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ORIGINAL ARTICLE

Retrospective Study

Roles of biochemistry data, lifestyle, and inflammation in identifying abnormal renal function in old Chinese

Chao-Hung Chen, Chun-Kai Wang, Chen-Yu Wang, Chun-Feng Chang, Ta-Wei Chu

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Abstract

BACKGROUND

The incidence of chronic kidney disease (CKD) has dramatically increased in recent years, with significant impacts on patient mortality rates. Previous studies have identified multiple risk factors for CKD, but they mostly relied on the use of traditional statistical methods such as logistic regression and only focused on a few risk factors.

AIM

To determine factors that can be used to identify subjects with a low estimated glomerular filtration rate (L-eGFR < 60 mL/min per 1.73 m^2) in a cohort of 1236 Chinese people aged over 65.

METHODS

Twenty risk factors were divided into three models. Model 1 consisted of demographic and biochemistry data. Model 2 added lifestyle data to Model 1, and Model 3 added inflammatory markers to Model 2. Five machine learning methods

were used: Multivariate adaptive regression splines, eXtreme Gradient Boosting, stochastic gradient boosting, Light Gradient Boosting Machine, and Categorical Features + Gradient Boosting. Evaluation criteria included accuracy, sensitivity, specificity, area under the receiver operating characteristic curve (AUC), F-1 score, and balanced accuracy.

RESULTS

A trend of increasing AUC of each was observed from Model 1 to Model 3 and reached statistical significance. Model 3 selected uric acid as the most important risk factor, followed by age, hemoglobin (Hb), body mass index (BMI), sport hours, and systolic blood pressure (SBP).

CONCLUSION

Among all the risk factors including demographic, biochemistry, and lifestyle risk factors, along with inflammation markers, UA is the most important risk factor to identify L-eGFR, followed by age, Hb, BMI, sport hours, and SBP in a cohort of elderly Chinese people.

Key Words: Biochemistry data; Lifestyle; Machine learning; Renal function

Core Tip: This is a retrospective study that used five machine learning methods to evaluate the impact of lifestyle and chronic inflammation in identifying subjects with abnormal estimated glomerular rates among elderly Chinese subjects. Our results showed that uric acid is the most important risk factor (inflammatory marker), followed by age, hemoglobin, body mass index, sport hours, and systolic blood pressure.

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INTRODUCTION

The number of global people suffering chronic kidney disease (CKD) and acute kidney injury is approaching 850 million. CKD is expected to emerge as the 5th cause of death by the year of 2040, and 2nd by 2100 as the global population continues to age. CKD progresses through five stages based on the estimated glomerular filtration rate (eGFR). A decrease in eGFR value to 15 mL/min per 1.73 m^2 is defined as end stage renal disease according to Kidney Disease: Improving Global Outcome. In the United States, there are approximately 80000 patients with end stage renal disease, 71% of whom are presently on dialysis[1]. A similar trend is found in Taiwan. Data from Taiwan's National Health Insurance agency indicates that the prevalence of CKD increased from 1.3 million to 2.2 million from 2005 to 2014[2], while Tsai *et al*[3] found a 15.45% prevalence in a study cohort of 106094 subjects, of which 9.06% were in CKD stages[4]. The determinants were found to be diabetes, hypertension, and metabolic syndrome[4].

Subjects with CKD have a significantly higher chance to have cardiovascular diseases and cerebrovascular disease (stroke, transient ischemic attack, *etc*.), along with associated cognitive dysfunction. Even in early stage CKD, the appearance of albuminuria could be regarded as a representative systemic vascular injury[5].

Many studies have examined the risk factors for CKD. Hannan *et al*[6] found that lifestyle factors such as smoking cessation and exercise significantly retard the onset of CKD. They also reported that increased waking during was associated with a higher risk for CKD. Imig *et al*[7] found that inflammation and immune system activation are common underlying mechanisms for CKD. However, it should be noted that these previous studies have not been subject to meta-analysis and used traditional statistical analysis methods.

In recent years, machine learning (Mach-L) techniques have been widely applied in the field of medicine. Mach-L uses the current computing power to achieve our goal automatically through a computer algorithm[8]. Mach-L can capture nonlinear relationships in the data and complex interactions among multiple predictors, allowing it to potentially outperform conventional multiple logistic regression for diseases[9]. However, to date, no study has applied Mach-L to identifying the risk factors for CKD. The present study, we 1236 healthy elderly Chinese subjects. Five different Mach-L methods were applied to predict high or low eGFR levels (H-eGFR: ≥ 60, L-eGFR < 60 mL/min/1.73 m^2, dependent variable). The independent variables were divided into three models: Model 1: Demographic and biochemistry data; Model 2: Model 1 + lifestyle factors (income, education level, smoking, drinking, sleeping hour, and sport hours); Model 3: Model 2 + inflammatory markers (IM). This study sought to determine whether adding lifestyle and/or IM to Model 1 would increase the prediction accuracy for L-eGFR in elderly Chinese by applying state-of-the-art Mach-L methods.

