Quality of life and psychopathology of patients awaiting kidney/pancreas transplants

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Summary

Objective
Patients awaiting kidney/pancreas transplants are suffering from end-stage renal disease (ESRD) or severe insulin dependent diabetes mellitus (IDDM), which may contribute to renal insufficiency with or without other medical complications such as diabetic neuropathy. Such patients may experience psychopathological distress that can impair their daily lives. The aim of this study was to assess the QOL, lifetime and current DSM-IV Axis-I and II disorders, sub-threshold mood and panic-agoraphobic phenomenology in a large sample of ESRD and IDDM patients waiting kidney-pancreas transplants.

Methods
Consecutive transplant candidates of both genders aged between 18 and 65 years were enrolled (n = 227). Axis-I and -II diagnoses were determined by experienced clinicians using SCID-I and II. Patients were also administered MOODS-SR (self-report) and PAS-SR questionnaires to assess mood and panic-agoraphobic spectrum, and the Q-LES-Q questionnaire to assess QOL, enjoyment and satisfaction.

Results
The prevalence of current Axis-I disorders was 13.2%. The most common current axis-I disorders were agoraphobia (4.8%) and major depressive episode (4.0%). No difference in the distribution of Axis I disorders between the two groups (ESRD and IDDM) was found. QOL among the sample study was overall poorer than that of a healthy adult control population.

Conclusions
The prevalence of current mental disorders was approximately three times higher compared to the general Italian population, emphasising that the need for transplantation plays an important role in patients’ psychopathology and underlines the importance of careful evaluation of sub-syndromal symptoms.

Key words
Transplants • Spectrum symptoms • Quality of life

Introduction
Chronic physical illnesses represent an increasingly major public health concern. Elevated levels of stress inevitably affect chronically-ill individuals as they deal with physical pain, difficult diagnostic procedures, treatment side-effects and hospital admissions which have a strong impact on the quality of life; these patients show an increased risk of psychological distress compared to the general population1. Moreover, the relationship between psychological status and clinical outcomes after organ transplant has long been matter of debate2. Patients awaiting kidney/pancreas transplants are suffering from end-stage renal disease (ESRD) or severe insulin dependent diabetes mellitus (IDDM), which may contribute to renal insufficiency with or without other medical complications such as diabetic neuropathy. Such patients may experience psychopathological distress that can impair their daily lives.

Impairment of daily well-being and quality of life may be remarkably affected by dietary restrictions, intensive insulin therapy and monitoring3. In the advanced phases of ESRD and IDDM, the impact of the illness on quality of life perceived by the patient can be relevant. Health-related quality of life (HRQL) is currently used as an important outcome parameter to assess. The level of subjective well-being is determined by several dimensions such as physical status of the patient, state of mind, functional competence in everyday life and impact on interpersonal relationships4. HRQL represents the patient’s assessment of the impact of a disease and its treatment on daily life, well-being and functioning. HRQL is considered by some researchers essential for understanding the impact of the disease and its treatment on health outcomes. Scientific evidence has demonstrated the utility of self-reported outcomes in evaluating a broad range of health care interventions5.

Most of the literature on quality of life (QOL) of patients
Psychopathology of transplant candidates

