Transplant International ISSN 0934-0874

REVIEW

Quality of life following organ transplantation

Patrizia Burra[1] and Manuela De Bona[2]

1 Gastroenterology Section, Department of Surgical and Gastroenterological Sciences, Padua University, Padua, Italy
2 Gastroenterology Unit, S. Maria del Prato Hospital, Feltre, Italy

Keywords
pregnancy, quality of life, schooling, sexual function, sport, transplantation, work.

Correspondence
Patrizia Burra, MD, Liver Gastroenterology Transplantation, Department of Surgical and Gastroenterological Sciences, University Hospital, Via Giustiniani 2, 35128 Padova, Italy. Tel.: +39 049 8212892; fax: +39 049 8760820; e-mail: burra@unipd.it

Received: 22 August 2006
Revision requested: 27 September 2006
Accepted: 20 November 2006

doi:10.1111/j.1432-2277.2006.00440.x

Summary

Organ transplantation is a procedure that can save and prolong the life of individuals with end-stage heart, lung, liver, kidney, pancreas and small bowel diseases. The goal of transplantation is not only to ensure their survival, but also to offer patients the sort of health they enjoyed before the disease, achieving a good balance between the functional efficacy of the graft and the patient's psychological and physical integrity. Quality of life (QoL) assessments are used to evaluate the physical, psychological and social domains of health, seen as distinct areas that are influenced by a person's experiences, beliefs, expectations and perceptions, and QoL is emerging as a new medical indicator in transplantation medicine too. This review considers changes in overall QoL after organ transplantation, paying special attention to living donor transplantation, pediatric transplantation and particular aspects of QoL after surgery, e.g. sexual function, pregnancy, schooling, sport and work.

Introduction

Organ transplantation is a procedure that can save and prolong the life of individuals with end-stage heart, lung, liver, kidney, pancreas and small bowel diseases. Improved surgical techniques and new immunosuppressive drugs have led to transplantation being performed in increasing numbers of patients with excellent results in terms of survival [1–3]. The increase in the number of transplanted patients has given rise to a new socio-medical community of transplanted people, characterized by specific psychopathological and clinical features.

Clinically, transplanted people may have medical complications because of their immunosuppressive therapy, both in the short term (hypertension, diabetes, renal failure, hypertrichosis, gingival hyperplasia, etc.) and in the long term (chronic allograft dysfunction, recurrence of previous organ disease, *de novo* neoplasia). In the psychological sphere, transplanted people show changes in their relationships with their families and the medical staff, both because of their lengthy chronic disease and because of the transplant surgery, experienced as a ritual of death and rebirth to a new life [4]. Regaining bodily integrity is often complex because people have difficulty in accepting the new organ as part of the own body and not as a separate identity. Returning to physical activity, social relationships and work after transplant surgery may also be associated with psychopathological distress [5,6].

The goal of transplantation is not only to ensure their survival, but also to offer patients much the same state of health as they enjoyed before the disease, achieving a balance between the functional efficacy of the graft and patient's psychological and physical integrity. That is why a change has been seen in the evaluation of medical intervention in the field of organ transplantation, as in other medical fields [7,8]. Previously used parameters, such as clinical judgment, biochemical and instrumental tests and survival rates, have been integrated with new indicators evaluating the relationship between the costs (both human and economic) and benefits of any intervention in terms of quality of life (QoL) [9,10]. The question is not only whether and how long a patient will survive, but also how any treatment may affect the patient's QoL.

Quality of life

Definition

The term QoL was first used about 50 years ago in the USA in relation to socio-economic research in the field of 'well-being', identified as the satisfaction of people's needs [11]. It became central to debates on issues as diverse as the adequacy of governmental protection of the environment, the thoroughness of international development plans [12], and the ethically acceptable termination of medical treatment for incapacitated neonates, comatose accident victims and other people on life support systems [13].

In the medical field, interest in QoL has steadily increased since 1948, when the World Health Organization defined health as being not only the absence of disease and infirmity, but also the presence of physical, mental and social well-being [14]. The term QoL refers to the physical, psychological, and social domains of health, seen as distinct areas that are influenced by a person's experiences, beliefs, expectations, and perceptions [15]. This definition reflects two fundamental concepts: (i) that health has multiple dimensions (physical, mental and social) and (ii) that health is more than the absence of disease. There has been an increasing consensus regarding the centrality of a patient's feelings in the assessment of health status. The conventional outcomes considered as important endpoints by clinicians need to be integrated with patients' opinions of their health, reflecting how they really feel, and how much their disease affects their way of life. As expectations regarding health and the ability to cope with limitations and disability can greatly affect a person's perception of health and satisfaction with life, two people with the same objective health status may have a very different QoL.

Measuring QoL

The concept of QoL is difficult to define because of its multidimensional aspects and is also difficult to quantify. According to the WHO [15], the main domains of QoL are: (i) the physical domain, which includes independence in activities of daily living and symptoms of disease; (ii) the psychological domain, involving emotional, cognitive and behavioral status; and (iii) the social domain, how people perceive their role and relationship with other people.

Because many of the components of QoL cannot be observed directly, they are typically assessed according to the classical principles of item-measurement theory [9]. Psychometric tools are used to explore each domain using groups of questions (items). The number of items is a crucial feature of any such tool, because it influences the sensitivity of the assessment and the questionnaire's acceptance by the subject. Answers are converted into numerical scores that are then combined to yield 'scale scores', which may be further combined to yield domain scores or other summary scores of statistical interest. Questionnaires may be administered by means of interviews or self-administered.

Generic QoL tools are used in general populations to assess a wide range of domains applicable to a variety of states of health, conditions and diseases. They are usually not specific to any particular disease and are therefore most useful in conducting general research and drawing comparisons between different diseases. A generic instrument can provide a basis for comparing a sample of patients with other groups of chronically ill patients or with normative general population data [16,17]. Generation of such QoL data can potentially help both medical decision makers and policy planners evaluate the impact of a chronic disease and allocate medical resources for treatment of patients with chronic diseases [18]. All these generic instruments are sensitive to QoL modifications due to any kind of intervention (medical, surgical, or social) and they evaluate both physical dimension (health status and health perception) and mental or psychological dimension (including a psychopathological assessment). The main differences among these instruments are related to the degree to which they emphasize objective when compared with subjective dimensions, the extent to which various domains are covered (i.e. the number of items and categories), and the format of the questions. The most used are the Nottingham Health Profile (NHP) [19], Sickness Impact Profile (SIP) [20], Short-Form 36 (SF-36) [21], LEIPAD Quality of Life [22].

Disease-specific instruments focus on the domains most relevant to the disease or condition under study and on the characteristics of patients in whom the condition is most prevalent. Disease-specific instruments are most appropriate for clinical trials in which specific therapeutic interventions are being evaluated. As for organ transplantation, the most relevant are the Liver Transplant Database Quality of Life Questionnaire (LTD QoL) [23], and the End-Stage Renal Disease Symptom Checklist-Transplantation Module (ESRD-SCL) [24].

Despite the high number of both generic and disease-specific instruments, up to now there is no consensus about the 'gold standard' instrument to measure QoL, and this may limit the comparability of the results. A limitation of generic profiles is that they may not focus adequately on the area of interest for a specific patient or disease, and may lack the sensitivity to detect important changes in status over time. Disease-specific instruments, in contrast, are designed to relate more closely to traditional clinical disease measures, and have the potential for increased responsiveness [16]. Some researchers seem to have concluded that in the absence of an accepted standard, the best strategy is to multiply the number of questionnaires employed to explore different aspects of health-related QoL [16].