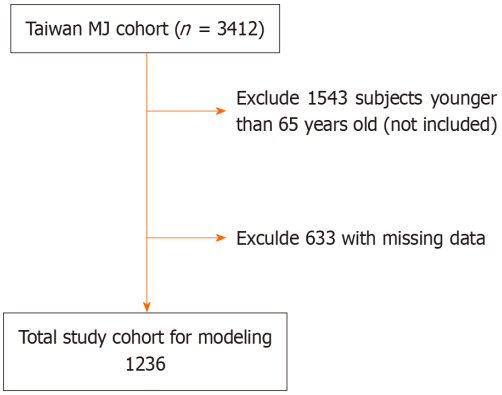

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Figure 1 Flowchart of sample selection from the MJ chronic kidney disease study cohort.

MATERIALS AND METHODS

Patient selection

Data for this study were sourced from the Taiwan MJ cohort, an ongoing prospective cohort of people undergoing health examinations conducted by the MJ Health Screening Centers in Taiwan[10]. These examinations cover more than 100 important biological indicators, including anthropometric measurements, blood tests, imaging tests, *etc.* Each participant completed a self-administered questionnaire to collect personal information and family medical history, current health status, lifestyle, physical exercise, sleep habits, and dietary habits[11]. The MJ Health Database only includes participants who provided informed consent. All or part of the data used in this research were authorized by and received from MJ Health Research Foundation (Authorization Code: MJHRF2020022A). Any interpretations or conclusions described in this paper do not represent the views of MJ Health Research[12]. The study protocol was approved by the Institutional Review Board of the Tri-Service General Hospital, National Defense Medical Center (IRB No.: KAFGHIRB 109-46). A total of 3412 healthy participants were enrolled. After excluding subjects for various causes, a total of 1236 subjects remained for analysis, as shown in Figure 1.

On the day of the study, senior nursing staff recorded the subject's medical history, including information on any current medications, and a physical examination was performed. The waist circumference was measured horizontally at the level of the natural waist. The body mass index (BMI) was calculated as the participant's body weight (kg) divided by the square of the participant's height (m). The systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using standard mercury sphygmomanometers on the right arm of each subject while seated.

Following previously published protocols, the procedures for collecting demographic and biochemical data are as follows[13]. After fasting for 10 h, blood samples were collected for biochemical analyses. Plasma was separated from the blood within 1 h of collection and stored at 30 °C until the analysis of fasting plasma glucose (FPG) and lipid profiles. FPG was measured using the glucose oxidase method (YSI 203 glucose analyzer; Yellow Springs Instruments, Yellow Springs, OH, United States). Total cholesterol and triglyceride (TG) levels were measured using the dry multilayer analytical slide method with a Fuji Dri-Chem 3000 analyzer (Fuji Photo Film, Tokyo, Japan). Serum high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol concentrations were analyzed using an enzymatic cholesterol assay, following dextran sulfate precipitation. A Beckman Coulter AU 5800 biochemical analyzer was used to determine the urine albumin/creatinine ratio by turbidimetry.

Table 1 defines the 19 baseline clinical variables, categorized into three models (Table 2). Model 1 included sex, age, BMI, blood pressure, FPG, aspartate aminotransferase (AST), alanine aminotransferase (ALT), uric acid (UA), HDL-C, TG, and eGFR; Mode 2 added drinking, daily sleeping and sport hours; Model 3 added white blood cell (WBC) count, hemoglobin (Hb), alkaline phosphatase (ALP), γ-glutamyl transferase (γ-GT), and high sensitivity c-reactive protein (hsCRP). All these variables were regarded as independent variables. At the same time, the dependent variable was categorical and subjects with H-eGFR were defined as 0 while those with L-eGFR were defined as 1 (L-eGFR < 60 mL/min/1.73 m^2).

Traditional statistics

Data are represented as the mean ± SD. Student's *t* test was used to evaluate the differences of continuous data between H-eGFR and L-eGFR subjects. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant. Statistical analyses were performed using SPSS 10.0 for Windows (SPSS, Chicago, IL, United States).

