ORIGINAL ARTICLE

The impact of the donors' and recipients' medical complications on living kidney donors' mental health

Lotte Timmerman¹, Mirjam Laging¹, Reinier Timman², Willij C. Zuidema¹, Denise K. Beck¹, Jan N.M. IJzermans³, Michiel G.H. Betjes¹, Jan J.V. Busschbach², Willem Weimar¹ & Emma K. Massey¹

1 Department of Internal Medicine, Section Nephrology and Transplantation, Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands

2 Department of Psychiatry, Section Medical Psychology and Psychotherapy, Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands

3 Department of General Surgery, Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands

Correspondence

Lotte Timmerman, Erasmus Medical Center, Department of Internal Medicine – Section Nephrology & Transplantation, P.O. Box 2040, 3000 CA Rotterdam, The Netherlands. Tel.: +31 10 70 32442; fax: +31 10 43 66372:

e-mail: l.timmerman.1@erasmusmc.nl

SUMMARY

A minority of living kidney donors (between 5–25%) have poor psychological outcomes after donation. There is mixed evidence on the influence of medical complications on these outcomes. We examined whether medical complications among donors and recipients predicted changes in donors' mental health (psychological symptoms and well-being) between predonation and 1 year postdonation. One-hundred and forty-five donors completed questionnaires on mental health predonation and 3 and 12 months postdonation. Number of recipient rehospitalizations and donor complications (none; minor; or severe) were obtained from medical records at 3 and 12 months after surgery. Multilevel regression analyses were used to examine the association between medical complications and changes in donors' mental health over time after controlling for sociodemographic characteristics. We found that donor complications (P = 0.003) and recipient rehospitalizations (P = 0.001) predicted an increase in donors' psychological symptoms over time. Recipient rehospitalizations also predicted a decrease in well-being (P = 0.005) over time; however, this relationship became weaker over time. We conclude that medical complications experienced by either the donor or recipient is a risk factor for deterioration in donors' mental health after living kidney donation. Professionals should monitor donors who experience medical complications and offer additional psychological support when needed.

Transplant International 2016; 29: 589-602

Key words

living donors, nephrectomy, prospective studies, psychological adaptation, psychosocial aspects, well-being

Received: 14 August 2015; Revision requested: 28 October 2015; Accepted: 15 February 2016; Published online: 16 March 2016

Introduction

Many studies have shown that a minority of living kidney donors (between 5–25%) experience suboptimal psychological outcomes after living kidney donation [1–6]. It is important to identify these donors and anticipate by support and guidance needs. Various studies highlight the influence of complications among

donors and recipients on donors' mental health, but the results are mixed and limited by methodological issues.

Two studies showed that donors who had a longer recovery period [7] or complications after donation [7,8] had a lower score on the mental component of quality of life postdonation. Minz *et al.* [9] also found that donors' self-reported health is related to depressive symptoms postdonation. Contrary to these results, two

other studies did not find a relationship between the number of donors' hospitalization days or occurrence of medical complications and psychological outcomes after donation [5,10].

Mixed results were also found on the relationship between medical complications among recipients and donors' mental health postdonation. While various studies found no association between recipients' medical complications and donors' quality of life [7,10–12] or satisfaction with life [13], Giessing *et al.* [8] found an association between unfavorable recipient outcomes and a lower quality of life among donors. Two other studies similarly found that donors who perceived the health status of their recipients as worse had more psychological problems than other donors [14,15].

The contradictory findings might be partly explained by the different aspects of mental health that were measured in the studies, for instance measuring quality of life is not the same as measuring psychological symptoms. Research would benefit from measuring overall mental health, instead of just separate aspects of mental health as measured in these previous studies. Models of overall mental health such as that of Keyes *et al.* [16] stipulate the importance of both positive and negative aspects of mental health, defined as well-being and psychological symptoms, respectively. Well-being consists of factors such as satisfaction with life, personal growth, and social contribution [16]. Psychological symptoms consist of factors such as a depressive mood and cognitive problems.

Moreover, the results of most studies were hampered by a retrospective design [7,8,11–13,17]. Consequently, it is possible that donors who reported negative medical experiences already had a lower mental health score predonation and their score postdonation is unrelated to complications during the donation process. Furthermore, a number of studies [9,14,15] based their conclusions on donors' perceptions of their own or recipients' medical complications and thus offer insight into the association between the donors' subjective interpretation of medical complications and donors' mental health. A potential bias in such studies is that a person's mood and mental health status can have an influence on the frequency and intensity of reported physical complaints [18]. Therefore, to explore the relationship between the donors' and recipients' medical complications and donors' mental health, a prospective study is necessary in which complications are measured with objective measures.

Furthermore, it is important to control for the potential influence of sociodemographic characteristics on psychological outcomes, as these characteristics are

related to donors' mental health postdonation [7,11]. Knowledge of the relationship between such characteristics and mental health can also help to identify donors who may need extra monitoring and psychological support.

To summarize, we investigated the extent to which objectively measured indicators of donors' and recipients' medical complications were related to the absolute level or change in donors' overall mental health between predonation and postdonation after controlling for sociodemographic characteristics.