Quality of life and transplantation

In transplantation medicine, as in other medical fields, the traditional 'biomedical model' of health based on molecular biology, genetics, physiology and biochemistry [7] is being integrated with the 'social science model' of health, based on psychosocial and economic grounds [25]. The high cost of transplantation, at a time when health-care expenditure is under severe scrutiny, induces its proponents to defend the procedure on the strength of both 'lives saved' and 'QoL gained' [9].

Interest in QoL as an outcome variable of transplantation surgery has prompted an increasing number of publications, from 117 between 1989 and 1993 to 3500 by the end of 2005 (http://www.ncbi.nlm.nih.gov).

Quality of life and heart transplantation

Heart transplantation has a more dramatic impact on life expectancy and QoL than when other organs are involved because the heart is seen as the keeper of life and the focus of feelings. A significant overall improvement in QoL is perceived immediately after the operation, as demonstrated by numerous studies in the last 10 years [26–30]. The impact of improved physical condition on psychological distress is already evident 3 months after transplant surgery and is mainly due to the improvement in cardiopulmonary, neuromuscular and emotional symptoms [31]. Any early post-transplant dermatological, neurological and gastrointestinal complications related to the immunosuppressive therapy is associated with a greater psychological distress and this, together with compliance problems, is a predictor of physical morbidity and mortality 1–3 years after surgery [32].

Recent data confirm the better long-term QoL after transplantation too [33–35]. Fisher *et al.* [34] showed that this was evident not only in the physical domain (home management, mobility, ambulation, eating behavior, body care and movement, sleep and rest) and social dimension (social interaction, recreation and pastimes, etc), but also in the psychological dimension (depression, emotion, etc). The improvement was stable up to 5 years after the surgery and was not correlated with age, rejection episodes, preoperative medical parameters or medication. Concerning age in particular, recent anesthesiological and surgical advances have enabled transplantation to be offered to patients more than 54 years old, with mortality and morbidity rates as good as in younger patients, and an even better QoL in terms of emotional reactions [36].

These good results in terms of QoL have been confirmed in a group of 69 patients surviving up to 13 years after transplantation, all of them in fairly good physical health and with a QoL similar to that of the general population of equivalent familial, social and occupational status [35]. Livi *et al.* [37] showed an improvement in self-care, life expectancy, physical status, and depression/anxiety in patients up to 8 years after transplantation by comparison with patients in the waiting list, but found no improvements in social relationships or cognitive functioning after surgery.

Predictors of QoL after heart transplantation are primarily psychological. A study on 232 patients showed that 66% of the variance in QoL was explained by psychological factors (less stress, more information forthcoming from health-care providers, better perception of health, more effective coping), together with older age and fewer complications [38]. As a clinical determinant, the severity of heart disease before surgery has a strong impact on QoL: patients who were more severely ill before transplantation were less satisfied with their lives and felt they were not doing as well; they experienced more family-related stress and used more negative coping strategies than less severely ill patients. Patients transplanted for dilative cardiomyopathy were more psychologically distressed (anxiety, depression, phobic anxiety and psychoticism) than patients transplanted for ischemic heart disease [37].

Quality of life and lung transplantation

In the 1992 Report of the American Thoracic Society Workshop on Lung Transplantation, there was no mention of QoL or reference to knowledge gaps related to QoL outcomes. Information on this topic is recent and based on a relatively small number of patients with a short follow-up. Current studies confirm that successful lung transplantation largely reverses the energy and physical mobility deficiencies reported by transplant candidates and these improvements persist for at least several years after transplant surgery [39–42]. In a group of 108 adult German-speaking lung transplant recipients, 75% were very satisfied with the outcome of transplant surgery and 92% would opt for the procedure again; the side effects of immunosuppression proved to be a major factor influencing their QoL [43].

Recipients who developed obliterative bronchiolitis syndrome experience a decline in their QoL, and the domain particularly affected are physical and social functioning, with a higher level of anxiety and depression [42]. Stilley *et al.* [44] reported that nearly half of their patients showed clinically significant distress in the areas of depression, anxiety, and anger–hostility after transplantation. Pretransplant psychiatric history, educational level, and post-transplant support from carers and health concerns were the most important independent variables correlating with the recipients' psychological outcome.

Quality of life and kidney and pancreas transplantation

Overall QoL significantly improves after kidney transplantation [45–48]. Particular attention has been focused on QoL in dialyzed patients because dialysis represents an alternative to kidney transplantation, which is not always a life-saving procedure (as it is in the case of the heart or liver).

Cameron *et al.* [49] compared emotional distress and psychological well-being across renal replacement therapies, i.e. continuous ambulatory peritoneal dialysis (CAPD), home- and in-center hemodialysis (CHD) and transplantation. Successful renal transplantation was associated with less distress and more well-being than either type of dialysis. CAPD was associated with more well-being than CHD; and CHD was associated with more distress than home hemodialysis.

In a group of 68 patients evaluated while on the waiting list and again 6 and 12 months after transplantation, Hathaway *et al.* [50] showed a significant improvement in all QoL domains. This improvement occurred early (within the first 6 months after surgery) and remained stable during the follow-up. When predictors were analyzed, three parameters influenced 20–54% of the variability in QoL, i.e. number of hospital admissions (representing early morbidity after transplantation), work (representing economic autonomy) and social support.

A recent Japanese study reported that the improved QoL after transplantation was mainly related to the social and physical domains, although it did not reach the same level as in the healthy population, particularly in relation to the perception of overall health [51].

Although transplantation dramatically improves QoL, there are racial, gender and socio-cultural differences in how it is perceived after surgery. Afro-Americans achieved a less marked improvement than Caucasian-Americans in the affective and functional measures of QoL [52]; women scored consistently lower than men and reported improvements mainly in functional ability, while perceptions of self-image remained low [52,53]; higher economic and educational levels were associated with a higher perception of overall QoL after transplantation [53].

Quality of life also improves significantly in patients who have combined kidney and pancreas transplants for diabetes and end-stage renal disease. Successful pancreas transplants were shown to stabilize or improve neuropathy and prevent any recurrence of diabetic nephropathy in simultaneous kidney grafts [54–56]. Although many patients developed medical complications (caused by long-term diabetes-related complications and immunosuppressive therapy), more positive health perceptions, improved social interactions and greater vitality and energy were significantly associated with successful pancreas–kidney transplantation [57].

Quality of life and liver transplantation

The first studies on QoL after liver transplantation were performed using generic tools on small groups of patients with a short follow-up, but overall QoL appeared to improve after transplantation [58–62]. Methodologically better results emerged from longitudinal studies providing a dynamic assessment of QoL changes before and after transplantation in the same group of recipients. The first longitudinal study was conducted by Tarter *et al.* [63], who evaluated changes in QoL in 53 patients studied when listed for liver transplantation and then at least 2 years after surgery, who were compared with 35 healthy controls. Overall QoL improved significantly after surgery in all domains, but only the physical domain reached levels similar to those of the control population, whereas the psycho-physical domains remained lower. These findings were further confirmed by Bravata *et al.* [64] on a meta-analysis of 49 studies reporting data on 3576 transplant recipients: QoL domains affected by physical health showed higher improvement after transplantation than those affected by psychological functioning.

As for the sample size considered, the most important study so far is the longitudinal one by Belle *et al.* [23], who studied QoL in 346 patients over 7 years, before surgery and in the first year afterwards, using the first specific tool for evaluating QoL after liver transplantation, the LTD QoL [23]. QoL was significantly improved by surgery and became similar to that of healthy people.

