

QUALITY OF LIFE AND PHYSICAL ACTIVITY AFTER LIVER TRANSPLANTATION. LITERATURE REVIEW

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Abstract Liver transplantation has become one of the most effective treatments for end-stage renal disease. For patients, however, the decision to have orthotopic liver transplantation (OLT) is often made in an effort to improve their quality of life and to reduce their risk of mortality and morbidity. Quality of life is an important aspect of therapy for transplant patients because this category reflects the subjective evaluation of one's own life in the physical, psychological and social dimensions. One of the means to achieve a better quality of life is not only good health, but also physical activity. Physical activity has been demonstrated to be of significance not only in the assessment of fitness levels but also could be of importance in long term recovery process after major surgical operations. The aim of this study was a review of literature showing the improved quality of life in patients after liver transplantation as well as the influence of physical activity on their physical health, mental health and quality of life after transplantation. Longitudinal data showed remarkable improvement of common domains of QOL comparing pre- and post-transplant items. Gender, occupation and regular physical activity have an influence on the quality of life after liver transplantation.

Key words quality of life; liver transplantation; physical activity

Introduction

Liver transplantation surgery (LTx) provides patients with a chance to return to an active life. Above all, LTx saves patients from premature death, and in doing so delivers an opportunity for continued development and a normal life. In recent years the follow up treatment of patients has taken into account assessments of their quality of life, where this measurement is used as a marker of the effectiveness of the treatment. One of the means to achieve a better quality of life is not only better health, but also physical activity. Regular exercise has a long-term positive impact on recovery following various surgical procedures including transplants, giving patients the opportunity to return to an active life in their families, society and also in their professional life.

Naturally, quality of life improves considerably following LTx. Nevertheless, transplant recipients still show lower health related quality of life (HRQOL) scores than the general population (Masala et al., 2012). Regular

physical activity has been demonstrated to be of significance in the long term recovery process following LTx, and to positively affect the quality of life (Painter et al., 2001). However, many LTx recipients remain sedentary (Beyer et al., 1999; Kallwitz et al., 2013) and their low physical activity contributes to the development of post LTx metabolic abnormalities and cardiovascular complications, the third leading cause of long-term mortality following LTx (Beyer et al., 1999; Watt et al., 2010). Yet to date there has only been limited data on factors related to low physical activity and impaired HRQOL in LTx recipients.

Therefore, this paper reviews the body of research on the improvement of quality of life in post LTx patients, and on the influence of physical activity on their physical health, mental health and quality of life (QOL).

The concept and measurement of quality of life

HRQOL is a multi-dimensional concept that includes subjective evaluations in domains related to physical, mental, emotional and social functioning, in the context of a disease or disability and its treatment (World Health Organization, 1998). The evaluation of HRQOL denotes an effort to define how the variables within the dimensions of health relate to the specific measurements that have been found to be of importance to the subjects (Ware, 1995). With subsequent improvements in medical treatments effecting a prolonged survival, HRQOL has emerged as an important clinical issue.

HQOL is an important measure in the treatment of chronic diseases. It quantifies the subjective evaluation of a patient's life in physical, psychological and social spheres. HRQOL takes into account the natural course of the disease, its consequences and outcomes, and reflects the individual patient's perspective on the disease. It is increasingly frequently emphasized that an analytical approach is not sufficient in the care of the chronically ill. In these patients, it is often difficult and sometimes impossible to draw a line between physical and psychological aspects of the disease (Pietrzykowska et al., 2007). The questionnaires used in quality of life evaluations can be divided into general, specific and mixed types. The general surveys assess physical, psychological and intellectual functions, independently of health and coexisting diseases, and can be applied in the general population. However, it is recommended to use disease-specific scales, such as the Sickness Impact Profile, Nottingham Health Profile and Medical Outcomes Survey Short Form 36 (SF-36), WHOQOL 100, and Quality of Life (QOL) by Ferrans and Powers in the general version (Chrobak, 2009).