Proposed machine learning scheme

Models to predict H- or L-eGFR and rank risk factors were constructed using five different Mach-L methods: Multivariate adaptive regression splines (MARS), eXtreme Gradient Boosting (XGBoost), stochastic gradient boosting (SGB), Light Gradient Boosting Machine (LightGBM), and Categorical Features + Gradient Boosting (CATboost) to construct models for predicting whether to have H- or L-eGFR and to identify the importance of the aforementioned risk factors. These

Table 1 Demographic, biochemistry, and lifestyle information of the participants

	Low eGFR	High eGFR
Number	180	1056
Age (yr)	72.1 ± 5.9	69.5 ± 4.6[c]
Sleep time (h)	5.89 ± 1.10	6.1 ± 1.15[a]
Drinking duration	4.76 ± 4.37	5.25 ± 5.74
Sport hours	205.6 ± 36.2	204.4 ± 36.3
Body mass index (kg/m^2)	23.9 ± 3.4	23.7 ± 3.2
White blood cell count (10^3/μL)	5.94 ± 1.75	5.58 ± 1.40[b]
Hemoglobin (g/dL)	13.8 ± 1.5	14.0 ± 1.3
Fasting plasma glucose (mg/dL)	108.2 ± 19.3	108.2 ± 21.5
Alkaline phosphatase (IU/L)	67.8 ± 19.2	66.6 ± 22.2
Serum glutamic oxaloacetic transaminase (IU/L)	27.3 ± 11.3	26.0 ± 12.8
Serum glutamic pyruvic transaminase (IU/L)	25.4 ± 14.7	25.8 ± 19.2
γ-glutamyltransferase (IU/L)	28.5 ± 28.7	27.1 ± 35.5
Systolic blood pressure (mmHg)	131.2 ± 18.9	127.4 ± 18.1[b]
Diastolic blood pressure (mmHg)	75.6 ± 11.2	74.6 ± 10.6
Triglyceride (mg/dL)	121.4 ± 71.4	114.5 ± 67.3
High density lipoprotein cholesterol (mg/dL)	57.4 ± 14.3	59.6 ± 16.0
Uric acid (mg/dL)	6.53 ± 1.48	5.56 ± 1.3
High sensitivity C-reactive protein (mg/L)	2.52 ± 5.08	2.11 ± 4.35[c]
eGFR	74.8 ± 10.1	53.02 ± 6.8

[a]$P < 0.05$.
[b]$P < 0.01$.
[c]$P < 0.005$.
eGFR: Estimated glomerular filtration rate.

Mach-L methods have been used in various healthcare applications and do not have prior assumptions regarding data distribution[14-23].

MARS is a nonparametric and nonlinear statistical method in which several linear segments with different gradients are used to automatically examine the nonlinearity and dependency between multidimensional input and output variables, and then generate the final optimum nonlinear prediction model[24].

XGBoost is a gradient boosting technology based on an SGB optimized extension[25]. It trains and assembles many weak models sequentially using the gradient boosting method of outputs, which achieves a better prediction performance. In XGBoost, the Taylor binomial expansion is used to approximate the objective function and arbitrary differentiable loss functions to accelerate model construction and convergence process[26]. XGBoost then applies a regularized boosting technique to penalize model complexity and correct overfitting, thus increasing model accuracy[25].

SGB is a tree-based gradient boosting learning algorithm that combines both bagging and boosting techniques to minimize the loss function to solve the overfitting problem of traditional decision trees[23]. In SGB, many stochastic weak learners of trees are sequentially generated through multiple iterations, in which each tree concentrates on correcting or explaining errors of the tree generated in the previous iteration. That is, the residual of the previous iteration tree is used as the input for the newly generated tree. This iterative process is repeated until the convergence condition or a stopping criterion is reached for the maximum number of iterations. Finally, the cumulative results of many trees are used to determine the final robust model.

LightGBM is a decision tree-based distributed gradient boosting framework that uses advanced histograms. In each iteration, it learns the approximate value of the decision tree residuals based on one-side sampling and negative gradient fitting[27].

CatBoost is a gradient-boosting decision tree technique in which sequential boosting methods are combined with gradient boosting and multiple categorical features[28]. In CatBoost, the tree combinations and categorical features generated through gradient boosting are aggregated into a sequence to generate the final model.

Figure 2 presents the proposed prediction and important variable identification scheme that combines the five Mach-L methods. First, patient data were collected to prepare the dataset. The dataset was then randomly divided into an 80%

Table 2 Variables contained in three models

	Model 1	Model 2	Model 3
Age	√	√	√
Body mass index	√	√	√
Systolic blood pressure	√	√	√
Diastolic blood pressure	√	√	√
Fasting plasma glucose	√	√	√
Serum glutamic oxaloacetic transaminase	√	√	√
Serum glutamic pyruvic transaminase	√	√	√
Uric acid	√	√	√
High density lipoprotein cholesterol	√	√	√
High sensitivity C-reactive protein	√	√	√
Triglyceride	√	√	√
Estimated glomerular filtration rate	√	√	√
Sleep time		√	√
Drinking duration		√	√
Sport hours		√	√
White blood cell count			√
Hemoglobin			√
Alkaline phosphatase			√
γ-glutamyltransferase			√
High sensitivity C-reactive protein			√

training dataset for model building and a 20% testing dataset for model testing. In the training process, the hyperparameters of each Mach-L method must be tuned to construct an effective model. In this study, a 10-fold cross-validation technique was used for hyperparameter tuning.

