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Monocyte–lymphocyte ratio is a valuable predictor for diabetic nephropathy in patients with type 2 diabetes

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Abstract

Diabetic nephropathy (DN) is serious threat to human health. Therefore, early prediction of its occurrence is important. This study aimed to assess the predictive significance of monocyte–lymphocyte ratio (MLR) for DN.

A total of 301 patients with type 2 diabetes (T2D), including 212 T2D patients without diabetic-related complications and 99 DN patients, were enrolled. Peripheral white blood cells were measured before treatment to calculate MLR, and the risk factors and predictive significance for T2D and DN were assessed.

T2D patients without diabetic-related complications had higher MLR than control patients ($P < .01$). However, MLR was significantly higher in DN patients than in T2D patients without diabetic-related complications ($P < .001$). According to MLR quartiles, higher MLR in DN patients was correlated with higher serum creatinine, estimated glomerular filtration rate, and urinary albumin excretion (UAE) levels ($P < .01$ or $P < .001$). Furthermore, MLR was positively correlated with UAE level ($R^2 = 0.5973$; $P < .01$) and an independent predictor for DN (odds ratio: 7.667; 95% confidence interval [CI]: 3.689–21.312; $P < .001$). The area under the receiver-operating characteristic (ROC) curve for MLR was 0.874 (95%CI: 0.830–0.918, $P < .001$). When the optimal cutoff value was 0.23, the sensitivity and specificity of MLR for DN prediction were 0.85 and 0.74, respectively.

The present findings suggest that MLR is a powerful independent predictor for DN.

Abbreviations: AUC = area under the curve, BMI = body mass index, CI = confidence interval, CKD = chronic kidney disease, CysC = cystatin C, DN = diabetic nephropathy, eGFR = estimated glomerular filtration rate, FPG = fasting plasma glucose, HB = hemoglobin, HbA1c = glycosylated hemoglobin, MLR = monocyte–lymphocyte ratio, ROC = receiver-operating characteristic, SBP = systolic blood pressure, SCr = serum creatinine, SNK = Student–Newman–Keuls, T2D = type 2 diabetes, TSH = thyroid-stimulating hormone, UAE = urinary albumin excretion, WBC = white blood cell.

Keywords: diabetic nephropathy, monocyte–lymphocyte ratio, predictor, type 2 diabetes

1. Introduction

As the third leading cause of mortality, diabetes is the most common noncommunicable chronic disease in developed and developing countries,[1] and represents a serious threat to human health worldwide.[2] Microvascular complications are frequent and serious complications of diabetes.[3] Among these complications, diabetic nephropathy (DN) is the main factor that leads to kidney failure.[4] DN typically manifests as progressive deterioration in kidney function, including augmented glomerular filtration rate, glomerular hypertrophy, and urinary leakage of albumin.[5] Moreover, DN is associated with poor outcomes[6] and acts as a unique predictor of mortality in diabetes patients.[7] Therefore, early identification of the risk for diabetes and microvascular complications provides an opportunity to introduce preventive measures to stop or delay disease onset,[8] which can decrease the morbidity and mortality of patients with type 2 diabetes (T2D).

Studies have shown that many biomarkers can reflect the presence of microvascular damage in T2D patients, and are associated with the risk of microangiopathy and T2D development.[9–12] Furthermore, various biomarkers have been recognized to play potential roles in the diagnosis and prognosis of DN.[13] Our previous studies demonstrated that thyroid-stimulating hormone (TSH) and free triiodothyronine[14] as well

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as fibrinogen[15] can be used to predict DN. Therefore, routine laboratory indicators can be used as predictors for DN risk.

Inflammation is common in patients with chronic kidney disease (CKD), and its prevalence is inversely correlated with level of kidney function and positively associated with magnitude of proteinuria.[14] In recent years, the role of inflammation in progression of diabetic kidney disease has been emphasized.[15] Therefore, inflammation is certain to play an important role in DN progression, and the determination of inflammatory markers would be of great value for DN diagnosis and treatment. Studies have shown that many inflammatory factors and markers, including C-reactive protein, interleukin-1, interleukin-6, and tumor necrosis factor-α, are closely related to end-stage organ injury in diabetes, and play important roles in DN risk assessment and prediction.[16–19] Furthermore, the relationships between white blood cell (WBC) subtypes and inflammatory state of DN have been evaluated in different degrees.[20,21] Monocyte–lymphocyte ratio (MLR), a new inflammatory marker, has an important role in the prediction and prognosis of tumors and cardiovascular diseases.[22,23] However, the associations of MLR with T2D and DN remain unclear. Therefore, the purpose of this study was to explore the predictive significance of MLR in the development of T2D and occurrence of DN.

