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# A clinical nomogram for predicting renal calculus of university teachers

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**Abstract. – OBJECTIVE: To establish a prediction model of renal calculus for university teachers to help them prevent renal calculus scientifically. This study involves a specific group of university teachers. We collected the physical examination index of 1043 university teachers in the Hubei University of Chinese Medicine in 2018 to build the model. We also used the physical examination data of 968 teachers in 2019 to verify the model.**

**MATERIALS AND METHODS: We used Lasso regression to screen the factors and logistic regression analysis to establish the model.**

**RESULTS: The models of this study included sex, age, DBP, TC, HDL. C, CEA, UA, ALT, GGT, HB, pH, RBC, RDW, and CLYMPH. Among these, sex, TC, ALT, HB, and LYMPH present high risks in the model. The result is of great significance related to the research of university teachers suffering from renal calculus. The C-index is 0.715, and the AUC is 0.7064.**

**CONCLUSIONS: Based on the results of this study, we suggest that physical examination indicators can predict the risk of renal calculus and the individual probability of prevalence in specific groups. According to the risk of each physical examination index, it is possible to effectively prevent the occurrence of renal calculus in certain high-risk groups through lifestyle changes.**

*Key Words:*

Renal calculus, University teacher, Risk, Nomogram.

## Introduction

Renal calculus or nephrolithiasis is a common disease in urology[1]. It is formed by specific components of urine in the kidney. These components lead to a series of diseases related to urinary system symptoms[2,3]. It is well known that, globally, renal calculus is a highly prevalent disease[4], it has been estimated that its prevalence rate is as high as 14.8%[5], and the incidence of this disease keeps increasing each year[6-8].

According to the clinical predictions of renal calculi, the pathogenesis of renal calculi is complex. It includes genetic, metabolic, and environmental factors[9-11]. The risk factors are related to age, male sex, race[12], dietary habits[11,13], obesity[14,15], hypertension, gout, chronic kidney disease, etc[15]. Understanding the pathogenesis and risk factors for the prevention and treatment of renal calculus is urgently needed.

Previous studies have shown that the occurrence of renal calculus has a link with occupations[16]. Due to the nature of certain occupations, specific groups of people do not drink enough liquid to dilute urine[16]. University teachers are a representative group of people[17]. Due to continuously working for long hours and moving around in classes, university lecturers have reduced the necessary amount of water to be healthy. As a result, it is likely to lead to renal calculus formation in the long run. However, such occupational renal calculi have received little attention[17], and as of yet, a specific population renal calculi model has not been established.

Our hospital undertakes medical examinations of school staff, collects reliable data, and uses data mining techniques to build clinical predictive models that allow for early detection of potential health risks and further intervention and moderation. Between the year 2018 and 2019, the prevalence of nephrolithiasis was 21.5% and 19.3%, respectively, among the physically examined teacher population, a level higher than the general population, the reasons of which are worth investigating. Based on the physical examination data, we provide early warning of teachers who may develop nephrolithiasis and screen for factors related to the development of nephrolithiasis for further research.

It is essential to pay close attention to the physical condition of these teachers to reduce the prevalence of renal calculus among university teachers. Therefore, in this study, the renal calcu-



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lus model of university teachers was established by collecting the physical examination indexes of university teachers. By gaining an insight into the relationship between these indexes and the occurrence of renal calculus, it will be helpful to scientifically guide the high-risk groups to prevent the occurrence of renal calculus. It will also be helpful to change their bad living habits effectively. The success of this study is undoubted of great significance for these high-risk patients.

## Materials and Methods

### Study Subjects and Inclusion of Risk Indicators

This study is a retrospective study. Data from the 2018 and 2019 physical examinations of Hubei University of Chinese Medicine staff in Huangjiahu Hospital were selected. The physical examination data were separated into two parts. The data cohorts from 2018 about 1043 medical examinations related to the teaching staff were used as data sets for modelling. Moreover, in the data cohorts from 2019, about 968 teaching staff were used as validation data sets. This study extracted the basic information of teaching staff, laboratory examination, and imaging examination results. The most basic information includes sex and age at the time of medical examination. Laboratory indicators include systolic blood pressure, diastolic blood pressure, pH, urine specific weight, Helicobacter pylori test, thyrotropin, total cholesterol, triglyceride, high-density lipoprotein, low-density lipoprotein, blood glucose, carcinoembryonic antigen, urea, creatinine, uric acid, alanine aminotransferase, glutamic oxaloacetic transaminase, r glutamic acid transferase, total protein, globulin, total bilirubin, white blood cells, red blood cells, hemoglobin, mean hemoglobin, mean hemoglobin, mean hemoglobin concentration, platelet, erythrocyte distribution width, mean blood cell number, neutrophil, lymphocyte count, lymphocyte count, lymphocyte count, lymphocyte count, eosinophil. Basophil, neutrophil ratio, lymphocyte ratio, monocyte ratio, eosinophil ratio, and basophil ratio. Using the imaging examination results to determine whether the patient has renal calculus is the endpoint of this study.