Materials and methods

Participants

All potential donors who underwent medical screening for living kidney donation at Erasmus Medical Center between July 2011 and September 2012 received a patient information form about the study. This cohort included both specified and unspecified donors [19]. Specified donors are persons who donate their kidney to an emotionally and/or genetically related recipient, while unspecified donors donate their kidney anonymously to an unrelated and unknown person. One week before the final appointment of the predonation screening with the nephrologist, the researcher (LT) called the potential donor to ask whether he/she would participate if he/she was approved for donation. Potential donors who did not speak the Dutch language sufficiently or did not live in the Netherlands were not eligible for this study.

Procedure

All those approved for donation were asked to complete questionnaires immediately after the final appointment with the nephrologist (baseline measurement). Participants were asked to complete the same questionnaires immediately after evaluation at the outpatient clinic 3 months (second measurement) and 1 year after donation (third measurement). The questionnaires were explained by a psychologist (LT, ML, EM, or DB) and were either completed in a private room at the outpatient clinic or at home and returned by post. Indicators of medical complications among donors and recipients and donors' sociodemographic characteristics were obtained at 3 and 12 months after the operation from medical records.

This study was approved by the institutional review board of Erasmus Medical Center (MEC-2011-271). All

participants signed an Informed Consent form prior to participation.

Measures

Sociodemographic characteristics

Donors' sociodemographic characteristics are depicted in Table 1. We categorized the relationship between donor and recipient into two groups: unspecified and specified donors. The specified donors were subdivided into five categories: partners, children, parents, siblings, and others (e.g., friends, neighbors).

Mental health

Psychological symptoms: The Brief Symptom Inventory [BSI: 20,21] (Cronbach's $\alpha = 0.96$) was used to measure the presence of psychological symptoms, such as anxious and depressive feelings [20]. An example item is: "In the past 2 weeks, how often did you feel lonely?". The participant rated the extent to which he/she experienced the 53 symptoms in the past 2 weeks on a 5point scale from totally not (0) to very much (4). The mean was calculated, a higher score indicates more symptoms. Psychological symptoms was further operationalized as "negative affect" as measured by the negative affect subscale of the "Positive And Negative Affect Schedule" [PANAS-NA: 22,23] (Cronbach's $\alpha = 0.86$). The Positive And Negative Affect Schedule (PANAS) consists of statements reflecting participant's positive and negative states or emotions. An example of a statement reflecting a negative state is "scared". The participant rated the extent to which he/she experienced the affective states in the past 2 weeks on a 5-point scale from very little or not at all (1) to very much (5). Mean scores were calculated.

Well-being: The Dutch Mental Health Continuum-Short Form [MHC-SF: 24,25] was used to measure well-being (Cronbach's $\alpha=0.89$) [25]. The participant rated how often he/she experienced 14 different feelings of well-being in the past month from *never* (0) to *every day*. An example item is: "In the past month, how often did you feel satisfied?". Mean scores were calculated. Well-being was also operationalized using the "positive affect" subscale of the PANAS (PANAS-PA: Cronbach's $\alpha=0.89$) [22]. While the MHC-SF only minimally measures a person's affect, the PANAS measures affect/emotions in more detail. An example of a statement reflecting a pos-

Table 1. Sociodemographic characteristics of participants (N = 145)

Sociodemographic characteristics	n	%
Median age (range)	56 (20–83)	
Gender		
Men	70	48.3
Women	75	51.7
Employment		
Paid employment	87	60.0
Retired/voluntary work/unemployed	58	40.0
Marital status		
Married/living together	96	66.2
Single/divorced/widowed	49	33.8
Highest level of education		
Primary/secondary school	47	32.4
Further education	95	65.5
Missing	3	2.1
Religious affiliation		
Yes	74	51
No	66	45.5
Missing	5	3.4
Native country		
The Netherlands	129	89.0
Other country	16	11.0
Native language		
Dutch	131	90.3
Other language	14	9.7
Children		
Yes	114	78.6
No	31	21.4
Relationship with recipient		
Unspecified	16	11.0
Specified		
Partner	48	33.1
Child	18	12.4
Parent	12	8.3
Sibling	28	19.3
Other	23	15.9
Cohabitation with the recipient	60	44.4
Yes	60	41.4
No	69	47.6
Not applicable (unspecified donors)	16	11.0

itive state is "interested". Mean scores were calculated (range: 1-5).

Medical complications

The occurrence of medical complications among donors was used and summed for 0–3 months and 4–12 months after donation to align with the measures of psychological factors at 3 and 12 months post donation. Complications were coded into categories by a nephrologist (WW): no complication, minor complication, or

severe complication. Donors' medical information was anonymized before coding. The classification was inspired by the Clavien-Dindo Classification of Surgical Complications [26] and adapted to the situation of living kidney donors. We chose to use less categories, as there was little variation in complications and there were no life-threatening complications. Minor complications were expected to have a limited impact on the donors' life and needed minimal or no medical intervention, while severe complications were expected to have much impact on the donors' life and needed a more invasive intervention, such as a blood transfusion (See Table 3 for details of the classification). For the analyses, minor complications were assigned one point and severe complications two points. Consequently, severe complications have twice the influence on the "complication score" than minor complications. In case of multiple complications, the points assigned to each complication were summed. Eventually, the complication score gives an indication of both severity and number of complications.

Number of rehospitalizations (at Erasmus Medical Center or another hospital) were used as an indicator of medical complications among recipients and were summed for 0–3 months and 4–12 months after the operation. We chose to use number of rehospitalizations as this is an indicator of recurrent medical problems among recipients. Rehospitalizations for biopsies were also included, as biopsies are only performed in case of suspicion of kidney failure, which is an important indicator of recipients' medical complications. Due to the low incidence of graft failure (n = 2) and death among recipients (n = 2), it was impossible to use these independently as indicators of medical complications. As unspecified donors did not know their recipient, they had no data on this item.