As for the factors affecting the perception of QoL after surgery, pretransplant clinical data, medical complications and immunosuppressive therapy did not emerge as determinants [65–68], whereas liver disease etiology (viral, metabolic, cholestatic, neoplastic) does influence QoL after transplantation. Hepatitis C virus (HCV) recurrence after liver transplantation is reportedly the major determinant of both clinical and psychological outcome after surgery [69,70]; patients with recurrent HCV had a lower QoL than either those transplanted for other liver disease etiologies or those transplanted for HCV-related cirrhosis who experienced no HCV recurrence in the graft [71–73]. Psychological distress was apparent early and affected the scores for depression, anxiety, paranoid ideation and psychoticism [73]. Patients transplanted for alcohol-related cirrhosis (an indication often questioned because of the risk of recidivism) reported a QoL just as high as patients transplanted for other etiologies, with lower levels of anxiety and depression [74,75].

Quality of life and intestinal transplantation

Intestinal transplantation has become a standard treatment for intestinal failure in patients with life-threatening complications of total parenteral nutrition, but QoL evaluation in this setting is still scanty.

The most relevant report comes from Sudan *et al.* [76], who evaluated 29 pediatric intestinal transplant recipients (a mean 5 years after surgery, at a mean age of 11 years), who perceived their physical and psychosocial functioning as being the same as for normal school children; their parents, however, perceived their children as having a worse general health and physical functioning after intestinal transplantation than their peers.

Quality of life and living donors

Organ shortages and steadily increasing waiting times for cadaveric transplants have forced the medical community to look for alternatives, including living donation for kidney and liver transplantation. Follow-up reports concerning living donor experiences are short term and primarily focus on medical outcome. Available data on health-related QoL issues for living donors are currently limited and little information is available regarding factors associated with QoL. Living donor kidney transplantation is considered a safe and effective treatment for end-stage renal disease [77]. Living nephrectomy for transplantation is naturally of no direct benefit to the donor other than an increase in self-esteem, but at least it is an extremely safe procedure, with a worldwide overall mortality rate of 0.03% [78]. Donor risks include short-term surgical risk as well as long-term risks of impaired renal function, hypertension and psychological problems [79]. Long-term studies with a follow-up of 20–30 years after kidney donation have shown no significant differences in donor survival compared with nondonor siblings [79]. Most donors reported a high QoL, with a boost in self-esteem and a greater sense of well-being: 96% felt it was a positive experience. Living kidney donation has no detrimental effect on the physical and psychological well-being of donors a year after the operation. In a prospective, longitudinal cohort study, the effect of donating a kidney was investigated before and a year after operation [80]: before the donation, the donors' mean QoL score in the physical domain was significantly higher than the UK value for a healthy person; 6 weeks after surgery, it dropped to UK normative levels, then improved again at 1 year. Donors were not concerned about living with one kidney, and most of them would donate again, if this were possible. In retrospect, the surgical method (laparoscopic versus open donor nephrectomy) did not affect donors QoL or willingness to donate [81].

As for the recipients, the specific impact of transplantation on recipients of living related donor or cadaveric kidneys and their QoL has received little attention. These different forms of transplantation may prompt different emotional responses, albeit with no apparent difference in QoL; for instance, guilt feelings appear to be particularly prominent in living related donor transplantation [82].

Living donor liver transplantation (LDLT) is more controversial and has received criticism in the medical and lay community [77]. It provides potential recipients with timely transplantation, but entails a potentially significant risk to the donor. After resection of the right hepatic lobe, healthy donors can suffer postoperative complications and there have even been a few cases of death. Little research has been done, however, on the psychological issues for living donors before and after LDLT. Most donors felt the experience had changed their lives for the better, and more than 90% would donate again [83]. Walter *et al.* [84] reported that donors' overall QoL before LDLT was higher than in the normal population and remained on a level with healthy people even after LDLT, despite significant reductions in the scores for 'physical health' and 'living conditions'. Postoperative complications had no significant influence on QoL after transplantation. A growing body of literature confirms that the QoL of donors after LDLT is high, indicating a positive psychosocial outcome for the majority of donors, irrespective of donation-related complications [85–87]. The major concern is represented by physical complaints, and postoperative pain in particular.

Quality of life and pediatric transplantation

Measuring QoL is difficult in children and adolescents, and this is reflected in the few suitable tools available. Several instruments rely on the opinions of a proxy (parent or carer), but self-assessment by the child is preferable wherever possible. The need for self-reporting by the child is supported by the inconsistency observed between assessments made by children and proxies. Although QoL measurement is challenging, it is arousing a growing interest in the pediatric setting, particularly in the field of transplantation, where data are very scanty.

Pediatric and adult organ transplantation differ in many ways, but one of the most significant differences lies in the impact of the end-stage organ disease and transplantation on growth and development in pediatric patients, which are important determinants of their QoL. Numerous facets of transplantation may have an impact on growth and development: age is a primary factor, with younger recipients exhibiting the greatest catch-up growth; graft function is important, because a reduced glomerular filtration rate correlates with poor growth in kidney recipients, and the need for re-transplantation is associated with impaired growth in liver recipients; for immunosuppression, the use of corticosteroids is avoided or reduced because of their adverse impact on growth and mood; then there is the risk of post-transplant infectious complications, including lymphoproliferative disease [88]. Although generally improved after transplantation, QoL in pediatric recipients differs significantly according to the type of organ involved, and this is related to the impact of the end-stage organ disease on the children's physical, psychological and social development.

In the last 10 years, more than 2600 pediatric patients have undergone heart transplantation, and the survival rate at 10 years is 65%, with excellent short- and long-term results in terms of overall survival, graft survival, and rejection-free intervals [89]. Pollock-BarZiv *et al.* [90] reported the first QoL study on 10 adolescent heart transplant recipients, who had an excellent perceived QoL and psychological well-being, comparable with healthy controls. Subscale results for physical, social, and emotional function provided evidence of a positive response to transplantation. These results are consistent with other reports, showing that the majority of children and adolescents are capable of a healthy psychological function after heart transplantation [91,92].

Lung transplantation has been performed in small numbers of infants, children and adolescents since 1990 and, by comparison with adults, the numbers remain small today. The main indication for lung transplantation in children is severe pulmonary vascular disease, which is most commonly associated with developmental abnormalities or congenital heart disease; cystic fibrosis is the dominant indication in older childhood and adolescence. Data on QoL are scanty but confirm a huge improvement in overall QoL after transplantation. Post-transplant complications related to viral infections and post-transplant lymphoproliferative disease are more common and more likely to be severe and life-threatening than in adult recipients and strongly affect perceived QoL [93].

Even less experience has been gained in the field of QoL and pediatric intestinal transplantation. There is only one report on this matter: Sudan *et al.* [76] evaluated the perception of QoL in pediatric recipients and their parents and found that, beyond the perioperative period, intestinal transplant recipients perceived their physical and psychosocial functioning as being much the same as normal school children. Parental proxy assessments differed, with parents perceiving a worse than normal general health and physical functioning for intestinal transplant recipients.

Quality of life improves significantly after pediatric liver transplantation. It is reportedly excellent in patients transplanted for inherited metabolic disorders [94] and also in children under 5 years old [95]. Avitzur *et al.* [96] assessed health status 10 years after pediatric liver transplantation in 32 children, confirming a high self-reported QoL in the long term, despite chronic extrahepatic morbidities (Epstein–Barr virus-related malignancies in 22% of patients, severe chronic renal failure in 77%, mild chronic anemia in 59%, hypertension in 25%). A critical review of the health-related QoL of children and adolescents after liver transplantation suggested an improvement in health-related QoL by comparison with their pretransplant status, with a QoL that tended to be worse than for their healthy peers and better than for those with other chronic diseases [97].

