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Differences in perceived health status between kidney transplant recipients and dialyzed patients are based mainly on the selection process

Rosenberger J, van Dijk JP, Prihodova L, Majernikova M, Nagyova I, Madarasova Geckova A, Roland R, van den Heuvel WJA, Groothoff JW. Differences in perceived health status between kidney transplant recipients and dialyzed patients are based mainly on the selection process. Clin Transplant 2010; 24: 358–365. © 2009 John Wiley & Sons A/S.

Abstract: Kidney transplantation offers longer survival, less morbidity and lower costs than dialysis. It is also believed to improve quality of life. The aim of this study was to compare prospectively the perceived health status (PHS) of dialyzed patients on a waiting list with kidney transplant recipients after transplantation, matched for age, gender and comorbidity. The sample consisted of 93 dialyzed patients on a waiting list for deceased-donor kidney transplantation and 87 incident transplant recipients. A total of 62 dialyzed patients were matched for age, gender and comorbidity with 62 transplant recipients. PHS was measured using the SF-36 questionnaire. Data from baseline and after 12 months were compared between the groups. Patients on dialysis had worse physical (49 ± 21) and mental (59 ± 18) PHS than transplant recipients (56 ± 21 and 64 ± 18 , $p \leq 0.05$), but when matched pairs were compared, no differences in PHS were found. After 12 months, PHS did not change significantly in either group. The PHS of patients after kidney transplantation is better than that of those on dialysis. However, this fact is significantly influenced by the selection procedure, as only some dialyzed patients are put onto the waiting list while others were actually transplanted. The differences disappear with matching.

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Key words: dialysis – kidney transplantation – quality of life – perceived health status – selection – SF-36

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Kidney transplantation offers longer survival and less morbidity than dialysis. Moreover, the cost of transplantation is lower (1). It is also reported that quality of life is improved after kidney transplantation (2, 3). While research into graft and patient survival after transplantation is quite impressive, studies focusing on quality of life, functional status or perceived health status are less

common. Comparisons of health status between patients after transplantation and those remaining on dialysis are even less frequent and most were published more than 10 yr ago. In general, two different populations are usually evaluated. When considering deceased-donor kidney recipients, one should be aware that patients being transplanted come from a group of dialyzed patients who have

been put on a waiting list. A patient's first step towards getting on such a list is an evaluation, and only if no contraindications are found, is s/he placed on the waiting list. The second step takes place when a suitable organ is available: the patient's actual condition is checked again before transplant surgery. Transplantation is performed only if there are no contraindications. Transplant surgeons commonly choose the very best candidates for transplantation carefully. In some published studies, transplant recipients had only half as much coronary and peripheral vascular disease than patients on dialysis (4), and only 2.5% of incident patients with end-stage renal disease undergo transplantation as their initial modality of treatment (5), which is in contrast to published guidelines (6). Any comparison of the health status of transplant recipients to patients on dialysis is therefore biased by these two selection processes, resulting in a comparison of young and relatively healthy patients to older and more ailing ones (7).

The majority of research papers that explore differences in quality of life between kidney transplant recipients and dialyzed patients date from more than 10 yr ago (from 1984 till 1996) and are cross-sectional in design. Over the past 10–15 yr dialysis technology and immunosuppressive treatment have changed considerably. The indication criteria for starting dialysis and for considering transplantation have also changed. These shifts have definitely altered the characteristics of our patient sample when compared to samples from previous periods. Another problem is the number of transplant patients recruited in these studies, ranging between 30 and 144 (8–14). Studies with larger samples are rare, the exceptions being the study by Muthny and Koch, who included 761 transplanted, 290 hemodialyzed and 68 peritoneal dialysis patients (15); the study by Gudex with 367 transplanted, 144 hemodialyzed and 93 peritoneal dialysis patients (16); the study by Wight et al. with 228 transplanted, 183 hemodialyzed and 109 peritoneal dialysis patients (3); and the study by Reimer et al. with 149 transplanted and the same number of both hemodialyzed patients and healthy controls (17). All of the cited studies found better quality of life in transplant recipients when compared to dialyzed patients, but some of their authors noted the heterogeneity within their samples. The differences in age between (younger) transplanted and (older) dialyzed patients are the most common findings (3, 8, 11, 15), but different lengths of time for treatment (3, 8, 15) and unequal gender proportions (15) are reported as well. In contrast to earlier findings, Morris and Jones did not find any striking differences in quality of life