Statistical analyses

Firstly, we examined whether participants (donors who completed at least one measurement) differed on sociodemographic characteristics from nonparticipants (donors who refused to participate or were not approached due to logistical issues). Independent *t*-tests were used for the continuous data and chi-squared tests for categorical data.

Secondly, we explored changes in donors' mental health over time by describing basic statistics (median and ranges) of the difference scores between postdonation and predonation scores. In addition, we examined how many donors showed an increase, decrease, and no change in the mental health outcomes over time based on the reliable change indexes [RCIs, 27]. Using the RCI, one can determine whether an individual change score on a measure is large enough that it is unlikely that this change is the consequence of measurement error and can therefore be considered as a "real change" [27]. RCIs for the BSI and MHC-SF reported by Timmerman *et al.* [4] were used: The RCI for the BSI is RCI = 0.14 for men and RCI = 0.19 for women; the RCI for the MHC-SF is RCI = 0.78. RCIs for the PANAS-NA and PANAS-PA were calculated using the standard deviations (SD = 0.71 and SD = 0.53, respectively) and internal consistencies ($\alpha = 0.87$ and $\alpha = 0.77$, respectively) of the Dutch version of the PANAS [28].

Mixed modeling, also referred to as multilevel regression models, was used to examine whether sociodemographic characteristics and medical complications among donors and recipients were related to the absolute level or change in psychological outcomes. Mixed modeling is an intention to treat analysis that can efficiently handle data with missing and unbalanced time points and corrects for the bias of missing time points [29]; therefore all available data points were included in the analyses. Furthermore, multilevel analyses have more power to find effects than analyses like MANOVA [30,31]. Because the BSI and the PANAS-NA were not normally distributed these were transformed with logistic transformations [32]. Our models had two levels: the participant was the upper level, and their repeated measures was the lower level. We determined the most appropriate structure for the models: models with either an unstructured covariance structure, variance component structure, or a random intercept only were tested. Using the likelihood ratio test using restricted maximum likelihood [33,34], we determined whether a subsequent model was an insignificant, thus permitted reduction of the more elaborate model.

In a first step, we conducted separate multilevel regression models for the four mental health outcomes, to select potentially relevant sociodemographic variables (P < 0.01). Due to variation in time between baseline measurement and surgery, date of surgery was coded 0 for the variable "time (months)" and "time to surgery (months)" was entered as an additional covariate in each model. In addition, one of the sociodemographic characteristics and its interaction with time were entered in each model.

In a second step, we conducted final multilevel regression models for the four mental health outcomes. The covariates were as follows: time, time to surgery, the selected sociodemographic variables from step 1 (P < 0.01), a medical complication indicator (either complication score of the donor or number of recipient rehospitalizations), and its interactions with time. Each model was conducted twice: (i) for donor complications and (ii) for recipient rehospitalizations, resulting in eight models. The medical complications of the donor and recipient were not included in the same model, as unspecified donors have no data on the recipients' rehospitalizations and would therefore automatically be excluded from all analyses. Therefore, in the second analyses, only specified donors were included. Medical complication indicators were time varying: All donors were assigned 0 at baseline, indicators of medical complications till 3 months after donation were added to the second measurement, and indicators between 4-12 months after donation were added to the third measurement. Consequently, the medical complication covariate shows whether it was related to change in mental health after donation and the interaction with time indicates whether this relationship changed between 3 and 12 months. Nonsignificant covariates were removed step by step until a parsimonious model was reached. Figures were made for the models of mental health outcomes that had a significant relationship with either donor complications or recipient rehospitalizations.

For all analyses, we used spss version 21.0 (IBM Corporation, Armonk, NY, USA). In the univariate analyses, a P-value < 0.05 was considered statistically significant, while in the multilevel regression models, a P-value < 0.01 was considered statistically significant due to multiple testing.

Results

Participants

Between July 5, 2011 and September 13, 2012, 185 potential living kidney donors were approved for donation and subsequently donated their kidney. All donors underwent laparoscopic nephrectomy. Twelve donors were excluded from participation due to language or living abroad. Eighteen donors were not approached for the first measurement due to logistical issues, for example screening in another hospital. Six of these donors participated from the second measurement onwards, and two donors only participated at the third measurement. One hundred and forty-five donors completed at least one measurement (response rate was 84%) and are

referred as "participants" (See Figure 1, for the number of participants and nonparticipants at the three measurements). Eight donors dropped out during the study (6%) and three donors completed the first and third but not the second measurement (2%).

Descriptive statistics

Participants' sociodemographic characteristics are depicted in Table 1. We found that participants did not significantly differ from nonparticipants on sociodemographic characteristics except for native country and religious affiliation: More participants were born in the Netherlands and were less likely to have a religious affiliation than nonparticipants.

Donors' scores on the questionnaires did not differ according to method of completion (in the clinic versus at home).

Donors donated their kidney a median of 2.5 (range 0.1–21.7) months after baseline. Median time between the operation and second measurement was 3.0 (range 2.1–7.6) months and between the operation and third measurement 12.3 (range 11.2–17.5) months.

