Perceived health status after kidney transplantation

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CHAPTER 2

Are differences in perceived health status between kidney transplant recipients and dialysed patients based on a selection bias?

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Abstract

Background: Kidney transplantation offers longer survival, less morbidity and lower costs than dialysis. It is believed that it improves quality of life as well. The aim of present study was to compare perceived health status (PHS) of dialysed patients on waiting list with kidney transplant recipients 3 months after transplantation, matched for age, gender and co-morbidity.
Methods: Out of 103 dialysed patients 45 on waiting list for cadaveric kidney transplantation were matched for age, gender and co-morbidity to 42 incident transplant recipients. An interview was conducted to collect socio-demographic variables. PHS was measured by the SF-36, social support by Social Support List Discrepancies questionnaire. Medical data were retrieved from patients' medical records.
Results: Patients on dialysis had worse physical (37.7±23.3) and mental

(50.6±19.4) PHS than transplant recipients (54.2±20.5 and 60.7±20.0, $p \leq 0.001$ and $p \leq 0.01$, respectively). If transplanted patients were compared to their matched pairs on waiting list, no differences in PHS were found.
Conclusions: PHS after kidney transplantation is much better than on dialysis. However, this fact is significantly influenced by a selection bias as only some dialysed patients are put onto waiting list and some of them are actually transplanted. When the correction of this bias is done using matching criteria, differences in PHS disappear.

Introduction

Kidney transplantation offers longer survival, less morbidity than dialysis and the cost of transplantation is lower as well [1]. It is also reported that quality of life after kidney transplantation is improved [2,3].

While research into graft and patient survival after transplantation is quite impressive, studies focused at 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 mostly published more than ten years ago. In general, two different populations are usually evaluated. When considering a recipient of cadaveric kidney, one should be aware that patients who are being transplanted are coming from a waiting list. As the first step, a patient's status is evaluated and only if no contraindications are found, a patient is placed on waiting list. As the second step, when a suitable organ is available, a patient is checked again before transplant surgery. It is common that transplant surgeons carefully choose the very best candidates for transplantation. In some published studies, transplant recipients had half as much coronary and peripheral vascular disease than patients on dialysis [4]. In summary, two processes of selection are happening before a patient is transplanted. Therefore, any comparison of health status of transplant recipients to patients on dialysis is twicely biased, resulting in comparison of young and relatively healthy to older and more ill patients [5].

The majority of research papers that explore differences in quality of life between kidney transplant recipients and dialysed patients is outdated (from 1984 till 1996) and has a cross-sectional design. Another problem is the number of transplant patients recruited in these studies varying between 30 and 144 [6-12]. Research with larger samples is rare, the exceptions are the study by Muthny and Koch who included 761 transplanted, 290 hemodialysed and 68 peritoneal dialysis patients [13], the study by Gudex with 367 transplanted, 144 hemodialysed and 93 peritoneal dialysis patients [14], the study by Wight et al. with 228 transplanted, 183 hemodialysed and 109 peritoneal dialysis patients [3], and the study by Reimer et al. with 149 transplanted, the same number

of hemodialysed patients and healthy controls [15]. All cited studies found better quality of life in transplant recipients when compared to dialysed patients, but some of their authors pointed at heterogeneity within their samples. The differences in age between (younger) transplanted and (older) dialysed patients are the most common findings [3,6,9,13], but different time on treatment [3,6,13] and unequal gender proportions [13] are reported as well. Contrasting with earlier findings, Morris and Jones did not prove striking differences in quality of life between 69 transplanted and 24 home hemodialysis patients. Although the authors found reduced quality of life in 24 hospital hemodialysis patients compared to that of transplant recipients, but also to that of home hemodialysis patients [16]. Another study without significant differences in quality of life was published by Johnson et al. Twenty kidney transplant recipients were compared to 10 hemodialysed patients on the waiting list for kidney transplantation, 19 hemodialysed patients not on waiting list and 10 failed transplants. Only the last category displayed a diminished quality of life [17].

Very few studies with repeated evaluations of quality of life before and then 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. [10], 23 in the study by Kutner et al. [18] and 27 in the study by Russell et al. [19]. Three larger studies were published – Jofre et al. followed 88 kidney transplant recipients [20], Laupacis et al. 168 [2] and Manninen et al. 226 [21]. All papers, except for Kutner et al., studied only transplant recipients without any control group.

It is evident that perceived health status is influenced by age, gender, education, employment status, social support, side-effects of treatment, co-morbidity, and not only by the success of transplantation [22]. Because dialysis and transplant patients differ in these variables, their perceived health status is different too [17].

With aiming at these facts the present study was designed as the comparison of perceived health status between dialysed patients on waiting list for cadaveric transplantation and incident kidney transplant recipients 3 months after kidney transplantation, matched for age, gender and co-morbidity. To our knowledge, few papers with similar approach have been published, however without exploring differences between dialysed and transplanted patients [23] or without matching them for co-morbidity [15].