between 69 transplanted and 24 home hemodialysis patients. The authors found reduced quality of life in 24 hospital hemodialysis patients compared with transplant recipients, but also when compared with home hemodialysis patients (18). Another study showing no significant differences in quality of life was published by Johnson et al. Twenty kidney transplant recipients were compared to 10 hemodialyzed patients on a waiting list for kidney transplantation, 19 hemodialyzed patients not on a waiting list and 10 failed transplants. Only the latter category showed diminished quality of life (19).

Very few studies with repeated evaluations of quality of life before and after transplantation have been published on this topic. Three studies contain a low number of transplanted patients – 16 in the study by Park et al. (12), 23 in the study by Kutner et al. (20) and 27 in the study by Russell et al. (21). Three larger studies have been published: Jofre et al. tracked 88 kidney transplant recipients, finding improvement in the Karnovsky Scale and Sickness Impact Profile scores after transplantation compared to pre-transplant scores, but with differences among genders (22); Laupacis et al. observed a 20% improvement in health-related quality of life (measured by the Sickness Impact Profile and Time Trade-Off Technique) in 168 transplant recipients, 76 of whom were followed-up two yr after transplantation (2); and Manninen et al. followed-up 226 transplant recipients and found improved work capacity among those with a functioning graft (23). All of these papers, except for Kutner et al., studied only transplant recipients without any control group.

Our previous research focused on medical and non-medical determinants of perceived health status after transplantation. We found that perceived health status, as a very complex construct, is influenced by age, gender, education, employment status, social support, side-effects of treatment and comorbidity, and not only by the success of transplantation. The largest proportion of variability in perceived health status is attributed to age and comorbidity (24). Because dialysis and transplant patients differ in these variables, their perceived health status differs, too (19). Therefore, the central hypothesis was formulated that perceived health status in patients with chronic kidney disease is much more dependant on age, gender, and comorbidity than on mode of therapy. In focusing on these facts, the present study was designed as a comparison of perceived health status between dialyzed patients on a waiting list for deceased-donor kidney transplantation and incident kidney transplant recipients three months after kidney transplantation, matched for age,

gender and comorbidity, with prospective follow-up after 12 months. This is a rather unique study as only a few papers with a similar approach have been published: Franke et al. studied 80 dialyzed patients before and after transplantation focusing on the role of social support and psychological distress rather than on exploring differences between dialyzed and transplanted patients (25); Reimer et al. compared quality of life in 149 transplant recipients, 149 dialyzed patients and 149 healthy controls matched for age and gender, but without matching them for comorbidity, finding the quality of life of transplant recipients to be comparable with that of healthy controls (17).

Materials and methods

Sample and procedures

Two patient cohorts were examined – patients on dialysis and those after transplantation. Two waves of data collection were performed: one at baseline (three months after transplantation in transplant group), the second after 12 months. Dialysis patients on a waiting list for deceased-donor kidney transplantation were identified and matched for age (in decades), gender and comorbidity category with incident kidney transplant recipients from the same region. Comorbidity was evaluated using information about comorbid diseases from medical records based on Wright's comorbidity index criteria (26). Patients were then stratified as low-risk category (no comorbidity), intermediate-risk (one comorbid condition) or high-risk (more than one comorbid condition).

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

Dialysis patients

Altogether 169 dialyzed patients from four different dialysis centers in the Slovak Republic were invited to participate, but 18 patients refused or provided incomplete data (a response rate of 89.3%). Out of these 151 respondents, 93 patients were on waiting lists for deceased-donor kidney transplantation. Non-respondents did not differ from participants either in age or gender. All patients from the four dialysis centers which agreed to participate were included except for 15 with severe dementia and two with mental retardation (dementia or mental retardation were listed in their medical records). Only patients currently on a waiting list for transplantation were included for statistical analysis. All respondents fulfilling the

inclusion criteria were invited to participate in a follow-up examination 12 months after the baseline interview, but eight of them (8.6%) did not respond or provided incomplete data.

