The change in glomerular volume and its clinicopathological impact after kidney transplantation

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【*Background and Aim*】

Both immunological and nonimmunological factors affect graft function after kidney transplantation. Such factors include acute rejection, calcineurin inhibitor toxicity, and the recurrence of glomerulonephritis. Glomerular enlargement or glomerular sclerosis due to glomerular hyperfiltration secondary to increased renal blood flow may also affect graft function. Although the glomerular volume (GV) in baseline biopsy specimens predicts late allograft function, the relationship between allograft function and annual changes in GV after kidney transplantation is unclear. We investigated the change in GV after kidney transplantation and its clinicopathological relationship with graft function. Glomerular density (GD), a factor associated with GV, was also investigated.

【*Methods*】

The study enrolled 23 patients who underwent transplantations from 2005 to 2012. All patients had stable kidney function without an episode of rejection or any complications that decreased graft function. We measured GV using the Weibel-Gomez method and GD using 0- and 1-hour biopsy specimens (baseline controls) and 1-year biopsy specimens as follows: $GV = (GA)^{3/2} \times \beta/d$ and GD = nonsclerotic glomerular number/renal cortical area. We also investigated the association between changes in the GV and GD and various clinical parameters, including graft function, proteinuria, and effective renal plasma flow (ERPF). The ERPF was calculated from a MAG 3 renogram.

【*Result*】

The patients' clinical characteristics are shown in Table 1. The ERPF was significantly increased 1 year after kidney transplantation. In contrast, the level of proteinuria was significantly decreased (Figure 1). Although the GD did not change, GV was significantly increased 1 year after kidney transplantation (Figure 2). Neither the baseline nor the 1-year GV and GD were correlated with the estimated glomerular filtration rate (eGFR), proteinuria, or ERPF at 1 year. On the other hand, ⊿GV was correlated with ⊿proteinuria (1 year − 1 month after transplantation) ($P < 0.05$, $r_s = -0.467$) and eGFR at 1 year ($P < 0.05$, $r_s = -0.449$) (Figure 3).

Table 1: Clinical characteristics

Variable	Mean±SD	Range
Donor age (y)	56.9±9.45	(36-69)
Donor gender (male/female)	10/13	-
Recipient age (y)	36.0±9.54	(22-50)
Recipient gender (male/female)	15/8	-
Body Mass Index (kg/m2)	21.3±4.31	(16.5-35.7)
Body Surface Area (m2)	1.65±0.18	(1.33-2.02)
SBP (mmHg)	129.3±11.8	(110-152)
DBP (mmHg)	77.7±9.96	(58-96)
Graft weight (g)	175.3±57.1	(120-340)

Figure 1: The changes of graft function, proteinuria and ERPF

	Baseline	at 1 year	P value
Serum Creatinine (mg/dl)	1.36±0.07	1.34±0.07	NS
eGFR (ml/min/1.73m2)	48.7±2.99	48.3±2.64	NS
Proteinuria (mg/day)	136.9±19.7	77.3±13.4	<0.05
ERPF (mL/min/1.73m²) (n=15)	208.1±9.19	259.8±10.6	<0.01

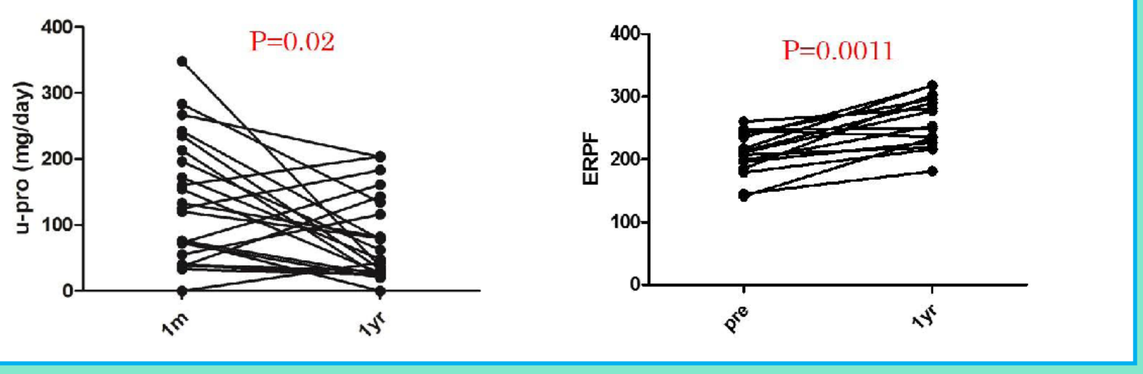


Figure 2: The changes of GD and GV after transplantation

	baseline	at 1 year	p value
GV (μm³)	2464524±165369	3164306±226448	<0.01
GD	2.24335±0.14563	1.98904±0.18668	NS

