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RESEARCH ARTICLE

Correlation Between Microinflammatory Status and Proteinuria in Simple obesity

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Abstract

Objective: To investigate the correlation between microinflammatory status and proteinuria in patients with simple obesity.

Methods: A total of 224 patients with simple obesity who underwent bariatric surgery in the Department of Bariatric Metabolism of our hospital from January 2018 to December 2019 were selected. According to the urinary microalbumin level, the patients were divided into no proteinuria group, microalbuminuria group and massive proteinuria group. The changes of urinary microalbumin, BMI, and microinflammatory indicators (NLR, TG/HDL, FIB) before and after bariatric surgery were observed, and the relationship between microinflammatory indicators and urinary microalbumin was analyzed

Results: 1. The body weight and BMI of patients increased gradually with the increase of urinary microalbumin level ($P < 0.01$), and the levels of NLR and TG/HDL also increased ($P < 0.01$). 2. Three months after Bariatric surgery, with the decrease of body weight and BMI, the urinary microalbumin level of patients decreased compared with that before surgery ($P < 0.05$), and the NLR and TG/HDL levels also decreased significantly ($P < 0.05$). 3. Urinary microalbumin level was positively correlated with body weight, BMI, TG/HDL, and NLR ($P < 0.05$). Logistic regression analysis showed that body weight, BMI, NLR and TG/HDL were risk factors for proteinuria in patients with simple obesity. The ROC curve analysis of BMI, NLR and TG/HDL could accurately predict the occurrence of proteinuria.

Conclusions: 1. Obesity is a risk factor for albuminuria, and the degree of obesity is positively correlated with albuminuria. 2. Microinflammatory status plays an important role in the development of proteinuria in patients with simple obesity. 3. Weight loss through surgery can reduce proteinuria in patients, and the mechanism may be related to the reduction of inflammation.

Keywords: Obesity; Proteinuria; Micro inflammation; Weight-Loss Surgery

Introduction

Chinese Library Classification Number R696+.2 Document identification code A Simple obesity is the most common type of obesity, which can cause many problems, including proteinuria, and leads to the end-stage renal disease that should be paid attention to. However, the mechanism of obesity causing proteinuria is still unclear. Some studies suggest that it may be related to hemodynamic changes, inflammatory response, renin-aldosterone system activation, insulin resistance, and so on, among which inflammation is an important factor[1].In this study, urine microalbumin and microinflammatory indicators (NLR, TG/HDL, FIB) were detected in patients with simple obesity before and after bariatric surgery to explore the correlation between microinflammatory status and proteinuria, so as to provide theoretical basis and methods for the prevention and treatment of proteinuria.

Materials and Method

Subjects: A total of 224 patients with simple obesity who underwent bariatric surgery in the Department of Bariatric Metabolism, the Fourth Hospital of China Medical University from January 2018 to December 2019 were selected as the research subjects. Inclusion criteria :(1) age ≥18 years old (2) According to the "Adult Weight Determination" issued by the National Health and Family Planning Commission, PRC in 2013,[2]A BMI of 28 kg/m or more^2(3) This study was approved by the ethics committee of our hospital, and all subjects signed informed consent. Exclusion criteria: (1) renal disease: glomerulonephritis; Nephrotic syndrome; Chronic autoimmune diseases; CKD3 stage and above. (2) A history of drug use for renal damage (3) Severe infections and malig nant tumors occurred 1 month before and during the study (4) Patients with hypertension, diabetes, coronary heart disease, heart failure, hematopoietic system diseases, etc.

Research Methods

Clinical Data Collection: gender, age, history of diabetes, hypertension, coronary heart disease and other past medical history. Blood pressure, height, and weight were measured, with BMI= weight/height^2.

Collection of Laboratory Indicators: Fasting blood of the elbow vein was collected on the second day of admission: Neutrophil count (Neu) and lymphocyte count (Lym) were detected by Siemens 2120 blood cell analyzer, and neutrophil lymphocyte ratio (NLR) was calculated. Serum creatinine (Cr), triglyceride (TG), high density lipoprotein (HDL), triglyceride high density lipoprotein ratio (TG /HDL) and fibrinogen (FIB) were measured by automatic biochemical analysis ADVIA2400 instrument. Urine microalbumin was measured by immunoturbidimetry with Siemens 2400 in morning urine. NLR, TG/HDL and FIB were used to evaluate the microinflammatory status. Three months after surgery, the patients returned to the hospital to check the above indexes again