2. Materials and methods

2.1. Patient population

A total of 301 patients with T2D were finally enrolled in the study. The patients comprised 193 males and 108 females aged 37 to 85 years from the Department of Endocrinology, Zhejiang Provincial People's Hospital, China between October 2015 and December 2016. T2D patients without diabetes-related complications and those with nephropathy only before treatment in hospital were included in the study. All patients with T2D were diagnosed according to the criteria in the 2013 Diabetes Guideline from the China Diabetes Association.[24] Patients who exhibited the following characteristics were included:

1) typical symptoms of diabetes (polyuria, polydipsia, unexplained weight loss);
2) random blood glucose level ≥11.1 mmol/L;
3) fasting plasma glucose (FPG) level ≥7.0 mmol/L or 2-hours post-challenge glucose level in oral glucose tolerance test ≥11.1 mmol/L.

Any atypical symptoms were confirmed on a different day. Meanwhile, patients with DN were diagnosed according to the diagnostic standards for DN in the Mogensen DN diagnostic criteria.[25] The following exclusion criteria was used:

1) diabetic complications except DN;
2) primary liver and kidney dysfunctions;
3) cardiovascular and cerebrovascular diseases;
4) malignancies;
5) acute inflammation or infections; and
6) postoperative status.

Before in-hospital treatment, clinical histories, risk factors, physical examination findings, clinical and biological data, and routine laboratory tests were collected. The total patients were divided into 2 groups: T2D without diabetic-related complications group (n = 202) and DN group (n = 99). At the same time, 101 healthy controls (age, sex, and race-matched) were included in the study. The control subjects came from the healthy management center at the hospital, and had not taken any drugs in the 2 weeks before sample collection. Informed consent was obtained from the controls and patients, and an ethical approval was not necessary because the present study was not involved human beings or experimental subjects.

2.2. Laboratory assays

Before treatment, venous blood samples were collected in sodium citrate or EDTA-K_2-containing and anticoagulant-free vacutainer tubes (Becton Dickinson, Mountain View, CA) after an overnight fast. Total WBC, monocyte, lymphocyte, and hemoglobin (HB) levels were measured by an automatic hematological analyzer and commercially available reagents (BC-6900; Mindray Inc., Shenzhen, China). The analyzer was well calibrated, and an internal quality analysis was well performed. Sera were obtained from the blood samples without anticoagulants by centrifugation at $1500 \times g$ for 10 min at room temperature. Subsequently, the levels of other biochemical indexes including FPG, glycosylated hemoglobin (HbA1c), cystatin C (CysC), serum creatinine (SCr), and TSH were measured. A CKD-EPI equation was used to calculate the estimated glomerular filtration rate (eGFR) based on CysC, according to the following formula: $\text{eGFRcys} = 33 \times (\text{CysC}/0.8)^{-0.449}$ [−1.328 if CysC > 0.8 mg/L] $\times\, 0.996^{\text{age}} \times$ (0.932 if female).[26] Whole urine during 24 h was collected from the patients and controls, and the urine albumin concentrations were measured by a biochemical analyzer. Subsequently, the urinary albumin excretion (UAE) in 24 h was calculated. At the same time, the biological and clinical data of the patients and controls (age, sex, and body mass index for all subjects; T2D-related and pathological data before in-hospital treatment for all patients) were collected and reviewed.

2.3. Statistical analysis

Data were initially tested for distribution normality by the Kolmogorov–Smirnov test, and normally distributed data were presented as mean ± standard deviation. One-way analysis of variance was used to analyze the differences among controls, T2D patients, and DN patients, as well as among quartiles, and differences between 2 groups were subsequently analyzed by the Student–Newman–Keuls (SNK) test. Samples with normal and non-normal data distributions were analyzed by Student's t test and the Mann–Whitney U test, respectively. The chi-square test was used for categorical variables (sex and occurrence of elevated systolic blood pressure). Multivariate logistic regression analyses were performed to calculate the odds ratio and 95% confidence interval (95% confidence interval [CI]) for T2D and DN. Pearson analysis was used to assess the correlation of MLR with UAE level. A receiver-operating characteristic (ROC) curve was constructed, and the area under the curve (AUC) was calculated to evaluate the predictive power of the independent risk factors. All statistical analyses were performed using the SPSS 20.0 statistical package (SPSS, Chicago, IL). A value of $P < .05$ was considered statistically significant.