The training dataset was further randomly divided into a training dataset to rebuild the model with a different set of hyperparameters and a validation dataset for model validation. All possible hyperparameter combinations were investigated using a grid search. The best performing model in terms of accuracy, sensitivity, specificity, area under the receiver operating characteristic (AUC) curve, F-1 score, and balanced accuracy (Table 3) for the validation dataset was taken as the more accurate one. In the present study, AUC obtained from each Mach-L method was averaged and used as the comparator for the accuracy of the three models. We also ranked the corresponding variable importance. Using different Mach-L methods produces different risk rankings because of the different modeling characteristics. Therefore, we integrated the risk importance ranking to enhance the stability and integrity. After averaging, rank 1 is the most critical factor for L-eGFR.

All methods were performed using R software version 4.0.5 and R-Studio version 1.1.453 with the required packages installed (http://www.R-project.org; https://www.rstudio.com/products/rstudio/).

RESULTS

Table 1 summarizes the demographic data of the 1236 participants (mean ± SD). The mean age was significantly higher in subjects with low eGFR (72.1 ± 5.9 *vs* 69.5 ± 4.6 years old). Alcohol consumption was expressed as the multiple of the drinking frequency, alcohol percentage, and drinking duration. Exercise habits were expressed as the multiple of the intensity of the exercise, frequency, and the whole duration. Lifestyle results were consistent across both groups. Interestingly, the high eGFR group was found to have significantly higher sleep hours (6.1 ± 1.15 *vs* 5.89 ± 1.10 h). SBP was significantly higher in the low eGFR group (131.2 ± 18.9 *vs* 127.4 ± 18.1 mmHg), but not DBP. For the laboratory data, only WBC count and hsCRP were higher in the low eGFR group (5.94 ± 1.75 *vs* 5.58 ± 1.40 × 103/μL for WBC count and 2.52 ± 5.08 *vs* 2.11 ± 4.35 mg/L for hsCRP).

Table 3 summarizes the results for accuracy, sensitivity, specificity, AUC, F-1 score and BA derived from each model. Each value was found to increase from Model 1 to Model 3. Since the AUC represents the most important accuracy indicator for a given model, it is listed as the most important one in Table 4, which shows the average AUC values. The mean increased from 0.6144 for Model 1 to 0.776 for Model 3, indicating that, as risk factors were added, the mean AUC

Table 3 Results of five different machine learning methods in three different models

Model	Methods	Accuracy	Sensitivity	Specificity	AUC	F1-score	BA
Model 1	MARS	0.689	0.717	0.519	0.633	0.799	0.618
	XGboost	0.715	0.753	0.482	0.602	0.820	0.617
	SGB	0.596	0.590	0.630	0.599	0.715	0.610
	LightGBM	0.731	0.771	0.482	0.615	0.831	0.626
	Catboost	0.549	0.518	0.741	0.623	0.664	0.629
Model 2	MARS	0.689	0.683	0.731	0.693	0.792	0.707
	XGboost	0.632	0.617	0.731	0.663	0.744	0.674
	SGB	0.762	0.802	0.500	0.666	0.854	0.651
	LightGBM	0.767	0.808	0.500	0.646	0.857	0.654
	Catboost	0.637	0.635	0.654	0.663	0.752	0.644
Model 3	MARS	0.767	0.801	0.622	0.760	0.848	0.711
	XGboost	0.762	0.763	0.757	0.786	0.838	0.760
	SGB	0.777	0.789	0.730	0.814	0.851	0.759
	LightGBM	0.741	0.750	0.703	0.776	0.824	0.726
	Catboost	0.819	0.897	0.487	0.744	0.889	0.692

AUC: Area under receiver operating characteristic curve; BA: Balanced accuracy; MARS: Multivariate adaptive regression splines; XGBoost: eXtreme Gradient Boosting; SGB: Stochastic gradient boosting; LightGBM: Light Gradient Boosting Machine; CATboost: Categorical Features + Gradient Boosting. Model 1: Demographic and biochemistry data; Model 2: Model 1 + lifestyle factors; Model 3: Model 2 + inflammation factors.