Descriptive statistics—Change in mental health over time

The RCI calculation of the PANAS resulted in an RCI = 0.71 for the PANAS-NA and an RCI = 0.70 for the PANAS-PA. Table 2 shows that for the majority of donors, the mental health outcomes remained stable; however, for a minority of donors, the scores increased or decreased over time.

Descriptive statistics—Medical complications

Eighty-eight donors (61%) experienced at least one complication between baseline and 3 months after donation, 45 donors (31%) experienced at least one complication between 4 and 12 months after donation. A minority had missing data: four donors (3%) between baseline and 3 months after donation and 15 donors (10%) between 4 and 12 months after donation. The remaining donors did not experience a complication. See Table 3 for the prevalence of each complication.

Fifty-five recipients (43%) were rehospitalized at least once between baseline and 3 months after transplantation; 68 recipients (53%) were rehospitalized at least once between 4 and 12 months after transplantation.

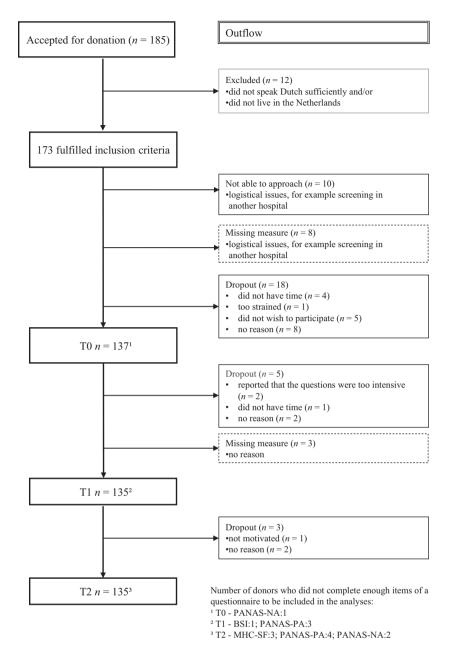


Figure 1 Flowchart of participants.

Four recipients (3%) had missing data on both measurements. The remaining recipients were not rehospitalized (See Table 4, for details on the occurrence of recipient rehospitalizations).

Influence of donors' medical complications on change in donors' mental health

The model with the best fit for all scores had only a random intercept (See Table 5, for the final models with donor complications included as predictor).

Psychological symptoms & negative affect

Psychological symptoms (BSI) increased significantly over time. More or more severe complications among donors were related to an increase in psychological symptoms over time (see Figure 2, for a visual representation of this relationship). Age was negatively related to psychological symptoms: Younger donors had a higher level of psychological symptoms across the donation process.

Negative affect (PANAS-NA) increased significantly over time. Donor complications were not related to

Table 2. Descriptive statistics of changes in mental health outcomes between predonation and postdonation (N = 145)

	Difference scores	Changes based on the reliable change indexes			
	Median (range)	Decrease, %	No change, %	Increase, %	
Brief symptom inventory (range 0–4)					
3 months after donation—baseline	0.00 (-0.60 to 1.75)	9.4	73.4	17.2	
1 year after donation—baseline	0.02 (-0.89 to 2.38)	6.3	73.2	20.5	
Positive and negative affect schedule—	negative affect (range 1–5)				
3 months after donation—baseline	0.00 (-1.40 to 2.40)	3.1	91.4	5.5	
1 year after donation—baseline	0.00 (-1.80 to 2.60)	4.0	92.7	3.2	
Mental health continuum- short form (ra	ange 0–5)				
3 months after donation —baseline	-0.14 (-1.86 to 2.14)	14.0	76.7	9.3	
1 year after donation—baseline	-0.14 (-2.21 to 1.50)	19.4	73.4	7.3	
Positive and negative affect schedule—positive affect (range 1–5)					
3 months after donation—baseline	-0.10 (-2.40 to 2.67)	23.8	63.5	12.7	
1 year after donation—baseline	-0.10 (-1.70 to 1.90)	22.6	68.5	8.9	

Table 3. Classification of minor versus severe complications of the donor and prevalence of complications (N = 145)

	0–3 months after donation	4–12 months after donation	Tota n
No complications	53	85	138
Minor complications	72	43	115
Wound infection, wound was not opened	6		6
Bleeding/hematoma, without blood transfusion	14		14
Urinary tract infection: once	7	3	10
Urinary retention, less than a week (during hospitalization)	2		2
Pain without intervention	23	17	40
Fatigue	15	11	26
Itchiness	2	1	3
Atrial fibrillation	1		1
Incontinence	1	1	2
Dyspnea		1	1
Edema	1		1
LUTS/oliguria		7	7
Scar correction (cosmetic reasons)		1	1
Dizziness		1	1
Severe complications	28	5	33
Wound infection, wound had to be opened	15		15
Bleeding/hematoma, with blood transfusion	4		4
Urinary tract infection, more than once			
Urinary retention, more than a week	1		1
Epididymitis	1	1	2
Nerve damage	3	2	5
Pneumonia/pneumothorax	2		2
Rehospitalization	1	1	2
Respiratory infection	1	•	1
Scar tissue surgically removed		1	1
Missing	4	15	19

change in negative affect over time. Age was negatively related to negative affect: Younger donors had a higher negative affect score across the donation process. The interaction between time and marital status was negatively related to negative affect over time: A greater increase in negative affect over time was found among donors who did not have a partner.

