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Reduced quality of life in living kidney donors: association with fatigue, societal participation and pre-donation variables

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Summary

Health related quality of life (HRQoL) of living kidney donors on average is good, but some donors experience a low HRQoL after donation. This study assessed the prevalence of reduced HRQoL and explored associations with pre- and post-donation variables. 316 donors (response rate 74%) who donated a kidney between 1997 and 2009 filled in a questionnaire. HRQoL was measured using the Short-Form 36; fatigue using the Multidimensional Fatigue Inventory; societal participation using the Utrecht Scale for Evaluation of Rehabilitation-Participation. Donors on average had better HRQoL than the general population. However, 12% had a reduced physical (PCS) and 18% a reduced mental (MCS) HRQoL. Donors with reduced HRQoL reported greater fatigue ($P < 0.01$), lower societal participation ($P < 0.01$) and showed a trend towards statistical significance in experiencing more donor–recipient relationship changes ($P = 0.07$). Prior to donation, donors with reduced PCS had a higher BMI ($P < 0.05$) and more often smoked ($P < 0.05$). Donors with reduced MCS had higher expectations ($P < 0.05$). Reduced HRQoL is associated with higher BMI, smoking and higher expectations prior to donation. These results may be used to develop a screening instrument to select donors at high risk for reduced HRQoL.

Introduction

Kidney transplantation using living donors is increasingly performed worldwide. Literature has shown that donors on average have the same or better health related quality of life (HRQoL) [1–3] than a healthy population and that they return to pre-donation HRQoL levels post donation [4,5]. However, a small part of the donors experience a low HRQoL after donation, especially regarding psychological functioning [1,6,7]. It is unknown which pre-donation variables may predict such a negative effect on HRQoL. Furthermore, some donors report an increased fatigue after donation, which may limit them in their participation in leisure activities [4]. However, this fatigue might be the result of ageing and not related to donating a kidney. Therefore HRQoL of donors should be standardized to the age-specific HRQoL of the general population.

Previous studies have shown that people hesitate to donate a kidney, because they are concerned about their own longterm health [8,9]. It is known that the donor's mortality pattern is similar to that in the general population, the majority dying of cardiovascular diseases and malignancies [10], that their blood pressure may increase

post donation with 5-mm Hg per 5–10 years more than the rise due to normal aging [11], and that their renal function deteriorates with increasing age, but similar to what is seen among healthy subjects [10]. However, we do not know whether increasing blood pressure or other medical consequences after donation [12] explain differences in HRQoL between donors. Research shows that people are able to adapt or learn to deal with such medical consequences of an illness or surgery, and that the effect on HRQoL is smaller than healthy people expect [13,14]. The extent to which differences in HRQoL between living kidney donors are explained by differences in kidney function, increased blood pressure or other medical consequences has not been studied so far.

This study therefore determines the HRQoL of living kidney donors in the short and long term post donation, assesses the prevalence of reduced HRQoL and explores which variables are associated with this reduced HRQoL. This will add to existing literature not only which part of the donors experience reduced HRQoL, and its association with fatigue and societal participation, but also which pre-donation variables are associated with reduced HRQoL so that it becomes possible to develop a screening tool to select donors at risk for reduced HRQoL.

Material and methods

Study population

The study is a retrospective follow up study among all donors who donated a kidney at the Leiden University Medical Center (LUMC) between 1997 and 2009. The study was approved by the Medical Ethical Committee of the LUMC.

Questionnaires were sent to all living kidney donors (n = 426) in September 2010. On a response form they could indicate whether they wanted to participate or not. If not, they were asked for their reason for non-participation and to rate their current health status using a single question. If donors did not respond within 1 month we sent a reminder. In case of missing answers donors were contacted. Of the 426 questionnaires, 17 were returned by the postal service (unknown address), 2 donors appeared to be deceased (not mentioned in the hospital information system) with unknown cause of death, and 20 donors replied that they did not want to participate. 73 Donors did not return the response form. Thus, 316 of the 426 donors completed the questionnaire (response rate of 74.2%).

