



Review Article

QUALITY OF LIFE AFTER LIVER TRANSPLANTATION

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Abstract

We have searched articles published in various journals world wide on quality of life (QoL) after liver transplantation through internet; 38 articles were available through our searching process. After reviewing all papers we have found that there is no transplant specific assessment tool for measuring QoL after liver transplantation. General tools are used for assessment of QoL of these patients. Pretransplantation QoL are severely affected when compared to normal healthy volunteers. Hepatocellular carcinoma and cholestatic etiologies have higher QoL scores than those related to alcohol or viral hepatitis. Post-transplantation QoL scores are not affected by the etiology of the original liver cirrhosis, but transplant recipient scores continue to remain significantly lower than those of healthy patient controls. The QoL scores improve during initial time after liver transplantation, but decreases in the long term. It may be due to decreases in the physical function and bodily pain domains as the patient's age increases, develops osteoporosis from long-term intake of steroids, and chronic rejection process. It is also addressed that QoL is not good in patients with Hepatitis C after liver transplantation. The development of a QoL assessment tool specific to transplantation could help to more accurately assess factors that alter post-transplantation QoL.

Introduction

It is essential to understand the quality of life (QoL) after surgery for any disease, particularly important in liver transplantation (LT) recipients because the magnitude of the program is huge. The surgery involves two lives in case of living donor related liver transplantation (LDLT), one life and brain death related donor in case of deceased donor liver transplantation (DDLT). A lot of investigations are needed for selecting

the donor and also for checking the fitness of the recipient. The availability of suitable donor liver is also extremely less. The complexity of law for procurement of donor liver makes the liver transplantation program more difficult. A good infrastructure, huge skilled manpower, requirement of special instruments, and pre-, per-, postoperative medications makes the surgery more expensive for patients. Considering these facts it is important to know the QoL after liver transplantation. If the QoL is not favorable the existence of this program will be questionable; on the contrary if it is favorable the question of more expansion of the program will come ahead. There are numerous assessment tools for measuring QoL after LT published in various journals. Studies also published on the comparison result of QoL in cirrhotic patients before LT and QoL after LT using these measurement tools. Valid articles published on these issues are collected

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for discussing the pros and cons of quality of life after liver transplantation.

QoL tools

There are a number of tools used to measure QoL in transplant recipients¹⁻³

- a) Generic assessment tools; i) Medical Outcome Short Form 36: (role physical, bodily pain, physical functioning, general health, vitality, social functioning, role emotional, and mental health). ii) Age-specific assessment tool (physical function, self-care, depression/anxiety, cognition, sexual function, and life satisfaction). iii) Sickness Impact Profile (sleep and rest, emotional behavior, body care and movement, home management, mobility, social interaction, ambulation, alertness, behavior, communication, work, recreation and pastimes, and eating).
- b) Specific assessment tools; Chronic Liver Disease Questionnaire (abdominal symptoms, activity, emotional function, fatigue, systemic symptoms, and worry).
- c) Mental health-focused tools: Beck Depression Inventory (depression, anxiety, hostility, phobic anxiety, paranoid ideation, somatization, obsessive compulsiveness, and interpersonal sensitivity). d) Functional performance tools (Functional performance by the measurement of observable characteristics of physical functioning at 10-point intervals). The most widely used generic QoL instrument is the Short Form 36 (SF-36)⁴. Specifically, the SF-36 assessment focuses on the evaluation of disease effects on physical, functional, emotional, and social categories of a patient's life⁴. Scores from each dimension are then transformed into a scale in which 100 represents good health and 0 represents poor health. Sixty-eight percent of the general population is expected to score between 40 and 60. Serious depressive symptoms would be expected to decrease the mental health scale by 25 to 30 points; a chronic medical condition is associated with a physical functioning scale decrement of 20 to 25 points. In the last decade, the SF-36 survey has become the most frequently used QoL instrument for LT recipients. The QoL of patients with liver disease is assessed with Chronic Liver Disease Questionnaire (CLDQ)⁵. The CLDQ includes 29 items separated into 6

domains (abdominal symptoms, activity, emotional function, fatigue, systemic symptoms, and worry). These tools were used in various institutes worldwide to study the QoL in patients with cirrhosis before transplantation and after transplantation. We have collected several published articles and discussed on pre-transplant QoL, the effect of LT on QoL within first 6 months, the effect of LT on QoL in the long term, the effect of LT on QoL in patients with hepatitis C, the effect of LT on Employment and QoL and the effect of LT on Gender.

