Glomerular density and progression

Sir,
We have recently read with great interest the article by Tsuboi et al. [1], which examines glomerular metrics in progressive idiopathic membranous nephropathy. In patients with proteinuria (>1 g/day), low glomerular density was predictive of a loss of renal function in this disease.

In the accompanying editorial, Fogo [2] reminds us that glomerular density is a relative metric, with tubulointerstitial volume being the denominator. Interstitial fibrosis is actually a consequence of both reduction in tubulointerstitial volume and excess matrix accumulation. In the same way that a deflated balloon contains the same amount of material in a smaller volume, renal fibrosis is accompanied by a reduction in renal size [3] due to collapse of the renal parenchyma, a process enhanced by myofibroblast-mediated contraction [4]. A similar process occurs in skin wound healing, where the drawing together of wound edges by tissue contraction is an important part of wound closure. More direct evidence comes from examining the histology in experimental renal infection and scarring [5]. Being a primarily tubulointerstitial model of injury, the glomeruli are largely unaffected during fibrosis, with increasing density of glomeruli therefore providing a direct measure of parenchymal collapse. There are obvious differences between the elegant observations of Tsuboi et al. [1] and our tubulointerstitial disease corollary [5]. In their case, in a form of primary glomerular disease, less glomeruli per area of cortex was a worse prognostic feature. In our studies in a primarily tubulointerstitial disease, increasing glomerular density occurred with renal damage. However, these two observations may well be part of a continuum. Our morphometric studies in experimental renal infection indicate that glomerular density decreases acutely in association with interstitial oedema, increased cellularity and fibrogenesis. The contraction of renal parenchyma occurs later. A progressive increase in fibrous scar tissue in this model is therefore a combined effect of an early increase in collagen expression and a later collapse of the renal
parenchyma [5]. Consistent with this, as Tsuboi et al. [1] point out, severe chronic lesions may characterize already advanced injury.

In conclusion, there is an increasing body of evidence that even simple structural metrics shed much light on progression of renal injury. There should be more studies to dissect these complex pathophysiologies, if targeted interventions are to be developed.

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