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COMMENTARY

Proposal of classification of "chronic kidney disease (CKD) with diabetes" in clinical setting

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Abstract

The natural history of typical and classical "diabetic nephropathy" has been described as high levels of albuminuria and subsequent renal function decline. However, recent decades, the cases, who show the reduced glomerular filtration rate (GFR) without the progression of albuminuria, has been increased. "Diabetic kidney disease (DKD)" is a concept that widely recognizes the pathophysiological change induced by diabetes as the onset and progressive factor of renal injury and renal function decline, regardless of the level of albuminuria. However, we may confuse that "chronic kidney disease (CKD) with diabetes" is "DKD". Therefore, to choose the appropriate treatment that should be prioritized in the clinical setting, we propose that "CKD with diabetes" is classified as "DKD", "non-DKD (NDKD) with diabetes" or "combined disease of DKD and NDKD".

Keywords Diabetic kidney disease · Chronic kidney disease · Non-diabetic kidney disease · Diabetes

Diabetic kidney disease (DKD) is a concept that widely recognizes the pathophysiological change induced by diabetes as the onset and progressive factor of renal injury and renal function decline, regardless of the level of albuminuria [1]. However, in the current clinical setting, the definition of DKD is vague. It may be misunderstood that all "chronic kidney disease (CKD) with diabetes" may mean "DKD", because the boundaries between "CKD with diabetes" and "DKD" are also unclear. Therefore, to choose the appropriate treatment that should be prioritized in the clinical setting, we propose that "CKD with diabetes" is classified as "DKD", "non-DKD (NDKD) with diabetes" or "combined disease of DKD and NDKD" (Fig. 1) [2]. Diabetes, in particular type 2 diabetes, is often comorbid with other lifestyle-related diseases including hypertension, obesity, dyslipidemia and hyperuricemia, which are recognized as deterioration factors in both renal and cardiovascular diseases, and they also accelerate renal injury and renal function decline. The aim of treatment for DKD is to suppress both the progression to end-stage renal disease and the onset of cardiovascular disease (CVD), because CKD, particularly DKD, is associated with increased CVD morbidity and mortality [3]. Therefore, multifactorial treatment including control of glucose, blood pressure, lipid and uric acid levels using appropriate drugs, and improvement of obesity is recommended for the suppression of progression of both DKD and CVD [4–6]. In the clinical setting, we propose that DKD is recognized as "CKD with diabetes" that preferentially needs multifactorial treatment against metabolic disorders, including primarily diabetes. DKD may contain multiple renal pathologies, including nephrosclerosis due to hypertension, renal changes associated with atherosclerosis, obesity-related glomerulopathy and gouty nephropathy. Additionally, aging may contribute to the progression of DKD, and aging-related pathological changes such as glomerular and tubulo-interstitial fibrosis may co-exist in diabetic kidneys. However, it is impossible to perform renal biopsy for evaluating renal pathology to diagnose DKD, in all patients with both CKD and diabetes. Therefore, the clinical diagnosis of DKD is comprehensively conducted by individual clinical courses and examinations, including blood, urine, and morphological evaluation of the kidney using computed tomography. In the natural course of typical and classical diabetic nephropathy, the onset of microalbuminuria and its progression to macroalbuminuria

