131 Quality of Life in Liver Cirrhosis

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Abstract: Liver cirrhosis is a chronic condition imposing a considerable burden on patients, families, health care, and society. Assessment of health-related quality of life (QOL) is particularly important for these patients in view of the paucity of therapies substantially improving their survival except for liver transplantation. To date several investigators employing numerous generic and disease-specific QOL measurement instruments have reported poor QOL in these patients irrespective of the etiology of liver disease. Apart from the severity and complications of liver cirrhosis several disease-specific symptoms (such as pruritus, muscle cramps, sleep disturbance, sexual dysfunction, fatigue, and gastrointestinal symptoms) have been shown to be of importance in determining QOL in this patient group. Liver transplantation has been repeatedly shown to improve QOL. However, some of the few studies evaluating the impact of other medical interventions on QOL in cirrhotics have demonstrated that various treatment modalities may improve survival or decrease complication risk but they do not invariably improve patients' QOL which stresses the need for rigorous selection of patients suitable for a specific type of treatment. Last, the value cirrhotic patients place on the state of their health differs from that assigned by physicians. Thus, in cost-utility analysis, which is based on quality-adjusted life years, utilities should be based on patient reports.

List of Abbreviations: *AUSQUAL,* Austin quality of life scale; *BDI,* Beck depression inventory; *BSI,* brief symptom inventory; *CC,* compensated cirrhosis; *CLDQ,* chronic liver disease questionnaire; *CLD-QOL,* chronic liver disease quality of life questionnaire; *DC,* decompensated cirrhosis; *GSRS,* gastrointestinal symptom rating scale; *HAD,* hospital anxiety and depression index; *LDQOL,* liver disease quality of life instrument; *LDSI,* liver disease symptom index; *LTX,* liver transplantation; *MELD,* model for end-stage liver disease; *MFI-20,* multidimensional fatigue index – 20; *NC,* non-cirrhotic control patients; *NHP,* Nottingham health profile; *PGWBI,* psychological general well-being index; *QOL,* quality of life; *SF-36,* 36-item short form health survey; *SIP,* sickness impact profile; *TIPS,* transjugular intrahepatic portosystemic shunt

1 Introduction

Liver cirrhosis is defined histologically as a diffuse process with liver cell necrosis/apoptosis, fibrosis, and regenerative nodules. There are several causes of liver cirrhosis, the most common being high alcohol consumption, hepatitis C, hepatitis B, non-alcoholic steatohepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, or autoimmune hepatitis (Sherlock and Dooley, 2002). Cirrhosis (apart from other features peculiar to the cause) results in two major events: hepatocellular failure and portal hypertension. Important complications of liver cirrhosis include, but are not limited to, esophageal varices, ascites, hepatic encephalopathy, hepatic failure with jaundice, and hepatocellular cancer (Sherlock and Dooley, 2002). Cirrhosis has also been associated with varying degrees of malnutrition (Kalaitzakis et al., 2006; Sherlock and Dooley, 2002). Apart from liver transplantation, no specific cure exists for liver cirrhosis to date (*Table 131-1*).

Liver cirrhosis is a chronic condition imposing a considerable burden on families, health care, and society. Assessment of health-related quality of life (QOL), which is meant to give the patients' perspective on the burden of disease, is particularly important for patients with liver cirrhosis because of the paucity of therapies substantially improving survival, other than liver transplantation. Hepatocellular failure and portal hypertension as well as their complications

Table 131-1
Key facts of liver cirrhosis

Liver cirrhosis is a diffuse histological process with liver cell necrosis/apoptosis and replacement of the hepatic parenchyma by fibrotic tissue and regenerative nodules
Liver cirrhosis is mainly caused by high alcohol consumption, hepatitis C, hepatitis B, primary biliary cirrhosis, primary sclerosing cholangitis, autoimmune hepatitis, or non-alcoholic steatohepatitis
Liver cirrhosis might lead to complications such as esophageal varices and variceal bleeding, ascites, hepatic failure with jaundice, hepatic encephalopathy, and hepatocellular cancer
Apart from liver transplantation, no specific cure exists for liver cirrhosis to date

The table summarizes key facts about definition, etiology, complications, and therapy of liver cirrhosis

and various symptoms (pruritus, fatigue, muscle cramps, gastrointestinal symptoms) that frequently accompany liver cirrhosis have, in addition to contributing to morbidity and mortality, adverse effects on the patients' sense of well-being.

2 Assessment of Quality of Life in Patients with Liver Cirrhosis

Assessment of QOL is usually performed by using multi-item questionnaires which are completed by patients themselves thus reflecting their subjective experience of the impact of disease on daily activities and well-being (Borgaonkar and Irvine, 2000). Generic health-related QOL instruments may be used in any population irrespective of underlying disease, whereas disease-specific instruments are constructed for a particular disease. Combining generic and disease-specific instruments in usually recommended as it allows comparisons between diseases and within disease groups (Borgaonkar and Irvine, 2000).

