RESEARCH ARTICLE

Dynamics and Liver Disease Specific Aspects of Quality of Life Among Patients with Chronic Liver Disease in Yunnan, China

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Abstract

Background: Patients with chronic liver diseases (CLD) may have compromised health related quality of life (HRQoL). Hepatitis B virus (HBV) infection has long been the leading cause of CLD including liver cancer and cirrhosis. Knowledge on different symptom profiles of CLD should help in development of comprehensive treatment and patient care plans. Objective: To access the facets of HRQoL in chronic liver diseases throughout their spectrum of severity. Materials and Methods: A cross-sectional study was conducted in the First Affiliated Hospital of Kunming Medical University in Yunnan Province of China. Both out- and inpatients undergoing treatment protocols for different HBV related liver disease states were consecutively collected from December 2012 to June 2013. ANOVA was used to compare the mean scores of EQ-5D and chronic liver disease questionnaire (CLDQ) among 5 disease groups. The relationship between demographic variables predicting global CLDQ scores and the domains of CLDQ was analysed. Results: A total of 1040 patients including 520 without complications, 91 with compensated cirrhosis, 198 with decompensated cirrhosis, 131 with HCC and 100 with liver failure were recruited. All domains of CLDQ, the means of EQ-5D value and EQ VAS exhibited significant decline with worsening of disease severity from uncomplicated HBV to liver failure. The multivariate regression demonstrated the reduction of mean scores of CLDQ domain at advanced stage. Patients with liver failure and HCC had more HRQoL impairment than other disease states. No effect of patient gender was found. Patient age was associated with 'fatigue' and 'worry' domains (p=0.006; p=0.004) but not with other domains and global scores of CLDQ and ED-5D. Conclusions: The HRQoL in chronic hepatitis B patients is greatly affected by disease states. Care for HBV-related diseases should consider not only the outcomes of treatment strategies but also improvement in patient wellbeing.

Keywords: HBV - chronic liver disease - liver cancer - cirrhosis - quality of life

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Introduction

Chronic hepatitis caused by HBV may progress to cirrhosis and death from liver failure, and chronic HBV infection is the major cause of hepatocellular carcinoma (HCC) worldwide (Lee, 1997). It is estimated that more than half a million Chinese people die annually from end-stage liver diseases (Lesmana et al., 2006). In Chinese patients with chronic HBV infection, the infection leads to a striking increase in the risk of cirrhosis, HCC, and liver-related premature mortality (Beasley et al., 1981).

Patients with chronic liver disease had a variety of symptoms which influenced their life activities and quality of life (QOL). Symptoms varied with type of liver disease (Younossi et al., 2001; Ong and Younossi, 2005). Knowledge on different symptom profiles of liver diseases may help in the development of comprehensive treatment plans. Researchers had found that patients with liver diseases had more impaired health related quality of life (HRQL) than the general population in the USA (Younossi et al., 2001).

The instruments and techniques used to assess quality of life vary according to the identity of the respondent. Generic instruments are used in general populations to assess a wide range of domains applicable to a variety of health states and diseases (Guyatt et al., 1993). They are usually use for conducting general survey research on health and making comparisons between disease states but not useful for any particular disease state or susceptible population of patients (Guyatt et al., 1993). Disease-

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specific instruments focus on assessment of the domains most relevant to the disease (Younossi et al., 1999) while they could not be used to compare QOL in two different diseases.

Despite the importance of health related quality of life (HRQoL) for patients with chronic liver diseases, few investigators have assessed quality of life in these patients with diverse diseases. We evaluated the impact on HRQoL of the spectrum of chronic liver diseases by clarifying differences in HRQoL by type and severity of the disease.

Materials and Methods

Study design

A cross-sectional study was conducted from December 2012 to June 2013. The information was consecutively collected from both outpatients and inpatients undergoing treatment protocols for different liver diseases states at the First Affiliated Hospital of Kunming Medical University in Yunnan province of China, the largest comprehensive hospital in Yunnan. It was a level three of first-class hospital having a department for liver disease and infectious disease and was one of the two hospitals in Kunming allowing patients with liver diseases to be admitted for treatment.

The study protocol was approved by the Institutional Ethical Committee of the Prince of Songkla University, Thailand, and the First Affiliated Hospital of Kunming Medical University in Yunnan province, China, where the study was carried out.

