Transplant International ISSN 0934-0874

ORIGINAL ARTICLE

# Adherence, depression and quality of life in patients on a renal transplantation waiting list

Beril Akman,[1] Murathan Uyar,[1] Baris Afsar,[1] Siren Sezer,[1] Fatma Nurhan Ozdemir[1] and Mehmet Haberal[2]

1 Department of Nephrology, Baskent University Hospital, Ankara, Turkey
2 Department of General Surgery, Baskent University Hospital, Ankara, Turkey

**Keywords**
adherence, quality of life, renal transplantation, waiting list.

**Correspondence**
Beril Akman, Baskent Universitesi Hastanesi, Nefroloji Bölümü, 5. Sok. No:48, 06490 Bahçelievler, Ankara, Turkey. Tel.: +090 (0) 312 2238684; fax: +090 (0) 312 2130034; e-mail: dr.berilakman@gmail.com

Received: 31 August 2006
Revision requested: 29 September 2006
Accepted: 10 April 2007

doi:10.1111/j.1432-2277.2007.00495.x

## Summary

To study nonadherence, and its relationship with depression and quality of life (QOL) in patients on a cadaveric renal transplantation waiting list (RTWL). In 86 RTWL patients (56 men/30 women), there were 49 nonadherent patients (age, 46.8 ± 21.8 years) and 37 adherent patients (age, 42.8 ± 12.1 years). Clinical nonadherence was defined as skipping or shortening dialysis sessions, interdialytic weight gain (IDWG) of >5.7% body weight, a predialysis potassium level of >6 mEq/l and a predialysis phosphate level of >7.5 mg/dl. For each study subject, marital status, level of education duration of dialysis, prior renal transplantation, IDWG, predialysis blood urea nitrogen (BUN) value and creatinine, potassium, phosphate levels were recorded as were scores from the short form-36 and Beck depression inventory (BDI). A high IDWG (33.7% of the subjects) was the most common nonadherence pattern noted. Age, sex, marital status, duration of dialysis, prior transplantation, comorbid conditions the predialysis BUN values, the levels of creatinine, potassium, and phosphate were not significantly different between the two groups ($P > 0.05$). The level of education was higher in adherent group ($P = 0.018$). QOL and BDI scores were negatively correlated ($P = 0.001$, $r = -0.561$). Nonadherent patients had lower QOL ($P = 0.04$) and higher depression scores ($P = 0.01$) than did adherent patients. Of the depressed patients, 77.8% had a comorbid condition. Nonadherence was only associated with BDI scores (OR, 2.146; CI, 2.052–2.350; $P = 0.002$). In dialysis patients, close monitoring of adherence, early diagnosis of depression, and the treatment of disease may further enhance QOL during the waiting period for a cadaveric renal transplant.

## Introduction

The efficacy of any therapy depends not only on the appropriate choice of medication, but also on the active cooperation of the patient in adhering to the therapeutic regimen prescribed by healthcare professionals. That cooperation which is vital to therapeutic success is defined as 'adherence,' i.e., the extent to which the patient's behavior coincides with his or her clinical directives. However, this type of essentail compliance is usually defined in terms of its opposite 'nonadherence', which refers to the patients failing to comply 'with medical recommendations'.

In patients who experience chronic renal failure, the global assessment of nonadherence is difficult and considerable effort has been devoted to identifying the various factors effecting adherence in that population [1–7]. Various approaches have been used to study nonadherence [8–10]. '*Clinical nonadherence*' has been assessed by documenting clinically measurable events, such as compliance with diet, the dialysis prescription and the medication

© 2007 The Authors
Journal compilation © 2007 European Society for Organ Transplantation

regimen [8,9]. Skipping or shortening dialysis sessions is considered nonadherence as is dietary noncompliance revealed by the patients' serum potassium, phosphate and blood urea nitrogen (BUN) levels, interdialytic weight gain (IDWG) and failure to adhere medication regimen, which can be assessed by evaluating patients' serum phosphate level [9].

