The capillary web gets lost in diseased kidneys

Main functions of the kidney are regulating ions, pH, fluid balance and blood pressure and disposing of metabolic waste products. These functions are dependent on properly working renal blood vessels, including the smallest ones, the so called renal microvasculature or peritubular capillaries.

Chronic kidney disease (CKD) is a serious, life-threatening condition. It is estimated that more than 10% of the world population suffer from CKD and the numbers are rising. Virtually all kidney diseases of various causes eventually lead to CKD, which is characterized by scarring, i.e. replacement of functional renal tissue by connective tissue termed renal fibrosis. It has been known, that one of the characteristics of CKD and renal fibrosis are also characterized by reduction of the number of peritubular capillaries.

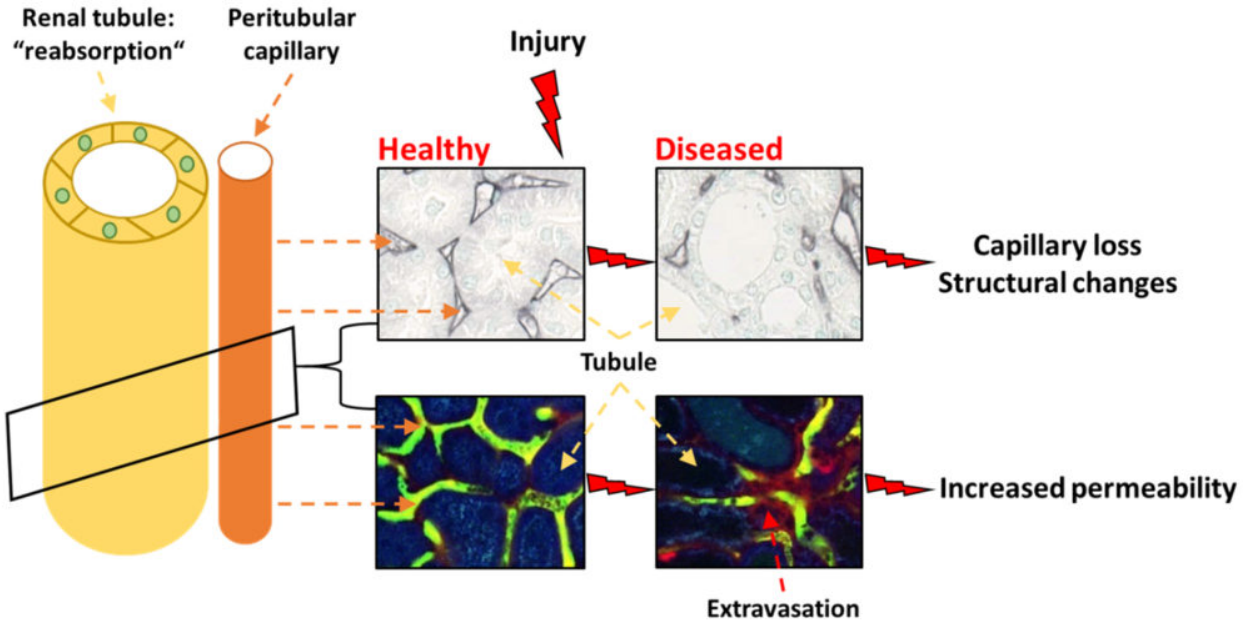

Fig. 1.

In our study, we have described various aspects of peritubular capillary alterations in CKD. We have used different animal models of CKD and fibrosis, which enabled us the analyses in a time-dependent manner as fibrosis and CKD develops, which is not possible in humans. We have adapted histological methods for quantification of peritubular capillaries and confirmed that in all models of CKD, independently of the underlying disease, renal fibrosis was associated with prominent loss of peritubular capillaries, so called microvascular rarefaction. Furthermore, we have assessed the functionality of peritubular capillaries by analyzing their "leakiness", or permeability,

which is not observed in healthy state. In fibrosis, in all models, renal microvasculature became strongly leaky. We have also developed a method to observe this leakiness in living animal using the so-called two-photon in vivo microscopy, which could visualize microvascular dysfunction in real time. Finally, we have performed quantitative analyses of ultrastructural alterations of peritubular capillaries using electron microscopy, i.e. on a subcellular level in high-magnification. These data showed that pathological alterations appear already very early during disease. We could apply the latter method not only in animal models but also human kidney tissues and showed, that both patients and animal showed similar pathological alterations in peritubular capillaries. This showed that animal models of CKD and renal fibrosis are relevant to study microvascular alterations in CKD and renal fibrosis.

Taken together, our study showed that the renal peritubular capillary web, an essential functional unit of the kidney, is lost and undergoes prominent ultrastructural and functional alterations in CKD and fibrosis. These data support the hypothesis, that therapy targeting renal microvasculature might represent a valuable target for the treatment of chronic kidney disease.

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Regardless of etiology, progressive renal disease causes ultrastructural and functional alterations of peritubular capillaries.
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