Well-being

Well-being (MHC-SF) did not change over time, and donor complications were not related to change in wellbeing over time. Religious affiliation was positively

Table 4. Prevalence of recipient rehospitalizations till 3 and 12 months after transplantation (N = 145)

Number of recipient rehospitalizations	0–3 months after transplantation <i>n</i>	4–12 months after transplantation <i>n</i>
0	70	57 ²
1	28 ¹	25
2	15	14 ³
2 3 4 5 6	5	12
4	6	9
5		3
	1	
7 8		2
		2
9		1
Missing	4	4
Not applicable (unspecified donor)	16	16

¹One of these recipients died and one recipient had kidney failure during the research period

related to well-being: Religious donors had a higher well-being across the donation process than nonreligious donors.

Positive affect (PANAS-PA) did not change over time and donor complications were not related to change in positive affect over time. Unemployment was negatively related to positive affect: employed donors had a higher positive affect during the donation process than donors who were retired, unemployed, or had voluntary work.

Influence of recipients' medical complications on change in donors' mental health

The model with the best fit for all scores had only a random intercept. See Table 6, for the final models with recipient rehospitalizations included).

Psychological symptoms & negative affect

When recipients' complications were used as covariates in the model, psychological symptoms (BSI) did not change over time. A greater number of recipient rehospitalizations were related to an increase in psychological symptoms over time (See Figure 3, for a visual representation of this relationship). Consistent with the earlier model of the BSI, younger donors had a higher level of psychological symptoms.

Recipient rehospitalizations and its interaction with time did not significantly predict negative affect (PANAS-NA).

Table 5. Final models with donors' medical complications included and donors' mental health as outcome, after removing the nonsignificant covariates (N = 145)

	b	SE b	Р	95% CI	
Psychological symptoms (Brief Symptom Inventory)					
Intercept	-2.620	0.404	< 0.001	-3.420; -1.821	
Time (months)	0.024	0.008	0.005	0.007; 0.041	
Complication score of the donor	0.208	0.069	0.003	0.073; 0.342	
Age	-0.019	0.007	0.010	-0.034; -0.005	
Negative affect (PANAS-NA)					
Intercept	-1.750	0.361	< 0.001	-2.462; -1.037	
Time (months)	0.036	0.013	0.005	0.011; 0.061	
Age	-0.022	0.007	0.001	-0.035; -0.009	
Marital status	0.062	0.207	0.765	-0.346; 0.470	
Time × marital status	-0.048	0.015	0.002	-0.078; -0.018	
Well-being (MHC-SF)					
Intercept	2.801	0.108	< 0.001	2.587; 3.015	
Religious affiliation	0.407	0.156	0.010	0.099; 0.715	
Positive affect (PANAS-PA)					
Intercept	3.033	0.067	< 0.001	2.901; 3.164	
Unemployment	-0.436	0.105	< 0.001	-0.644; -0.229	

²One of these recipients died during the research period.

³One recipient had a kidney failure during the research period.

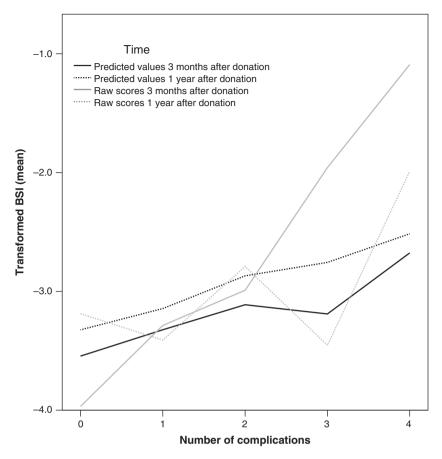


Figure 2 Relationship between complication score of the donor and the raw scores of the transformed BSI and the predicted values of this relationship based on the multilevel regression model as depicted in Table 5.

Table 6. Final models for the relationship between recipients' medical complications and donors' mental health, after removing the nonsignificant covariates (n = 129)

	b	<i>SE</i> b	Р	95% CI
Psychological symptoms (Brief Symptom In	iventory)			
Intercept	-2.374	0.422	< 0.001	-3.208; -1.539
Recipient rehospitalizations	0.130	0.039	0.001	0.053; 0.207
Age	-0.021	0.008	0.008	-0.037; -0.006
Negative affect (PANAS-NA)				
Intercept	-2.614	0.186	< 0.001	-2.981; -2.247
Time (months)	0.035	0.014	0.012	0.008; 0.063
Marital status	-0.303	0.224	0.178	-0.746; 0.139
Time × marital status	-0.049	0.017	0.004	-0.082; -0.016
Well-being (MHC-SF)				
Intercept	3.001	0.088	< 0.001	2.827; -3.175
Time (months)	-0.011	0.006	0.097	-0.023; 0.002
Recipient rehospitalizations	-0.147	0.053	0.005	-0.251; -0.044
Time × recipient rehospitalizations	0.014	0.005	0.004	0.005; 0.023
Positive affect (PANAS-PA)				
Intercept	2.976	0.068	< 0.001	2.842; 3.110
Unemployment	-0.360	0.110	0.001	-0.576; -0.143

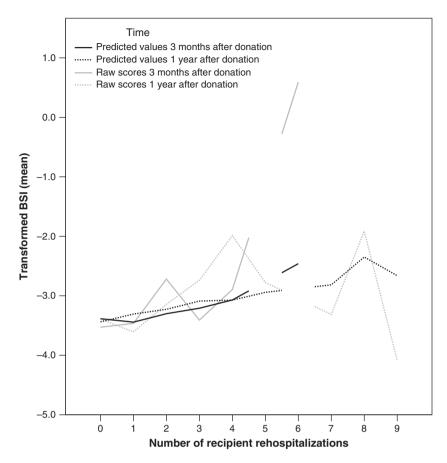


Figure 3 Relationship between number of recipient rehospitalizations and the raw scores of the transformed BSI and the predicted values of this relationship based on the multilevel regression model as depicted in Table 6.