Patient recruitment

The recruited patients were older than 20 years old and were categorized into five groups, namely (1) chronic hepatitis B; (2) compensated hepatitis B cirrhosis; (3) decompensated hepatitis B cirrhosis; (4) hepatocellular carcinoma (HCC); (5) liver failure based on the International Classification of Disease (ICD) 10th version diagnosis criteria (WHO, 2012). The diagnosis criteria of the diseases mentioned above were based on the Chinese standard guidelines (Ministry of Public Health of P.R.C.; Chinese Society of Hepatology and Chinese Society of Infectious Diseases, 2011) developed by the Ministry of Health of People's Republic of China and the American Association for the Study of Liver Diseases guideline (AASLD) (Ghany MG et al., 2009). The eligible participants considered active in treatment procedures were recruited from the hospital. Those patients with toxic, drug induced, and autoimmune hepatic diseases as well as those who could not communicate in Chinese had been excluded.

Measurement

The EQ-5D is the most widely used generic preference based measure of health-related quality of life which has been validated in many different patient populations. The descriptive system has 5 dimensions (mobility, self-care, usual activity, pain/discomfort and anxiety/depression) and each has 3 response levels (no problems, some problems, and extreme problems) which create 243 unique health states. Most of the EQ-5D value sets have been obtained using a representative sample of the general population, thereby ensuring that they represent the societal perspective. This set of values can be applied to people's self-reported descriptions of their HRQL to generate health-related utility values. Utility valuations for all 243 EQ-5D health states are based on time-trade-off (TTO) valuations technique. The visual analog scale (VAS) technique on the other hand, asks people to indicate where, on a vertical thermometer-like scale ranging from best imaginable health to worst imaginable health, they think a health state should be positioned. The EQ VAS self-rating records the respondent's own assessment of their health status (The EuroQol Group, 1990; Brooks, 1996).

Since China is a big country comprising many minority populations, there has been no study of TTO for the whole country or for Yunnan province which has 21 minorities. Thus, in this study we decided to use the Thailand TTO value set to generate the EQ-5D values. The reasons behind this decision were that Dai was one of the minority groups in Yunnan and Thailand was the closest country where a study of TTO had been published (Tongsiri S., 2009).

The Chronic Liver Disease Questionnaire (CLDQ) (Younossi et al., 1999) is a standardized self-administered questionnaire designed to assess liver-disease specific HRQL instrument. It contains 29 items divided into six domains as follow: (1) abdominal symptoms (AS) (2) fatigue (FA) (3) systemic symptoms (SS) (4) activity (AC) (5) emotional function (EF) (6) worry (WO). The scores for each domain were on a 7-point Likert scale ranging from 1 corresponding to the maximum frequency ("all of the time") to 7 the minimum ("none of the time"). Domain scores were the means of the items contained and the global score was the mean of all domains. The CLDQ questionnaires were formally translated from the original versions and validated in Chinese-speaking patients (Xincai et al., 2012).

Data collection

Outpatients visiting the clinic and inpatients hospitalized during the study period who qualified participation criteria were invited to join the study and to complete questionnaires when they had signed the informed consent. For inpatients, the basic information (i.e. demographic characteristics, disease conditions) was extracted from inpatients electronic medical record databases. The same procedures followed those for outpatients. The other sections of the questionnaire of the Chinese version were required the inpatients to fully fill out during the hospital stay. And those seriously ill persons who lost their ability to answer the questions or were under their family dependent assistance, attending family members were asked to assist finishing the questionnaire. Epidata software was used for data entry after finishing data collection.

Statistical analysis

The R software (version 3.0.1) was used to perform data analysis (R Core Team, 2013). Descriptive statistics

for characteristics of patients were conducted. Categorical variables were described as number and percentage. Continuous variables were presented as mean and SD or median and IQR if not normally distributed.

Domain score was calculated from the average score of all items of that domain (Younossi et al., 1999). We used ANOVA to compare the mean scores of EQ-5D and CLDQ among 5 disease groups. Chi-square test was used in comparing the ratios for disease groups when one or more cross-tabulated cell had at least five subjects; otherwise, Fisher's exact test was used. We computed Spearmen correlation coefficient between the EQ-5D and CLDQ. All tests were two-sided with an overall significance level of 0.05. The relationship between independent variables predicting global CLDQ scores and the different domains of CLDQ questionnaire was analysed using multivariate regression model.

