Self-rated health and mortality after kidney transplantation

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Part II

Self-rated health as a health outcome

Chapter 4

Factors associated with self-rated health after kidney transplantation – a prospective study

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Abstract

Background

This prospective study explores and compares the relationship between patients' self-rated health (SRH) after kidney transplantation (KT) at different follow-up periods and its medical and non-medical predictors over time.

Methods

Patients (N=128) who completed a questionnaire (the SRH question of the SF-36 and the End-Stage Renal Disease Symptom Checklist–Transplantation Module) were enrolled. Clinical data were retrieved from medical files. The sample was stratified into early (N=89) and late (N=39) cohorts according to time since KT at baseline. Linear regression was used to identify predictors of SRH at follow-up.

Results

In both cohorts a change in Glomerular filtration rate (GFR) over time remained a predictor of SRH; in the early cohort age was an additional predictor; in the late cohort a change in transplantation-associated psychological distress over time and the number of late acute rejection episodes during the observation period were additional predictors.

Conclusions

Improvement in GFR over time predicted better SRH at each period after KT. Decreased transplantation-associated psychological distress and fewer late acute rejection episodes seemed to predict better SRH at a later follow-up period. Despite these observations higher SRH was associated with better clinical outcomes.

Key words

kidney transplantation, self-rated health, glomerular filtration rate, rejection, side-effects of immunosuppressant

Introduction

Self-rated health (SRH) is considered a reliable indicator of mortality and morbidity in patients with end-stage renal disease (ESRD).[1,2] Thong et al. investigated the predictive utility of SRH, measured shortly after the start of dialysis, on mortality and found SRH to be an independent predictor of mortality in dialysis patients at up to 7 years follow-up.[3] Spiegel et al. indicated in their systematic review of end-stage renal disease the importance of self-reported health as it is connected with traditional biomarkers.[4] Avitzur et al. explored SRH in pediatric patients who are 10-year survivors of transplantation and who had an excellent graft function and a high self-reported quality of life.[5] Thus, SRH seems to be a predictor of future health status and becomes an important outcome criterion in the evaluation of medical treatment of ESRD.[6]

In previous studies of patients after kidney transplantation (KT) improvements in SRH have been found to be associated with younger age, male gender, higher education, higher socioeconomic status, higher social support, lower number of comorbidities, and not only with the success of the transplantation.[7] Studies in ESRD have focused mainly on associations between components of better self-perceived health and objective factors of higher graft function.[8,9] The subjective evaluation of the side-effects of immunosuppressant[10] as well as rejection episodes continues to be a significant problem in long-term attrition of graft function[11], and also seem to be connected to poorer self-rated health.[10]

To our knowledge there is only one study analyzing the associations between a change in objective factors over time and SRH at follow-up.[12] In addition, studies comparing predictors in SRH in prospective studies stratified by time after KT are lacking. Thus, the aim of this study was a) to explore changes over time in the medical and non-medical factors associated with self-rated health, and b) to compare their associations with self-rated health according to time since transplantation.

Materials and Methods

Sample and procedures

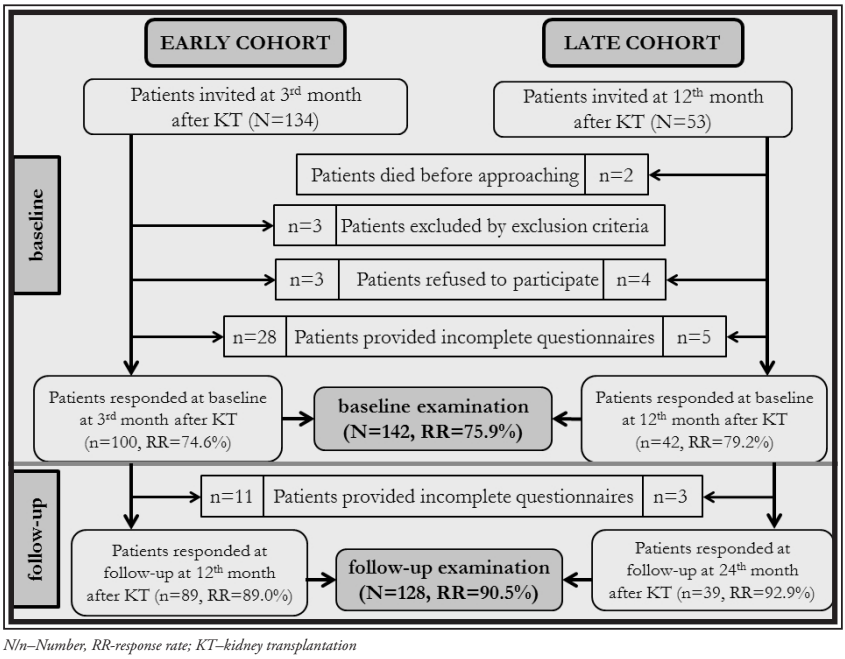
A total of 187 kidney transplant recipients in their 3rd (N=134) and 12th (N=53) month after successful transplant surgery at the Transplant Centre of Kosice from the eastern region of Slovakia were invited to participate at baseline examination. The sample was stratified according time since KT at baseline and two cohorts of patients were formed – early patients (3 months after KT at baseline) and late patients (12 months after KT at baseline). The follow-up examination took place at the 12th month after KT for the early cohort and at the 24th month after KT for the late cohort. All patients with a functional transplanted kidney (N=142) who agreed to participate were included. The baseline examination for our sample occurred in the third and twelfth month after a successful KT, because on one hand the first 3 months after KT are usually considered as the most problematic period connected to dramatic changes, increased morbidity and even mortality[13], and on the other hand an improvement in self-perceived health most often occurs during the first 2 years after KT.[14] The exclusion criteria were the presence of mental retardation, organic psycho-syndrome, severe dementia, or other psychiatric diseases mentioned in the medical record; therefore, 3 (1.6%) patients were excluded at the baseline examination, 7 patients (3.7%) refused to participate, 33 (17.6%) provided incomplete questionnaires and 2 (1.1%) died