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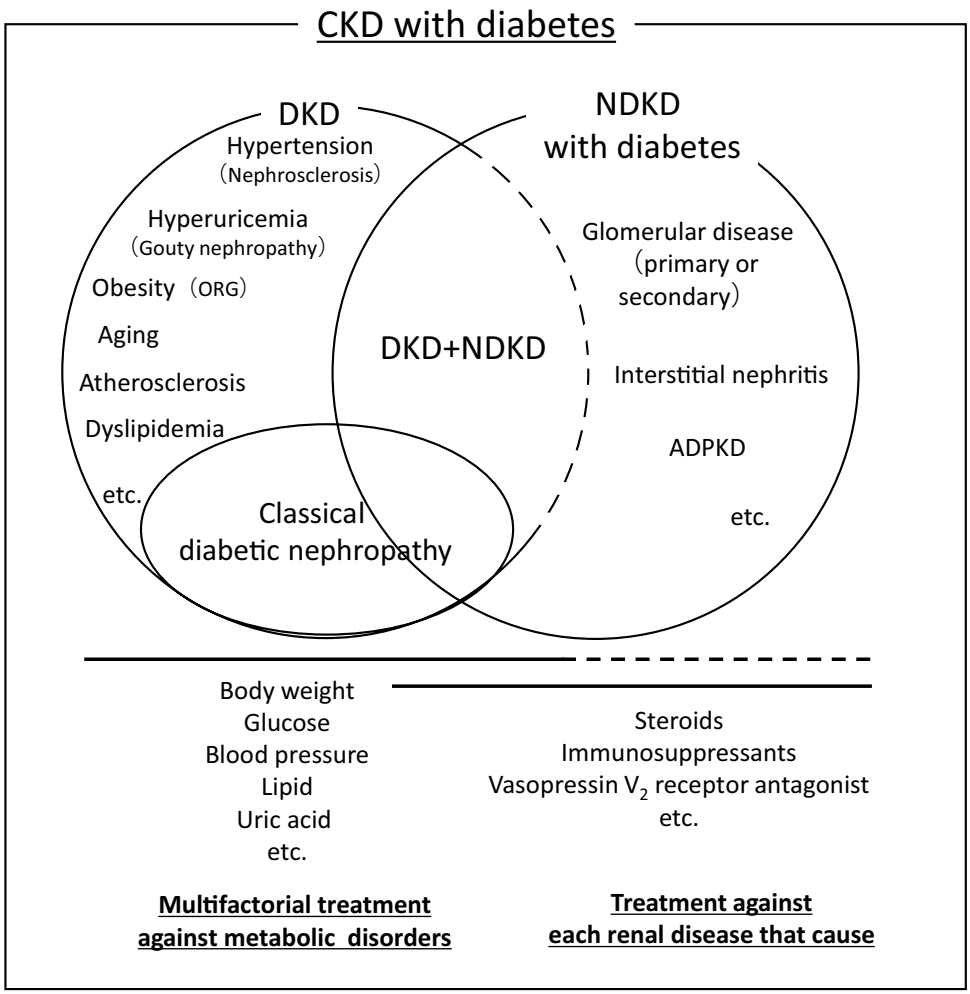

Fig. 1 Classification of CKD with diabetes. *DKD* diabetic kidney disease, *NDKD* non-DKD, *ORG* obesity-related glomerulopathy, *ADPKD* autosomal dominant polycystic kidney disease

or persistent proteinuria which is accompanied by gradual renal function decline, are important. However, the level of albuminuria is not necessarily crucial for the diagnosis of DKD.

On the other hand, we should suspect the onset of NDKD, when the diabetic patients have the rapidly increased proteinuria and progression of renal function decline which is not consistent with the course of DKD, the existence of significant microscopic or macro-hematuria, the significant increased tubular damage markers or the existence of family history of hereditary renal disease. Additionally, in the cases that have other diseases causing renal injury, such as autoimmune diseases, we should consider about the onset of NDKD. NDKD includes primary or secondary glomerular diseases, autosomal dominant polycystic kidney disease (ADPKD) and interstitial nephritis, etc. (but dose does not include classical diabetic nephropathy). For the diagnosis of NDKD, excluding ADPKD, we should consider performing renal biopsy to evaluate renal pathology in a clinical setting, if patients have no contraindications for receiving renal biopsy. When the pathological diagnosis by renal biopsy is not possible, we need to make a clinical diagnosis of NDKD by individual clinical features to determine the appropriate treatment. Additionally, when the diabetic patients without CKD have the onset of NDKD, or when the patients with NDKD have the onset of diabetes, it is recognized as "NDKD with diabetes". "NDKD with diabetes" should be distinguished from DKD from the viewpoint of choosing priority treatments such as steroids, immunosuppressants or vasopressin V_2 receptor antagonist [7–9] (Fig. 1), because the diabetic state is not mainly and directly involved in the pathogenesis of those renal diseases. Additionally, in the case that the preceding NDKD merges with DKD or in the case that the preceding DKD merges with NDKD, it should be recognized as the "combined disease of DKD and NDKD (DKD + NDKD)". "DKD + NDKD" deals separately with "NDKD with diabetes", from the viewpoint of more emphasis on multifactorial treatment and against metabolic disorders including diabetes, in addition to specific treatment for NDKD (Fig. 1). However, NDKD with diabetes may progress to DKD + NDKD

in the clinical course. Therefore, the border between NDKD and DKD + NDKD may be vague, and it is shown as dotted line (Fig. 1).

Compliance with ethical standards

Conflict of interest The authors declare that there are no conflicts of interest associated with this manuscript.

Human rights statement and informed consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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