Transplanted patients

A group of 127 incident kidney transplant recipients three months after transplant surgery from the same region of the Slovak Republic were invited to participate, but 40 patients refused or provided incomplete data, so 87 patients remained (a response rate of 68.5%). Non-respondents did not differ from participants either in age or gender. All newly transplanted patients with a functional graft who agreed to participate were included except for one with mental retardation (mental retardation was listed in the medical record). All respondents were invited to participate in a follow-up examination 12 months after their transplantation, but 33 of them (37.9%) did not respond or provided incomplete data.

Matching procedure

Respondents included for analysis were matched for age, gender and comorbidity index. For age-matching, 10 yr difference was tolerated. In addition, matched patients had to be of the same gender and have the same comorbidity index. At baseline, 62 matched pairs were identified. For the follow-up examination, 33 patients on a waiting list and 41 transplant patients remained for analysis.

Measures

All participants were interviewed by trained personnel. The interview focused on basic demographic information (age, gender), education (elementary, secondary or university), employment status (employed full-time or part-time, and not employed – disabled, retired or unemployed), house-keeping activities (measured in hours per week spent shopping, cooking, cleaning, or caring for family members) and family status (single, married, divorced or widowed).

Perceived health status was measured using the Short Form Health Survey (SF-36). The SF-36 is a 36-item questionnaire for the assessment of perceived health status (27). It consists of eight subscales which can be combined as a physical summary component and a mental summary component. All sub-scales as well as the summary components are presented as scores between 0 and 100, with higher scores indicating better health

status. The validity and reliability of the SF-36 have been validated in patients with renal disease, including those after kidney transplantation (3, 25, 28, 29). Skalska et al. validated the questionnaire in the Czech population (which is very similar to the Slovak population, as we used to be one country in past) (30). Cronbach's α in the present sample was 0.94.

Information about medical variables was taken from patient medical records. Medical variables were as follows: dialysis modality, either current or in the past (categorized as hemodialysis, peritoneal dialysis or both methods), length of dialysis period (either current or before transplantation), primary nephrologic diagnosis, and the presence of comorbidity. Information about current serum creatinine and current immunosuppression protocol was retrieved in the group of transplanted patients as well.

Statistics

Frequencies, means and standard deviations were calculated for the sample description. Differences in continuous variables between dialysis and transplant patients as well as between dialysis patients on waiting lists and transplant patients were analyzed using the Mann–Whitney *U*-test and Wilcoxon signed ranks test. Differences in categorical variables between dialysis and transplant patients as well as between dialysis patients on waiting lists and transplant patients were analyzed with the chi-square test and Fisher exact test. SPSS 16.0 was used for statistical analyses.

Results

Out of 151 dialyzed patients 93 were on a waiting list for deceased-donor kidney transplantation (mean age 49.2 ± 11.9 yr, 54 males and 39 females). The mean age of the group of 87 transplanted patients was 46.6 ± 13.1 yr (49 males, 38 females). After matching, 124 patients (62 dialyzed patients on waiting list and 62 transplant recipients) remained for analysis.

Follow-up data 12 months following baseline evaluation are available for 33 dialyzed patients on a waiting list and 41 kidney transplant recipients. The reasons for lack of follow-up data are as follows. Two (2.2%) waiting-list patients and three (3.4%) transplant recipients died; eight (8.6%) waiting-list patients and 33 (37.9%) transplant recipients refused to give informed consent or provided incomplete questionnaires; 20 (21.5%) waiting-list patients were transplanted; 14 (15.1%) waiting-list patients were not yet 12 months after baseline evaluation and five (5.7%) transplant recipients were not yet 12 months after transplantation; two (2.2%) waiting-list patients and one (1.1%) transplant recipient were lost to follow-up; and five (5.4%) waiting-list patients no longer fit the inclusion criteria.

