

# Prospective Measurement of Urinary Microalbumin in Living Kidney Donor Nephrectomy: Toward Understanding the Renal Functional Recovery Period

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## Abbreviations and Acronyms

CKD = chronic kidney disease

DTPA = diethylenetriamine pentaacetic acid

eGFR = estimated glomerular filtration rate

IB = implantation biopsy

IgA = immunoglobulin A

MA = microalbuminuria

MDRD = Modification of Diet in Renal Disease

UACR = urinary albumin-to-creatinine ratio

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Study received institutional review board approval.

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**Purpose:** We determined the clinical implications of perioperative urinary microalbumin excretion in relation to renal function after living donor nephrectomy.

**Materials and Methods:** Between August 2010 and January 2013, 259 donors undergoing live donor nephrectomy were enrolled in the study. The donor urinary albumin-to-creatinine ratio was measured perioperatively, and changes in perioperative urinary albumin-to-creatinine ratio and the implications of preoperative microalbuminuria (urinary albumin-to-creatinine ratio 30 mg/gm or greater) were investigated. The relationships between perioperative urinary albumin-to-creatinine ratio and recovery of renal function and implantation biopsy histology were also analyzed.

**Results:** Mean  $\pm$  SD preoperative urinary albumin-to-creatinine ratio was  $7.1 \pm 12.7$  mg/gm. The urinary albumin-to-creatinine ratio was increased after 1 day ( $24.7 \pm 18.9$  mg/gm,  $p < 0.001$ ) and stabilized after 1 month ( $10.3 \pm 10.7$  mg/gm,  $p < 0.001$ ). Preoperative microalbuminuria was not associated with perioperative estimated glomerular filtration rate during a followup period of 6 months but was associated with histological abnormalities. Donors with a higher urinary albumin-to-creatinine ratio before donation, even in the normal range, consistently had an increased postoperative urinary albumin-to-creatinine ratio. A ROC curve analysis showed that age, preoperative estimated glomerular filtration rate and 1-month postoperative urinary albumin-to-creatinine ratio were highly predictive of delayed recovery of renal function (AUC 0.884,  $p < 0.001$ ). The 1-month postoperative urinary albumin-to-creatinine ratio was associated with delayed recovery of renal function (OR 1.05 for each 0.1 mg/gm increase,  $p = 0.021$ ).

**Conclusions:** Donors with higher preoperative urinary albumin-to-creatinine ratio levels require close observation because there is a greater possibility of microalbuminuria developing after donation even if the ratio is within the normal range. A higher urinary albumin-to-creatinine ratio was also associated with delayed recovery of renal function and histological abnormalities.

**Key Words:** kidney transplantation, albuminuria, delayed graft function, nephrectomy, living donors

KIDNEY pathology or damage due to acute injury can lead to proteinuria.<sup>1</sup> Proteinuria can be measured by

24-hour urine collection, which is difficult and cumbersome for the donor. Urinary microalbumin, a potential

substitute for measuring proteinuria, is more convenient because it can be checked in spot urine samples.<sup>2</sup> Currently microalbuminuria is more frequently measured because precise and simple methods for estimating microalbumin in urine are available.<sup>3</sup> It is usually expressed as the urinary albumin-to-creatinine ratio to compensate for hydration status.<sup>4</sup> Normally UACR is less than 30 mg/gm.<sup>5</sup>

Numerous studies have been performed to investigate the implications of MA. McCullough et al concluded that albuminuria is a typical marker of CKD in young adults, whereas reduced estimated glomerular filtration rate is the most frequent abnormality in elderly people with CKD.<sup>6</sup> A study in a large Canadian cohort demonstrated that MA is a risk factor for end stage renal disease even in patients whose eGFR is relatively normal (greater than 60 ml/minute/1.73 m<sup>2</sup>).<sup>7</sup> Moreover, a UACR value greater than 10 mg/gm is a predisposing factor for all cause mortality and cardiovascular mortality in the general population.<sup>8</sup>

