The Association between the Extracellular water-to-total body water ratio and Albuminuria in Chinese type 2 diabetes mellitus patients (#111956)

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The Association between the Extracellular water-to-total body water ratio and Albuminuria in Chinese type 2 diabetes mellitus patients

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Background .
Diabetic kidney disease (DKD) is a common complication in patients with type 2 diabetes (T2DM), and early screening and diagnosis are crucial for preventing end-stage renal disease (ESRD). The extracellular water/total body water (ECW/TBW), as measured by bioelectrical impedance analysis (BIA), may be closely associated with the development of DKD. This study aimed to evaluate the relationship between ECW/TBW and albuminuria in T2DM patients and to explore its potential as an early diagnostic tool.
Methods .
This study included 1,034 T2DM patients. Demographic information, medical history, medication use, and laboratory test results were collected, including glycated hemoglobin (HbA1c), creatinine, lipid profile, and the urine albumin-creatinine ratio (UACR). BIA was used to measure parameters such as ECW/TBW. Multivariate logistic regression analysis explored the correlation between ECW/TBW and UACR. Ultimately, two simple nomograms were established to predict macroalbuminuria from patients with normoalbuminuria and microalbuminuria, respectively.
Results . The ECW/TBW increased significantly with rising UACR levels. Multivariate logistic regression analysis showed that ECW/TBW was significantly associated with macroalbuminuria compared to both normo-albuminuria and microalbuminuria (OR = 2.136, 95% CI: 1.562-2.921, P < 0.001; and OR = 1.925, 95% CI: 1.378-2.691, P < 0.001, respectively). In the analysis stratified by renal function, a similar relationship was found only in patients with eGFR ≥ 60 mL/min/1.73 m^2 (OR = 2.161, 95% CI: 1.570~2.974, P < 0.001) but not in patients with eGFR < 60 mL/min/1.73 m^2. Finally, two nomograms for predicting macroalbuminuria were established. The C-index of the nomogram model for

predicting the macroalbuminuria in patients with normoalbuminuria was 0.795 (95% CI: 0.752 - 0.838), and the C-index of the nomogram model for predicting the macroalbuminuria in patients with microalbuminuria was 0.761 (95% CI: 0.711 - 0.812). Conclusions . This study demonstrated a significant correlation between the ECW/TBW and UACR levels in Chinese T2DM patients. In patients with normal or mildly impaired renal function (eGFR ≥ 60mL/min/1.73 m^2), ECW/TBW was significantly associated with macroalbuminuria, potentially serving as a diagnostic marker for macroalbuminuria.

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Abstract

Background.

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Methods.

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Results.

The ECW/TBW increased significantly with rising UACR levels. Multivariate logistic regression analysis showed that ECW/TBW was significantly associated with macroalbuminuria compared to both normo-albuminuria and microalbuminuria (OR = 2.136, 95% CI: 1.562-2.921, P < 0.001; and OR = 1.925, 95% CI: 1.378-2.691, P < 0.001, respectively). In the analysis stratified by renal function, a similar relationship was found only in patients with eGFR ≥ 60 mL/min/1.73 m² (OR = 2.161, 95% CI: 1.570~2.974, P < 0.001) but not in patients with eGFR < 60 mL/min/1.73 m². Finally, two nomograms for predicting macroalbuminuria were established. The C-index of the nomogram model for predicting the macroalbuminuria in patients with normoalbuminuria was 0.795 (95% CI: 0.752 - 0.838), and the C-index of the nomogram model for predicting the macroalbuminuria in patients with microalbuminuria was 0.761 (95% CI: 0.711 - 0.812).

Conclusions.

This study demonstrated a significant correlation between the ECW/TBW and UACR levels in

Chinese T2DM patients. In patients with normal or mildly impaired renal function (eGFR ≥ 60mL/min/1.73 m²), ECW/TBW was significantly associated with macroalbuminuria, potentially serving as a diagnostic marker for macroalbuminuria.

Keywords

Type 2 diabetes mellitus; Diabetic kidney disease; Extracellular water/total body water ratio; Bioelectrical impedance analysis; Albuminuria; Nomogram

Introduction

Diabetes mellitus (DM) has become one of the major public health challenges globally and a significant health threat. According to the Diabetes Atlas of the International Diabetes Federation, 537 million adults worldwide were diagnosed with diabetes in 2021, with this number projected to rise to 784 million by 2045. Among these patients, more than 90% have type 2 diabetes mellitus (T2DM), and it is estimated that 6.7 million adults died from diabetes or its complications in 2021, accounting for 12.2% of all-cause mortality[1]. Diabetic kidney disease (DKD), one of the most common microvascular complications of diabetes, affects approximately 30–40% of diabetic patients[2,3]. DKD is the leading cause of end-stage renal disease (ESRD)[4] and significantly increases the risk of cardiovascular disease and mortality[5].

