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Psychosocial and physical outcome following kidney donation—a retrospective analysis

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Summary

Living renal donation is of benefit to the allograft recipient. Careful analysis of the donor outcome is necessary with respect to the medical condition, socioeconomic status, and health-related quality of life. All living kidney donors of the Transplant Center at Heidelberg were included. Renal function and comorbidities were assessed. HRQoL and fatigue symptoms were determined by self-reporting validated test systems [Short-Form 36 (SF-36), Multidimensional Fatigue Inventory (MFI-20), Patient Health Questionnaire (PHQ)]. In total, 430 of 519 living renal donors were eligible to participate: 295 living donors (68.6%) provided informed consent (age at donation 49 ± 11 years) with a median time after donation of 77 (24–484) months. Renal function was lower compared with predonation (66 ± 15 ml/min vs. 88 ± 14 ml/min). Blood pressure remained stable (128 ± 14 mmHg vs. 129 ± 15 mmHg) with an increase of 56 donors receiving antihypertensive treatment (27.1% vs. 19%). The SF-36 physical component summary score was significantly better for both genders compared with the general population; the SF-36 mental component summary score was lower for female donors, caused by a reduced role functioning. Prevalence of fatigue was increased in female donors between the ages of 40 and 59 years. Renal function and blood pressure were as expected from previous studies. Concerning the psychosocial outcome, female donors might be at risk of impairments postdonation. Future evaluations will confirm and specify whether these results are necessary.

Introduction

Living kidney transplantation provides the optimal treatment of patients with end-stage renal disease, with living kidney donation becoming more common worldwide [1,2]. Intraoperative surgical problems are rare [3], and most living donors have a good medical health status and good levels of health-related quality of life (HRQoL) compared with the general population [4–8].

Despite positive long-term outcomes, more recent data have identified some donors with increased medical risks (end-stage renal disease, mortality, hypertension) and psychosocial risks [7,9,10]. Further long-term studies focusing on medical and psychosocial outcomes for living kidney donors are necessary [11].

The current thorough renal donor evaluation and the extensive database of our Transplant Center with pre- and postdonation data allow us to review the long-term medical, psychosocial, and HRQoL outcome of kidney donors. The study objectives included a detailed analysis of the medical outcome and the psychosocial status and the HRQoL, assessed by standardized and validated test systems in a representative sample of living donors.

Methods

Study population

The study was designed to evaluate the medical, psychosocial, and HRQoL outcomes of living kidney donors. At the Heidelberg Transplant Center, a regular clinical follow-up after donation—including a medical history, laboratory, and body examination—is performed annually. Psychological counseling is carried out on each donor and recipient before transplantation and, where indicated, after transplantation. All 519 kidney donors at the Heidelberg Transplant Center from 1967 to June 2011 were identified.

Donors with language barriers or no existing current addresses were excluded. Invitation letters, including the questionnaires, were sent to 430 eligible donors, asking them to participate. In the case of no response, donors were contacted by telephone. Demographic and psychosocial data were obtained from 295 donors (68.6%) by a structured questionnaire, which included special items addressing the physical and medical follow-up. In addition, medical history, clinical data, laboratory, and extensive body examination results were collected during the regular visits at the Transplant Center prior to living donation and yearly thereafter. Home blood pressure was measured after 10 min of seated rest. The glomerular filtration rate (GFR) was estimated by the Chronic Kidney Disease Epidemiology (CKD-epi) formula [12]. Evaluation of HRQoL, as well as screening for depression, anxiety and fatigue, was performed using validated tests. A representative German adult cohort served as the control group for each questionnaire [13–15].

According to the Center's practice, a medically low-risk population is eligible for donation. Body mass index should be <35 kg/m^2 and blood pressure has to be well controlled with at least two antihypertensives (systolic/diastolic blood pressure <140/90 mmHg). Donors with diabetes or impaired fasting glucose concentrations as well as donors with obvious psychiatric diseases are not accepted as living renal donors.

The study was performed according to the Declaration of Helsinki 2000 and the Declaration of Istanbul 2008, and approved by the institutional Ethics Committee. Written informed consent was obtained from all participating donors.

Questionnaires

Questionnaires were mailed, self-administered, and returned in prepaid envelopes. The questionnaires included the Short-Form 36 (SF-36) [16], the Multidimensional Fatigue Inventory 20 (MFI-20) [17,18], the Patient Health Questionnaire (PHQ) [19,20], and some additional questions related to kidney donation.

Short-Form 36 (SF-36)

The SF-36 is a self-assessment of day-to-day function and well-being over the previous 4 weeks. The SF-36 contains eight multi-item subscales: general health perceptions, physical functioning, physical role (role limitations due to physical problems), bodily pain, general mental health, vitality (vitality, energy, fatigue), emotional role (role limitations due to emotional problems), and social functioning. Each transformed subscale has a range from 0 to 100 (100 = optimal function) [16]. Subscales are combined into a physical and mental component summary score (PCS and MCS) and standardized to the age and gender distribution of the German adult population. The SF-36 was evaluated in a representative German adult cohort of 6964 persons ranging in age from 17 to 79 years [13].

Multidimensional Fatigue Inventory 20

The MFI-20 is a 20-item self-administered questionnaire developed to assess fatigue and to reflect feelings over the previous few days [17]. The MFI-20 consists of five subscales: general fatigue, physical fatigue, mental fatigue, reduced activity, and reduced motivation. Each subscale includes four items on a five-point Likert scale with higher scores indicating a higher level of fatigue. In addition, a total score within the range of 20 to 100 is reported [18]. The MFI-20 was evaluated in a representative German adult cohort of 2037 persons [14].

Patient Health Questionnaire

Depression was measured with the depression part of the Psychosomatic Health Questionnaire PHQ-9 [19]. The PHQ-9 is the summary of nine items on a three-point scale, with higher scores indicating more depressive symptoms within the previous 4 weeks. Somatization was measured using the PHQ-15 somatic symptom module [20], which consists of 15 items on somatic symptoms and answered on a three-point scale. The total PHQ-15 score ranges from 0 to 30 and scores of ≥5, ≥10, and ≥15 represent mild, moderate, and severe levels of somatization, respectively. The reliability and validity of the PHQ-9 and PHQ-15 are high in clinical healthcare settings [19,20]. The PHQ was evaluated in a representative German adult cohort of 2066 men and women [15].

