Project Name: The association between serum urea nitrogen to creatinine ratio and the survival in patients with DKD.
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Study unit: Guangdong Provincial People's Hospital
Sponsor: Guangdong Provincial People's Hospital

Background

In 2013, the prevalence of adult diabetes in China was as high as 10.9%, with the number of patients exceeding 100 million. Diabetic kidney disease (DKD), as one of the main microvascular complications of diabetes, occurs in 20% ~ 40% of diabetes. Furthermore, Diabetes-related chronic kidney disease, the leading cause of chronic kidney disease, has become a serious public health problem and brought huge economic burden. How to realize the early prevention and treatment of DKD and improve its clinical outcomes raises our concerns.

Previous studies have shown that a low-protein diet (LPD) can retard renal function decline in patients with CKD mainly through the improvement of glomerular hyperfiltration/hyperfusion and tubule-interstitial damage, inflammation and fibrosis. The lower the baseline dietary protein intake (DPI), the slower the progression toward ESRD. Each 0.1 g/kg per day higher DPI at baseline was associated with a loss of kidney function that was faster by approximately 0.064 ml/min per year. In 2020, standards of medical care in diabetes of American diabetes Association (ADA) recommended for people with nondialysisdependent CKD to maintain DPI approximately 0.8 g/kg body weight per day. Previous studies provided some methods for dietary assessment such as 24-hour dietary recalls, food diaries and food frequency questionnaires, which exist limitations including:(1)reliance on patient's memory, compliance and communication ability; (2)reliance on interviewer's skills, comprehensiveness and prompts;(3)lack of ability to represent a longer period. Maroni formula, which tests 24-hour urine urea nitrogen, is a relatively objective and common method to evaluate protein intake, but can't be generalized due to its complexity and uncertainty. Joel D et.al found that serum urea nitrogen to creatinine ratio (sUCR) correlated closely with protein intake and knowledge of its relation to protein intake could be used to determine the degree of protein restriction. In our previous study, the mathematical model between sUCR and DPI was preliminarily established after modeling and verification, and has obtained the patent.

Protein restriction is a basic but important life intervention to improve the prognosis of DKD patients. How to calculate DPI in a simple and effective way to overcome the complexities and errors of existing methods attracts our attentions. In this study, we hypothesize sUCR can be applied to evaluate of protein intake during the follow-up periods and predict the survival in patients with DKD.

Object

To evaluate the prognostic value of sUCR in the progression of DKD.

Methods

This study is a multicenter, retrospective cohort study. We select patients diagnosed with DKD since January 2012. The present study is performed according to the principles of the Declaration of Helsinki and has been approved by the Ethics Committee of Guangdong Provincial People's Hospital.

Study population

We screen DKD patients aged 18-70 years with CKD stages 1-4. DKD was defined as those diagnosed by pathological biopsy, or those with eGFR <60 ml/min per 1.73 m_2, or presence of clinically detectable albuminuria over 3 months which is caused by diabetes. Patients who undergo infection, severe liver disease, malignant tumor, acute heart failure, gastrointestinal hemorrhage, pregnancy are excluded.

Data collection

At baseline and every medical visit, therapeutic relevant information will be collected. Data mainly include demographic characteristics(age, gender, place of residence, marriage status, education degree), lifestyle(smoking, drinking, exercise), clinical characteristics(body mass index, blood pressure, duration , history of CVD, complications, nutrition situation), laboratory indexes(serum creatinine, blood urea nitrogen, glycosylated hemoglobin, urinary albumin to creatinine ratio, 24-hour urinary albumin, 24-hour urine urea nitrogen, etc.). History of cardiovascular disease including coronary artery disease, congestive heart failure, stroke, and peripheral vascular disease were ascertained by self-report or doctor's diagnosis.

Outcomes

Patients are followed for survival until they reach the end of the study, whichever happen first, or are censored because they lose contact or the follow-up interval is less than one month. The outcomes are all-cause death, a composite of end-stage kidney disease (dialysis, transplantation, or a sustained estimated GFR of <15 ml per minute per 1.73 m_2, or increasing by 50% of the serum creatinine level from baseline. Evaluated GFR was calculated using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula.

Statistics

Data are presented as mean ±SD for continuous variables and as a number(percentage) for categorical variables. According to mean sUCR and ΔsUCR (fluctuation of sUCR over time, meaning monthly rate of change), patients are divided into four groups. The relationship between baseline characteristics among the four groups was compared by using one-way analysis of variance test, Kruskal-Wallis test or Chi-squared test where appropriate. Survival rates are estimated using Kaplan Meier analysis, and the significance of differences are analyzed using the log-rank test. Cox proportional hazard regression analysis is used to assess the association between the clinical outcomes and mean sUCR and ΔsUCR. In multivariate analysis, we enter variables using a P value of <0.10 as the selection criterion or considered clinically significant. Hazard ratios (HRs) are presented with 95% CIs. All statistical analysis was performed with the use of SPSS (version 19.0, SPSS, Chicago, USA) and Prism 7.0 (GraphPad Software, San Diego, CA, USA). A two-tailed P value <0.05 was considered to be statistically significant.