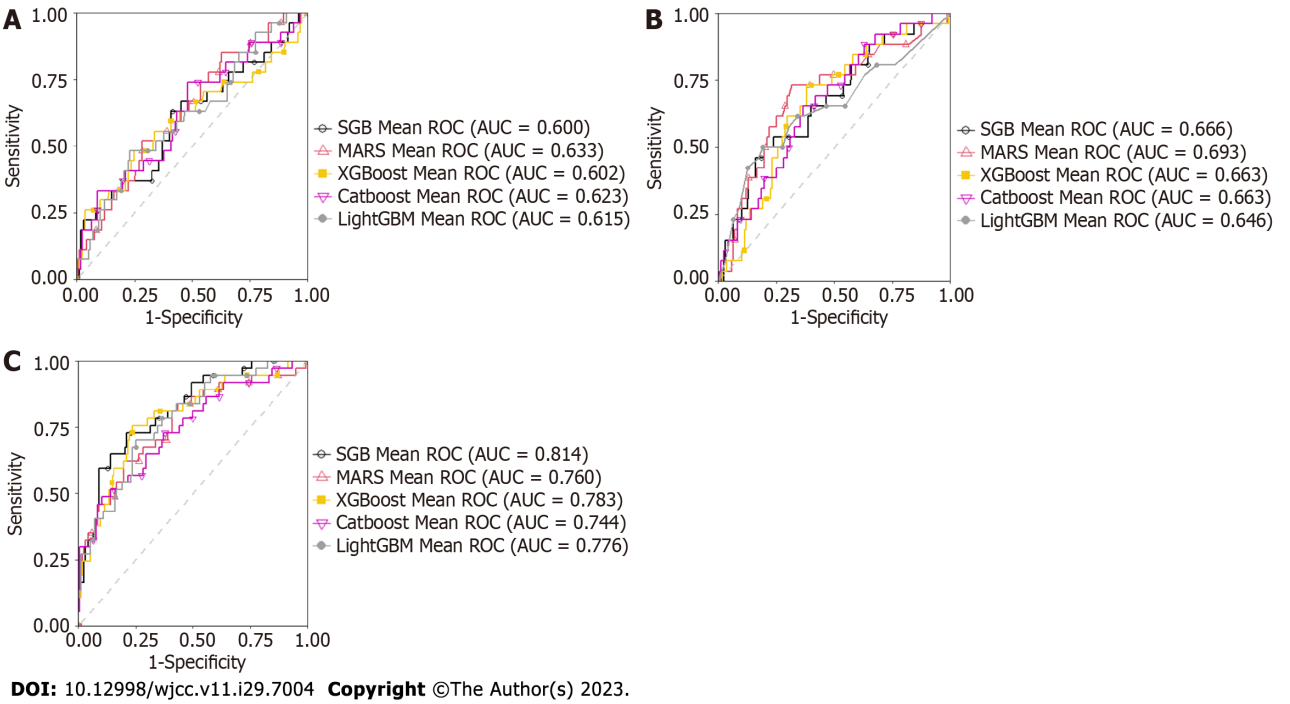

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Figure 2 Area under receiver operating characteristic curve derived from five different machine learning methods in different models. A: Model 1; B: Model 2; C: Model 3. MARS: Multivariate adaptive regression splines; XGBoost: eXtreme Gradient Boosting; SGB: Stochastic gradient boosting; LightGBM: Light Gradient Boosting Machine; CATboost: Categorical Features + Gradient Boosting. Model 1: Demographic and biochemistry data; Model 2: Model 1 + lifestyle factors; Model 3: Model 2 + inflammation factors.

Table 4 Area under receiver operating characteristic curve derived from five different machine learning methods of the three different models

Model/AUC	Model 1	Model 2	Model 3
MARS	0.633	0.693	0.760
XGboost	0.602	0.663	0.786
SGB	0.599	0.666	0.814
LightGBM	0.615	0.646	0.776
Catboost	0.623	0.663	0.744
Mean	0.6144	0.6662	0.776

AUC: Area under receiver operating characteristic curve, MARS: Multivariate adaptive regression splines; XGBoost: eXtreme Gradient Boosting; SGB: Stochastic gradient boosting; LightGBM: Light Gradient Boosting Machine; CATboost: Categorical Features + Gradient Boosting. Model 1: Demographic and biochemistry data; Model 2: Model 1 + lifestyle factors; Model 3: Model 2 + inflammation factors.