Statistical analyses

All analyses were performed using IBM SPSS Statistics, version 18 (SPSS Inc., Chicago, IL, USA). Values are presented as mean (SD) or *n* (%). Clinical variables were compared among groups using the chi-square test for categorical variables and Student's *t*-test or Mann–Whitney–Wilcoxon test for continuous variables. $P < 0.05$ was considered to indicate statistical significance. Linear regression analysis was

performed, identifying variables that predicted a poor HRQoL outcome, fatigue, or depression. Variables with a significant univariate correlation and lacking multicollinearity were included in each model.

Results

Study population

In total, 430 of 519 living renal donors were eligible to participate (Fig. 1). Eleven previous living kidney donors (median time after donation 245 (43–555) months) had already died (two from cancer, three from cardiac disease, two from liver cirrhosis, and four unknown). Informed consent was provided and clinical data as well as completed questionnaires were returned by 295 living donors [106 (35.9%) male]. Nonresponding donors were younger than the responding donors at the time of donation (43 ± 11 vs. 49 ± 11 years, $P < 0.001$) and at the time of questionnaire distribution (55 ± 14 vs. 57 ± 11 years, $P = 0.041$).

In the responding donor cohort, the mean age at donation was 49 ± 11 years, with 19 donors over the age of 65 years. The median time after donation was 77 (24–484) months, with 85 (28.8%) donors being ≥10 years postdonation. Donors' demographics and socioeconomic data are given in Table 1. Minimal invasive donation was performed in 10 (3.4%) donors, and 31 (10.5%) donors had a flank incision. Most of the donors were first-degree relatives [mother $n = 78$ (26.4% of total); father $n = 58$ (19.7%); (brother $n = 15$ (5.1%); sister $n = 32$ (10.8%)] and second-degree relative spouses [wife $n = 69$ (23.4%); husband $n = 24$ (8.1%)].

Renal function postkidney donation

In general, the estimated glomerular filtration rate was significantly lower after donation (66 ± 15 ml/min vs. 88 ± 14 ml/min, $P < 0.001$; Table 2) with >30% decrease in 109 (36.9%) and >50% decrease in two donors. Aging contributed to postdonation GFR with a mean GFR of 78 ± 19 ml/min in donors ≤40 years at the time of follow-up, 69 ± 14 in donors aged 41–60 years, and 61 ± 13 ml/min in donors aged >60 years. Linear regression analysis showed the age at the time of donation ($P = 0.04$), basal renal function ($P = 0.002$), and systolic blood pressure ($P = 0.04$) as predictors of the reduction in eGFR.

Protein excretion was 0.046 ± 0.059 g/l before donation and 0.058 ± 0.062 g/l postdonation. Significant protein excretion (≥150 mg/l) was noted in 7/295 (2.4%) donors before donation and in 17/295 (5.8%) donors postdonation.

Blood pressure postkidney donation

Systolic and diastolic blood pressure were comparable before and postkidney donation; the mean arterial blood

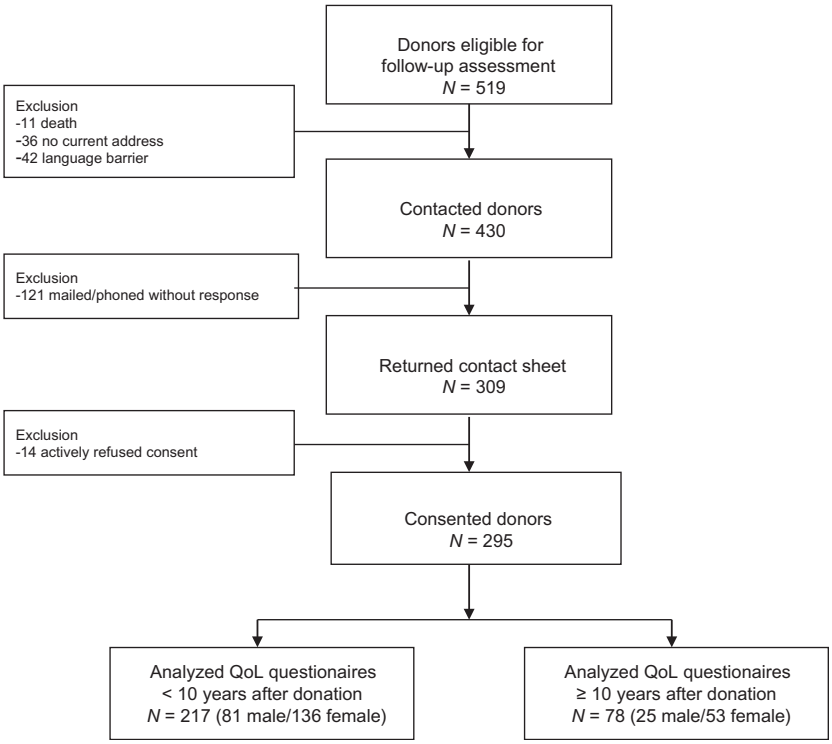

Figure 1 Donor flow chart.

Table 1. Donors' demographics, all donors, and separated by gender.

