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ORIGINAL ARTICLE

One- and five-year follow-ups on blood pressure and renal function in kidney donors

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Summary

It is considered safe to donate a kidney if internationally accepted medical criteria are fulfilled. However, some donors have encountered hypertension, proteinuria and impaired renal function after donation. The study was based on retrospective data on 908 donors, donating in the period 1997–2007. Preoperative and follow-up data were collected from patient files and the Norwegian Living Donor Registry. Follow-up data were available for 665 donors at 1 year after donation, and 256 donors at 5 years after donation. We calculated the estimated glomerular filtration rate (eGFR) using the four variable Modification of Diet in Renal Disease equation. At 1 and 5 years after donation, the prevalence of hypertension was 11.7% and 27.1% respectively compared to 2.6% before donation. Proteinuria was present in 3.3% and 1.6% at 1 and 5 years. Mean eGFR was 56.1 ± 10.8 ml/min/1.73 m^2 at 1 year and 61.0 ± 11.8 ml/min/1.73 m^2 at 5 years. Mean blood pressure was 122.5 ± 10.6/76.2 ± 7.5 mmHg at donation (n = 908), 124.3 ± 14.2/77.9 ± 8.2 mmHg at 1-year (n = 649) and 127.2 ± 15.4/78.8 ± 8.3 mmHg at 5-year follow-ups (n = 247). We found no evidence of further decline in renal function beyond the initial decrement following nephrectomy.

Introduction

Despite its advantages, living kidney donation remains a complex ethical, moral and medical issue. International consensus exists on evaluations and screening of potential donors prior to donation [1]. For reasons of increased demand for organs, some transplant centres now are willing to accept marginal living donors with older age, obesity, well-controlled hypertension or low-normal glomerular filtration rate (GFR). Since the 1970s, follow-up studies on previous kidney donors have been performed with generally reassuring results [2–9]. However, there have been concerns about methodological weaknesses with some of these studies [3,4,10,11].

Regular and long-term follow-up of all kidney donors is recommended [1,12]. Previous donors in general are considered healthy and thus regular follow-up visits may be difficult to accomplish. There are currently no established guidelines detailing follow-up duration and intervals, and follow-up routines vary considerably among different centres [13].

The main purpose of this study was to describe the prevalence of hypertension, proteinuria and renal function in living kidney donors at 1 and 5 years after kidney donation.

Materials and methods

In Norway, all kidney transplantations are performed at one centre. Predonation work-up and postdonation follow-up of recipients and donors are performed in each county by the local nephrology department in cooperation with

the transplant centre. Data of all living kidney donors in Norway have since 1997 been entered in a living donor registry [14]. Each data registration includes a basic medical examination with blood and urinary samples. Preoperative and follow-up data were collected from patient files and the Norwegian Living Donor Registry. The study was approved by the regional ethics committee.

Hypertension was defined as blood pressure above 140/90 mmHg and/or use of blood pressure lowering medication. Proteinuria was examined by dipstick, 24-h urine collection or albumin/protein-creatinine ratio, and was reported as present (>300 mg/day) or not.

Creatinine was measured preoperatively at the transplantation centre, and at follow-up at the donor's local hospital. During the study period, creatinine assays throughout Norway were standardized to accommodate clinical use of the Modification of Diet in Renal Disease (MDRD) formula [15]. Creatinine clearance was measured before donation, but was not available at follow-up.

Using the MDRD formula [16], we calculated the estimated glomerular filtration rate (eGFR) at 1 and 5 years after donation [17–20]. For reasons of concerns regarding imprecision and tendency to underestimate true GFR, we did not calculate prenephrectomy eGFR.

Preoperative data consisted of height, weight, body mass index (BMI), age, gender, current smoking, systolic and diastolic blood pressure, creatinine, cholesterol and fasting glucose. When the blood pressure measured the day before surgery differed from the measurement obtained during donor evaluation, the lowest value was chosen. Follow-up data consisted of creatinine, eGFR, presence of proteinuria (>300 mg/day), systolic and diastolic blood pressure, and use of blood pressure lowering medication.