Nonadherence is an important problem during dialysis therapy as it has been related with patient outcome [11] and reported to occur 2–50% of people undergoing hemodialysis [12]. It has also been reported to occur in 2–68% of patients who have undergone renal transplantation [13]. Rovelli *et al.* [14] stated that 'after 3 months post-transplant, nonadherence causes more graft losses than uncontrollable rejection in adherent patients'. Nonadherence has been found to contribute for up to 25% of late deaths and 13–24% of late renal graft losses in the post-transplant period [15].

The assessment of nonadherence in the pretransplant period is of particular importance, because evidence from patients with other chronic conditions including those associated with renal transplantation shows that past nonadherence is predictive of future nonadherence [16,17]. When the contributing factors for nonadherence were analyzed in candidates for heart, liver, or lung transplantation, depression was identified as a major risk factor in both transplant [10,18] and nontransplant populations [19]. Nonadherence may also be a barrier to achieving and improved quality of life (QOL) during dialysis therapy and can negatively affect patients' outcome who are waiting for a renal transplant [20].

Because nonadherence during dialysis therapy may be a risk factor for similar behavior after renal transplantation, we studied the incidence of nonadherence, factors that contribute to that behavior, and the effect of noncompliance on QOL in patients on a cadaveric renal transplant waiting list.

## Patients and methods

Eighty-six renal patients on a waiting list for cadaveric renal transplantation (56 men, 30 women; aged, 44.6 ± 17.0 years) at Baskent University Hospital were included in this study. All patients were undergoing hemodialysis sessions of 4–5 h duration, three times per week with a hemophane membrane. The patients were divided into two groups according the to absence (group 1; $n = 49$; patient age, 46.8 ± 21.8 years; duration of hemodialysis, 83.9 ± 48.7 months) or presence (group 2; $n = 37$; patient age, 42.8 ± 12.1 years; duration of hemodialysis, 96.5 ± 45.2 months) of adherence.

In this study, 'Clinical nonadherence' was defined as the presence of one or more of the following behaviors or conditions: skipping of more than one dialysis session or shortening a dialysis session by more than 10 min in 2 months, a serum potassium concentration of >6.0 mEq/l, a phosphate level of >7.5 mg/dl, or an IDWG of >5.7% of body weight [8,12]. IDWG was defined by the amount of weight lost during a hemodialysis session and is presented as the percentage of body weight lost. IDWG was calculated from the most recent hemodialysis treatment before enrollment, and the potassium and the phosphate measurements were those obtained on the enrollment date. Nonadherence measures of IDWG, and the levels of the potassium, and the phosphate were adjusted so that all patients would have their predialysis weight measured and blood drawn at second dialysis session of the week (to ensure comparability). Skipping dialysis or shortening the session was evaluated for the 60 days immediately prior to enrollment.

From the patients' medical records at the time of enrollment, we abstracted demographic data (age, sex, marital status, educational level, number of months of treatments with dialysis, and prior renal transplantation history) and data on comorbid conditions which were defined as any of the following 19 summary comorbid diseases according to the Charlson comorbidity index [21] myocardial infarction, congestive heart failure, cerebrovascular disease, peripheral vascular disease, chronic pulmonary disease, dementia, connective tissue disease, peptic ulcer, mild liver disease, diabetes mellitus, hemiplegia, moderate-severe renal disease, diabetes with end-organ damage, tumors, leukemia, lymphoma, moderate-severe liver disease, metastatic solid tumors or HIV/AIDS [21].

Biochemical evaluation of predialysis levels of BUN, and serum levels of creatinine, potassium, and phosphate was performed. Serum phosphate was measured by the calorimetric method using a Beckman Cx-7 autoanalyzer (Beckman Instruments Inc., Fullerton, CA, USA); all others were by standard laboratory techniques.

The Beck depression inventory (BDI) was administered to each patient by the same psychologist. No acutely interfering illness was present at the time the test was given. The BDI scale consists of 21 questions that are answered on a 4-point Likert scale, in which 0 represents the absence of a problem and 3 represents an extreme problem, with a total score range of 0–63. For example, the score for feeling sad, ranges from 0 ('I don't feel sad') to 3 ('I am so unhappy that I cannot stand it'). Examples of other cognitive feelings surveyed are guilt, disappointment, failure, and decision-making. The somatic items of the BDI assess such issues as fatigue and sleep function. For example, the score for fatigue, ranges from 0 ('I do not get more tired than usual') to 3 ('I am too tired to do anything'). The scores were interpreted, and the patients were grouped into four stages as follows: <4 (no

© 2007 The Authors
Journal compilation © 2007 European Society for Organ Transplantation 

depression), 5–9 (mild depression), 10–18 (mild-moderate depression), 19–29 (moderate-severe depression), 30–63 (severe depression) [22]. Data were interpreted with regard to each of those stages and the presence of depression.