3. Results

3.1. Basic characteristics of the T2D patients and controls

In this study, 301 consecutive patients with confirmed diagnosis of T2D were enrolled. The median age at diagnosis was 61 years

Table 1

Comparisons of the basic characteristics of the patients and controls.

Variables	Controls	T2D patients without complications	DN patients	P
n	101	202	99	
Age, yr$^{\Delta}$	56 (33–79)	57 (37–84)	63 (37–85)	.143
Sex (M/F)	68/33	(131/71)	(62/37)	.231
Disease course (yr)$^{\Delta}$	ND	5.5 (2.0–13.1)	10.0 (4.2–20.1**	<.001
Elevated SBP, n	ND	51	27	.371
BMI, kg/m^2	24.5 ± 2.5	28.1 ± 4.3*	28.4 ± 4.7*	.012
HB, g/L	123.5 ± 12.8	121.2 ± 13.3	121.1 ± 13.0	.522
MLR	0.20 ± 0.13	0.26 ± 0.15*	0.42 ± 0.19**	<.001
SCr (μmol/L)	80.3 (43.2–95.2)	85.3 (49.6–118.7)	142.2 (50.2–205.5)**	<.001
eGFP, mL/min$^{\Delta}$	113.5 (93.2–136.8)	111.3 (86.1–133.1)	79.3 (62.3–103.1)**	<.001
HbA1c, %	5.89 ± 1.02	7.16 ± 1.78*	7.18 ± 2.10	.175
TSH, U/L	1.86 ± 0.99	1.79 ± 0.62	3.03 ± 1.13**	<.001
FPG, mmol/L	5.68 ± 1.02	7.27 ± 2.70	7.50 ± 2.48	.220
WBC (×10^9/L)	5.81 ± 1.65	6.49 ± 1.88*	6.95 ± 2.11	<.001
UAE, mg/24h$^{\Delta}$	10.2 (0.3–15.4)	13.2 (0.2–52.1)	45.3 (0.7–1782.0)**	<.001

BMI = body mass index; DN = diabetic nephropathy; eGFR = estimated glomerular filtration rate; FPG = fasting plasma glucose; HB = hemoglobin; HbA1c = glycosylated hemoglobin; MLR = monocyte–lymphocyte ratio; *P* value: comparisons of the 3 groups by one-way analysis of variance; SBP = systolic blood pressure; SCr = serum creatinine; T2D = type 2 diabetes mellitus; TSH = thyroid-stimulating hormone; UAE = urinary albumin excretion; WBC = white blood cell.

†Data were presented as mean ± standard deviation, except for variables marked with ($^{\Delta}$) presented as median (range).

* $P < .01$ vs controls.

** $P < .001$ vs T2D patients without diabetic-related complications, by the SNK test.

(range: 37–85 years), and male patients constituted the majority of the group ($n = 193$, 64%). Compared with controls and T2D patients without diabetic-related complications, DN patients exhibited increased TSH, MLR, and UAE levels, and decreased SCr and eGFR levels ($P < .001$). However, the HbA1c, WBC, and MLR levels in T2D patients without diabetic-related complications were higher than those in controls ($P < .01$). Detailed comparisons of the clinical and biological characteristics of the patients and controls are presented in Table 1.

3.2. Characteristics of T2D patients according to MLR quartiles

A total of 202 T2D patients without diabetic-related complications were enrolled in the study. The clinical and biological characteristics of the study population according to MLR quartiles are presented in Table 2. Patients with higher MLR were more likely to have higher TSH and WBC levels ($P < .05$ or $P < .001$). Both disease course and occurrence of elevated systolic blood pressure (SBP) showed significant differences between different MLR quartiles ($P < .05$).

3.3. Characteristics of DN patients according to MLR quartiles

A total of 99 patients with DN were enrolled in the study. The clinical and biological characteristics of the patients according to MLR quartiles are presented in Table 3. There were increases in SCr, eGFR, HbA1c, TSH, WBC, and UAE levels from the lowest to highest MLR quartiles in DN patients ($P < .01$ or $P < .001$). Both

Table 2

Clinical and biological characteristics of T2D patients without diabetic-related complications according to MLR quartiles.