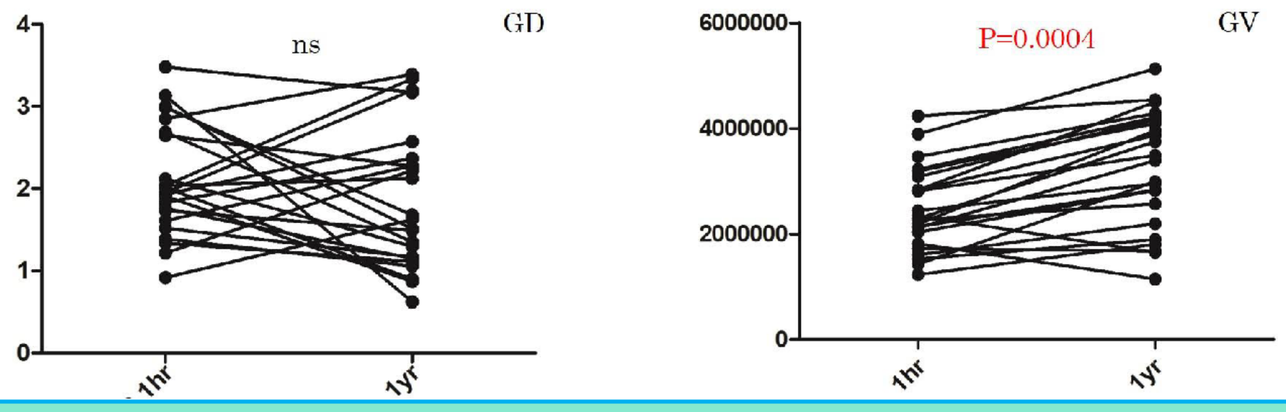
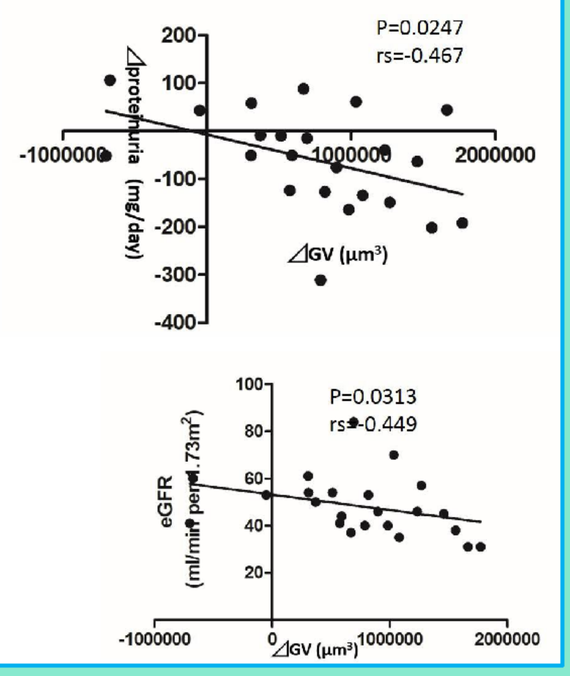


Figure 3: The correlations between ⊿GV and clinical parameters

	⊿GV p-value
age	ns
s-BP	ns
BMI	ns
BSA	ns
graft weight	ns
estimated GFR at 1year (mL/min/1.73m²)	0.0313
urinary protein excretion at 1 year (mg/day)	ns
⊿urinary protein excretion (1yr - 1m: mg/day)	0.0247
ERPF at 1 year	ns
⊿ERPF	ns



【*Discussion*】

- ***Glomerular enlargement and kidney function***

A previous report demonstrated that at 4 months after transplantation, the GV was correlated with the creatinine clearance rate. Furthermore, patients with chronic allograft nephropathy (CAN) had smaller glomeruli than did patients without CAN, and the glomeruli of patients with CAN did not enlarge. Based on these observations, the authors suggested that glomerular enlargement was a necessary condition for renal adaptation. In our study, although ⊿GV was correlated with a lower eGFR 1 year after kidney transplantation, additional follow-up is needed to determine the long-term effect of glomerular enlargement on graft function.

- ***Glomerular enlargement and proteinuria***

Urinary protein excretion was significantly lower at 1 year than at 1 month after transplantation, and patients with glomeruli that could enlarge showed a greater decrease in their proteinuria. Glomerular enlargement may be a renal adaptation mechanism and might be related to the improvement in proteinuria after kidney transplantation. On the other hand, it is well known that hyperfiltration induces glomerular enlargement and consequently leads to secondary focal segmental glomerular sclerosis (FSGS) with massive proteinuria. Indeed, we reported a case of secondary FSGS in a patient with enlarged glomeruli, the cause of which was thought to be hyperfiltration induced by an imbalance in body size and uncontrolled diabetes. Thus, it is important to identify which factors will break the capacity of glomeruli to enlarge as a renal adaptation mechanism.

- ***Glomerular enlargement and ERPF***

Because the ERPF was significantly higher at 1 year than at 1 month after transplantation, we assumed that ⊿GV was also related to the ERPF or ⊿ERPF. However, there were no significant correlations between them. Both increased renal blood flow and other various factors that increase intraglomerular pressure might be associated with glomerular enlargement.

【*Conclusion*】

Glomerular enlargement may be a form of renal adaptation to glomerular hyperfiltration after kidney transplantation.

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