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Serum fibrinogen predicts diabetic ESRD in patients with type 2 diabetes mellitus

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ABSTRACT

Aims: Although increased serum fibrinogen level was often observed in patients with diabetic nephropathy (DN), its association with DN severity and progression remains unclear. The aim of this study was to investigate the relationship between the serum fibrinogen levels and clinicopathological features and renal prognosis in Chinese patients with type 2 diabetes mellitus (T2DM) and DN.

Methods: A total of 174 patients with T2DM and biopsy-proven DN were enrolled. Patients were stratified by the quartiles of serum fibrinogen levels; Q1: <3.30 g/L; Q2: between 3.30 and 4.00 g/L; Q3: between 4.00 and 4.74 g/L; Q4:≥4.74 g/L. The renal outcomes were defined by reaching end stage renal disease (ESRD). The influence of serum fibrinogen levels on renal outcomes was evaluated using Cox regression analysis.

Results: The factors associated with higher level of fibrinogen (Q3 and Q4) were diabetic retinopathy, low e-GFR, high proteinuria and severe glomerular and tubulointerstitial lesions. Importantly, in adjusted analysis, higher levels of fibrinogen were independently related with a greater risk of reaching ESRD with a hazard ratio (HR) of 1.64 per standard deviation (SD) of the natural log-transformed fibrinogen concentration (95%CI, 1.22–2.20; $p = 0.001$). In reference to the Q1, the risk of renal failure increased by quartiles of the serum fibrinogen level: the HRs were 7.12 for the Q2 (95%CI, 2.29–22.16; $p = 0.001$), 5.77 for Q3 (95% CI, 1.99–16.75; $p = 0.001$), and 8.81 for Q4 (95%CI, 2.79–27.80; $p < 0.001$).

Conclusions: These findings suggested that the elevated serum levels of fibrinogen were associated with diabetic ESRD in patients with T2DM.

1. Introduction

Diabetic nephropathy (DN), recently also referred to as diabetic kidney disease (DKD), is one of the most serious microvascular complications in patients with diabetes. It has been reported by Center for Disease Control and prevention (CDC) in 2017 that approximately 44% of the patients initiating end stage renal disease (ESRD) treatment had diabetes ranked as the leading cause of ESRD (ESRD-D) in the United State [1,2]. In addition, Afkarian et al. [3] observed that DN

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carries with it a 10-year mortality rate of up to 31% in patients with type 2 diabetes mellitus (T2DM) [3]. Early detection and better management of DN in patients with T2DM may delay its progression to ESRD, and improve its complications and outcomes [1].

Although several clinical and nephropathologic factors including proteinuria, e-GFR and glomerular and tubulointerstitial lesions have been evidenced to be associated with the poor renal outcomes [4–6], the reports regarding the relationship between the serum fibrinogen, as one of hemostatic markers, and DN were very limited. Lin et al. [7] and Dalla Vestra et al. [8] reported that the serum levels of fibrinogen were associated with reduced renal function, proteinuria and glomerular basement membrane (GBM) thickness in the cross-section studies. And Wang et al. [9] observed that the urinary fibrinogen was correlated with the risk for progression of CKD to ESRD. However, whether the serum fibrinogen levels related with disease progression in patients with DN remains unclear.

Hence, in this retrospective cohort study we aimed to explore whether the serum fibrinogen as a noninvasive biomarker could predict renal prognosis in 174 Chinese patients with T2DM and biopsy-proven DN.

2. Materials and methods

2.1. Study design and patients

This is a retrospective cohort study including DM patients who underwent clinical renal biopsy at the West China Hospital of Sichuan University between 2009 and 2016, and had a pathologic diagnosis of DN. The diagnosis and classification of DM was based on the criteria of the American Diabetes Association (ADA) [10] and DN was according to the standards of the Renal Pathology Society (RPS) in 2010 [11]. The inclusion criteria were (1) age ≥18 years old, (2) a diagnosis of T2DM, (3) the diagnosis of DN proven by renal biopsy, and (4) e-GFR >15 mL/min/1.73 m [2]. Subjects with non-T2DM, superimposed systemic diseases or other glomerular disease were excluded. If patients had begun the dialysis treatment before kidney biopsy or been followed up less 1 year, they were also excluded. (Fig. 1) This study has been approved by the ethics committee of West China Hospital of Sichuan University. The study protocol was in compliance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Written informed consent was obtained from all individual patients when hospitalized.

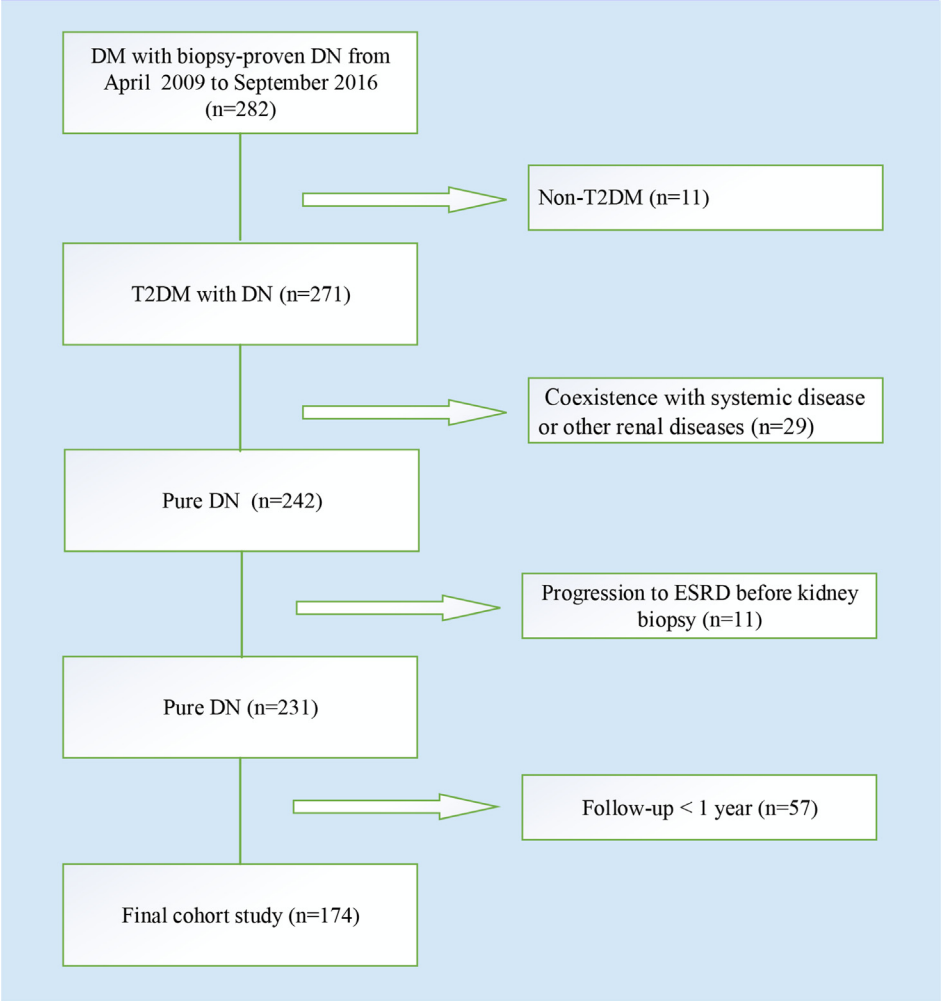

Fig. 1 – Flowchart of study participants. DN, diabetic nephropathy. ESRD, end stage renal disease.