Demographic and socioeconomic variables are described in Table 1. We observed a trend towards older age in the dialysis group (however, differences were not significant). Medical variables are presented in Table 2. The majority of patients had hemodialysis as their elimination modality, but this was less frequent in the transplanted group than in

Table 1. Basic characteristics of all dialyzed patients on a waiting list, all transplanted patients, and matched pairs of patients on a waiting list and after transplantation

	D-WL (N = 93)	Tx (N = 87)	Matched D-WL (N = 62)	Matched Tx (N = 62)
Age (yr)	49.2 ± 11.9	46.6 ± 13.1	46.5 ± 11.3	48.0 ± 12.2
Gender (%)				
Male	58.1	56.3	61.3	61.3
Female	41.9	43.7	38.7	38.7
Education (%)				
Elementary	55.5	59.2	50.0	59.0
Secondary	35.6	35.2	37.1	36.1
University	8.9	5.6	12.9	4.9
Employment status (%)				
Employed	11.8	10.3	14.5	11.3
Not employed	88.2	99.7	85.5	88.7
Housekeeping (h/wk)	21 ± 16	20 ± 19	22 ± 15	18 ± 18
Family status (%)				
Single	19.2	25.0	19.2	27.7
Married	74.0	64.3	80.8	63.7
Divorced	0.0	3.6	0.0	4.3
Widowed	6.8	7.1	0.0	4.3

Figures are percentages or means ± standard deviations.
D-WL, dialysis patients on a waiting list; Tx, transplanted patients.

	D-WL (N = 93)	Tx (N = 87)	Matched D-WL (N = 62)	Matched Tx (N = 62)
Dialysis modality (%)				
Hemodialysis	88.3*	73.6	86.7	72.6
Peritoneal dialysis	10.5	11.1	13.3	11.3
Both modalities	1.2***	15.3	0.0***	16.1
Dialysis duration (yr)	3.6 ± 3.6	3.9 ± 2.7	3.5 ± 3.6	4.0 ± 2.8
Primary diagnosis (%)				
Glomerulonephritis	31.5	38.0	33.9	35.5
Tubulointerstitial nephritis	26.9	29.6	25.8	27.4
Diabetic nephropathy	4.5	11.3	4.8	12.9
Polycystic kidneys	11.2*	2.8	8.1	3.2
Other or unknown	25.9	18.3	27.4	21.0
Co-morbidity (%)				
Diabetes mellitus	12.2*	29.8	13.2*	31.2
Hypertension	93.2	100.0	90.6	100.0
Heart diseases	39.2	32.8	34.0	36.7
Stroke	12.2	8.6	11.3	10.2
Hepatitis	5.4	7.3	5.7	8.7
Severe anemia (Hb < 100 g/L)	24.7**	12.0	26.4***	10.2
Cancer	8.1*	0.0	9.4*	0.0
Severe bone disease	19.0	19.0	20.8	22.4
Co-morbidity index (%)				
low-risk	6.7	13.9	6.5	6.5
intermediate-risk	48.3	44.4	48.4	48.4
high-risk	45.0	41.7	45.2	45.2
Serum creatinine (μmol/l)		137 ± 56		134 ± 46
Immunosuppression (%)				
CsA + MMF + P		80.4		78.3
Tac + MMF + P		16.4		17.4
CsA + MMF		1.8		2.2
Tac + MMF		1.8		2.2

Table 2. Medical characteristics of all dialyzed patients on a waiting list, all transplanted patients, and matched pairs of patients on a waiting list and after transplantation

Figures are percentages or means ± standard deviations.

D-WL, dialysis patients on a waiting list; Tx, transplanted patients; CsA, cyclosporin A; MMF, mycophenolate mofetil; P, prednisone; Tac, tacrolimus.

*Significant difference when compared to transplanted patients ($p \leq 0.05$).

**Significant difference when compared to transplanted patients ($p \leq 0.01$).

***Significant difference when compared to transplanted patients ($p \leq 0.001$).

the waiting list group ($p \leq 0.05$). There were more patients who switched elimination therapy (from peritoneal dialysis to hemodialysis or vice versa) in the transplant group compared to dialysis patients on a waiting list ($p \leq 0.001$). Patients on dialysis differed significantly from those after transplantation in their primary nephrologic diagnosis – there were more polycystic kidney diseases ($p \leq 0.05$) among the dialyzed patients. Dialyzed patients on a waiting list had severe anemia ($p \leq 0.01$) and cancer ($p \leq 0.05$) more often when compared to transplant recipients. On the other hand, diabetes mellitus was more frequent among transplant recipients ($p \leq 0.05$), and when the comorbidity index was calculated, an insignificant trend towards higher morbidity was observed among dialyzed patients.