	MLR quartile				
Variables	Q1 (0.02–0.20)	Q2 (0.21–0.28)	Q3 (0.29–0.37)	Q4 (0.38–0.57)	P
n	75	56	43	28	
Age (yr)$^{\Delta}$	55 (37–70)	56 (60–74)	58 (40–77)	61 (38–84)	.142
Sex (M/F, n)	48/27	37/19	28/15	18/10	.097
Disease course (yr)$^{\Delta}$	2.5 (2.0–7.9)	3.5 (2.2–8.5)	4.0 (2.5–10.2)	6.5 (2.9–13.1)	<.001
Elevated SBP (n, %)	16 (21.3)	12 (21.4)	13 (30.2)	10 (35.7)	.045
BMI (kg/m^2)	28.2 ± 3.5	28.2 ± 3.2	27.7 ± 3.8	28.3 ± 4.0	.202
HB (g/L)	120.6 ± 13.2	123.5 ± 13.0	119.8 ± 13.1	120.3 ± 12.4	.112
SCr (μmol/L)	62.3 (50.2–95.3)	68.2 (53.3–91.5)	76.8 (59.1–97.5)	77.3 (49.6–105.5)	.156
eGFP (mL/min)$^{\Delta}$	110.1 (94.2–127.3)	103.1 (89.3–120.4)	101.3 (90.3–127.9)	105.2 (86.1–133.1)	.245
HbA1c (%)	7.02 ± 1.32	7.33 ± 1.20	7.15 ± 1.35	7.21 ± 1.17	.021
TSH (U/L)	1.53 ± 1.00	1.83 ± 0.89	1.98 ± 0.97	2.83 ± 1.03	<.001
FPG (mmol/L)	7.21 ± 2.55	7.30 ± 2.30	7.38 ± 2.06	7.35 ± 2.56	.123
WBC (×10^9/L)	6.40 ± 1.65	6.46 ± 1.51	6.63 ± 1.85	6.58 ± 1.75	.043
UAE (mg/24 h)$^{\Delta}$	13.9 (0.2–37.8)	14.3 (0.6–44.1)	15.2 (0.7–52.1)	16.2 (0.8–50.0)	.078

BMI = body mass index; eGFR = estimated glomerular filtration rate; FPG = fasting plasma glucose; HB = hemoglobin; HbA1c = glycosylated hemoglobin; MLR = monocyte–lymphocyte ratio; *P* value: comparisons of the 3 groups by one-way analysis of variance; SBP = systolic blood pressure; SCr = serum creatinine; T2D = type 2 diabetes mellitus; TSH = thyroid-stimulating hormone; UAE = urinary albumin excretion; WBC = white blood cell.

†Data were presented as mean ± standard deviation, except for variables marked with ($^{\Delta}$) presented as median (range).

Table 3

Clinical and biological characteristics of DN patients according to MLR quartiles.

Variables	MLR quartile				P
	Q1 (0.04–0.30)	Q2 (0.31–0.41)	Q3 (0.42–0.63)	Q4 (0.64–1.19)	
n	24	32	23	20	
Age (yr)$^{\Delta}$	62 (37–78)	58 (42–81)	59 (40–85)	63 (38–82)	.187
Sex (M/F, n)	15/9	20/12	14/8	13/8	.176
Disease course (yr)$^{\Delta}$	5.5 (4.2–10.5)	8.1 (6.4–16.2)	11.2 (8.3–19.0)	16.7 (11.2–20.1)	<.001
Elevated SBP (n, %)	5 (20.8)	8 (25.0)	7 (30.4)	7 (35.0)	<.001
BMI (kg/m^2)	27.5 ± 3.7	28.8 ± 3.0	28.9 ± 4.0	28.4 ± 4.1	.199
HB (g/L)	120.1 ± 11.0	122.2 ± 12.2	121.0 ± 12.4	120.7 ± 11.0	.102
SCr (μmol/L)	62.3 (50.2–85.3)	78.2 (53.3–101.5)	96.8 (69.5–137.5)	112.3 (89.6–205.5)	<.001
eGFP (mL/min)$^{\Delta}$	105.2 (79.3–120.3)	94.3 (72.4–113.4)	88.5 (66.2–105.8)	79.2 (62.3–94.0)	<.001
HbA1c (%)	7.12 ± 1.70	7.21 ± 1.56	7.15 ± 1.61	7.24 ± 1.70	<.001
TSH (U/L)	2.86 ± 0.92	2.99 ± 1.01	3.10 ± 1.09	3.23 ± 1.05	<.001
FPG (mmol/L)	7.35 ± 2.24	7.54 ± 2.16	7.78 ± 2.06	7.82 ± 2.24	.002
WBC (×10^9/L)	6.71 ± 1.45	6.89 ± 1.56	7.01 ± 1.75	7.28 ± 2.10	.003
UAE (mg/24 h)$^{\Delta}$	13.6 (0.7–26.6)	14.1 (1.4–40.0)	33.2 (4.2–82.5)	219.0 (26.8–1782.0)	<.001

