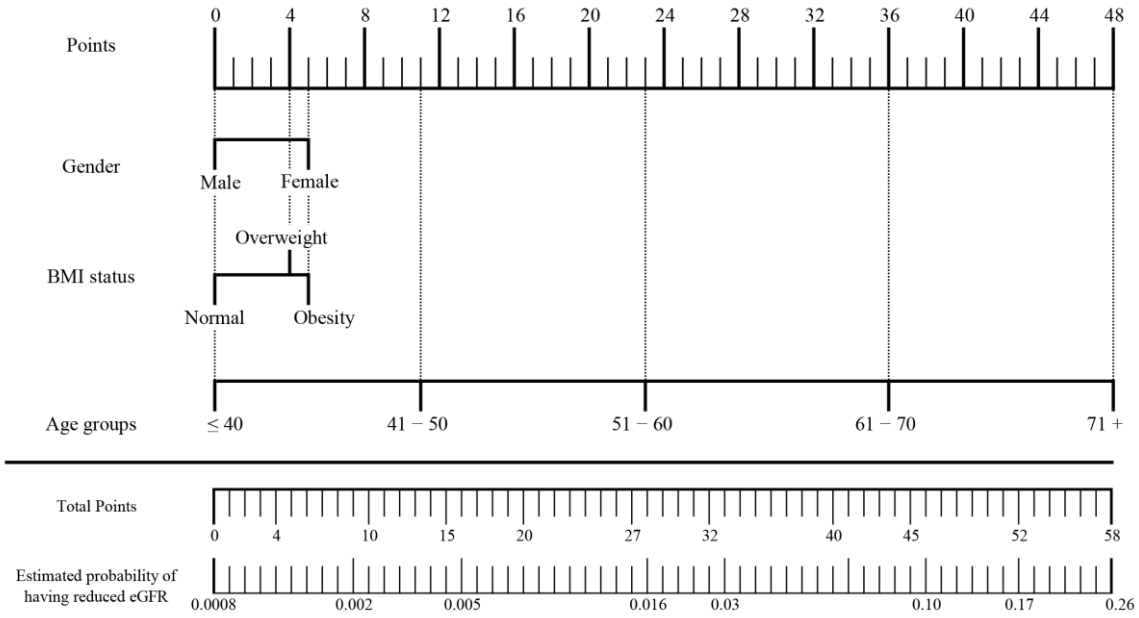

Figure 2. Nomogram for identifying reduced eGFR from asymptomatic working population using non-invasive variables. Abbreviation: BMI, body mass index; eGFR, estimated glomerular filtration rate. Overweight was defined as BMI between 23−24.9 kg/m^2 and obesity was defined as BMI≥25 kg/m^2 in this Asian population. To use the nomogram, first, draw a straight upward line to the "Points" axis and determine the points contributed by gender. Repeat the same process for BMI status and age group. Second, get the total points by adding the points from gender, BMI status and age group. Last, find the point in the "Total Points" axis and draw a straight downward line to the "Estimated probability of having reduced eGFR" and read the estimated probability. For an obese (5 points) female subject (5 points) aged 77 years (48 points), the total points were 58, and the corresponding probability of having reduced eGFR was 0.26.

Table 1. Demographic and Clinical Characteristics of the 2012 Study Population According to the Reduced eGFR Diagnosis, Urumqi, China, 2012

	Overall participants (*n* = 14374)	**Normal eGFR (*n* = 14080)**	**Reduced eGFR (*n* = 294)**	***P* value [a]**
Age, years	45.3 (14.3)	44.8 (13.9)	68.6 (11.8)	<0.001
Sex				0.493
Male	8153 (56.7%)	7992 (56.8%)	161 (54.8%)	
Female	6221 (43.3)	6088 (43.2%)	133 (45.2%)	
BMI[b]	24.5 (3.5)	24.5 (3.5)	25.4 (3.4)	<0.001
BMI status[c]				<0.001
Normal weight	5043 (35.1%)	4977 (35.3%)	66 (22.4%)	
Overweight	3303 (23.0%)	3242 (23.0%)	61 (20.7%)	
Obesity	6028 (41.9%)	5861 (41.6%)	167 (56.8%)	
Systolic BP, mm Hg	122.8 (19.3)	122.5 (19.1)	134.9 (21.5)	<0.001
Diastolic BP, mm Hg	78.2 (12.8)	78.1 (12.8)	79.8 (13.1)	0.030
Hypertension	3640 (25.3%)	3501 (24.9%)	139 (47.3%)	<0.001
Serum creatinine, μmol/L	77.2 (19.7)	76.3 (14.0)	123.5 (85.7)	<0.001
eGFR, mL/minute/1.73 m^2	95.5 (16.4)	96.5 (15.2)	51.0 (10.0)	<0.001
Fasting blood glucose, mmol/L	4.8 (1.5)	4.8 (1.4)	5.5 (2.3)	<0.001
Total cholesterol, mmol/L	4.5 (1.3)	4.5 (1.3)	4.8 (1.3)	<0.001
Triglycerides, mmol/L	1.8 (1.5)	1.8 (1.5)	2.2 (1.9)	0.001
HDL-cholesterol, mmol/L	1.0 (0.7)	1.0 (0.7)	0.9 (0.8)	0.350
LDL-cholesterol, mmol/L	1.8 (1.4)	1.8 (1.4)	1.8 (1.5)	0.637

Abbreviation: BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; HDL, high density lipoprotein; LDL, low density lipoprotein; SD, Standard deviation.

