Loss of Renal Peritubular Capillaries in Hypertensive Patients is Detectable by Urinary Endothelial Microparticle Levels

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Hypertension, an important cause of chronic kidney disease, is characterized by peritubular capillary (PTC) loss. Circulating levels of endothelial microparticles (EMPs) reflect systemic endothelial injury. We hypothesized that systemic and urinary PTC-EMPs levels would reflect renal microvascular injury in hypertensive patients. We prospectively measured by flow-cytometry renal vein, inferior vena cava, and urinary levels of EMPs in essential (EH, n=14) and renovascular (RVH, n=24) hypertensive patients, and compared them with peripheral blood and urinary levels in healthy volunteers (HVs, n=14). PTC-EMPs were identified as urinary exosomes positive for the PTC marker plasmalemmal-vesicle-associated protein. In 7 RVH patients, PTC and fibrosis were also quantified in renal biopsy, and in 18 RVH patients, PTC-EMPs were measured again 3 months after continued medical therapy with or without stenting (n=9 each). Renal vein and systemic PTC-EMPs levels were not different among the groups, whereas their urinary levels were elevated in both RVH and EH vs. HVs (56.8±12.7 and 62.8±10.7 vs. 34.0±17.8%, both p≤0.001). Urinary PTC-EMPs levels correlated directly with blood pressure and inversely with estimated glomerular filtration rate. Furthermore, in RVH, urinary PTC-EMPs levels correlated directly with stenotic-kidney hypoxia, histological PTC count, and fibrosis, and inversely with cortical perfusion. Three months after treatment, the change in urinary PTC-EMPs levels correlated inversely with a change in renal function (r=-0.582, p=0.011). Therefore, urinary PTC-EMPs levels are increased in hypertensive patients, and may reflect renal microcirculation injury, whereas systemic PTC-EMPs levels are unchanged. Urinary PTC-EMPs may be useful as novel biomarkers of intrarenal capillary loss.