Grouping: According to the level of microalbuminuria, the patients were divided into three groups: no proteinuria group (uri nary microalbumin < 30mg/L, n= 90), microproteinuria group (30mg/L≤ urinary microalbumin < 200mg/L, n=92), and massive proteinuria group (urinary microalbumin ≥200mg/L, n=42). Patients with preoperative proteinuria and completed 3-month follow-up were divided into preoperative and postoperative paired group (n=65)

Statistical Methods: All data were analyzed by the SPSS26.0 software. Measurement data with normal distribution were represent ed as (x±s), and non-normal distribution data were represented as median (interquartile range) [M(QR)]. One-way ANOVA was used to compare the normal distribution of measurement data between groups, and Kruskall-Wallis H test was used to compare the non-normal distribution of measurement data. Chi-square was used for comparison of enumeration data between groups^{2}Inspection. Positive Pearson correlation analysis was used for normal distribution and Spearman correlation analysis was used for non-normal distribution of the relationship between urinary microalbumin and other indicators. Paired sample t-test was used for normal distribution and Wilcoxon test for non-normal distribution between the two groups. Logistic regression analysis was used to screen the risk factors of proteinuria and the relative risk of each factor. ROC curve was used to evaluate the predictive value. $P < 0.05$ was considered statistically significant.

Results

Comparison of Data Between Groups:

Statistical analysis showed that there were no significant differences in gender, age, and Scr level among the three groups (P > 0.05). There were significant differences in body weight, BMI, NLR, TG/HDL and FIB levels among the three groups (P < 0.05). With the increase of proteinuria, the levels of body weight, BMI, TG/HDL, NLR and FIB also increased gradually (P < 0.05) (Table 1).

Table 1: Comparison of data levels between groups in adults with simple obesity before surgery [(X ±s), M(QR)]¯

Factors	No proteinuria group (n=90)	Microproteinuria group (n=92)	Macroproteinuria group (n=42)	P
Age (years)	29.82±8.35	28.41±7.13	30.00±8.12	> 0.05
Gender (male/female)	21/69	25/67	20/22	> 0.05
Weight (Kg)	110.60±26.70	120.46±27.28[a]	141.20± 29.00[ab]	< 0.001
BMI(Kg/m^2)	38.44±7.62	41.94±8.59[a]	48.61±8.50[ab]	< 0.05
Scr(umol/L)	54.43±13.00	54.20±12.87	55.24±9.66	> 0.05
TG/HDL	1.41 (0.59)	1.61 (1.20)[a]	3.10±1.14[ab]	< 0.001
NLR	1.76 (0.82)	2.15 (1.23)[a]	2.95 (0.97)[ab]	< 0.001
FIB(g/L)	3.30 (0.91)	3.64 (1.02)[a]	3.58 (0.57)[a]	< 0.05
Umalb (mg/L)	17.75 (10.72)	49.55 (23.70)[a]	468.83 (369.40)[ab]	< 0.001

Note A represents P < 0.05 compared with the group without proteinuria, and
B represents P < 0.05 compared with the group with microproteinuria

Changes of Proteinuria and Inflammatory Indicators in Patients After Bariatric Surgery:

The paired sample test showed that with the weight loss, the proteinuria also decreased, and the microinflammatory factors NLR and TG/HDL also decreased, and the differences were statistically significant (P < 0.05) (Table 2).

Table 2: Comparison of observation indexes before and after bariatric surgery [(X ± S), M(QR)]¯

To observe	weight	BMI	NLR	TG/HDL	Umalb
Preoperative	120.04 + / - 29.37	41.60 + / - 9.04	2.24 (1.09)	1.98 (1.65)	49.50 (34.7)
3 months after surgery	103.39 + / - 24.99[a]	35.87 + / - 7.57[a]	1.83 (0.86)[a]	1.55 (1.08)[a]	23.40 (18.6)[a]

Note: A indicates statistically significant difference before and after bariatric surgery (P < 0.05)

Correlation Analysis of Urinary Microalbumin Level with Body Weight and Inflammatory Indicators:

The urinary microalbumin level was related to the body weight, BMI, NLR, TG/HDL and FIB levels of patients. Therefore, Pearson and Spearman bivariate analysis was used to explore the correlation between urinary microalbumin and FIB. The results showed that urinary microalbumin level was positively correlated with body weight, BMI, TG/HDL, and NLR (P < 0.05) (see Table 3).

