

# Do dialysis- and transplantation-related medical factors affect perceived health status?

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## Abstract

*Background:* Quality of life and perceived health status (PHS) are important indicators of patient care together with morbidity, mortality and health-care resource utilization. The aim of this study is to explore how various medical conditions might influence perceived health status.

*Methods:* The study sample consisted of 128 kidney transplant recipients. PHS was measured using the self-administered SF-36 questionnaire. Stepwise linear regression analysis of 17 demographic, dialysis-, transplantation- and co-morbidity-related factors was performed in order to explore predictors of worse PHS.

*Results:* Older age, female gender, lower education, increased number of hospitalizations during the dialysis period and diabetes mellitus were identified as significant predictors of worse PHS. Age was the most important predictor of PHS, explaining 23.3 % of variance in the SF-36

physical component and 4.4 % in the SF-36 mental component. Between age groups, major differences were found in predictors of perceived health status – serum creatinine was the most important for patients younger than 45 years and the number of hospitalizations for patients of 45 years and over.

*Conclusions:* Biological and medical factors are significant predictors of the physical component of PHS, although they can explain only up to one third of its variance. Other dimensions of PHS are weakly influenced by these medical parameters. It seems important to evaluate perceived health status separately among the age groups because they differ in their predictors.

## **Introduction**

Kidney transplantation is the method of choice among renal replacement therapies due to its superior results in morbidity, mortality, cost utilization and quality of life in comparison with dialysis <sup>1,2</sup>. A wide range of factors is already known to influence morbidity and mortality of transplanted patients. Less information is available about those variables that have an impact on quality of life.

The World Health Organization Quality of Life (WHOQoL) assessment group has defined quality of life as 'Individuals' perception of their position in life in the context of the culture and the value system in which they live and in relation to their goals, expectations, standards and concerns' <sup>3</sup>. Quality of life according to the WHO definition <sup>3</sup> is a multidimensional construct comprising physical, mental, social and economic components <sup>3-5</sup>. Spilker's hierarchical model includes overall quality of life, separate domains of quality of life, as well as a third level covering more specific aspects of each domain <sup>5</sup>. Due to the complexity of each domain there are many factors that can influence quality of life somehow, including demographic, psychosocial and medical parameters. It is for this reason that so many different methods are used for evaluation of quality of life <sup>6</sup>. Depending on the method chosen, various factors are identified as predictors of good or bad quality of life. The major problem in this field is the lack of clear definitions and measures for quality of life and the related terms. Quality of life is an umbrella term and is often interchanged with perceived health status, functional status, self-rated health or health-related quality of life <sup>7</sup>. It is evident that various disease-specific parameters that can affect health are important factors in quality of life. Many researchers therefore call it "health-related quality of life" <sup>8</sup>, while others refuse such simplification and prefer term "perceived health status" <sup>7</sup>. In this research paper the authors have decided to use the term perceived health status because it seems the most appropriate. Despite the uncertainty in definitions health-related quality of life or perceived

health status is not a mere construct devoid of clinical relevance. Recent research has shown that it is a very important predictor of other outcomes in patients with chronic renal disease <sup>8,9</sup>.

The research into quality of life after kidney transplantation is mostly focused on the description of its determinants using univariate statistics. With these methods, a variety of medical and non-medical factors have been identified as characteristics of perceived health status. Unfortunately, research with more proper analysis of predictive variables is scarce. Searching the literature, we identified six such studies <sup>2,10-14</sup>. Griva et al. found among 347 transplant recipients that worry about the transplant is a predictor of the mental component of SF-36, whereas age, income, co-morbidity and time on dialysis predict the results in the physical component of SF-36 <sup>11</sup>. The study by Siegal et al. analyzed 3676 kidney transplant recipients on cyclosporin-based immunosuppression. The authors found significant influence of co-morbid conditions on perceived health status, but they rated joint and eye diseases as the most important psychological problems, as well as the presence of side-effects of immunosuppression. In their study the presence of co-morbidity was assessed by patient self-referral, which could decrease the true frequency level of various diseases <sup>14</sup>. A longitudinal study of 68 patients by Hathaway et al. identified employment status, 6-months hospital admittance, age, education and social support to be predictors of perceived health status <sup>12</sup>. Wight et al. compared cohorts of 292 dialysis and 228 transplanted patients and they found higher age, female gender and lower hemoglobin to be predictors of worse physical functioning in kidney transplant recipients. As the most important predictor they reported age <sup>2</sup>. Julius et al. studied a cohort of 459 end-stage renal disease patients including transplanted patients. Race, age, diabetes mellitus as primary cause of renal failure, co-morbidity and modality of treatment were significantly related to physical dysfunction. However, Julius et al. did not describe separate analysis exclusively for transplanted patients <sup>13</sup>. Fujisawa et al. analyzed 117 transplanted patients and found serum creatinine to be the predictor of results in physical functioning, general health perceptions and vitality scales of the SF-36 questionnaire <sup>10</sup>. All but the last two above-mentioned studies identified mostly non-medical factors as predictors of perceived health status; of the biological and medical variables, age and co-morbidity are the most relevant.