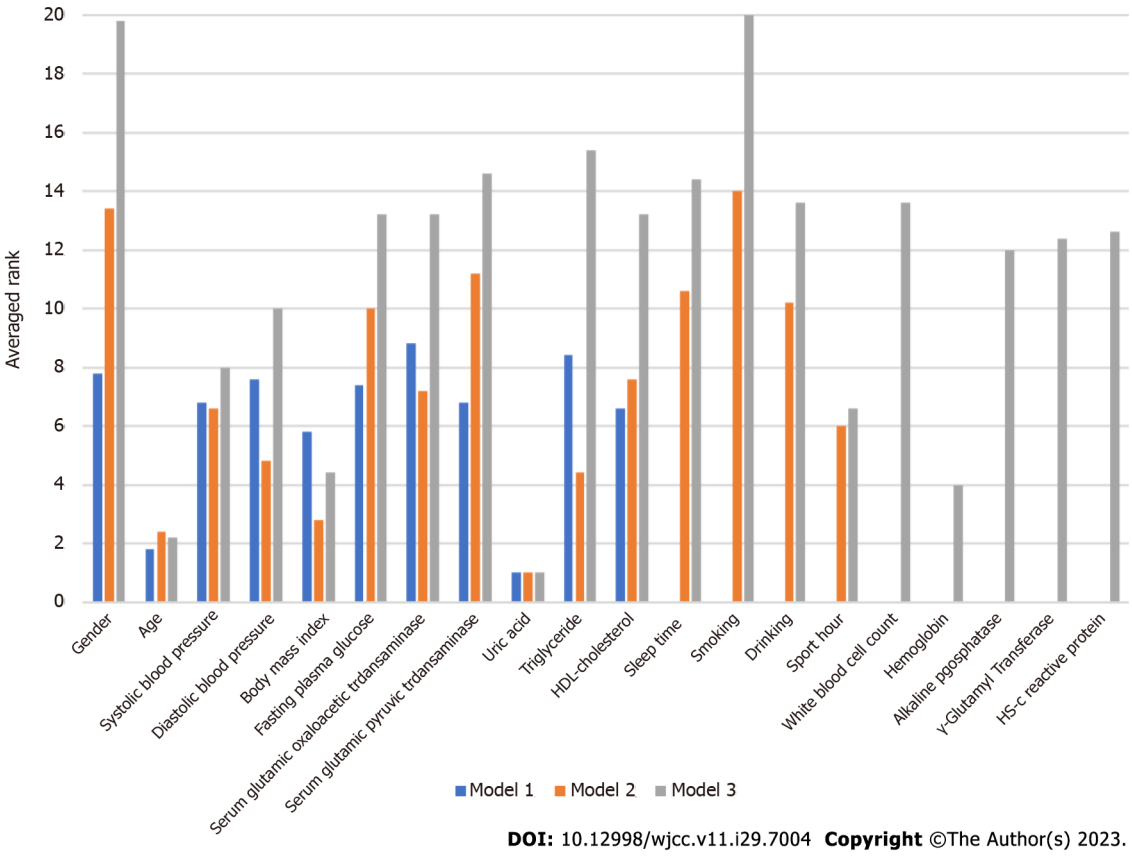

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Figure 3 Averaged ranks of importance for each risk factor in three different models. Model 1: Demographic and biochemistry data; Model 2: Model 1 + lifestyle factors; Model 3: Model 2 + inflammation factors.

increased in each for different Mach-L methods. Not surprisingly, Model 3 had the best AUC. Finally, the importance rankings for the three models are, respectively, shown in Tables 5-7. In Model 1, the most important risk factor was UA, followed by age, BMI, HDL-C, SBP, and GPT. When lifestyle factors were added, the ranking changed to UA, age, BMI, TG, DBP, and sport hours. Finally, integrating inflammation factors, the most important risk factor was UA, followed by age, Hb, BMI, sport hours, and SBP. The AUC of each model is, respectively, shown in Figures 2 to 3, while Table 3 presents the numerical values of the changes to each model. As shown in Figure 2, Model 3 had the highest AUC value. Figure 3 first compares the relative importance of each variable in the models, with color coded in blue, orange, and grey, respectively, for Models 1-3. The figure shows that gender was of greater importance in Model 1 than in Model 3, where a lower value indicated greater importance. Next, comparing columns of the same color allows for a clear observation of the relative importance of the various factors in each model. For example, UA was the most important variable in Model 3, followed by age and BMI.