HRQoL, fatigue and societal participation

The Short Form-36 (SF-36) questionnaire was used to assess the donor's current HRQoL [15–18]. Since the donors differed on the time passed since donation (between <1 years and 13 years), we were able to reconstruct the HRQoL by time since donation. The SF-36 is the most widely used and validated general HRQoL questionnaire, which has been translated into several languages. The SF-36 has undergone reliability and validity testing in the Netherlands [18] and has already been used to measure HRQoL in living kidney donors [2,19]. It includes 36 questions assessing 8 health domains [15–18] that are used to compute the physical component summary (PCS) and the mental component summary (MCS) scores. The component summary scores are standardized to the general Dutch population, using the Dutch regression coefficients, so that a score of 50 is the reference value (the expected HRQoL) for the Dutch population of that age and gender. A reduced HRQoL was defined as a PCS or MCS lower than 45, because a 5-point difference is regarded as clinically relevant [20] and which is 10% lower than the average expected HRQoL in the general population (standardised for age and gender). Given that the average HRQoL in living kidney donors is known to be higher on average than the general population [1–3], a cut-off of 45 means that these donors do not only have a 10% lower score than the general population, but can be considered very low compared to the average HRQoL scores among other donors.

We also measured the donor's current fatigue and societal participation in a more specific way than is measured with the generic SF-36 questionnaire, since these may be influenced by donation. Fatigue was measured with the Multidimensional Fatigue Inventory (MFI-20) [21], which covers the following dimensions of fatigue: (i) general fatigue; (ii) physical fatigue; (iii) mental fatigue; (iv) reduced motivation and (v) reduced activity. In each of the five subscales, scores range from 4 to 20, with higher scores indicating greater fatigue. Participation was measured using the Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-Participation) [22]. The USER-Participation covers three aspects of societal participation: frequency of participation, restriction in participation and satisfaction with participation. In each of the three subscales, scores range from 0 to 100, with higher scores indicating higher frequency of participation, fewer restrictions in participation and more satisfaction with participation.

Post-donation medical outcomes and experienced relationship changes

To assess whether kidney function is associated with a reduced HRQoL we collected post donation data from the medical records of donors regarding urine concentration of protein and albumin and serum concentration of creatinine. Serum creatinine was used to calculate the renal clearance with the Cockcroft formula [23]. In addi-

tion, data were collected on other medical outcomes as blood hemoglobin and blood pressure. All measurements concerned the last visit at the outpatient clinic, so that this measurement was as close as possible to the measurement of HRQoL.

To assess whether reduced HRQoL is associated with changes in the donor–recipient relationship that are experienced after donation, donors were asked whether they had experienced such relationship changes after donation. Relationship changes were measured using self-constructed questions, which were based on face-to-face interviews and focus groups. Included items were frequency of contact with recipients (seeing each other, doing activities together, contact by phone or computer) as well as a valuation of their contact. First, donors were asked to rate their frequency of contact (as well as valuation) before donation and then to rate their current frequency of contact compared with the situation before donation. These changes could be rated on a 5-point scale (much more frequent, more frequent, as frequent, less frequent and far less frequent as before donation). Changes in how they valued the relationship were rated on a 5-point scale, including a direction indicating a positive or negative change (much better, slightly better, as good as, worse, much worse than before donation).

Pre-donation medical variables and expectancies

To assess which pre-donation variables may be associated with a reduced HRQoL after donation, we retrospectively collected data from the medical records: age, gender, height, weight, smoking, urine protein concentration, blood hemoglobin and renal clearance. In addition, we collected data on blood pressure, cardiovascular events in the medical history, thrombosis and diabetes, because these are prevalent disorders in the general population, but also increase the risk of developing chronic kidney disease [24]. Cardiovascular events were defined as acute myocardial infarction or other forms of chronic ischemic heart disease, heart failure, peripheral vascular disease or cerebral vascular disease consistent with the cardiovascular diseases included in the Charlson Index for comorbidity [25]. Disorders included in these categories were further defined following the International Classification of Diseases 9 (ICD9). The last pre-donation measurements were used.