### Statistical Analysis

The extracted basic information and laboratory results were considered as independent variables. The imaging results were considered as dependent variables, regardless of whether renal calculus existed or not. The dependent variables in this study were two-classified variables. They were groups with renal calculus and without renal calculus. In addition, preprocessing was performed on all included data, missing data were removed, and value was assigned to the data. The data is divided into modeling data sets and verification data sets. Statistical analysis was carried out using r software, where $p<0.05$ corresponds to statistical significance. The modeling dataset selected variables by lasso regression, and the estimated regression parameters were evaluated by penalty coefficient lambda (λ) (Figure 1). If the penalty coefficient was significant, it implied no effect on the estimated regression parameters. However, some coefficients may shrink to zero as λ decreases. Lasso logistic regression analysis was used to construct the prediction model and to draw the line diagram. The model that incorporated the above selected independent variables was developed and presented as the nomogram; it was then evaluated by the identification ability, calibration, besides clinical efficacy (Figure 2).

The identification of the model can be evaluated by the c index, the area under the roc curve, and the c index is between 0.5-1. A more considerable value is helpful for improved prediction performance of the model. The calibration diagram was used to evaluate the calibration (Figure 3), and it was used to reflect the relationship between the observed and predicted values. Moreover, the probability of consistency between the predicted value of the c index and the observed value is equivalent to the area under the curve (ROC). The optimal cutoff value was selected by roc analysis (Figure 4) and determined by maximizing the Youden index. Decision curve analysis was carried out to determine the clinical effectiveness of the model (Figure 5). Finally, the c index was used to verify the model and evaluate the accuracy.

## Results

Following careful screening according to the same inclusion and exclusion criteria, in 2018, 1043 patients were included in the development group. In 2019, 968 patients were selected in the validation group. The C-index was 0.715 (95% confidence interval[CI], 0.67972–0.75028) and