	All donors *N* = 295	Male donors *N* = 106	Female donors *N* = 189	Significance *P*
Gender, *n* (%)		106	189	–
Age at the time of donation (years), mean (SD)	49 (11)	51 (11)	49 (11)	0.2
Age at the time of assessment (years), mean (SD)	58 (11)	59 (11)	58 (11)	0.3
Time after donation (months), mean (SD)	101 (72)	97 (75)	103 (71)	0.5
Side of donation, *n* (%)				
Right kidney	137 (46.4)	48 (45.3)	89 (47.1)	0.8
Left kidney	158 (53.6)	58 (54.7)	100 (52.9)	
Smoking, *n* (%)				
Smoker	28 (9.5)	11 (10.4)	17 (9.0)	0.4
Nonsmoker	256 (86.8)	93 (87.7)	163 (86.2)	
Unknown	11 (3.7)	2 (1.9)	9 (4.8)	
Relationship to recipient, *n* (%)				
Child (son/daughter)	4 (1.4)	2 (1.9)	2 (1.1)	0.08
Parent (father/mother)	136 (46.1)	58 (54.7)	78 (41.3)	
Sibling (brother/sister)	47 (15.9)	15 (14.2)	32 (16.9)	
Spouse (husband/wife)	93 (31.5)	24 (22.6)	69 (36.5)	
Other related	6 (2.0)	1 (0.9)	5 (2.6)	
Friends, emotionally related	7 (2.4)	5 (4.7)	2 (1.1)	
Other unrelated	2 (0.7)	1 (0.9)	1 (0.5)	
Marital status at survey, *N* (%)				
Married or living together	218 (73.9)	85 (80.2)	133 (70.4)	0.01
Separated, divorced	34 (11.5)	8 (7.5)	26 (13.8)	
Widowed	27 (9.2)	4 (3.8)	23 (12.2)	
Unmarried/single	16 (5.4)	9 (8.5)	7 (3.7)	
Immigrated from another country, *n* (%)				
All	33 (11.2)	15 (23.6)	18 (9.5)	0.1
Of the European Union	17 (5.8)	10 (9.4)	7 (3.7)	
Out of the European Union	16 (5.4)	5 (4.7)	11 (5.8)	
Educational graduation, *n* (%)				
High school	70 (23.7)	34 (32.1)	36 (19.0)	0.09
Middle school	81 (27.5)	26 (24.5)	55 (29.1)	
Primary school	123 (41.7)	39 (36.8)	84 (44.4)	
Extraordinary school	4 (1.4)	1 (0.9)	3 (1.6)	
No graduation	5 (1.7)	0	5 (2.5)	
Unknown	12 (4.1)	6 (5.7)	6 (3.2)	
Employment at the time of donation, *n* (%)				
Working full time	122 (41.4)	78 (73.6)	44 (23.3)	<0.001
Working part time	75 (25.4)	2 (1.9)	73 (38.6)	
Student	2 (0.7)	1 (0.9)	1 (0.5)	
Housewife/houseman	42 (14.2)	0	42 (22.2)	
Unemployed	6 (2.0)	1 (0.9)	5 (2.6)	
Pension	38 (12.9)	19 (17.9)	19 (10.1)	
Unknown	10 (3.4)	5 (4.7)	5 (2.6)	
Donor income at the time of donation, *n* (%)				
<25 000€	86 (29.2)	15 (14.2)	71 (37.6)	<0.001
25 000–50 000€	87 (29.5)	44 (41.5)	43 (22.8)	
50 000–100 000€	31 (10.4)	22 (20.8)	9 (4.8)	
>100 000€	4 (1.4)	3 (2.8)	1 (0.5)	
Unknown	87 (29.5)	22 (20.8)	65 (34.3)	
Donor medical insurance, *n* (%)				
General insurance	220 (74.6)	78 (73.6)	148 (78.3)	0.5
Private insurance	36 (12.2)	17 (16.0)	22 (11.6)	
General + private insurance	22 (7.5)	7 (6.6)	12 (7.4)	
Unknown	17 (5.8)	4 (3.8)	7 (3.7)	

Table 1. continued

	All donors $N = 295$	Male donors $N = 106$	Female donors $N = 189$	Significance P
Medication, *n* (%)				
Any medication	86 (29.2)	25 (23.6)	61 (32.3)	0.1
Antihypertensive	56	24	32	
Antidiabetics	0	0	0	
Antilipids	11	5	6	
Diuretics	9	3	6	
Analgesics	6	1	5	
Proton pump inhibitor	3	0	3	
Psychiatric disorder	7	1	6	
Thyroid medication	18	1	17	
Others	25	7	18	

pressure and pulse pressure were stable (Table 2). Systolic blood pressures >140 mmHg were noted in 35 (11.9%) donors before donation and 36 (12.2%) postdonation; a significant increase (>30%) was noted in 7 (2.4%) of the donors. Diastolic blood pressure >90 mmHg was noted in 20 (6.8%) donors before and 11 (3.7%) donors postdonation; a significant increase (>30%) was noted in 11 (3.7%). Mean arterial pressure (MAP) >105 mmHg was documented in 41 (13.9%) donors before and in 35 (11.9%) donors postdonation; a significant increase (>30%) was noted in 7 (2.4%) donors. Pulse pressure >65 mmHg was documented in 14 (4.7%) donors before and in 18 (6.1%) donors postdonation; an increase (>30%) was noted in 48 (16.3%) donors.

Antihypertensive medication was administered to 56 (19.0%) donors before and to 80 (27.1%) donors postdonation (Table 2). New onset or worsening of hypertension, defined as *de novo* antihypertensives or >30% increase of MAP, was documented in 38 (12.9%) donors.

Hospitalization postkidney donation

Hospitalization after kidney donation was necessary in 25 (8.5%) donors (eight incisional hernia, two wound-healing problems, two cardiovascular diseases, 13 others). All donors with an incisional hernia had a horizontal incision.

Drug treatment

At the time of donation, 86 (29.2%) donors were on drug treatment, whereas at the time of the last follow-up, daily medication was being taken by 113 (38.3%) donors (Table 2), including 33 (11.2%) donors on *de novo* antihypertensives, 11 donors on *de novo* statins, one donor on *de novo* antidiabetic drug, and five donors on *de novo* antidepressants or other psychotropic agents.

Socioeconomic outcome

One-year after donation, 110/287 (38.3%) donors were employed full-time with eight donors showing a decrease in employment time [one from full-time to part-time employment, one from full-time to low income or unemployment, two from part-time to low income or unemployment, two from full-time to illness (one classified as mild depression by PHQ, one intercurrent illness with recovery), two from part-time to housewife]. Changes in employment were caused by health status in 13/214 (6.1%) donors.

One-year postdonation, the mean income increased in four donors (change from part- to full-time employment, professional development) and decreased in 15 donors (six retirements, three reduced physical capacities, one unemployment, two for macroeconomic reasons, and three on parental leave).

Donor medical insurance remained unchanged in 280/285 (98.2%) donors 1-year postdonation.

Family interaction and professional activities

In the self-rating questionnaire, 247 (83.7%) donors reported that kidney donation did not affect family life or professional activities, with 25 donors confirming a positive effect and 23 donors complaining of negative effects.

