

## Department of Internal Medicine

### Division of Nephrology and Hypertension

---

Takashi Yokoo, *Professor*  
Makoto Ogura, *Associate Professor*  
Kazushige Hanaoka, *Assistant Professor*  
Nobuo Tsuboi, *Assistant Professor*

Keitaro Yokoyama, *Associate Professor*  
Yoichi Miyazaki, *Associate Professor*  
Masato Ikeda, *Assistant Professor*  
Ichiro Ohkido, *Assistant Professor*

#### General Summary

Our department is one of the largest nephrology departments in Japan and includes all subspecialties of nephrology, i.e., from early chronic kidney disease with proteinuria to dialysis and kidney transplantation. Therefore, our research groups are investigating diverse subjects and aim to eventually find new therapeutic strategies and mechanisms of disease progression, which may help decrease the number of patients with end-stage renal diseases.

#### Research Activities

##### *Studies on immunoglobulin A nephropathy*

We demonstrated that steroid pulse therapy with tonsillectomy had an independent effect on the disappearance of proteinuria (Nephrol Dial Transplant 2014). We also analyzed the prognostic factor that affects the recurrence of immunoglobulin A nephropathy after steroid pulse therapy (under revision).

##### *Studies on low glomerular density in glomerular diseases*

Our studies showed that low glomerular density was strongly associated with the prognosis of various glomerular diseases (Clin Kidney J 2014, Hypertens Res 2015, Am J Hypertens 2015). Collaborative research about the estimation of nephron numbers in Japanese patients is in progress.

##### *Studies of hypertension and renal damage*

We analyzed renal histopathological findings in relation to ambulatory blood pressure values. Only the severity of interstitial damage exhibited a significant association with an increased value of ambulatory blood pressure (Hypertens Res 2015).

##### *Studies of chronic kidney disease-mineral and bone disease*

In basic research, we evaluated the effects of chronic kidney disease on the transcription factor glial cells missing 2 (*Gcm2*), which is indispensable to parathyroid gland and epigenetic variations.

Also, we analyze functions of glial cells missing 1 (*Gcm1*), which is a homolog of *Gcm2*. In a clinical study we clarified that ferric citrate hydrate, a novel iron-based phosphate binder, decreased concentrations of fibroblast growth factor 23. Because novel iron-based

phosphate binders increase serum ferritin levels (CJASN 2014), we evaluate that there is no association between mortality and anemia related parameters included ferritin, hemoglobin, and transferrin saturation among patients undergoing dialysis with the registry data of the Japanese Society for Dialysis Therapy (NDT 2014).

#### *Studies of peritoneal dialysis*

We confirmed the availability of combined therapy with peritoneal dialysis and hemodialysis using outcomes of combined therapy in a cohort of more than 100 patients (Blood Purification 2014). Moreover, we found that survival outcome of combined therapy was not worse than that of peritoneal dialysis or hemodialysis (Blood Purification 2014). We are evaluating peritoneal injury using laparoscopy.

#### *Study of renal transplantation*

1. We investigated the significance of caveolin 1 immunoreactivities in peritubular capillaries in patients who have undergone the transplantation of kidney from living related donors. 2. We analyzed the effect of medullary ray injury early after kidney transplantation on the graft survival. 3. We examined the difference between ABO-compatible and ABO-incompatible kidney transplantation regarding cytomegalovirus infection.

#### *Renal protective effects of azilsartan in adenine-induced renal failure model rats*

We examined the mechanism of the renal protective effects of azilsartan in a rat model of renal failure. Daily urinary sodium excretion was decreased in the nonmedication group, and azilsartan suppressed the decreasing sodium excretion. Sympathetic nerve activity was elevated by azilsartan. Blood pressure was not elevated in this experimental model; therefore, because azilsartan greatly suppressed blood pressure, it did not suppress sympathetic nervous system, as previously reported.

#### *Central blood pressure and activity of the renin-angiotensin-aldosterone system*

We examined the relationship between central blood pressure (CBP) and the renin-angiotensin-aldosterone system in patients with primary aldosteronism and essential hypertension. The gap between central blood pressure (CBP) and brachial systolic blood pressure (SBP) increased with the plasma aldosterone concentration in essential hypertension. In primary aldosteronism, the CBP-SBP gap was significantly higher than that in essential hypertension. This study suggests that, even if SBP is well controlled, the kinetics of CBP indicate a different tendency from SBP as the renin-angiotensin-aldosterone system increases and might increase the risk of cardiovascular events.

#### **Publications**

**Yokoyama K.** New Developments in CKD-MBD. New aspects in phosphate binders (in Japanese). *Clin Calcium*. 2014; **24**: 1815-23.

**Okamoto H, Haruhara K, Kamejima S, Mafune H, Manabe M, Kanzaki G, Mashiko H (Mashiko Hosp), Yokoo T.** Is granular formulation of lanthanum carbonate more effective than chewable tab-

lets? *Ther Apher Dial*. 2014; **18** Suppl 1: 23-7.

**Maruyama Y, Yokoyama K, Nakayama M, Higuchi C, Sanaka T, Tanaka Y, Sakai K, Mizuiri S, Otsuka Y, Kuriyama S, Maeba T, Iwasawa H, Nakao T, Hosoya T (Tokyo Women's Med Univ, Toho Univ, Asao Kidney Clin, Tokyo Med Univ); EARTH (Evaluation of**

**the Adequacy of Renal replacement Therapy) study group.**

Combined therapy with peritoneal dialysis and hemodialysis: a multicenter retrospective observational cohort study in Japan. *Blood Purif.* 2014; **38**: 149-53.