Pre-transplant QoL

Several studies assessed the QoL of cirrhotic patients and they found that it is clearly compromised in patients with cirrhosis when compared with the general population. In a study Saab et al.⁶ found that ascites and/or encephalopathy (component of Child-Turcotte-Pugh score) were significantly correlated with QoL score. These findings were confirmed by a study by Estraviz et al.⁹ showing that Child-Turcotte-Pugh (CTP) classifications could be correlated with pre-transplantation QoL scores. The study found that CTP class A patients had significantly higher overall QoL scores than CTP class C patients. Specifically, CTP class A patients had significantly higher scores in the SF-36 physical functioning, general health, vitality, and social functioning domains as well as its mental summary component in comparison with CTP class C patients. In another study by Kanwal et al.⁸ showed that QoL scores actually predicted mortality in patients with cirrhosis. All these studies support that the severity of liver disease correlate with QoL scores.

The etiology of liver disease also seems to affect pre-transplantation QoL scores. Estraviz et al.⁹ compared QoL of patient with alcohol-induced hepatitis, hepatitis B virus (HBV), hepatitis C virus (HCV), hepatocellular carcinoma (HCC), and cholestatic etiologies of liver cirrhosis prior to OLT. The study found significant differences between the different etiologies in all areas of SF-36 domain QoL scores except the bodily pain domain. Within the physical functioning domain, the physical role domain, and the physical summary component of the SF-36, QoL scores were highest for the HCC patients, followed by those with cholestatic disease and then those with HBV/HCV viral etiologies and the lowest scores were held by the patients with alcohol-induced cirrhosis⁹. For the vitality, social functioning, emotional role, mental health, and general

health domains as well as the mental summary component scores of the SF-36, QoL scores were again highest for HCC and cholestatic patients, but within these domains, patients with alcoholic-induced cirrhosis had higher QoL scores than patients with HBV/HCV-induced liver cirrhosis.

LT effects on QoL within the first 6 months

QoL in cirrhotic patient is decreased before LT and it varies among the etiology of cirrhosis as discussed in above section. In contrast, during the first 6 months after LT the overall QoL is increased, and the etiology of liver cirrhosis does not appear to affect post-transplantation QoL scores. Estraviz et al.⁹ showed that at 6 months post-LT, mean QoL scores were no different between HCC, cholestatic, alcohol-induced, and HBV/HCV indications for LT. This change from QoL differences observed before transplantation was explained by HBV/HCV and alcohol induced cirrhosis patients experiencing significantly larger QoL score gains within the general health, physical functioning, bodily pain, vitality, and social functioning domains as well as the physical summary component of the SF-36 in comparison with the HCC and cholestatic liver disease patients⁷. Similarly, at 6 months post-LT, there were no significant differences observed in the mean QoL scores between the observed CTP groups. This was again explained by pre-LT CTP class B and C patients achieving much greater QoL score gains postoperatively in comparison with CTP class A patients¹⁰. A study by Bryan et al.⁷ also confirmed that CTP class C patients experience significantly larger QoL score gains in comparison with CTP class A patients after LT. Studies show that SF-36 QoL scores remain significantly lower for LT recipients compared to healthy patient controls^{7,11,12}. However, multiple studies show that LT recipients do enjoy statistically significant increased QoL scores early after LT in comparison with pre-transplantation scores¹³⁻¹⁶. Telles-Correia et al.¹³ recently showed that at 1 month after LT, there is a statistically significant improvement in the SF-36 mental and physical component QoL scores in comparison with the scores before LT. Similarly, Ratcliffe et al.¹⁴ showed that at 3 months post-LT, there is a statistically significant increase in QoL scores in all SF-36 domains except bodily pain. A study by Younoussi et al.¹² showed increased QoL scores in every SF-36 domain within the first 6 months post-LT. Likewise, Krasnoff et al.¹⁵ studied post-LT QoL scores at 2, 6, 12, and 24 months

after LT. The study found that there was a significant increase in SF-36 physical function, role function, bodily pain, and general health domain scores at both 2 and 6 months.

LT effects on QoL in the long term

However, these widespread gains in QoL scores within first 6 months are not universally sustained in the long term, and improvements in QoL scores appear to have several limitations. In a systematic review of the longitudinal studies comparing pretransplant and posttransplant SF-36 physical domain QoL scores, Tome et al.¹¹ found improvements in the SF-36 general health, physical function, and social functioning domain scores in the post-LT group in comparison with pre-LT scores. The study also found significant improvements in the mental health domains, specifically in the depression and anxiety QoL scores. However, by 1 year post-LT, SF-36 mental health domain QoL scores had plateaued and actually decreased beyond 1 year post-LT. Similarly, a study by Goetzmann et al.¹⁶ found that although LT recipients experienced increased QoL scores within the SF-36 physical function, role physical, bodily pain, social function, and role emotional domains at both 6 and 12 months post-LT, mental health and social function domain QoL scores began to decline by 12 months post-LT. Likewise, Ratcliffe et al.¹⁴ aforementioned study found that by 24 months after LT, all prior QoL score improvements seen at 3 months were sustained except those in the mental health and role emotional domains, both of which began to decline at that time. These findings were confirmed by multiple studies showing that depression and anxiety QoL scores significantly improve during the 6 months after transplantation, but these higher scores plateau by 1 year post-LT^{11,17,18,20}. In fact, multiple studies have shown QoL scores measuring depression, anxiety, and overall psychological well-being actually begin to worsen during post-operative years 1 through^{5,21-23}. Thus, even years after LT, QoL scores of LT recipients continue to be lower than those of unaffected controls in the general population, most specially in the mental health domains^{7,9,11}. Other factors besides the decreases in the mental domain QoL score also negatively affect long-term QoL after LT. During postoperative years 1 through 5, episodes of acute cellular rejection and patient age over 60 years decrease QoL scores by decreasing both the physical functioning domain and physical component scores