DKD often presents with no obvious clinical symptoms in its early stages, and its progression is insidious, leading to delays in treatment. Currently, the primary methods for timely diagnosis of DKD include regular monitoring of the urine albumin-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR). However, in clinical practice, not all patients undergo regular screening and monitoring. A cross-sectional survey in China, which included 9,886 T2DM patients, revealed that while the prevalence of chronic kidney disease (CKD) was 32.5%, the awareness rate was only 26%, and the screening rate was 55.3%[6]. Although several new biomarkers have emerged in recent years[7], various approaches, such as genomics, proteomics, metabolomics, urine exosome analysis, and high-throughput screening, have provided valuable insights into DKD screening. However, these methods lack convenience. Therefore, simpler and

more accessible early warning measures are needed for patients.

Body composition analysis (BIA) can evaluate the water content and distribution in different parts of the human body by measuring the electrical impedance of various tissues. The accuracy and repeatability of BIA had been validated[8,9], and it is closely related to the gold-standard tracer dilution technique for assessing fluid status. BIA has been widely used in clinical practice to assess volume control in patients undergoing renal replacement therapy[11]. Recent studies have shown that increased extracellular fluid is significantly associated with decreased renal function in non-end-stage DKD patients[12,13], suggesting that extracellular fluid expansion is closely linked to the development of DKD. Albuminuria, a key clinical manifestation of DKD, is an important marker for CKD progression[14] and an independent cardiovascular risk factor[15]. A study by Hanako Nakajima reported that, in a Japanese cohort of T2DM patients with eGFR ≥ 30 mL/min/1.73 m², an increased proportion of extracellular fluid was significantly associated with albuminuria, supporting the feasibility of predicting albuminuria by monitoring extracellular fluid proportion[16]. However, few studies have specifically examined the relationship between extracellular fluid ratio and albuminuria in T2DM patients.

This study aims to investigate the association between the extracellular water ratio, as measured by BIA, and albuminuria levels in a Chinese T2DM population. Furthermore, it seeks to explore the relationship between these two parameters across different renal function stratifications based on eGFR, with the goal of identifying a rapid and effective method for screening patients with DKD.

Materials & Methods

Study population

Between August 2022 and May 2024, patients with T2DM admitted to our institution were continuously screened. The inclusion criteria were as follows: (1) diagnosis of T2DM; (2) age ≥ 18 years; (3) underwent bioelectrical impedance analysis (BIA) for body fluid composition analysis; and (4) tested UACR. The exclusion criteria were as follows: (1) incomplete data, (2) presence of other kidney diseases, and (3) severe liver disease. This study was approved by the

Institutional Review Board of the Medical Ethics Committee of Tangdu Hospital, Fourth Military Medical University, China (No. K202207-05), and complied with the principles of the Declaration of Helsinki . All participants provided written informed consent prior to participation in the study.

Data collection

Demographic data, including the duration of T2DM, smoking history (defined as smoking at least one cigarette per day for at least six months), and alcohol consumption history (defined as consumption for at least one year), were collected. The medication history of the patients was recorded, including the use of Antidiabetic drugs and antihypertensive drugs, such as insulin, metformin hydrochloride, sodium-glucose cotransporter 2 inhibitors (SGLT-2i), glucagon-like peptide 1 receptor agonists (GLP-1RA), renin–angiotensin–aldosterone system (RSAS) inhibitors, calcium channel blockers (CCB), and diuretics. Height and weight were measured by a trained nurse in the morning while the patients were fasting. Blood pressure was measured using a standard sphygmomanometer after the patients had rested for 10 minutes in a seated position.

Laboratory indicators, including glycated hemoglobin (HbA1c), creatinine, and lipid profile including total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) were collected，after an overnight fast. eGFR uses the CKD-EPI formula[17], eGFR = a × (Scr / b) c × (0.993) ^{age}. a: female = 144, male = 141; b: female = 0.7; male = 0.9; c: female, Scr ≤ 0.7 mg/dl = -0.329, Scr > 0.7 mg/dl = -1.209; male, Scr ≤ 0.9 mg/dl = -0.411; Scr > 0.9 mg/dl = -1.209. Urine albumin and creatinine concentrations were measured from midstream urine after waking up, and the UACR was calculated. The participants were devided into three groups: normo-albuaminuria (UACR <30 mg/g), microalbuaminuria (30-300 mg/g) and macroalbuaminuria (UACR > 300 mg/g).

After an overnight fast, extracellular fluid (ECW), intracellular water (ICW), total body water (TBW), and ECW/TBW were measured using a bioelectrical impedance analyzer (BIA, Serial Number: 270CEFEE, Biospace, South Korea). Additional measurements included body fat percentage, waist-to-hip ratio and skeletal muscle mass.