The emotional relationship between donors and recipients was rated as stable or even better in 274/284 (96.5%) donors. Negative changes in emotional relationships attributed to donation were cited by 10/295 donors; six donors attributed the negative change to the kidney donation.

Effect of donation on self-rated health condition

Overall, self-rated general health condition was rated as at least good in 263 (89.2%) donors (22 excellent, 84 very good, 157 good), whereas 32 donors stated fair ($n = 30$) or even poor health ($n = 2$) condition at the time of the last

Table 2. Clinical, laboratory, and socioeconomic data in living donors (n = 295) at baseline and after kidney donation.

	At the time of donation	At the time of survey	Significance P
Demographics			
Age (years), mean (SD)	49 (11)	58 (11)	<0.001
Gender (male), *n* (%)	106	106	—
Time after donation (months), mean (SD)	—	101 (72)	—
Renal function			
S-creatinine (mg/dl), mean (SD)	0.82 (0.16)	1.08 (0.22)	<0.001
CKD-epieGFR (ml/min), mean (SD)	93 (14)	66 (15)	<0.001
Blood ureanitrogen (mg/dl), mean (SD)	62 (15)	77 (19)	<0.001
Protein excretion (g/l), mean (SD)	0.047 (0.060)	0.051 (0.065)	0.07
Other laboratory data			
Uric acid (mg/dl), mean (SD)	5.08 (1.39)	5.96 (1.52)	<0.001
Glucose (mg/dl), mean (SD)	94 (18)	93 (14)	0.07
HbA1c (%),mean (SD)	5.5 (0.5)	5.49 (0.41)	0.4
Triglyceride (mg/dl), mean (SD)	115 (70)	146 (86)	<0.001
Cholesterol (mg/dl), mean (SD)	210 (40)	214 (38)	0.03
Total protein (g/l), mean (SD)	74 (5)	75 (4)	0.3
Albumin (g/l), mean (SD)	45 (4)	45 (3)	0.4
C-reactive protein (mg/l), mean (SD)	1.61 (3.26)	3.09 (6.24)	0.005
Hemoglobin (g/dl), mean (SD)	14.0 (1.3)	14.1 (1.1)	0.9
Hematocrit (l/l), mean (SD)	0.41 (0.04)	0.42 (0.03)	<0.001
Leukocytes (/nl), mean (SD)	6.86 (1.84)	6.65 (1.81)	0.02
Ferritin (µg/l), mean (SD)	98 (100)	70 (73)	0.3
Clinical data			
Body mass index (kg/m^2), mean (SD)	25.7 (4.3)	26.2 (4.4)	<0.001
Systolic blood pressure (mmHg), mean (SD)	128 (14)	129 (15)	0.4
Diastolic blood pressure (mmHg), mean (SD)	80 (9)	80 (8)	0.9
Mean arterial pressure (mmHg), mean (SD)	96 (10)	97 (9)	0.7
Pulse pressure (mmHg), mean (SD)	47 (10)	49 (13)	0.3
Ultrasound, mean (SD)			
Length persisting kidney	113 (9)	120 (10)	<0.001
Parenchyma persisting kidney	19 (2)	19 (2)	0.5
Medication, *n* (%)			
Any medication	86 (29.2)	113 (38.3)	<0.001
Antihypertensive	56 (19.0)	80 (27.1)	
Antidiabetics	0	1	
Antilipids	11	17	
Diuretics	9	27	
Analgesics	6	4	
Proton pump inhibitor	3	10	
Psychiatric disorder	7	8	
Thyroid medication	18	17	
Others	25	36	

Conversion factors for units: serum creatinine in mg/dl to µmol/l, ^{x}88.4; urea nitrogen in mg/dl to mmol/l, ^{x}0.357; uric acid in mg/dl to µmol/l, ^{x}59.48; glucose in mg/dl in mmol/l, ^{x}0.05551; triglycerides in mg/dl to mmol/l, ^{x}0.01129; cholesterol in mg/dl to mmol/l, ^{x}0.02586; ferritin in µg/l to pmol/l, ^{x}2.247.

follow-up. In 96.6% of the donors, donation did not affect the general health condition.

A total of 97.6% of the donors felt fully informed about kidney donation (specifically, 12 too detailed, 174 very good, 82 satisfactory, 16 fair, nine poor). In general, 256 (87%) donors reconfirmed again their willingness to donate a kidney, whereas five donors denied their willingness and 31 were uncertain. In contrast, 278 (93%) donors would again donate the kidney to the specific recipient.

Donors' HRQoL

Detailed donors' SF-36 profiles adjusted to gender are provided in Table 3. Overall, physical health was significantly better compared with the German population [PCS scores 54.50 (9.56) vs. 48.36 (9.42), $P < 0.0001$] (Table 3a). Donors reported significantly better or comparable quality of life relative to the German adult population in all but one domain (Table 3b). The role function of female donors was rated lower by living kidney donors compared with the German population [79.52 (35.01) vs. 86.74 (28.99), $P = 0.006$], resulting in a lower overall MCS in donors compared with the German population [MCS scores 49.17 (12.03) vs. 50.87 (8.82), $P = 0.02$]. Figure 2 illustrates PCS and MCS scores in living kidney donors compared with the German general population, separated by gender and age.

Table 3. Donors' Short-Form-36 Health survey (SF-36) profile and comparison to the German general population [43]: (a) renal donors compared with German references; (b) renal donors separated by gender and compared with German references

(a) Renal donors compared with German references

		Percentage of donors with above or below average scores based on their gender and age		
SF-36 scores	Mean (SD)	<2 SD *n* (%)	Within ±2 SD *n* (%)	>2 SD *n* (%)
Physical component summary score (PCS)	54.50 (9.56)	4 (1.4)	268 (97.5)	3 (1.1)
Mental component summary score (MCS)	49.17 (12.03)	36 (13.1)	239 (86.9)	0