[a] *P* values refer to comparisons between subjects with and without reduced eGFR, using Student's t test or Pearson's χ^2 test.

[b] BMI = weight (kg)/height $(m)^2$.

[c] Overweight was defined as BMI between 23−24.9 kg/m^2 and obesity was defined as BMI≥25 kg/m^2 in this Asian population.

Table 2. Comparison of Demographic and Clinical Characteristics between the Training Dataset and the Internal or External Testing Dataset, Respectively, Urumqi, China, 2012 and 2015

Characteristic	2012 study population[a]		*P* value[b]	2015 study population	*P* value[c]
	Training dataset (*n* = 9621)	Internal testing dataset (*n* = 4753)		External testing dataset (*n* = 4371)	
Age, years	45.4 (14.3)	45.2 (14.3)	0.448	41.8 (11.7)	<0.001
Sex					<0.001
Male	5456 (56.7%)	2697 (56.7%)		2786 (63.7%)	
Female	4165 (43.3%)	2056 (43.3%)		1585 (36.3%)	
BMI[d]	24.5 (3.5)	24.5 (3.6)	0.612	24.7 (4.4)	0.016
BMI status[e]					
Normal weight	3347 (34.8%)	1696 (35.7%)	0.358	1601 (36.6%)	<0.001
Overweight	2222 (23.1%)	1081 (22.7%)		728 (16.7%)	
Obesity	4052 (42.1%)	1081 (41.6%)		2042 (46.7%)	
Systolic BP, mm Hg	122.8 (19.3)	122.6 (19.2)	0.415	125.6 (22.5)	<0.001
Diastolic BP, mm Hg	78.2 (12.8)	78.0 (12.9)	0.348	76.8 (15.0)	<0.001
Hypertension	2436 (25.3%)	1204 (25.3%)	0.988	971 (22.2%)	<0.001
Serum creatinine, μmol/L	77.2 (19.7)	77.3 (19.6)	0.778	75.4 (17.8)	<0.001
eGFR, mL/minute/1.73 m^2	95.5 (16.4)	95.6 (16.5)	0.815	97.1 (16.2)	<0.001
Reduced eGFR (n, %)	194 (2.0%)	100 (2.1%)	0.522	47 (1.1%)	<0.001
Fasting blood glucose, mmol/L	4.8 (1.5)	4.8 (1.4)	0.979	—	
Total cholesterol, mmol/L	4.5 (1.3)	4.5 (1.3)	0.125	—	
Triglycerides, mmol/L	1.9 (1.5)	1.8 (1.5)	0.254	—	
HDL-cholesterol, mmol/L	1.0 (0.7)	1.0 (0.7)	0.395	—	
LDL-cholesterol, mmol/L	1.8 (1.4)	1.8 (1.4)	0.979	—	

Abbreviation: BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; HDL, high density lipoprotein; LDL, low density lipoprotein; SD, Standard deviation.

[a] Around 2/3 of the 2012 study population were randomly selected as the training dataset and the remaining as the internal testing dataset.

[b] *P* values refer to comparisons between subjects training dataset and internal testing dataset, using Student's t test or Pearson's χ^2 test.

[c] *P* values refer to comparisons between subjects training dataset and external testing dataset, using Student's t test or Pearson's χ^2 test.

[d] BMI = Weight (kg)/height $(m)^2$.

[e] Overweight was defined as BMI between 23−24.9 kg/m^2 and obesity was defined as BMI≥25 kg/m^2 in this Asian population.

Table 3. Cross-Sectional Analysis of the Association between Non-invasive Variables and Reduced eGFR using Stepwise Logistic Regression in the Training Dataset

Risk factors	β-Coefficient	OR	95% CI	*P* value	Score
Age group, years					
≤ 40	–	1	–	–	–
41 − 50	1.12	3.05	1.16 − 8.04	0.024	11
51 − 60	2.27	9.64	3.94 − 23.58	0.000	23
61 − 70	3.64	38.22	16.19 − 90.19	0.000	36
71 +	4.76	117.06	51.02 − 268.60	<0.001	48
BMI status [a]					
Normal	–	1		–	
Overweight	0.43	1.55	1.09 − 2.19	0.014	4
Obesity	0.47	1.60	1.10 − 2.34	0.014	5
Gender					
Male	–	1	–	–	–
Female	0.46	1.58	1.17 − 2.14	0.003	5

Abbreviation: BMI, body mass index; OR, odds ratio; CI, confidence interval.

[a] Overweight was defined as BMI between 23−24.9 kg/m^2 and obesity was defined as BMI≥25 kg/m^2 in this Asian population.

Table 4. Discrimination and Calibration of the Final Model in the Training, Internal and External testing dataset, respectively

	Model discrimination		**Model calibration**
	AUC	**95%CI**	**Hosmer-Lemeshow test (*P value*)**
Training dataset (*n* = 9,621)	0.887	0.865 - 0.909	0.955
Internal testing dataset (*n* = 4,753)	0.894	0.861 - 0.926	0.798
External testing dataset (*n* = 4,371)	0.880	0.829 - 0.931	0.397

Abbreviation: AUC, Area under receiver operating characteristic curve; CI, confidence interval.