Clinical Investigation Into Plasma Neutrophil Gelatinase-Associated Lipocalin and Body Adipose Tissue Associated With Remaining Renal Function in Living Kidney Donor

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ABSTRACT

Objective. Plasma neutrophil gelatinase-associated lipocalin (pNGAL) is known to increase in proportion to the degree and period of renal damage. This study aimed to evaluate the clinical relevance of pNGAL and body adipose tissue to remaining renal function in living kidney donors.

Methods. Between July 2013 and February 2015, 75 live kidney donors were enrolled. Visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT) and VAT/SAT ratio were measured in preoperative CT scan which performed before surgery. We analyzed the correlation among the variables (VAT, SAT, and VAT/SAT ratio), eGFR and pNGAL. ΔpNGAL-max(=Maximum pNGAL-measures), ΔpNGAL-min(=Minimum pNGAL-measures), ΔeGFR-max(=Maximum eGFR-measures) and ΔeGFR-min(=Minimum eGFR-measures) were also analyzed.

Results. The highest value of pNGAL (207.46 ± 76 ng/mL) was observed on postoperative day 7, and the lowest value of eGFR (57.52 ± 11.20 mL/min/1.73 m^2) was also measured on postoperative day 7. A significant correlation was found between ΔpNGAL, VAT, and VAT-to-SAT ratio. Moreover, a significant correlation between ΔpNGALmin and ΔeGFRmin was revealed. Also, VAT-to-SAT ratio was correlated with ΔeGFRmin during the all of the follow-up periods, and it was also correlated with ΔpNGALmin until postoperative day 3.

Conclusion. There was a correlation between the elevation of pNGAL until post-operative day 5 and the decrease of eGFR after living donor nephrectomy. VAT-to-SAT ratio had a significant correlation with both ΔpNGALmin and eGFRmin. Given the metabolism of pNGAL, the increase of pNGAL seemed to be affected as a consequence of body adipose tissue.

KIDNEY transplantation is an important role in the treatment of end-stage renal disease. Because an organ from living kidney donor provides better graft function than those from deceased donors, it has become a significant source for kidney transplantation [1,2]. The safety of living donors postnephrectomy has become a subject of study throughout the years. Higher occurrences of end-stage renal disease in living donors compared with matched healthy persons have been demonstrated [2,3]. Furthermore, an increase in the long-term risk of all-cause mortality in donors is more likely compared with healthy controls [2,4]. For these reasons, in addition to inflicting an injurious

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procedure on a healthy donor candidate, living donor criteria should prioritize donor safety as it continues to accommodate increasing demand. Efforts must be made to continuously update the donor selection criteria [5].

A reduction in nephrons after donor nephrectomy causes compensatory hyperfiltration of the remaining contralateral kidney [6]. In the absence of severe sequelae during this period, the increase in the level of acute kidney injury markers may be used in the management of the remaining kidney [6–9]. A reported novel marker of acute kidney injury, plasma neutrophil gelatinase-associated lipocalin (pNGAL), has been shown to be a useful early predictor of AKI [9–11]. As an indicator of significant kidney injury, urine and pNGAL have been shown to have similar predictive value [9,12,13].

A significant relationship between the baseline body mass index (BMI) and the risk of chronic kidney disease has been reported [9,14]. The increased amount of visceral fat tissue and other related disorders of homeostasis can lead to an increased secretion of proinflammatory cytokines and hormones leading to both acute and chronic changes in the kidney [15].

Our study investigated the possible associations among pNGAL and body adipose tissue with the residual renal function postnephrectomy in living kidney donors.

MATERIALS AND METHODS

The study protocol was reviewed and approved by the Institutional Review Board of our institution, and all subjects supplied written informed consent. Between July 2013 and February 2015, 75 living kidney donors were enrolled in this study. All donor nephrectomies were performed by 2 surgeons by video-assisted mini-incision surgical technique [16].

Preoperative evaluation was done including routine blood tests, diethylenetriaminepentaacetic acid renal scans, and computed tomography (CT) angiography for all living kidney donors. After surgery, lab tests were performed daily for 3 days until the patients were discharged.