Statistical analysis

All statistical analyses were performed using SPSS version 26.0. Continuous variables were expressed as means ± standard deviations, and categorical variables were expressed as proportions. One-way analysis of variance (ANOVA) was used for normally distributed continuous variables, while nonparametric tests were used for variables that were not normally distributed. Chi-square tests were used for categorical variables. Multivariate logistic regression analysis was employed to examine factors affecting UACR in T2DM patients.Finally, two predictive models for macroalbuminuria were constructed, nomograms were depicted and used to evaluate the prediction accuracy through ROC curve analysis, and were evaluated by the concordance index (C-index) and the calibration curve. *P*-value < 0.05 was considered statistically significant.

Results

Baseline characteristics

A total of 1,034 patients with T2DM were enrolled in this study, the baseline characteristics were shown in Table 1. Among the participants, 640 (58.4%) had normo-albuminuria, 244 (23.6%) had microalbuminuria, and 150 (14.5%) had macroalbuminuria. Patients with microalbuminuria and macroalbuminuria had a longer duration of diabetes, were more often male, had higher blood pressure, more extracellular fluid, higher creatinine levels, lower eGFR, higher lipid levels, and a higher proportion use insulin, diuretics and antihypertensive medications ($P < 0.05$) (Table 1).

Comparative analysis of ECW/TBW across various anatomical regions among three UACR groups.

To further investigate whether the variations in ECW/TBW among different albuminuria groups were associated with specific anatomical regions, patients were categorized into two groups based on the median ECW/TBW for distinct body segments, including the left upper limb, right upper limb, trunk, and left lower limb, and the differences in ECW/TBW across distinct UACR groups were expressed as percentages.The results indicated that as UACR increased, the ECW/TBW across all anatomical regions exhibited a gradual increase (Figure 1) (Supplementary

Table), suggesting that the relationship between ECW/TBW and UACR has no anatomical regional specificity.

Analysis of the relationship between ECW/TBW and UACR groups

Multifactorial logistic regression models examined the association between ECW/TBW and UACR. In comparison to the normo-albuminuria group, ECW/TBW demonstrated a significant correlation with macroalbuminuria ($P < 0.001$), while no significant association was observed with microalbuminuria. Similarly, In comparison to microalbuminuria group, ECW/TBW remained significantly associated with macroalbuminuria ($P < 0.001$) (Table 2), indicating a robust association between ECW/TBW and macroalbuminuria. Given that no significant difference in ECW/TBW was observed between the normo-albuminuria and microalbuminuria groups, further analysis was conducted to elucidate the relationship between ECW/TBW and macroalbuminuria by dividing patients into two groups: one comprising those with normo-albuminuria plus microalbuminuria and another consisting of those with macroalbuminuria. Binary logistic regression models were employed to assess differences in ECW/TBW between these two cohorts; the results consistently revealed a significant association between ECW/TBW and macroalbuminuria ($P < 0.001$) (Table 3).

Furthermore, to investigate whether the association between ECW/TBW and macroalbuminuria differs among patients with varying grades of renal function, participants were categorized into two groups based on eGFR: one group with eGFR < 60 mL/min/1.73 m² and another with eGFR ≥ 60 mL/min/1.73 m². The relationship between ECW/TBW and macroalbuminuria was assessed in these two groups using binary logistic regression models. It was found that in patients with eGFR ≥ 60 mL/min/1.73 m², ECW/TBW demonstrated a significant association with macroalbuminuria ($P < 0.001$). Conversely, in patients with eGFR < 60 mL/min/1.73 m², no significant association between ECW/TBW and macroalbuminuria was identified; this indicates that in T2DM patients with preserved renal function (eGFR grades 1-2), a significant association exists between ECW/TBW and macroalbuminuria (Table 3).

Development and validation of an individualized prediction model

Based on multivariate logistic regression models, two predictive models were developed to

estimate the risk of macroalbuminuria, targeting individuals with normoalbuminuria and microalbuminuria, respectively. Model A predicts the progression from normoalbuminuria to macroalbuminuria (Figure 2), while Model B predicts the progression from microalbuminuria to macroalbuminuria (Figure 3). Both models incorporated variables including age, sex, duration of type 2 diabetes, use of SGLT2 inhibitors, systolic blood pressure, and the ECW/TBW ratio. Corresponding nomograms were constructed for each model (Figures 2A and 3A), where each variable's contribution to macroalbuminuria risk is represented by a specific point value. The total risk score was calculated by summing the points of all variables, providing an individualized estimate of macroalbuminuria risk in patients with type 2 diabetes.