of the SF-36^{11,24,25}. Krasnoff et al.¹⁵ also showed that patients' SF-36 general health domain QoL scores plateau 12 months after LT. Very few studies have evaluated LT effects on QoL scores beyond 5 years after LT. One study by Desai et al.²⁵ evaluated OLT-QoL scores between postoperative years 10 and 30. Beyond 10 years post-OLT, transplant age over 60 decreases SF-36 physical functioning and role physical domain QoL scores. Osteoporosis decreases QoL scores through decreases in the physical function and bodily pain domains as well as decreases in the physical component and mental component scores²⁵. In addition, post-LT complications and chronic rejection decrease QoL scores via decreased physical function, bodily pain, role physical, social functioning, and role emotional domain scores as well as decreased mental component summary scores of the SF-36.2. Concern has been raised about the effects of the etiology of liver disease on long-term QoL scores, particularly among LT recipients with alcohol-induced cirrhosis as an indication. However, Cowling et al.²⁶ showed that alcohol-related and non-alcohol-related LT recipients appear to experience similar QoL scores, and they return to society to lead similarly active and productive lives for years after LT. In fact, studies show that HCV appears to be the only etiology of liver disease to negatively affect long-term QoL scores.^{13,18,23}

It is clear from above discussion that both mental and physical component of QoL decreases as the time passes after LT. The reason may be due to ageing process, development of osteoporosis, long-term use of immunosuppressive drugs, development of chronic cellular rejection, recurrent infection of transplanted liver by HCV infection and alcohol induced liver cirrhosis by resumption to alcohol consumption.

HCV induced liver disease and QoL after LT

HCV is the most common indication for LT in the United States and Europe. However, recurrent infection is universal, and recurrent disease can lead to graft

failure in approximately 20% of transplant recipients within 5 years. Studies suggest that QoL scores experienced by LT recipients transplanted for HCV are lower than those of LT recipients transplanted for other indications such as HBV or alcoholic cirrhosis.¹⁹ These findings suggest that diseases that recur appear to have a particularly pronounced effect on patient QoL scores post-LT. Indeed, multiple studies have shown that QoL scores for recipients transplanted

for HCV are lower within the SF-36 QoL bodily pain and social function domains. In addition, both the physical and mental component SF-36 QoL scores are also low^{16,22-24,28}. However, studies designed to investigate this effect have shown that decreased QoL scores do not correlate with the timing of any actual physical consequences of recurrent liver disease, the statistical occurrence of cirrhosis, or any medical complications of a patient's disease recurrence. Thus, what accounts for patients reporting lower generalized QoL scores? It appears that the impact of HCV recurrence on QoL as reported by post-LT patients is complicated by recipients' knowledge of their own viral status. For instance, a study conducted by Rodger et al. found that patients informed of HCV recurrence before taking QoL surveys scored lower than those with HCV recurrence who did not know their serostatus^{29,30}. Patients assessed at both 6 and 12 months post-LT show that the psychological stress associated with disease recurrence is perceived as being more disabling and is a greater contributor to depression than any physical impairment secondary to disease sequelae^{23,31}. In nontransplant patients, HCV recurrence is known to decrease QoL, usually because the antiviral therapy used to treat this recurrence is known to decrease QoL scores during treatment^{29,32,33}. However, LT recipients transplanted for HCV report this decrease in QoL with the knowledge of HCV recurrence alone, without antiviral therapy or physical sequelae of recurrent disease.

