EDITORIAL

Korean J Intern Med 2013;28:544-546
http://dx.doi.org/10.3904/kjim.2013.28.5.544

KJIM

Does nondiabetic renal disease exacerbate diabetic nephropathy in patients with type 2 diabetes?

Cheol Whee Park

Division of Nephrology, Department of Internal Medicine, Seoul St. Mary's Hospital, The Catholic University of Korea College of Medicine, Seoul, Korea

See Article on Page 565-572

Diabetic nephropathy (DN) is one of the major complications of diabetes mellitus (DM). It is estimated that 20% to 40% of DM patients will develop a diabetic renal disease. Currently, DN is the leading cause of end-stage renal disease worldwide, including in Korea, and has become a serious economic burden to the healthcare system in Korea [1]. However, renal diseases other than DN, a heterogeneous group of renal lesions, also occur frequently in patients with diabetes.

Renal biopsy is considered to be a major part of the clinical practice of nephrology, because the information it provides is critical in making a specific diagnosis and decisions for patient management and for the evaluation of disease activity and prognosis [2]. Due to its invasiveness, however, renal biopsy is not routinely performed in diabetic patients presenting with proteinuria alone.

Thus, the diagnosis of DN is almost always based on clinical findings and supported by persistent proteinuria without hematuria, hypertension, and progressive decline in renal function. The validity of this clinical approach is well-established in type 1 diabetes, but not in those with type 2 diabetes [3]. It is not uncommon for patients with a 7- to 10-year history of type 1 DM to have demonstrated diabetic retinopathy (DR) and a history of microalbuminuria. These patients present no evidence of sudden-onset marked proteinuria, hematuria, abnormal kidney size, or other renal disease [4-7].

Unfortunately, most of our knowledge of DN in type 2 diabetes patients is derived from studies of patients with type 1 DM [2,3]. Furthermore, nondiabetic renal diseases (NDRD), either isolated or superimposed on an underlying DN, have been reported, and the prevalence of biopsy-proven NDRD in type 2 patients varies from 10% to 85% [8-10]. It is well-known and generally accepted that it is difficult to reverse DN, whereas some cases of NDRD are readily treatable and remittable with appropriate treatment. However, DN and NDRD coexist in some diabetic patients. In summary, it is important to distinguish NDRD from DN and to identify features that discriminate between NDRD and DN, because this could assist clinicians in making a rapid and appropriate diagnosis, resulting in more effective management.

In this issue of *The Korean Journal of Internal Medicine*, Byun et al. [11] found that shorter duration of diabetes, higher hemoglobin A1c (HbA1c), and the absence of DR are independent

Received: June 19, 2013
Accepted: June 25, 2013

Correspondence to
Cheol Whee Park, M.D.
Division of Nephrology, Department of Internal Medicine, Seoul St. Mary's Hospital, The Catholic University of Korea College of Medicine, 222 Banpo-daero, Seocho-gu, Seoul 137-701, Korea
Tel: +82-2-2258-6038
Fax: +82-2-599-3589
E-mail: cheolwhee@hanmail.net

Copyright © 2013 The Korean Association of Internal Medicine
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0/) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

pISSN 1226-3303
eISSN 2005-6648
http://www.kjim.org

predictors of NDRD, and that NDRD is associated with better renal outcomes with specific treatment, such as steroids and immunosuppressants. Additionally, patients with a history of hematuria were more likely to have NDRD. A large meta-analysis study showed that clinical predictors allowing discrimination of NDRD from DN were: 1) absence of DR, 2) shorter DM duration, 3) lower HbA1c, and 4) lower blood pressure. They also found no difference in age, 24-hour urinary protein excretion, serum creatinine, glomerular filtration rate, or blood urea nitrogen concentrations in patients with NDRD and DN [12]. The results of that study are quite similar to those of the authors [13] with the exception of blood pressure. Byun et al. [11] also found that immunoglobulin A (IgA) nephropathy was the most common lesion, followed by membranous nephropathy, crescentic glomerulonephritis, and tubulointerstitial nephritis, in order of frequency. In contrast, a report from Malaysia showed that the causes of NDRD in type 2 diabetes, in decreasing order of frequency, were acute interstitial nephritis, glomerulonephritis, hypertensive renal disease, and acute tubular necrosis [14]. A recent study from China reported that IgA nephropathy was the most common NDRD, followed by tubulointerstitial lesion, membrano-proliferative glomerulonephritis, and membranous nephropathy [12]. The high prevalence of IgA nephropathy as the most common NDRD in type 2 diabetes patients in these two studies is consistent with their geographic distribution, in which IgA nephropathy is the most common glomerulonephritis in the general population. This reflects the prevalence patterns of glomerular disease in adults in the general population [15,16]. From the results of these studies, we may cautiously conclude that IgA nephropathy is the most common NDRD in East Asian diabetic patients. Another interesting finding of Byun et al. [11] was that the rate of decline in renal function was faster in patients with DN compared with those with NDRD alone or with DN. The authors' explanation was that patients with DN had a shorter duration and lower degree of severity of diabetes and a higher incidence of potentially treatable renal diseases, such as IgA nephropathy and membranous nephropathy. These findings are consistent with a previous report demonstrating that a shorter duration of diabetes and the presence of potentially treatable NDRD had a favorable prognosis in type 2 diabetes [14].

