

Quality of Life as an Indicator of the Effectiveness of Simultaneous Pancreas-Kidney Transplantation

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Abstract

The meaning of quality of life has evolved to become a multidimensional and integrative concept that includes both objective and subjective criteria. Simultaneous pancreas-kidney transplantation aims not only to increase survival but also to improve health-related quality of life. Studies of health-related quality of life in simultaneous pancreas-kidney transplantations show that the improvement achieved in some dimensions can surpass values in the general population, but without reaching overall levels of health-related quality of life in this population. Qualitative studies and those analyzing psychological variables show that many patients have anxiety or identity disorders. Simultaneous pancreas-kidney transplant recipients fear graft loss, and the transplant represents not just physical but also imaginary and symbolic implantation of the other person's organs. Health-related quality of life assessments show that age, gender, years since diabetes onset, time under renal replacement therapy, and time since simultaneous pancreas-kidney transplantation have significant effects. Future studies should perform temporal evaluations to determine the variations produced after simultaneous pancreas-kidney transplantation and combine quantitative and qualitative methods to provide more exhaustive information on this topic. (Trends in Transplant. 2008;2:69-77)

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Key words

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Introduction

Diabetes mellitus (DM) is one of the main causes of terminal renal failure. At 10-15 years after DM onset, diabetic nephropathy affects 30% of patients and, when these patients require renal replacement therapy (RRT), survival is lower than that in nondiabetic patients¹. Currently, the 2000 and 2003 recommendations of the American Diabetes Association (ADA) establish that simultaneous pancreas-kidney (SPK) transplantation should be considered the treatment of choice in diabetic patients under RRT with dialysis, while pancreatic transplantation alone should be considered in diabetic patients without terminal renal failure but with unacceptably poor metabolic control and quality of life (QOL)². Islet cell transplantation is still considered an experimental treatment^{3,4}.

The indications for SPK transplantation center on patients with diabetes mellitus type 1 (DM1) and terminal renal failure, but do not exclude patients with diabetes mellitus type 2 (DM2) and terminal renal failure. The aim of SPK transplantation is to restore renal function and blood glucose levels to normal values, allowing insulin and dialysis therapy to be discontinued, some of the complications of DM1 to be stabilized or improved, and health-related quality of life (HR-QOL) to be increased. For patients and their families, SPK transplantation is an idealized solution to end the physical and psychological distress caused by the disease. This procedure represents the recovery of "health" and freedom, the end of suffering, and not having to depend on a machine or on insulin to continue living⁵. However, a functioning SPK transplant is not synonymous with cure, since the complications of DM1 may persist, immunosuppressive therapy carries secondary risks, the need for life-long medication and medical follow-up continues, and some patients may experience physical and/or psychological disturbances.

Since the first pancreas transplant in 1966, more than 25,000 diabetic patients throughout the world have undergone this procedure. In Spain, the first pancreatic transplant was performed in the Hospital Clínic de Barcelona in 1983. Since then,

more than 600 pancreatic transplants have been performed, most of which have been SPK transplants^{4,6}. From 2000, the number of pancreatic transplants performed rose substantially, increasing from an average of 22.7 per year in the period 1993-1999 to 94 in 2006. Of the 540 pancreatic transplants performed between 1999 and 2006, 472 were SPK, 48 were pancreatic, and 20 were multiorgan transplantations⁶. In Spain, 68% of kidney transplants and 70% of pancreatic transplants continued to function at five years⁶. In the Hospital Clínic de Barcelona, from 2000-2006, one-year survival in patients, kidney transplants, and pancreatic transplants was 97.8, 95.6, and 89.7%, respectively, and five-year survival was 97.8, 89.7, and 86.8%, respectively⁷.

Health professionals have traditionally given priority to the study of clinical features in transplant recipients. However, in the last decade, interest in patients' subjective perception of QOL has increased. Health-related quality of life assessment has emerged as a new medical indicator of therapeutic and health services' effectiveness⁸. It includes the aspects of QOL most closely related to the experience of the disease and to the treatment and follow-up required – aspects which could potentially be modified by the health system.