Results

Descriptive results

Characteristics of the study subjects were summarized in Table 1. Of the 1040 HBV infected patients including 520 with no complication, 91 with compensated cirrhosis, 198 with decompensated cirrhosis, 131 with HCC and 100 with liver failure diseases. Overall mean age was 45 years old (ranging from 20 to 83). Patients with HCC were the oldest while those without HBV complication were the youngest. The number of males in patients with HBV was two times more than females; while the ratio was three times for patients with other disease groups. Except ethnics, the distribution of other demographic variables among different disease groups was all significantly different.

Table 1. Demographic Characteristic of the Recruited Patients

	HBV	Com-pensated	Decom-pensated	HCC	Liver failure	*p* value
Total	520	91	198	131	100	
Age mean(SD)	40(13.8)	48(11.3)	49(11.8)	56(11.1)	44(12.3)	<0.001
Gender						<0.001
male	340 (65.4)	77 (84.6)	154 (77.8)	104 (79.4)	75 (75)	
female	180 (34.6)	14 (15.4)	44 (22.2)	27 (20.6)	25 (25)	
Ethnic						0.119
Han	458 (88.1)	80 (87.9)	177 (89.4)	118 (90.1)	97 (97)	
others	62 (11.9)	11 (12.1)	21 (10.6)	13 (9.9)	3 (3)	
Marital status						<0.001
unmarried	130 (25)	4 (4.4)	14 (7.1)	9 (6.9)	6 (6)	
married	390 (75)	87 (95.6)	184 (92.9)	122 (93.1)	94 (94)	
Education						<0.001
illiteracy	40 (7.7)	13 (14.3)	30 (15.2)	26 (19.8)	4 (4)	
low educate	354 (68.1)	70 (76.9)	142 (71.7)	92 (70.2)	83 (83)	
high educate	126 (24.2)	8 (8.8)	26 (13.1)	13 (9.9)	13 (13)	
Occupation						<0.001
blue-collar	208 (40)	42 (46.2)	74 (37.4)	49 (37.4)	27 (27)	
white-collar	216 (41.5)	37 (40.7)	95 (48)	54 (41.2)	33 (33)	
unemploy	96 (18.5)	12 (13.2)	29 (14.6)	28 (21.4)	40 (40)	
Family history						<0.001
no	312 (60)	78 (85.7)	145 (73.2)	108 (82.4)	81 (81)	
yes	208 (40)	13 (14.3)	53 (26.8)	23 (17.6)	19 (19)	

Health Related Quality of Life (HRQoL) scores in patients with HBV-related diseases

The EQ-5D results for the patients with HBV-related diseases were listed in Table 2. The mean utility value varied significantly in different disease groups. In all subdomains of CLDQ, the means of EQ-5D value and EQ VAS exhibited the gradual order of quality of life from HBV > compensated cirrhosis > decompensated cirrhosis > HCC > liver failure. Most of the differences between groups of patients were statistically significant when the mean score in one group was compared against that in the others. Exceptions were between the groups of HBV and compensated cirrhosis in AS, FA, WO domains of CLDQ, and between HCC and liver failure in EQ-5D.

The HCC group had HRQoL scores measured with the EQ-5D VAS somewhat better than patients with decompensated cirrhosis, but there was no statistically significant difference of the mean scores (p=0.18) and utility value (p=1.0) between the two groups. Patients with liver failure had significantly impaired health as measured with both the EQ-5D VAS and utility value compared to other diseases in all dimensions. Patients with HBV had significantly higher mean EQ-5D utility value and VAS scores when compared with those patients with other disease groups.