Quality of life was evaluated with the short form-36 (SF-36 form) developed by Ware and Sherbourne [23]. The SF-36 consists of eight subclasses: General health, bodily pain, physical functioning, physical role, vitality, social functioning, mental health and emotional role. Patients' responses to the 36 questions on the SF-36 were used to determine scores for the mental component summary and the physical component summary. Total score is the sum of these two components. SF-36 items and scales are scored so that a higher score indicates better functioning and the pain scale is scored so that a high score indicates freedom from pain. We calculated the SF-36 score, if the respondent answered at least half of the items on a multi item scale as devised by Ware *et al.* [24] and a higher score indicated a better QOL. The validity and reliability of the Turkish version of SF-36 has been demonstrated by Koçyigit *et al.* [25]. In this study, groups 1 and 2 were compared according to results from the SF-36 form and BDI, as well as demographic, clinical, and laboratory data.

This study have been reviewed by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in an appropriate version of the 2000 Declaration of Helsinki (http://www.wma.net/e/policy/b3.htm). All of the patients gave their informed consent prior to their inclusion in the study.

Statistical analyses were performed using SPSS software (Statistical Package for the Social Sciences, version 11.0; SPSS Inc., Chicago, IL, USA). All numeric variables are expressed as mean ± standard deviation (SD). Intergroup differences in the parameters were analyzed and compared using the Student *t* and Spearman correlation analysis. Nominal parameters were analyzed with chi-squared test. Multivariate logistic regression analyses were performed to asses the independent effects of several variables including age, sex, marital status, educational level, number of moths of dialysis treatment, prior renal transplantation, comorbid conditions, and BDI scores. These results were measured by odds rations (ORs) and their 95% confidence intervals (CIs) based on logistic regression models. A value for $P < 0.05$ was considered statistically significant.

## Results

Of the 86 patients studied, 24.4% had undergone prior renal transplantation, and 31.3% had a comorbid disease. The demographic data and nonadherence behaviors of each group are summarized in Table 1. The number of patients who demonstrated each nonadherence measure is shown in detail Tables 2 and 3. No significant difference was found between the groups regarding age, sex, marital status, number of months on dialysis treatment, prior transplantation or presence a of comorbid condition ($P > 0.05$). There were no uneducated patients in the adherent group ($P = 0.018$). High IDWG (33.7%) was the most common nonadherence behavior. The predialysis BUN value and the levels of serum creatinine,potassium and phosphate were not different between groups ($P > 0.05$) (Table 4). QOL and BDI scores were significantly different between the groups (Table 5). Of the patients who were depressed, 77.8% had a comorbid condition QOL and BDI scores were negatively correlated ($P = 0.001$, $r = -0.561$). The multivariate logistic regression analysis showed that nonadherence was associated only with BDI scores (OR, 2.146; CI, 2.052–2.350; $P = 0.002$) (Table 6).

## Discussion

End-stage renal failure greatly restricts a patient's lifestyle via the imposed dialysis regimen, dietary and fluid restrictions, treatment with multiple medications that can cause

**Table 1.** Demographic characteristics of group 1 and group 2.

| | Group 1 ($n = 49$) | Group 2 ($n = 37$) | *P*-value |
|---|---|---|---|
| Age (years) | 46.8 ± 21.8 | 42.8 ± 12.1 | >0.05 |
| Sex (%) | | | |
| Male | 67.3 | 62.2 | >0.05 |
| Female | 32.7 | 37.8 | |
| Number of months on dialysis | 83.9 ± 48.7 | 96.5 ± 45.2 | >0.05 |
| Marital status (%) | | | |
| Single | 30 | 27.3 | >0.05 |
| Married | 70 | 72.7 | |
| Educational level (%) | | | |
| Uneducated | 15 | 0 | 0.018 |
| High school | 75 | 45.5 | |
| University | 10 | 54.5 | |
| Previous renal transplantation (%) | 40 | 36.4 | >0.05 |
| Presence of comorbid disease (%) | 90 | 81.8 | >0.05 |