Well-being

Over the whole model, well-being (MHC-SF) did not change over time. However, a greater number of recipient rehospitalizations were significantly related to a decrease in well-being over time. The interaction between time and recipient rehospitalizations was also significant, indicating that the negative relationship between recipient rehospitalizations and well-being is stronger the first months after donation and weaker 1 year after donation (see Figure 4, for a visual representation of this relationship).

Recipient rehospitalizations and its interaction with time did not significantly predict positive affect (PANAS-PA).

Discussion

In this study, we provide new insights into the impact of the donors' and recipients' medical complications on donors' mental health after living kidney donation by investigating this question in a prospective cohort study. Findings from previous research were inconclusive, and these studies were limited by retrospective designs, subjective measures, and measurement of single components of mental health. We examined medical complications objectively and measured overall mental health. The results showed more or more complex medical complications experienced by either the donor or the recipient is a risk factor for deterioration in donors' mental health after living kidney donation. A greater deterioration in mental health over time was found among donors who did not have a partner.

On the basis of these results, we recommend that professionals monitor the mental health of living kidney donors who experience complications themselves and/or recipient rehospitalizations. We do not recommend that all donors who experience such unfavorable medical outcomes receive psychological support as standard, as routine psychological treatment after a life event is not effective and could even have a detrimental effect for some individuals [35]. We therefore recommend that professionals monitor the need for psychological support among these donors and refer them for additional

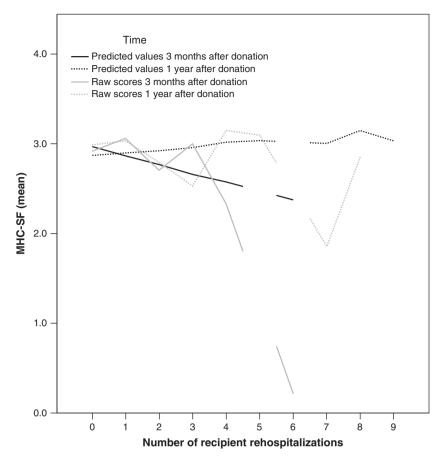


Figure 4 Relationship between number of recipient rehospitalizations and the raw scores of the MHC-SF and the predicted values of this relationship based on the multilevel regression model as depicted in Table 6.

psychological support when indicated. Extra attention is needed in case of extreme negative medical outcomes, such as graft failure or recipients' death, as earlier research revealed that these donors often have difficulties in expressing their need for additional psychological support [36]. This difficulty also emphasizes the needs for monitoring.

A number of sociodemographic risk factors were identified that may characterize donors needing greater psychological support during the donation process. These were a lack of a partner, younger age, no religious affiliation, and being unemployed. These donors were more likely to have poorer mental health (changes) across the donation process.

We note that descriptive statistics of this study showed that the variability in changes in donors' mental health is small: For the majority of donors, the mental health outcomes remained stable; however, for a minority of donors, the scores increased or decreased over time. These results are positive and highlight that additional psychological interventions will only be necessary for a minority of donors.

Which psychological intervention techniques could be used to prevent deterioration in donors' mental health? To our knowledge, there are no guidelines or studies on effective psychological interventions that help donors to cope with medical complications. Our suggestions for appropriate psychological interventions are as follows: supportive counseling, acceptance-focused interventions [37,38], stress-reducing techniques [39], or grief therapy [40]. Furthermore, we highlight the importance of educating potential living donors about the risks of medical complications after donation/transplantation and the potential impact on donors' mental health. This is in line with conclusions from earlier research that improving the informed consent process of donors will contribute to positive psychological outcomes after donation, for instance by increasing realistic expectations before donation [41], increasing knowledge about living donation/ transplantation [42], and reducing ambivalence against donation [43]. These interventions should be performed by a clinical psychologist who is trained in the interventions. We encourage future research on the effectiveness of these interventions among donors.

A striking result of the current study is that donors' and recipients' medical complications predicted psychological symptoms over time, but was unrelated to negative affect. Similarly, recipients' medical complications predicted well-being over time, but was unrelated to positive affect. These results make clear that medical complications have an influence on the more long-term, stable components of mental health (e.g., psychological symptoms) rather than mood/emotions. In addition, these results and the finding that divergent sociodemographic characteristics were related to different aspects of mental health demonstrate that mental health consists of various components, which are influenced by different factors [25,44].

It is likely that not all donors will react to medical complications (their own or those of the recipient) in the same way. Psychological processes are likely to influence the impact of medical complications on mental health outcomes, for example some donors may cope more effectively, have more social support than other donors, or have unrealistic expectations about their recovery process prior to donation. It is feasible that such factors have an influence on donors' mental health, as they are proved to have an influence on the psychological impact of other kinds of surgery [45,46] and other events [47,48]. For example, the study by Burker et al. [45] showed that patients who were undergoing lung transplantation were more often distressed if they had a maladaptive coping style, such as avoidance. The influence of these psychological factors on mental health outcomes in the case of living kidney donation has yet to be investigated.