awaiting transplants focuses on the substantial decrements in QOL experienced during end-stage chronic diseases, including impairments in both physical and mental health domains. In recent years, increasing attention has been given to the individual characteristics of patients affected by chronic disease, concentrating emphasis on social situations, socioeconomic status, perceptions and responses to the illness, to physicians/healthcare providers, spouses and families and the effects they may have on the transplant outcome. Anxiety and depression may be induced by chronic illness, obviously contributing to the perception of QOL in psychological and social domains as well as the physical domain. Indeed, during hospitalisation for ESRD and IDDM, affective disorders have been described as the most common psychiatric hospitalisation for ESRD and IDDM, affective disorders have been theorised that depression possibly affects medical outcomes in ESRD patients through modification of immunologic and stress responses, impact on nutritional status and/or reduction of compliance with, or access to, prescribed dialysis and medical regimens. In the majority of transplant programs, a psychiatrist evaluates potential candidates for psychosocial aptness to transplantation. Actually, although psychiatric and psychological screenings for disease are standardised, the psychosocial criteria for transplantation are not. There are only few studies on the prevalence, diagnosis and treatment of depression in this population using accurate, well-defined diagnostic criteria and appropriate epidemiologic methods. Although a depressive mood or depressive symptomatology may be expected in some transplant candidates, there are few systematic clinical reviews using well-defined diagnostic criteria and appropriate epidemiological methods to assess the psychopathology of waiting list patients. The aim of this study was to assess lifetime and current DSM-IV (Diagnostic and Statistical Manual of Psychiatric Disorders, 4th Edition) Axis-I and II disorders, quality of life and sub-threshold mood and panic-agoraphobic phenomenology in a large sample of ESRD and IDDM patients awaiting kidney-pancreas transplants.

Materials and methods

Study sample

The study sample included consecutive transplant candidates of both genders, aged between 18 and 65 years, seeking treatment at the Outpatient Division of General and Transplantation Surgery of the University Hospital of Pisa, between March 2003 and October 2008. Exclusion criteria were mental retardation, illiteracy or poor knowledge of the Italian language. The diagnostic assessment was conducted by psychiatrists trained and certified to the use of the interviews using the SCID-I (Structured Clinical Interview for DSM-IV Axis-I) for DSM-IV diagnoses and the SCID-II (Structured Clinical Interview for DSM-IV Axis-II) for personality disorders.

The Ethics Committee at the Azienda Ospedaliera Universitaria Pisana reviewed and approved all study procedures, and all participants gave written informed consent after receiving a complete description of the study and having the opportunity to ask questions. The work described in the present article was carried out in accordance with the Code of Ethics of the World Medical Association for experiments involving humans.

Instruments

The MOODS-SR (Mood Spectrum Instrument-Self-Report) is a self-report instrument derived from the corresponding structured interview that explores features associated with mood disorders. It consists of 161 items coded as present or absent for one or more periods of at least 3-5 days over a lifetime. For some questions exploring temperamental features or the occurrence of specific events the duration is not specified because it would not be applicable. Items are organised into 3 manic-hypomanic and 3 depressive domains exploring mood, energy and cognition, plus a domain that explores disturbances in rhythmicity (i.e. changes in mood, energy and physical well-being according to the weather, the season and phase of menstrual cycle) and in vegetative functions, including sleep, appetite and sexual activity. The sum of the scores of the three manic-hypomanic domains constitutes the manic-hypomanic component and that of the three depressive domains “the depressive component”. Both the interview and self-report have been shown to be valid, reliable and suitable for administration to patients and normal controls. Factor analysis is a statistical method used to describe variability among observed, correlated variables in terms of a potentially lower number of unobserved variables called factors. Two factor analyses of the depressive and manic components of MOODS-SR spectrum identified 6 depressive factors and 9 manic-hypomanic factors: “Depressive mood”, “Psychomotor retardation”, “Suicidality”, “Drug/illness-related depression”, “Psychotic features” and “Neurovegetative symptoms”. The factors of mania/hypomania are: “Psychomotor Activation”, “Creativity”, “Mixed Instability”, “Sociability/Extraversion”, “Spirituality/Mysticism/Psychoticism”, “Mixed Irritability”, “Inflated self-esteem”, “Euphoria” and “Wastefulness/Recklessness”. The lifetime self-report panic/agoraphobic spectrum (PAS-SR) consists of 114 items coded as present or absent items for one or more periods of at least 3 to 5 days in the lifetime.
The factor analysis of the lifetime PAS-SR has identified 10 factors: “panic symptoms”, “agoraphobia”, “claustrophobia”, “separation anxiety”, “fear of losing control”, “drug sensitivity and phobia”, “medical reassurance”, “rescue object”, “loss sensitivity” and “reassurance from family members”.