Table 3: Correlation analysis between clinical parameters and urinary microalbumin in patients with preoperative proteinuria

Clinical parameters	weight	BMI	NLR	TG/HDL	FIB
Correlation coefficient R	0.326[b]	0.348[b]	0.298[a]	0.217[a]	0.104

Note: A indicates statistically significant correlation, P < 0.05;
B indicates statistically significant correlation (P < 0.001)

Logistic Regression Analysis of Risk Factors for Albuminuria in Patients with Simple Obesity:

We included proteinuria as the dependent variable, and weight, BMI, NLR and TG/HDL as independent variables in the Logistic regression analysis. The results showed that weight, BMI, NLR and TG/HDL were independent risk factors for proteinuria in patients with simple obesity (P < 0.05). With the increase of body weight, BMI, NLR and TG/HDL, the possibility of proteinuria was increased (Table 4).

Table 4: Risk factors for proteinuria in simple obesity

The independent variables	weight	BMI	NLR	TG/HDL
The OR value	1.063[a]	1.333[a]	1.020[a]	1.068[a]

Note: A indicates statistically significant OR, P < 0.05

Predictive Analysis of BMI and Microinflammation Indicators for Proteinuria in Patients with Simple Obesity:

The area under the ROC curve of BMI, NLR and TG/HDL were 0.646, 0.663 and 0.644, respectively.95%CI were 0.571-0.722, 0.588-0.738, 0.570-0.719, respectively. The optimal cut-off points were 36.31, 2.042, 1.709, respectively. The sensitivities were 0.765, 0.652, 0.522, respectively. The specificity were 0.461, 0.633, 0.767, respectively. All P values were < 0.001. It can accurately predict the occurrence of proteinuria in patients with simple obesity. (Figure 1).

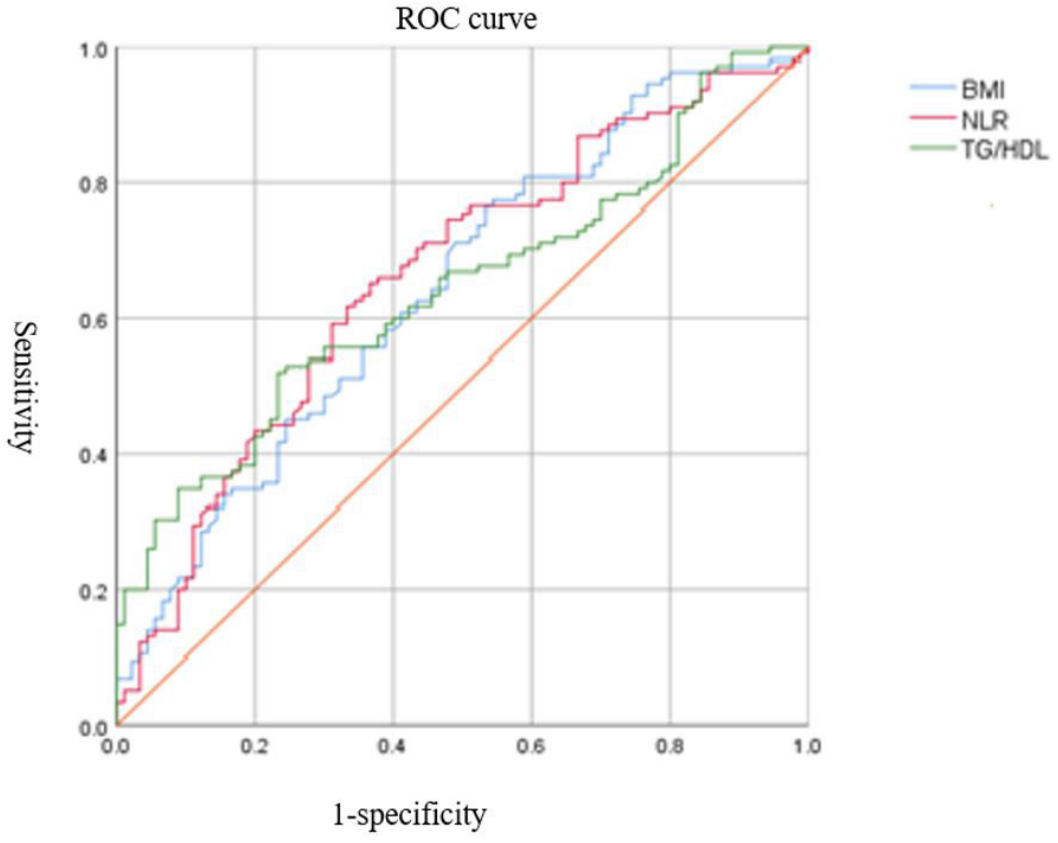

Figure 1: ROC curve assessment of BMI, NLR, TG/HDL on the occurrence of proteinuria