(b) Renal donors separated by gender and compared with German references

	Male kidney donors *n* = 275 (SD)	Male German population *n* = 6967	Significance *P*	Female kidney donors *n* = 275	Female German population *n* = 6967	Significance *P*
Physical component summary score (PCS)	56.11 (12.15)	49.26 (8.89)	<0.001	53.57 (10.46)	47.49 (9.82)	<0.001
Mental component summary score (MCS)	51.27 (23.55)	51.92 (8.02)	0.6	47.95 (12.08)	49.85 (9.41)	0.04
Physical functioning (PF)	92.73 (22.12)	88.18 (18.49)	<0.001	84.13 (21.47)	82.77 (22.18)	0.4
Role perception (RP)	90.95 (19.12)	85.53 (30.02)	0.02	80.98 (34.84)	79.22 (34.70)	0.5
Bodily pain (BP)	86.43 (20.88)	71.04 (25.36)	<0.001	81.19 (25.26)	63.89 (25.87)	<0.001
General health perception (GH)	74.46 (15.73)	66.83 (17.60)	<0.001	72.45 (17.97)	66.03 (18.66)	<0.001
Vitality (VT)	66.08 (28.43)	62.58 (17.06)	0.09	60.20 (19.90)	57.57 (18.22)	0.07
Social functioning (SF)	91.27 (18.33)	88.63 (18.29)	0.09	84.97 (22.73)	84.24 (21.12)	0.7
Role functioning (RE)	88.57 (7.56)	91.58 (23.78)	0.3	79.52 (35.01)	86.74 (28.99)	0.006
Mental health (MH)	77.06 (11.72)	75.22 (15.29)	0.3	71.94 (18.83)	68.89 (17.51)	0.1

Data are mean (standard deviation, SD).

Depression and somatoform disorders (PHQ-9 and PHQ-15)

Depression was detected in 22 donors by the PHQ-9 questionnaire (16 mild, four moderate, two severe). The mean depression score was 3.59 (3.99). Somatoform disorders detected by the PHQ-15 questionnaire showed 32 (10.8%) donors with a mean somatoform syndrome score of 5.32 (5.33).

Donor fatigue symptoms (MFI-20)

Nearly, all donors rated fatigue symptoms assessed by the MFI-20 questionnaire comparable to or even better than the German adult population (Fig. 3). Physical fatigue or mental fatigue above the average results of the general population was detected in 43 (15%) and 50 (17%) of the donors. Detailed analysis revealed female donors ranging in age from 40 to 59 years were a more vulnerable population for general and physical fatigue, whereas female and male donors aged <40 or older than 59 years reported comparable or lower fatigue symptoms relative to the general population in all domains.

Fatigue subscales as well as the MFI-20 total score and PHQ-9 depression sum scale correlated significantly (general fatigue: $r = 0.754$, $P < 0.001$; Table 4). Depressive disorders, including minor symptoms, were noted in 24 of 29 (82.8%) donors with signs of fatigue (general fatigue score >2 SD of German population). Fatigue scores correlated inversely with quality of life assessed by the SF-36 physical and mental component score (Table 4).

Linear regression analysis

The MCS was predicted by five variables: disturbances in concentration and memory, brooding, reduced motivation (fatigue scale), depression sum score (PHQ-9), and partnership problems ($R^2 = 0.734$) (Table 5a). The PCS was predicted by four variables: health concerns, muscle weakness, arthralgia, and deterioration of athleticism ($R^2 = 0.520$) (Table 5b). Health status of the recipient did not independently predict MCS or PCS. General fatigue was determined by depression symptoms (PHQ-9 sum scale), exhaustion, muscle weakness, the burden of caring for a family member, and having nobody to talk to ($R^2 = 0.727$) (Table 5c). The depression sum scale was predicted by MCS, PCS, sleeplessness, exhaustion, having nobody to talk to, stress at work or school, emotional distress, scar numbness or prickling, and financial difficulties ($R^2 = 0.784$) (Table 5d).

Discussion

Living kidney donors reported an overall good clinical outcome after kidney donation; renal function was expectedly