**Table 2.** Frequencies of measurable nonadherence patterns.

| Nonadherence patterns | *n* | % |
|---|---|---|
| Skipping/shortening | 18 | 20.9 |
| Hyperkalemia | 4 | 4.7 |
| Hyperphosphatemia | 12 | 14 |
| High IDWG | 29 | 33.7 |

IDWG, interdialytic weight gain.

© 2007 The Authors

**Table 3.** Distribution of nonadherence behavior in cadaveric renal transplantation waiting list patients.

| Nonadherence patterns | *n* |
|---|---|
| Skipping/shortening | 11 |
| Hyperkalemia | 2 |
| Hyperphosphatemia | 6 |
| Hyperphosphatemia and skipping/shortening | 1 |
| High IDWG | 18 |
| High IDWG and hyperkalemia | 1 |
| High IDWG and hyperphosphatemia | 4 |
| High IDWG and skipping/shortening | 4 |
| High IDWG and hyperkalemia and skipping/shortening | 1 |
| High IDWG and hyperphosphatemia and skipping/shortening | 1 |

IDWG, interdialytic weight gain.

**Table 4.** Predialysis blood urea nitrogen, creatinine, potassium and phosphate levels of the groups.

| | Group 1 ($n = 49$) | Group 2 ($n = 37$) | *P*-value |
|---|---|---|---|
| Predialysis blood urea nitrogen (mg/dl) | 77.9 ± 17.5 | 81.1 ± 24.7 | >0.05 |
| Predialysis serum creatinine (mg/dl) | 11.1 ± 2.5 | 11.5 ± 3.0 | >0.05 |
| Predialysis serum potassium (mEq/l) | 5.1 ± 0.7 | 4.8 ± 0.7 | >0.05 |
| Predialysis serum phosphate (mg/dl) | 5.3 ± 1.9 | 5.3 ± 1.3 | >0.05 |

**Table 5.** The QOL and BDI scores of the groups.

| | Group 1 ($n = 49$) | Group 2 ($n = 37$) | *P*-value |
|---|---|---|---|
| QOL | 80.8 ± 11.2 | 92.2 ± 10.6 | 0.04 |
| BDI | 19.8 ± 13.8 | 10.2 ± 8.6 | 0.01 |

QOL, quality of life; BDI, Beck depression inventory.

**Table 6.** Multivariate logistic regression analysis of risk factors for nonadherence.

| | Multivariate analysis | | |
|---|---|---|---|
| Risk factors for nonadherence | OR | 95% CI | *P*-value |
| Age (years) | 0.986 | 0.959–1.013 | 0.298 |
| Sex (male,female) | 1.255 | 0.514–3.067 | 0.618 |
| Marital status (married, unmarried) | 1.143 | 0.223–5.886 | 0.873 |
| Education (educated, uneducated) | 1.256 | 0.501–3.145 | 0.627 |
| Transplantation history(p/a) | 0.857 | 0.118–3.918 | 0.842 |
| Comorbid conditions(p/a) | 2.000 | 0.241–16.612 | 0.521 |
| HD duration (months) | 1.006 | 0.995–1.017 | 0.273 |
| BDI scores | 2.146 | 2.052–2.350 | 0.002 |

p/a: presence absence; HD, hemodialysis; BDI, Beck depression inventory.

adverse effects and the management of multiple comorbid conditions. Nonadherence with various aspects of treatment is a common problem both during dialysis therapy and after renal transplantation, and that noncompliance is understandable from the patient's perspective. However, the pretransplantation identification of organ recipients who are likely to be noncompliant would be ideal. Demographic factors may affect the adherence behavior in dialysis patients. The groups of patients in our study were similar in terms of age and sex. Adherent patients were receiving hemodialysis therapy longer than those who were nonadherent, but that factor did not effect adherence in our study.