Despite the strengths of this study such as a high response rate and low attrition over time, a number of limitations should be taken into consideration. Firstly, more participants were born in the Netherlands and were less likely to have a religious affiliation than non-participants. Extra efforts should be made to recruit non-native and religious donors in future research to enhance the generalizability of our results. Secondly, the follow-up period of this study is limited to 1 year and we were therefore not able to examine the impact of kidney failure or recipient's death on psychological outcomes of the donor due to the low incidence of

these events. Prospective studies with a longer follow-up period investigating the influence of medical factors on donor psychological outcomes could add important insights to this area.

We conclude that medical complications experienced by either the donor or recipient is a risk factor for deterioration in donors' mental health after living kidney donation. This information should be added to education programs for potential living kidney donors. Furthermore, professionals should monitor the mental health of donors who experience medical complications and offer additional support when needed. Future research is needed to explore which psychosocial factors, such as personal resources, are in addition to medical complications related to mental health after living kidney donation.

Authorship

LT: participated in research design, collected the data, analyzed the data and wrote the manuscript. ML and DB: contributed to data collection, contributed to writing of the manuscript. RT: participated in data analysis, contributed to writing of the manuscript. MB: participated in data analysis and contributed to writing of the manuscript. JVB, WW, WZ and JJ: participated in research design and contributed to writing of the manuscript. EM: participated in research design, contributed to data collection, participated in data analysis and contributed to writing of the manuscript.

Funding

Erasmus Medical Center.

Conflicts of interest

The authors have declared no conflicts of interest.

Acknowledgements

We thank all donors who participated in the study and the data managers and transplant coordinators who assisted with logistics of this study.

REFERENCES

- Clemens KK, Thiessen-Philbrook H, Parikh CR, et al. Psychosocial health of living kidney donors: a systematic review. Am J Transplant 2006; 6: 2965.
- Dew M, Myaskovsky L, Steel J, DiMartini A. Managing the psychosocial and financial consequences of living donation. Curr Transplant Rep 2014; 1: 24.
- 3. Rodrigue JR, Schutzer ME, Paek M, Morrissey P. Altruistic kidney donation to a stranger: psychosocial and functional outcomes at two US

- transplant centers. *Transplantation* 2011; **91**: 772.
- 4. Timmerman L, Laging M, Westerhof G, et al. Mental health among living kidney donors: a prospective comparison with matched controls from the general population. *Am J Transplant* 2015; 15: 508.
- Timmerman L, Zuidema WC, Erdman RAM, et al. Psychologic functioning of unspecified anonymous living kidney donors before and after donation. *Transplantation* 2013; 95: 1369.
- Smith GC, Trauer T, Kerr PG, Chadban SJ. Prospective psychosocial monitoring of living kidney donors using the SF-36 health survey. *Transplantation* 2003; 76: 807
- 7. Gross CR, Messersmith EE, Hong BA, et al. Health-related quality of life in kidney donors from the last five decades: results from the RELIVE study. Am J Transplant 2013; 13: 2924.
- Giessing M, Reuter S, Schönberg B, et al. Quality of life of living kidney donors in Germany: a survey with the validated Short Form-36 and Giessen Subjective Complaints List-24 questionnaires. Transplantation 2004; 78: 864.
- Minz M, Udgiri N, Sharma A, et al. Prospective psychosocial evaluation of related kidney donors: Indian perspective. Transplant Proc 2005; 37: 2001.
- Smith GC, Trauer T, Kerr PG, Chadban SJ. Prospective psychosocial monitoring of living kidney donors using the Short Form-36 Health Survey: results at 12 months. *Transplantation* 2004; 78: 1384.
- 11. Sommerer C, Feuerstein D, Dikow R, et al. Psychosocial and physical outcome following kidney donation a retrospective analysis. *Transpl Int* 2015; **28**: 416.
- Clemens K, Boudville N, Dew MA, et al.
 The long-term quality of life of living kidney donors: a multicenter cohort study. Am J Transplant 2011; 11: 463.
- 13. Messersmith EE, Gross CR, Beil CA, et al. Satisfaction with life among living kidney donors: a RELIVE study of long-term donor outcomes. *Transplantation* 2014; **98**: 1294.
- 14. Kroencke S, Fischer L, Nashan B, Herich L, Schulz K-H. A prospective study on living related kidney donors' quality of life in the first year: choosing appropriate reference data. *Clin Transplant* 2012; **26**: E418.
- Schweitzer J, Seidel-Wiesel M, Verres R, Wiesel M. Psychological consultation before living kidney donation: finding out and handling problem cases. *Transplantation* 2003; 76: 1464.
- 16. Keyes CL. Mental illness and/or mental health? Investigating axioms of the