Generic and disease-specific instruments that have been used in different studies evaluating QOL in liver cirrhosis are shown in *Table 131-2*. The most commonly used generic instrument is the 36-item short form health survey (SF-36), a 36-item self administered questionnaire encompassing eight physical and mental health domains and two physical and mental summary scales (Sullivan et al., 2002). The SF-36 has been thoroughly tested for validity and reliability in a variety of patient populations and it may be used to evaluate change in health status over time (Sullivan et al., 2002). To date, four health-related QOL instruments have been constructed for use in patients with chronic liver disease: the chronic liver disease questionnaire (CLDQ) (Younossi et al., 1999), the liver disease quality of life instrument in persons with advanced chronic liver disease (LDQOL) (Gralnek et al., 2000), the liver disease symptom index (LDSI) (van der Plas et al., 2004), and the chronic liver disease quality of life (CLD-QOL) questionnaire (Lee et al., 2008) (*Table 131-1*). The CLDQ, LDSI, and LDQOL were developed in Western patient populations (Gralnek et al., 2000; van der Plas et al., 2004; Younossi et al., 1999) whereas the CLD-QOL was developed in an Asian patient population who live in different social and cultural environment compared to Western patients (Lee et al., 2008). Apart from their English versions, the CLDQ has been validated in German (Hauser et al., 2004b), Italian (Rucci et al., 2005), and Spanish-speaking patients (Ferrer et al., 2006) and the LDQOL in Spanish-speaking patients (Casanovas Taltavull et al., 2003).

Table 131-2

Generic and disease-specific instruments used in different studies evaluating quality of life in liver cirrhosis

Generic instruments
Assessment of health-related quality of life
The 36-item short-form health survey (SF-36) (Hauser et al., 2004a; Marchesini et al., 2001; Younossi et al., 2001b)
Nottingham health profile (NHP) (Bianchi et al., 2003; Marchesini et al., 2001)
Sickness impact profile (SIP) (Groeneweg et al., 1998; Prasad et al., 2007; Tarter et al., 1992)
Austin quality of life scale (AUSQUAL) (Moore et al., 2000)
Quality of life index (Gulberg et al., 2002)
Assessment of mental health
Brief symptom inventory (BSI) (De Bona et al., 2000)
Beck Depression Inventory (BDI) (Bianchi et al., 2005; Singh et al., 1997)
Hospital anxiety and depression (HAD) (Hauser et al., 2004a)
Psychological general well-being index (PGWBI) (Bianchi et al., 2005)
Assessment of gastrointestinal symptoms
Gastrointestinal symptom rating scale (GSRS) (Kalaitzakis et al., 2006)
Assessment of fatigue
Multidimensional fatigue index-20 (MFI-20) (van der Plas et al., 2003)
Assessment of sexual function
International index of erectile function (Toda et al., 2005)
Liver disease-specific instruments
Chronic liver disease questionnaire (CLDQ) (Younossi et al., 1999)
Liver disease quality of life instrument in chronic liver disease (LDQOL) (Gralnek et al., 2000)
Liver disease symptom index (LDSI) (van der Plas et al., 2004)
Chronic liver disease quality of life (CLD-QOL) questionnaire (Lee et al., 2008)

A wide variety of generic and disease-specific questionnaires have been used in studies of health-related quality of life in liver cirrhosis. Relevant references provided in the table are indicative and not exhaustive

3 Liver Cirrhosis and Health-Related QOL

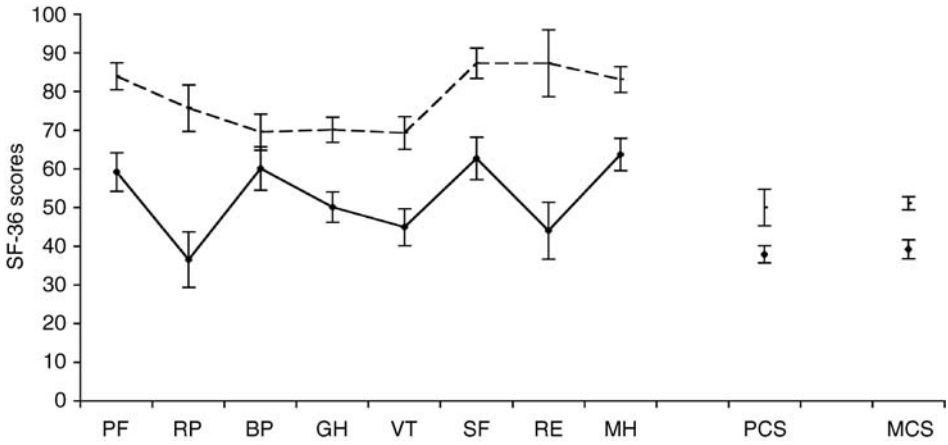
Several studies have shown that both physical and mental dimensions of health-related quality of life are affected in patients with chronic liver disease in general and liver cirrhosis in particular (Bianchi et al., 2005; Hauser et al., 2004a; Kalaitzakis et al., 2006; Marchesini et al., 2001; Singh et al., 1997; van der Plas et al., 2003; Younossi et al., 2001b) (*Figure 131-1*).