after baseline; thus 142 (75.9%) patients were included in the analysis. At follow-up, 14 (9.9%) provided incomplete questionnaires, resulting in 128 patients with a functional transplanted kidney (a response rate of 90.1%) at the follow-up examination. Figure 4.1 presents more detailed information about the participants.

Data collection took place from 2003 to 2010 in Kosice. Patients provided information about sociodemographic variables and filled in the questionnaires. All participants were interviewed during regular outpatient clinical visits by trained personnel independent of the transplant team. Medical data were retrieved from medical records.

Only patients who signed informed consent prior to the study were included. The local Ethics Committee in Kosice approved the study.

Figure 4.1 Flow chart diagram of the participants



N/n–Number, RR-response rate; KT–kidney transplantation

Measures

Sociodemographic data included age and gender.

Self-rated health (SRH) was measured using the first question of the Short Form Health Survey (SF-36).[15] The SF-36 questionnaire consists of eight subscales: physical functioning, physical role limitations, bodily pain, vitality, general health perception, social functioning, emotional role limitations, and mental health.[15,16] All of the eight subscales are coded and transformed into a scale from 0 (poor health) to 100 (excellent health) in which they are presented as standard SF-36 scores between 0 and 100, with higher scores indicating better health status.[15] Self-rated health can be also determined in this way from a single item in the SF-36. The validity and reliability of the SF-36 and its first item have been confirmed in

patients with renal disease, including those after KT.[8,16-18]

Side-effects of immunosuppressive treatment were assessed by the End-Stage Renal Disease Symptom Checklist – Transplantation Module (ESRD SCL-TM), which consists of six subscales: limited physical capacity (10 items), limited cognitive capacity (8 items), cardiac and renal dysfunction (7 items), side effects of corticosteroids (5 items), increased growth of gum and hair (5 items), and transplantation-associated psychological distress (8 items).[19] This questionnaire can be used to measure the side-effects of immunosuppressive treatment as well as its disease-specific distress.[19] For each item the patient can rate the severity of the symptom on a subscale from 0 (not at all) to 5 (extremely). The scores for the subscales are transformed into a scale score by dividing the severity index score by the number of items in the subscales.[19] Higher scores indicate a higher level of side-effects from immunosuppressive treatment. In this sample Cronbach's α was 0.89 for limited physical capacity, 0.87 for limited cognitive capacity, 0.85 for cardiac and renal dysfunction, 0.81 for side effects of corticosteroids, 0.85 for increased growth of gum and hair and 0.84 for transplantation-associated psychological distress.

Clinical data were retrieved from medical files. These included serum creatinine, weight, duration of dialysis (in years), current immunosuppressive treatment, function immediately after KT, number of early acute rejection episodes, number of late acute rejection episodes and chronic renal allograft dysfunction during the observation period. Glomerular filtration rate (GFR) was calculated using the Cockroft-Gault formula.[20] Rejection episodes (early acute, late acute and chronic renal allograft dysfunction) were diagnosed after biopsy according to the Banff 2009 update diagnostic categories for renal allograft biopsies.[21] An early acute rejection episode was defined as an acute rejection episode occurring within 3 months; a late acute rejection episode was defined as the last acute rejection episode occurring after 3 months independently of a previous early acute rejection episode.[22,23]