Despite many studies in this field there are still doubts about the importance of medical factors for perceived health status after kidney transplantation <sup>4</sup>. The direct relationship between adverse medical conditions and mortality is well known in nephrology. Diabetes, cardiovascular morbidity and anemia are the conditions most negatively associated with survival. An important question then arises – do medical factors play a similar role in perceived health status and its dimensions?

The aim of this study is to explore how various medical conditions controlled for basic demographic factors might influence perceived health status in patients after kidney transplantation.

## **Subjects and methods**

### **Patients**

Out of 208 adult kidney transplant recipients with a functioning graft, transplanted more than 3 months ago and less than 7 years ago, 128 responded and returned the completed questionnaire (response rate 61.5 %). Nonresponders did not differ either in age, gender, education or employment status significantly from the analysed group ( $p=0.125$ ,  $0.505$ ,  $0.062$  and  $0.093$ , respectively). Data collection took place from September 2002 to February 2004 in two transplant centers in Slovakia (Košice and Bratislava). Five patients with severe dementia or mental retardation were not invited to participate (the only exclusion criterium). All patients signed an informed consent before the interview. The local ethical committee approved the study.

### **Methods**

Patient medical records were searched for information about their dialysis treatment before transplantation (hemodialysis, peritoneal dialysis or both methods), dialysis duration before transplantation, number of hospitalizations before and after transplantation, graft source (cadaveric, living), time since transplantation, number of acute rejection episodes, current immunosuppressive therapy, current serum creatinine and the presence or lack of co-morbid diseases (hypertension, heart disease, diabetes mellitus, stroke, peripheral artery disease, anemia, cancer, bone disease, other clinically relevant serious diseases).

Each patient completed the SF-36 questionnaire form. The Short-Form Health Survey (SF-36) is a 36-item questionnaire for assessment of perceived health status. The SF-36 consists of 8 sub-scales: bodily pain, physical functioning, physical role limitations, general health perceptions, vitality, emotional role limitations, mental health, and social functioning. The first four sub-scales can be combined as the physical summary component and the last four as the mental summary component. All sub-scales as well as the summary components are presented as scores between 0 and 100, with higher scores meaning better health. The validity and reliability of SF-36 have been tested in patients with renal disease, including those after kidney transplantation<sup>2,9,10</sup>. Skalská et al. validated the questionnaire in the Czech population<sup>15</sup>. The Cronbach  $\alpha$  in the present sample was 0.83, while the Cronbach  $\alpha$  for each sub-scale varied between 0.76 (for emotional role limitations) and 0.91 (for physical functioning).

## Statistics

Stepwise linear regression was used for analysis of relation between gender, age, education, employment status, medical characteristics and the SF-36 sub-scales. The analyses were performed with the total patient sample as well as with the sample divided into patients younger than 45 years and those aged 45 years and more.

Gender, age, education and employment status were used for demographic description of the patient sample.

Dialysis-related factors were considered to be: type of dialysis treatment before transplantation, duration of dialysis treatment and number of hospitalizations during dialysis period (none, 1-3, 4-5, or more than 5).

Transplantation-related characteristics were as follows: time since transplantation, number of hospitalizations after transplantation (none, 1-3, 4-5, or more than 5), number of acute rejection episodes, current immunosuppressive protocol and current serum creatinine.

