A New Quantitative Classification of Diabetic Nephropathy by Morphometric Analysis

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Dear Sir,

The pathological stage of diabetic nephropathy had been traditionally evaluated using Gellman's criteria [1], on the basis of 4 grades according to the severity of diffuse glomerular lesions. It is generally accepted that the histopathological staging ensures the reliable diagnostic criterion of diabetic nephropathy. However, a wide discrepancy remains among pathologists as to on which basis they discriminate the degree of mesangial area expansion. Therefore, a new quantitative classification of diabetic nephropathy is needed. We attempted to clarify a new histopathological staging of diabetic nephropathy using 30 patients with type 2 diabetes mellitus who underwent renal biopsy (19 males and 11 females, serum creatinine concentrations 0.3–1.8 mg/dl). Tissue specimens obtained by percutaneous renal biopsy were processed for morphometric evaluation by light microscopy. Serial sections 3 μ m thick were cut and stained with periodic acid Schiff. The severity of diffuse glomerular changes was graded on a scale of D1 through D4 according to Gellman's criteria [1] by a single consultant pathologist as follows: D1 (local lesion present within each glomerulus and focal lesion present within the kidney); D2 (mesangial thickening is diffuse within the glomerulus and generalized throughout the kidney); D3 (capillary lumina are narrowed and obliterated only locally); and D4 (the lumen is generally narrowed and the

entire glomerulus is ischemic and appears to be hyalinized). The severity of glomerular lesions was also estimated by quantitative morphometric studies [2]. Briefly, PAS-stained specimens were analyzed using a color image processor (SPICCA-II, Olympus Co., Tokyo, Japan) measuring glomerular

area (GA) and mesangial area (MA). The GA was defined as inner area of glomerular tuft outline, and the mesangial rate (MR%) was defined as the ratio of MA to GA.

The mean value of MR% was $14.4 \pm 2.1\%$ in D1, $19.7 \pm 3.0\%$ in D2, $25.3 \pm 2.3\%$ in D3, and $35.2 \pm 2.5\%$ in D4. There

Fig. 1. Correlation between the grades of diffuse glomerular lesions evaluated by Gellman's criteria and mesangial rate (MR%) estimated by computer-assisted quantitative morphometric analysis.

was a significant correlation between MR% and the grade of diffuse lesions (D) assessed by Gellman's criteria ($MR\% = 6.65 \times D + 7.05$, $r = 0.939$, $p < 0.0001$) (fig. 1). Stages of diabetic nephropathy were classifiable into four classes by the discriminating analysis. Class 1 proved to comprise 10 cases with their MR% under 16.9%; class 2, 10 cases with their MR% between 17.0 and 23.6%; class 3, 5 cases with their MR% between 23.7 and 30.2%, and class 4, 5 cases with their MR% over 30.3%. Urinary albumin excretion rate (62 ± 12 mg/24 h, 435 ± 195 , $3,175 \pm 1,147$, and $5,605 \pm 2,560$, respectively) and creatinine clearance (108 ± 26 ml/min, 96 ± 36 , 63 ± 30 , and 50 ± 16 , respectively) significantly differed among the four groups.

In the pioneer paper in the field of renal pathology in diabetic nephropathy by Gellman et al. [1], it had been previously used for evaluating the severity of diffuse glomerular lesions. However, diagnosis according to this criteria is quite prone to remarkable interobserver variation. In later years, morphometric analysis using the stereologic techniques of electron microscopy have been widely investigated in diabetic nephropathy [3–5]. The stereologic technique of electron microscopy is an exacting but time consuming procedure, whereas the computer-assisted quantitative morphometric analysis used in our study is processed to obtain a similar precise evaluation. It could provide a valid routine investigation with advantageous clinical implications.

References

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