- complete state model of health. *J Consult Clin Psychol* 2005; **73**: 539.
- 17. de Groot IB, Stiggelbout AM, van der Boog PJM, Baranski AG, Marang-van de Mheen PJ. Reduced quality of life in living kidney donors: association with fatigue, societal participation and predonation variables. *Transpl Int* 2012; 25: 967.
- Brown KW, Moskowitz DS. Does unhappiness make you sick? The role of affect and neuroticism in the experience of common physical symptoms. *J Pers* Soc Psychol 1997; 72: 907.
- Dor FMF, Massey EK, Frunza M, et al. New classification of ELPAT for living organ donation. *Transplantation* 2011; 91: 935.
- 20. de Beurs E, Zitman F. De Brief Symptom Inventory (BSI): De betrouwbaarheid en validiteit van een handzaam alternatief voor de SCL-90 [The Brief Symptom Inventory (BSI): the reliability and validity of a practical alternative for the SCL-90] Maandblad Geestelijke Volksgezondheid 2006; 61: 120.
- Derogatis LR. BSI Brief Symptom Inventory: Administration, Scoring, and Procedure Manual (4th Ed.). Minneapolis, MN: National Computer Systems, 1933; pp. 1–85.
- 22. Boon MTG, Peeters FPML. Affectieve dimensies bij depressie en angst [Dimensions of affectivity in depression and anxiety]. *Tijdschrift voor Psychiatrie* 1999; 41: 109.
- Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol* 1988; 54: 1063.
- Keyes CLM. The subjective wellbeing of America's youth: toward a comprehensive assessment. Adolesc Fam Health 2006; 4: 3.
- Lamers SM, Westerhof GJ, Bohlmeijer ET, ten Klooster PM, Keyes CL. Evaluating the psychometric properties of the Mental Health Continuum-Short Form (MHC-SF). J Clin Psychol 2011; 67: 99.
- Clavien PA, Barkun J, De Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009; 250: 187.
- Jacobson NS, Truax P. Clinical significance: a statistical approach to defining meaningful change in psycho therapy research. J Consult Clin Psychol 1991; 59: 12.
- 28. Engelen U, De Peuter S, Victoir A, Van Diest I, Van den Bergh O. Verdere validering van de Positive and Negative Affect Schedule (PANAS) en

- vergelijking van twee Nederlandstalige versies[Further validation of the Positive and Negative Affect Schedule (PANAS) and comparison of two Dutch version]. Gedrag en Gezondheid 2006; 34: 89.
- Tabacknick B, Fidell L. Using Multivariate Statistics. Boston, MA: Pearson Education, 2007: 781 pp.
- 30. Gueorguieva R, Krystal JH. Move over ANOVA: progress in analyzing repeatedmeasures data and its reflection in papers published in the archives of general psychiatry. Arch Gen Psychiatry 2004; 61: 310.
- Quené H, van den Bergh H. On multilevel modeling of data from repeated measures designs: a tutorial. Speech Commun 2004; 43: 103.
- 32. Lesaffre E, Rizopoulos D, Tsonaka R. The logistic transform for bounded outcome scores. *Biostatistics* 2007; **8**: 72.
- Singer J, Willett J. Applied Longitudinal Data Analysis – Modeling Change and Event Occurrence. Oxford, UK: Oxford University Press, 2003; pp. 1–644.
- Verbeke G, Molenberghs G. Linear Mixed Models for Longitudinal Data. New York, NY: Springer, 2000; pp. 1–570.
- Emmerik vAAP, Kamphuis JH, Hulsbosch AM, Emmelkamp PMG. Single session debriefing after psycho logical trauma: a meta-analysis. *Lancet* 2002; 360: 766.
- Haljamäe U, Nyberg G, Sjöström B. Remaining experiences of living kidney donors more than 3 yr after early recipient graft loss. Clin Transplant 2003; 17: 503.
- Hayes SC. Acceptance and commitment therapy, relational frame theory, and the third wave of behavioral and cognitive therapies. *Behav Ther* 2004; 35: 639.
- 38. Hayes SC, Luoma JB, Bond FW, Masuda A, Lillis J. Acceptance and commitment therapy: model, processes and outcomes. *Behav Res Ther* 2006; **44**: 1.
- Lehrer P, Woolfolk R, Sime W. Principles and Practice of Stress Management. New York, NY: The Guilford Press, 2007; pp. 1–734.
- Worden J. Grief Counseling and Grief Therapy. A Handbook for the Mental Health Practitioner. New York, NY: Springer Publishing Company, 2009; pp. 1–314.
- 41. Tong A, Chapman JR, Wong G, Kanellis J, McCarthy G, Craig JC. The motivations and experiences of living kidney donors: a thematic synthesis. *Am J Kidney Dis* 2012; **60**: 15.
- 42. Timmerman L, Ismail S, Luchtenburg A, et al. Exploring knowledge about dialysis, transplantation, and living donation among patients and their

- living kidney donors. Int J Behav Med 2015; 22: 580.
- 43. Dew MA, DiMartini AF, DeVito Dabbs AJ, *et al.* Preventive intervention for living donor psychosocial outcomes: feasibility and efficacy in a randomized controlled trial. *Am J Transplant* 2013; 13: 2672.
- 44. Merz EL, Roesch SC. Modeling trait and state variation using multilevel factor analysis with PANAS daily diary data. *J Res Pers* 2011; **45**: 2.
- 45. Burker E, Evon D, Sedway J, Egan T. Appraisal and coping as predictors of psychological distress and self-reported physical disability before lung transplantation. *Prog Transplant* 2004; 14: 222.
- 46. Schelling GMD, Richter MMS, Roozendaal BP, *et al.* Exposure to high stress in the intensive care unit may have negative effects on health-related
- quality-of-life outcomes after cardiac surgery. *Crit Care Med* 2003; **31**: 1971.
- 47. Lazarus RS. Stress and Emotion. A New Synthesis. New York, NY: Springer Publishing Company, Inc., 1999; pp. 1–320.
- 48. Ursin H, Eriksen HR. The cognitive activation theory of stress. *Psychoneuroendocrinology* 2004; **29**: 567.