The global and six domain scores among disease groups are showed for comparison in Figure 1. All domains of CLDQ scale declined significantly with worsening of disease severity from HBV to liver failure. There was statistical significant difference among diverse disease groups by ANOVA test. Liver failure patients had the poorest HRQL as measured by the global CLDQ scale and the six CLDQ subscales. The extent of impaired CLDQ varied in the six domains. The most severely affected domains were FA in the physical health and WO in the psychological health aspect. The mean scores of systemic symptoms (SS) domain were higher than other domain scores for all disease states (Table 2). While EQ-5D was

Table 2. Mean scores of CLDQ and EQ-5D results

Total	HBV 520	Compensated 91	Decompensated 198	HCC 131	Liver failure 100	*p* value (ANOVA)
Abdominal Symptoms	5.6 (1.6)	5.3 (1.7)	4.1 (1.7)	3.3 (1.7)	2.9 (1.5)	<0.001
Fatigue	5.2 (1.4)	5.0 (1.6)	4.4 (1.7)	3.6 (1.4)	2.7 (1.4)	<0.001
Systemic Symptoms	5.8 (1)	5.3 (1.3)	4.5 (1.5)	3.7 (1.6)	3.1 (1.5)	<0.001
Activity	5.7 (1.3)	5.2 (1.8)	4.3 (1.9)	3.5 (1.9)	2.7 (1.3)	<0.001
Emotional Function	5.5 (1.4)	5.0 (1.4)	4.5 (1.6)	3.7 (1.4)	2.8 (1.4)	<0.001
Worry	5.2 (1.7)	4.8 (1.6)	4.2 (1.8)	3.2 (1.5)	2.7 (1.3)	<0.001
Global CLDQ	5.5 (1.1)	5.0 (1.3)	4.4 (1.4)	3.5 (1.3)	2.9 (1.3)	<0.001
Utility scores	0.8 (0.2)	0.7 (0.2)	0.6 (0.3)	0.6 (0.3)	0.0 (0.2)	<0.001
EQ VAS	72 (13.7)	58.2 (14.9)	47.6 (23.4)	50.6 (16.9)	36.4 (17.2)	<0.001

Abbreviations: CLDQ: chronic liver disease questionnaire; EQ-5D VAS: EQ-5D visual analogy scale

Table 3. Multivariate Model in Quality of Life, Adjusted for Gender, Age, and Other Demographic Characteristics

Variable	HBV	Compensated	Decompensated	HCC	Liver failure	Age	Gender (female vs male)
CLDQ							
AS**	ref.	-0.25 (-0.62, 0.12)	-1.5 (-1.78, -1.23)	-2.25 (-2.59, -1.91)	-2.61 (-2.97, -2.26)	0 (-0.01, 0.01)	0.06 (-0.16, 0.29)
FA**	ref.	-0.33 (-0.67, 0.01)	-0.92 (-1.17, -0.67)	-1.74 (-2.05, -1.43)	-2.56 (-2.89, -2.24)	0.01 (0, 0.01)*	-0.19 (-0.4, 0.02)
SS**	ref.	-0.48 (-0.77, -0.18)	-1.34 (-1.56, -1.13)	-2.11 (-2.37, -1.84)	-2.64 (-2.92, -2.37)	0 (-0.01, 0)	-0.01 (-0.19, 0.16)
AC**	ref.	-0.54 (-0.9, -0.18)	-1.39 (-1.66, -1.12)	-2.22 (-2.55, -1.89)	-3.03 (-3.37, -2.68)	0 (-0.01, 0.01)	0.01 (-0.22, 0.23)
EF**	ref.	-0.54 (-0.87, -0.22)	-1.07 (-1.31, -0.82)	-1.9 (-2.2, -1.61)	-2.66 (-2.97, -2.35)	0 (0, 0.01)	-0.14 (-0.34, 0.06)
WO**	ref.	-0.5 (-0.87, -0.13)	-1.13 (-1.41, -0.86)	-2.27 (-2.61, -1.93)	-2.59 (-2.94, -2.23)	0.01 (0, 0.02)*	-0.14 (-0.37, 0.09)
Global**	ref.	-0.47 (-0.75, -0.19)	-1.19 (-1.4, -0.98)	-2.06 (-2.31, -1.8)	-2.66 (-2.92, -2.39)	0 (0, 0.01)	-0.09 (-0.26, 0.08)
EQ-5D							
Utility Scores**	ref.	-0.09 (-0.14, -0.04)	-0.16 (-0.2, -0.12)	-0.13 (-0.18, -0.08)	-0.75 (-0.8, -0.7)	0 (0, 0)	-0.02 (-0.06, 0.01)
EQ VAT**	ref.	-12.6 (-16.41, -8.8)	-23.03 (-25.87, -20.18)	-16.82 (-20.31, -13.33)	-34.23 (-37.87, -30.58)	-0.05 (-0.13, 0.02)	0.41 (-1.84, 2.66)