Model performance was evaluated using receiver operating characteristic (ROC) curves, calibration curves, and decision curve analysis (DCA). ROC analysis demonstrated that Model A achieved an AUC of 0.795 (95% CI: 0.752–0.838; Figure 2B), while Model B achieved an AUC of 0.761 (95% CI: 0.711–0.812; Figure 3B), indicating robust predictive accuracy. Calibration curves showed excellent agreement between predicted probabilities and observed outcomes (Figures 2C and 3C). Hosmer-Lemeshow tests confirmed good model calibration (Model A: P=0.469; Model B: P=0.197). DCA further evaluated the clinical utility of the nomograms, demonstrating high net clinical benefit for predicting macroalbuminuria across a threshold probability range of 0% to 80% (Figures 2D and 3D). These findings underscore the strong predictive performance, clinical applicability, and decision-support value of the two nomogram models.

Discussion

Early diagnosis and intervention of diabetic kidney disease (DKD) are critical for preventing end-stage renal disease (ESRD) and mitigating the risk of cardiovascular complications[19,20]. However, owing to the subtle early manifestations of DKD, many patients remain unscreened or undiagnosed promptly, resulting in delayed treatment. This study demonstrated that among patients with T2DM, the ECW/TBW exhibited a strong correlation with the incidence of macroalbuminuria, particularly among those classified as eGFR grades 1 and 2. Suggesting that

ECW/TBW has the potential to early identify macroalbuminuria in T2DM patients, which is essential for effective clinical management and improved prognosis.

This study further revealed that in T2DM patients, the ECW/TBW increased significantly with rising UACR, confirming the positive correlation between increased extracellular fluid ratio and albuminuria. A previous study by Wang Y et al. explored the use of BIA to assess fluid status in CKD patients, showing that the proportion of extracellular water was closely related to renal function decline[21]. Nakajima's study focused on patients with eGFR grades 1-3, revealing a strong association between increased extracellular fluid and albuminuria, and proposed that the ECW/ICW ratio could serve as a potential indicator for predicting albuminuria[16]. Our study extended these findings to include T2DM patients with eGFR grades 4-5 and replaced the ECW/ICW ratio with the ECW/TBW. Therefore, our study indicated that ECW/TBW and UACR levels demonstrate consistent trends across varying stages of renal function in patients with T2DM, suggesting the universal applicability of this indicator among T2DM patients with differing kidney function.

This study also revealed that in T2DM patients, the ECW/TBW increased significantly with rising UACR, confirming the positive correlation between increased extracellular fluid ratio and albuminuria. A previous study by Wang Y et al. explored the use of BIA to assess fluid status in CKD patients, showing that the proportion of extracellular water was closely related to renal function decline[20]. Nakajima's study focused on patients with eGFR grades 1-3, revealing a strong association between increased extracellular fluid and albuminuria, and proposed that the ECW/ICW ratio could serve as a potential indicator for predicting albuminuria[16]. Our study extended these findings to include T2DM patients with eGFR grades 4-5 and replaced the ECW/ICW ratio with the ECW/TBW. Therefore, our study indicated that ECW/TBW and UACR levels demonstrate consistent trends across varying stages of renal function in patients with T2DM, suggesting the universal applicability of this indicator among T2DM patients with differing kidney function.

The observed increase in ECW/TBW may result from either an elevation in extracellular water

(ECW) or a reduction in intracellular water (ICW). In this study, both ECW and ICW were found to rise with increasing levels of albuminuria; however, the increase in ECW was more pronounced, resulting in a higher ECW/TBW. The causal relationship between albuminuria and increased extracellular water (ECW) remains ambiguous, potentially linked to a reduction in plasma colloid osmotic pressure resulting from albumin loss. Our data indicate that patients with macroalbuminuria exhibit the lowest serum albumin levels. Furthermore, the development of albuminuria is influenced by multiple factors, including inflammation, oxidative stress, and hemodynamic disturbances. For instance, inflammation may enhance capillary permeability, leading to fluid redistribution. However, the predictive capacity of ECW/TBW was most pronounced in patients with chronic kidney disease (CKD) stages 1-2, while it significantly diminished in those with CKD stages 3-5. In advanced CKD, reduced estimated glomerular filtration rate (eGFR) and impaired water and sodium excretion likely play a more pivotal role in fluid imbalance, thereby attenuating the correlation between ECW/TBW and proteinuria. Consequently, our study not only corroborated Nakajima's findings regarding the predictive value of extracellular fluid ratio in early-stage CKD patients but also emphasized the limitations of this indicator in CKD stages 3-5. This highlights the heterogeneity among patients at different CKD stages and underscores the significance of ECW/TBW for detecting macroalbuminuria in individuals with preserved renal function.