In the non-matched sample, dialysis patients on a waiting list reported worse physical (48.5 ± 21.4) and mental (58.6 ± 18.1) perceived

health status than patients after kidney transplantation (55.7 ± 18.1 and 63.6 ± 18.2 , $p \leq 0.05$, respectively). When patients after kidney transplantation were compared to their matched pairs on a waiting list, no differences in perceived health status were found (Table 3). After the follow-up 12 months later, the physical perceived health status of all waiting-list patients worsened, by 4.8 ± 14.8 , and mental perceived health status improved by 0.1 ± 18.1 (the change is not significant). Physical and mental perceived health status of kidney transplant recipients improved by 0.4 ± 14.4 and 1.5 ± 15.6 , respectively (also not significant). When matched pairs were compared with regard to a change in perceived health status, the differences between patients on a waiting list and those after transplantation were also not significant. In addition, the change of perceived health status was highly variable in both groups; there were as many patients with

Table 3. Perceived health status (SF-36) of all dialyzed patients on a waiting list, all transplanted patients, and matched pairs of patients on a waiting list and after transplantation

	D-WL (N = 93)	Tx (N = 87)	Matched D-WL (N = 62)	Matched Tx (N = 62)
Physical perceived health status (baseline)	48.5 ± 21.4*	55.7 ± 20.7	48.2 ± 22.1	52.3 ± 19.8
Mental perceived health status (baseline)	58.6 ± 18.1*	63.6 ± 18.2	57.0 ± 18.7	59.7 ± 18.9
	N = 42	N = 45	N = 33	N = 41
Physical perceived health status (follow-up)	47.7 ± 19.5	54.7 ± 19.0	50.0 ± 18.5	53.6 ± 18.7
Mental perceived health status (follow-up)	60.1 ± 18.5	64.2 ± 17.0	62.0 ± 18.4	63.4 ± 17.0
Change in physical health status	-4.8 ± 14.2	0.4 ± 14.4	-5.3 ± 15.3	0.0 ± 14.3
Change in mental health status	0.1 ± 18.1	1.5 ± 15.6	1.0 ± 19.5	1.3 ± 15.8

Figures are percentages or means ± standard deviations.
 D-WL, dialysis patients on a waiting list; Tx, transplanted patients.
 *Significant difference when compared to all transplanted patients (p ≤ 0.05).

dramatic improvement as with dramatic worsening (Table 3).

Discussion

The present study confirms that patients after kidney transplantation feel better than those on dialysis (15). The physical component of perceived health status in particular is improved in transplant patients. In contrast to previous research, we show that this is not the case when the perceived health status of transplant recipients is compared to that of their dialysis matched pairs (having the same age, gender and comorbidity) on a waiting list.

We evaluated the perceived health status of incident kidney transplant recipients three months after their transplant surgery. Three months after transplantation seems to be sufficient time for most patients’ wounds to heal and for them to adapt to their new life situation. The frequency of medical visits, blood tests and doses of immunosuppressive drugs are reduced as well. In addition, there is evidence that after three months the risk of death is comparable between transplant recipients and patients on waiting lists (31). Perceived health status remained stable 12 months after transplantation. On the other hand, the same (not significant) trend is visible in their matched dialysis pairs on a waiting list.

Our findings are not in line with previous research, and we think it is important to discuss the possible reasons. Although the majority of papers have confirmed sharp differences in age between the general dialysis population and kidney transplant recipients (2, 8, 10, 11, 15, 18), this fact is often neglected when interpreting results. In the present study, the sample of all (non-matched) dialyzed patients was older than transplant recipients by an average of 10 yr (data for dialyzed

patients not on a waiting list for transplantation are not shown in the tables). There are other demographic and social variables which are potential confounders. Our sample did not reveal significant differences in these variables, despite the fact that dialyzed patients in our sample had a different distribution of family status than patients after transplantation.