Evolution of the concept of quality of life

Interest in the study of QOL, or the "good life" goes back to ancient times. Aristotle stated that to achieve human happiness, certain external elements influencing happiness were required⁹. However, the current concept of "quality of life" and scientific interest in its measurement is relatively recent. In the 1950s, concerned by growing industrialization and the social changes generated after the Second World War, some social researchers undertook studies aimed at determining the population's wellbeing. At first, these studies used objective, quantifiable, economic and social indicators. In 1954, the United Nations constructed a system of indicators to measure QOL that included the dimensions of health, diet, working conditions, housing, leisure time, social

security, transport, human freedoms, the environment, and education¹⁰. Thus, the level of life was defined as the point at which the population's overall needs were met. These studies progressively evolved, leading to the notion of "quality of life", understood as a multidimensional and integrative concept that includes both objective and subjective criteria. Quality of life evaluations consider the subject's material environment together with the social environment, viewing the person as an active subject and protagonist of action. Calman¹¹ defined QOL as "*the gap between a person's expectations and achievements*".

Health status and disease have classically been evaluated through quantitative data on morbidity, disability, mortality, and survival in individuals or populations and the results have been interpreted by health professionals. However, these data are insufficient to evaluate health, which is a complex, multidimensional, and constantly evolving concept. In 1946, the World Health Organization defined health as "a state of complete physical, mental, and social wellbeing and not just the absence of disease"¹². This definition viewed health in positive terms and included social and mental dimensions, but did not manage to satisfy all collectives. The difficulty of finding a satisfactory definition of health is not due to a semantic problem, but rather to the nature of health as a polymorphous and changing state, making it a complex reality. A study performed in Barcelona (Spain) with distinct population groups revealed that health is a multidimensional concept involving physical, psychological, social, educational, economic, political, religious, and philosophical factors and varies according to group¹³. Blaxter¹⁴ indicates the importance of psychological and social factors and states that health is a fluid concept that depends on variables such as age and sex. For Modolo¹⁵, health is a cultural concept linked to the needs of people and their environment as well as being a way of perceiving and dealing with these needs.

After health was recognized to be much more than the absence of disease and that its meaning differs from one society to another – even

among persons from the same social group – the concept of HR-QOL appeared in the 1970s. However, there is no absolute consensus on the conceptual model of HR-QOL or on how it should be measured. For Patrick and Erickson¹⁶, HR-QOL is the value assigned to duration of life modified by the impairments, functional states, perceptions, and social opportunities that are influenced by disease, injury, treatment, or policy". For Whiting¹⁷, HR-QOL is the measurement and quantification of the subjective perspective of patients on distinct aspects related to health. After reviewing the definitions, Shumaker and Naughton¹⁸ proposed the following: subjective evaluation of the influence of health status, healthcare, and health promotion on the ability of individuals to maintain a level of functioning that allows them to perform activities important to them, and that affects their general wellbeing. The most important dimensions that include HR-QOL are: social, physical, and cognitive functioning, mobility and self-care, and emotional wellbeing. Although different, the most important aspects of all definitions are that they emphasize the subjective evaluation made by an individual of his or her own QOL and include a limited and defined number of dimensions.

Measurement of health-related quality of life

Health-related quality of life is usually measured through standardized questionnaires, either self-administered or administered through a personal interview. Several instruments to establish an approach to HR-QOL measurement have been developed, mainly in Anglo-Saxon countries. These instruments can be divided into generic and specific. Specific instruments focus on aspects of QOL related to a specific disease or clinical situation; these instruments can be specific to a disease (transplants, diabetes, cancer, ischemic heart disease), to a function (sexuality, fatigue, treatment adherence), or to a population group (adolescents, the elderly). In contrast, generic instruments are independent of diagnosis and consequently can be applied to any population or disease²⁰. Specific questionnaires lack the breadth of generic instruments, but can be more sensitive

to the aspects of QOL influenced by a specific disease²¹. Independently of whether or not there are specific instruments to evaluate HR-QOL, selecting the most suitable instrument in a particular context or situation is essential. According to Donovan, et al.²², the characteristics of a good instrument for measuring QOL are suitability to the health problem to be measured, and accuracy, validity, and sensitivity in detecting changes over time or among individuals; these instruments should also be based on data generated by the patients themselves and be well accepted by patients, health professionals, and researchers. The use of original HR-QOL instruments in other cultures, countries, or languages requires that they be validated, a process for which a series of guidelines on their translation, adaptation and evaluation of the measurement properties have been established. In 2002, the Scientific Advisory Committee of the Medical Outcomes Trust²³ defined eight necessary attributes that should be taken into account to validate a HR-QOL instrument: conceptual model, validity, reliability, sensitivity to change, interpretability, administration, alternative formats, and cross-cultural adaptation.