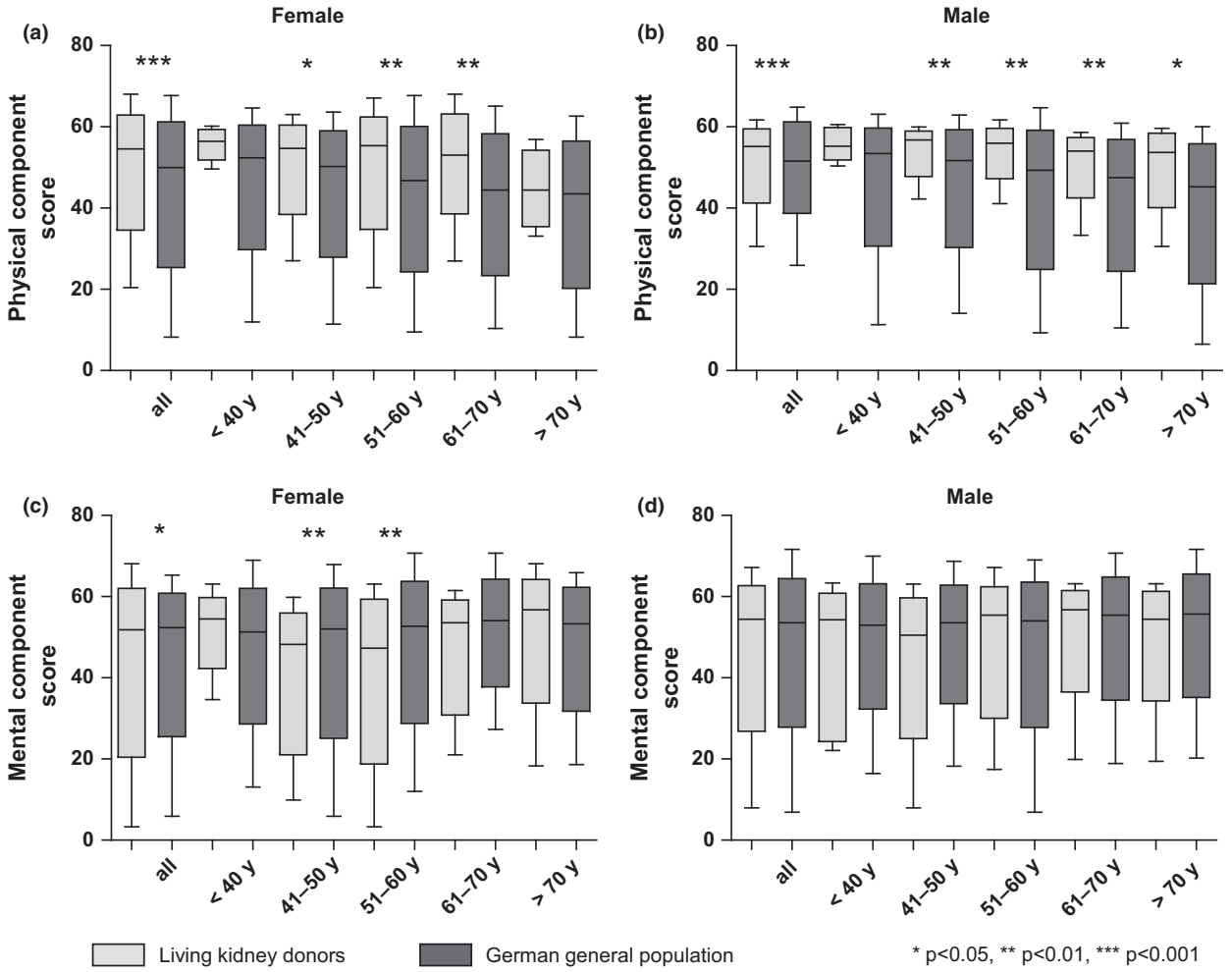

Figure 2 Health-related quality of life assessed by the Short-Form-36 questionnaire in living kidney donors compared with the German general population [13], separated by gender and age: (a) physical component score (PSC) in female donors compared with female German general population; (b) physical component summary score (PCS) in male donors compared with male German general population; (c) mental component score (MCS) in female donors compared with female German general population; (d) MCS in male donors compared with male German general population. Light gray bars, donors; dark gray bars, German general population; *, $P < 0.05$, **, $P < 0.01$, ***, $P < 0.001$.

lower compared with before the donation; none of the donors showed severe renal insufficiency or end-stage renal failure. Blood pressure remained stable with an increased number of donors receiving antihypertensive treatment. Socioeconomic status, including professional activities, income and medical insurance, remained unchanged. HRQoL, as assessed by the SF-36 PCS score, was favorable for both genders.

The study provided new information about female donors, with an overall MCS score lower in comparison with the general female German population. This was because of a reduced role functioning of women. Prevalence of fatigue did not differ from, or was even lower compared with the general German population, except for general and physical fatigue in female donors aged between 40 and 59 years. Overall, there was no increased incidence of depression or somatoform syndromes postkidney donation. However, fatigue and depressive syndromes correlated significantly.

The present study demonstrates the results of an extensive evaluation of living kidney donors with a mean time after donation of 77 (24–484) months postdonation, and with nearly 30% of donors being ≥10 years postdonation. None of the donors died as a result of kidney donation or suffered from end-stage renal disease (ESRD). These data concur with reports showing a similar or even better survival rate for kidney donors and reduced ESRD risk, compared with controls matched for age, gender, and ethnic groups [5,21,22]. Good or excellent health status was reported by 89.2% of the donors.

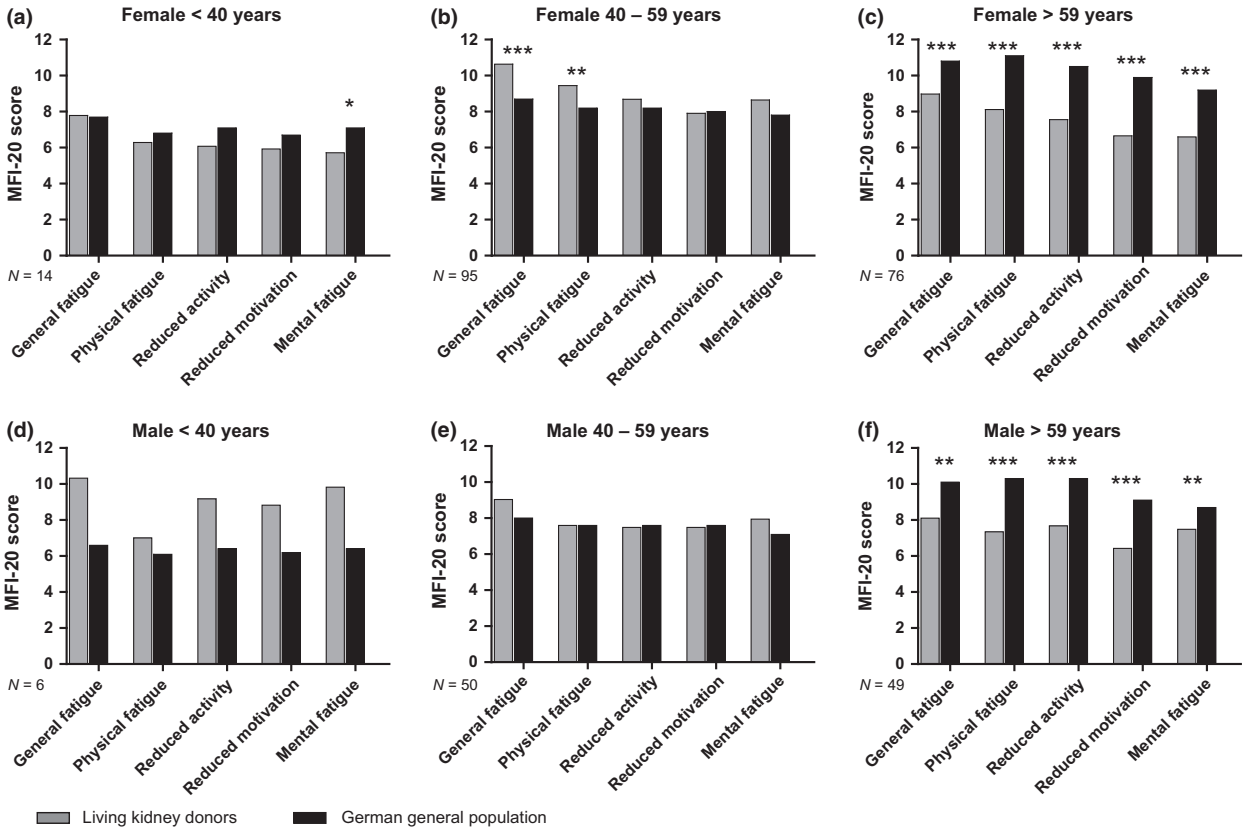

Figure 3 Fatigue symptoms assessed by the MFI-20 questionnaire in living kidney donors compared with the general population [14], separated by age and gender: (a) females aged <40 years (n = 14); (b) females aged 40–59 years (n = 95); (c) females aged >59 years (n = 76); (d) male aged <40 years (n = 6); (e) male aged 40–59 years (n = 50); (f) male aged >59 years (n = 49). Gray bars, donors; black bars, German general population; *, $P < 0.05$, **, $P < 0.01$, ***, $P < 0.001$.