Short Form-36 (SF-36) is the most often used. The SF-36 was developed to measure eight of the most important areas of health. The results from the SF-36 enables comparisons across a broad range of conditions, and between studies on health-related QOL in the same settings [4]. It contains 36 items grouped into 8 domains in the areas of physical health (physical functioning, physical role limitation, bodily pain, general health) and mental health (vitality, social functioning, emotional role limitation, mental health). Each domain is scored from 0 to 100 points, with higher scores indicating a better HRQOL. Two summary scores, a physical component and a mental component, are obtained as mean values calculated from the appropriate domains (Ware et al., 1992; 1993).

Definition and evaluation of physical activity

Physical activity is one of the factors that affects the health of patients before and after transplantation. Physical activity is usually associated with a significant improvement in functional abilities and health, and can often prevent or reduce the severity of certain disease. The results of numerous studies affirm that regular physical exercise undertaken at different intensities increases the resistance and exercise capacity of most patients in

almost all groups following transplants (kidney, lung, liver, heart, bone marrow). With properly selected physical activity, transplant recipients can obtain results comparable to healthy individuals at a similar age (Kjaer et al. 1999).

One method of assessing physical activity is via a questionnaire for specific ages, conditions and types of activity (regular, daily and weekly). Questionnaires that evaluate shorter periods of time are more accurate; such data allows assessment of the energetic consumption of the body, which is important in evaluating the intensity of the effort for disease prevention. It is important to use simple, inexpensive and easy to perform questionnaires. Each type of physical activity can be expressed in MET (metabolic equivalent) units, counting intensity by the number of days and time in minutes. MET is a unit of energy related to oxygen consumption at rest, i.e. 3.5ml O₂/kg/min [22].

The common questionnaires in adult studies are: Minnesota Leisure Time Physical Activity Questionnaire (MLTPAQ), Paffenbarger Physical Activity Questionnaire (PPAQ), Stanford Usual Activity Questionnaire (SUAQ) and the Seven-Day Activity Recall (SDPAR). MLTPAQ covers physical activity in leisure time over the last 12 months. It contains several categories of activity: walking, general activity, water sports, winters sports, garden activity and housework. The intensity of activity is divided into 3 degrees: low (<4 MET), medium (4–6 MET) and large (>6 MET). The PPAQ questionnaire seeks information about activity in the past year as well as in the last week, but with no specific kinds of sports or housework, and is used to describe usual physical activity. The Stanford Usual Activity Questionnaire assesses activity in leisure time in the last 3 months, based on "yes" or "no" answers. The intensity of physical activity is described as moderate, high or very high. The SDPAR questionnaire is based on activity during occupation and leisure time in the last 7 days and categorizes small (<4 MET), medium (4–6 MET) and high activity (>6 MET) (Desai et al., 2008; Nowak, 2006; Pereira et al., 1997).

Firstly, we believe that this is an opportune moment to undertake a systematic review of post LTx QOL, in which particular attention is paid to studies using the SF-36. We review specific aspects of QOL after LTx, including available data on whether gender influences post LTx QOL, and review employment as a marker of QOL. Then we evaluate the impact of selected aspects of physical activity in patients following liver transplantation.

Assessment of health-related quality of life studies using the SF-36 in LTx patients

Several studies have shown that HRQOL improves considerably following LTx. Nevertheless, transplant recipients demonstrate lower HRQOL scores and remain less physically active than the general population (Cordoba et al., 2003; Hauser et al., 2004; Younossi et al., 2000; 2001; Belle et al., 1997; Bona et al., 2000; Gross, 1999). This refers in particular to those subjects with liver cirrhosis complicated by hepatic encephalopathy, ascites or pruritus (Arguedas et al., 2003; Les et al., 2010; Marchesini et al., 2001; Wunsch et al., 2013). However, several HRQOL parameters are also impaired in non-cirrhotic patients with chronic liver diseases, such as those suffering from primary biliary cirrhosis (PBC) (Mells et al., 2013; Selmi et al., 2007; Huet et al., 2000). QOL improved following liver transplantation in all domains compared to the preoperative status (Sainz-Barriga et al., 2005; Aberg et al., 2012; Dupuis-Girod et al., 2010; Sirivatanauksorn et al., 2012).