Although this study did not identify a significant predictive value for the ECW/TBW in detecting microalbuminuria, it demonstrated substantial clinical relevance in predicting macroalbuminuria. In contrast to microalbuminuria, macroalbuminuria is frequently an irreversible pathological condition[22,23] and markedly increases the risk of progression to end-stage renal disease (ESRD)[24]. While microalbuminuria is regarded as an early marker of diabetic kidney disease (DKD), it does not consistently predict the development of ESRD.[25]. The risk of developing ESRD within ten years in patients with macroalbuminuria is 9.3 times higher than in patients with normo-albuminuria[26]. A meta-analysis of 28 cohorts with follow-up periods of up to 10 years showed that a 30% reduction in UACR lowers the risk of ESRD by 20-32%, particularly among

patients exhibiting higher baseline UACR, where the intervention effect is more pronounced[27]. These findings underscore that early identification and intervention in patients with macroalbuminuria can not only delay chronic kidney disease (CKD) progression but also significantly mitigate the risk of ESRD and associated complications.

Recently, novel drugs such as SGLT2 inhibitors and non-steroidal selective mineralocorticoid receptor antagonists have been proven to reduce albuminuria and protect the heart and kidneys in patients with diabetic nephropathy[28-31]. Studies have shown that both SGLT2 inhibitors and MRAs can reduce albuminuria by 30% to 50%[32-35]. During treatment aimed at reducing albuminuria, improvements in the ECW/TBW may reflect reductions in fluid overload and stabilization of renal function, which could guide further adjustments in therapy. For patients with macroalbuminuria, continuous monitoring of the ECW/TBW is valuable for dynamically evaluating treatment efficacy and preventing further progression of kidney disease.

Additionally, the progression rates of DKD demonstrate significant variability among patients,, influenced by factors such as genetic susceptibility, persistent hyperglycemia, and hypertension. Some patients may rapidly progress from normo-albuminuria to macroalbuminuria. Regular monitoring of the ECW/TBW provides an effective tool for individualized management, especially for high-risk patients with quickly progressing diseases. Tracking changes in the ECW/TBW can help adjust intervention measures promptly and optimize treatment strategies.

Innovation

This study is innovative as it is the first to demonstrate the predictive ability of the ECW/TBW for albuminuria in T2DM patients across different CKD stages, particularly its ability to independently predict macroalbuminuria in the early stages of CKD. By integrating clinical indicators such as age, diabetes duration, and blood pressure, the prediction accuracy was significantly enhanced. Furthermore, this study validated the utility of the extracellular water ratio, determined by BIA, as a convenient and low-cost predictive tool for albuminuria, making it especially suitable for resource-limited settings. These findings provide new insights into the early screening and management of renal injury in T2DM patients.

Limitations

Although this study provides a novel approach for the early screening of DKD, there are several limitations. Firstly, as a cross-sectional study, it does not establish a causal relationship. Secondly, while BIA offers the advantages of simplicity and high repeatability, its accuracy can be affected by the patient's condition (e.g., oedema). Future studies should validate the causal relationship between the extracellular water ratio and albuminuria through prospective cohort studies and assess the utility of this indicator in different T2DM subgroups. Additionally, although this study confirmed the predictive value of the extracellular water ratio in T2DM patients with better renal function, its role in advanced CKD patients remains unclear. Future research should explore how to integrate noninvasive tools like BIA with traditional indicators (e.g., UACR and eGFR) to develop a multidimensional early screening model for T2DM patients with advanced renal impairment, optimizing the diagnosis and treatment of DKD.

Conclusion

This study demonstrated that the ECW/TBW, as measured by BIA, was significantly correlated with albuminuria levels in Chinese patients with T2DM. Notably, the ECW/TBW showed potential in predicting macroalbuminuria among individuals with preserved renal function. These findings provided a novel tool for the early diagnosis of DKD and offer clinicians additional options for patient monitoring in resource-limited settings. Future research should further investigate the clinical applications of this method and validate its efficacy across diverse patient populations through large-scale longitudinal studies.

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Figure 1

Comparison of the ECW/TBW ratio across different body regions among three participant groups.

Patients were categorized based on the median ECW/TBW ratios of various body regions, and the differences in ECW/TBW across distinct UACR groups were expressed as percentages.

Figure 2

Model for predicting macroalbuminuria in T2DM patients with normal albuminuria.

(A) Nomogram model for predicting the development of macroalbuminuria in T2DM patients with normal albuminuria. (B) Receiver operating characteristic (ROC) curve of the prediction model. AUC: Area under the curve. (C) Calibration curve of the nomogram model. (D) Decision curve analysis (DCA) of the prediction model.