Co-morbidity was evaluated as the presence or lack of the following diseases: hypertension, heart disease, diabetes mellitus, stroke, and other serious co-morbidity. The model did not separately explore some co-morbid diseases of possible importance, such as heart failure, anemia, peripheral vascular disease, bone disease or cancer. There is evidence that these co-morbid conditions can have an impact on perceived health status after kidney transplantation<sup>16</sup>, but they were not included in our analysis as individual variables due to their low occurrence among the patients in our sample. We decided to create the variable "all other serious co-morbid conditions" for this purpose. For separate assessment of these potential medical factors a larger study is needed, which should definitely contain more patients with severe co-morbidity. For the same reason neither graft source nor the number of secondary transplantations were added into the model, despite the existence of studies identifying some differences in quality of life depending on these variables<sup>11</sup>.

SPSS for Windows 11.0.1 was used for statistical analysis. The level of significance was set to  $p < 0.05$ . The tests were two-tailed.

## Results

The analyzed sample consisted of kidney transplant recipients with mean age 48.6 years; at average 28 months since their transplantation; and a median serum creatinine of 137.8  $\mu\text{mol/l}$  (1.56 mg/dl). Approximately two thirds of the sample were males, and the patients were on hemodialysis treatment before transplantation for median 2.6 years. All but three patients had a kidney from a cadaveric donor. Hypertension and heart disease were the most common co-morbid diseases among the patients

(96.1 % and 31.2 %, respectively). The predominant immunosuppressive protocol was based on cyclosporin and mycophenolate mofetil (45.7 % with prednison and 10.1 % without prednison), and fewer patients were treated with the older protocol based on combination of cyclosporin and azathioprin (12.2 % cyclosporin + azathioprin + prednison, 3.2 % prednison + azathioprin, 12.8 % cyclosporin + prednison and 6.4 % cyclosporin alone). A more detailed description of the sample is given in Table 1 and Table 2.

Means and standard deviations for the eight SF-36 sub-scales for the whole sample were as follows: bodily pain  $61.0 \pm 26.5$ , physical functioning  $63.6 \pm 25.6$ , physical role limitations  $46.9 \pm 40.7$ , general health perceptions  $45.1 \pm 21.6$ , vitality  $53.4 \pm 19.6$ , emotional role limitations  $61.7 \pm 42.0$ , mental health  $64.2 \pm 18.6$ , social functioning  $63.1 \pm 26.8$ . The summary physical component score was  $55.2 \pm 20.9$ , and the summary mental component score was  $60.2 \pm 18.5$ .

Table 3 shows the results of stepwise linear regression analysis of the relationships between the selected model of parameters and the dimensions of the SF-36 questionnaire. The physical component of SF-36 was negatively associated with older age, lower education and higher number of hospitalizations during the dialysis period, while the mental component was negatively affected only by lower education and older age. The following variables played a significant role in prediction of worse results in the eight SF-36 sub-scales: older age, lower education, female gender, higher number of hospitalizations during dialysis period and presence of diabetes mellitus.

When the patient sample was split into two age groups, major differences were found (Table 4). In the group of younger patients (younger than 45 years), the most important predictor of the physical dimension of SF-36 was serum creatinine (SCr). Increased SCr was associated with worse results in the physical component of SF-36 including its physical functioning and general health perceptions sub-scales. On the other hand, the mental component of SF-36 was only influenced by education. Among older patients (45 years and more) presence of diabetes mellitus, more hospitalizations during the dialysis period and after transplantation predicted worse perceived health status.

## Discussion

In general, perceived health status in the sample of transplanted patients measured by SF-36 sub-scales is lower than HRQoL in the healthy population. The results indicate that some degree of physical restriction still persists among our patients despite successful transplantation. In addition, high standard deviations (especially in the emotional and physical role limitations sub-scales) indicate major differences within the

patient sample. Similar findings of floor and ceiling effect in these two dimensions are described by other authors <sup>2,10</sup>.

The preliminary univariate analysis of the effect of various medical factors on perceived health status found that many variables have significant association with some of the SF-36 sub-scales (the results are not shown here). These findings are in accordance with other studies <sup>16,17</sup>. The heterogeneity of our sample could have produced these results. Some studies have already pointed out that case mix may strongly influence the interpretation of findings, giving importance to variables which are not in fact significant <sup>2,18</sup>. For this reason, more complicated models and statistical methods should be considered to eliminate such misleading interpretations. This is also the reason why we chose to construct a model consisting of 17 possible bio-medical factors that can predict outcomes on SF-36, and why we analyzed it using stepwise linear regression.