4 Etiology of Liver Cirrhosis and Health-Related QOL

Most studies have not detected any difference in health-related QOL indices among patients with liver cirrhosis of different etiologies (Hauser et al., 2004a; Kalaitzakis et al., 2006; Marchesini et al., 2001). However, some controversy exists with some authors reporting that

Figure 131-1

Health-related quality of life assessed as SF-36 domain and summary scores (means and 95% confidence intervals) in patients with liver cirrhosis (continuous line, n = 128) and healthy controls (dashed line, n = 299) (Kalaitzakis et al., 2006) (reproduced with permission from the publisher Taylor & Francis). Lower scores indicate poorer health-related quality of life. Patients with liver cirrhosis showed poorer health-related quality of life assessed by the 36-item short-form health survey (SF-36) compared to controls from the general population. All SF-36 indices and summary scores were significantly lower in patients with cirrhosis compared to controls except that for bodily pain. *SF*-36, the 36-item short form health survey; *PF*, physical functioning; *RP*, role limitations caused by physical health problems; *BP*, bodily pain; *GH*, general health perceptions; *VT*, vitality; *SF*, social functioning; *RE*, role limitations caused by emotional problems; *MH*, mental health; *PCS*, physical component summary; *MCS*, mental component summary. The PCS and MCS are summaries of the physical and mental SF-36 indices



both physical and mental dimensions of QOL are less impaired in patients with cholestatic disease than in those with hepatocellular disease (Younossi et al., 2001b). Also, chronic hepatitis C has been reported to have a negative impact on health-related QOL of end-stage liver disease patients (Kanwal et al., 2004) but patients with hepatitis C cirrhosis have not been found to differ in health-related QOL from patients with cirrhosis of other etiologies (Björnsson and Kalaitzakis, unpublished data). Health-related QOL in hepatitis C is dealt with elsewhere in this book. Patients with alcoholic cirrhosis generally do not differ from patients with other cirrhosis etiologies but those with active alcohol abuse have been reported to have increased psychological distress and increased depression scores compared to abstainers (Bianchi et al., 2005).

5 The Impact of Severity and Complications of Liver Cirrhosis on Health-Related QOL

Factors that have been reported to be associated with impairment of QOL in these patients include cirrhosis severity (Bianchi et al., 2005; Kalaitzakis et al., 2006; Marchesini et al., 2001; van der Plas et al., 2003; Younossi et al., 2001b), complications of portal hypertension such as hepatic encephalopathy (Arguedas et al., 2003; Marchesini et al., 2001), ascites

(Marchesini et al., 2001), hepatocellular carcinoma (Bianchi et al., 2003), daily medications especially loop diuretics (Marchesini et al., 2001), comorbidities (Marchesini et al., 2001), and nutritional status impairment (Norman et al., 2006). A recent large study, in which patients with chronic liver disease (n = 489), compensated liver cirrhosis (n = 391), decompensated liver cirrhosis (n = 84), and transplanted patients (n = 186) were included, showed that all patients with chronic liver disease, including compensated and decompensated cirrhotics, have compromised health-related QOL compared to controls from the general population (van der Plas et al., 2003). However, when compared to patients with chronic liver disease without cirrhosis QOL was impaired mainly in patients with decompensated cirrhosis (*Figure 131-2*). Furthermore, severity of liver cirrhosis expressed as the Child-Pugh and the MELD (model for end-stage liver disease) score has been reported to be related to health-related QOL indices (Kalaitzakis et al., 2006; Kanwal et al., 2004; Saab et al., 2005). Interestingly the Child-Pugh score has consistently been shown to be more strongly associated to health-related QOL than the MELD score (Kalaitzakis et al., 2006; Kanwal et al., 2004; Saab et al., 2005). This may be due to that the Child-Pugh score encompasses ascites and hepatic encephalopathy which have been shown to be independent predictors of QOL in cirrhosis (Arguedas et al., 2003; Marchesini et al., 2001) apart from biochemical parameters whereas the MELD score is derived solely from biochemical parameters.

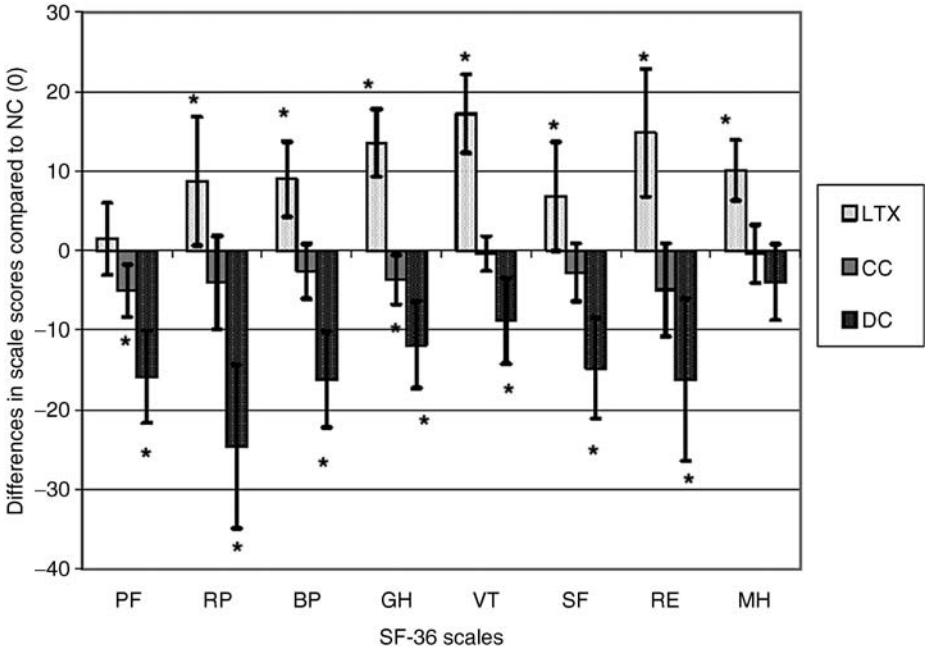
5.1 Hepatic Encephalopathy and Impairment of Health-Related QOL