BMI = body mass index; DN = diabetic nephropathy; eGFR = estimated glomerular filtration rate; FPG = fasting plasma glucose; HB = hemoglobin; HbA1c = glycosylated hemoglobin; MLR = monocyte–lymphocyte ratio; *P* value: comparisons of the 3 groups by one-way analysis of variance; SBP = systolic blood pressure; SCr = serum creatinine; TSH = thyroid-stimulating hormone; UAE = urinary albumin excretion; WBC = white blood cell.

[†]Data were presented as mean ± standard deviation, except for variables marked with ($^{\Delta}$) presented as median (range).

disease course and occurrence of elevated SBP showed significant differences between different MLR quartiles ($P < .001$).

3.4. Regression analysis of risk factors for T2D and DN

The variables showing differences for T2D and DN patients according to MLR quartiles in above-mentioned results were further assessed, and we also included MLR and FPG. The association of each variable with the risk for T2D and DN was analyzed separately. A multivariate analysis was performed in controls and T2D patients without diabetic-related complications, and the results revealed that all variables except for disease course and HbA1c level were not independently correlated with T2D without diabetic-related complications (Table 4). A further multivariate analysis in T2D patients with DN and without diabetic-related complications demonstrated that disease course, elevated SBP, TSH, and MLR were independent risk factors for DN, and all of these variables were significantly associated with DN (all $P < .01$) (Table 5).

3.5. Correlation of MLR with UAE level in DN patients

In this study, Pearson correlation analysis was performed to evaluate the correlation of MLR with UAE level. The result revealed a close association of MLR with UAE level ($R^2 = 0.5973$; $r = 0.773$; $P < .01$). The detailed results are presented in Figure 1.

Table 4

Results of regression analysis of risk factors for T2D.

Variables	OR	95%CI	P
Disease course	1.701	1.201–3.432	<.01
Elevated SBP	1.012	0.978–1.060	>.05
FPG	1.086	0.988–1.042	>.05
HbA1c	1.312	1.101–1.711	<.01
TSH	1.001	0.991–1.012	>.05
WBC	0.998	0.776–1.532	>.05
MLR	1.020	0.998–1.031	>.05

FPG = fasting plasma glucose; HbA1c = glycosylated hemoglobin; MLR = monocyte–lymphocyte ratio; SBP = systolic blood pressure; TSH = thyroid-stimulating hormone; WBC = white blood cell.

3.6. Results of the ROC curve analysis of MLR for DN prediction

Using the data for the patients, a ROC curve analysis was performed to assess the predictive power of MLR for DN. The ROC analysis demonstrated that MLR had a high AUC (AUC: 0.874; 95%CI: 0.830–0.918; $P < .001$) for prediction of DN. When the optimal cutoff value was set at 0.23, the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of MLR were 0.85%, 0.74%, 0.87%, 0.91%, and 82%, respectively. The data are presented in Figure 2.

4. Discussion

The present study measured MLR and various biochemical markers in 301 patients with T2D. We also assessed the

Table 5

Results of regression analysis of risk factors for DN.

Variables	OR	95%CI	P
Disease course disease	1.955	1.222–3.859	<.001
SCr	1.021	0.956–1.021	>.05
eGFP	1.044	0.977–1.032	>.05
Elevated SBP	3.442	2.01–5.761	<.001
FPG	1.086	0.988–1.042	>.05
HbA1c	1.012	0.981–1.011	>.05
TSH	2.001	1.345–4.226	<.001
WBC	0.998	0.776–1.532	>.05
MLR	7.667	3.689–21.312	<.001

eGFR = estimated glomerular filtration rate; FPG = fasting plasma glucose; HbA1c = glycosylated hemoglobin; MLR = monocyte–lymphocyte ratio, SBP = systolic blood pressure, SCr = serum creatinine, TSH = thyroid-stimulating hormone, WBC = white blood cell.