Knowing the results from univariate analyses it was surprising that only a few variables proved to be significant predictors of perceived health status in regression analysis. Age is the strongest factor, explaining 23.3 % of variance in the physical and 4.4 % in the mental component of SF-36. More advanced age predicts worse results independently from other factors. When considering the eight sub-scales of SF-36, age is very important for the physical functioning, pain and general health perceptions sub-scales (explaining from 9.4 to 26.2 % of variance); in other sub-scales it plays a significant, but less important role. These results are in accordance with previous research <sup>11,12,17</sup>.

Number of hospitalizations during the dialysis period is a significant predictor of worse results in the physical component of SF-36 and in two sub-scales, but its contribution is less than 5 %. In contrast to previous research <sup>12</sup>, our study did not find the number of hospitalizations after transplantation to be a significant predictor of perceived health status. A possible reason for this is in the cross-sectional approach we followed, resulting in the situation that each patient was questioned in a different time period after transplantation. The type of immunosuppressive treatment is not a significant predictor of perceived health status. One possible explanation for this surprising fact is that combination therapy is usually used. The protocols consist of several drugs and their doses vary in different time periods with quick tapering after first weeks after transplant surgery. Therefore differences in adverse effects are visible even within each protocol group. Rosenberger et al. have pointed out this issue in their research <sup>19</sup>. Our study found that presence of diabetes mellitus weakly predicts worse scores in the physical and emotional role limitations sub-scales, and other co-morbid conditions are not significant factors at all. Heart disease predicted worse results in the physical role limitations, mental health and pain sub-scales. Its influence was borderline and non-significant. These results are in contrast to other studies <sup>11,13,14,16,17</sup>. However, from these papers only the studies by Griva et al., Siegal et al.

and Julius et al. used a similar approach to the one we followed, and the other authors performed univariate statistical procedures <sup>11,13,14</sup>.

Another model including the Wright co-morbidity index was evaluated in addition to the described model of medical factors. Co-morbidity indices are commonly used for analysis of the effect of various diseases on clinical outcomes <sup>16,17</sup>. The Wright co-morbidity index consists of combined information about age and co-morbidity, making it potentially more sensitive. When we used it in our model instead of separate age and specific co-morbid conditions, we found it to be a significant predictor of perceived health status, although the explanation of variance was lower than in the previously presented model.

With regard to physical functioning it was found that serum creatinine is a borderline, non-significant predictive factor for perceived health status. Serum creatinine is the crucial parameter for assessment of graft function, so one can assume that it should also play an important role in perceived health status <sup>10</sup>. In general our results do not support this theory. On the other hand, when we separately analyzed the sub-group of patients younger than 45 years, serum creatinine became the only important factor for the physical component of SF-36, including its physical functioning and general health perceptions sub-scales (creatinine explained from 13.3 to 16.5 % of variance). In the group of older patients creatinine plays no role; the number of hospitalizations before transplantation predict physical functioning and mental health instead. In addition, fewer hospitalizations after transplantation is a predictor of better general health perceptions and vitality, and presence of diabetes mellitus predicts worse results in the physical and emotional role limitations sub-scales. These results indicate that significant differences exist between age groups. In older patients serious co-morbid conditions that require medical attention (represented by number of hospitalizations) and presence of diabetes mellitus decrease perceived health status, in contrast to younger patients, in whom kidney function is the main predictor of results in SF-36. Similar results for the relationship between SCr and perceived health status are presented by Fujisawa et al. Comparing our patient sample with the patients from that study, differences in age are visible. Patients after transplantation in that sample were younger than our patients ( $43.9 \pm 9.1$  vs.  $48.6 \pm 12.0$  years). The patients studied by Fujisawa et al. are therefore similar to those from our "young" sub-sample, and so their results are also similar <sup>10</sup>.

Perceived health status does not share the same predictors with quantity of life, represented by graft and patient survival. Medical variables, which are highly evaluated by physicians and form their center of attention, do not seem to play a crucial role from the patients' perspective. Other factors are rather more important, including age, gender, adverse effects of treatment <sup>19,20</sup> and compliance. Another category includes socio-demographic and economic factors <sup>12</sup>.