Methods

Sample and procedures

Two patient cohorts were examined – patients on dialysis and those after transplantation. The protocol was designed to examine 100 dialysis patients, 50 of them who are on waiting list for cadaveric kidney transplantation,

and to match those on waiting list for age (in decades), gender and co-morbidity category with 50 incident kidney transplant recipients from the same region. Co-morbidity was evaluated using the information about co-morbid diseases from medical records based on criteria for Wright co-morbidity index [24]. Thereafter patients were stratified into low-risk category (no comorbidity), intermediate-risk (one co-morbid condition) and high-risk (more than one co-morbid condition).

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

Dialysis patients

The group of 109 dialysed patients from four different dialysis centers in the Slovak Republic was invited to participate, 6 patients refused or provided incomplete data (response rate 94.5 %). Out of these, 45 patients (and 3 nonresponders) were on a waiting list for cadaveric transplantation. Nonresponders did not differ from participants whether in age or gender. All patients who agreed with their participation were included except for fifteen with severe dementia and two with mental retardation (dementia or mental retardation were listed in their medical records).

Transplanted patients

The group of 61 incident kidney transplant recipients three months after their transplant surgery from the same region of Slovak Republic was invited to participate, 19 patients refused or provided incomplete data. 42 patients remained (response rate 68.9 %). Nonresponders did not differ from participants whether in age or gender. All patients with a functional graft who agreed with their participation were included except for one with mental retardation (mental retardation was listed in the medical record).

After matching for age, gender and co-morbidity index, 31 dialysis (on waiting list) and 31 transplant patients remained for analysis.

Measures

All participants were interviewed by a trained individual. The interview was focused on basic demographic information (age, gender), education (categorized as elementary, secondary or university), employment status (categorized as employed for full-time or part-time and not employed – disabled, retired or unemployed), house-keeping activities (measured in hours per week spent for shopping, cooking, clearing, or caring for family members), family status (categorized as 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 assessment of perceived health status [25]. It consists of 8 sub-scales which can be combined

as the physical summary component and the 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 SF-36 have been tested in patients with renal disease, including those after kidney transplantation [3,23,26,27]. Skalska et al. validated the questionnaire in the Czech population [28]. The Cronbach's α in the present sample was 0.94.

Social support was measured using the Social Support List Discrepancies questionnaire (SSL-D). The items in this questionnaire are grouped into 6 scales and they can be computed into a summary score (higher score indicates better social support). The validity and reliability of this questionnaire have been previously tested in various patient populations [29,30]. The Cronbach's α of the questionnaire in the present research was 0.88.

Information about medical variables was taken from patients' 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, presence of co-morbidity. Information about current serum creatinine and current immunosuppression protocol were searched in the group of transplanted patients as well.

Statistics

Descriptive statistics were used for sample description. Differences in continuous variables between dialysis and transplant patients as well as between dialysis on waiting list patients and transplant patients were analysed by t-test. Differences in categorical variables between dialysis and transplant patients as well as between dialysis on waiting list patients and transplant patients were analysed by χ^2-test. SPSS 12.0.2 was used for statistical analyses.

Results

Out of 103 dialysed patients with mean age of 55.9 ± 14.1 years (63 males, 40 females) 45 were on waiting list for cadaveric kidney transplantation (mean age 48.6 ± 12.7 years, 27 males and 18 females). The mean age of the group of 42 transplanted patients was 45.5 ± 12.5 years (26 males, 16 females). After matching, 62 patients (31 dialysed patients on waiting list and 31 transplant recipients) remained for analysis.

Demographic, socio-economic variables and social support are described in Table 1. Patients on dialysis were significantly older than patients after transplantation ($p \leq 0.001$). There were significantly less single ($p \leq 0.05$)

and more widowed ($p \leq 0.05$) persons among dialysed patients. When matched pairs were compared, no significant differences in demographic, socio-economic variables and social support were found.

Medical variables are presented in Table 2. Majority of patients had hemodialysis as their elimination modality, but it was more frequent in the dialysed group than in the transplanted group ($p \leq 0.01$). There were more cases who switched the elimination therapy in the transplant group when compared to whole dialysis patients ($p \leq 0.01$) or dialysis patients on waiting list ($p \leq 0.01$). Patients on dialysis differed significantly from those after transplantation in their primary nephrologic diagnosis – there were less glomerulonephritis ($p \leq 0.01$) and more polycystic kidney diseases ($p \leq 0.05$) among dialysed patients. Marked differences were found in co-morbid conditions as dialysed patients more frequently suffered from heart diseases ($p \leq 0.001$) and severe anemia ($p \leq 0.01$). Dialysed patients on waiting list had more often severe anemia when compared to transplant recipients ($p \leq 0.05$). When co-morbidity index was calculated, two thirds of dialysed patients belonged to high-risk category and one quarter to intermediate-risk category. Among transplant recipients these ratios were nearly reversed ($p \leq 0.001$). Patients on waiting list did not differ significantly from those after transplantation in distribution of their co-morbidity index. When matched pairs were compared, no significant differences in medical variables were found except for more frequent anemia among dialysed patients ($p \leq 0.05$).