Expectations before donation may influence the donor's emotional reactions and behavior after donation. We therefore used the living donation expectancies questionnaire to measure potential donor's expectancies [26]. Respondents were asked to think back to the time before donation, and to answer questions on expectations prior to donation grouped into the following 4 scales: interpersonal benefit (7 items), personal growth (13 items), Quid pro Quo (5 items), and health consequences (6 items). Each item has five response options, with higher scores indicating higher expectations.

Donors were also asked whether they expected prior to donation that donor–recipient relationship changes would occur after donation.

Analyses

We first assessed the donors' average HRQoL, overall and by time since donation, and compared it with the average HRQoL in the general Dutch population using a one-sample *t*-test. We assessed whether HRQoL differed depending on the time passed since donation in years using correlation analysis. If no differences were observed, we created three groups of time since donation: ≤5 years post donation, 5–10 years post donation and >10 years post donation. Within each of these three groups we compared the average HRQoL of our living kidney donors to the average HRQoL in the general Dutch population, both for the 8 domains and the 2 component summary scores.

Next, we assessed what proportion of donors had reduced HRQoL and compared donors with and without reduced HRQoL on pre-donation variables to assess possible associations using a *T*-test (in case of continuous variables) or chi-square test (in case of categorical variables). The pre-donation variables were BMI, blood pressure, urine protein and albumin concentration, blood hemoglobin, renal clearance, smoking, cardiovascular event and expectations prior to donation. All factors that showed a significant univariate relationship ($P < 0.10$) were entered in a multiple logistic regression analysis.

Furthermore, we assessed whether HRQoL was associated with fatigue and societal participation using linear regression analysis. Thereafter, it was assessed whether donors with reduced HRQoL differed in their self-reported fatigue and societal participation compared to donors without reduced HRQoL using a *T*-test. Finally, we assessed whether post-donation kidney function represented by renal clearance, urine protein and albumin concentration, and other post-donation medical outcomes such as blood pressure and blood hemoglobin as well as experienced donor–recipient relationship changes were associated with reduced HRQoL using a *T*-test (in case of continuous variables) or chi-square test (in case of categorical variables). A *P*-value smaller than 0.05 was considered statistically significant in all analyses; a *P*-value between 0.05 and 0.10 was considered a trend towards statistical significance.

Results

The characteristics of the donor population are shown in Table 1. Of all donors 35% were male. The mean age at

donation was 51.7 years and the mean time since donation was 5 years (range 0.9–13.5 years). Most of the donors had donated a kidney to a first degree relative (child, father/mother) or to a second degree relative (brother, sister).

To assess whether our results were affected by response bias, we asked both the non-respondents and respondents to answer a single question about their current health status (item 1 of the SF-36). Of the 20 non-respondents 15 completed this question; they all reported a good to excellent health status. Within the group of respondents 91% reported a good to excellent health status, so that based on these data and the overall good response rate (74%) it is likely that the respondents are representative for the total group of donors.

Donors' overall HRQoL and HRQoL by time since donation

Figure 1 shows that both the PCS and MCS did not differ depending on time passed since donation ($r = -0.05$ $P = 0.34$ for PCS and $r = -0.04$ $P = 0.48$ for MCS).

Health related quality of life of the donors overall and stratified by time since donation in three equal time period groups are thus shown in Table 2. HRQoL of our donors on average was significantly better than the general Dutch population in all domains and the physical component summary score (Table 2). The mental component summary score was not significantly different from the score in the general population. Also, within the three groups of time since donation, each group of donors had higher HRQoL scores than the general population on all domains and for both component summary scores (Table 2). Furthermore, the PCS and MCS did not differ depending on the relationship with the recipient (first degree, second degree, partner or other) ($P = 0.45$ and $P = 0.93$ respectively). For comparability with other studies, we also calculated the PCS and MCS using the American regression coefficients, which were 53.7 (8.3) and 52.7 (8.2) respectively.