Statistics

The Mann-Whitney U-test and Chi-square test were used to check the differences between respondents and non-respondents. Frequencies, means and standard deviations were calculated for the sample description. Bivariate analyses were used for determining the strength and direction of the association between SRH at baseline and follow-up in both cohorts stratified by time after transplantation and the others factors. Stepwise linear regression was performed in order to identify the predictors of SRH at follow-up in the cohorts stratified by time after transplantation (early cohort means 3 months and late cohort means 12 months at baseline). The independent variables were age, gender, change in all six subscales of the ESRD SCL-TM questionnaire over time (between baseline and follow-up examination) and SRH at baseline from the SF-36 questionnaire, the change in GFR over time (between baseline and follow-up examination), duration of dialysis (in years), the number of early acute rejection episodes, the number of late acute rejection episodes and chronic renal allograft dysfunction during the observation period. The Statistical Package for the Social Science (SPSS Inc. Chicago, IL, USA) version 16.0 was used for statistical analyses.

Results

No significant differences were found between respondents and non-respondents regarding age, gender and medical factors or between patients who provided complete and incomplete data; in addition, no significant differences regarding the independent variables were found between the cohorts stratified by time after transplantation at baseline and at follow-up.

In both cohorts the side-effects of immunosuppressive treatment and the mean limited physical capacity significantly increased over time (between baseline and follow-up) ($p \leq 0.01$); on the other hand, the mean transplantation-associated psychological distress significantly decreased over time ($p \leq 0.05$). The mean SRH significantly increased over time ($p \leq 0.001$) as did the mean GFR over time ($p \leq 0.001$). Other variables did not significantly differ from baseline to follow-up. The pairwise associations for SRH at baseline and follow-up in the cohorts with each of the factors are indicated in Table 4.1. Table 4.1 displays more detailed information.

Gender, the change in five subscales of the ESRD SCL-TM over time (limited physical capacity, limited cognitive capacity, cardiac and renal dysfunction, the side-effects of corticosteroids, and increased growth of gum and hair), duration of dialysis, the number of early acute rejection episodes during the observation period and chronic renal allograft dysfunction during the observation period were not predictors associated with SRH at follow-up in the regression models of the stratified cohorts.

Table 4.1 Sociodemographic, psychological, and medical characteristics of the sample at baseline and at follow-up

		baseline (N=142)		follow-up (N=128)	
		N or mean	% or SD	N or mean	% or SD
Time after KT during reviewing	3months	100	70.5	0	0
	12months	42	29.5	89	69.5
	24months	0	0	39	29.5
Age	Mean±SD	48.7*	12.7	49.7*	12.7
Gender	Male	79	55.6	70	54.7
	Female	63*#	44.4	58	45.3
End-Stage Renal Disease Symptom Checklist Transplantation Module	Limited physical capacity	1.51*	0.97	**1.77***#	0.97
	Limited cognitive capacity	1.22*	0.82	1.31*	0.86
	Side effects of corticosteroids	1.09	0.92	1.08	0.78
	Cardiac and renal dysfunction	1.04*	0.81	1.07*	0.84
	Increased gum and hair growth	0.76	0.92	0.78	0.86
	Transplantation associated psychological distress	1.28*	0.85	**1.17***#	0.81
Self-rated health	Mean±SD	47.82	24.55	**57.66**	24.43
Glomerular filtration rate (ml/s)	Mean±SD	0.99	0.28	**1.12***#	0.37
Function immediately after KT	immediate function	74	52.1	66	51.6
	delayed function	68	47.9	62	48.4
Immunosuppression treatment at the time of interview	CsA+MMF+P	84	59.2	80	62.5
	Tac+MMF+P	40	28.2	39	30.5
	Tac+MMF	3	2.1	1	0.8
	CsA+MMF	10	7.0	8	6.2
	SIR+MMF+P/ SIR+MMF	5	3.5	0	0
Duration on dialysis (in years)		3.65	2.44	3.51	2.32
Number of early acute rejection episodes during observation period		0.32*	0.55	0.31*	0.53
Number of late acute rejection episodes during observation period		0.15#	0.36	0.15#	0.35
Chronic renal allograft dysfunction during observation period		0.14	0.35	0.13#	0.32

N–Number, SD–Standard deviation; KT–kidney transplantation
*Significant differences between baseline and follow-up are flagged: **bold font**; determining the strength of the association between SRH and each variable are flagged:*
**-SRH in the early cohort, #-SRH in the late cohort*

The regression model of the early cohort (N=89) explained 66.2% of SRH variance at follow-up. A change in GFR over time contributed significantly to this model, as did age and SRH at baseline.

The regression model of the late cohort (N=39) explained 60.4% of SRH variance at follow-up. A change in GFR over time contributed significantly to this model, as did a change in transplantation-associated psychological distress over time, the number of late acute rejection episodes during the observation period and SRH at baseline. More detailed information is presented in Table 4.2.