Patients on dialysis on waiting list and not on waiting list together reported worse physical (37.7 ± 23.3) and mental (50.6 ± 19.4) perceived health status than patients after kidney transplantation (54.2 ± 20.5 and 60.7 ± 20.0, $p \leq 0.001$ and $p \leq 0.01$, respectively). If patients after kidney transplantation were compared to their matched pairs on waiting list, no differences in perceived health status were found (Table 3).

Discussion

The present study confirmed the fact that patients after kidney transplantation feel better than those on dialysis [13]. Physical component of perceived health status is reduced in dialysis patients in particular. In contrast to previous research, we have shown that this is not true when comparing perceived health status of transplant recipients to their matched pairs (with the same age, gender and co-morbidity) on waiting list.

Majority of papers confirmed sharp differences in age between general dialysis population and kidney transplant recipients [2,6,8,9,13,16]. In the present study, the sample of all dialysed patients was older than transplant recipients in average of 10 years. There are other demographic,

social variables and social support, which are potential confounders. Our sample did not present significant differences in these variables, despite in dialysed patients was a different distribution of family status from those after transplantation.

It is common to control for medical variables in graft or patient survival analyses. Dialysed patients in the present research suffered more from cardiovascular diseases and anemia when compared to transplant recipients. But in the research focused on differences in quality of life among various end-stage renal disease treatment modalities this is often neglected. Primary diagnosis or co-morbidity is usually presented, but seldom included into analyses [3,8]. However, the best way how to avoid confounding is to stratify the sample or to conduct a matched pairs study.

The present study has some weaknesses to be mentioned. The number of participants was not high as we included 145 patients with end-stage renal disease treated by dialysis or transplantation. Majority of studies on this topic contained a similar number of patients, but there are exceptions, unfortunately with no matching [13] or matching for age and gender only [15]. The design of our research was cross-sectional, therefore it is not possible to evaluate the effect of time after transplant surgery. In contrast to our approach, Laupacis et al. evaluated 168 patients within the period of 19.5 months and found an improvement in health status 6 months after transplantation [2]. It seems to be of value to continue in our study and examine all participants after one year. But it is necessary to calculate with the fact that small fraction of dialysed patients on waiting list would move to transplant category, reducing the sample [18]. Another problem of the interpretation of present research is in the tool, which was used. The SF-36 is the questionnaire designed for evaluation of perceived health status. This mesure is definitely not equal to quality of life, as the later term covers much broader aspects. So, the differences in instruments might be the source of contrary conclusions.

Perceived health status after kidney transplantation is much better than on dialysis. However, this statement is significantly influenced by a selection bias as only some dialysed patients are put onto waiting list and some of them are actually transplanted. When the correction of this bias is done using matching criteria (age, gender and co-morbidity), differences in perceived health status disappear. The consequences for clinical practice are aimed at the group of patients on dialysis awaiting for transplantation. They expect improvement in their health status after successful transplantation, but are often encountered with new health complaints, including adverse effects of immunosuppressive drugs, fear from rejection and infection or anxiety about long-term kidney function [31-34]. Therefore intensive attention should be paid not only to transplant recipients, but to patients on waiting list as well.

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Table 1 Basic characteristics of all dialysed patients, dialysed patients on waiting list, all transplanted patients, and the matched pairs of patients on waiting list and after transplantation

		D N = 103	WL N = 45	Tx N = 42	matched WL N = 31	matched Tx N = 31
age (years)		55.9±14.1***	48.6±12.7	45.5±12.5	46.6±12.3	46.7±13.3
gender	male	61.2 %	60.0 %	61.9 %	67.7 %	67.7 %
	female	38.8 %	40.0 %	38.1 %	32.3 %	32.3 %
education	elementary	60.2 %	64.5 %	51.9 %	61.3 %	54.8 %
	secondary	32.0 %	28.9 %	33.3 %	29.0 %	38.7 %
	university	7.8 %	6.7 %	4.8 %	9.7 %	6.5 %
employment status	employed	10.5 %	17.8 %	17.1 %	22.6 %	19.4 %
	not employed	89.5 %	82.2 %	82.9 %	77.4 %	80.0 %
housekeeping (hours/week)		17.8±14.7	22.3±13.2	19.7±18.5	23.6±13.3	17.6±16.8
family status	single	12.6 % *	22.2 %	29.3 %	19.4 %	33.3 %
	married	71.8 %	73.3 %	65.9 %	80.6 %	60.0 %
	divorced	1.9 %	0.0 %	4.9 %	0.0 %	6.7 %
	widowed	13.6 % *	4.4 %	0.0 %	0.0 %	0.0 %
social support (SSL-D)		56.2±12.4	57.2±12.5	55.0±10.9	59.4±10.8	54.2±9.9

figures are percentages or means ± standard deviations

D – dialysis patients, WL – dialysis patients on waiting list, Tx – transplanted patients