Biological and medical factors are significant predictors of the physical component of SF-36, although they can explain only up to one third of its variance. Other dimensions of perceived health status are weakly influenced by these medical parameters. Patients should be assessed with regard to their age, because the main differences exist between the younger and the older patients. In the group of younger patients kidney function is the best predictor of SF-36 in contrast to the older patients, who are more affected by co-morbidity.

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**Table 1** Description of the patient sample (N=128)

<b>variable</b>		<b>N</b>	<b>% or mean with SD (range)</b>
<b>gender</b>	male	79	61.7 %
	female	49	38.3 %
<b>age</b>			48.6 ± 12.3 years (18-74)
<b>dialysis treatment before transplantation</b>	hemodialysis	93	72.7 %
	peritoneal	20	15.6 %
	both	15	11.7 %
<b>duration of dialysis</b>			2.6 years (0.1-35)
<b>number of hospitalizations during dialysis period</b>	0	7	5.7 %
	1-3	72	58.5 %
	4-5	20	16.3 %
	> 5	24	19.5 %
<b>graft source</b>	cadaver donor	125	97.7 %
	living donor	3	2.3 %
<b>secondary transplantation</b>		4	3.1 %
<b>time since transplantation</b>			28 months (3-84)
<b>number of hospitalizations after transplantation</b>	0	52	40.9 %
	1-3	60	47.2 %
	4-5	11	8.7 %
	> 5	4	3.1 %
<b>number of acute rejection episodes</b>			0.53 ± 0.66 (0-3)
<b>current serum creatinine</b>			137.8 µmol/l (75-444.4)
			1.56 mg/dl (0.85-5.05)

**Table 2** Description of co-morbid diseases in the patient sample (N=128)

<b>variable</b>		<b>N</b>	<b>%</b>
<b>hypertension</b>	yes	123	96.1 %
	no	5	3.9 %
<b>coronary artery disease</b>	yes	40	31.2 %
	no	88	68.8 %
<b>heart failure</b>	yes	8	6.2 %
	no	120	93.8%
<b>diabetes mellitus</b>	yes	27	21.1 %
	no	101	78.9 %
<b>stroke</b>	yes	12	9.4 %
	no	116	90.6 %
<b>peripheral vascular disease</b>	yes	4	3.1 %
	no	124	96.9 %
<b>anemia (hemoglobin less than 100 g/l)</b>	yes	7	5.5 %
	no	121	94.5 %
<b>lymphoma</b>	yes	1	0.8 %
	no	127	99.2 %
<b>bone disease with fractures</b>	yes	4	3.1 %
	no	124	96.9 %
<b>other serious co-morbidity</b>	yes	96	75.0 %
	no	32	25.0 %

**Table 3** Linear regression analysis of significant relations between selected variables and SF-36 in total sample

SF-36 sub-scale	variables	R <sup>2</sup> change	β	95 % CI	p
<b>physical component summary</b>	age	23.3 %	-0.509	-1.089; -0.574	0.000
	education	4.5 %	0.214	1.568; 9.680	0.007
	dialysis hospitalization	2.4 %	-0.172	-7.814; -0.429	0.029
<b>mental component summary</b>	education	7.7 %	0.261	2.042; 9.967	0.003
	age	4.4 %	-0.229	-0.575; -0.081	0.010
<b>bodily pain</b>	age	13.0 %	-0.389	-1.116; -0.047	0.000
	dialysis hospitalization	4.1 %	-0.220	-1.161; -0.165	0.010
<b>physical functioning</b>	age	26.2 %	-0.505	-0.267; -0.146	0.000
	education	5.5 %	0.227	0.517; 2.450	0.003
	dialysis hospitalization	3.4 %	-0.199	-2.032; -0.307	0.008
<b>physical role limitations</b>	education	6.5 %	0.233	0.126; 0.825	0.008
	age	4.6 %	-0.194	-0.047; -0.002	0.030
	diabetes mellitus	2.8 %	-0.191	-1.404; -0.067	0.031
<b>general health vitality</b>	age	9.4 %	-0.318	-0.166; -0.049	0.000
	age	7.8 %	-0.264	-0.134; -0.028	0.003
	education	4.0 %	0.219	0.234; 1.927	0.013
<b>emotional role limitations</b>	education	5.8 %	0.242	0.110; 0.665	0.007
	diabetes mellitus	4.3 %	-0.225	-1.206; -0.158	0.011
<b>mental health</b>	education	4.5 %	0.230	0.303; 2.354	0.012
<b>social functioning</b>	education	7.6 %	0.289	0.311; 1.261	0.001