Pre-donation variables associated with reduced HRQoL

Twelve percentage of the donors had a reduced PCS and 18% a reduced MCS. Donors with reduced PCS on average had a slightly higher BMI (26 vs. 25, $P = 0.09$), much more often smoked (41% vs. 25%, $P < 0.05$) and showed a trend towards higher expectations regarding health consequences ($P = 0.07$) prior to donation (Table 3). Donors with and without reduced PCS did not differ in blood pressure, kidney function, percentage of cardiovascular events and expected relationship changes (Table 3). In a multivariate logistic regression analysis BMI ($P < 0.05$) and smoking had a significant ($P < 0.05$) independent association with reduced PCS (data not shown).

Table 1. Characteristics of the donor population (Leiden University Medical Center, 316 living kidney donors).

Characteristics	Donors ($n = 316$)
Gender, % male	35.4
Age during donation, mean (SD)/median (range)	51.7 (11.4)/ 52.6 (25.1–76.8)
Time since donation in years, mean (SD)	5.07 (3.2)
Donor relationship to recipient*, number (%)	
First degree	87 (27.7)
Second degree	84 (26.8)
Partner	104 (33.1)
Other/unrelated	39 (12.4)
Educational level†, number (%)	
Basic	23 (7.5)
Intermediate	197 (64.2)
High	87 (28.3)

SD, standard deviation.
*Missing data for 2 donors.
†Missing data for 9 donors.

Donors with reduced MCS (18%) did not differ in BMI, blood pressure, kidney function, percentage of cardiovascular events compared to donors without reduced MCS (Table 3), but on average had higher expectations regarding interpersonal benefits ($P < 0.05$), health consequences ($P < 0.05$) and quid pro quo ($P = 0.07$) prior to donation (Table 3). Higher scores on expected health consequences meant that they had more negative thoughts on whether they would be in a lot of pain and discomfort or would feel anxious or depressed after donation. Both groups did not differ in their expectations regarding donor–recipient relationship changes ($P > 0.10$). In a multivariate logistic regression analysis, expectations regarding health consequences had a signifi-

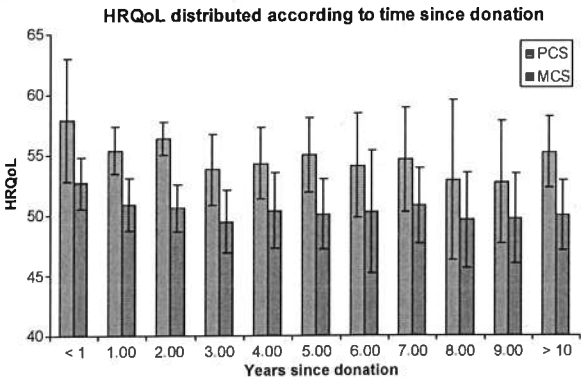

Figure 1 Health related quality of life (HRQoL) by time since donation (Leiden University Medical Center, 316 living kidney donors). PCS, Physical Component Score; MCS, Mental Component Score.

Table 2. Average Health related Quality of Life (SF-36) scores for all donors (n = 316) and stratified by time since donation.

	PF	RP	BP	GH	VT	SF	RE	MH	PCS	MCS
General Dutch population	85.2 (23.1)	79.5 (35.4)	80.5 (24.4)	71.3 (20.8)	68.6 (19.2)	85.1 (21.5)	83.1 (32.7)	75.9 (17.6)	50 (10.0)	50 (10.0)
All donors	91.5 (16.7)	87.1 (29.2)	88.0 (19.8)	80.6 (19.3)	71.3 (18.5)	88.3 (19.0)	89.7 (26.3)	79.8 (15.2)	54.8 (8.4)	50.3 (8.1)
P-value	**<0.01**	**<0.01**	**<0.01**	**<0.01**	**0.01**	**<0.01**	**<0.01**	**<0.01**	**<0.01**	0.53
Time since donation										
<5 yr (59%)	92.2 (15.7)	88.1 (28.6)	89.0 (18.4)	80.8 (19.5)	71.6 (19.2)	89.7 (17.7)	89.5 (26.4)	80.2 (15.5)	55.2 (7.6)	50.4 (8.1)
5–10 yr (30%)	90.1 (18.3)	83.6 (32.2)	85.8 (22.6)	80.1 (19.0)	70.5 (17.9)	85.9 (21.6)	89.5 (26.7)	79.4 (15.1)	54.0 (9.7)	50.1 (8.0)
>10 yr (11%)	91.0 (17.1)	91.9 (22.8)	88.7 (18.7)	81.4 (19.5)	71.2 (16.4)	87.1 (18.1)	91.2 (25.0)	78.6 (14.1)	55.2 (8.9)	50.0 (8.6)

Results are presented as mean (standard deviation). Significant differences are in bold.
PF, physical functioning; RP, role-physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role-emotional; MH, mental health; PCS, Physical Component Score; MCS, Mental Component Score.