Several studies have suggested that there are distinct clinical and pathological features in diabetic patients with DN complicating NDRD. These patients have some of the clinical and pathological features of DN, which include a high prevalence of DR, a long duration of diabetes, poor glycemic control, and a lack of history of hematuria [8-12]. As some cases of NDRD are remittable and, in some cases, treatable if correctly intercepted, leading to completely different renal outcomes, the importance of accurate diagnosis cannot be understated. It is well-known that the only way to distinguish NDRD from DN is renal histology. However, the prevalences of NDRD are not uniform, which is likely to be due to differences in study populations and/or selection criteria. Thus, larger, multicenter, randomized, prospective studies are needed to confirm these preliminary findings. There is an urgent need to identify features that can discriminate between NDRD and DN; this could provide clinicians with more objective, reliable, and safe diagnoses, leading to more effective medical management.

Conflict of interest

No potential conflict of interest relevant to this article is reported.

Acknowledgments

This study was supported by a grant from the Korean Health Technology R&D Project, Ministry of Health and Welfare, Republic of Korea (C.W.P.) (No. A111055).

REFERENCES

1. Jin DC, Ha IS, Kim NH, et al. Brief report: renal replacement therapy in Korea, 2010. Kidney Res Clin Pract 2012;31:62-71.
2. Mather HM, Chaturvedi N, Kehely AM. Comparison of prevalence and risk factors for microalbuminuria in South Asians and Europeans with type 2 diabetes mellitus. Diabet Med 1998;15:672-677.
3. Soni SS, Gowrishankar S, Kishan AG, Raman A. Non

diabetic renal disease in type 2 diabetes mellitus. Nephrology (Carlton) 2006;11:533-537.
4. Kramer HJ, Nguyen QD, Curhan G, Hsu CY. Renal insufficiency in the absence of albuminuria and retinopathy among adults with type 2 diabetes mellitus. JAMA 2003;289:3273-3277.
5. Lin YL, Peng SJ, Ferng SH, Tzen CY, Yang CS. Clinical indicators which necessitate renal biopsy in type 2 diabetes mellitus patients with renal disease. Int J Clin Pract 2009;63:1167-1176.
6. Mak SK, Gwi E, Chan KW, et al. Clinical predictors of non-diabetic renal disease in patients with non-insulin dependent diabetes mellitus. Nephrol Dial Transplant 1997;12:2588-2591.
7. Mauer SM, Chavers BM, Steffes MW. Should there be an expanded role for kidney biopsy in the management of patients with type I diabetes? Am J Kidney Dis 1990;16:96-100.
8. Olsen S, Mogensen CE. How often is NIDDM complicated with non-diabetic renal disease? An analysis of renal biopsies and the literature. Diabetologia 1996;39:1638-1645.
9. Nzerue CM, Hewan-Lowe K, Harvey P, Mohammed D, Furlong B, Oster R. Prevalence of non-diabetic renal disease among African-American patients with type II diabetes mellitus. Scand J Urol Nephrol 2000;34:331-335.
10. Prakash J, Sen D, Usha, Kumar NS. Non-diabetic renal disease in patients with type 2 diabetes mellitus. J Assoc Physicians India 2001;49:415-420.
11. Byun JM, Lee CH, Lee SR, et al. Renal outcomes and clinical course of nondiabetic renal diseases in patients with type 2 diabetes. Korean J Intern Med 2013;28:565-572.
12. Zhuo L, Zou G, Li W, Lu J, Ren W. Prevalence of diabetic nephropathy complicating non-diabetic renal disease among Chinese patients with type 2 diabetes mellitus. Eur J Med Res 2013;18:4.
13. Liang S, Zhang XG, Cai GY, et al. Identifying parameters to distinguish non-diabetic renal diseases from diabetic nephropathy in patients with type 2 diabetes mellitus: a meta-analysis. PLoS One 2013;8:e64184.
14. Chong YB, Keng TC, Tan LP, et al. Clinical predictors of non-diabetic renal disease and role of renal biopsy in diabetic patients with renal involvement: a single centre review. Ren Fail 2012;34:323-328.
15. Chang JH, Kim DK, Kim HW, et al. Changing prevalence of glomerular diseases in Korean adults: a review of 20 years of experience. Nephrol Dial Transplant 2009;24:2406-2410.
16. Woo KT, Chan CM, Chin YM, et al. Global evolutionary trend of the prevalence of primary glomerulonephritis over the past three decades. Nephron Clin Pract 2010;116:c337-c346.

http://dx.doi.org/10.3904/kjim.2013.28.5.544