Role of endothelial dysfunction in the development of albuminuria

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Chronic Kidney Disease (CKD) is strongly associated with cardiovascular disease (CVD). Individuals with CKD are more likely to die of CVD than to develop kidney failure. Albuminuria is strongly associated with risk for CVD and common in the patients with diabetes, metabolic syndrome and hypertension. Moreover, epidemiological data suggest that 5-7% of the general population have increased urinary albumin excretion.

Elucidation of pathogenetic mechanisms of albuminuria will give us better understandings of underlying mechanisms between CKD and CVD. Both glomerular hyperfiltration and endothelial dysfunction are believed to be implicated with development of albuminuria. To elucidate the pathogenetic mechanisms of albuminuria, we have developed the techniques by which we could visualize the micro-circulation in the kidney using two-photon laser microscopy. We have also developed the novel techniques to detect reactive oxygen species (ROS) and nitric oxide (NO) simultaneously in the tissue specimen.

Using these techniques, we have found impaired bioavailability of NO and increased oxidative stress in the small arterioles and glomeruli in the disease conditions. Permeability of macromolecules in the glomerular vascular walls were deteriorated at the same time in these conditions. Finally, we would like to show how renin angiotensin blockage by angiotensin II receptor blocker (ARB) could ameliorate endothelial dysfunction and hyperpermeability of macromolecules.

Keywords: endothelial dysfunction, oxidative stress, nitric oxide, albuminuria