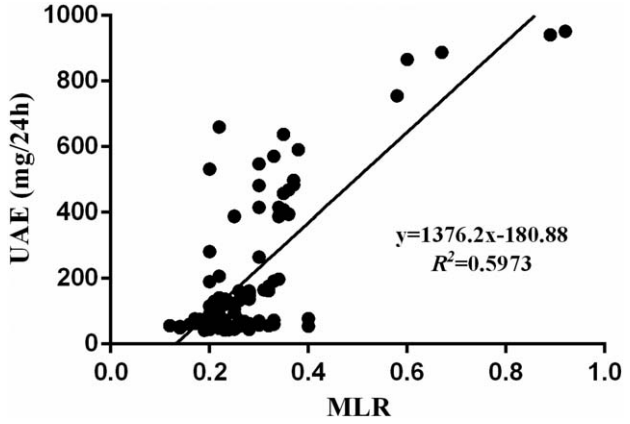

Figure 1. Correlation of MLR and UAE level in patients with diabetic nephropathy. MLR = monocyte–lymphocyte ratio, UAE = urinary albumin excretion.

association of MLR with T2D and DN. Two of the major findings in the study were that elevated MLR was significantly correlated with risk of DN, and that MLR can be used as a predictor for DN.

Patients with diabetes exhibited abnormalities of biochemical parameters in the present study, consistent with other studies and associated with metabolic disorders.[16,17,27] The low level of chronic inflammatory response induced by abnormal metabolism is closely related to the occurrence of diabetes and DN, and various immune and inflammatory cells, such as monocytes, lymphocytes, and neutrophils, and many cytokines are involved in the occurrence and development of diabetes and DN.[28,29] Therefore, much attention has been paid to the changes in WBC subtypes for the diagnosis and treatment of DN. In the present study, the WBC and MLR levels were higher in patients with T2D than in controls, and DN patients had higher MLR and other biological and biochemical indicators, indicating that T2D patients may exhibit more significant inflammatory reactions. Thus, the findings suggest that monocytes and lymphocytes may play important roles in the occurrence and development of T2D and DN, resulting from ongoing chronic inflammatory reactions. Therefore, observation of the changes in monocytes and lymphocytes in peripheral blood will have important significance for DN risk assessment. Our findings further showed that increased MLR was correlated with abnormalities in SCr, eGFR, and UAE levels, which are closely correlated with kidney function, and demonstrated a close relationship between