Renal transplantation offers the best renal replacement therapy for most children with end-stage renal disease, improving their potential for growth and nutrition, neurodevelopment and QoL [98]. Self-assessment of QoL of 139 children and adolescents remaining on alternative therapies for end-stage renal disease showed that QoL among transplanted children is better than in the dialysis groups, in terms of physical activity as well as physical and social well-being [99]. These results are confirmed in a longitudinal prospective study with a 5-year follow-up after transplantation, which showed that overall QoL improved but did not reach the healthy control level [100]. Despite impressive short-term improvements in QoL, significant long-term problems remain unsolved, particularly in relation to severe immunosuppression-related side effects (including nephrotoxicity and *de novo* malignancy), which are especially relevant for pediatric recipients who will need to take the treatment for several decades – in fact, comorbidities are the most important determinant in children's QoL after transplantation [100].

Special aspects of quality of life after transplantation

Sexual function

Sexual dysfunction is highly prevalent among people with end-stage organ disease, with a strong impact on their QoL and a multifactorial pathogenesis, due to both disease-related and psychological factors. A survey of sexual concerns among 768 organ transplant recipients showed that transplantation had a positive impact on sexuality: 69.9% reported having intimate relationships, 66.7% were satisfied with their relationship, and only 26% were not sexually active. Different organ transplant groups did not differ significantly regarding satisfaction, sexual function, or QoL [101].

In males with severe chronic liver disease, the incidence of erectile dysfunction is reportedly higher than 70% and this correlates with older age and protein malnutrition [102]. Liver transplantation improves all sexual function domains: erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction [103]. Despite reproductive and hormone function abnormalities, sexuality in cirrhotic women waiting for liver transplantation strongly correlates with depression [104]. A year after surgery, 70% of female recipients indicated satisfaction with their relationships, 75% had weekly intercourse and 70% experienced orgasm with intercourse [104], although sexual functioning remained significantly worse in women than in men [105].

As for heart disease, the severity of ischemic coronary disease, age, diabetes and hypertension has a negative effect on quality of erectile function [106], but sexual concerns are commonly experienced (but seldom voiced) after heart transplantation. Sexual dysfunction in men included impotence, ejaculation problems, altered libido, and avoidance of sexual opportunities. Contributing factors to these sexual difficulties were fear of death during coitus, effects of medication on interest and ability to function, body-image concerns, depression, uncertainty about the sexuality of the donor, and altered roles and responsibilities within the family [107].

Renal transplantation has varying effects on sexual function: 35% of patients only reported an improvement in overall sexual function after surgery, although hormone profiles had largely returned to normal [108]. Sexual desire increased significantly compared with 6 months pretransplant, but about 25% of men and women remained sexually dysfunctional [109]. Erectile dysfunction regresses after renal transplantation, but remains common (35.8%), with a multifactorial pathogenesis: hemoglobin level, diabetes mellitus and/or peripheral neuropathy have a significant and independent negative impact on erectile function [110].

Sirolimus, one of the newer immunosuppressive agents, has recently been shown to impair gonadal function in male heart and kidney transplant recipients, reducing total testosterone levels and increasing gonadotropic hormone levels, but it remains to be seen whether sirolimus affects other aspects of sexual function [111,112].

Pregnancy

Organ transplantation offers the best prospect of pregnancy in fertile women with various types of end-stage organ disease. Based on data from the USA National Transplantation Pregnancy Registry (NTPR), more than 70% of post-transplant pregnancies end in a successful live birth [113]. Experience comes mainly from kidney transplants [114–116], followed by the liver [117–119] and heart [120,121]. Most pregnancies do not significantly affect graft function, but are associated with significant obstetric problems. A 30-year study in Sweden on pregnancy outcome before and after organ transplantation showed a high frequency of pre-eclampsia (22%), preterm birth (46%), low birthweight (41%), small size for gestational age (16%) and infant death (5% before the age of 1 year) for deliveries after organ transplantation, but no significant increase in congenital malformation rate was seen [122]. Cesarean section is required in 30–50% of patients due to obstetric or maternal concerns. In the presence of stable graft function, stable maintenance immunosuppression and no evidence of hypertension, patients are more likely to have successful outcomes. Although fertility is restored early (<6 months), the current recommendation is to wait at least 2 years after transplantation before pregnancy [122].

A survey in Italy on 67 pregnancies in women with a transplanted kidney, liver or heart confirms complications at term in 25%, hypertension being the most frequent (16%); two transplant rejections were reported and 59% of the babies were born at term [123].

Successful pregnancies have been reported in recent years under different immunosuppressive regimens (cyclosporine, azathioprine, prednisolone, and tacrolimus), but the optimal treatment for the maximum safety of mother and fetus remains unclear. Few data are available on the newer immunosuppressants, such as mycophenolate mofetil and sirolimus, so these agents are not recommended [113].

Whether recipients should breastfeed remains controversial; recent reports in the literature and the NTPR data appear to be in favor of breastfeeding [124].

Schooling

With the increasing use and better survival rates of liver, heart and lung transplantation for children with end-stage disease, attention is focusing on the long-term psychological and social implications of these procedures. Up to 40% of chronically ill children and adolescents experience problems at school, including learning difficulties, social maladjustment and problems with peer relationships. Little is known about the school performance of children after transplantation, and data are mostly extrapolated from assessments of their overall QoL.

A significant number of children experienced difficulties at school after successfully undergoing heart or heart–lung transplantation, and their performance was significantly worse than that of healthy children. Contrary to expectations, educational problems were more prevalent in the medium term, rather than soon after transplantation. Initial diagnosis was a salient factor in post-transplant psychological functioning at school: children with congenital heart disease had more academic and behavioral difficulties than those with cardiomyopathy or cystic fibrosis [125].

Conversely, school performance was found to improve after renal transplantation: in a series of 47 children observed for 10–20 years after their operation, with a 10-year survival rate of 89%, all except three with mental retardation were, or had been, attending normal day care or normal school [126]. These results are consistent with the experience of Uddin *et al.* [127], who evaluated 57 children with a cumulative patient survival of 87% at 10 years; 25 of the 29 school-age children with a functioning graft were attending full-time school in a class appropriate for their age and nine of the 13 older patients were working full-time, and two part-time.

As for liver transplantation, Fouquet *et al.* [128] reported a good long-term survival for pediatric cases transplanted for biliary atresia, showing an overall patient survival rate of 82% at 10 years with normal growth rates and schooling in the majority of recipients: 63 of 80 children were attending normal schools and 55 children (69%) had suffered no delay in the education. These results are consistent with the SPLIT (Studies of Pediatric Liver Transplantation) [129] outcomes of 640 children after transplantation, reporting that 89% of school-age children were in school full-time 18 months after surgery. When pediatric liver transplantation for metabolic disorders was compared with cases of nonmetabolic disease, results were excellent for survival, clinical and biochemical outcomes and QoL. All the school-age children were not more than 1 year behind schedule, except for those with pretransplant developmental delays, who remained in special education [130].

Sports

Most transplanted people report a better QoL not only in psychological and social, but also in physical domains after surgery, returning to the same sort of physical activity as before their chronic illness. Yet little is known, at present, about physical exercise and sports after transplantation.

People who have received a heart, lung, liver, kidney or pancreas transplant have different whole-body and organ reactions to both acute exercise and regular physical training than healthy people. The majority of cardiovascular, hormonal and metabolic changes in response to acute exertion are maintained after transplantation, but organ denervation in heart transplant recipients reduces the speed with which heart rate increases in response to exercise. Sympathetic denervation impairs normal insulin and renin response to exercise in pancreas and kidney recipients, respectively. In contrast, hepatic glucose production is not inhibited in liver transplant recipients during exercise, and lung denervation does not affect the ability to increase ventilation during physical exertion. With a few precautions, organ transplant recipients can exercise and do training, obtain similar effects to those achieved in the healthy population of similar age [131].