Table 3. Associations between pre-donation medical variables, expectations and health related quality of life (Leiden University Medical Center, 316 living kidney donors).

Donors	PCS < 45 n = 36 (11.5%)	PCS ≥ 45 n = 278 (88.5%)	*P*-value	MCS < 45 n = 55 (17.5%)	MCS ≥ 45 n = 259 (82.5%)	*P*-value
Medical variables						
BMI, mean (SD)	26.2 (3.9)	25.2 (3.3)	**0.08**	25.9 (3.7)	25.2 (3.3)	0.13
Systolic blood pressure, mean (SD)	133.3 (18.7)	134.2 (15.4)	0.72	135.4 (18.9)	134.0 (15.1)	0.55
Diastolic blood pressure, mean (SD)	81.2 (9.3)	81.6 (8.2)	0.79	81.2 (8.5)	81.6 (8.3)	0.73
Renal clearance, mean (SD)	96.1 (21.1)	97.6 (23.5)	0.72	98.5 (22.4)	97.2 (23.4)	0.70
Albumin, mean (SD)	12.5 (11.1)	11.2 (16.8)	0.65	12.4 (16.0)	11.1 (16.6)	0.60
Total protein, mean (SD)	0.15 (0.06)	0.15 (0.07)	0.91	0.16 (0.07)	0.15 (0.06)	0.49
Hemoglobin, mean (SD)	8.77 (0.71)	8.84 (0.69)	0.60	8.74 (0.74)	8.85 (0.68)	0.31
% Smoking	41.2	24.9	**0.01**	35.3	25.0	0.21
% Cardiovascular event	2.8	2.9	0.91	1.9	3.1	0.57
Expectancies						
Interpersonal benefit, mean (SD)	16.2 (5.8)	15.3 (5.2)	0.31	17.0 (5.0)	15.1 (5.2)	**0.02**
Personal growth, mean (SD)	33.9 (9.2)	35.2 (9.2)	0.41	36.2 (8.3)	34.9 (9.4)	0.34
Health consequences, mean (SD)	12.2 (3.6)	11.1 (3.3)	**0.07**	12.8 (3.8)	10.9 (3.1)	**< 0.01**
Quid pro quo, mean (SD)	9.5 (3.3)	9.4 (3.1)	0.87	10.1 (3.4)	9.2 (3.0)	**0.07**
Expected relationship changes						
% yes	11.1	6.5	0.30	9.1	6.6	0.56
% maybe	11.1	15.8	0.46	16.4	15.1	0.84
% not thought about it at that moment	19.4	21.2	0.81	27.3	19.7	0.21
% no	58.3	56.2	0.83	47.3	58.7	0.12

BMI, Body Mass Index; Significant differences are in bold.

cant ($P < 0.05$) independent association with reduced MCS (data not shown). No difference was found between donors of whom the recipient had graft failure (immediate or later), graft loss or died, with the other donors in the expectations they reported to have had prior to donation (data not shown). This suggests that donors who reported more negative expectations are not just donors with worse outcomes in the recipient.

Association of HRQoL with fatigue, societal participation and other post-donation outcomes

A higher PCS/MCS after donation was associated with less fatigue (all subscales of the MFI-20) and better societal participation (all three subscales of the USER-P) (data not shown). Donors with reduced PCS and MCS subscales reported significantly higher fatigue on all dimensions of the MFI-20 (Table 4) and lower societal participation both in terms of frequency and satisfaction, as well as more restrictions. Comparing the fatigue scores with the scores obtained in a sample of 139 individuals from the Dutch general population [27], then donors without reduced PCS/MCS report less fatigue while donors with reduced PCS/MCS clearly have higher fatigue scores indicating more fatigue than the general population, particularly for general and physical fatigue (Table 4).