Physical function is a strong benefactor of liver transplantation (Dupuis-Girod et al., 2010). Patients report reductions in feelings of loneliness, anxiety and hopelessness, allowing a higher quality of social interactions (Duffy et al., 2010). Sainz-Barriga et al. reported improvements in all domains of QOL except the psychological domain (Sainz-Barriga et al., 2005). Similarly, Bravata et al. (2001) in meta-analysis concluded that generally there were improvements in the patients' general health, physical health, daily activity functioning and sexual functioning. There was, however, less consistent evidence of improvement in psychological health, including social isolation

and social functioning. Those findings are consistent with studies on recipients of other organ transplants (lung, kidney and heart) which also found the post transplantation quality of life of organ recipients is better than their pre-transplantation quality of life, particularly in physical health domains (Bravata et al., 1999).

In a Danish study published in 2002, 130 liver transplant recipients were assessed via SF-36 against the Multidimensional Fatigue Inventory and Hospital Anxiety and Depression Scale. They self-reported poorer health than the general population in physical but not in mental areas, and they experienced physical rather than mental fatigue. Diagnosis was found to be a predictor of postoperative physical function and fatigue because patients with an alcoholic or cryptogenic cirrhosis background had significantly poorer physical function and experienced more physical fatigue than patients with other diagnoses. Work status and survival time after LTx had a significant effect on post-operative physical function and fatigue – occupation and a post LTx time of 4 to 5 years were associated with better physical function and less physical fatigue than not working and a shorter post-LTx time (Aadahl et al., 2002).

Gender differences

Analyzing the gender of patients, Kober et al. reported that men had lower QOL scores after LTx than women (Kober et al., 1999). In another composite analysis published in 1999, Bravata et al. concluded that there were no differences between the sexes in post-LTx QOL, although the authors commented on the scarcity of studies dealing with this topic (Bravata et al., 1999). Moore came to the same conclusion in a single-center prospective study of 10 LTx recipients compared to normal controls (Moore et al., 2000).

Cowling reported a study specifically designed to consider whether gender influenced QOL outcome after LTx (Cowling et al., 2004). Among 88 male and 61 female LTx recipients who matched for prevalence of HCV infection and who had received QOL assessment pre-LTx, men displayed higher levels of health-related QOL than women at 1 and 2 years following LTx (Cowling et al., 2004). The differences were partially corrected after adjustment for educational level. A similar result was reported by Spanish investigators who reported that psychosocial adjustment after LTx was reported higher in males compared to female recipients (Blanch et al., 2004). Similarly, in research by Kotarska et al. HRQOL was significantly worse in female patients in the majority of the SF-36 domains (Kotarska et al., 2014).

Employment

There is a clear consensus in literature that patients are more likely to feel better after liver transplantation if they were professionally active after the surgery. The possibility to return to work after liver transplantation also depends on the type of work previously held (Loinaz et al., 1999; Sahota et al., 2006; Adams et al., 2006). Interestingly, despite the socio-cultural differences that could affect work patterns and perceptions of QOL, these same results were found among transplant recipients in Japan (Kita et al., 1996), Taiwan (Shih et al., 2000), Sweden (Hellgren et al., 1998) and the United States (Bravata et al., 2001).

According to the study carried out by Aadahl et al. (2002), patients with a low PF (physical functioning)) are often unemployed and more frequently experience fatigue than those engaged in any educational or working activity. An association between external stimuli through work and a sense of fatigue is also suggested in a Dutch study, which observed that an unemployed patient is less stimulated/ motivated, and by being less active is more exposed to fatigue; thus, the patient has a reduced physical function (de Rijk et al., 1999). Patients who return to work have a better QOL perception.