These results have also been confirmed in the pediatric setting: kidney transplanted children have a good tolerance of physical exercise, although they are smaller and have a higher body mass index than age-matched healthy controls [132].

Work

An important goal of transplantation is to enable patients to return to work, and improving employment outcomes for transplant recipients can positively contribute to a patient's identity, self-esteem, and QoL [133]. Detailed information on the working lives of transplanted patients is limited, mainly because employment after transplantation is generally considered among the QoL aspects evaluating social relationships. The return to work rates reported in the literature vary widely, moreover, from as low as 20% to as high as 80% [134].

A recent survey on 263 patients with heart, liver and lung transplants showed that relatively few patients (roughly one in four of the total sample) reported that they were working full- or part-time [135].

Clinical and demographic variables influence the return to work after heart transplantation. In a longitudinal study on 237 heart transplant patients, only 17% of patients were working before their operation, when compared with 26% who were working by 1 year afterwards. Patients who were working either pre- or post-transplant were more likely to have jobs that were less physically demanding. Factors significantly associated with return to work after heart transplant were better functional ability, higher education, fewer endocrine problems, fewer acute rejection episodes and shorter heart transplant waiting time [136].

The improvement in QoL associated with combined kidney–pancreas transplantation provides an added incentive for diabetics with renal insufficiency to seek employment. At the time of transplantation, in fact, 39% of kidney–pancreas transplant patients and 33% of kidney-alone transplant patients were working at least 20 h a week, but significantly more kidney–pancreas recipients (73%) than kidney-alone recipients (27%) were working. Additionally, pretransplant employment was independently associated with post-transplant work status [137].

Better results are reported after liver transplantation. Parolin *et al.* [138] showed that more than 75% of patients were unable to work because of their end-stage liver disease before liver transplantation, but 68% of patients returned to work within a mean 5.9 months after surgery. Reasons for inactivity after liver transplantation were early retirement, unemployment and physical disability. Postoperative complications and functional status did not predict post-transplantation employment levels [139]. There were no significant differences between alcohol-related and nonalcohol-related transplant recipients in the proportions of those in employment, and students [140].

Conclusions

Health-related QoL has become a frequently used outcome in clinical and health policy settings in the last two decades, as expression of the centrality of patients' point of view in the assessment of health status. The role of QoL evaluation is crucial particularly with respect to therapies involving the allocation of scarce resources, such as organ transplantation.

Organ transplantation represents the treatment of choice for many patients with end-stage organ diseases, with good outcome from a technical standpoint. In this setting, the goal is whether and how long a patient will survive, but also with what restrictions on QoL is such a treatment procedure associated, in terms of patients' ability to function both from a physical and psychosocial standpoint, and the effect on their perceived sense of well-being.

Most published studies report that the impact of transplantation on recipients' QoL is dramatic. The improvement is significant and perceived early after surgery, with larger gains in the dimensions of QoL most affected by physical health and more modest improvements in areas affected by psychosocial functioning. Despite these good results, overall QoL after organ transplantation seems lower than expected, whether the aim of transplantation is to restore the same level of QoL which patients had before developing an organ failure or a QoL as the same level of the healthy people. This discrepancy may be related to medical complications after surgery, to psychological difficulties in psychosocial adjustments and coping strategies, but also to the limits of the research on the field of QoL following transplantation. In fact, the literature on QoL is heterogeneous, with different methodologies and instruments, applied to small number of patients in the majority of cases, and based on cross-sectional more than longitudinal prospective studies. However, more detailed and comprehensive data are needed in the field of organ transplantation and in the growing experience of pediatric transplantation and living-related organ transplantation, to focus attention on patient groups at higher risk of a lower QoL. New strategies are needed to support and inform patients on the waiting list and after organ transplantation. Measures aiming to improve rehabilitation in specific targeted areas may enable patients to resume a more fulfilling life after their transplantation surgery.

References

1. Wood RP, Ozaki CF, Ktz SM, Monsour HP, Dyer CH, Johnston TD. Liver transplantation. The last ten years. *Surg Clin North Am* 1994; **74**: 1133.
2. NITp – Iss. La situazione dei trapianti in Italia e in Europa. *Panorama Sanità* 1996; **2**: 14.
3. UNOS. *Annual Report of the US Scientific Registry of Transplant Recipients and the Organ Procurement and Transplantation Network*. Contract Numbers 240-93-0051 and 240-93-0052. Health Resources and Services Administration, Division of Organ Transplantation, 1994.
4. Rauch JB, Kneen KK. Accepting the gift of life: heart transplantation recipients' post-operative adaptive tasks. *Soc Work Health Care* 1989; **14**: 47.
5. Dew MA, Myaskovsky L, Switzer GE, DiMartini AF, Schulberg HC, Kormos RL. Profiles and predictors of the course of psychological distress across four years after heart transplantation. *Psychol Med* 2005; **35**: 1215.
6. Muehrer RJ, Becker BN. Life after transplantation: new transitions in quality of life and psychological distress. *Semin Dial* 2005; **18**: 124.
7. Bergner M. Quality of life, health status and clinical research. *Med Care* 1989; **27**(Suppl.): S148.
8. Wilson I, Cleary P. Linking clinical variables with health-related quality of life. *JAMA* 1995; **273**: 59.
9. Testa MA, Simonson DG. Assessment of quality-of-life outcomes. *N Engl J Med* 1996; **334**: 835.
10. Kanwal F, Hays RD, Kilbourne AM, Dulai GS, Gralnek IM. Are physician-derived disease severity indices associated with health-related quality of life in patients with end-stage liver disease? *Am J Gastroenterol* 2004; **99**: 1726.
11. De Leo D. La qualità di vita: aspetti teorici. In: Burra P, Naccarato R, eds. *Qualità di vita nei trapianto d'organo*. Padova: Tipografia Albignasego, 1998: 1.
12. National Wildlife. Quality of life (environmental quality index). *Natl Widl* 1994; **32**: 38.
13. Brock D. Quality of life measures in health care and medical ethics. In: Nussbaum M, Sen S, eds. *Quality of Life*. Oxford: Clarendon Press, 1993: 95.
14. World Health Organization. Constitution of the World Health Organization. In: *World Health Organization. Handbook of Basic Documents, 5th edn*. Geneva: Palais des Nations, 1952: 3.
15. World Health Organization. *Quality of Life in Health Care*, Workshop, Geneva, Switzerland, 11–16 February 1991.