Zrinyi *et al.* [4] reported that as the number of family members living with a dialysis patient increased, the caloric intake of that patient also increased. In that study, dialysis patients living with family members demonstrated increased serum phosphate levels and IDWG [4]. In our study, we evaluated only the marital status of the patients and did not find such a relationship between marital status and any of the adherence behaviors.

When the education status of both groups was analyzed, we found that there were no uneducated patients in the adherent group. Therefore, we presumed that that education level was an important factor in adherence to therapy. However, we found no relationship in our logistic regression model between education level and nonadherence.

Among the nonadherence measures, a high IDWG was the most common nonadherent behavior, which was followed in order of prevalence by skipping or shortening dialysis sessions. According to the results of Euro-DOPPS, the most commonly reported nonadherent behavior in France and Italy was also a high IDWG [8]. A limitation of our study may be the use of hemophane membranes for hemodialysis because the use of synthetic (high-flux) membranes might have shortened the dialysis sessions and might thus have discouraged patients from skipping or shortening those sessions.

As expected, depressed patients on a cadaveric renal transplantation waiting list (RTWL) had higher rate of comorbid conditions than did their nondepressed counterparts. The logistic regression analysis revealed that the presence of a comorbid condition did not independently affect adherence behavior in that patient group. However, depression in addition to the comorbid condition was found to be important in the evaluation of the nonadherence in a patient on a cadaveric RTWL.

Patients waiting for a cadaveric renal donor have been reported to be at greater risk for anxiety and more severe depressive disorders than are patients with a living-related donor [26]. We observed that prior renal transplantation had no effect on nonadherence, depression or QOL in our study groups. We found depressed patients on a cadaveric transplant waiting list had a tendency to nonadherent behavior during hemodialysis therapy. Depression and nonadherence further decreased QOL during the renal transplant waiting period in our patients.

© 2007 The Authors
Journal compilation © 2007 European Society for Organ Transplantation 

Shapiro *et al.* [27] emphasized the necessity of preoperative screening for nonadherence. Of course, organ recipients with preoperative risk factors for postoperative nonadherence are not usually excluded a priori from transplantation, but if possible risk factors for noncompliance can be eliminated, such patients may convert to adherent behavior while waiting for their transplant. The waiting period can be stressful so patients with multiple risk factors for noncompliance (a comorbid condition, depression, etc) can be evaluated for referral to receive appropriate psychosocial therapy. If such patients receive a transplant, the transplantation team must remember that these organ recipients are 'high-risk patients' who require much more attention, care, and guidance than do recipients identified as adherent.

To our knowledge, this study is among the few that have established a relationship between the QOL, depression, and adherence among patients on a waiting list for renal transplantation. Although the parameters we evaluated were applied to only a small number of noncompliant recipients, our study highlights the importance of monitoring adherence (fulfilling therapeutic, dietary and medication requirements) during the waiting period for a cadaveric renal transplant. We have shown that pretransplant behavior may signal the degree of post-transplant adherence. We also emphasize the importance of diagnosing depression in patients on a waiting list for renal transplantation because treating that depression may improve adherence. The diagnosis and treatment of depression are especially important in renal transplant recipients with a comorbid condition. Close monitoring of adherence behavior, early diagnosis, and the treatment of depression in those patients may further enhance the QOL during the waiting period for cadaveric renal transplant.