Donors with reduced PCS showed a trend towards a higher albumin level on average ($P = 0.07$), but renal

Table 4. Associations between health related quality of life and post-donation fatigue and societal participation (Leiden University Medical Center, 316 living kidney donors).

Donors	PCS < 45 n = 36 (11.5%)	PCS ≥ 45 n = 278 (88.5%)	P-value	MCS < 45 n = 55 (17.5%)	MCS ≥ 45 n = 259 (82.5%)	P-value	General Dutch population [27]
General Fatique, mean (SD)	14.0 (4.2)	7.6 (3.8)	**<0.01**	13.1 (4.8)	7.4 (3.5)	**<0.01**	9.9 (5.2)
Physical Fatique, mean (SD)	15.0 (3.5)	6.4 (3.1)	**<0.01**	11.7 (4.8)	6.5 (3.4)	**<0.01**	8.8 (4.9)
Reduced Activity, mean (SD)	12.6 (4.4)	6.8 (3.0)	**<0.01**	10.9 (4.3)	6.7 (3.0)	**<0.01**	8.7 (4.6)
Reduced Motivation, mean (SD)	11.3 (4.1)	6.6 (2.9)	**<0.01**	10.5 (4.3)	6.5 (2.7)	**<0.01**	8.2 (4.0)
Mental Fatique, mean (SD)	10.4 (5.1)	7.3 (3.5)	**<0.01**	10.7 (5.0)	7.0 (3.2)	**<0.01**	8.3 (4.8)
User_P frequency, mean (SD)	28.3 (11.1)	36.0 (8.2)	**<0.01**	31.3 (10.0)	35.9 (8.5)	**<0.01**	
User_P restrictions, mean (SD)	42.1 (11.3)	52.9 (6.3)	**<0.01**	46.1 (11.1)	35.9 (8.5)	**<0.01**	
User_P satisfaction, mean (SD)	67.1 (17.4)	88.7 (13.9)	**<0.01**	78.4 (17.7)	87.9 (15.0)	**<0.01**	

Significant differences are in bold.

clearance did not differ between donors with and without reduced PCS (Table 5). Donors with reduced MCS had a lower blood hemoglobin level post donation ($P < 0.05$) and showed a trend towards more often experiencing donor–recipient relationship changes post donation ($P = 0.07$) (Table 5). Although the numbers are small, the general trend seems to be that donors with a reduced MCS less often experienced increased contact or joint activities with the recipient after donation, and less often reported a better way of contact, involvement in their life and relationship.

Discussion

On average our donors demonstrated a better HRQoL compared to the general Dutch population both in the short and long term post donation. Part of the donors nevertheless, experienced a reduced HRQoL, had a higher level of fatigue, a lower level of societal participation, and showed a trend towards more often experiencing donor–recipient relationship changes. A reduced PCS was associated with a higher BMI and smoking prior to donation and a reduced MCS with higher expectations regarding

Table 5. Associations between post-donation outcomes, experienced donor–recipient relationship changes and health related quality of life (Leiden University Medical Center, 316 living kidney donors).