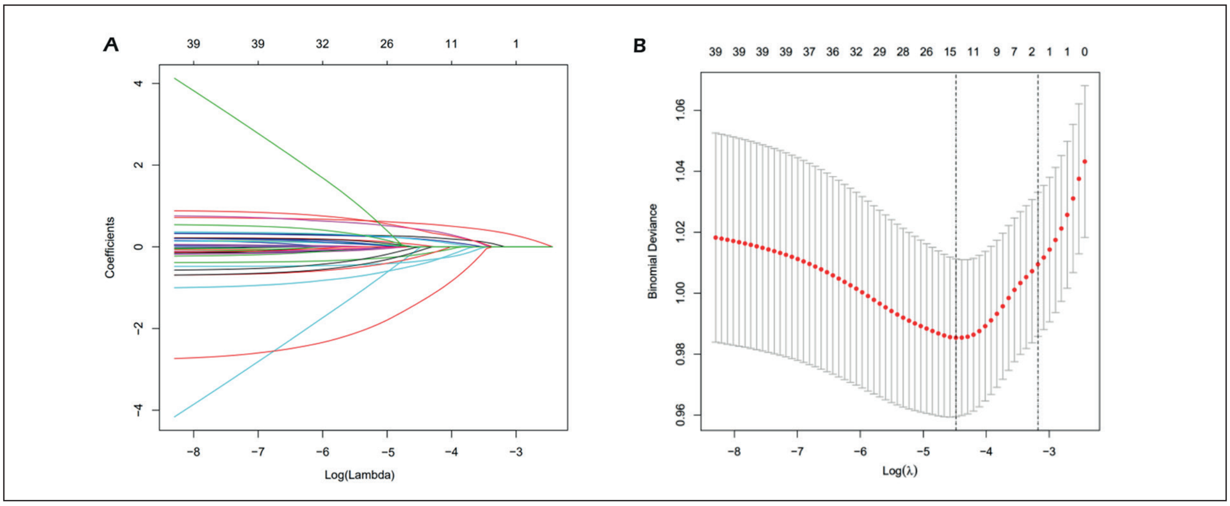


**Figure 1.** Demographic and clinical feature selection using the LASSO binary logistic regression model. Considering all the relevant variables, the minimum λ value was 0.0130943. **A,** LASSO coefficient profiles of the 41 features. A coefficient profile plot was produced according to the log(lambda) sequence. **B,** The binomial deviance curve was plotted against log(lambda/λ). Dotted vertical lines were drawn at the optimal values, where optimal lambda resulted in 14 features with nonzero coefficients.

0.673 (95% confidence interval [CI], 0.63086–0.71514) for the development and validation cohorts, respectively. It implies discrimination in the model. Based on the development cohort, 41 variables were reduced to fourteen potential predictors. Fourteen variables (age, sex, DBP,

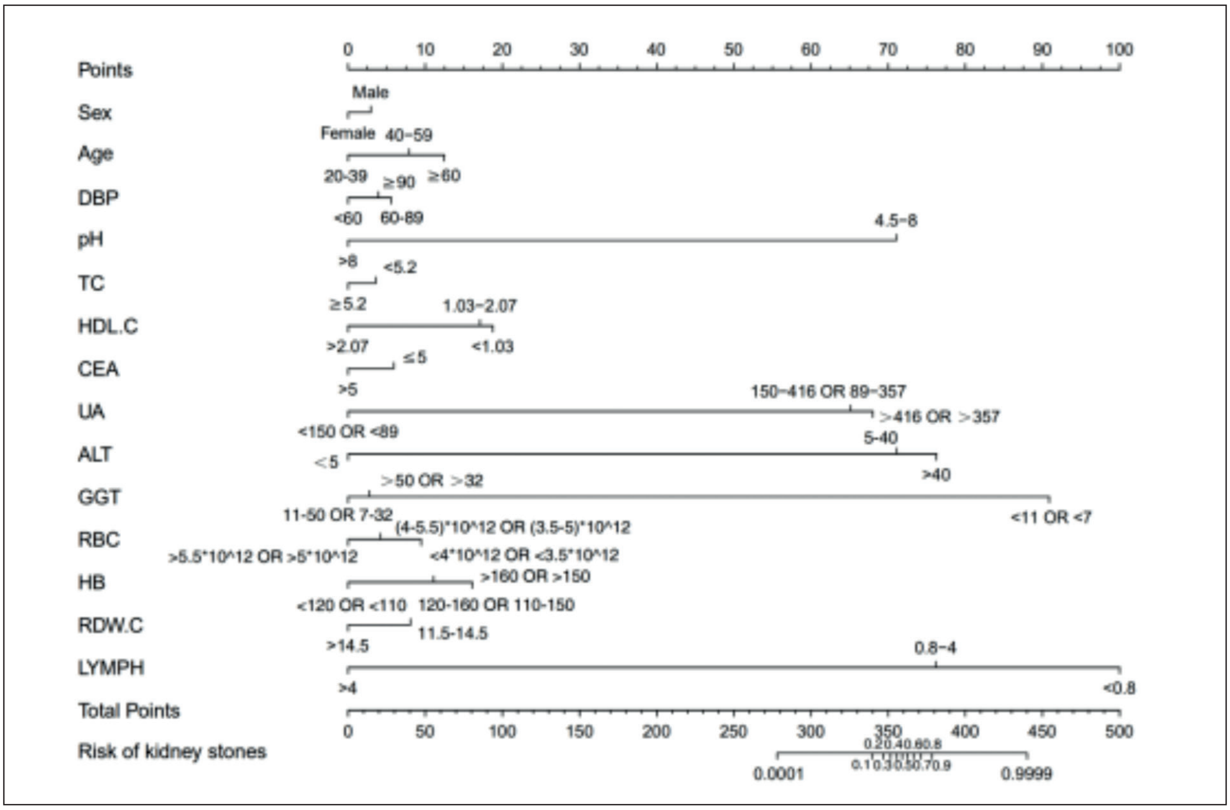


**Figure 2.** Based on the results, a prediction model, followed by a nomogram predicting the risk of renal calculus in university teachers was established.