Employment and QoL after LT

A surrogate marker of recipients' post-transplant functional status in society may be employability. Approximately 45% of LT recipients actually return to work after transplantation, and studies have demonstrated that better QoL is associated with post-transplantation employment^{16,32}. In a study of over 300 LT recipients, Aberg et al.³⁴ showed that employed LT recipients experienced better QoL than unemployed recipients. The study found that patients transplanted for chronic liver diseases such as HBV or HCV returned to work in numbers similar to those of patients transplanted for acute liver failure and HCC³². Thus, the transplant indication does not appear to be a contributing factor to post-LT employment rates³². Likewise, the severity or duration of liver dysfunction prior to transplantation does not appear to correlate with employment rates after LT^{32,35}. Aberg et al.'s study did find that patients transplanted at a younger

age were more often able to return to work after LT³². It also showed that an earlier return to employment after LT was associated with higher QoL scores (eg, patients who returned to work in 6 months had higher QoL scores than those who waited 1 to 2 years to return to work)³². Saab et al.⁶ also studied employment and its effects on QoL after LT. The study found that employment rates after transplantation were higher in LT recipients who did not receive disability income coverage prior to transplantation, in patients who had health maintenance organization (HMO) or preferred provider organization (PPO) insurance, in patients who worked at least 20 to 40 hours per week prior to transplantation, and in patients who did not have diabetes. The study concluded that lower rates of post-LT employment were associated with lower QoL scores within the physical health domains, specifically the SF-36 QoL physical functioning and role physical domains⁶. Thus, both studies concluded that employment after LT is an indicator for higher QoL scores. In addition, lack of employment after LT appears to be more greatly influenced by prior socioeconomic factors rather than severity of pre-transplantation or post-transplantation disease^{6,32,35}.

Gender and QoL after LT

Several studies have examined the effects of gender on post-LT QoL scores, and there appear to be conflicting data. A meta-analysis conducted by Bravata and Keeffe³⁶ concluded that there were no significant differences in QoL score reports on the basis of gender, but the study commented on the scarcity of reports in the literature on the topic. Moore et al.³⁷ concurred with Bravata et al.'s findings, but their study had an extremely small patient population, with only 10 LT candidates and 10 healthy controls. In contrast, Kober et al.³⁸ reported that men actually had lower QoL scores after LT than female recipients. The largest study to date, conducted by Cowling et al.²⁶ reported that female gender lowers QoL scores post-LT. The authors compared 88 male and 61 female LT recipients and showed that male recipients reported overall higher QoL scores than females²⁶. When they controlled for disparities in education, they found that in the more highly educated population, males continued to have higher QoL scores than females. Among the less educated patients, there were no differences found between male and female QoL scores²⁶. Thus, studies with larger patient populations that also match socioeconomic factors such as education, income

levels, and marriage are needed before gender influences on QoL post-LT can definitively be determined. No studies have been explained why QoL after LT is better in male and educated peoples than female and non educated or less educated peoples. More studies may be required on this issue for getting the appropriate answer.

Limitations

There are several limitations for interpreting QoL data. First of all, data are based on patient self-reporting. Secondly, many studies are performed in the outpatient settings. Thus, patients who are lost from transplant program, or died or too ill to be seen as outpatients may not be captured in many quality of life data. This inherently excludes patients in poor condition at the time of assessment as well as those who have died. The third limitation to interpret QoL is the timing of assessment because the QoL assessment started after discharge from the hospital in follow up visit. The recipient, who had complications after LT, had physical, mental, social and financial sufferings. These are not reflected in those studies. The fourth limitation is that there is no transplant-specific QoL instrument routinely used. Most studies used SF-36 or disease-specific instruments that are related to one particular disease (eg, the CLDQ for recurrent hepatitis C). Finally economic and education status are not routinely assessed in many QoL instruments. Both economic status and level of education affect not only a patient's medical decision making but also a patient's perception of quality of life.

Conclusion

On the basis of above discussion we can conclude that pretransplantation QoL scores are affected by the etiology of liver cirrhosis, with hepatocellular and cholestatic etiologies having higher QoL scores than those related to alcohol or viral hepatitis. Post-transplantation QoL scores are not affected by the etiology of the original liver cirrhosis, but transplant recipient scores continue to remain significantly lower than those of healthy patient controls. During the first 6 months after liver transplantation, the majority of physical and mental components of QoL scores improve, but these increases are not sustained in the long term. At 1 year after liver transplantation, emotional and mental QoL scores begin to decrease. During postoperative years 1 to 5, episodes of acute cellular rejection and patient age over 60 years

decrease physical function and overall QoL scores. Beyond 5 years after orthotopic liver transplantation, age over 60, osteoporosis, and episodes of chronic rejection decrease health-related quality of life scores through decreases in the physical function and bodily pain domains. Hepatitis C as an indication for liver transplantation is an independent factor in decreasing post-transplantation QoL scores. Further studies are necessary that include a complete evaluation of the effects of gender, socioeconomic status, education, and ethnicity in order to better understanding of the factors influencing post-liver transplantation QoL scores. The development of a QoL assessment tool specific to transplantation could help us to more accurately assess factors (such as immunosuppression) that alter post-transplantation QoL.

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