16. Guyatt GH, Feeny DH, Patrick DL. Measuring health-related quality of life. *Ann Intern Med* 1993; **118**: 622.
17. Patrick DL, Deyo RA. Generic and disease-specific measures in assessing health status and quality of life. *Med Care* 1989; **27**: S217.
18. Patrick DL, Erickson P. *Health Status and Health Policy: Quality of Life in Health Care Evaluation and Resource Allocation*. New York: Oxford University Press, 1993.
19. Hunt SM, McKenna SP, McEwen J, Backett EM, Williams J, Papp E. A quantitative approach to perceive health status: a validation study. *J Epidemiol Community Health* 1980; **34**: 281.
20. Gilson BS, Gilson JS, Bergner M, *et al.* The sickness impact profile. Development of an outcome measure of health care. *Am J Public Health* 1975; **65**: 1304.
21. Brazier JE, Harper R, Jones NM, *et al.* Validating the SF-36 health survey questionnaire: new outcome measure for primary care. *BMJ* 1992; **305**: 160.
22. De Leo D, Diekstra RF, Lonnqvist J, *et al.* LEIPAD, an internationally applicable instrument to assess quality of life in the elderly. *Behav Med* 1998; **24**: 17.
23. Belle SH, Porayko MK, Hoofnagle JH, Lake JR, Zetterman RK, for the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Liver Transplantation Database (LDT). Changes in quality of life after liver transplantation among adults. *Liver Transpl Surg* 1997; **3**: 93.
24. Franke GH, Reimer J, Kohnle M, Luetkes P, Maehner N, Heemann U. Quality of life in end-stage renal disease patients after successful kidney transplantation: development of the ESRD symptom checklist-transplantation module. *Nephron* 1999; **83**: 31.
25. Wilson I, Cleary P. Linking clinical variables with health-related qualiy of life. *JAMA* 1995; **273**: 59.
26. Hunt SA, Rider AK, Stinson EB *et al.* Does cardiac transplantation prolong life and improve its quality? An update report. *Circulation* 1976; **54**(Suppl. 6): III 56.
27. English TA, Wallwork J. Heart and heart–lung transplantation. Papworth Hospital 1979 to 1987. *Clin Transpl* 1989; **1**: 73.
28. O'Brien BJ, Buxton MJ, Ferguson BA. Measuring the effectiveness of heart transplant programmes: quality of life data and their relationship to survival analysis. *J Chronic Dis* 1987; **40**(Suppl. 1): 137S.
29. Lough ME, Lindsey AM, Shinn JA, Stotts NA. Life satisfaction following heart transplantation. *J Heart Transplant* 1985; **4**: 446.
30. Bunzel B, Grundbock A, Laczkovics A, Holzinger C, Teufelsbauer M. Quality of life after orthotopic heart transplantation. *J Heart Lung Transplant* 1991; **10**: 455.
31. Jalowiec A, Grady KL, White-Williams C, *et al.* Symptom distress three months after heart transplantation. *J Heart Lung Transplant* 1997; **16**: 604.
32. Dew MA, Kormos RL, Roth LH, Murali S, DiMartini A, Griffith BP. Early post-transplant medical complicance and mental health predict physical morbidity and mortality one to three years after heart transplantation. *J Heart Lung Transplant* 1999; **18**: 549.
33. Molzahn AE, Burton JR, McCormick P, Modry DL, Soetaert P, Yaylor P. Quality of life of candidates for and recipients of heart transplantation. *Can J Cardiol* 1997; **13**: 141.
34. Fisher DC, Lake KD, Reutzel TJ, Emery RW. Changes in health-related quality of life and depression in heart transplant recipients. *J Heart Lung Transplant* 1995; **14**: 373.
35. Hetzer R, Albert W, Hummel M, *et al.* Status of patients presently living 9 to 13 years after orthotopic heart transplantation. *Ann Thorac Surg* 1997; **64**: 1661.
36. Rickenbacher PR, Lewis NP, Valantine HA, Luikart H, Stinson EB, Hunt SA. Heart transplantation in patients over 54 years of age. Mortality, morbidity and quality of life. *Eur Heart J* 1997; **18**: 870.
37. Livi U, Volpe B, Scarso P, Ponton P, Cozzi MT. La qualità di vita dopo trapianto di cuore. In: di Burra P, De Bona M, Rupolo G, Naccarato R, eds. "*Qualità di vita nei trapianti d'organo*" *a cura*. Albignasego (Pd): Tipolitografia Roma snc, 1999: 65.
38. Grady KL, Jalowiec A, White-Williams C. Predictors of quality of life in patients at one year after heart transplantation. *J Heart Lung Transplant* 1999; **18**: 202.
39. TenVergert EM, Essink-Bot ML, Geertsma A, van Enckevort PJ, de Boer WJ, van der Bij W. The effect of lung transplantation on health-related quality of life: a longitudinal study. *Chest* 1998; **113**: 358.
40. Stavem K, Bjortuft O, Lund MB, Kongshaug K, Geiran O, Boe J. Health-related quality of life in lung transplant candidates and recipients. *Respiration* 2000; **67**: 159.
41. MacNaughton KL, Rodrigue JR, Cicale M, Staples EM. Health-related quality of life and symptom frequency before and after lung transplantation. *Clin Transplant* 1998; **12**: 320.
42. Van Den Berg JW, Geertsma A, van Der Bij W, *et al.* Bronchiolitis obliterans syndrome after lung transplantation and health-related quality of life. *Am J Respir Crit Care Med* 2000; **161**: 1937.
43. Smeritschnig B, Jaksch P, Kocher A, *et al.* Quality of life after lung transplantation: a cross-sectional study. *J Heart Lung Transplant* 2005; **24**: 474.
44. Stilley CS, Dew MA, Stukas AA, *et al.* Psychological symptom levels and their correlates in lung and heart–lung transplant recipients. *Psychosomatics* 1999; **40**: 503.
45. Russell JD, Beecroft ML, Ludwin D, Churchill DN. The quality of life in renal transplantation. A prospective study. *Transplantation* 1992; **54**: 656.
46. Yoshimura N, Ohmori Y, Tsuji T, Oka T. Quality of life in renal transplant recipients treated with cyclosporine: 4 year follow-up. *Transplant Proc* 1994; **26**: 2542.
47. Ohkubo M. The quality of life after kidney transplantation in Japan: result from a nation wide questionnaire. *Transplant Proc* 1995; **27**: 1452.