The Q-LES-Q (Quality of Life Enjoyment and Satisfaction Questionnaire) is a self-report measure of quality of life, enjoyment and satisfaction. The 16-item version used in the present study includes 14 items exploring general activities as well as 2 items measuring overall satisfaction. Items are scored on a Likert scale (1 = very little to 5 = extremely). The 14 items evaluated each subject’s satisfaction with his or her physical health; social relations; ability to function in daily life; ability to get around physically; mood; family relations; sexual drive and interest; ability to work on hobbies, work, leisure time activities; economic status; household activities; living/housing situation; overall sense of well-being. There are two global items, number 15 and 16, that are not included in the Q-LES-Q total score: medication and life satisfaction and contentment over the last week. The total score is the sum of the first 14 items and is expressed as a percentage of the total score of 70.

Statistical analyses

Baseline demographic and clinical variables of patients with nephropathy were compared to patients with diabetes using a chi-square test or Fisher’s exact test (categorical variables), T-test (continuous variables with normal distribution), or Mann-Whitney Test (skewed variables), as appropriate. A stepwise linear regression analysis was carried out to assess the relationship between quality of life and the lifetime MOODS-SR and PAS-SR factors in the total sample and in patients with nephropathy and diabetes, separately.

Analyses were conducted using SPSS, version 15 (SPSS Inc., Chicago, Ill). Data were presented as means and standard deviation (± SD) or percentages.

Results

Characteristics of the sample

Of the 227 patients waiting for a kidney and/or pancreas transplant, 130 (57.3%) were males and 97 (42.7%) females; 58.9% of subjects were married, 38.7% had a high school diploma and 61.5% were employed (Table I). The primary illness responsible for the transplant was: complicated type I diabetes mellitus in 177 patients (78%) and nephropathy in 50 patients (22%). The onset of type I diabetes was on average at 16 years, significantly earlier than the onset of nephropathy (Table I).

Axis I and II disorders

Table II presents current and lifetime prevalence of Axis I Psychiatric Disorders in the overall sample, and in patients with nephropathy and diabetes. The prevalence of lifetime Axis I Psychiatric Disorders in the overall sample was 15.9%.

The most common lifetime Axis-I disorders were Major Depressive Episode (9.7%), Panic Disorder (3.5%) and...
Bipolar II Disorder (3.1%). Of the 36 subjects with at least one disorder, 5 (2.2%) met criteria for two diagnoses. Female patients showed a higher frequency of lifetime depression than male patients (N = 17, 17.5% vs N = 5, 3.8%, respectively, ×2 = 11.88, p = 0.001), but no differences were found for the other Axis I disorders.

**Psychiatric disorders**

The prevalence of current Axis-I disorders was 13.2%. The most common current Axis-I disorders were Agoraphobia (4.8%) and Major Depressive Episode (4.0%) (Table II). In the overall sample, 64 (28.2%) subjects met criteria for Axis-II disorders (Table III); of those, 13 (5.7%) met...
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TABLE IV.
Total scores (mean ± SD) of lifetime MOODS-SR and PAS-SR and in Q-LES-Q.

<table>
<thead>
<tr>
<th></th>
<th>All subjects (N = 227)</th>
<th>Nephropathy (N = 50)</th>
<th>Diabetes (N=177)</th>
<th>Mann-Whitney test and p</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOOD-SR-LT</td>
<td>32.7 (21.4)</td>
<td>30.9 (22.1)</td>
<td>33.0 (21.1)</td>
<td>Z = -0.72 p = 0.470</td>
</tr>
<tr>
<td>PAS-SR-LT</td>
<td>18.4 (18.2)</td>
<td>18.1 (17.7)</td>
<td>18.5 (15.6)</td>
<td>Z = -0.46 p = 0.643</td>
</tr>
<tr>
<td>Q-LES-Q</td>
<td>54.6 (15.1)</td>
<td>58.3 (15.1)</td>
<td>53.5 (15.1)</td>
<td>Z = -2.56 p = 0.010</td>
</tr>
</tbody>
</table>