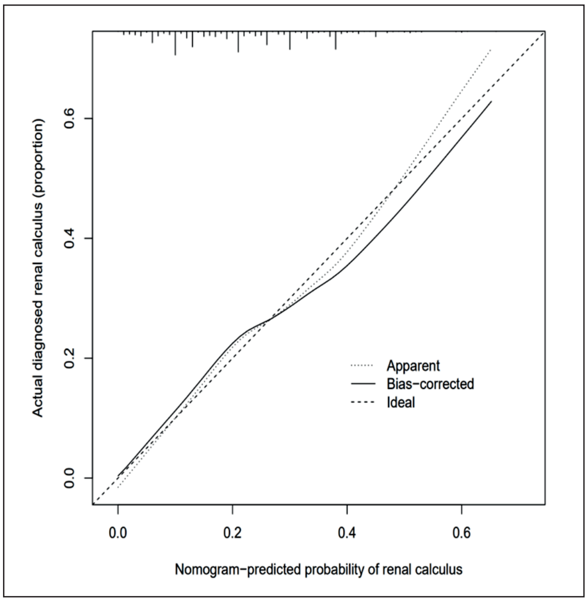


**Figure 3.** The calibration curve of the nomogram, which was used for the prediction of nephrolith in university teachers exhibited good agreement in this cohort.

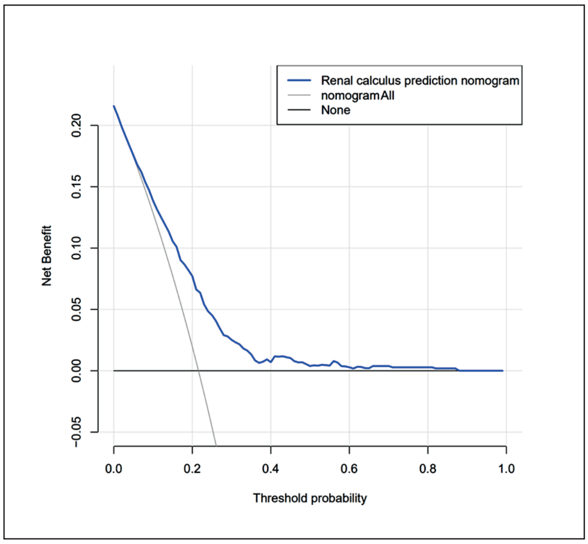


**Figure 5.** The decision curve analysis showed that, if the threshold probability of a patient ranged from 1% to 87%, using this nomogram to predict nephrolith in university teachers, was far more beneficial than the scheme. Within this range, the net benefit was comparable.

TC, HDL. C, CEA, UA, ALT, GGT, HB, pH, RBC, RDW.C, and lymph) in the final model with non-zero coefficients were used.

Table I shows the distribution of baseline characteristics of the development cohort stratified by nephrolithiasis. There are no differences between these queues. However, significant differences were found in the baseline characteristics between patients with nephrolithiasis and university teachers. In the present study, LASSO binary logistic regression was used for constructing the prediction model.

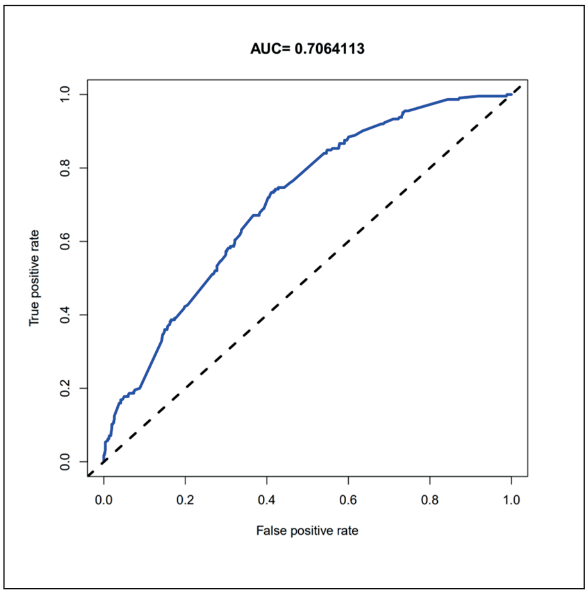


**Figure 4.** The AUROC value of the development group was 0.7064.

According to this Prediction model (Figure 2), we can roughly predict the risk of kidney stones in university teachers. For example, the following characteristics were assigned to a participant, a male teacher (3 points), aged 45 years old (8 points), DBP was 86 mmHg (6 points), pH was 7.2 (71 points) TC was 4.9 mmol/L (4 points), HDL.C was 2.01 mmol/L (17 points), CEA was 4.5 µg/L (6 points), UA was 518 umol/L (68 points), ALT was 38 U/L (71 points), GGT was 48 U/L (0 points), RBC was 4.2* $10^{12}$ (4 points), HB was 150 g/L (11 points), RDW.C was 13.5 (8 points), and LYMPH was 3.1* $10^{9}$ (76 points). Accordingly, his collective number of points was 353 points, for him, the risk of nephrolith was approximately 30%. The results of this calculation are helpful for doctors to make clinical decisions.