A reduction in nephrons after donor nephrectomy causes compensatory hyperfiltration of the contralateral remnant kidney, which can cause proteinuria.<sup>9</sup> MA can also easily occur after kidney donation.<sup>10</sup> However, to our knowledge no information on the significance of preoperative MA in kidney donors is available, and few studies evaluating the association between perioperative urinary albumin excretion and recovery of donor renal function have been reported in the literature.<sup>9</sup> Therefore, this study was conducted to assess the relationship between MA and kidney donor renal function. Our hypotheses were 1) donors with MA before nephrectomy may have worse remnant renal function, 2) MA is associated with delayed recovery of renal function and 3) MA can reflect histological abnormalities in implantation biopsies.

## MATERIALS AND METHODS

A total of 259 donors who underwent living donor nephrectomy at our institution between August 2010 and January 2013 were enrolled in the study. Donor data were prospectively recorded and archived. All donor nephrectomies were performed by 2 surgeons using video-assisted mini-incision surgery as previously reported.<sup>11-13</sup> All donors underwent DTPA renal scans and computerized tomography angiography, and provided 24-hour urine samples. Donors with a 24-hour urine creatinine clearance less than 80 ml/minute/1.73 m<sup>2</sup> and an eGFR less than 80 ml/minute/1.73 m<sup>2</sup> on preoperative examinations were excluded from the matched living kidney transplantation in accordance with our institutional donor criteria. The institutional review board approved this study (4-2013-0421) and all subjects provided written, informed consent.

## Renal Function and Urinary Microalbumin

Urinary microalbumin and serum creatinine were determined for all donors preoperatively, on postoperative day 1, and 1, 3, and 6 months after the procedure. Renal function was estimated with the MDRD formula. Urinary microalbumin was measured by an immunoturbidimetric method using an AU680 automated chemistry analyzer (Beckman Coulter, Inc., Brea, California). Because hydration status or dilution of urine can affect the concentration of urinary microalbumin, UACR was used as a measure of MA.<sup>4</sup> The normal range of UACR is defined as less than 30 mg/gm.<sup>5</sup> Differences between donors with MA before the operation and normal donors were investigated. Because some studies have reported that UACR values greater than 10 mg/gm are clinically important, despite being in the normal range,<sup>8,14</sup> we classified the donors into those with an increased UACR (10 mg/gm or greater) and those with UACR less than 10 mg/gm. Delayed recovery of renal function was defined as MDRD-eGFR less than 60 ml/minute/1.73 m<sup>2</sup> at 6 months after kidney donation.<sup>15</sup>

## Implantation Biopsy

Histological examinations were performed only in donors who agreed to IB before donor nephrectomy. After transplantation of the procured allograft IB was performed in the operating theater immediately before reperfusion. All biopsy samples were examined by light microscopy, and additional immunofluorescence and electron microscopic analyses were performed if needed.<sup>16</sup> Histological abnormalities were scored according to the 2007 Banff classification.<sup>17</sup> Global glomerulosclerosis was defined as at least 5% of all observed glomeruli showing sclerotic changes. The median number of observed glomeruli was 17. Unexpected IgA nephropathies were also counted.

## Statistical Analysis

Continuous data are presented as means  $\pm$  SD. Differences between the 2 groups were analyzed using Student's t-test for continuous variables and Fisher's exact test and Pearson's chi-square test for categorical variables. Paired samples were analyzed using the paired Student's t-test. Logistic regression analysis was performed to model the value of different parameters in predicting delayed recovery of kidney function. A value of  $p < 0.05$  was considered statistically significant. Statistical analyses were performed using SPSS® version 20.0.

## RESULTS

### Donor Characteristics

Donor characteristics are summarized in the table. Mean age was  $40.6 \pm 11.6$  years, 40.9% of donors (106) were male and most donor nephrectomies (82.2%) were performed on the left side. No donors had diabetes but 8 had hypertension that was well controlled with medication. Mean preoperative MDRD-eGFR was  $96.5 \pm 16.7$  ml/minute/1.73 m<sup>2</sup>. No donors had proteinuria in preoperative 24-hour urine samples.

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