Postdonation Anemia in Living Kidney Donors

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ABSTRACT

Background. The effect of nephrectomy on development of anemia in living kidney donation has not been well studied. We hypothesized that the remaining kidney volume and function after donation are determinants of hemoglobin (Hb) concentration and postdonation anemia (PDA).

Methods. We studied 398 living kidney donors (LKDs) who donated from January 2001 to December 2013. Demographic variables, hematologic variables, renal mass, and renal function were investigated as factors associated with PDA with the use of univariate and multivariable logistical regression analysis. Renal mass was determined from kidney volume measured with the use of computerized tomographic scans.

Results. Prevalence of PDA in LKDs was 11.8% at a median follow-up time of 601 days. In univariate analyses, PDA was more prevalent in women than in men (72% vs 28%; $P = .048$). Age and race were not associated factors. Kidney volume was lower in donors with PDA than in those without PDA (326 ± 52 mL vs 368 ± 70 mL; $P < .001$). Donors with and without PDA had similar predonation and postdonation glomerular filtration rates. In the multivariable logistic regression analysis, total kidney volume and predonation anemia remained as independent factors associated with PDA.

Conclusions. PDA is prevalent after living kidney donation, with donor kidney volume and predonation hemoglobin levels being independent determinants for PDA.

RENAL transplantation is considered to be the treatment of choice for patients with end-stage renal disease, and living kidney donation is known to be the superior form of transplantation compared with deceased donation because it offers better graft and patient survival [1]. Long-term outcomes of living kidney donors have become an important area of attention. It has been shown that renal excretory function is well preserved after nephrectomy owing to compensatory increase in function of the remaining kidney [2]. However, it is unclear whether non–filtration-related endocrine functions of the kidney, such as erythropoietin secretion and consequently hemoglobin production, are similarly preserved after donation.

The kidneys play a vital role in erythropoiesis, because the renal cortex is the primary source of erythropoietin production. Erythropoietin is a glycoprotein hormone that regulates the erythrocyte blood mass by stimulating red blood cell generation in the bone marrow [3]. The decrement of renal function as a consequence of nephron loss and interstitial fibrosis is associated with inadequate production of erythropoietin which leads to reduced erythrocytosis, with anemia being a common finding in the majority of patients with chronic kidney disease [4]. This matter is important because untreated anemia is associated with high risks of morbidity and mortality due mainly to cardiovascular disease and stroke [5].

Living kidney donors lose ~50% of renal mass with a similar loss in renal function immediately after nephrectomy. Renal function recovers to 60%–70% of baseline within 10–14 days and ~70%–80% in the long term owing to compensatory renal hyperfiltration [6–9]. Similarly, there is also compensatory hypertrophy of the remaining kidney

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Table 1. Donor Characteristics Associated with Postdonation Anemia: Univariate Analyses

Donor Characteristics	All Donors ($n = 398$)	Donors with No Anemia ($n = 351$; 88.2%)	Donors with Anemia ($n = 47$; 11.8%)	*P* Value
Age (y)	41 ± 11	41 ± 11	41 ± 9	.71
African American race	40 (10.1%)	33 (9.4%)	7 (14.9%)	.24
Female sex	235 (59.0%)	201 (57.3%)	34 (72.3%)	.048
BSA (m^2)	1.9 ± 0.3	1.9 ± 0.3	1.9 ± 0.2	.42
Total kidney volume (mL)	364 ± 70	368 ± 70	326 ± 52	<.001
Total kidney volume adjusted for BSA (mL/m^2)	332 ± 59	335 ± 60	308 ± 39	.010
Preoperative eGFR ($mL/min/1.73\ m^2$)	113 ± 31	113 ± 31	115 ± 34	.63
eGFR at last follow-up ($mL/min/1.73\ m^2$)	67 ± 14	67 ± 14	67 ± 14	1.00
Predonation anemia	23 (5.8%)	11 (3.1%)	12 (25.5%)	<.001
Preoperative Hb (g/dL)	14.0 ± 1.4	14.0 ± 1.1	11.4 ± 0.9	<.001
Preoperative hematocrit (%)	41.8 ± 3.2	42.1 ± 3.0	39.1 ± 3.6	<.001
Preoperative MCV (fL)	89 ± 5	89 ± 5	87 ± 5	.002
Preoperative MCHC (g/dL)	34 ± 1	34 ± 1	33 ± 1	<.001
Follow-up time (d)	394.0 (188.0–758.0)	400.0 (197.0–764.0)	254.0 (23.0–436.0)	.003
Smokers	57 (17.3%)	49 (16.3%)	8 (22.9%)	.44
Glomerulosclerosis	61 (20.6%)	55 (20.6%)	6 (20.7%)	.99
Arteriosclerosis	118 (39.9%)	101 (37.8%)	17 (36.2%)	.030
Interstitial fibrosis/tubular atrophy	41 (13.9%)	38 (14.2%)	3 (10.3%)	.56
Any chronic change	160 (54.1%)	141 (52.8%)	19 (65.5%)	.19

