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Editorial Comment

EDITORIAL COMMENT

The large spectrum of renal disease in diabetic patients

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Abstract

The prevalence of diabetic nephropathy (DN) among diabetic patients seems to be overestimated. Recent studies with renal biopsies show that the incidence of non-diabetic nephropathy (NDN) among diabetic patients is higher than expected. Renal impairment of diabetic patients is frequently attributed to DN without meeting the KDOQI criteria or performing renal biopsy to exclude NDN. In this editorial, we update the spectrum of renal disease in diabetic patients and the impact on diagnosis, prognosis and therapy.

Key words: CKD, diabetes mellitus, diabetic nephropathy, GFR, kidney transplantation

Diabetes mellitus (DM) is one of the most important health problems worldwide, and its prevalence is increasing. One of the complications of DM is diabetic nephropathy (DN), which is responsible for over 40% of cases of chronic kidney disease requiring dialysis or kidney transplantation in the Western world [1–3].

The natural history of DN in patients with type 1 DM is well characterized because we know the precise time of DM onset [1]. Classically, these patients develop microalbuminuria, followed by macroalbuminuria in the first 15 years of DM. After 20 years of DM, progressive loss of glomerular filtration rate (GFR) develops. The majority of these patients have diabetic retinopathy [4]. However, the natural history of renal disease in adults with DM type 2 is controversial. Before diagnosis, type 2 DM has usually evolved over several years but has remained unnoticed [1, 4].

In 2007, KDOQI guidelines described characteristics of diabetic patients that indicate DN involvement, namely the presence of macroalbuminuria or microalbuminuria with diabetic retinopathy, or in type 1 DM patients, over 10 years of DM [5]. In addition, the guidelines summarize the characteristics that suggest the presence of non-diabetic nephropathy (NDN): absence of diabetic retinopathy, fast decline of renal function, fast increase in proteinuria or nephrotic syndrome, refractory hypertension, active urinary sediment or signs or symptoms of systemic disease or >30% reduction in GFR within 2–3 months after starting the blockade of the renin–angiotensin–aldosterone system (RAAS).

In this issue of *CKJ*, Yuan *et al.* addressed the accuracy of a clinical diagnosis of DN among diabetic patients following the criteria proposed by the KDOQI guidelines [6]. Around 20% of patients did not meet KDOQI criteria for DN in type 2 DM, suggesting a significant overestimation of DN in this population. This high proportion of NDN matches previous publications which demonstrated that about a third of patients with DM have biopsy-proven NDN [7–9]. The gold standard for diagnosis is renal biopsy. Renal biopsy in diabetic patients has focused on identifying NDN, because these patients have different prognosis and therapy. The most frequent biopsy indications in diabetic patients are nephrotic syndrome, nephrotic proteinuria in patients with < 5 years of DN evolution, microhaematuria, acute kidney injury and unexplained decline of renal function [7]. Several groups have studied renal biopsies from diabetic patients [7, 10–14], showing that the most frequent NDN diagnoses are IgA nephropathy, membranous nephropathy and focal segmental glomerulosclerosis.

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Different studies have shown that patients with DN have a worse renal prognosis [12, 15, 16] and that the prevalence of NDN is high in diabetic patients. Therefore, it is important to accurately classify diabetic patients for ND or NDN.

Yuan *et al.* studied the differential characteristics between patients meeting clinical criteria to diagnose DN according to KDOQI and misclassified patients. They showed that those patients lacking KDOQI-predicted DN were more likely to have an active urine sediment and less likely to have developed macroalbuminuria or retinopathy prior to end-stage renal disease. Using the binary logistic regression analysis, diabetic retinopathy was the only factor independently associated with patients who met KDOQI criteria [6].

Kidney biopsy studies in diabetic patients have found predictive factors for NDN: absence of diabetic retinopathy, low glycosylated haemoglobin, worse renal function, lower level of proteinuria, the presence of microscopic haematuria, older age and shorter DM evolution [7, 10–17]. Although the Yuan *et al.* cohort is small and the diagnostic method was usually not renal biopsy, the results are in line with prior reports [6]. However, recent studies have shown that patients with biopsy-proven DN may be normoalbuminuric [18]. Thus, further studies with larger cohorts and ideally renal biopsy confirmation are necessary to find factors better predicting NDN in type 2 diabetic patients. These studies may help to design novel diagnostic tools to be applied by physicians in daily clinical practice.

New therapeutic agents for the treatment of DN have recently been characterized. Endothelin receptor antagonists, sodium-glucose co-transporter 2 inhibitors, incretins and agents targeting inflammation/fibrosis are probably the most promising candidates on top of the classical RAAS blockers [2, 19]. Therefore, it is mandatory that patients with diabetic renal disease are adequately classified, differentiating clearly those with DN and those with NDN. In addition, among those with DN, a reliable classification within different pathological categories [20, 21] will be of great value to individualize treatment strategies.

In conclusion, the study by Yuan *et al.* suggests that a clinical diagnosis of DN may be a mislabel and that these patients need to be further categorized. Thus, in the future a more accurate identification and classification of kidney disease in every DM patient will facilitate the choice of a suitably targeted and individualized therapy. Further studies are still necessary with larger and multi-centre cohorts. This approach may change the spectrum of diagnosed renal disease in diabetic patients in the near future. An improved classification of renal lesions in diabetic patients may lead to optimized therapeutic approaches and outcomes.

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Conflict of interest statement

None declared.

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