*: p value <0.05; **: p value <0. 01; AS: Abdominal symptoms; FA: Fatigue; AC: Activity; EF: Emotional function; WO: Worry

Table 4. Correlation between CLDQ and EQ-5D

	AS	FA	SS	AC	EF	WO	Global CLDQ	EQ VAS	Utility value
Abdominal Symptoms	1	0.6	0.7	0.7	0.6	0.6	0.7	0.4	0.4
Fatigue	0.6	1	0.7	0.8	0.8	0.7	0.9	0.3	0.3
Systemic Symptoms	0.7	0.7	1	0.7	0.7	0.6	0.8	0.4	0.4
Activity	0.7	0.8	0.7	1	0.7	0.6	0.8	0.3	0.4
Emotional Function	0.6	0.8	0.7	0.7	1	0.8	0.9	0.4	0.4
Worry	0.6	0.7	0.6	0.6	0.8	1	0.9	0.3	0.3
Global CLDQ	0.7	0.9	0.8	0.8	0.9	0.9	1	0.4	0.4
EQ VAS	0.4	0.3	0.4	0.3	0.4	0.3	0.4	1	0.5
Utility value	0.4	0.3	0.4	0.4	0.4	0.3	0.4	0.5	1

Abbreviations: AS: Abdominal symptoms; FA: Fatigue; SS: Systemic symptoms; AC: Activity; EF: Emotional function; WO: Worry; CLDQ: chronic liver disease questionnaire; EQ-5D VAS: EQ-5D visual analogy scale

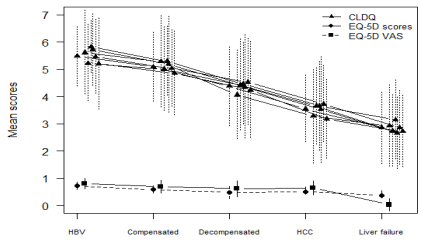

Figure 1. Distribution of CLDQ in Each Domain and EQ-5D. (EQ-5D VAS plot is derived by EQ-5D VAS/100 to make the line comparable with EQ-5D scores)

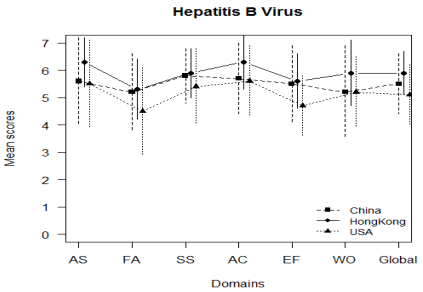

Figure 2. Comparison of CLDQ Scores of HBV Patients in Each Domain in this Study (labeled China), Hong Kong, and the United States of America

designed to measure general QOL, the trends of change through the spectrum of the disease was rather similar to the CLDQ which was disease-specific measurement. The striking phenomenon was a marked decrease in EQ VAS from HCC to liver failure which was the end stage of the disease spectrum.

In order to observe the difference of mean CLDQ cores between every pair of disease group, Pairwise comparison using Student t test on mean CLDQ scores in overall and six domains was performed (the results not display in table). Compared with HBV patients, the CLDQ scores in patients with compensated cirrhosis as measured by SS, AC, EF domains and global scores decreased with statistical significance while they did not significantly decrease by AS, FA, WO domains. The difference in CLDQ scores among patients with HCC and liver failure were not significant by AS domain, although HCC patients had less impairment than liver failure patients as measured by AS domain scores of CLDQ. The rest of disease groups, pairwise comparison of CLDQ scores showed statistically significant declined with severity of disease progression.

To assess how diagnosis of different types of chronic liver disease related to the global CLDQ score while controlling for socio-demographic factors, multivariate regression demonstrated a reduction in mean scores of CLDQ domain at advanced stage of liver disease after controlling the potential confounders such as age and gender. The results are displayed in Table 3.

There was no variable except the states of liver disease to be retained in the final model at p<0.05. Patients with liver failure had more HRQoL impairment than those with other disease states. No effect of patient gender was found in different domains. Patient age was associated with FA and WO domains (p=0.006; p=0.004). Other domains and global scores of CLDQ and ED-5D scores were not affected by age.