Values are presented as *n* (%), mean ± SD, or median (interquartile range).
Abbreviations: BSA, body surface area; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration.

after donation by 20%–30% [9,10]. Hypothetically, if erythropoietin production mirrors renal mass, donors may lose an average 25% of their endocrine capacity, which may predispose to postdonation anemia, especially if other risk factors were present and/or predonation hemoglobin levels were at the lower limit of normal. However, some small studies have reported no significant change in hematocrit or hemoglobin in living kidney donors after uninephrectomy [11,12]. Romero et al further concluded that erythropoietin levels in fact increases in the 1st 3 months in living kidney donors after donation and then remains constant [13]. Therefore, whether nephrectomy leads to postdonation anemia in living kidney donors remains unclear. Expanding our knowledge about anemia after donation in living kidney donors may have implications for informed consent and postdonation medical care. We hypothesized that the remaining kidney volume and function following donation are determinants of postdonation anemia.

METHODS

The Internal Review Board at the Cleveland Clinic approved the present study. A chart review was performed on 965 living kidney donors aged ≥18 years who donated from January 2001 to December 2013 at the Cleveland Clinic. We identified 398 living kidney donors with renal volume measurements and ≥1 year of follow-up after nephrectomy, assuming resolution of the acute surgical blood loss by then.

All living donors underwent a comprehensive clinical evaluation before donation. This included anthropometric measurements, blood pressure, and blood work, including serum creatinine. Living donors at our institution are followed at ~1 month, 3–6 months, and then annually for ≥2 years. During follow-up visits, donors underwent measurement of weight, blood pressure, hemoglobin, hematocrit, and serum creatinine routinely. Blood samples were collected before nephrectomy, on postoperative day 1, and during follow-up visits. Predonation glomerular filtration rate (GFR) and postdonation GFRs were calculated with the use of the Chronic Kidney Disease Epidemiology Collaboration equation. Serum creatinine levels were assayed with the use of a standardized isotope dilution mass spectrometry analyzer. Kidney mass of the remnant kidney was determined from kidney volume as measured with the use of multidetector computerized tomographic scans. Kidney volume was calculated in cubic centimeters (cc) and then adjusted for body surface area (mL/m^2) [14]. Kidney histology was obtained from implant biopsies routinely performed at the time of donation per protocol before reperfusion of the transplanted kidney. Chronic histologic changes in the implant biopsies were reported by 2 renal pathologists and were characterized by the following: >5% global glomerulosclerosis, >5% arteriosclerosis, and >5% interstitial fibrosis and tubular atrophy.

The primary outcome analyzed was the occurrence of postdonation anemia as defined by hemoglobin level after donation at the last follow-up. Anemia was defined with the use of the World Health Organization criteria of hemoglobin <12 g/dL in women and <13 g/dL in men. We investigated factors associated with postdonation anemia, including demographic variables, hematologic variables, kidney volume, kidney function, and chronic histologic changes in the implant biopsies.

Statistical Analysis

Statistical analyses were performed with the use of SAS 9.3 and JMP 9.0 statistical software (SAS Institute, Cary, North Carolina). Student *t* test was used to compare continuous variables, and chi-square and Fisher exact tests were used to examine differences between normally and nonnormally distributed categoric variables, respectively. Univariate analyses were done for the continuous and