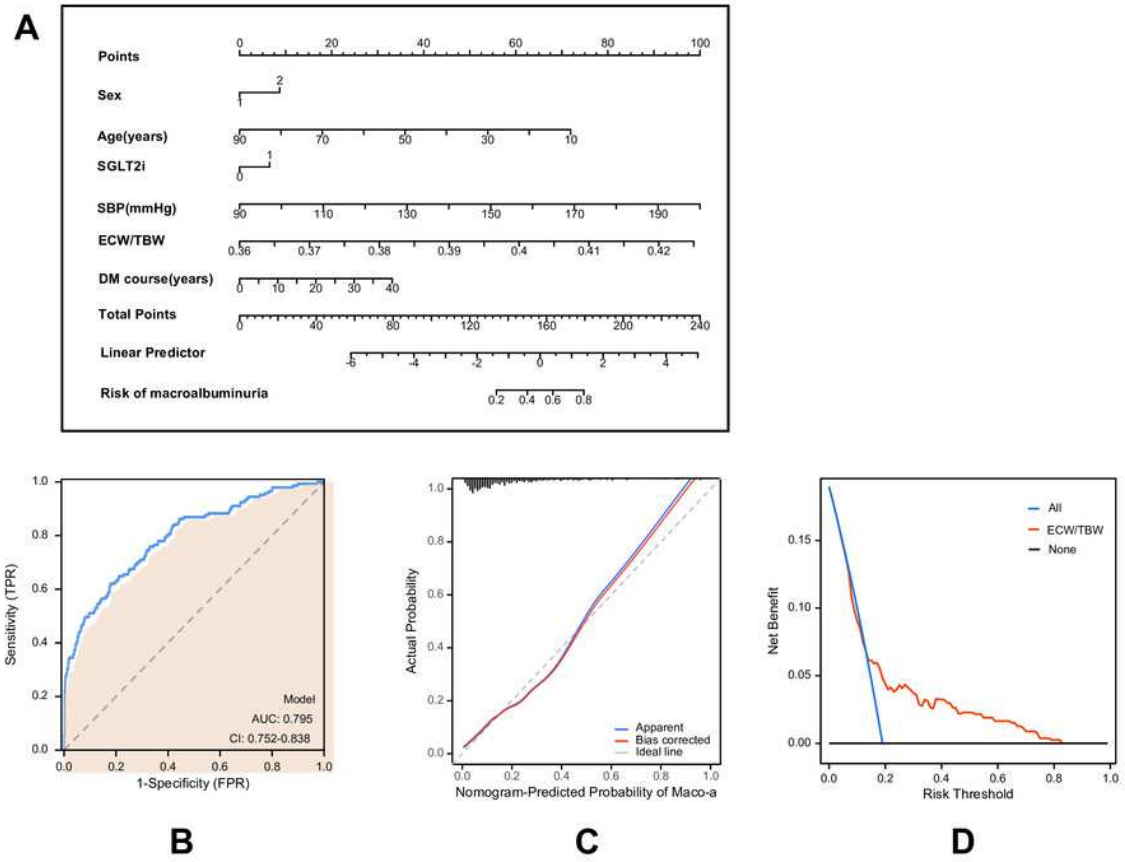

Figure 3

Model for predicting macroalbuminuria in T2DM patients with microalbuminuria.

(A) Nomogram model for predicting the development of macroalbuminuria in T2DM patients with microalbuminuria. (B) Receiver operating characteristic (ROC) curve of the prediction model. AUC: area under the curve. (C) Calibration curve of the nomogram model. (D) Decision curve analysis (DCA) of the prediction model.