Donors	PCS < 45 N = 36 (11.5%)	PCS ≥ 45 N = 278 (88.5%)	P-value	MCS < 45 N = 55 (17.5%)	MCS ≥ 45 N = 259 (82.5%)	P-value
Outcomes on kidney function						
Renal clearance, mean (SD)	78.2 (20.0)	78.1 (20.2)	0.99	80.3 (20.3)	77.6 (20.1)	0.41
Albumin, mean (SD)	64.2 (276.5)	12.6 (49.8)	**0.07**	11.7 (22.1)	21.1 (117.6)	0.60
Total protein, mean (SD)	0.18 (0.35)	0.11 (0.11)	0.11	0.10 (0.06)	0.12 (0.18)	0.41
Other outcomes						
Systolic blood pressure, mean (SD)	130.1 (15.2)	129.1 (14.1)	0.70	129.2 (12.4)	129.3 (14.6)	0.98
Diastolic blood pressure, mean (SD)	81.1 (8.1)	81.5 (7.4)	0.77	81.1 (5.9)	81.5 (7.8)	0.77
Hemoglobin, mean (SD)	8.55 (0.86)	8.54 (0.67)	0.96	8.36 (0.70)	8.58 (0.69)	**0.04**
Experienced donor–recipient relationship changes*						
Yes (%)	8 (23.5)	59 (22.2)		16 (32.0)	51 (20.4)	
No (%)	26 (76.5)	207 (77.8)	0.86	34 (68.0)	199 (79.6)	**0.07**
% increased						
Face-to-face contact	5 (14.7)	30 (11.2)		5 (9.8)	30 (11.9)	
Joint activities	2 (5.9)	23 (8.6)		4 (7.8)	21 (8.3)	
Contact by phone/computer	2 (5.9)	28 (10.4)		5 (9.8)	25 (9.9)	
% Improved						
Way of contact	6 (17.6)	27 (10.0)		5 (9.8)	28 (11.1)	
Involvement in their life	6 (17.6)	23 (8.6)		4 (7.8)	25 (9.9)	
Way of empathizing with each other	4 (11.8)	23 (8.6)		4 (7.8)	23 (9.1)	
Relationship	6 (17.6)	28 (10.4)		4 (7.8)	30 (11.9)	
Understanding	6 (17.6)	24 (8.9)		6 (11.8)	24 (9.5)	
Conversations	4 (11.8)	22 (8.2)		6 (11.8)	20 (7.9)	

Significant differences are in bold.

*Donors who indicated that their recipient was deceased (n = 7), were not included in the analysis.

health consequences prior to donation. No association of reduced HRQoL with kidney function prior to or post donation was found.

The study has some limitations. First, the study is a cross-sectional retrospective study. Donor HRQoL has not been evaluated prior to donation, so that it is possible that the reduced HRQoL in these donors was already present before donation, and that it is not associated with the kidney donation itself. Even if this were true, it is likely that the higher BMI and smoking were also associated with reduced HRQoL prior donation, so that these can still be used to identify high risk donors to educate them on e.g. smoking behaviour, in particular if the reduced HRQoL would worsen due to donation. Furthermore, respondents were asked retrospectively about their expectations prior to transplantation so that we have to be careful with interpreting the association found between reduced mental HRQoL and expectations in this study. Higher expectations might lead to disappointment or regret and thereby result in a lower mental HRQoL. With respect to health consequences, donors with reduced mental HRQoL more often reported more negative thoughts on expecting pain and discomfort or feeling anxious and depressed after donation. This may either reflect their current mental state of mind, or be an accurate representation of their expectancies prior to donation. It is also possible that a lower mental HRQoL leads to recalling the negative thoughts prior to donation, to a greater extent than in donors with higher mental HRQoL. Our study thus shows that there is an association between HRQoL and expectations prior to donation, but the direction of this association should be further investigated in a prospective study. Finally, this study concerns a single center study. As a result the sample size of donors does not reflect all donors in the Netherlands. However, because the HRQoL in our population was comparable to that of other centers [19] we feel our population is representative for the Dutch donor population.

Our donor population on average reported better HRQoL compared with the general population of the same age and sex, which has also been shown by studies in other countries [28,29] both in the short and long term after donation. A comparison with a healthy sample would have been preferable, since the general population also includes subjects with diseases, whereas living donors constitute a selective sample chosen for their good health. However, such a healthy sample was not available so that a comparison with the general population standardized by age and sex was the best possible option. The present study adds to existing studies that a proportion of donors nevertheless experienced a reduced mental or physical HRQoL, a higher level of fatigue and a lower societal participation, and that a higher BMI, smoking and higher expectations prior to donation are associated with such a reduced HRQoL. Since HRQoL estimates were standardized for age and gender to the general Dutch population, these results cannot simply be the result of general ageing.