Patients with liver cirrhosis are prone to develop cognitive dysfunction termed hepatic encephalopathy. Clinical manifestations of hepatic encephalopathy range from subtle intellectual and personality changes to coma (Sherlock and Dooley, 2002). Hepatic encephalopathy is diagnosed according to certain clinical criteria. However, it is well-recognized that even patients without clinically overt hepatic encephalopathy may have subtle cognitive dysfunction identifiable only by means of psychometric tests (minimal hepatic encephalopathy) (Sherlock and Dooley, 2002). Tarter and colleagues applied the sickness impact profile (SIP) and a psychometric test battery to 130 nonalcoholic patients whom they examined before and 3 years after liver transplantation (Tarter et al., 1992). They found that there was a substantial improvement from the pretransplant to the posttransplant periods across almost all dimensions of QOL. Psychometric test scores explained up to 20% of the variance in magnitude of change from pre- to post- surgery. Thus the investigators concluded that severity of hepatic encephalopathy is associated with posttransplantat improvement in QOL (Tarter et al., 1992). Hepatic encephalopathy has also been shown to be independently related to the physical functioning and role-emotional SF-36 domains in a large multicenter study in which 544 patients with cirrhosis were enrolled (Marchesini et al., 2001). In another study investigating the possible effect of hepatic encephalopathy on health-related QOL 160 consecutive patients with liver cirrhosis undergoing pretransplantation evaluation were included (Arguedas et al., 2003). Hepatic encephalopathy was assessed clinically as well as by means of a psychometric test and QOL was assessed by means of the SF-36 (Arguedas et al., 2003). Patients with hepatic encephalopathy (overt or minimal) had decreased physical and mental component summary scores compared to patients without encephalopathy (*Figure 131-3*).

Minimal hepatic encephalopathy has been shown to impair daily functioning as assessed by means of the sickness impact profile in 179 outpatients with liver cirrhosis (Groeneweg et al., 1998). One study by Schomerus et al investigated the potential role of hepatic encephalopathy

Figure 131-2

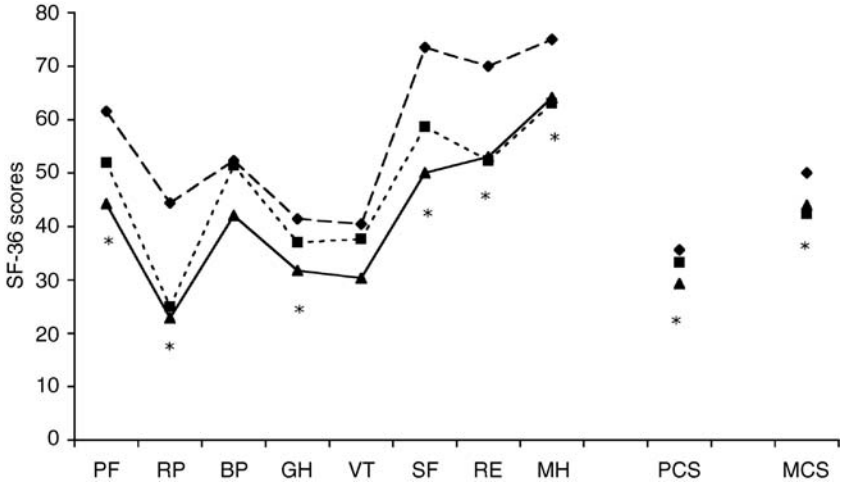
Health-related quality of life assessed as SF-36 domain score differences (means and 95% confidence intervals) between non-cirrhotic patients with chronic liver disease (n = 489) (NC), and patients with compensated liver cirrhosis (n = 391) (CC), decompensated liver cirrhosis (n = 84) (DC), and transplanted patients (n = 186) (LTX). Differences are adjusted for gender, age, educational level, etiology, use of liver disease medication, use of psychopharmaca, and comorbidity (reproduced from van der Plas et al. (2003) with permission). Positive values indicate higher (better) and negative values poorer health-related quality of life SF-36 scores compared to controls (NC, non-cirrhotic patients with chronic liver disease). This figure illustrates that health-related quality of life is impaired mainly in patients with decompensated and not compensated cirrhosis compared to patients with chronic liver disease without cirrhosis (NC). Patients having received a liver transplant have better health-related quality of life in most dimensions compared to NC. * Scale score of subgroup is significantly different ($p < 0.05$) from scale score of controls (NC). *SF-36*, the 36-item short form health survey; *NC*, non-cirrhotic patients with chronic liver disease; *CC*, compensated cirrhosis; *DC*, decompensated cirrhosis; *LTX*, liver transplantation; *PF*, physical functioning; *RP*, role limitations caused by physical health problems; *BP*, bodily pain; *GH*, general health perceptions; *VT*, vitality; *SF*, social functioning; *RE*, role limitations caused by emotional problems; *MH*, mental health. @ 2003 van der Plas et al; licensee BioMed Central Ltd. Open Access Article: verbatim copying and redistribution of this article are permitted in all media for any purpose, provided this notice is preserved along with the article's original URL (http://www.biomedcentral.com/1471–230X/3/33)



in working capacity in patients with cirrhosis (Schomerus and Hamster, 2001). A total of 110 outpatients with liver cirrhosis who were not willingly unemployed were enrolled in the study and underwent extensive psychometric testing. Forty-four percent were receiving disability pension. The authors found that although the working group and the group of patients on