48. Witzke O, Becker G, Franke G, Binek M, Phillipp T, Haemann U. Kidney transplantation improves quality of life. *Transplant Proc* 1997; **29**: 1569.
49. Cameron JI, Whiteside C, Katz J, Devins GM. Differences in quality of life across renal replacement therapies: a meta-analytic comparison. *Am J Kidney Dis* 2000; **35**: 629.
50. Hathaway DK, Winsett RP, Johnson C, *et al.* Post kidney transplant quality of life prediction models. *Clin Transplant* 1998; **12**: 168.
51. Tsuji-Hayashi Y, Fukuhara S, Green J, *et al.* Health-related quality of life among renal-transplant recipients in Japan. *Transplantation* 1999; **68**: 1331.
52. Johnson CD, Wicks MN, Milstead J, Haerwig M, Hathaway DK. Racial and gender differences in quality of life following kidney transplantation. *Image J Nurs Sch* 1998; **30**: 125.
53. Rebollo P, Ortega F, Baltar JM, *et al.* Health-related quality of life (HRQoL) in end stage renal disease (ESRD) patients over 65 years. *Geriatr Nephrol Urol* 1998; **8**: 85.
54. Sutherland DER, Gores PF, Farney AC, *et al.* Evolution of kidney, pancreas and islet transplantation for patients with diabetes at the University of Minnesota. *Am J Surg* 1993; **166**: 465.
55. Gaber AO, Cardoso S, Pearson S, *et al.* Improvement in autonomic function following combined pancreas–kidney transplantation. *Transplant Proc* 1991; **23**: 1660.
56. Muller-Felber W, Landgraf R, Scheuer R, *et al.* Diabetic neuropathy 3 years after successful pancreas and kidney transplantation. *Diabetes* 1993; **42**: 1482.
57. Bruce DS, Newell KA, Josephson MA, *et al.* Long-term outcome of kidney–pancreas transplant recipients with good graft function at one year. *Transplantation* 1996; **62**: 451.
58. Starzl TE, Koep LJ, Schroter GPJ, Halgrimson CG, Porter KA. The quality of life after liver transplantation. *Transplant Proc* 1979; **11**: 252.
59. Colonna JO, Brems JJ, Hiat JR, *et al.* The quality of survival after liver transplantation. *Transplant Proc* 1988; **20**: 594.
60. Lowe D, O'Grady JG, McEwen J, Williams R. Quality of life following liver transplantation: a preliminary report. *J R Coll Gen Pract* 1990; **24**: 43.
61. Kuchler T, Kober A, Broelsch C, Kremer B, Henne-Bruns D. Quality of life after liver transplantation. *Clin Transplant* 1991; **5**: 94.
62. Bonsel J, Essink-Bot ML, Klompaker IJ, Slooff MJH. Assessment of the quality of life before and following liver transplation. *Transplantation* 1992; **53**: 796.
63. Tarter RE, Switala JA, Arria A, Plail J, Van Thiel D. Quality of life before and after orthotopic hepatic transplantation. *Arch Intern Med* 1991; **151**: 1521.
64. Bravata DM, Olkin I, Barnato AE, Keeffe EB, Owens DK. Health-related quality of life after liver transplantation: a meta-analysis. *Liver Transpl Surg* 1999; **5**: 318.
65. De Bona M, Rupolo G, Ponton P, *et al.* The effect of recurrence of HCV infection on quality of life after liver transplantation. *Transpl Int* 1998; **11**: 475.
66. Brown ES, Suppers T. Mood symptoms during corticosteroid therapy: a review. *Harv Rev Psychiatry* 1998; **5**: 239.
67. Di Martini AF. Neuropsychiatric side effects of FK506 vs cyclosporine A. First week postoperative findings. *Psychosomatics* 1997; **38**: 565.
68. Scholler G, Rose M, Neuhans R. Comparison of cyclosporine A and FK506 with regard to complaints and psychosocial characteristics before and after liver transplantation. *Transplant Proc* 1997; **29**: 2491.
69. Terrault NA, Wright TL. Hepatitis C virus in the setting of transplantation. *Semin Liver Dis* 1995; **15**: 92.
70. Feray C, Gigou M, Samuel D, *et al.* The course of hepatitis C virus reinfection after liver transplantation. *Hepatology* 1994; **20**: 1137.
71. Dickson RC, Wright RM, Bacchetta MD, *et al.* The quality of life of hepatitis B and C patients after liver transplantation. *Clin Transplant* 1997; **11**: 282.
72. Singh N, Gayowski T, Wagener MM, Marino IR. Quality of life, functional status, and depression in male liver transplant recipients with recurrent viral hepatitis C. *Transplantation* 1999; **67**: 69.
73. De Bona M, Ponton P, Ermani M, *et al.* The impact of liver disease and medical complications on quality of life and psychological distress before and after liver transplantation. *J Hepatol* 2000; **33**: 609.
74. Wiesner RH, Lombardero M, Lake JR, Everhart J, Detre KM. Liver transplantation for end-stage alcoholic liver disease: an assessment of outcomes. *Liv Transpl Surg* 1997; **3**: 231.
75. De Bona M, Burra P, Foti F, *et al.* Quality of life changes after liver transplantation in alcoholic and non alcoholic patients. *Ital J Gastroenterol Hepatol* 1997; **29**(Suppl. 2): A25.
76. Sudan D, Horslen S, Botha J, *et al.* Quality of life after pediatric intestinal transplantation: the perception of pediatric recipients and their parents. *Am J Tranplant* 2004; **4**: 407.
77. Rudow DL, Chariton M, Sanchez C, Chang S, Serur D, Brown RS. Kidney and liver living donors: a comparison of experiences. *Prog Transplant* 2005; **15**: 185.
78. Bruzzone P, Pretagostini R, Poli L, Rossi M, Berloco PB. Ethical considerations on kidney transplantation from living donors. *Transplant Proc* 2005; **37**: 2436.
79. Najarian JS. Living donor kidney transplants: personal reflections. *Transplant Proc* 2005; **37**: 3592.
80. Lumsdaine JA, Wray A, Power MJ, *et al.* Higher quality of life in living donor kidney transplantation: prospective cohort study. *Transpl Int* 2005; **18**: 975.
81. Giessing M, Reuter S, Deger S, *et al.* Laparoscopic versus open donor nephrectomy in Germany: impact on donor health-related quality of life and willingness to donate. *Transplant Proc* 2005; **37**: 2011.

82. Griva K, Ziegelmann JP, Thompson D, *et al.* Quality of life and emotional responses in cadaver and living related renal transplant recipients. *Nephrol Dial Transplant* 2002; **17**: 2204.
83. Parolin MB, Lazzaretti CT, Lima JH, Freitas AC, Matias JE, Coelho JC. Donor quality of life after living donor liver transplantation. *Transplant Proc* 2004; **36**: 912.
84. Walter M, Dammann G, Papachristou C, *et al.* Quality of life of living donors before and after living donor liver transplantation. *Transplant Proc* 2003; **35**: 2961.
85. Miyagi S, Kawagishi N, Fujimori K, *et al.* Risks of donation and quality of donors' life after living donor liver transplantation. *Transpl Int* 2005; **18**: 47.
86. Verbesey JE, Simpson MA, Pomposelli JJ, *et al.* Living donor adult liver transplantation: a longitudinal study of the donor's quality of life. *Am J Transplant* 2005; **5**: 2770.
87. Coelho JC, Parolin MB, Baretta GA, Pimentel SK, de Freitas AC, Colman D. Donor quality of life after living donor transplantation. *Arq Gastroenterol* 2005; **42**: 83.
88. Fine RN. Growth following solid-organ transplantation. *Pediatr Transplant* 2002; **6**: 47.
89. Gabrys CA. Pediatric cardiac transplants: a clinical update. *J Pediatr Nurs* 2005; **20**: 139.
90. Pollock-BarZiv SM, Anthony SJ, Niedra R, Dipchand AI, West LJ. Quality of life and function following cardiac transplantation in adolescents. *Transplant Proc* 2003; **35**: 2468.
91. DeMaso DR, Douglas Kelley S, Bastardi H, O'Brien P, Blume ED. The longitudinal impact of psychological functioning, medical severity, and family functioning in pediatric heart transplantation. *J Heart Lung Transplant* 2004; **23**: 473.
92. Wray J, Radley-Smith R. Beyond the first year after pediatric heart or heart–lung transplantation: changes in cognitive function and behaviour. *Pediatr Transplant* 2005; **9**: 170.
93. Mallory GB, Spray TL. Pediatric lung transplantation. *Eur Respir J* 2004; **24**: 839.
94. Kayler LK, Merion RM, Lee S, *et al.* Long-term survival after liver transplantation in children with metabolic disorders. *Pediatr Transpant* 2002; **6**: 295.
95. Cole CR, Bucuvalas JC, Hornung RW, *et al.* Impact of liver transplantation on HRQoL in children less than 5 years old. *Pediatr Transplant* 2004; **8**: 222.
96. Avitzur Y, De Luca E, Cantos M, *et al.* Health status ten years after pediatric liver transplantation – looking beyond the graft. *Transplantaton* 2004; **78**: 566.
97. Taylor R, Franck LS, Gibson F, Dhawan A. A critical review of the health-related quality of life of children and adolescents after liver transplantation. *Liver Transplant* 2005; **11**: 51.
98. Krmar RT, Eymann A, Ramirez JA, Ferraris JR. Quality of life after kidney transplantation in children. *Transplantation* 1997; **64**: 540.
99. Rubik J, Grenda R, Jakubowska-Winecka A, Dabrowska A. Quality of life in children and adolescent with end-stage renal disease treated with dialysis and kidney transplantation. *Pol Merkuriusz Lek* 2000; **8**: 280.
100. Qvist E, Narhi V, Apajasalo M, *et al.* Psychosocial adjustment and quality of life after renal transplantation in early childhood. *Pediatr Transplant* 2004; **8**: 120.
101. Hart LK, Milde FK, Zehr PS, Cox DM, Tarara DT, Fearing MO. Survey of sexual concerns among organ transplant recipients. *J Transpl Coord* 1997; **7**: 82.
102. Toda K, Miwa Y, Kuriyama S, *et al.* Erectile dysfunction in patients with chronic viral liver disease: its relevance to protein malnutrition. *J Gastroenterol* 2005; **40**: 894.
103. Coelho JC, Matias JE, Zeni Neto C, de Godoy JL, Canan Junior LW, Jorge FM. Sexual function in males undergoing liver transplantation. *Rev Assoc Med Bras* 2003; **49**: 413.
104. Parolin MB, Rabinovitch I, Urbanetz AA, Scheidemantel C, Cat ML, Coehlo JC. Impact of successful liver transplantation on reproductive function and sexually in women with advanced liver disease. *Transplant Proc* 2004; **36**: 943.
105. Blanch J, Sureda B, Flavia M, *et al.* Psychosocial adjustment to orthotopic liver transplantation in 266 recipients. *Liver Transplant* 2004; **10**: 228.
106. Greenstein A, Chen J, Miller H, Matzkin H, Villa Y, Braf Z. Does severity of ischemic coronary disease correlate with erectile function? *Int J Impot Res* 1997; **9**: 123.
107. Tabler JB, Frierson RL. Sexual concerns after heart transplantation. *J Heart Transplant* 1990; **9**: 397.
108. Tsujimura A, Matsumiya K, Tsuboniwa N, *et al.* Effect of renal transplantation on sexual function. *Arch Androl* 2002; **48**: 467.
109. Schover LR, Novick AC, Steinmuller DR, Goormastic M. Sexuality, fertility, and renal transplantation: a survey of survivors. *J Sex Marital Ther* 1990; **16**: 3.
110. El-Bahnasawy MS, El-Assmy A, El-Sawy E, *et al.* Critical evaluation of the factors influencing erectile function after renal transplantation. *Int J Impot Res* 2004; **16**: 521.
111. Kaczmarek I, Groetzner J, Adamidis I, *et al.* Sirolimus impairs gonadal functions in heart transplant recipients. *Am J Transplant* 2004; **4**: 1084.
112. Lee S, Coco M, Greenstein SM, Schechner RS, Tellis VA, Glicklich DG. The effect of sirolimus on sex hormone levels of male renal transplant recipients. *Clin Transplant* 2005; **19**: 162.
113. Sivaraman P. Management of pregnancy in transplant recipients. *Transplant Proc* 2004; **36**: 1999.
114. Gutierrez MJ, Acebedo-Ribo M, Garcia-Donaire JA, *et al.* Pregnancy in renal transplant recipients. *Transplant Proc* 2005; **37**: 3721.
115. Pour-Reza-Gholi F, Nafar M, Farrokhi F, *et al.* Pregnancy in kidney transplant recipients. *Transplant Proc* 2005; **37**: 3090.
116. Fischer T, Neumayer HH, Fischer R, *et al.* Effect of pregnancy on long-term kidney function in renal transplant