Remarkably, kidney function had no impact on HRQoL. If reduced HRQoL would be strongly associated with donating a kidney, we would have expected a difference in renal clearance between donors with and without reduced physical HRQoL. One of the explanations may be that kidney function would have to worsen much more than is the case in living donation, to have an influence on HRQoL. It thus seems more likely that the reduced HRQoL is due to a combination of factors around kidney donation, among which kidney function only has a small influence, for instance the donor's HRQoL prior to donation and factors like smoking and a high BMI before donation. Pre-donation BMI and smoking were independently associated with a reduced physical HRQoL, as they are in the general population and within other populations [30–32]. The reason for these associations may be the increased risks during surgery, since it is more difficult to access the kidney in people with higher BMI and will thus generally require longer operating time. This may increase the risks of complications after surgery and consequently recovery. The same may be true for smokers, given the effect this has on the vascular system. It is thus possible that being a donor has an additional small (negative) effect on HRQoL besides smoking behavior and higher BMI, but that the effect on kidney function was too small to be detected in the present study. This should be further explored in a future comparative study of donors and matched healthy non-donors, as done by Clemens *et al.* [3] but where these variables were not included.

The percentage of donors with reduced mental health (18%) corresponds to what is found in the literature, in which studies among kidney donors report percentages of reduced mental functioning between 10% and 25%. However, the way mental functioning is measured varies between studies, which might explain the variation in percentage of donors with mental problems between studies. For example, Reimer reported that one out of eight donors (13%) experienced mental distress measured with the Brief Symptom Inventory [7]. Wiedebusch found that 25% of the donors experienced depressive symptoms screened with the hospital anxiety and depression scale (HADS) [33]. In the present study a generic HRQoL questionnaire was used and our results regarding proportion of donors with reduced mental health fit within the range reported in the literature.

It is known that expectations before an event often influence emotional and behavioural reactions after the

event [34]. The findings of Rodrigue *et al.* [26] suggest that donor candidates with high expectations are more likely to be classified as having some level of psychosocial risk. Transplant centers in the US also identified that unrealistic expectations should be considered as a relative or absolute contraindication to donation [35]. In this study, we found that donors with reduced mental HRQoL had higher pre-donation expectations regarding health consequences than donors without reduced mental HRQoL. These results seem to be consistent with the previous findings and might be used to develop a screenings tool to select those donors at risk for a reduced HRQoL if confirmed in a prospective study, to discuss their expectancies so that these are realistic. One of the possibilities may be to use the Donor Expectancies Questionnaire as part of the screening, so that discussing these becomes more structured than in the current screening. Extreme scores may for instance be used as a contraindication as done in the US [35]. However, we must keep in mind that donors were asked to think back to the time before donation, so our results might be influenced by recall bias, where donors with reduced MCS were perhaps more likely to remember that they had more negative thoughts regarding health consequences. Furthermore, donors with reduced MCS tended to more often experience changes in the donor–recipient relationship after donation. Another study found that the donation led to family conflicts in 11% of the cases, but whether this influences HRQoL was not investigated [7]. Taken together this suggests that it is important to further analyze the donor–recipient relationship post donation prospectively in a larger donor population, because it might have an impact on mental HRQoL after donation.

The present study has shown that donors on average had a HRQoL better than or equal to the Dutch general population, both short term and long term after donation. However, 12–18% of the donors had a reduced HRQoL, a higher level of fatigue and a lower societal participation and showed a trend towards more often experiencing relationship changes after donation. A higher BMI, smoking and higher expectations regarding health consequences prior to donation are associated with reduced HRQoL. Our results can be used to develop a screening instrument to select those donors at risk for a reduced HRQoL. These donors should be informed and educated about the possibility of reduced HRQoL (e.g. as a result of smoking behaviour) and may be monitored more closely after donation so that early detection of problems is possible. Furthermore, the expectations of high risk donors on various domains should be discussed to ensure that these are realistic, to prevent potential conflicts or disappointment after donation.

Authorship

IBG: analyzed the data and wrote the first draft of the manuscript; PJMB, AMS and AGB: helped with interpretation of the data and writing the manuscript; PJM: conceived the study and its design, participated in the statistical analyses and interpretation of the data, and writing the manuscript. All authors have read and approved the final manuscript.

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