Figure 131-3

Health-related quality of life assessed as mean SF-36 domain score and summary scores in patients with liver cirrhosis without hepatic encephalopathy (dashed line, n = 23), with minimal hepatic encephalopathy (dotted line, n = 36), and with overt hepatic encephalopathy (continuous line, n = 89). Lower scores indicate poorer health-related quality of life. Patients with hepatic encephalopathy (overt and minimal) showed poorer health-related quality of life assessed by the 36-item short-form health survey (SF-36) compared to cirrhotic patients without hepatic encephalopathy. * Statistical significance by analysis of variance. The Child-Pugh score did not differ significantly among groups ($p > 0.05$). *SF-36*, the 36-item short form health survey; *PF*, physical functioning; *RP*, role limitations caused by physical health problems; *BP*, bodily pain; *GH*, general health perceptions; *VT*, vitality; *SF*, social functioning; *RE*, role limitations caused by emotional problems; *MH*, mental health; *PCS*, physical component summary; *MCS*, mental component summary. The PCS and MCS constitute summaries of the physical and mental SF-36 indices. Data from Arguedas et al. (2003)



disability pension did not differ in severity or complications of liver cirrhosis (including overt hepatic encephalopathy) the latter group scored worse in psychometric tests evaluating psychomotor function and personality (Schomerus and Hamster, 2001). It was concluded that minimal hepatic encephalopathy might be implicated in impaired working capability of patients with liver cirrhosis (Schomerus and Hamster, 2001).

5.2 Minimal Hepatic Encephalopathy and Fitness to Drive

Published data suggest that minimal hepatic encephalopathy impairs fitness to drive (Bajaj et al., 2008; Wein et al., 2004). A total of 48 patients with liver cirrhosis (34 with and 14 without minimal hepatic encephalopathy according to psychometric testing) were enrolled in a prospective study evaluating their ability to drive a car by means of a standardized on-road driving test (Wein et al., 2004). Patients with compared to those without minimal hepatic encephalopathy required a higher number of interventions by driving instructors to prevent

accidents (Wein et al., 2004). Patients with minimal hepatic encephalopathy have also been reported to have impaired navigations skills on a driving simulator which is correlated with impairment in response inhibition and attention (Bajaj et al., 2008). In view of these data it is not surprising that a study investigating the reported occurrence of traffic violations and motor vehicle accidents by means of an anonymous driving history and behavior questionnaire which was sent to 200 cirrhotics without overt hepatic encephalopathy and 100 age/education matched controls found that cirrhotics have a higher self-reported occurrence of violations and accidents compared to controls (Bajaj et al., 2007). In the same study minimal hepatic encephalopathy was the only risk factor (odds ratios: 4.2:7.6) for violations and accidents selected in multivariate analysis (Bajaj et al., 2007).

6 The Impact of Cirrhosis-Related Symptoms on Health-Related QOL

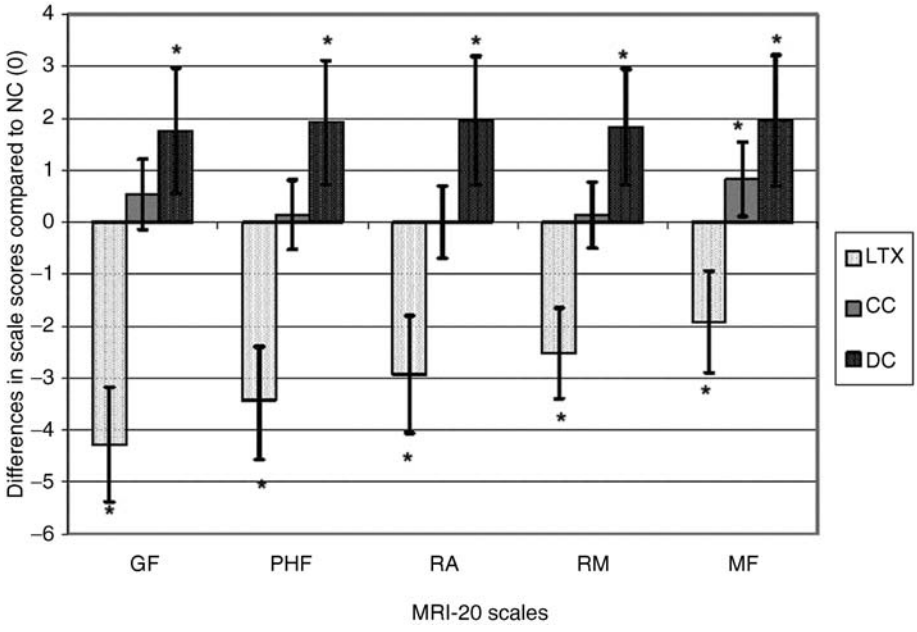
Non-life threatening subjective symptoms of cirrhosis, frequently underscored by physicians, have been reported to be of concern in patients with liver cirrhosis. Thus, disease-specific instruments for assessment of health-related QOL include several symptoms affecting these patients (Gralnek et al., 2000; Lee et al., 2008; van der Plas et al., 2004; Younossi et al., 1999). In a multicenter study assessing QOL in 544 patients with liver cirrhosis, pruritus affected 26% and muscle cramps affected 36% of included patients and were found to be more closely associated with poor QOL than major, even life-threatening events (Marchesini et al., 2001). Sleep disturbance is also common in cirrhosis affecting 48% of these patients and it was found to be unrelated to clinical parameters and cognitive impairment in one study on 44 cirrhotic patients without clinically overt hepatic encephalopathy (Cordoba et al., 1998). Sexual dysfunction is another common complaint among cirrhotics and impotence affects 70% of alcoholic patients with cirrhosis and 25% of non-alcoholic cirrhotic patients ($p < 0.05$) (Cornely et al., 1984). In another study in which 53 male patients with liver cirrhosis were included erectile dysfunction was found to affect 92% of patients (Toda et al., 2005). To date no published study has particularly evaluated sexual dysfunction and its impact on dimensions of health-related QOL in both genders.