The majority of patients undergoing liver transplantation are of working age (28–59 years) at the time of surgery, with up to half being employed at the time of follow-up. The overall rate of employment declined after 5 years, with 67% retired at 8 years (Sainz-Barriga et al., 2005; Aberg et al., 2012). Across the studies assessing employment, patients returning to work post-operatively reported higher QOL scores (Sainz-Barriga et al., 2005; Aberg et al., 2012; Cowling et al., 2000). Employment status differed according to the etiology of the liver disease. Rates of resumption of work were highest in primary sclerosing cholangitis, and lowest in acute liver failure, primary biliary cirrhosis and alcoholic liver disease (Ho JK et al., 2006).

Assessment of physical activity after liver transplantation

Common to all candidates before transplantation is an impaired physical performance level that not only interferes with the ability to perform leisure-time exercise, but often also limits the ability to perform even simple physical tasks such as climbing stairs (Badenhop, 1995). It has been widely described that after receiving a donor organ these patients reported improved quality of life and were frequently able to successfully return to employment (Tarter et al., 1991).

The US Surgeon General's Report on Physical Activity and Health states that "regular physical activity appears to improve health-related quality of life by enhancing psychological well-being and improving physical functioning in persons compromised by poor health" (Office of the US Surgeon General, 1996). This report also states that regular physical activity reduces many of the cardiovascular comorbidities and risk factors often seen in longer term transplant recipients. Thus, it seems justified to further investigate the contribution of physical activity in HRQOL. Improvements in self-related physical functioning result from exercise training in other patient populations (Painter et al., 2000) and it is well documented that self-reported physical functioning is highly predictive of outcomes (e.g. hospitalization and mortality).

Health-related quality of life and physical activity

Systematic physical activity contributes to better QOL (Masala et al., 2012; Dupuis-Girod et al., 2010; Rongies et al., 2011; Painter et al., 2001; Kirchner et al., 2006). Greater involvement in social and physical activities is attributed to the amelioration of physical symptoms, fatigue and worry related to CLD (Sirivatanaucksorn et al., 2012). Active patients achieved better scores in the domains of physical functioning, bodily pain, general health, social functioning, emotional role limitations, and physical and mental component summary scores. The physical component summary scores of active individuals achieved levels similar to the general population.

Physical activity after surgery is also associated with health benefits in addition to QOL, such as decreases in surgical complications and new onset comorbidities following surgery (Masala et al., 2012; Painter et al., 2001). Painter et al. report significant differences in SF-36 scores between transplant recipients who were physically active and those who were sedentary. In another study of the same group from 2001, they indicated that physical activity is related to HRQOL after LTx independently of other coexisting medical conditions. Patients who participated in regular physical activity had significantly higher scores on all physical scales and physical component scale (PSC). The regression model, which included age, gender, time post transplantation, re-transplantation, recurrence of hepatitis C and a number of comorbid conditions, showed that both the number of comorbid conditions and participation in physical activity were significant independent contributors to the physical functioning scale and PCS (Painter et al., 2001; Lubkowska et.al., 2015).

Gender differences

Payne demonstrated that regular physical activity improves the general health of patients after liver transplantation (Payne et al., 1996). Kotarska et al. noted that female patients remained significantly less active than male subjects. In many reports males reveal a higher level of activity in all age groups. Men are more likely to undertake regular exercise and more frequently (Kotarska et al., 2014; Malina, Bouchard, 2003; Ainsworth, 2000). It has been found that younger patients after LTx are more physically active. Overweight and obesity reduce physical activity and deteriorate the quality of life (Painter et al., 2001; Osiński, 2002). Although an age-related decrease in fitness and exercise capacity is physiologically inevitable, this may occur at a different pace and intensity and may even be delayed by a maintained or increased physical activity (Osiński, 2002). Studies confirm that obesity and overweight in patients after LTx coincides with low levels of physical activity. They also show lower levels of physical activity among Polish women, which could be related to their lifestyle. The etiology of the disease and time following transplantation had no influence on the physical activity of individuals.