dialysis hospitalization – number of hospitalizations during dialysis period, tx hospitalization – number of hospitalization after transplantation, SCr – serum creatinine, R<sup>2</sup> change – % of explained variance (adjusted), β – standardized β coefficient, CI – confidence interval, p – p-value of significance

**Table 4** Linear regression analysis of significant relations between selected variables and SF-36 in the group of patients younger than 45 years<sup>Y</sup> and in the group of patients aged 45 and more years<sup>0</sup>

SF-36 sub-scale	variables	R <sup>2</sup> change	B	95 % CI	p
<b>physical component summary</b>	<sup>Y</sup> SCr	9.6 %	-0.344	-0.141; -0.010	0.026
	<sup>0</sup> gender	6.0 %	-0.266	-20.403;-2.047	0.017
	<sup>0</sup> education	4.8 %	0.243	0.620; 11.289	0.029
<b>mental component summary</b>	<sup>Y</sup> education	11.8 %	0.374	1.941; 16.773	0.015
	<sup>0</sup> employment status	6.8 %	0.301	6.836; 40.934	0.007
	<sup>0</sup> tx hospitalization	5.0 %	-0.248	-11.410;-0.811	0.024
<b>bodily pain</b>	<sup>Y</sup> dialysis hospitalization	7.4 %	-0.311	-1.750;-0.022	0.045
	<sup>0</sup> SCr	7.0 %	0.287	0.004; 0.026	0.010
<b>physical functioning</b>	<sup>Y</sup> SCr	16.5 %	-0.380	-0.031; -0.006	0.006
	<sup>Y</sup> education	8.1 %	0.405	0.712; 3.639	0.005
	<sup>Y</sup> gender	8.0 %	-0.317	-4.393;-0.349	0.023
	<sup>0</sup> dialysis hospitalization	7.4 %	-0.283	-2.858;-0.423	0.009
	<sup>0</sup> education	5.8 %	0.262	0.325; 2.975	0.015
<b>physical role limitations</b>	<sup>Y</sup> education	10.1 %	0.351	0.112; 1.422	0.023
	<sup>0</sup> diabetes mellitus	4.9 %	-0.250	-1.649;-0.109	0.026
	<sup>0</sup> gender	3.7 %	-0.219	-1.479;-0.003	0.049
<b>general health</b>	<sup>Y</sup> SCr	13.3 %	-0.393	-0.037; -0.005	0.010
	<sup>0</sup> tx hospitalization	4.1 %	-0.231	-2.635;-0.032	0.045
<b>emotional role limitations</b>	<sup>Y</sup> education	12.3 %	0.380	0.151; 1.209	0.013
	<sup>0</sup> diabetes mellitus	5.6 %	-0.262	-1.331;-0.111	0.021
<b>mental health</b>	<sup>Y</sup> education	10.7 %	0.359	0.384; 4.132	0.019
	<sup>0</sup> employment status	6.3 %	0.262	0.929; 9.497	0.018
	<sup>0</sup> dialysis hospitalization	3.9 %	-0.223	-2.203; -0.037	0.043
<b>vitality</b>	<sup>0</sup> employment status	5.1 %	0.268	4.428; 41.964	0.016
	<sup>0</sup> tx hospitalization	4.0 %	-0.228	-11.951;-0.286	0.040
<b>social functioning</b>	<sup>Y</sup> education	9.5 %	0.308	0.164; 22.382	0.047
	<sup>0</sup> education	6.9 %	0.263	1.366; 15.645	0.020

dialysis hospitalization – number of hospitalizations during dialysis period, tx hospitalization – number of hospitalization after transplantation, SCr – serum creatinine, R<sup>2</sup> change – % of explained variance (adjusted), B – standardized B coefficient, CI – confidence interval, p – p-value of significance

**Conflict of interests:** none declared