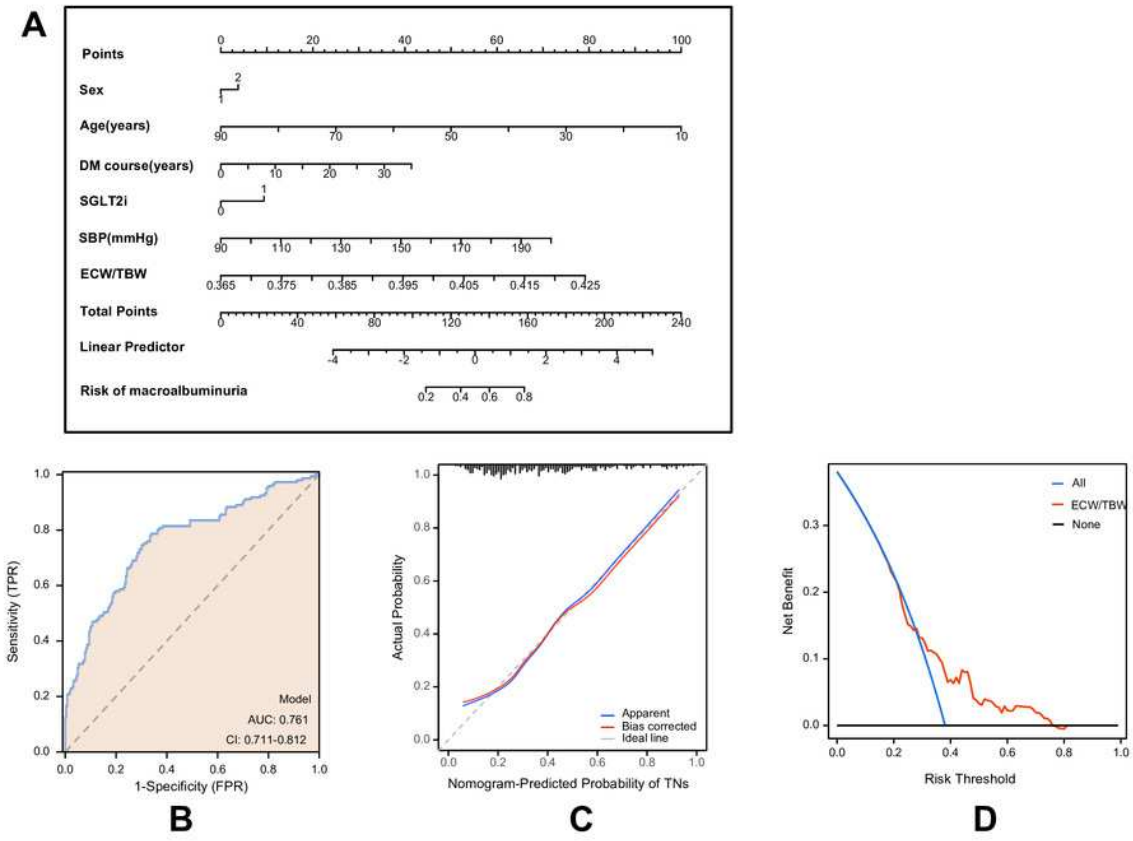

Table 1(on next page)

Characteristics of study pa tients

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Table 1 Characteristics of study patients

Variables	Total	Normo-albuminuria	Microalbuminuria	Macroalbuminuria	*P*
n (%)	1034	640 (61.90)	244 (23.60)	150 (14.50)	—
Age (years)	54.40±12.87	54.02±12.76	55.48±11.94	54.27±14.66	0.315
Male, n (%)	722 (69.80)	425 (66.40)	182 (74.50)	115 (76.70)	0.009
Duration of diabetes (years)	8 (3, 14)	8 (2, 13)	8 (3, 14)	10 (4, 18)	<0.001
Smoking, n (%)	358 (34.70)	220 (34.40)	86 (35.40)	52 (34.70)	0.965
Systolic pressure (mmHg)	130.71±16.29	127.99±14.37	131.23±17.17	141.75±17.97	<0.001
Diastolic pressure (mmHg)	82.41±10.09	81.33±9.73	82.69±10.00	86.66±10.65	<0.001
BMI (kg/m^2)	25.74±3.71	25.56±3.67	25.95±3.51	26.15±4.16	0.125
Body composition					
Body fat mass (kg)	23.30±10.80	23.17±10.54	24.01±11.51	22.67±10.67	0.436
Body fat percentage (%)	29.21±7.84	29.40±7.76	29.01±7.61	28.68±8.51	0.541
Skeletal muscle mass (kg)	27.58±5.31	27.30±5.35	27.88±4.96	28.30±5.62	0.07
Waist-to-hip ratio	0.92±0.07	0.92±0.07	0.93±0.06	0.91±0.08	0.059
ICW (kg)	22.74±4.08	22.54±4.09	23.02±3.83	23.13±4.36	0.13
ECW (kg)	14.34±2.46	14.13±2.42	14.48±2.30	14.98±2.77	0.001
TBW (Kg)	38.88±9.34	38.65±9.69	39.65±9.21	38.60±7.91	0.338
ECW/TBW ratio (%)	38.71±1.19	38.58±0.76	38.70±0.88	39.27±1.19	<0.001
HbA1c (%)	8.60±2.19	8.45±2.19	8.67±1.98	9.11±2.45	0.009
Creatinine (μmol/L)	60 (51, 71)	59 (50, 67)	60 (49, 71)	76 (56, 113)	<0.001
eGFR (mL/min/1.73 m^2)	102.79±23.17	106.71±16.85	103.15±20.65	85.37±37.98	<0.001
＜60 mL/min/1.73 m^2, n (%)	54 (5.20)	6 (0.90)	8 (3.30)	40 (26.70)	<0.001
≥60 mL/min/1.73 m^2, n (%)	980 (94.80)	634 (99.10)	236 (96.70)	110 (73.30)	
Albumin (g/L)	44.21±6.32	44.38±6.21	45.23±5.82	41.81±7.02	<0.001
TC (mmol/L)	4.47±1.52	4.34±1.25	4.43±1.99	5.09±1.56	<0.001
TG (mmol/L)	2.17±2.02	2.12±2.01	2.01±1.37	2.66±2.76	0.028
LDL-C (mmol/L)	2.49±0.98	2.42±1.00	2.43±0.82	2.88±1.04	<0.001

