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Diabetic kidney disease: Is there a non-albuminuric phenotype in type 2 diabetic patients?

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ABSTRACT

Background: Albuminuria was widely considered as the first clinical sign of diabetic kidney disease (DKD), which is why it has traditionally been used as a screening test for DKD. However, increasing evidence has shown that a significant number of type 2 diabetes mellitus (DM) patients have a decreased glomerular filtration rate (GFR) without significant albuminuria, known as non-albuminuric DKD (NA-DKD). The aim of this study was to determine the prevalence and the demographic and clinical characteristics of patients with NA-DKD.
Methods: This was a 1-year retrospective study that included 146 type 2 diabetic patients with GFR < 75 mL/min followed-up in a diabetes outpatient department. Patients were divided into two groups according to their ACR status – NA-DKD and albuminuric DKD (A-DKD).
Results: Of the 146 patients included in the study, 53.4% had A-DKD and 46.6% had NA-DKD. According to the multivariable analysis performed, patients with NA-DKD tended to be older ($p = 0.021$), female ($p = 0.045$) and with a lower GFR ($p = 0.004$) than A-DKD patients.

There was no difference between the groups in terms of body mass index, metabolic control of DM, duration of DM diagnosis and prevalence of metabolic syndrome.
Conclusions: The majority of patients with DKD had albuminuria, but a significant proportion had a non-albuminuric phenotype (46.6% in this population). These patients exhibit distinct clinical features that could have screening, therapeutic and prognosis implications.

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Enfermedad renal diabética: ¿hay un fenotipo de no albuminuria en diabéticos tipo 2?

Palabras clave:
Enfermedad renal crónica
Diabetes tipo 2
Sin albuminuria

RESUMEN

Introducción: La albuminuria fue ampliamente considerada como el primer signo clínico de la enfermedad renal diabética (DKD), por lo que se ha utilizado tradicionalmente como prueba de detección para DKD. Sin embargo, el aumento de la evidencia ha demostrado que un número importante de pacientes con diabetes mellitus tipo 2 (DM) tenían disminución de la filtración glomerular (TFG), sin albuminuria significativa (DKD sin albuminuria (NA-DKD). El objetivo de este estudio fue determinar la prevalencia y las características demográficas y clínicas de los pacientes con NA-DKD.

Métodos: Este fue un estudio retrospectivo de un año que incluyó a 146 diabéticos tipo 2 con TFG < 75 ml/min seguidos en el departamento de diabetes. Los pacientes fueron divididos en 2 grupos de acuerdo a su estado de ACR NA-DKD y DKD albuminúrica (A-DKD).

Resultados: De los 146 pacientes incluidos en el estudio, 53,4% tienen A-DKD y 46,6% tienen a NA-DKD. En comparación con los pacientes con A-DKD, aquellos con NA-DKD eran más propensos a ser de mayor edad (p = 0,021), a ser mujeres (p = 0,045) y tenían una TFG menor (p = 0,004), datos confirmados en el análisis multivariante.

El índice de masa corporal, el control metabólico de la DM, la duración del diagnóstico de DM y la prevalencia de síndrome metabólico no fueron diferentes entre los grupos.

Conclusiones: La mayoría de los pacientes con DKD presentan albuminuria, pero una proporción significativa tiene un fenotipo de no albuminuria (46,6% en esta población). Estos pacientes presentan características clínicas diferentes, lo que podría tener relevancia en la proyección, el pronóstico o implicaciones terapéuticas.

Introduction

Diabetes mellitus (DM) is the leading cause of chronic kidney disease (CKD) and end stage renal disease (ESRD) in developed countries.[1] In diabetic patients, early detection of diabetic kidney disease (DKD) is of critical importance.

Albuminuria was widely accepted as the earliest marker of DKD progression and was traditionally used as a screening test for DKD.[1] Since 1980s, renal disease in diabetes has been classified in stages defined by increased albuminuria/proteinuria levels (normo-micro-macro). Classically, the development of macroalbuminuria or overt proteinuria marked the initiation of faster glomerular filtration ratio (GFR) declining.[2]

However, several studies have criticized this definition in the last decades. They described progressive declining of GFR without significant albuminuria in subjects with type 1 or type 2 diabetes, i.e. a non-albuminuric DKD (NA-DKD).[3,4] Although declining GFR can occur without albuminuria, the development of advanced CKD stages seems to be strongly dependent on the progression to albuminuria greater than 300 mg/dL.[5] The majority of the studies found that the rising in albuminuria is accompanied by GFR decline.[3–5] These findings suggested that decreased GFR could be, for some group of diabetics, an early marker of DKD.

In the last few years, the traditional concept of the natural history of DKD has changed. This evidence has led the American Diabetes Association (ADA) to recommend the screening of DKD based on the albumin excretion ratio (AER) and estimated GFR (eGFR).[2]

In addition, albuminuria as a marker of glomerular lesion progression has some limitations because of its intra-patient variability and possibility of spontaneous regression (in over 50% of patients with lower levels of albuminuria),[6] in contrast with GFR that has low variability and infrequent improvement.

Growing evidence has shown that there is a continuous relationship between the level of albuminuria and the decline of GFR and cardiovascular (CV) risk. It should be noted that the levels of urinary AER, even within normal ranges, are positively correlated with the declining of GFR and cardiovascular risk.[7–10]

The prevalence and which patients develop NA-DKD are not completely defined.

The aim of this study was to evaluate the prevalence and the demographic and clinical characteristics of type 2 diabetic patients with NA-DKD.

Subjects and methods

Study design

This was an observational, 1-year retrospective, single-centre study of a cohort of type 2 diabetic patients followed in an outpatient department.

Population

From the 731 patients followed in a diabetes outpatient department of our Hospital between 09/2012 and 09/2013, 457