Data were reported as mean ± SD. Paired *t*-test and McNemar's test were performed as appropriate. When performing multiple comparisons, the Bonferroni correction was applied. Statistical analyses were performed using SPSS version 16 (SPSS Inc., Chicago, IL, USA).

Results

At our centre, a total of 908 living kidney donations were performed during 1997–2007. Preoperative donor characteristics were available for all donors, and are shown in Table 1.

Follow-up data (Table 2) were available for 665 donors at 1 year after donation, and 256 donors at 5 years after donation. At 1-year follow-up, 11.7% (n = 76/649) of donors were hypertensive based on blood pressure >140/90 mmHg or use of antihypertensive medication, a significant ($P < 0.001$) increase compared with the prevalence prior to donation. Mean blood pressure was 124.3 ± 14.2/77.9 ± 8.2 mmHg. Sixteen donors were using

Table 1. Baseline data n = 908.

	Total (n = 908)		One-year data (n = 665)		Five-year data (n = 251)	
Variable	n	Means (SD), frequencies (%)	n	Means (SD), frequencies (%)	n	Means (SD), frequencies (%)
Height, cm	901	171.9 (9.1)	659	171.9 (9.2)	250	171.2 (9.0)
Weight, kg	907	75.3 (13.0)	665	75.1 (13.0)	256	73.7 (12.7)
BMI, kg/m^2	901	25.4 (3.3)	659	25.3 (3.2)	250	25.0 (3.1)
Age, years	908	47.5 (11.7)	665	47.5 (11.8)	256	47.5 (11.7)
Male	908	373 (41.1)	665	276 (41.5)	256	98 (38.3)
Smoking	853	298 (34.9)	622	217 (32.6)	233	87 (37.3)
Creatinine clearance, ml/min	814	115.0 (29.0)	607	113.5 (29.0)	218	110.8 (31.6)
Preoperative creatinine, μmol/l	908	76.5 (13.0)	665	77.1 (13.1)	256	81.4 (9.7)
Creatinine first postoperative day, μmol/l	908	114.7 (20.6)	665	114.8 (20.8)	256	113.0 (18.7)
Creatinine at discharge*, μmol/l	908	111.8 (20.7)	665	112.0 (20.6)	256	113.7 (19.0)
Postoperative eGFR†, ml/min/1.73^2	908	51.7 (8.7)	665	51.7 (9.0)	256	51.9 (8.5)
eGFR at discharge*, ml/min/1.73^2	908	53.4 (9.4)	665	53.3 (9.4)	256	51.6 (8.6)
S-cholesterol, mmol/l	859	5.4 (1.0)	621	5.5 (1.1)	251	5.6 (1.1)
S-glucose, mmol/l	839	5.1 (0.5)	603	5.1 (0.5)	244	5.1 (0.5)
Systolic blood pressure, mmHg	908	122.5 (10.6)	665	122.4 (10.4)	256	122.5 (10.1)
Diastolic blood pressure, mmHg	908	76.2 (7.5)	665	76.4 (7.3)	256	76.1 (6.8)
Hypertension‡	905	26 (2.5)	665	17 (2.6)	256	7 (2.7)

P-value calculated by chi-square or *t*-test.
*Mean hospital stay was 7 days.
†Estimated glomerular filtration rate by MDRD equation.
‡Hypertension defined as BP over 140/90 or use of medication.

Table 2. Follow-up data on 703 kidney donors.