criteria for two disorders and 1 (0.4%) subject met criteria for four disorders. The most common Personality Disorder was Obsessive-Compulsive Disorder (20.3%), followed by Paranoid Disorder (4.8%) and Oppositional Disorder (3.1%). Of the 50 patients with nephropathy, 5 (10%) had a lifetime Axis-I disorder, 7 (14.0%) a current Axis-I disorder and 16 (32.0%) a Personality Disorder. Of the 177 patients with diabetes, 31 (17.5%) had a lifetime axis-I disorder, 23 (13.0%) a current Axis-I disorder and 48 (27.1%) a personality disorder. No significant differences were found in the diagnostic distribution between patients with diabetes and those with nephropathy.

Mood spectrum and panic-agoraphobic spectrum phenomenology

Mood and panic-agoraphobic spectrum scores were examined in 226 subjects out of 227, because one patient failed to complete the assessment. Table IV shows mean scores on the MOODS-SR and the PAS-SR total scores, in patients with nephropathy and diabetes. Mood and panic-agoraphobic spectrum total scores did not differ between patients with type I diabetes mellitus and with nephropathy. When analysing factor scores of the MOODS-SR and PAS-SR spectra, we found that only the rescue object factor of the lifetime PAS-SR was significantly higher in patients with diabetes compared to those with nephropathy (0.9 ± 1.0 vs 0.5 ± 0.9, respectively Z = -2.57, p = 0.010). Lifetime MOODS-SR factors were not significantly different among the two diseases (all p > 0.05).

Quality of life

The mean Q-LES-Q score was lower in patients with type I diabetes than in patients with nephropathy (Table IV). Areas of higher dissatisfaction were physical health, sexual interests and homework with no differences between the two diseases (Figure 1).

Using a stepwise linear regression model, we found that, in the overall sample, Q-LES-Q total score was negatively associated with depressive mood factor (â = -0.40, t = -6.23, p < 0.001) of the depressive component of the MOODS-SR, with mixed irritability (â = -0.24, t = -3.18, p = 0.002), inflated self-esteem (â = -0.21, t = -2.73, p = 0.007) factors of the manic/hypomanic component of the MOODS-SR and with separation anxiety factor (â = -0.27, t = -4.01, p < 0.001) of the PAS-SR. Moreover, the quality of life was positively associated with sociability/extraversion factor (â = 0.19, t = 2.64, p = 0.009) of the manic/hypomanic component of the MOODS-SR.

Significant associations between quality of life and MOODS-SR and PAS-SR factors in patients with diabetes and in patients with nephropathy are shown in Table V. In patients with nephropathy, the quality of life was negatively associated only with psychotic features of the depressive component of the MOODS-SR. In patients with diabetes, the quality of life was positively associated with creativity factor of the manic/hypomanic component of the MOODS-SR and negatively with depressive mood factor of the depressive component of the MOODS-SR, mixed irritability and inflated self-esteem factors of the manic/hypomanic component of the MOODS-SR and separation anxiety factor of the PASSR.

Discussion

In our study, lifetime depression was the disorder most represented both in the ESRD (6%) and IDDM (10.7%) subgroups. These results confirm and expand our preliminary data on this matter. These rates were consistent with the prevalence estimation reported in the general Italian population. In our sample, current Generalised Anxiety Disorder (GAD) was significantly more represented in ESRD (6%) than IDDM (0.6%). The reasons for this difference in the prevalence of GAD between the 2 groups is not known. We can speculate that chronic kidney disease remains asymptomatic and unrecognised for a long time. Therefore, the time elapsed between diagnosis and transplantation in ESRD patients is usually much shorter than in IDDM patients who are often aware...
of their disease since childhood, and are already accustomed to therapies and hospitalisation at the time that transplantation is proposed. However, in our sample, the prevalence of current mental disorders (13.2%) and major depression (4.0%) was around three times higher compared to the current prevalence in the general Italian population (3.2% and 1.4%, respectively). These data confirm epidemiological studies indicating that diabetic patients (both type I and type II) present depressive symptomatology and that depressive symptoms are common among ESRD patients, especially after

![Graph showing areas of dissatisfaction in quality of life for nephropathy and diabetes.](image)

**FIGURE 1.**
Areas of dissatisfaction of quality of life. In both nephropathy and diabetes, the areas of higher dissatisfaction were physical health, sexual interest and homework.