Table 5 Rank importance of risk factors in model 1, from the most important to the least

Variable	MARS	XGboost	SGB	LightGBM	Catboost	AVG
Uric acid	1	1	1	1	1	1
Age	1	2	2	2	2	1.8
Body mass index	11	3	8	4	3	5.8
HDL-cholesterol	11	4	4	9	5	6.6
Systolic blood pressure	11	6	5	5	7	6.8
Serum glutamic pyruvic transaminase	4	9	7	10	4	6.8
Fasting plasma glucose	5	10	10	3	9	7.4
Diastolic blood pressure	11	5	6	8	8	7.6
Gender	3	8	11	7	10	7.8
Triglyceride	11	11	3	6	11	8.4
Serum glutamic oxaloacetic transaminase	11	7	9	11	6	8.8

AVG: Average of the rank of importance; MARS: Multivariate adaptive regression splines; XGBoost: eXtreme Gradient Boosting; HDL: High-density lipoprotein; SGB: Stochastic gradient boosting; LightGBM: Light Gradient Boosting Machine; CATboost: Categorical Features + Gradient Boosting. Model 1: Demographic and biochemistry data; Model 2: Model 1 + lifestyle factors; Model 3: Model 2 + inflammation factors.

Table 6 Rank importance of risk factors in model 2, from the most important to the least

Variable	MARS	XGboost	SGB	LightGBM	Catboos	AVG
Uric acid	1	1	1	1	1	1
Age	2	2	2	4	2	2.4
Body mass index	2	5	2	2	3	2.8
Triglyceride	7	4	5	1	5	4.4
Diastolic blood pressure	3	7	3	9	2	4.8
Sport hours	4	6	6	10	4	6
Systolic blood pressure	14	1	4	3	11	6.6
Serum glutamic oxaloacetic transaminase	6	8	8	5	9	7.2
HDL-cholesterol	14	3	7	8	6	7.6
Fasting plasma glucose	14	10	10	6	10	10
Drinking	5	12	12	14	8	10.2
Sleep time	14	9	9	14	7	10.6
Serum glutamic pyruvic transaminase	14	11	11	7	13	11.2
Gender	14	13	14	14	12	13.4
Smoking	14	14	14	14	14	14

AVG: Average of the rank of importance; MARS: Multivariate adaptive regression splines; XGBoost: eXtreme Gradient Boosting; HDL: High-density lipoprotein; SGB: Stochastic gradient boosting; LightGBM: Light Gradient Boosting Machine; CATboost: Categorical Features + Gradient Boosting. Model 2: Model 1 + lifestyle factors.

Table 7 Rank importance of risk factors in model 3, from the most important to the least

Variable	MARS	XGboost	SGB	LightGBM	Catboost	AVG
Uric acid	1	1	1	1	1	1
Age	1	2	2	2	4	2.2
Hemoglobin	4	4	6	3	3	4
Body mass index	7	3	3	7	2	4.4
Sport hours	3	8	4	5	13	6.6
Systolic blood pressure	5	6	20	4	5	8
Diastolic blood pressure	20	5	5	6	14	10
Alkaline phosphatase	20	7	11	12	10	12
γ-glutamyl transferase	20	13	8	9	12	12.4
Hs-C reactive protein	9	12	10	15	17	12.6
Fasting plasma glucose	20	9	20	10	7	13.2
Serum glutamic oxaloacetic transaminase	20	18	7	13	8	13.2
HDL-cholesterol	20	10	13	8	15	13.2
Drinking	20	14	12	16	6	13.6
White blood cell count	8	11	20	11	18	13.6
Sleep time	6	17	20	18	11	14.4
Serum glutamic pyruvic transaminase	20	16	14	14	9	14.6
Triglyceride	20	15	9	17	16	15.4
Gender	20	20	20	20	19	19.8
Smoking	20	20	20	20	20	20

AVG: Average of the rank of importance; MARS: Multivariate adaptive regression splines; XGBoost: eXtreme Gradient Boosting; HDL: High-density lipoprotein; SGB: Stochastic gradient boosting; LightGBM: Light Gradient Boosting Machine; CATboost: Categorical Features + Gradient Boosting. Model 3: Model 2 + inflammation factors.

DISCUSSION

The present study evaluated the effects of lifestyle and inflammation factors on eGFR changes in an elderly Chinese cohort. Our data show that, even though lifestyle and inflammation factors did have some predictive impacts for L-eGFR, the main determinants are still traditional factors that had been discussed extensively in previous work, including UA, age, Hb, BMI, sport hours, and SBP.

For all three models, the various Mach-L methods all selected UA as the key factor for determining L-eGFR, a finding supported by previous work. In a four-year longitudinal study, Liu *et al*[29] showed that compared to the highest quartile of UA, subjects with lower UA (quartile 1) are at lower risk for having reduced renal function [hazard ratio = 0.64, 95% confidence interval (0.49–0.85)]. Zhang *et al*[30] reviewed ten randomized controlled trials, finding that, following febuxostate treatment, eGFR was consistently and significantly lower than that in the non-treatment group. From such evidence, it could be concluded that through different mechanisms, hyperuricemia can lead to vascular obstruction and renal hypoperfusion[31].