Clinical utility of health-related quality of life evaluation

Several authors have identified problems that could limit the systematic application of HR-QOL evaluation in clinical practice. Among these are the difficulty of administering excessively long questionnaires that burden patients and are time-consuming for health professionals, logistic and economic problems in data analysis, and the lack of immediate results²⁴. Criticisms have also been made due to methodological difficulties and the consequent biases that can be produced by measuring HR-QOL²⁵, the lack of specific definitions of this concept in the various studies, and the lack of attention paid to the patients' feelings²⁶.

Health-related quality of life is essentially a subjective concept but, despite the difficulties and problems posed, measurement of this concept is arousing growing interest in medical research because the data obtained are an important source

of information for research related to health services²⁷. Systematic measurement of HR-QOL in patients could benefit the process of medical care^{28,29}. The results of HR-QOL research could aid the diagnosis of previously undetected functional and emotional problems, treatment follow-up, monitoring of disease progression and treatment response, and could improve communication between health professionals and health services users³⁰⁻³². Several theoretical models have been proposed to systematize the clinical use of HR-QOL evaluation^{33,34}. Callaghan, et al.³³ identified three stages in the application of HR-QOL results in clinical practice: firstly, the results of perceived health are transformed into specific diagnoses (link to evaluation); secondly, the health professional evaluates the needs perceived by the patients and the need for resources aimed at the specific causes of the dysfunction and plans interventions (link to resources); and thirdly, the health professional and user decide whether a new treatment should be started (link to action).

One of the greatest benefits expected from the clinical application of HR-QOL evaluation would be that of providing additional and hitherto unknown information to health professionals³⁵⁻³⁸. Several studies have been performed of the impact of HR-QOL evaluations before consultations on doctor-patient communication^{39,40}. In a study performed in patients with epilepsy, 63% of the physicians stated that the HR-QOL test had provided new information⁴¹. Equally, in transplant recipients, HR-QOL evaluation provided additional information that could not have been obtained through physiological measures⁴². Studies performed in oncology patients revealed that if the physician bore the results of the HR-QOL evaluation in mind, communication and the patient's HR-QOL improved over a six-month period⁴³. A review of 21 studies showed that when physicians knew the results of HR-QOL assessment, they made more diagnoses, especially related to mental health, and the services provided increased. However, no scientific evidence was found on the effect of HR-QOL assessment on patients' functional status or health⁴⁴.

Despite the theoretical conceptualization and the importance that HR-QOL assessment has acquired in the last few decades, as well as the increase in the number of publications on the subject, the effects on clinical practice have been scarce⁴⁵ except in oncology. Numerous studies of HR-QOL have been performed in transplantation, including some qualitative investigation, but little research has been performed on the contribution of HR-QOL evaluation to transplant-related clinical practice⁴⁶.

Results of questionnaire-based health-related quality of life assessment in simultaneous pancreas-kidney transplant recipients

To measure HR-QOL and explore the experience of disease and of SPK transplantation, we performed an observational, cross-sectional, ethnographic qualitative study in the Hospital Clínic de Barcelona between 2004 and 2005⁵. All patients who had undergone transplantation between 1998 and 2002 and in whom both grafts continued to function were included in the HR-QOL study. During this period, 90 SPK transplants were performed in the Hospital Clínic de Barcelona. At the start of the study, both grafts were functioning in 71 patients (78.8%). Of this group, two patients were excluded because they were followed-up in another province. The sample was composed of 69 patients, 41 men with a mean age of 41.78 ± 6.5 years, and 28 women with a mean age of 38.5 ± 7 years. Time since SPK transplantation ranged from 2-6 years. For the qualitative study, 10 patients with good communication skills (two for each year of the study) were selected.