6.1 Fatigue and Impairment of Health-Related QOL

Fatigue is another common complaint in patients with chronic liver disease. It has been the object of extensive investigation in patients with primary biliary cirrhosis in whom it is thought to have a negative effect on health-related QOL (Goldblatt et al., 2002; Huet et al., 2000) although fatigue has not been found to be a specific symptom of primary biliary cirrhosis in all studies (Björnsson et al., 2005). However, few of the patients included in these studies had frank liver cirrhosis and published data on fatigue in cirrhosis of other etiologies are scarce. A recent study performed in patients with chronic liver disease (n = 489), compensated liver cirrhosis (n = 391), decompensated liver cirrhosis (n = 84), and transplanted patients (n = 186) showed that all patients with chronic liver disease, including cirrhotic and transplanted patients, have increased fatigue indices compared to controls from the general population (van der Plas et al., 2003). However, when compared to patients with chronic liver disease without cirrhosis fatigue severity was increased mainly in

Figure 131-4

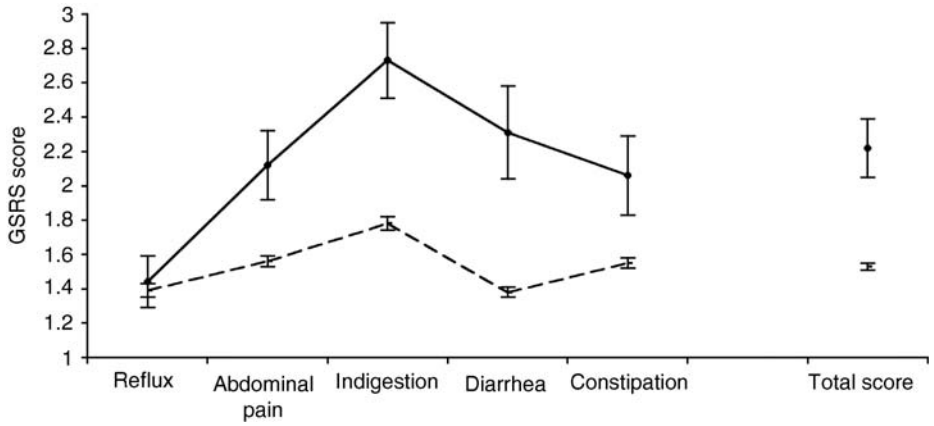
Fatigue assessed as multidimensional fatigue impact-20 scale score differences (means and 95% confidence intervals) between non-cirrhotic patients with chronic liver disease (n = 489) (NC), and patients with compensated liver cirrhosis (n = 391) (CC), decompensated liver cirrhosis (n = 84) (DC), and transplanted liver patients (n = 186) (LTX). Differences are adjusted for gender, age, educational level, etiology, use of liver disease medication, use of psychopharmaca, and comorbidity (reproduced from van der Plas et al. (2003) with permission). Positive values indicate increased and negative values decreased fatigue scores compared to controls (NC, non-cirrhotic patients with chronic liver disease). This figure illustrates that fatigue is increased mainly in patients with decompensated and not compensated cirrhosis compared to patients with chronic liver disease without cirrhosis (NC). Patients having received a liver transplant have decreased fatigue scores compared to NC.* Scale score of subgroup is significantly different ($p < 0.05$) from scale score of controls (NC). *NC*, non-cirrhotic patients with chronic liver disease; *CC*, compensated cirrhosis; *DC*, decompensated cirrhosis; *LTX*, liver transplantation; *GF*, general fatigue; *PHF*, physical fatigue; *RA*, reduction in activity; *RM*, reduction in motivation; *MF*, mental fatigue. @ 2003 van der Plas et al; licensee BioMed Central Ltd. Open Access Article: verbatim copying and redistribution of this article are permitted in all media for any purpose, provided this notice is preserved along with the article's original URL (http://www.biomedcentral.com/1471–230X/3/33)



patients with decompensated and not compensated cirrhosis (*Figure 131-4*). In another recent study in which 83 consecutive patients with liver cirrhosis undergoing pretransplantation evaluation were included, fatigue (assessed by means of the fatigue impact scale) was found to be increased in cirrhotics compared to controls from the general population and it was also associated with impaired QOL in these patients (Kalaitzakis and Björnsson, 2007). Mood disorders and low hemoglobin levels were reported to contribute to fatigue in cirrhotics