Age is well-known to be associated with decreased adaptive capacity which leads to morbidity and mortality[32]. In the present study, it is not surprising that age is the 2nd most important factor related to L-eGFR, and this result is consistent with most previous findings. The underlying pathophysiology for this phenomenon has been studied extensively, and loss of renal mass, hyalinization of the afferent capillary, sclerotic glomerular and tubulointerstitial fibrosis are the main causes, leading to reduced blood flow and ultrafiltration of the glomerular capillary along with reduced afferent arteriolar resistance, thus resulting in reduced eGFR[33].

In the present study, Hb level was the third most important risk factor for abnormal eGFR. It is well-known that CKD can cause anemia, and this correlation is strongly supported by the cornerstone study published in 2002 by Coresh *et al* [34] that found that, once the eGFR falls below 60 mL/min per 1.73 m^2, lower renal function is associated with a higher incidence of anemia[35]. On the other hand, anemia might also contribute to the deterioration of renal function. Subjects with anemia have lower exercise tolerance[36], poor left ventricular growth[37], and even higher risk of heart failure[38]. This suggests that even before the CKD, anemia might begin to damage renal function.

It is well-known that BMI is also related to eGFR. Few previous studies have examined this link. Chang *et al*[39] conducted a longitudinal study from 2008 to 2013 with 7357 CKD subjects, finding that subjects with a BMI < 18.5 kg/m^2 had lower eGFR declines compared to other BMI groups. Similar findings were also found in Japanese and Malaysians [40-42]. It is not surprising that higher body weight leads to poor renal function since obesity is related to various sequelae such as hyperglycemia, hypertension, dyslipidemia, and metabolic syndrome[43,44]. It must be stressed here that this is not a causal association, and further longitudinal studies are needed to elucidate our result.

Surprisingly, when sport hours was included in the model, it emerged as the 5th most important factor. An increasing number of publications have suggested that exercise is beneficial for many aspects of CKD. Regular exercise is recommended by the Renal Association Clinical Practice Guidelines to improve renal function[45]. The impact of exercise on renal function could be explained by reduced inflammation, nitric oxide, angiotensin II accumulation, and improved anabolic response in skeletal muscles[46].

High blood pressure is a well-known independent risk factor for decreased renal function[47-49]. The present study is the first to use Mach-L to identify SBP as the 6th most important factor. Our finding was not alone, and in a 7-year longitudinal study, Wang *et al*[50] followed 2383 rural Chinese between the ages of 40 and 60 years old, finding a dose-dependent relationship between blood pressure and eGFR. The highest rate of eGFR decline was observed among subjects with SBP over 140 mmHg (odds ratio 2.9, 95% confidence interval 1.6–5.1) or DBP over 90 mmHg (odds ratio 2.7, 95% confidence interval 1.6–4.6)[50]. Interestingly, both SBP and DBP were important for identifying H-eGFR and L-eGFR. This indicates that SBP and DBP have different and independent effects.

CONCLUSION

In conclusion, we have applied Mach-L techniques to identify and rank risk factors from demographic, biochemistry, and lifestyle factors along with inflammation markers for L-eGFR among elderly Chinese, finding that the most important factors are UA, age, Hb, BMI, sport hours, and SBP.

ARTICLE HIGHLIGHTS

Research background

The incidence of chronic kidney disease (CKD) has significantly increased in recent years, leading to substantial impacts on patient mortality rates.

Research motivation

Previous studies have identified various risk factors for CKD, but they mostly relied on traditional statistical methods, such as logistic regression, and focused only on a limited number of risk factors.

Research objectives

To evaluate the impact of lifestyle and chronic inflammation in identifying subjects with abnormal estimated glomerular rates among elderly Chinese elderly subjects.

Research methods

The main focus of this study is to utilize five machine learning methods (Mach-L) for identifying factors.

Research results

Our results showed that uric acid is the most important risk factor (inflammatory marker), followed by age, hemoglobin, body mass index, sport hours, and systolic blood pressure.

Research conclusions

The study highlights that among demographic, biochemistry, lifestyle risk factors, and inflammation markers, UA is the most crucial risk factor for identifying low estimated glomerular filtration rate in elderly Chinese individuals, followed by age, hemoglobin, body mass index, sport hours, and systolic blood pressure.

Research perspectives

Further longitudinal studies are warranted to validate and clarify the causal relationships between these factors and estimated glomerular filtration rate changes.

FOOTNOTES

Author contributions: Chen CH participated in the design and oversight of the study, and was involved in data collection; Wang CK participated in the design of the study and was involved in data collection; Wang CY was involved in data collection and assisted with data analysis; Chang CF drafted the manuscript and assisted with data analysis; Chu TW drafted the manuscript and assisted with data

analysis; all authors read and approved the final manuscript.

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