<p>| TABLE V. |
| Relationship between mood and anxiety spectrum factors and quality of life score (Q-LES-Q). |</p>
<table>
<thead>
<tr>
<th>Factors retained in stepwise linear regression models</th>
<th>Nephropathy (N = 50)</th>
<th>Diabetes (N = 177)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Standardised beta coefficients</td>
<td>T-test</td>
</tr>
<tr>
<td>MOODS-SR depressive component</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychotic features</td>
<td>-0.33</td>
<td>-2.30</td>
</tr>
<tr>
<td>Depressive mood</td>
<td>-0.44</td>
<td>-6.09</td>
</tr>
<tr>
<td>MOODS-SR manic/hypomanic component</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed irritability</td>
<td>-0.27</td>
<td>-3.22</td>
</tr>
<tr>
<td>Creativity</td>
<td>0.21</td>
<td>2.61</td>
</tr>
<tr>
<td>Inflated self-esteem</td>
<td>-0.22</td>
<td>-2.59</td>
</tr>
<tr>
<td>PAS-SR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Separation anxiety</td>
<td>-0.29</td>
<td>-3.81</td>
</tr>
</tbody>
</table>
the initiation of renal replacement therapy. Furthermore, high rates of depression have been reported among patients on haemodialysis. The prospect of organ transplantation, not just the chronic disease, may play an important role in the development of current psychopathology; in particular, the awareness of an imminent major surgical procedure and its possible complications, or the awaiting of inevitable surgery from a cadaveric donor may contribute to the development of anxiety and depression. Psychiatric assessment is required to identify personality traits that can reduce the good outcome of transplant procedures. The process of transplant requires a series of adaptations to modify physical and social functioning. Severe personality disorder has been proposed as a potential absolute or relative contraindication for transplantation. Our results show that Obsessive-Compulsive (O-C) disorder is the most prevalent personality disorder both in the overall sample and in the two sub-groups examined. Probably, the needful for dietary restrictions and attentive treatment compliance (e.g. insulin therapy) could affect the development of obsessive-compulsive behaviours. In our opinion, the need for structure and order of a typical obsessive-compulsive personality would be adaptive to the demands of transplantation before and after surgery. While it is known that there is a correlation between diabetes and anxiety symptoms, there are no recent studies that focus on the relationship between O-C symptoms and diabetes. However, one study showed an increase of O-C symptoms in children with diabetes compared to healthy controls, which was interpreted as psychological adjustment. Because type I diabetes usually onsets during childhood or adolescence, we can assume that these symptoms may represent the onset of an obsessive-compulsive personality disorder in adulthood.