We followed the patients for 6 months postoperatively. At 6 months, we identified the donors who showed estimated glomerular filtration rates (eGFR) lower than 60 mL/min/1.73 m^2 as the chronic kidney disease group. eGFRs were calculated using the Modification of Diet in Renal Disease formula. BMI was calculated by dividing the body weight in kilograms by the height in meters squared.

CT scans have been reported as the gold standard method for estimating visceral adiposity. Visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) were measured at the level of the umbilicus using CT according to a procedure described and validated previously. After the border of the intra-abdominal cavity was outlined on the CT image, the cross-sectional surface areas of the visceral fat and subcutaneous fat were calculated by a single urologist using Xelis CT software (INFINITT, Seoul, Korea), which electronically determined the adipose tissue area by setting the attenuation values for a region of interest within a range of −250 to 50 Hounsfield (Fig 1) [17].

Continuous data are presented as the mean ± standard deviation and categorical data as numbers (%). We used a linear mixed model analysis for repeated pNGAL measurements to determine the time

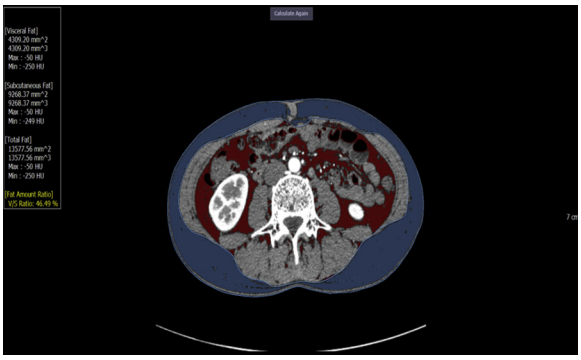

Fig 1. Axial computed tomography images of the level of the umbilicus used for assessment of abdomen adiposity. The red region represents the visceral adipose tissue, and the blue area represents the subcutaneous adipose tissue.

to stabilization. Also, we analyzed the correlation among the variables (VAT, SAT, and VAT-to-SAT ratio), eGFR, and pNGAL. The maximum pNGAL measures, minimum pNGAL measures (ΔpNGALmin), maximum eGFR measures, and minimum eGFR measures (ΔeGFRmin) were also analyzed. The correlation between pNGAL level, donor renal function, and adipose tissue was evaluated with Pearson linear correlation analysis. All data analyses were processed using SPSS software version 23.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA).

RESULTS

The study population consisted of 75 living donors with a mean age was 42.4 years who were followed for 6 months. Baseline demographic and characteristics of donors are summarized in Table 1. The mean BMI was 23.5 ± 2.6 kg/m^2. There were 33 male donors (44.0%) and 42 female donors (56.0%). Among the 75 surgeries, 13 (17.3%) were

Table 1. General Study Population Characteristics

No. of Donors	75
Sex (%)	
Male	33 (44)
Female	42 (56)
No. laterality (%)	
Left	62 (82.7)
Right	13 (17.3)
Age (y), mean ± SD	42.4 ± 11.3
BMI (kg/m^2), mean ± SD	23.6 ± 2.7
Preoperative eGFR (mL/min/1.73 m^2), mean ± SD	103.0 ± 19.7
ΔeGFR (mL/min/1.73 m^2), mean ± SD	48.52 ± 13.7
Preoperative pNGAL (ng/mL), mean ± SD	64.8 ± 23.1
pNGAL maximum (ng/mL), mean ± SD	208.5 ± 78.0
ΔpNGAL (ng/mL), mean ± SD	147.3 ± 69.3
Visceral adipose tissue (cm^3), mean ± SD	73.0 ± 41.6
Subcutaneous adipose tissue (cm^3), mean ± SD	117.5 ± 70.2
VAT-to-SAT ratio, mean ± SD	0.74 ± 0.54

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; pNGAL, plasma neutrophil gelatinase-associated lipocalin; SAT, subcutaneous adipose tissue; SD, standard deviation; VAT, visceral adipose tissue.