## Discussion

The formation of kidney stones or renal calculus is a common occurrence. Intense pain is the primary manifestation of the disease. Patients suffer severe pain daily. Establishing the cause of this disease has been the focus of current research.

**Table I.** Differences between baseline and clinical characteristics of training and validation groups.

| Variable | Training cohort (n = 1043) n (%) | Validation cohort (n = 968) n (%) |
|---|---|---|
| Sex | | |
| Female | 576 (55.2) | 559 (57.7) |
| Male | 467 (44.8) | 409 (42.3) |
| Age (years) | | |
| 20-39 | 321 (30.7) | 346 (35.7) |
| 40-59 | 336 (32.2) | 314 (32.4) |
| > = 60 | 386 (37.1) | 308 (31.9) |
| DBP (mmHg) | | |
| < 60 | 154 (14.8) | 207 (21.4) |
| 60-89 | 842 (80.7) | 714 (73.8) |
| > = 90 | 47 (4.5) | 47 (4.8) |
| TC (mmol/L) | | |
| < 5.2 | 845 (81.0) | 732 (75.6) |
| > = 5.2 | 198 (19.0) | 236 (24.4) |
| HDL.C (mmol/L) | | |
| < 1.03 | 38 (3.6) | 78 (8.0) |
| 1.03-2.07 | 978 (93.8) | 881 (91.0) |
| > 2.07 | 27 (2.6) | 9 (1.0) |
| CEA (ng/ml) | | |
| < = 5 | 986 (94.5) | 930 (96.1) |
| > 5 | 57 (5.5) | 38 (3.9) |
| UA (μmol/L) | | |
| < 149 or < 89 | 1 (0.1) | 1 (0.1) |
| 149-416 or 89-357 | 783 (75.1) | 660 (68.2) |
| > 416 or > 357 | 259 (24.8) | 307 (31.7) |
| ALT (U/L) | | |
| < 5 | 2 (0.2) | 2 (0.2) |
| 5-40 | 978 (93.8) | 905 (93.5) |
| > 40 | 63 (6.0) | 61 (6.3) |
| GGT (U/L) | | |
| < 11 or < 7 | 1 (0.1) | 0 |
| 11-50 or 7-32 | 945 (90.6) | 870 (89.9) |
| > 50 or > 32 | 97 (9.3) | 98 (10.1) |
| HB (g/L) | | |
| < 120 or < 110 | 27 (2.6) | 36 (3.7) |
| 120-160 or 110-150 | 971 (93.1) | 852 (88.0) |
| > 160 or > 150 | 45 (4.3) | 80 (8.3) |
| RDW.C | | |
| 11.5-14.5 | 991 (95.0) | 898 (92.8) |
| 14.5 | 52 (5.0) | 0 (7.2) |
| LYMPH | | |
| < 0.8*109 | 4 (0.4) | 2 (0.2) |
| 0.8-4.0*109 | 1033 (99.0) | 961 (99.3) |
| > 4*109 | 6 (0.6) | 5 (0.5) |
| PH | | |
| 4.5-8 | 1038 (99.5) | 963 (99.5) |
| > 8 | 5 (0.5) | 5 (0.5) |
| RBC | | |
| < 4* $10^{12}$ OR < 3.5* $10^{12}$ | 15 (1.4) | 6 (0.6) |
| (4-5.5)* $10^{12}$ OR (3.5-5)* $10^{12}$ | 988 (94.7) | 870 (89.9) |
| > 5.5* $10^{12}$ OR > 5*$10^{12}$ | 40 (3.8) | 92 (9.5) |