To evaluate HR-QOL, the SF-36 questionnaire was used. This was chosen because it is the most widely used instrument to evaluate HR-QOL in patients with DM1 and terminal renal failure under RRT as well as in patients with kidney and SPK transplants⁴⁷. The psychometric properties of this questionnaire have been evaluated in more than 400 articles⁴⁸ and all publications on the metric characteristics of the Spanish version of

the SF-36 demonstrate its reliability, validity, and sensitivity⁴⁹. For the qualitative study, an intensive case study was performed based on qualitative techniques: in-depth interviews, ethnographic descriptions, and participant observation.

In our study, 66.6% of the patients believed that their health was better than in the previous year and only 8.4% thought it had worsened. Multivariate analysis demonstrated that SPK transplantation was significantly associated with improved HR-QOL in all health dimensions⁵⁰. These results coincide with those of other studies showing better results in patients with terminal renal failure who received transplants than in those who remained under RRT with distinct dialysis techniques⁵¹⁻⁵⁴ and also coincide with those of studies showing the effectiveness of SPK transplantation in improving HR-QOL^{7,55-59}, achieving, in some dimensions, HR-QOL similar or even superior to that in the general population. Nevertheless, both our results and those of other authors show that overall HR-QOL is lower in transplant recipients than in the general population^{7,53-60}. In our study, the perception of general health was lower in men and women with SPK transplantation than in the Spanish general population.

Health-related quality of life does not depend on SPK transplantation alone. Multivariate analysis shows that in addition to SPK transplantation, other variables have a significant effect. These variables include, age, gender, years since onset of DM1, length of time under RRT, time since SPK transplantation, and socioeconomic factors.

Gender

In our study, female gender was negatively associated with the dimensions of mental health, bodily pain, vitality, role-emotional and physical function⁵⁰. In some studies in kidney transplant recipients, no differences were found according to sex, and better HR-QOL was even observed in women, mainly in the dimension of mental health^{42,61}. However, in most publications, female gender is associated with worse perceived health and HR-QOL, both in healthy individuals and female patients^{27,49,62}.

In men, the values for role-physical and role-emotional were significantly lower than those in the Spanish general population, even though values for the dimension of vitality were significantly higher than the mean for the Spanish general population. Women showed lower values than men in all dimensions of the test. However, fewer significant differences were found with the Spanish general population, possibly due to the smaller number of women in the sample, which reduced statistical power⁵⁰.

Age

Age has frequently been associated with worse QOL^{49,62-65}. In our study, age showed a negative but non-significant ($p = 0.051$) association with general health, but a positive association with mental health⁵⁰. This finding could be due to the relative youth of SPK transplant recipients. The negative effects of age on HR-QOL could be due to the effect of functional deterioration produced in older persons and not just to the effect of the disease, although the SF-36 may be able to discriminate between the effect of disease and treatment and that of age on HR-QOL⁴². The association between older age and better HR-QOL has been observed in patients under RRT and in kidney transplant recipients^{42,61}, and would be in agreement with other studies showing that having a chronic disease and being young is associated with psychological disorders and worse HR-QOL⁶⁶⁻⁶⁹. This association could be explained by the difficulty of young persons in having to cope with chronic health problems while still attempting to forge a life for themselves.

Years since onset of diabetes mellitus type 1 and length of time under renal replacement therapy

In our study, time since onset of DM1 was negatively associated with the dimensions of mental health and bodily pain. No significant differences were found due to length of time under RRT⁵⁰. Other studies of kidney transplant recipients have reported an association between length of time under RRT and a lower

overall physical score⁴² in HR-QOL assessment and an increase in posttransplantation psychological disorders⁷⁰. Some studies suggest that patients with prolonged treatment experience difficulties in adapting to the disease, treatment, lifestyle, and the stigma attached to their illness^{71,72}. Although SPK transplant recipients must also continue under treatment, RRT involves greater dependency and more apparent stigma.

Time since simultaneous pancreas-kidney transplantation

In our study, the highest HR-QOL scores were observed in patients with the most recent transplants. Patients receiving a graft in the previous year had values higher than those in the Spanish general population in the dimensions of role-physical, vitality, and role-emotional; a negative association was found in the dimension of physical function and no significant differences were found in the remaining dimensions, including perception of general health⁵⁰. These results are in agreement with those of other studies reporting reduced HR-QOL with the passage of time in patients receiving some type of transplantation^{8,61,73-75}. Some studies report that transplant recipients experience a state of euphoria in the first year after the procedure due to improvements in physical, social, sexual function, and employment^{76,77} and that HR-QOL scores tend to reach a peak and then decline⁷⁷. Other studies have shown that HR-QOL in transplant recipients undergoes temporal oscillations. A study in kidney transplant recipients showed that HR-QOL improved during the first six months after the procedure, then declined, and began to improve again three years after the procedure⁷⁸.