Table 4. Correlation between fatigue assessed by MFI-20 and depression (Patient Health Questionnaire, PHQ-9); somatoform disorders (PHQ-15) and quality of life (SF-36); Spearmen correlation coefficient r and significance *P* are shown.

	PHQ-9 depression sum score		PHQ-15 somatoform disorder		PHQ stress scale		SF-36 mental component score		SF-36 physical component score	
Subscale	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
General fatigue	0.754	<0.001	0.692	<0.001	0.628	<0.001	−0.689	<0.001	−0.494	<0.001
Physical fatigue	0.620	<0.001	0.600	<0.001	0.584	<0.001	−0.618	<0.001	−0.591	<0.001
Reduced activity	0.651	<0.001	0.565	<0.001	0.580	<0.001	−0.597	<0.001	−0.488	<0.001
Reduced motivation	0.563	<0.001	0.388	<0.001	0.471	<0.001	−0.552	<0.001	−0.365	<0.001
Mental fatigue	0.569	<0.001	0.478	<0.001	0.512	<0.001	−0.586	<0.001	−0.301	<0.001
MFI-20 Total Score	0.752	<0.001	0.655	<0.001	0.656	<0.001	−0.716	<0.001	−0.532	<0.001

This is comparable with previous evaluations with 91% of the donors categorizing their general health status as good or excellent [9].

Renal function postkidney donation was comparable with the results of recent evaluations. Kasiske *et al.* [23] showed an eGFR by CKD-epi formula of 65.5 ± 13.1 ml/min in 199 donors, 6 months postdonation. Another study of 253 living kidney donors that was performed between 1996 and 2007 in the Netherlands reported a reduction in renal function from 89 ± 14 to 56 ± 11 ml/min, representing a change in eGFR from 30% to 40% [24]. After a drop of renal function immediately postdonation, renal function improves within 12 months postdonation and remains stable thereafter [25].

Table 5. Linear regression analysis to identify co-factors of (a) mental component sum score (SF-36); (b) physical component score (SF-36); (c) general fatigue (Multidimensional Fatigue Inventory 20, MFI-20); (d) depression sum score (PHQ-9).

	Regression coefficient B	Standard error	Significance *P*
(a) Mental component sum score (SF-36); $R^2 = 0.734$			
Constant	42.983	3.897	<0.001
Disturbances in concentration and memory	2.549	0.719	<0.001
Brooding	2.635	0.623	<0.001
Reduced motivation (fatigue scale)	−0.871	0.170	<0.001
Depression sum score (PHQ-9)	−1.171	0.171	<0.001
Problems in partnership	−2.054	0.908	0.02
(b) Physical component score (SF-36); $R^2 = 0.520$			
Constant	44.819	3.923	<0.001
Concerns on health	−6.180	1.097	<0.001
Severe muscle weakness within the past 4 weeks	2.749	1.019	0.008
Severe arthralgia within the past 4 weeks	1.969	0.818	0.02
Deterioration of athleticism	−2.412	1.440	0.09
(c) General fatigue (MFI-20); $R^2 = 0.727$			
Constant	16.374	1.530	<0.001
Depression sum score (PHQ-9)	0.454	0.084	<0.001
Severe exhaustion within the last 4 weeks	−1.853	0.332	<0.001
Severe muscle weakness within the last 4 weeks	−0.863	0.320	0.008
Burden of caring for a family member	0.743	0.347	0.03
Not having anyone to talk to	−0.852	0.463	0.07
(d) Depression sum score (PHQ-9); $R^2 = 0.784$			
Constant	19.609	1.141	<0.001
Mental component score (SF-36)	−0.114	0.015	<0.001
Sleeplessness	−0.789	0.170	<0.001
Exhaustion	−0.896	0.210	<0.001
To have nobody to talk to	0.784	0.280	0.005
Physical component score (SF-36)	−0.042	0.015	0.006
Mental pressure in employment or school	0.599	0.230	0.01
Change in emotional balance compared to prior to donation (emotional distress)	−0.507	0.208	0.02
Scar numbness or prickling	−0.520	0.214	0.02
Financial difficulties	0.472	0.229	0.04

Some experimental studies in animal models have reported compensatory hemodynamic changes after reduction of renal mass; hyperfiltration damage, in addition to the age-dependent loss of renal function, has been discussed [26,27]. After donation, renal function deteriorates with increasing age, but similarly to that of healthy subjects [21]. Even with a reduced eGFR, our study shows an acceptable renal function in kidney donors with a mean follow-up of approximately 8 years.

Only 17 of our donors showed protein excretion after donation, with 1% of donors developing clinically significant proteinuria. The review of the literature shows a diverse incidence of proteinuria with reports of over 20% [28,29], whereas in other studies no increased proteinuria was documented compared with controls in the short-term and long-term donor follow-up [5]. A meta-analysis shows a pooled incidence of 10% as defined as >300 mg/d based on 24-h urine collection [30].

In the present study, blood pressure was stable. However, new onset or worsening of hypertension defined as *de novo* antihypertensive medication or >30% increase of MAP was documented in 12.9% of the donors. A hypertension risk was expected as a result of physiological alterations, such as hyperfiltration in the remaining kidney, changes in renin–angiotensin–aldosterone regulation, as well as more frequent clinical follow-ups [31,32]. A Canadian study found a hypertension diagnosis in 16.3% of living donors [32]. Other donor evaluations documented a lower blood pressure in kidney donors compared with controls and no increase in the use of antihypertensive drugs [5,23].