Variable	One-year follow-up (n = 665)		Five-year follow-up (n = 256)	
	n	Mean (SD), frequencies (%)	n	Mean (SD), frequencies (%)
Systolic bp, mmHg	649	124.3 (14.2)	247	127.2 (15.4)
Diastolic bp, mmHg	649	77.9 (8.2)	247	78.8 (8.3)
Hypertension*	649	76 (11.7)	247	67 (27.1)
Bp medication	649	16 (2.5)	247	43 (17.4)
Creatinine, μmol/l	653	106.5 (17.8)	252	96.7 (16.7)
eGFR†, ml/min/1.73 m^2	653	56.1 (10.8)	252	61.0 (11.8)
Proteinuria >300 mg/day	598	20 (3.3)	244	4 (1.6)
BMI, kg/m^2	629	25.5 (5.4)	161	26.1 (4.0)

Bp, blood pressure; BMI, body mass index.
*Hypertension was defined as systolic blood pressure >140, or diastolic blood pressure >90, or use of blood pressure medication.
†Estimated glomerular filtration rate by MDRD equation.

antihypertensive drugs. Uncomplicated hypertension was present before donation in 17 (2.6%) donors with available data at 1 year after donation; three of these used one blood pressure lowering medication and one used two. At 1 year, six were now normotensive and altogether six were using blood pressure medication. The remaining nine donors were still characterized as hypertensive, although they were not on antihypertensive therapy.

At 5-year follow-up, 27.1% were hypertensive, a significant ($P < 0.001$) increase from 1-year follow-up. Mean blood pressure was 127.2 ± 15.4/78.8 ± 8.3 mmHg. Forty-three donors used antihypertensive drugs. Seven donors who were hypertensive before donation had follow-up data at 5 years. Four were using one blood pressure medication, two were using two and one had become normotensive.

Blood pressure increased in donors with measurements both at donation and at 1-year follow-up (n = 649, 122.4 ± 10.5/76.3 ± 7.4 mmHg vs. 124.3 ± 14.2/77.9 ± 8.2 mmHg, $P = 0.002/P < 0.001$), as well as in donors with measurements both at 1- and 5-year follow-ups (n = 205, 124.2 ± 14.4/77.8 ± 8.3 mmHg vs. 127.1 ± 15.5/78.6 ± 8.2 mmHg, $P = 0.02/P = 0.4$).

Proteinuria 1 year after donation was present in 3.3% (n = 20/598) of donors (none before donation). At 5-year follow-up, 1.6% (n = 4/244) had proteinuria. Of the 20 donors with proteinuria at 1-year follow-up, eight had become negative, and 12 had missing data. Donors with proteinuria had a mean BMI of 25.4 kg/m^2 at baseline, similar to those without.

One year after donation, mean creatinine was 106.5 ± 17.8 μmol/l, eGFR was 56.1 ± 10.8 ml/min/1.73 m^2 and 68.8% of donors had eGFR <60 ml/min/1.73 m^2. At 5-year follow-up, mean creatinine was 96.7 ± 16.7 μmol/l, eGFR was 61.0 ± 11.8 ml/min/1.73 m^2 and 48.8% had eGFR <60 ml/min/1.73 m^2. The eGFR at discharge from the hospital was significantly correlated with both eGFR at 1- (r = 0.68) and 5-year (r = 0.66) follow-ups.

Between 1- and 5-year follow-ups (n = 211), there was an increase in eGFR of 1.7 ml/min/1.73 m^2 per year (53.7 ± 10.3 ml/min/1.73 m^2 vs. 60.4 ± 11.6 ml/min/1.73 m^2, $P < 0.001$). Creatinine values declined throughout the study period, with a corresponding increase in eGFR. The creatinine values obtained at 5 years after donation were obtained at the end of the period, with more laboratories having changed their creatinine assays causing a possible bias. Therefore, we also calculated mean eGFR from 1-year follow-ups performed at similar time points (year) to the 5-year follow-ups. This showed a higher mean eGFR at 58.1 ± 10.9 ml/min/1.73 m^2, however, still lower than the mean eGFR at 5-year follow-up.

Discussion

The main finding in this study is an increase in blood pressure after donation. After an initial decrement following nephrectomy, eGFR did not show any further decline between 1- and 5-year follow-ups.