Socioeconomic factors

Although some studies have reported no association between socioeconomic factors and HR-QOL⁴², others have found a strong correlation between socioeconomic position and HR-QOL⁷⁹. Our study did not include socioeconomic variables.

Results of perceived health and quality of life after simultaneous pancreas-kidney transplantation based on qualitative studies

In our study, we found that SPK transplantation leads to a restructuring of the recipient's experience. After years of disease, complications, and disability, a new kidney and pancreas are surgically implanted and the patient stops being diabetic and his or her terminal renal failure is cured. To describe this new situation, patients use the words miracle, reborn, or living again. Patients report that they have not only regained their "health", but also their skin color, the gleam in their eyes, vitality, social relationships, and, in some cases, sexual and reproductive function⁵.

However, after SPK transplantation, the complications of DM1, surgery and treatment persist to a greater or lesser extent, as do psychological disorders in some patients. The SPK transplant recipients fear graft loss and live with two organs from a cadaver that may differ from them in sex and age. The transplant entails not merely the physical but also the imaginary and symbolic implantation of another person's organs. In some patients, all of these factors can lead to anxiety and identity disorders. Nevertheless, patients minimize the problems because they compare them with their pretransplant situation. The change of life after SPK transplantation is also expressed with new perceptions to the extent that some values are lost and others adopted (spending time with friends and family, taking walks and being able to enjoy life again). For these patients, medicine is highly effective both scientifically and symbolically⁵. Other qualitative studies have also shown that SPK and kidney transplant recipients viewed the transplant as a gift of life and described themselves as being "reborn"^{66,80}. Nevertheless, there are also qualitative and quantitative studies that have described psychological problems, the difficulty of constructing a new identity, and identification with the donor in transplant recipients^{60,80-84}.

Summary

The aim of SPK transplantation is not only to increase survival but also to improve patients' HR-QOL. A good balance between functional efficacy of the graft and the patient's physical and psychological integrity are required⁸. An assessment of HR-QOL is important as it offers a person-centered rather than a disease-centered health outcome and provides information on how the patient feels independently of clinical data⁸⁵. The HR-QOL is frequently used as a synonym of self-perceived health, which has been shown to be useful in predicting morbidity and mortality in patients with terminal renal failure⁸⁶⁻⁸⁹.

In general, HR-QOL questionnaires have certain limitations, given the difficulty of being sufficiently flexible to adjust to the specific context in which patients live and cope with their disease, and the difficulty of knowing and understanding complex physical, psychological, and functional variables through a simple numerical evaluation. Moreover, HR-QOL instruments only evaluate the dimensions that patients experience directly and exclude other variables that also affect their health such as certain biological and socio-environmental characteristics. The aim of qualitative research is not to explain phenomena and generalize the results, but rather to understand phenomena, incorporating the other's perspective, bearing in mind the socio-cultural components and reality of the context in which these phenomena are produced. Qualitative investigation allows researchers to gain access to the world of emotions, feelings, and daily experiences, and insight into the impact of advanced technologies in patients, their facilities, and the social milieu of the individuals involved; this type of research also aids reflection on the social role of health professionals' practice. Listening to the patient's suffering can also help health professionals to be more human and authentic⁹⁰.

Interest in questionnaire-based HR-QOL evaluation lies in the possibility of registering patients' perceptions quantitatively or semiquantitatively; the results can be communicated and used

in practice for the purposes of description, evaluation, or comparison⁹¹. Qualitative research is more appropriate to understand patients' experience of the disease and their perceptions, beliefs, and needs, but is more complex and cannot cover the patients' entire universe.

In future, temporal evaluations should be performed to determine the variations produced over time after SPK transplantation. Quantitative and qualitative methods should be combined, and the perspective of gender should be investigated to understand the differences in the experience of disease and perceived health and QOL between men and women.

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