* – significant difference when compared to all transplanted patients ($p \leq 0.05$)

*** – significant difference when compared to all transplanted patients ($p \leq 0.001$)

Table 2 Medical characteristics of all dialysed patients, dialysed patients on waiting list, all transplanted patients, and the matched pairs of patients on waiting list and after transplantation

		D N = 103	WL N = 45	Tx N = 42	matched WL N = 31	matched Tx N = 31
dialysis modality	hemodialysis	88.3 % **	84.4 %	69.0 %	83.9 %	74.2 %
	peritoneal dialysis	7.8 %	13.3 %	9.5 %	16.1 %	9.7 %
	both modalities	3.9 % **	2.2 % **	21.4 %	0.0 %	16.1 %
dialysis duration (years)		3.7±3.5	4.0±3.7	4.2±2.8	3.4±2.9	4.2±2.8
primary diagnosis	glomerulonephritis	23.3 % **	33.3 %	47.6 %	38.7 %	41.9 %
	tubulointerstitial nephritis	32.0 %	26.7 %	35.7 %	19.4 %	41.9 %
	diabetic nephropathy	20.4 %	8.9 %	7.1 %	9.7 %	9.7 %
	polycystic kidneys	10.7 % *	8.9 %	0.0 %	8.7 %	0.0 %
	other or unknown	13.6 %	22.2 %	9.6 %	23.5 %	6.5 %
co-morbidity	diabetes mellitus	35.0 %	20.0 %	26.2 %	25.8 %	35.5 %
	hypertension	94.2 %	97.8 %	100.0 %	96.8 %	100.0 %
	heart diseases	63.1 % ***	46.7 %	28.6 %	35.5 %	25.8 %
	stroke	15.5 %	13.3 %	11.9 %	12.9 %	12.9 %
	hepatitis	10.7 %	8.9 %	9.5 %	6.5 %	6.5 %
	anemia	32.0 % **	26.7 % *	7.1 %	29.0 % #	6.5 %
	cancer	8.7 %	8.9 %	0.0 %	9.7 %	0.0 %
	bone disease	28.2 %	24.4 %	21.4 %	22.6 %	22.6 %
co-morbidity index	low-risk	3.9 %	6.7 %	7.1 %	9.7 %	9.7 %
	intermediate-risk	26.2 % ***	37.8 %	54.8 %	38.7 %	38.7 %
	high-risk	69.9 % ***	55.6 %	38.1 %	51.6 %	51.6 %
serum creatinine (µmol/l)				144 ± 48		148 ± 52
immuno-suppression	CsA + MMF + P			83.3 %		80.6 %
	Tac + MMF + P			14.3 %		16.1 %
	Tac + MMF			2.4 %		3.2 %

figures are percentages or means ± standard deviations

D – dialysis patients, WL – dialysis patients on waiting list, Tx – transplanted patients

CsA – cyclosporin A, MMF – mycophenolate mofetil, P – prednison, Tac - tacrolimus

* – a significant difference when compared to all transplanted patients ($p \leq 0.05$)

** – a significant difference when compared to all transplanted patients ($p \leq 0.01$)

*** – a significant difference when compared to all transplanted patients ($p \leq 0.001$)

– a significant difference when compared to matched transplanted patients ($p \leq 0.05$)

Table 3 Physical and mental perceived health status of all dialysed patients, dialysed patients on waiting list, all transplanted patients, and the matched pairs of patients on waiting list and after transplantation

	D N = 103	WL N = 45	Tx N = 42	matched WL N = 31	matched Tx N = 31
physical perceived health status	37.7 ± 23.3 ***	47.7 ± 22.0	54.2 ± 20.5	47.9 ± 22.9	51.7 ± 20.6
mental perceived health status	50.6 ± 19.4 **	55.9 ± 17.1	60.7 ± 20.0	58.2 ± 18.4	60.5 ± 19.9

figures are means ± standard deviations

D – dialysis patients, WL – dialysis patients on waiting list, Tx – transplanted patients

** – a significant difference when compared to all transplanted patients ($p \leq 0.01$)

*** – a significant difference when compared to all transplanted patients ($p \leq 0.001$)