It is common to control for medical variables in graft or patient survival analyses. Dialyzed patients in the present study suffered more from cancer and anemia when compared to transplant recipients, while diabetes was more common among transplanted patients. But this fact is often neglected in research focusing on differences in quality of life among various end-stage renal disease treatment modalities. Primary diagnosis, or comorbidity is usually presented but seldom included in the analyses (3, 10). Ultimately, the best measure against confounding factors is to stratify the sample or to conduct a matched pairs study, as we did in our study (32).

Another important argument for the interpretation of conflicting results is the different time of data collection in the studies. Russell et al. observed significant improvement in quality of life 30.9 months after transplantation in 27 patients on waiting lists who had been subsequently transplanted. This prospective study was published in *Transplantation* in 1992 (21). In the early 1990s Laupacis et al. evaluated 269 patients on waiting lists; 168 of them were subsequently transplanted. The authors prospectively followed-up patients for 24 months (data on about 76 patients were available at that time) and concluded that health-related quality of life improved by 23% six months after transplantation and remained improved thereafter (2). Unfortunately, since 1996, when this study was published in *Kidney International*, no similar

research paper has been presented. During the past 10–15 yr dialysis as well as transplantation practice has changed significantly. Comparing our transplanted patients with the population in the study published in 1996 by Laupacis et al. reveals visible differences: our patients were on average five yr older, spent twice as much time on dialysis and were less likely to be employed. These differences visibly show that older and more ailing patients are being transplanted today, which can surely affect outcomes (2).

The present study has some weaknesses that need to be mentioned. The number of participants was not high, as we included 180 patients with end-stage renal disease treated by dialysis or transplantation. The majority of studies on this topic contained a similar number of patients, but there are exceptions, unfortunately with no matching (15) or matching for age and gender only (17). We tried to manage the problem of case-mix by matching for age, gender and comorbidity index. However, even after matching the samples are not fully equal as there are more cases with anemia and cancer among dialyzed patients and more diabetics among transplant recipients. Less anemia in the transplant group is not surprising because it is connected with functioning kidneys while the higher proportion of diabetics among transplant recipients is due to the manifestation of post-transplant diabetes mellitus after application of steroids and calcineurin inhibitors. As these facts are a part of dialysis/transplantation, it is problematic to control for them. Another problem for the interpretation of the present research lies in the tool used. The SF-36 is a questionnaire designed for evaluation of perceived health status. This measure is definitely not equivalent to quality of life, as the latter term covers much broader aspects. The differences in instruments might therefore be the source of contrary conclusions. Survival bias might also be a source of inaccuracy in our results, because we invited transplant recipients with functional graft after three months. Including those with graft failure before the third month (or those who died) would decrease the differences between the groups. An additional problem is the follow-up after 12 months, as we were able to examine only 45% of the waiting-list patients and half of the transplant recipients. While power analysis at baseline provided acceptable results (power 46–72%), it was merely fair (up to 20%) upon follow-up examination. Continuation in this prospective research is therefore necessary, but problematic because a significant numbers of waiting-list patients are transplanted, die or move to a non-waiting list category during the follow-up period.

Our aim was to conduct a study coming from real life, and therefore we included all new transplant recipients from our centre as well as all waiting-list patients from four dialysis centers from the same region. This approach provides the opportunity to generalize the results to the whole transplant/waiting list population.

Perceived health status in patients is much better after kidney transplantation than in those on dialysis. However, this statement may be influenced by the selection procedure, as only some dialyzed patients are put onto a waiting list and some of them are actually transplanted. After applying matching criteria (age, gender and comorbidity), differences in perceived health status disappear. Some patients perceive a dramatic improvement of health status shortly after transplantation, while others perceive a negative experience. Individual characteristics (medical and non-medical) possibly play a more important role than the type of therapy. Patients on dialysis awaiting transplantation (together with their nephrologists) expect improvement in their health status after successful transplantation, but often encounter new health complaints, including the adverse effects of immunosuppressive drugs, fear of rejection and infection, or anxiety about long-term kidney function (33–36).

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Conflict of interests

None.

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