HDL-C (mmol/L)	1.10±0.33	1.09±0.36	1.07±0.27	1.17±0.28	0.015
Use of Insulin, n (%)	427 (41.30)	243 (38.00)	101 (41.40)	83 (55.30)	0.001
Use of SGLT-2 inhibitor, n (%)	168 (16.20)	101 (15.80)	35 (14.30)	32 (21.30)	0.165
Use of diuretics, n (%)	56 (5.40)	28 (4.40)	13 (5.30)	15 (10.00)	0.023
Use of RAAS inhibitor, n (%)	211 (20.40)	106 (16.60)	54 (22.10)	51 (34.00)	<0.001
Use of CCB, n (%)	261 (25.20)	140 (21.90)	59 (24.20)	62 (42.30)	<0.001

BMI, body mass index, ICW, intracellular water, ECW, extracellular water; TBW, total body water, HbA1c, glycated haemoglobin, eGFR, estimated glomerular filtration rate, TC, total cholesterol, TG, triglycerides, LDL-C, low-density lipoprotein cholesterol, HDL-C, high-density lipoprotein cholesterol, SGLT-2, sodium-dependent glucose transporters 2, RAAS, renin-angiotensin-aldosterone system, CCB, calcium channel blockers.

Table 2 Association between ECW/TBW ratio and UACR

	Unadjusted		**Model 1**		**Model 2**		**Model 3**	
	OR(95%CI)	***P***	OR(95%CI)	***P***	OR(95%CI)	***P***	OR(95%CI)	***P***
Normo-albuminuria	Ref.		Ref.		Ref.		Ref.	
Microalbuminuria	1.178 (0.989~1.404)	0.067	1.222 (1.000~1.494)	0.050	1.121 (0.902~1.393)	0.302	1.110 (0.890~1.383)	0.354
Macroalbuminuria	2.293 (1.866~2.817)	<0.001	2.646 (2.085~3.357)	<0.001	2.179 (1.606~2.95)	<0.001	2.136 (1.562~2.921)	<0.001
Microalbuminuria	Ref.		Ref.		Ref.		Ref.	
Macroalbuminuria	1.946 (1.545~2.450)	<0.001	2.164 (1.663~2.818)	<0.001	1.944 (1.404~2.691)	<0.001	1.925 (1.378~2.691)	<0.001

Modle1 adjusted for age, gender, duration of diabetes, BMI, and current smoker.

Modle2 adjusted for age, gender, duration of diabetes, BMI, Current smoker, Systolic pressure, Diastolic pressure, TC, TG, LDLC, HDLC, HbA1c, and creatinine.

Modle3 adjusted for age, gender, duration of diabetes, BMI, Current smoker, Systolic pressure, Diastolic pressure, TC, TG, LDLC, HDLC, HbA1c, creatinine, use of Insulin, SGLT-2 inhibitor, diuretics, RAAS inhibitor, CCB.

Table 3 Association between ECW/TBW ratio and UACR in different eGFR grades

	Unadjusted		**Model 1**		**Model 2**		**Model 3**	
	OR (95%CI)	*P*	OR (95%CI)	*P*	OR (95%CI)	***P***	OR (95%CI)	***P***

Normo+Microalbuminuria	Ref.		Ref.		Ref.		Ref.	
Macroalbuminuria	2.182 (1.790~2.660)	<0.001	2.484 (1.977~3.120)	<0.001	2.113 (1.507~2.836)	<0.001	2.081 (1.538~2.817)	<0.001
eGFR＜60 mL/min/1.73 m^2								
Normo+Microalbuminuria	Ref.		Ref.		Ref.		Ref.	
Macroalbuminuria	1.595 (0.903~2.820)	0.108	1.558 (0.794~3.056)	0.197	3.729 (0.632~22.003)	0.146	6.919 (0.273~175.3)	0.241
eGFR≥60 mL/min/1.73 m^2								
Normo+Microalbuminuria	Ref.		Ref.		Ref.		Ref.	
Macroalbuminuria	1.770 (1.400~2.237)	<0.001	2.285 (1.752~2.979)	<0.001	2.215 (1.620~3.027)	<0.001	2.161 (1.570~2.974)	<0.001

Modle1 adjusted for age, gender, duration of diabetes, BMI, and current smoker.

Modle2 adjusted for age, gender, duration of diabetes, BMI, Current smoker, Systolic pressure, Diastolic pressure, TC, TG, LDLC, HDLC, HbA1c, and creatinine.

Modle3 adjusted for age, gender, duration of diabetes, BMI, Current smoker, Systolic pressure, Diastolic pressure, TC, TG, LDLC, HDLC, HbA1c, creatinine, use of Insulin, SGLT-2 inhibitor, diuretics, RAAS inhibitor, CCB.