Figure 131-5

Gastrointestinal symptom severity assessed as gastrointestinal symptom rating scale (GSRS) scores (means and 95% confidence intervals) in patients with liver cirrhosis (continuous line, n = 128) and healthy controls (dashed line, n = 2,162) (Kalaitzakis et al., 2006) (reproduced with permission from the publisher Taylor & Francis). Higher scores indicated increased gastrointestinal symptom severity. Patients with liver cirrhosis show increased severity of gastrointestinal symptoms as assessed by the gastrointestinal symptom rating scale (GSRS) compared to controls from the general population. *GSRS*, gastrointestinal symptom rating scale



in general whereas in male patients low testosterone was related to increased fatigue severity indices (Kalaitzakis and Björnsson, 2007).

6.2 Gastrointestinal Symptoms and Impairment of Health-Related QOL

Gastrointestinal symptoms are also of concern in patients with liver cirrhosis. In one study (Kalaitzakis et al., 2006), gastrointestinal symptom severity was found to be increased in patients with liver cirrhosis compared to the general population (*Figure 131-5*). Recent weight loss as well as physical and mental dimensions of health-related QOL were independently related to gastrointestinal symptoms (Kalaitzakis et al., 2006).

7 The Impact of Psychological Distress on Health-Related QOL in Liver Cirrhosis

Psychological distress and depression are common in patients with liver cirrhosis (Singh et al., 1997). In one study, the impact of depression on QOL and outcome was investigated in patients with liver cirrhosis undergoing pretransplantation evaluation (Singh et al., 1997). A total of 81 patients were assessed by means of the Beck depression inventory (BDI) and 64% were determined to be depressed according to the Beck depression scores. Depressed patients

did not differ from those without depression in any demographic variable, severity or complications of liver cirrhosis, or survival following liver transplantation. However, the depressed group had significantly poorer perceived QOL compared to non-depressed patients. Among patients not receiving a transplant depressed patients had shorter survival compared to those without depression (Singh et al., 1997). In another study the BDI and the psychological general well-being index (PGWBI) were applied to 156 consecutive patients with liver cirrhosis (Bianchi et al., 2005). Patients with cirrhosis showed significantly lower global and domain PGWBI scores compared to a reference population indicating psychological distress and poor sense of well-being in this group of patients (Bianchi et al., 2005). Also, 57% of cirrhotics had BDI scores suggestive of depression. Logistic regression analysis identified the presence of sleep disorders as the independent variable more frequently associated with low domains PGWBI scores and the severity of liver cirrhosis, expressed as the Child-Pugh score, as the sole variable related to depression as detected by the BDI (Bianchi et al., 2005). The etiology of liver disease was not found to be related to psychological distress or depression in this study. However, within the subgroup of patients with alcoholic cirrhosis active drinkers had higher BDI scores compared to abstainers (Bianchi et al., 2005). Thus, patients with liver cirrhosis have signs of psychological distress and depression which affects health-related quality of life. Treatment of depression in cirrhosis seems to be important.

8 The Impact of Medical Interventions and Liver Transplantation on Health-Related QOL in Liver Cirrhosis

Patients with liver cirrhosis frequently undergo medical interventions aiming to reduce morbidity and in certain cases improve survival. Apart from medical therapy, such as diuretics for ascites, beta-blockers as prophylaxis for variceal bleeding, and lactulose for hepatic encephalopathy, they may undergo paracentesis or receive transjugular intrahepatic portosystemic shunt (TIPS) for ascites. Furthermore, they may undergo liver transplantation. Some previous studies have evaluated the effect of some of these interventions on health-related QOL in this patients group.

The number of daily medications as well as specific drugs have been implicated in the poor health-related QOL in patients with liver cirrhosis (Cordoba et al., 2003; Kalaitzakis et al., 2006; Marchesini et al., 2001). The number of daily medications and loop diuretics have been shown to affect QOL in cirrhotics of various etiologies (Marchesini et al., 2001) whereas beta-blockers and diuretics appear to have an important effect on QOL in cirrhotic outpatients with hepatitis C and prior decompensations (Cordoba et al., 2003). Also, daily lactulose use has been reported to be independently related to gastrointestinal symptom severity in patients with cirrhosis (Kalaitzakis et al., 2006). It is conceivable that medications may have been a surrogate marker for more severe liver cirrhosis with several complications in these studies but it cannot be excluded that certain side-effects of medications used might contribute to health-related QOL impairment in these patients. On the other hand, a recent randomized prospective study evaluating the effect of lactulose treatment on minimal hepatic encephalopathy and QOL in patients with cirrhosis showed that lactulose improves both cognitive function and QOL (Prasad et al., 2007). Improvement in health-related QOL in this study was related to the improvement in cognitive function as assessed by psychometric tests (Prasad et al., 2007). Furthermore, in patients with chronic hepatitis C and advanced fibrosis or cirrhosis

achievement of sustained virologic response after pegylated interferon and ribavirin therapy has been reported to improve health-related QOL and sexual health (Bonkovsky et al., 2007).