The correlation between CLDQ and ED-5D questionnaires

Using the cut points of correlation coefficient (r) as very high, high, moderate, low and very low correlation of |r| at 0.95, 0.8, 0.5, 0.3, all variables in Table 4 were positively correlated. There were low to weak correlations

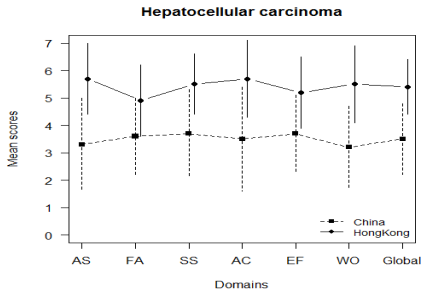

Figure 3. Comparison of CLDQ Scores of HCC Patients in each Domain in this Study (Labeled China) and Hong Kong

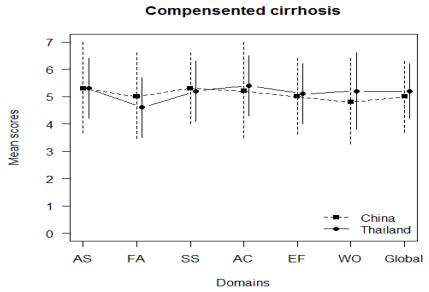

Figure 4. Comparison of CLDQ Scores of Compensated Cirrhosis Patients in Each Domain in this Study (labelled China) and Thailand

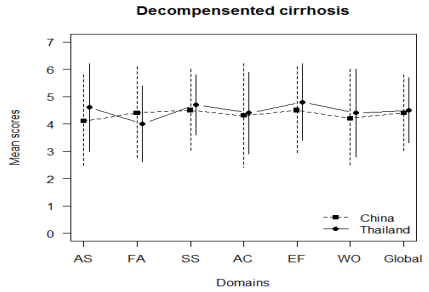

Figure 5. Comparison of CLDQ Scores of Decompensated Cirrhosis Patients in Each Domain in this Study (labelled China) and Thailand

between the CLDQ global score and each domain score with the EQ-5D utility scores and the EQ-5D VAS. The EQ-5D utility score had a low correlation with EQ-5D VAS. Moderate correlation among the 6 domains was detected. The Global CLDQ had high correlation with the six domains. Significant correlation was observed among various domains of the CLDQ.

Discussion

In summary, subjects under our study had different demographic background of the five disease states. As expected, various domains of CLDQ correlated among one another, but not with EQ-5D. Regression results revealed the order of QOL for different disease states varied with severity of the disease throughout the spectrum of disease development.

In this study we chose EQ-5D scale as the generic instrument and CLDQ as disease-specific one to evaluate quality of life of patients with HBV-related diseases. The original CLDQ was a well-developed and validated disease specific questionnaire for measuring QOL in CLD (Younossi et al., 1999). The results from generic and disease-specific questionnaires were in agreement with the fact that a marked decrease of QOL was seen in advanced stages of chronic liver diseases, and revealed the great impact of chronic liver disease progression stages on QOL. The results also illustrated that the decrease was not so obvious in EQ-5D utility value and VAS, especially for HCC and decompensated cirrhosis patients which were the states where the patients were going close to the end of life. The findings indicated that the quality of life score measured by EQ-5D, the generic instrument, was not as sensitive for this kind of disease as CLDQ, the disease-specific one.

With multivariate analysis to observe the QOL in various severity of liver disease development adjusted for age and gender effect illustrated that the CLDQ scores decreased with the severity of disease. The result was consistent with other studies which showed that patients with HBV-related diseases had a greatly impaired perceived health status. Patients with liver diseases usually had lower HRQL than normal population, and the deterioration of HRQL appeared with the increase in severity of liver diseases (Marchesini et al., 2001; Younossi et al., 2001; Arguedas et al., 2003; Chong et al., 2003; Cordoba et al., 2003).