In terms of diet, recent research has found that low animal protein intake and a high plant protein intake were associated with the risk of renal calculus[18]. In a study of data modeling, total cholesterol and fasting blood glucose have been proposed to predict the incidence of renal calculus[19]. On the other hand, using a nomogram has also been widely applied to identify multiple indicators of disease, especially with regards to cancer, which may reveal the associations within the disease[20]. In this study, the LASSO logistic regression model was adopted to filter the factors included in the following nomogram. According to the result of LASSO regression, sex, age, DBP, TC, HDL.C, CEA, UA, ALT, GGT, HB, pH, RBC, RDW.C, and LYMPH were selected as potential targets. According to the result of LASSO regression, sex, age, DBP, TC, HDL.C, CEA, UA, ALT, GGT, HB, pH, RBC, RDW.C, and LYMPH were selected as potential targets. Among these, sex, TC, ALT, HB, and LYMPH are also the correlative indicators in regression Analysis verification, and they are at high risks in the model. A majority of the participants included in this study were women. It should also be noted that males got higher points in the nomogram. Wood et al[21] highlighted that, compared to women, men excreted more calcium and oxalate, had lower urine pH and had higher supersaturation of uric acid. These factors are directly contributing to the occurrence of renal calculus. On the other hand, it was suspected that such a result might be connected to the dietary preferences of different genders. Through Logistic regression, older people are more likely to develop renal calculus, particularly those over-60s, who scored higher in the nomogram. Old age was associated with decreased calcium excretion, calcium oxalate supersaturation, calcium phosphate, and urinary pH[21]. Compared to individuals with normal blood pressure, renal calculus formation disproportionately affected patients with hypertension[22]. This study found evidence that high blood pressure increases the risk of renal calculus. Irrespective of SBP or DBP, it is well known that hypertension will also harm kidney function[23]. Research has shown that carotid IMT and CS levels in the CaOx ≥50% and CaP groups were all significantly higher than in the controls, which suggested a strong relationship between dyslipidemia, carotid atherosclerosis, and calcium renal calculus disease. A higher serum total cholesterol (TC) and low-density lipoprotein(LDL) were associated with lower urinary citrate and higher CS[24]. Ding Q pointed out that high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) levels were significantly lower in nephrolithiasis patients compared to the control group[25]. This is consistent with the demonstrations of the nomogram proposed in this study. The abnormalities of TC and HDL-C are collectively referred to as dyslipidemia. Previous studies have linked renal calculus with dyslipidemia due to a range of unhealthy life habits. As a standard clinical test indicator, CEA represents the tumor status and is associated with some non-tumor diseases. Prolonged inflammation or irritation due to renal calculi can induce glandular metaplasia of the urothelium or even malignant neoplasm[26]. Uric acid affects the body's pH, and it is closely related to the formation of renal calculus. In this statistic, the proportion of high uric acid is larger[27]. In the nomogram, interesting indicators of liver function were revealed, such as ALT and GGT. Huashi Pill inhibited the formation of stone crystals and reduced the insoluble calcium deposition. Furthermore, it also significantly improved liver functions by decreasing ALT and TBIL levels[28]. However, none of the studies have shown a direct link between ALT and renal calculus. Studies about these enzymes will thereby show the pathological status of the kidney. With regards to GGT, increased GGT activity leads to renal injury, which has been evidenced[29]. The fluctuation of RBC value and Hb value may be related to the bleeding of renal calculus. During the initial stages of the bleeding state, RBC decreased, while HB may be temporarily compensated, and RDW.C may also be increased. In clinical practice, urinary calculi are often accompanied by bacterial inflammation, closely related to immune cells. However, the relationship between lymphocytes and renal calculus has not been fully established.

The present study has some limitations. Firstly, the c-index of the training set is 0.715, and the c-index of the external validation set is 0.673. The predictive performance is insufficient. In addition, the score interval distribution of the rating table in the nomogram is relatively crowded. Hence, there may be some difficulties when used practically.

## Conclusions

Overall, this study provides a basis for clinicians and patients to self-diagnose the possibility of renal calculus (kidney stones) by constructing a nomogram. Simultaneously, it paves the way for future research aimed at establishing the causes of renal calculus.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

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### Statements

As the author of "A Clinical Nomogram for Predicting Recurrent Calculus of University Teachers", I would like to make the following statements. (1) All methods in this paper are implemented according to relevant guidelines and regulations. (2)This study was approved by the Ethics Committee of Huangjiahu Hospital of Hubei University of Chinese Medicine. (3) The clinical case information included in this study obtained the informed consent of the patients.

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