## References


1. Baines LS, Hamilton DN, Jindal RM. Compliance with hemodialysis and kidney transplantation: a psychotherapeutic perspective. *Transplant Proc* 2001; **33**: 1895.
2. Kobrin SM, Kimmel PL, Simmens SJ, Reiss D. Behavioral and biochemical indices of compliance in hemodialysis patients. *ASAIO Trans* 1991; **37**: M378.
3. Arici M, Altun B, Usalan C, *et al.* Compliance in hemodialysis patients: unanticipated monitoring of biochemical indices. *Blood Purif* 1998; **16**: 275.
4. Zrinyi M, Juhasz M, Balla J, *et al.* Dietary self-efficacy: determinant of compliance behaviours and biochemical outcomes in haemodialysis patients. *Nephrol Dial Transplant* 2003; **18**: 1869.
5. Morduchowicz G, Sulkes J, Aizic S, Gabbay U, Winkler J, Boner G. Compliance in hemodialysis patients: a multivariate regression analysis. *Nephron* 1993; **64**: 365.
6. Kimmel PL, Peterson RA, Weihs KL, *et al.* Behavioral compliance with dialysis prescription in hemodialysis patients. *J Am Soc Nephrol* 1995; **5**: 1826.
7. Hoover H. Compliance in hemodialysis patients: a review of the literature. *J Am Diet Assoc* 1989; **89**: 957.
8. Hecking E, Bragg-Gresham JL, Rayner HC, *et al.* Haemodialysis prescription, adherence and nutritional indicators in five European countries: results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). *Nephrol Dial Transplant* 2004; **19**: 100.
9. Leggat JE. Adherence with dialysis: a focus on mortality risk. *Semin Dial* 2005; **18**: 137.
10. De Geest S, Abraham I, Moons P, *et al.* Late acute rejection and subclinical noncompliance with cyclosporine therapy in heart transplant recipients. *J Heart Lung Transplant* 1998; **17**: 854.
11. Saran R, Bragg-Gresham JL, Rayner HC, *et al.* Nonadherence in hemodialysis: associations with mortality, hospitalization and practice patterns in the DOPPS. *Kidney Int* 2003; **64**: 254.
12. Leggat JE Jr, Orzol SM, Hulbert-Shearon TE, *et al.* Noncompliance in hemodialysis: predictors and survival analysis. *Am J Kidney Dis* 1998; **32**: 139.
13. Chisholm MA. Issues of adherence to immunosuppressant therapy after solid organ transplantation. *Drugs* 2002; **62**: 567.
14. Rovelli M, Palmeri D, Vossler E, Bartus S, Hull D, Schwaizer R. Noncompliance in organ transplant recipients. *Transplant Proc* 1989; **21**: 833.
15. Swanson MA, Palmeri D, Vossler ED, Bartus SA, Hull D, Schweizer RT. Noncompliance in organ transplant recipients. *Pharmacotherapy* 1991; **11**: 173S.
16. Douglas S, Blixen C, Bartucci MR. Relationship between pretransplant noncompliance and posttransplant outcomes in renal transplant recipients. *J Transpl Coord* 1996; **6**: 53.
17. World Health Organization. *Adherence to Long-term Therapies: Evidence for Action*. Switzerland: World Health Organization, 2003.
18. Dew MA, Kormos RL, Roth LH, *et al.* Early post-transplant medical compliance and mental health predict physical morbidity and mortality one to three years after heart transplantation. *J Heart Lung Transplant* 1999; **18**: 549.
19. DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk-factor for noncompliance with medical treatment: meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med* 2000; **160**: 2101.
20. Sehgal AR. Improving hemodialysis patient outcomes: a step-by-step approach. *Semin Dial* 2002; **15**: 35.
21. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol* 1992; **45(6)**: 613.
22. Beck AT, Steer RA, Garbin MG. Psychometric properties of the Beck depression inventory: twenty-five years of evaluation. *Clin Psychol Rev* 1988; **8**: 77.


© 2007 The Authors

23. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; **30**: 473.
24. Ware JE Jr, Kosinski M, Keller SD. *SF 36 Physical and Mental Health Summary Scales: A User's Manual*, 5th edn. Boston, MA: Health Assessment Lab, New England Medical Center, 1994.
25. Koçyigit H, Aydemir O, Fisek G, *et al.* Validity and reliability of Turkish version of SF-36. *J Drug Ther (Ilaç ve Tedavi Dergisi)* 1999; **12**: 102 (in Turkish).
26. Teran-Escandon D, Ruiz-Ornelas J, Estrada-Castillo JG, Barajas-Juarez L, Diaz-Martinez A. Anxiety and depression among renal transplantation candidates: impact of donor availability. *Actas Esp Psiquiatr* 2001; **29**: 91.
27. Shapiro PA, Williams DL, Foray AT, Gelman IS, Wukich N, Sciacca R. Psychosocial evaluation and prediction of compliance problems and morbidity after heart transplantation. *Transplantation* 1995; **60**: 1462.

© 2007 The Authors