8.1 Transjugular Intrahepatic Portosystemic Shunt (TIPS) and Health-Related QOL

TIPS is often used as an alternative to medical therapy and large-volume paracentesis in patient with cirrhosis and refractory ascites (Sherlock and Dooley, 2002). A successful TIPS may minimize the requirement for diuretics and the need for large-volume paracentesis with patients experiencing symptom relief (e.g., less shortness of breath and early satiety). However, TIPS may fail to resolve ascites in up to 50% of cases and patients may experience deterioration in QOL mainly due to development of hepatic encephalopathy. A study, in which 21 cirrhotic patients receiving TIPS due to ascites were included, evaluated QOL prior and post TIPS in a cross-over manner (Gulberg et al., 2002). QOL showed significant improvement post TIPS which was more pronounced in patients with complete response to therapy (Gulberg et al., 2002). A randomized study comparing the effect of TIPS versus medical therapy on QOL in patients with cirrhosis and refractory ascites, however, showed that the two therapeutic modalities led to similar changes in QOL (Campbell et al., 2005). Competing effects of hepatic encephalopathy post TIPS and of requirement for repeated large-volume paracentesis and hospitalizations in the medical therapy group probably account for the similar changes in health-related QOL (Campbell et al., 2005). These data indicate that physicians responsible for the care of patients with liver cirrhosis ought to apply rigorous criteria for selection of patients suitable for specific types of medical treatment.

8.2 Liver Transplantation and Health-Related QOL

Liver transplantation, the only curative treatment for liver cirrhosis, has been repeatedly shown to improve not only survival but also health-related QOL (Belle et al., 1997; De Bona et al., 2000; Gross et al., 1999; Karam et al., 2003; Moore et al., 2000; Sherlock and Dooley, 2002; Tarter et al., 1991). Transplanted patients have been shown to have higher health-related QOL indices compared to patients with compared to patients with chronic liver disease (*Figures 131-2 and 131-4*). Specifically both physical and mental dimensions of QOL have been reported to improve posttransplant (Belle et al., 1997; De Bona et al., 2000; Gross et al., 1999; Karam et al., 2003; Moore et al., 2000) including anxiety and depression (De Bona et al., 2000; Gross et al., 1999; Moore et al., 2000), cognitive function (Moore et al., 2000), and disease-related symptoms (Belle et al., 1997; Gross et al., 1999; Karam et al., 2003; Moore et al., 2000). However, when compared to the general population not all studies have shown a complete return of health-related QOL to normal status at least as far as certain QOL dimensions are concerned (Karam et al., 2003; Tarter et al., 1991).

9 Assessment of Utilities and Health-Related QOL in Liver Cirrhosis

Cost-utility analysis is an important approach to economic analysis and is based on quality-adjusted life years. It is important to appropriately define utilities for a particular

disease before any meaningful cost-utility analysis can be performed. Economic analyses of liver disease have traditionally relied on utility estimates from experts which may, however, differ from patients' direct experience and thus may be flawed. In one study, in which 120 patients with chronic liver disease (51% with cirrhosis) were enrolled, the validity of a widely used utility measure (Health Utility Index-2) was established and the decrement in health-related QOL associated with chronic liver disease was measured (Younossi et al., 2001a). Patients without cirrhosis and those with Child-Pugh A cirrhosis showed substantial decrement in utilities (0.82 and 0.83, respectively) in the range of patients surviving brain tumor. Those with Child-Pugh B and C cirrhosis showed greater decrement (0.67 and 0.56) that was in the range experienced by patients who survive a stroke (Younossi et al., 2001a). Another study compared physician-assigned and patient-assigned utilities for six clinical scenarios in cirrhosis (1) compensated cirrhosis, (2) decompensated cirrhosis, (3) hepatic encephalopathy, (4) spontaneous bacterial peritonitis, (5) variceal bleeding, and (6) hepatocellular cancer (Wells et al., 2004). Although physicians and patients assigned similar rankings to each health state, physician-assigned utilities were significantly different from those assigned by patients (Wells et al., 2004). The authors of both studies conclude that utilities should be based on patient reports (Wells et al., 2004; Younossi et al., 2001a).

10 Conclusions

Patients with liver cirrhosis have poor health-related QOL which is related not only to severity and complications of cirrhosis but also to cirrhosis-specific symptoms. Liver transplantation improves QOL but other medical interventions (aimed to improve survival and/or reduce morbidity) in cirrhotics have been demonstrated to improve or compromise patients' QOL. This suggests that there is a need for selection of patients most suitable for a specific type of treatment. Last, physician and patient-assigned utilities have been shown to differ significantly. Thus, in cost-utility analysis utilities should be based on patient reports.

Summary Points

- Liver cirrhosis is associated with poor health-related QOL.
- Severity and complications of liver cirrhosis (especially hepatic encephalopathy) are associated with poor health-related QOL whereas etiology of liver cirrhosis is not of major importance for QOL.
- Disease-specific symptoms such as pruritus, muscle cramps, sleep disturbance, fatigue and gastrointestinal symptoms have a negative impact on health-related QOL in patients with liver cirrhosis.
- Liver transplantation, the only curative treatment in liver cirrhosis, results in improvement of health-related QOL.
- Medical treatments aiming to improve survival or reduce mortality in patients with cirrhosis may not invariably improve health-related QOL which stresses the need for rigorous selection of patients suitable for specific therapies.
- Utilities for cost-utility analysis should be based on patient reports.

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