Elevated blood pressure is an exclusion criterion for accepting a potential donor [21]. In our study population, 26 donors with hypertension were allowed to donate, reflecting current international trends allowing donors with uncomplicated hypertension to donate, provided adequate follow-up is available [1,22]. At 1 and 5 years after donation, we found a significant increase in the prevalence of hypertension. However, six of 17 donors with hypertension before donation were normotensive after 1 year, suggesting some degree of 'white coat' hypertension during evaluation. We also found a significant increase in both systolic blood pressure and diastolic blood pressure at 1 year compared with predonation values. At 5 years, there was a further increase in systolic blood pressure from 1-year follow-up. The long-term consequences of developing hypertension after kidney donation might be associated with an increased risk of cardiovascular disease and progressive decline in renal function [23].

Several studies examining the risk of hypertension after kidney donation have been retrospective, without or with appropriate control groups, and with substantial loss of donors during follow-up [3,10]. Some long-term studies have demonstrated no increase in hypertension [5,7], whereas others have suggested donor nephrectomy to be associated with an increase in blood pressure [2,3,10,24].

There are some limitations to the interpretation of results on blood pressure in our study. Although our

health care system offers life-long follow-up free of charge, we also experience donors lost to follow-up. In contrast to predonation measurements, a slightly elevated blood pressure after donation will not necessarily lead to more frequent controls. More frequent visits to health care providers during follow-up may result in a higher frequency of diagnosed hypertension [24]. In the general population, every 10-mmHg increase in systolic blood pressure and 5-mmHg increase in diastolic blood pressure is associated with a 1.5-fold increase in death from ischaemic heart disease and stroke [25]. Whether an increase in blood pressure following kidney donation is similarly prognostic requires future consideration. Closer surveillance and early intervention in otherwise healthy adults could offset such risks and is a strong argument for mandatory life-long follow-up of kidney donors.

Several studies have demonstrated varying levels of increased proteinuria following kidney donation [6,26–29],and some have also suggested an increase in proteinuria with time after donation [4,6,30]. Meta-analyses support the notion that kidney donation increases proteinuria [2,4]. Common risk factors for proteinuria in the general population are hypertension, diabetes and obesity [31]. One report suggested an association between obesity and proteinuria after donor nephrectomy [32]. We did not find this association in our material.

Reassuringly, as in previous studies [2,4,30,33], we found no evidence of further decline in renal function after the initial decrement due to nephrectomy.

Differences in creatinine assays and ethnicity make absolute values of eGFR from different populations of previous kidney donors difficult to compare. A recent study based on registry data [34] found a postdonation mean eGFR of 56.1 ml/min/1.73 m^2 in Caucasians within 1-year postdonation, similar to our finding. Other studies have shown different values for eGFR [4,33,35] after donation. As the MDRD equation may underestimate renal function in previous kidney donors, true GFR may be slightly higher [17,19,20]. As eGFR at discharge is highly correlated with the value after 1 and 5 years, this parameter may be useful in deciding whether a donor may need more frequent follow-up visits.

The strength of this study is preoperative and follow-up data from a relatively large and representative sample of kidney donors with nearly complete baseline data. Limitations include blood pressure measurements, analysis of creatinine and donors lost to follow-up. It is difficult to estimate the possible impact of loss to follow-up in a single study. Two meta-analyses [3,4] have indicated that donors lost to follow-up are healthier than donors attending timed control visits.

In conclusion, we report an increase in blood pressure and increased frequency of hypertension after kidney donation. From 1 to 5 years post donation, there was no evidence of decline in renal function. Our findings support a conscientious follow-up of live kidney donors.

Authorship

GM: collected data, performed statistical analysis and participated in writing of the manuscript. IH and HB: participated in writing of the manuscript and statistical analysis. OØ, PF, KM and HH: participated in writing of the manuscript.

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