Employment

Low physical functioning is consistently reported following transplantation and is related to employment status, as well as overall quality-of-life ratings post transplantation. (Dew et al., 1997; Nicholas et al., 1994; Hicks et al., 1992; Hellger et al., 1998; Hunt et al., 1996). Reported symptoms before LTx include weakness, loss of range of motion, pain, and arthritis, primarily in the lower extremities. These symptoms may lead to limitations in physical activity and physical functioning, resulting in quality-of-life levels lower than those of the general population (Hellgren et al., 1998; Hunt et al., 1996; Bryan et al., 1998). Given the significant deterioration in function associated with physical inactivity and end-stage liver disease, it is reasonable to speculate that increased physical activity would attenuate or alleviate these symptoms post transplantation.

We earlier reported significant differences in SF-36 scores between transplant recipients who were physically active and those who were sedentary (Painter et al., 1997). Patients undertaking their professional work had significantly better SF-36 scores, mainly related to the physical aspects of well-being (i.e. physical functioning, physical role limitation, bodily pain, physical component summary and emotional role limitation) and were significantly more physically active than those out of work (pensioners). These observations are in agreement with selected studies in which persons that had an active work life had a significantly better HRQOL compared to those out of work (Masala et al., 2012; Aberg et al., 2012; 1995; Bownik et al., 2009). Liver transplant recipients experienced fatigue more frequently and demonstrated lower SF-36 physical functioning scores than those engaged in any educational or working activity (Aadahl, Hansen, 2002). This has been attributed to the fact that professional work provides external stimuli, and assists in the return to a normal lifestyle and social integration (de Rijk et al., 1995). Also, fulfillment of professional tasks and work satisfaction enhance their sense of independence. Thus, patients who remain out of work may potentially be less motivated and have more impaired physical activity than those with an active work life. Kotarska noted a significantly worse HRQOL in female patients in the majority of SF-36 domains (Kotarska et al., 2014).

Discussion

Traditionally, both clinicians and researchers have been mainly interested in two outcomes of liver transplantation: survival rate and postoperative complications. Liver transplantation is beneficial for long-term QOL as it provides persistent relief of symptoms. Survival rates after liver transplantation continue to improve across a majority of indicators, leading to increasing attention being placed on the well-being of patients after the procedure. However, compared to the standard population, LTx patients show considerable deficiencies, an observation that has been supported by a reduced QOL in specific patient cohorts and in particular domains. Moreover, physical activity has been demonstrated to be of significance, not only in the assessment of fitness levels, and could also be of importance in long term recovery processes following major surgical operations. Functional domains such as employment, emotional role limitation and physical activity are significant for liver transplant patients who are often young and of working age.

In the long-term, overall QOL scores and general health perception remain enhanced and comparable to the general population. However, physical functioning continues to be inferior compared with the general population despite marked improvements from preoperative physical functioning. Suboptimal physical health is likely to be a major contributor to the frequency of surgical morbidity, both early and late, compared to the general population (Yang et al., 2014).

It must be emphasized that the level of physical activity following transplantation is also an indicator of a patient's freedom from disease and capacity beyond undertaking normal daily activities. Clinicians may consider encouraging physical activity following surgery to improve HRQOL in addition to the well-known benefits of physical activity. Inpatient post-operative rehabilitation would be a useful consideration to optimize physical function (Cortazzo et al., 2005; MacDougall et al., 1980).

It can be assumed that a decrease in patient's physical activity may be related to the fact that they had not exercised much before the procedure and were still unwilling to exercise. They may also have unfounded fears regarding the adverse effects of post-procedure systematic exercise.

The systematic and reliable assessment of quality of life and physical activity in patients can bring important information about the areas which require significant changes. Such an assessment is increasingly often an important endpoint of many clinical trials. However, a lack of standardized testing methods for the assessment of quality of life and physical activity in patients after liver transplantation makes it difficult or impossible to compare studies from different centers, as well as preventing referencing results between similar studies.

Therefore, further research is necessary, as the information obtained during such studies can be of great use in the overall assessment of patients in terms of their physical and mental health, making it a valuable addition to the medical examination. This is especially important since most patients assess their physical and mental state prior to transplantation as poor.

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