recipients treated with cyclosporine and with azathioprine. *Am J Transplant* 2005; **5**: 2732.

117. Jain AB, Reyes J, Marcos A, *et al.* Pregnancy after liver transplantation with tacrolimus immunosuppression: a single center's experience update at 13 years. *Transplantation* 2003; **76**: 827.
118. Jabiry-Zieniewicz Z, Cyganek A, Luterek K, *et al.* Pregnancy and delivery after liver transplantation. *Transplant Proc* 2005; **37**: 1197.
119. Loreno M, Bo P, Senzolo M, Cillo U, Naoumov N, Burra P. Successful pregnancy in a liver transplant recipient treated with lamivudine for de novo hepatitis B in the graft. *Transpl Int* 2005; **17**: 730.
120. Yuh-Jer Shen A, Mansukhani PW. Is pregnancy contraindicated after cardiac transplantation? A case report and literature review. *Int J Cardiol* 1997; **60**: 151.
121. Miniero R, Tardivo I, Centofanti P, *et al.* Pregnancy in heart transplant recipients. *J Heart Lung Transplant* 2004; **23**: 898.
122. Kallen B, Westgren M, Aberg A, Olausson PO. Pregnancy outcome after maternal organ transplantation in Sweden. *BJOG* 2005; **112**: 904.
123. Miniero R, Tardivo I, Curtoni ES, *et al.* AIRT, NITp Outcome of pregnancy after organ transplantation: a retrospective survey in Italy. *Transpl Int* 2005; **17**: 724.
124. Armenti VT, Radomski JS, Moritz MJ, Gaughan WJ, McGrory CH, Coscia LA. Report from the National Transplantation Pregnancy Registry (NTPR): outcomes of pregnancy after transplantation. *Clin Transpl* 2003; **2**: 131.
125. Wray J, Long T, Radley-Smith R, Yacoub M. Returning to school after heart or heart–lung transplantation: how well do children adjust? *Transplantation* 2001; **72**: 100.
126. Englund M, Berg U, Tyden G. A longitudinal study of children who received renal transplants 10–20 years ago. *Transplantation* 2003; **76**: 311.
127. Uddin GM, Hodson EM. Renal transplantation: experience in Australia. *Indian J Pediatr* 2004; **71**: 137.
128. Fouquet V, Alves A, Branchereau S, *et al.* Long-term outcome of pediatric liver transplantation for biliary atresia: a 10-year follow-up in a single center. *Liver Transpl* 2005; **11**: 152.
129. SPLIT Research Group. Studies of Pediatric Liver Transplantation (SPLIT): year 2000 outcomes. *Transplantation* 2001; **72**: 463.
130. Kayler LK, Merion RM, Lee S, *et al.* Long-term survival after liver transplantation in children with metabolic disorders. *Pediatr Transplant* 2002; **6**: 295.
131. Kjaer M, Beyer N, Secher NH. Exercise and organ transplantation. *Scand J Med Sci Sports* 1999; **9**: 1.
132. Daudet G, Dupuis JM, Jocteur-Monrozier D, Reix P, Cochat P, Bellon G. Kidney transplanted child and sport practices. *Arch Pediatr* 2005; **12**: 273.
133. Callahan MB. Dollars and sense of successful rehabilitation. *Prog Transplant* 2005; **15**: 331.
134. Slapak M. Sport and transplantation. *Ann Transplant* 2005; **10**: 62.
135. Littlefield C, Abbey S, Fiducia D, *et al.* Quality of life following transplantation of the heart, liver, and lungs. *Gen Hosp Psychiatry* 1996; **18**(6 Suppl.): 36S.
136. White-Williams C, Jalowiec A, Grady K. Who returns to work after heart transplantation? *J Heart Lung Transplant* 2005; **24**: 2255.
137. Knight RJ, Daly L. The impact of pancreas transplantation on patient employment opportunities. *Clin Transplant* 2004; **18**: 49.
138. Parolin MB, Coelho JC, Costa PB, Pimentel SK, dos Santos-Neto LE, Vayego SA. Return to work of adults after liver transplantation. *Arq Gastroenterol* 2001; **38**: 172.
139. Hunt CM, Camargo CA, Dominitz JA, Clavien PA. Effect of post-operative complications on health and employment following liver transplantation. *Clin Transplant* 1998; **12**: 99.
140. Cowling T, Jennings LW, Goldstein RM, *et al.* Social reintegration after liver transplantation: findings in alcohol-related and non-alcohol-related transplant recipients. *Ann Surg* 2004; **239**: 93.