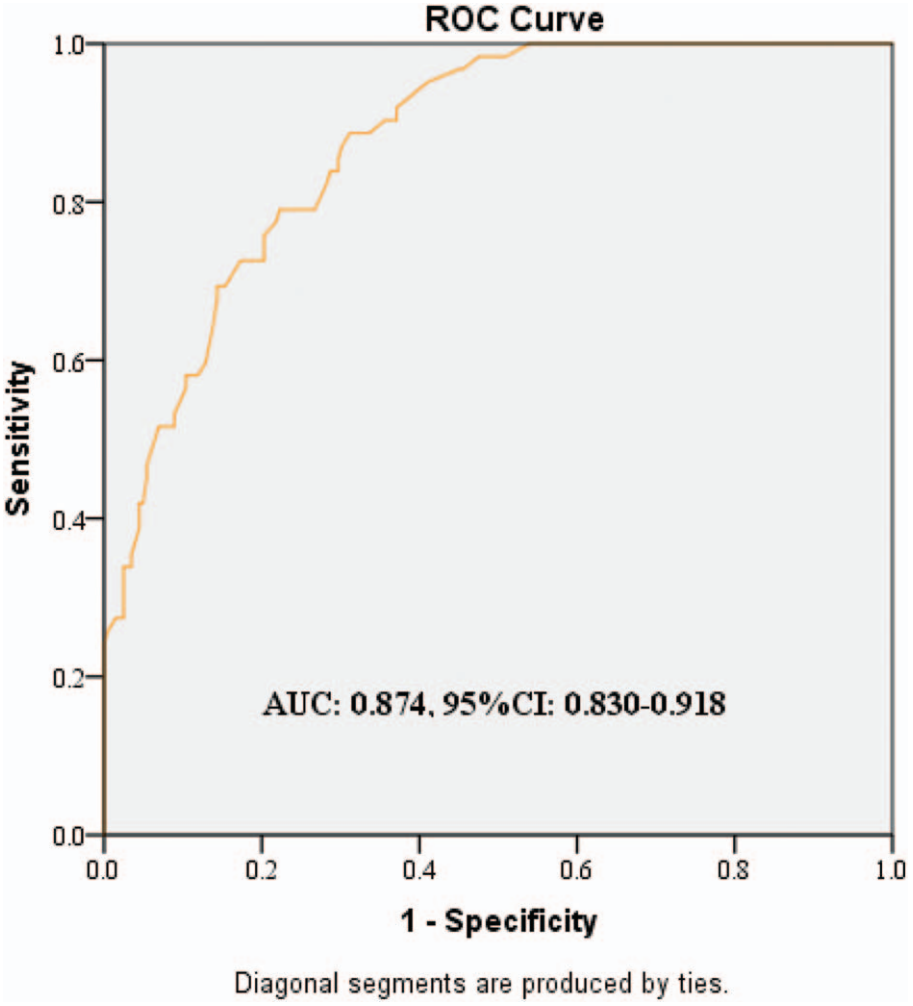

Figure 2. ROC curve of MLR for prediction of diabetic nephropathy. 95%CI = 95% confidence interval, AUC = area under the curve, MLR = monocyte–lymphocyte ratio, ROC = receiver-operating characteristic.

progression of T2D and MLR. Therefore, it will be of great value to explore the significance of MLR for T2D and DN risk assessment and prediction.

As a combined index that integrates monocytes and lymphocytes, MLR can amplify the evaluation effects of monocytes and lymphocytes for the occurrence and development of diseases related to inflammatory reactions, which is of great significance for the prediction and prognostic assessment of various diseases, including tumors, cardiovascular diseases, and diabetic retinopathy.[30–33] Therefore, to clarify the association of MLR with T2D and DN, we evaluated the differences in pathophysiological and biochemical indexes in all T2D patients with different MLR levels. Only a few indexes, such as WBC subtypes and TSH, showed notable differences in T2D patients without diabetic-related complications across the lowest to highest MLR quartiles, whereas many biochemical indexes, including SCr, eGFR, and UAE levels, had significant differences in DN patients, suggesting that increased MLR is closely related to the enhanced kidney injury in T2D patients. Thus, increased MLR has a close association with occurrence of T2D and DN, and MLR may be helpful for predicting the occurrence of T2D and DN.

To determine whether MLR can be used as a risk factor for T2D and DN, multivariate regression analyses were performed to assess the predictive significance of age, disease course, blood pressure, HbA1c, FPG, TSH, SCR, eGFR, and MLR for T2D and DN. The results showed that no biochemical variables were independent risk factors for T2D, while MLR and TSH were independent risk factors for DN, and MLR had a significantly higher adjusted hazard ratio than TSH. At the same time, MLR showed a positive correlation with UAE level in DN patients. Thus, our findings reveal that MLR is more closely related to severity of DN, and that increased MLR may indicate the risk of kidney injury in patients with T2D. To further evaluate the predictive value of MLR for DN risk, a ROC curve analysis was carried out. The AUC for MLR was 0.835, suggesting that MLR has high predictive power for DN. Furthermore, based on a cutoff value of 0.23, MLR exhibited high sensitivity, specificity, and diagnostic accuracy of 0.85%, 0.74%, and 82%, respectively, for prediction for DN. Therefore, the above results show that, as an independent risk factor, MLR has high predictive power for DN, and can act as a risk predictor for DN. Because MLR is calculated from WBC subtypes, it is more convenient, faster, and cheaper than other predictive indexes, and can be used as a valuable index to predict the development of T2D and occurrence of DN.

This study had 2 limitations. First, the study probably included some T2D and nephropathy patients with other complications that were not diagnosed before treatment. Therefore, the data from these patients could have produced some uncertain results, and may have influenced the predictive power. Second, patients with advanced DN may have increased the predictive power, and the patients were not stratified by disease condition of DN in this study. Therefore, it remained unclear whether there was a significant difference in MLR levels between the early and late stages of DN. Despite these limitations, the present study revealed that MLR has valuable predictive significance for DN.

5. Conclusions

The present study suggests that MLR cannot be used to predict T2D, but is a valuable predictor for DN. Further multiple-center and controlled prospective studies on large groups of patients may provide more definitive results.

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