Conclusion

Obesity has been recognized as a risk factor for kidney disease, and its related mechanisms are multifactorial. Among the metabolic effects, such as long-term microinflammatory states, that may affect renal structure and the function are important pathways. Micro-inflammation is a low-level, persistent inflammatory state that is caused by nonpathogenic microbial infection and characterized by elevated inflammatory factors. In a healthy state, there is a balance between adipokines to maintain energy homeostasis in the body. Excessive obesity and adipocyte dysfunction make adipose tissue the site of chronic low-grade inflammatory processes, which favor the production of proinflammatory adipokines. is microinflammatory process contributes to the development of various metabolic diseases, including the production of proteinuria, the development of CKD. Although the microinflammatory state has no obvious clinical symptoms, it plays a significant role in the progression of CKD. In recent years, a large number of data have shown that NLR is a possible predictor of morbidity and mortality in patients with malignant tumors and cardiovascular diseases [3]. The imbalance between neutrophils and lymphocytes is the basis of inflammatory response, and the higher the NLR value, the more severe the in-flammatory response. FIB is a soluble glycoprotein, which not only plays an important role in the coagulation system, but also plays an important pathophysiological role in aggravating the progression of renal diseases[4].A 3-year follow-up study of 338 patients with diabetes confirmed the ability of NLR to predict deterioration of renal function[5].In 80 patients with newly diagnosed type 2 diabetes, NLR was significantly and independently associated with the rate of 24-hour urinary albumin excretion and as an indicator of end-stage renal disease[6].The NLR of 205 obese patients with different urinary microalbumin levels was different before Bariatric surgery, and the NLR increased with the increase of proteinuria. The NLR level of patients with weight loss after Bariatric surgery significantly decreased with the decrease of proteinuria, which proved that NLR was positively correlated with urinary microalbumin. The is study further verified the close relationship between NLR and kidney disease. In this study, ANOVA showed differences in FIB level between groups ($P < 0.05$), but Pearson correlation analysis did not show a correlation between FIB level and urinary microalbumin, which was consistent with the previous observation by Wang et al., that FIB was associated with the risk of progression to ESRD in CKD [4]. There are some discrepancies between these studies, which may be related to the insufficient sample size.

In addition, a series of basic experiments and clinical studies have shown that lipid plays an important and independent role in the development of diabetic nephropathy and the decline of renal function [7]. High TG and low HDL levels play an important role in the progression of CKD, and higher TG/HDL is associated with a large decrease in eGFR[8]However, few data have shown the association between albuminuria and TG/HDL in patients with CKD. Our study found that the TG/HDL level in patients with simple obesity was different in different urinary microalbumin groups. With the increase of proteinuria level, the TG/HDL level also increased gradually, which was positively correlated with urinary microalbumin level.

For obesity-related renal diseases, we should make early diagnosis and intervention, and take various methods and approaches to prevent the occurrence and development of the diseases. There are many ways to lose weight, based on diet, which seems to be a major driver of changing the microbiome, and a high-fiber diet that promotes bacteria in the gut that produce short-chain fatty acids, which has been shown to be effective against obesity. In addition to diet, the most common approach is that exercise interventions, enhanced physical activity and physical exercise programs, resulting in weight loss, can improve cardiovascular risk. The way of drug weight loss is also being adopted by more and more people. Weight loss drugs such as glucagon-like peptides may play a role in preventing obesity-related kidney disease. The new bariatric surgery have been more and more widely used in our country. Surgical treatment of obesity-related comorbidities in severely obese adolescents is currently popular. The short-term results of bariatric surgery are very good, including weight loss and improvement in metabolic disease Bariatric surgery can not only reduce body weight, but also play a role in renal protection by reducing proteinuria and improving glomerular filtration rate[9, 10]. The latest article summarizes data on the effects of bariatric surgery on obesity-related kidney disease and DKD in adolescents with and without T2D, as well as potential mechanisms for the protective effects of bariatric surgery on the kidneys [11]. This study showed that proteinuria and microinflammatory factors decreased with weight loss after bariatric surgery.

In conclusion, microinflammatory status plays an important role in proteinuria in patients with simple obesity. BMI, NLR and TG/HDL are independent risk factors for proteinuria. Bariatric surgery reduces body weight and postoperative proteinuria, which may be related to inflammation. Therefore, early control of inflammation and weight loss can reduce the occurrence and development of proteinuria, which is also of great significance for the outcome and prognosis of chronic kidney disease.

Conflicts of Interest: All the authors have no conflicts of interest

Author Contribution Statement: Nan Jiang: designed the research protocol, implemented the research process, performed statistical analysis, and wrote the paper**;** Xiaowei Zhang: proposed research topic, collected data, revised the paper; Hang Liu: Chart design, participated in statistical analysis, thought analysis; Yong Wang, Hong Ding: Paper revision, literature search and reference books, paper review

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