Does Low Birthweight Have an Impact on Living Kidney Donor Outcomes?

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ABSTRACT

Introduction. Because nearly 30,000 people worldwide become living kidney donors each year, donor safety is of the utmost importance. Recent studies have shown that living kidney donation is associated with an increased relative risk for end-stage renal disease (ESRD). It is essential to determine which donors will be more likely to develop ESRD. One of the risk factors for ESRD in living kidney donors is hypertension and, because there are studies demonstrating that low birthweight is a risk factor for developing hypertension in adult life, we hypothesized that donors with low birthweight may be at higher risk of developing renal disease after donation.

Methods. Seventy-three living kidney donors were examined. Donors were divided into 2 cohorts: a group with low birthweight and group with normal birthweight. We checked whether the donor birthweight has an impact on the outcome of donor renal function and on the development of hypertension.

Results. Hypertension was observed statistically more frequent in the group with low birthweight ($P = .003$).

Conclusion. Glomerular filtration rate before kidney donation was found to be lower in the low-birthweight group.

COMPARED with deceased donor kidney transplantation, living donor kidney transplantation is associated with much better graft outcome, especially when done pre-emptively. Due to these excellent outcomes and the persisting deceased donor organ shortage, it has become the preferred approach to renal replacement therapy. Because nearly 30,000 people worldwide become living kidney donors each year [1], donor safety is of the utmost importance. Living kidney donation is a safe procedure, and minimally invasive techniques are predominantly used, with comparable outcomes for the different techniques [2]. However, recent studies have indicated that living kidney donation is associated with an increased relative risk for end-stage renal disease (ESRD) [3,4]. It is essential to determine which donors are more likely to develop ESRD. Hypertension is recognized to elevate the risk of developing chronic and end-stage kidney disease [5]. Although well-controlled hypertension is not a contraindication to becoming a living kidney donor, some studies [3,6] have suggested that hypertension is one of the risk factors for ESRD in living kidney donation.

Studies have demonstrated that low birthweight (LBW) is a risk factor for development of hypertension in adult life [7]. LBW, defined as <2.5 kg [8], regardless of gestational age, has also been linked with a higher risk of albuminuria and reduced glomerular filtration rate (GFR).

Living kidney donation results in a reduced renal (nephron) mass, which may lead to a diminished compensation capacity for renal injury [5], and hence higher prevalence of hypertension and renal disease in LBW patients [9].

As potential living kidney donors are sometimes those with LBW, we hypothesized that these people may be at

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Table 1. Donor Characteristics

	All Donors (n = 60)	LBW Donors (n = 17)	NBW Donors (n = 43)
Age (years)	46 (24–72)	49 (29–72)	42 (24–65)
Male, n (%)	23 (38)	2 (12)	21 (48)
BMI (kg/m^2)	25 (19–32)	24 (19–30)	25 (19–32)
≤25, n (%)	26 (43)	9 (53)	17 (39)
26–30, n (%)	30 (50)	7 (41)	23 (53)
>30, n (%)	4 (7)	1 (6)	3 (8)
Smoking, n (%)	13 (21)	3 (17)	10 (23)

Abbreviations: BMI, body mass index; LBW, low birthweight; NBW, normal birthweight.

higher risk of developing renal disease after the donation. Individuals born with LBW are recompensed for their lower nephron mass by hypertrophy of single nephrons, which is expressed by an increase in single nephron GFR. In the event of a unilateral nephrectomy (such as a living donor nephrectomy) in patients with a normal birthweight, many functional adaptations similarly take place in the remaining nephrons [10,11]. Potentially, it is possible that, in those with LBW who undergo donor nephrectomy, the compensatory mechanism is insufficient, thus leading to ESRD.

