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LETTER TO THE EDITOR

Hemodynamic Correction and Early Detection of Tubulointerstitial Fibrosis Prevent Disease Progression in Chronic Kidney Disease

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Two special issues that are relevant to the progression of chronic kidney disease (CKD) are the failure of early detection of tubulointerstitial fibrosis (TIF) and the unsettled pathogenesis of renal disease progression (RDP). With respect to the former, an early detection of TIF can be achieved by using a determination of fractional excretion of magnesium (FE Mg), which correlates directly with TIF since it reflects the tubular reabsorptive capability and intratubular wastage of magnesium in association with tubulointerstitial injury.[1] FE Mg is normal in minimal change disease or in acute glomerulonephritis with intact tubulointerstitial structure and is consistently elevated in conditions associated with TIF namely FSGS, IgM nephropathy with TIF, IgA N, reflux nephropathy, severe lupus nephritis, chronic glomerulonephritis and diabetic nephropathy[2] (unpublished data).

In accordance with the pathogenesis of RDP, a hemodynamically mediated mechanism has recently been proposed. In essence, an injury to the vascular compartment of the nephron (glomerular and postglomerular capillary) is usually associated with the initiation of a variety of glomerular diseases and has recently been documented that the glomerular endothelial dysfunction in respect to the reduction in renal perfusion ***precedes*** the development of TIF.[3] Indeed, an altered intrarenal hemodynamics so called ***hemodynamic maladjustment*** has been uniquely observed in a variety of CKDs.[4–7] It is characterized by a preferential constriction at the efferent arteriole by which it induces 1) proximally; the intraglomerular hypertension, capillary ballooning and podocyte injury[8–11] which aggravates in a vicious cycle pathogenesis (Fig. 1) and 2) distally; exaggeratedly reduces the

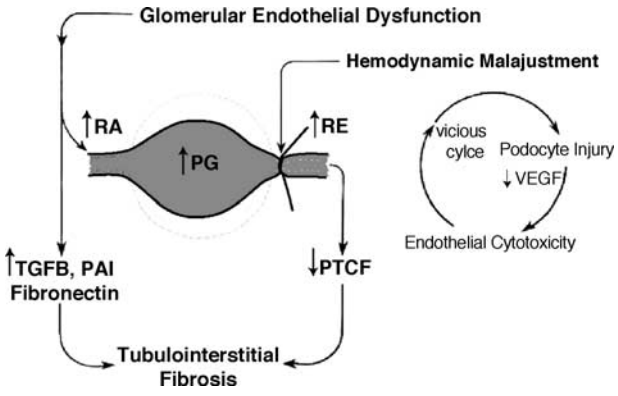

Figure 1. PG=intraglomerular hydrostatic pressure, PTCF=peritubular capillary flow, RA=afferent arteriole, RE=efferent arteriole, RPF=renal plasma flow. (*View this art in color at www.dekker.com.*)

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peritubular capillary flow which not only induces ischemic injury but also activates the profibrogenic pathway and therefore culminate in TIF.[12–15] A therapeutic correction of hemodynamic maladjustment with much higher doses of multi-drugs (vasodilators) than needed for maximal blood pressure control; has been repeatedly achieved to restore renal function with improved renal perfusion, GFR and prevent the RDP in CKD.[8,16–18]

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