Among diabetic subjects, opportunistic, alienated and explosive personality traits were found to be associated with poor management of the disease; patients with Cluster B dependent profiles exhibited poorer metabolic control than other patient profiles; in diabetic patients, non-compliance is often associated with borderline personality disorder. In the present report, the psychopathological sub-threshold features were assessed using validated spectrum instruments. Patients with diabetes showed higher levels of separation, anxiety and rescue object scores compared to patients with nephropathy. This factor includes items indicating the need to take objects such as an umbrella, a hat, a good luck charm or a bottle of water. In our context, this may be interpreted as a learned behaviour because patients with diabetes, since childhood, have associated the use of drugs and medical devices to safety. Furthermore, thirst is a common early symptom of diabetes or hyperglycaemia, which may justify the need for a water bottle everywhere. These results are in agreement with literature data showing that anxiety is an important comorbidity in patients with diabetes. Indeed, patients with diabetes and anxiety symptoms show increased diabetes symptoms burden, increased diabetes complication, increased pain, reduced QOL, increased depression and greater disability. In agreement with current literature data, the mean QOL among the overall sample was poorer than that of a healthy adult population. In our overall sample the QOL was positively associated with sociability/extraversion factor of the manic/hypomanic component of the MOODS-SR. Patients presenting this component have maintained openness to social contacts, avoiding the isolation that the disease can facilitate, thereby having a better QOL. The mean Q-LES-Q score was lower in patients with diabetes than in those with nephropathy confirming that diabetes may deeply affect several aspects of life. Despite the increasing interest in sub-threshold mood disorders and in QOL research, very little is known about the relationship between QOL and sub-threshold affective and anxiety symptoms in chronically-ill patients. We found significant negative associations between sub-threshold affective and anxiety symptomatology and QOL in both diabetic and nephropathic patients. Our results underline that in patients with diabetes, sub-threshold depressive mood, irritability, inflated self-esteem and separation anxiety are linked to increased functional and physical disability, decreased energy and interest in leisure, lower motivation, and impairment with family and social relationships. In patients with nephropathy, low levels of QOL were associated with the presence of psychotic features. This factor includes paranoid thoughts and psychotic symptoms that are widely reported in patients with major depressive episodes. Patients with kidney disease have a better QOL because the disease involves fewer complications than diabetes. We can speculate that only the presence of severe psychiatric symptoms may lead to impaired quality of life in ESRD patients. These data confirm previous observations concerning the relationship between syndromal and sub-syndromal depressive symptoms and quality of life or symptoms indirectly related to quality of life, such as psychosocial impairment and disability. Sub-threshold symptoms of depression or anxiety, may further increase psychosocial dysfunction in patients waiting for organ transplant.

Conclusions

An organ transplant procedure is generally the last therapeutic option of a long-standing chronic disease. The pre-surgical iter induces a significant psychological stress.
load, which can determine the onset of full-blown and/or sub-threshold mood or anxiety symptomatology and impairment of QOL.

Among subjects suffering from chronic physical illness, patients awaiting transplants represent a sub-group that deserves careful consideration. Routine assessment of psychosocial data of transplantation candidates has led to the investigation of psychosocial vulnerability as a potential predictor of post-transplant outcome, with the aim to identify patients at risk. Previous prospective studies have demonstrated that psychosocial variables are capable of predicting both psychosocial and physical outcomes after transplantation; pre-transplant psychiatric disorders have been shown to be predictors of lack of psychosocial adjustment after the operation, i.e., high pre-transplant anxiety or neuroticism values predict low post-transplant QOL. As such, professional assessment of QOL and psychosocial functioning at all the different stages of IDDM and chronic renal insufficiency (from early stages through to end-stages) can be extremely important for treatment outcome. In addition, appraisal of psychosocial variables such as cognitive beliefs, companionship and social networks that represent essential markers of psychosocial vulnerability may facilitate early identification of those patients at risk for psychosomatic and/or psychiatric symptoms after surgical intervention. Numerous reports describing the relationship between depression and the outcome of the surgery in renal transplant recipients suggest the importance of establishing this diagnosis, and it has been amply demonstrated that a depressive disorder can increase the risk of non-compliance to therapy. Emerging evidence shows that preoperatively assessed psychosocial variables can predict post transplantation psychopathological outcome among recipients of most organ types. Notwithstanding, little attention is dedicated to spectrum symptoms and their relationship to patient's QOL. At present, there is a lack of studies describing the psychopathology in terms of sub-threshold symptomatology and Axis I and II disorders using standardised interviews. Our findings underline the importance of careful evaluation of anxiety and depression symptoms during kidney/pancreas pre-transplant and post-transplant phases that involve subsyndromal symptoms evaluation. A systematic screening for depressive symptoms by means of self-report instruments, such as panic-agoraphobic instruments during the pre- and post-transplant phases, is valuable with particular attention to diabetic patients.

Conflicts of Interest

None.

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