MATERIALS AND METHODS

We examined a cohort of living kidney donors (n = 73) who underwent a laparoscopic donor nephrectomy at the Department of General Surgery and Transplantation, Medical University of Warsaw, Warsaw, Poland, between January 2012 and December 2015. All potential donors were screened according to current guidelines [12–14]. Thirteen donors who were lost to follow-up (<1 year follow-up) or with missing birthweights were excluded from the study. This resulted in a group of 60 Caucasian living kidney donors, both related and nonrelated (all left-sided donor nephrectomies), who were followed up for at least 12 months, with 33 of them observed for at least 24 months after donor nephrectomy.

The donor data analyzed included: donor birthweight (in grams; patients were asked to verify this information from their birth records); age at time of donor nephrectomy; sex; current and former smoking status; presence of hypertension (all potential donors have ambulatory blood pressure monitored, and those accepted must have well-controlled hypertension with a maximum of 2 antihypertensive medications); body mass index (BMI, kg/m^2); blood and urine test results (previous nephrectomy and 12 and 24 months after kidney donation); serum creatinine concentration (mg/dL); estimated GFR (mL/min) (using the Cockroft-Gault formula); parathyroid hormone (PTH, ng/mL); calcium level (Ca^{2+}, mg/dL); level of phosphate (PO_4^{3-}, mg/dL); proteinuria (g/dL) and albuminuria (mg/dL); and albumin:creatinine ratio. Split kidney function was evaluated by renal scintigraphy.

Calculations of nephron data were performed according to the formula: nephron number per kidney = 869,959 + [(donor birthweight (kg) − 3.34 kg) × 257,426] [7], and, as the mean predicted loss of glomeruli is 4500 per kidney per year between 18 and 70 years [8], the formula was adjusted for age as follows: nephron number per kidney − [4500 × (donor age − 18)].

Donors were divided into 2 cohorts: a group with LBW, and a control group with normal birthweight (NBW). We also aimed to determine whether donor birthweight has an impact on the outcome of donor renal function and on the development of hypertension.

Statistical tests were conducted using SPSS version 20.0 (IBM SPSS, Armonk, NY). $P < .05$ was considered significant. To determine the variability of the research variables over time (Ca^{2+}, PO_4^{3-}, proteinuria, albuminuria, PTH), taking into account the birthweight, analyses were performed in a scheme with repeated measurement (3) × 2, where 3 consecutive measurements of the variable in patients were treated as an intraobject factor (before donation and 12 and 24 months after surgery), whereas birthweight was an intergroup factor (NBW/NBW vs LBW/LBW). Because the general linear model in the repeated measurement scheme is relatively resistant to breaking the assumptions of the normality of the distribution and disturbance of equal number, the classical method of higher power was used; in each case, the variances in the variables were homogeneous, as shown by the Levene test. For calcium level, Mauchly's variance sphericity test was used and showed statistical significance [$\chi^2(2) = 9.06$, $P = .011$], which is why the test statistic was given with the correction for degrees of freedom; the value of the coefficient, $\varepsilon = 0.798$, suggested use of a Huynh-Feldt correction. For phosphate level and estimated GFR, the Greenhouse-Geisser correction was chosen [$\chi^2(2) = 17.53$, $P < .001$, $\varepsilon = .693$; and $\chi^2(2) = 24.60$, $P < .001$, $\varepsilon = 0.641$, respectively]. In other cases, the assumption of sphericity was not broken. To check the significance of the relationship between birthweight in the dichotomous and HA form, an independence test of 2 variables was carried out (chi-square test). The exact test result (likelihood ratio) based on the logistic regression method was used.

RESULTS

The group analyzed included 23 men (38.3%). Median age was 46 (range, 24–72) years at donor nephrectomy. Thirty-three donors were followed-up for 24 months and the remaining 27 were observed for at least 12 months, during

Table 2. Hypertension in the LBW and NBW Groups

Weight	Hypertension				
N (%)	No	Yes		No	Yes
NBW	91 (92.9)	7 (7.1)	Predonation	65 (90.3)	7 (9.7)
LBW	34 (73.9)	12 (26.1)	12 months postdonation	60 (83.3)	12 (16.7)

Abbreviations: LBW, low birthweight; NBW, normal birthweight.