**Sugano N, Yokoyama K, Kato N (Shinagawa Jin Clin), Hara Y, Endo S, Mitome J, Kin T (Kawagoe Ekimae Clin), Tokudome G, Kuriyama S, Hosoya T, Yokoo T.** Monitoring of body water composition by the simultaneous use of bio-electrical impedance analysis and Crit-Line® during hemodialysis. *Clin Exp Nephrol.* 2014; **18**: 944-51.

**Kobayashi A, Yamamoto I, Nakada Y, Kidoguchi S, Matsuo N, Tanno Y, Ohkido I, Tsuboi N, Yamamoto H, Yokoyama K, Yokoo T.** Successful treatment of BK virus nephropathy using therapeutic drug monitoring of mycophenolic acid. *Nephrology (Carlton).* 2014; **19** Suppl 3: 37-41.

**Okabe M, Miyazaki Y, Niimura F, Pastan F, Nishiyama A, Yokoo T, Ichikawa I, Matsusaka T** (<sup>1</sup>Tokai Univ, <sup>2</sup>Lab Mol Biol, <sup>3</sup>Kagawa Univ, <sup>4</sup>Vanderbilt Univ Med Ctr). Unilateral ureteral obstruction attenuates intrarenal angiotensin II generation induced by podocyte injury. *Am J Physiol Renal Physiol.* 2015; **308**: F932-7. Epub 2015 Feb 11.

**Nakada Y, Yamamoto I, Kobayashi A, Mafune A, Yamakawa T, Matsuo N, Tanno Y, Ohkido I, Yamamoto H, Yokoyama K, Yokoo T.** Acute vascular rejection during antituberculosis therapy in a kidney transplant patient. *Nephrology (Carlton).* 2014; **19** Suppl 3: 27-30.

**Kurashige M, Hanaoka K, Imamura M, Udagawa T, Kawaguchi Y, Hasegawa T, Hosoya T, Yokoo T, Maeda S** (<sup>1</sup>RIKEN Ctr). A comprehensive search for mutations in the PKD1 and PKD2 in Japanese subjects with autosomal dominant polycystic kidney disease. *Clin Genet.* 2015; **87**: 266-72.

**Yamanaka S, Yokote S, Yamada A, Katsuoka Y, Izuhara L, Shimada Y, Omura N, Okano HJ, Ohki T, Yokoo T.** Adipose tissue-derived mesenchymal stem cells in long-term dialysis patients display downregulation of PCAF expression and poor angiogenesis activation. *PLoS One.* 2014; **9**: e102311.

**Haruhara K, Tsuboi N, Koike K, Fukui A, Miyazaki Y, Kawamura T, Ogura M, Yokoo T.**

Renal histopathological findings in relation to ambulatory blood pressure in chronic kidney disease patients. *Hypertens Res.* 2015; **38**: 116-22.

**Furuya M, Yamamoto I, Kobayashi A, Nakada Y, Sugano N, Tanno Y, Ohkido I, Tsuboi N, Yamamoto H, Yokoyama K, Yokoo T.** Plasma cell-rich rejection accompanied by acute antibody-mediated rejection in a patient with ABO-incompatible kidney transplantation. *Nephrology (Carlton).* 2014; **19** Suppl: 31-4.

**Tanabe N, Takane K, Yokoyama K, Tanno Y, Yamamoto I, Ohkido I, Yokoo T.** Dialysate temperature adjustment as an effective treatment for baroreflex failure syndrome in hemodialysis patient. *BMC Nephrol.* 2014; **15**: 151.

**Haruhara K, Tsuboi N, Nakao M, Koike K, Fukui A, Miyazaki Y, Kawamura T, Ogura M, Yokoo T.** A case of glomerulopathy associated with the vascular endothelial growth factor inhibitor bevacizumab (in Japanese). *Nihon Jinzo Gakkaishi.* 2014; **56**: 600-5.

**Kuriyama S, Nakano T, Maruyama Y, Sugano N, Takane K, Suetsugu Y, Takahashi Y, Kobayashi C, Nishio S, Takahashi D, Kidoguchi S, Ichida K, Ohno I, Hosoya T, Yokoo T.** Relationship between serum uric acid levels and muscle strength/volume: a new insight from a large-scale survey (in Japanese). *Nihon Jinzo Gakkaishi.* 2014; **56**: 1260-9.

**Saikawa H, Yamaguchi Y, Ohno I, Hosoya T, Yokoo T.** Relationship between serum uric acid and renal histopathology in patients with chronic kidney disease (in Japanese). *Tsufu to Kakusan Taisha.* 2014; **38**: 109-16.

**Saikawa H, Ichida K, Ohno I, Hosoya T, Yokoo T.** Clinical feature and ABCG2 gene mutation of gouty kidneys diagnosed by abdominal ultrasonography (in Japanese). *Tsufu to Kakusan Taisha.* 2014; **38**: 117-28.

## Reviews and Books

**Yokoo T.** Kidney regeneration with stem cells: an overview. *Nephron Exp Nephrol.* 2014; **126**: 54-8.

**Tsuboi N, Kanzaki G, Koike K, Kawamura T, Ogura M, Yokoo T.** Clinicopathological assessment of the nephron number. *Clin Kidney J.* 2014; **7**: 107-14.