Readmission for acute conditions has become an important metric for healthcare systems in assessing the treatment success. In the present evaluation, approximately 8.5% of the donors were re-hospitalized after kidney donation; approximately 50% of these were possibly caused by donation (mostly wound problems). Schold *et al.* [33] reported a cumulative 3-year incidence of re-hospitalization of 9% following donation; readmission resulting from surgical complications in the early post-transplant period might be common [34].

The present study includes a detailed analysis of donors' quality of life (QoL) postkidney donation. As in several former evaluations, HRQoL was on average the same or even better in living kidney donors compared with the general population [6,7,35,36]. In 361 donors in the Netherlands, HRQoL was on average better than in the Dutch population, with 12% of donors presenting reduced physical and 18% reduced mental scores [9]. The percentage of 13% of donors with reduced mental health in the present study is on the lower scale of the previously reported percentages of lower mental functioning of between 9 and 25% [9,36,37]. However, a small proportion of living donors experience a reduction in HRQoL postdonation [35,37,38]. Remarkably, our study showed MCS scores being slightly lower for female donors; this was the result of a reduced role functioning. Comparable to previous studies, the blood

pressure, kidney function, and laboratory data, such as hemoglobin or total protein or cardiovascular events, did not contribute to PCS or MCS [9].

Discussion about an adequate control cohort for living kidney donors is ongoing [38]. Kroencke *et al.* [39] demonstrated better HRQoL compared with the general population, but lower scores compared with healthy controls.

As in a previous evaluation [9], the status of the recipient did not directly affect the psychosocial outcome in the present analysis. Other studies demonstrated recipients' poor health, death, or graft failure as significant predictors for poor quality of life of the donor [6,7,35,39]. This might be the result of a high rate of living donors (93.9%) and functioning allografts (84.5%) within the answering study cohort compared with other evaluations [36].

Depression is a prevalent condition in Germany and other countries, with approximately 5–10% of the population being affected [40,41]. In the present study, 7.8% of living kidney donors showed some depressive syndrome, with major depression in 2.1%. A systematic review combining data for more than 5000 living donors estimated that depression affects 5–23% of donors [6]. An Organ Procurement and Transplantation Network (OPTN) database analysis identified a cumulative frequency of depression diagnosis of 4.2%, 1-year postdonation and a significantly lower rate of depression diagnoses in kidney donors compared with an age and gender-matched nondonor cohort [42].

Some donors reported fatigue symptoms after donation, which may limit them in their participation in daily and leisure activities [9]. One explanation might be that these fatigue symptoms are the result of aging and are unrelated to kidney donation.

Our study showed additional interesting observations. In particular, older donors reported significantly fewer fatigue symptoms compared with the general population. Detailed analysis shows that fatigue was present in female donors aged between 40 and 59 years. This cohort represents an emotionally and physically highly engaged population. These results have important implications, because this cohort includes a considerable number of donors [5,7,36,43].

In addition, the presence of fatigue was closely associated with symptoms of depression. Correlation between fatigue and depression is documented [44]. With respect to living kidney donors, de Groot *et al.* [9] reported an association of higher PCS and/or MCS postdonation with less fatigue. In comparison to the Dutch population, donors with high PCS and/or MCS scores reported less fatigue, whereas donors with reduced PCS and/or MCS clearly had higher fatigue scores.

To our knowledge, the present study is the first detailed analysis of all living renal donors at one large renal transplant center in our country—including all parts of the outcome results. The effect of living renal donation on the clinical follow-up, socioeconomic and psychosocial outcome, quality of life, mental health, fatigue, and psychiatric symptoms were assessed. However, the study has some limitations. Only 68.6% of all donors at the Transplant Center provided informed consent and answered the questionnaires. Overall, this is an excellent result in questionnaire studies. However, missing data are an obstacle in all follow-up reports on living kidney donors. The inability or unwillingness to participate in such surveys raises questions on the representativeness of the results. The reasons for lack of response might be stress or feeling worse, but also feeling very well, which might be the reason for missing follow-up visits. In the present analysis, nonresponding donors were more likely to be male and younger at the time of donation and at the time of follow-up.

This is a longitudinal follow-up study concerning clinical and socioeconomic data, but it is a cross-sectional evaluation with respect to the health-related questionnaires. Donor HRQoL was not evaluated before the donation, so it is possible that the reduced QoL was already present prior to donation, without any association to the kidney donation itself. Overall, our donor cohort reported better HRQoL compared with the general German population of the same age and gender.

In addition, guidelines on psychosocial donor evaluation are inconsistent among various transplant centers and countries. There is a need for prospective psychosocial outcome studies on living donors and the use of uniform terminology to label psychosocial screening criteria [45]. The use of validated instruments as performed in the present study strengthened the outcome data.

Discussion on the optimal control cohort is ongoing. A comparison with a healthy population might be preferable. However, even a selected healthy cohort might not be adequate, as our and other data show that not all living kidney donors are completely healthy [8,46]; some may suffer from hypertension or metabolic disorders before the donation. In addition, a healthy general population will not undergo a surgical intervention comparable to kidney donation. This experience might have implications on psychological and mental follow-up.

In 96.6% of the donors, nephrectomy was performed by an open surgery. This might affect not only the physical but also the psychological outcomes. It might be debated whether self-esteem is affected by a long incision compared with a smaller invisible incision; and large flank scars might cause chronic pain. However, only some of the donors showed a large flank scar because the operating technique was changed to a small horizontal incision 15 years ago.

In conclusion, living kidney donors reported an overall good clinical outcome in the medium- and long-term

follow-up, with an expectedly reduced but stable renal function and a minor increase of hypertensive donors. The general physical and mental health is comparable with or even better than that of the general population. The present study shows some indication of female donors possibly being at higher risk of psychological problems after donation. However, this has to be assessed and specified in future clinical evaluations. Considering the result of this evaluation, clinical and psychological follow-up of living kidney donors should be intensified as blood pressure increased and GFR declined in several donors and depressive symptoms were obvious in several donors. Potential donors should be informed about the risk of depressive symptoms within the evaluation process, and psychological follow-up should be offered to donors.

Authorship

CS: research idea and study design. CS, DF, RD, MS, CM and VS: data collection. GR, DF and CS: statistical analysis. MH, PS and MZ: mentorship. Each author contributed intellectual content during writing of the manuscript.

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