Table 4.2: The regression models of significant predictors of SRH at follow-up in the cohorts: early (Model 1) and late (Model 2)

Models	Standardized Coefficients β	95% Confidence Interval
Model 1 in the early cohort (N=89); Adjusted R^2 0.662		
(Constant)		19.476;52.544
SRH at baseline	0.644***	0.484;0.744
change in GFR over time	0.569***	48.572;77.037
age	-0.160**	-0.553;-0.050
Model 2 in the late cohort (N=39); Adjusted R^2 0.604		
(Constant)		11.363;42.099
SRH at baseline	0.600***	0.326;0.859
change in GFR over time	0.555***	19.110;57.104
change in transplantation associated psychological distress over time	-0.338**	-14.810;-2.360
number of late acute rejection episode	-0.306*	-33.698;-2.975

*SRH–Self-Rated Health, GFR–Glomerular filtration rate; *-p<0.05, **-p<0.01, ***-p<0.001*

Discussion

In this study we a) explored changes over time in the medical and non-medical factors associated with self-rated health, and b) compared their associations with self-rated health at follow-up for early and late cohorts stratified by time since transplantation. Over a follow-up observation period in the early and late cohorts, self-rated health (SRH) and glomerular filtration rate (GFR) increased, and transplantation-associated psychological distress decreased. Previous studies have found an association between higher GFR rate and better SRH.[8,9]

In the early cohort worse SRH at baseline as well as at follow-up was associated with elderly, higher limited physical capacity, higher limited cognitive capacity, higher cardiac and renal dysfunction, higher transplantation-associated psychological distress and early acute rejection episodes. Additionally, worse SRH at baseline was associated with female gender and at follow-up with lower GFR. In the late cohort worse SRH at baseline as well as at follow-up was associated with late acute rejection episodes. Moreover, worse SRH at baseline was associated with female gender and at follow-up with lower GFR, higher limited physical capacity, higher transplantation-associated psychological distress and chronic renal allograft dysfunction. Associations between elderly, females, individual evaluations in disease-specific distress, rejection episodes and poorer well-being were also found.[7-9,18]

A change in GFR over time consistently predicted SRH at follow-up in both cohorts. Furthermore, better SRH at follow-up was predicted by fewer late acute rejection episodes during

the observation period in the late cohort after KT. Age was a predictor of SRH at follow-up in the early cohort only.

Our results indicate important differences in predictors of SRH at follow-up in the early cohort compared to the late cohort after KT. For the early cohort after KT, a change in GFR over time and age are predictors associated with SRH at follow-up. We have previously reported similar results in a smaller sample.[12] However, in the late cohort after KT, in addition to the change in GFR over time, the change in transplantation-associated psychological distress over time and the number of late acute rejection episodes during the observation period contributed significantly to the explanation of the variance in SRH at follow-up.

Late acute rejection episodes during the observation period seem to have a significant relationship to self-rated health at a late period after KT. So far late acute rejection episodes cause lower glomerular filtration rate and poor self-rated health; moreover, a decreased glomerular filtration rate predicts poor self-rated health, and not only when it occurs during late acute rejection episodes. Related to our results, Djamali et al. showed that decreased graft function after late acute rejection is associated with poor patient and allograft survival[24], which might be connected to poor self-rated health as well. Individual perceptions in disease-specific distress of transplantation also give the impression of having a significant relationship to self-rated health at a late period after KT. Similar to our findings, Drent et al. divided their group of transplanted patients into a short- and long-term cohorts and showed differences between these groups such that the long-term cohort reported more individual negative experiences than the short-term cohort[25]

Strengths and limitations

The strength of this study is its longitudinal design, which enabled us to explore changes in factors associated with SRH as well as the associations between these changes and SRH at follow-up in the early and the late cohorts stratified according to time after KT. Missing data are a limitation of this study; however, there were no differences in age and gender between respondents and non-respondents. On the other hand, all consecutive patients originating from one major transplant center in Slovakia over a number of years were asked to participate in the study to prevent selection bias.

Recommendations and implications

Results must be verified in a larger sample to allow for generalization. In addition, we only studied patients at baseline from 3 to 12 months after transplantation; therefore, prolonging the study period is necessary. Thus, in a future study pre-transplantation SRH is needed to further study its role in influencing post-transplantation SRH at follow-up. We could then verify whether SRH after KT remains dependent on the factors found in the cohorts before transplantation, or whether in a longer period after KT other variables become important. Furthermore, the pathways between psychological, physical and medical determinants associated with self-rated health should be studied.

Conclusion

Improvement in graft function over time predicted better SRH at each period of follow-up. Decreased transplantation-associated psychological distress did not seem to be important in the first year after KT but only beyond one year after KT. Moreover, fewer late acute rejection episodes seemed to predict better SRH at a late follow-up period. Despite these observations higher SRH was associated with better clinical outcomes.

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