Age and gender in univariate analysis were significantly different among the disease groups, while in multivariate analysis the effect of gender disappeared and that of age was observed in FA and WO domains of CLDQ. The difference of QOL between males and females was reported for particular domains of the HRQoL (Marchesini et al., 2001), and others also reported a lower HRQoL in women than men in chronic somatic diseases (Rodrigue and Baz, 2006; Pettersen et al., 2008). They discussed the differences between sexes were resulted from self-perception of health status. However, the gender effect on both CLDQ and EQ-5D scores was not demonstrated in patients with HBV-related disease in this study. Such the difference was not easy to explain and might be related to the difference in social culture in different populations. The patients' age only influenced the FA and WO domains of CLDQ scores. This was consistent with other studies in which the authors reported a weak influence of age on CLDQ scores in patients with chronic liver disease (Ware et al., 1994; Younossi et al., 2001).

In comparison of the mean score difference of CLDQ for any two disease states (pairwise comparison), the results indicated that most of the domains of CLDQ scores had significant differences in all comparisons except those of AS, FA, WO domains were not significantly lower among compensated cirrhosis compared with HBV patients. This may be due to the fact that cirrhosis of the liver usually occurs on the basis of chronic hepatitis B and the disease process is gradual and patients with early cirrhosis can compensate for the damage and have the ability to function normally. Therefore, the difference in QOL is not obvious between the two disease categories. During the decompensated stage of liver diseases, the liver can no longer be coping with its functions, then obvious

symptoms appear. Thus, in the present study the CLDQ scores decreased in all domains compared with HBV and decompensated cirrhosis diseases.

The results from comparison among different countries are shown in Figure 2. Comparison of CLDQ scores of HBV patients in each domain among Hong Kong, USA and this study in Yunnan (Younossi et al., 1999; Lam et al., 2009), the mean scores in six domains and global scores in this study were generally lower than those in the study in Hong Kong and the mean scores of AS, AC, WO and global was significant different by Student t test. The mean scores in the present study were higher than those in the US study. The mean scores of FA, SS, EF and global had statistical significance between the two countries. Figure 3 shows the comparison of CLDQ scores of HCC patients in each domain between Yunnan (this study) and Hong Kong (Lam et al., 2009). Patients with HCC in Hong Kong had statistically higher mean scores than those in Yunnan in every domain and the global scores of CLDQ.

The results of this study were different from that reported from Hong Kong although the patients had similar cultural background. The possible explanation was the study conducted in Hong Kong selected uncomplicated HBV patients as study sample and those patients were milder than our patients and thus resulted in higher patients' scores. Further studies are needed to verify the evidence. The study in USA was conducted in 1999. It seems that the QOL in patients with HBV had improved with the development of medical technics, thus the scores was higher in the current study in Yunnan than in the study in USA in the past. Social and cultural differences can confound the perception of QOL in disease-specific instruments as they are no way to adjust for those differences.

Figure 4 and Figure 5 show the comparison of CLDQ scores of compensated and decompensated cirrhosis patients in each domain between Yunnan and Thailand (Sobhonslidsuk et al., 2004). The mean scores in each domain were similar between the two countries except the mean score of FA domain in patients with compensated cirrhosis of Thai patients was lower than those in Yunnan with statistical significance (p=0.036). The possible reason may be because of the subjective self-evaluation of fatigue for patients. The similarity of the results of the two studies supports our decision to use Thai preference for EQ-5D instrument.

In conclusion, this study helps to provide a greater understanding of the impact of liver diseases and its treatment on patient wellbeing. The results of this study have shown that patients with either chronic hepatitis B or with complications caused by HBV, their psychological and mental stress are relatively large, their QOL has been greatly affected. Currently there has been no effective way to completely clear hepatitis virus from the patients; the treatment aims are not only focusing on drug therapy protocol to reduce viral load and enhancing their physical wellbeing but also enhancing psychological treatment on the patients. Meanwhile it is important to strengthen the broadcast of liver disease knowledge especially on the transmission and disease course since hepatitis B is a kind of infectious chronic disease, so that people can properly understand chronic hepatitis B and the elimination of prejudice to patients with chronic hepatitis B and more serious consequence. They deserve to get a better care to help them improve the quality of life.

The cross-sectional design of our study does not allow us to describe the progression of hepatitis B disease course as it relates to changes in HRQoL. Although most investigators endeavoured to exploit new targeted antiviral agents for treatment of HBV-related diseases, the major impact of patients with HBV-related diseases on HRQoL is deserving consideration. The success of future therapy for HBV-related diseases should concern not only in studying the treatment strategies of the disease but also in improving patient's HRQoL.

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