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Health-Related Quality of Life and Adjustment in Patients with Hepatocellular Carcinoma

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Abstract

The overall purpose of this thesis were to explore the impact of hepatocellular carcinoma (HCC) on patients' health-related quality of life (HRQOL), the significant predictors of adjustment outcomes, as well as to establish an adjustment model in patients with HCC. This thesis included three studies: systematic review, qualitative and quantitative study.

Systematic review. HCC and HRQOL relevant keywords were combined and 36 articles were recruited in this review. The main finding indicated patients with HCC had worse physical, emotional, and functional HRQOL; but better social/family HRQOL than the general population. The medical and physical variables associated with HRQOL also identified.

Qualitative study. Thirty-three patients with HCC in Taiwan were recruited, and semi-structured interview was used to collect data to explore patients' experience in illness journey. Four themes were identified, including the impact of disease, the illness perceptions of HCC, the information needs and the coping strategies. A preliminary model of illness adjustment was also developed.

Quantitative study. Standardized questionnaires were used to measure HRQOL, anxiety and depression, illness perceptions, coping, and social support; and demographic and physical variables were also collected (n=286). Patients with HCC had worse global HRQOL, physical, role, cognitive, social functioning, and more higher levels of depression than the general population; and the prevalence of anxiety, depression and emotional distress were 11.27%, 25.44%, and 20.14% respectively. Physical variables explained a significant amount of variance in all EORTC and HADS scores (R^2=.17-.62). Illness perceptions explained an additional 4.33%-31.80% of the variance in the EORTC and HADS scores after controlling for ECOG and α-FP.

Cognitive representations mediated the effects of ECOG on the EORTC and HADS scores, and coping mediated the effects of cognitive representations on psychological aspects of adjustment outcomes.

An adjustment model with multiple pathways was developed based on both quantitative and qualitative findings. Suggestions are made for improving clinical care for patients with HCC and future studies.

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List of Abbreviations

α-FP	Alpha Fetoprotein
AJCC	American Joint Committee on Cancer
BCLC	Barcelona Clinic Liver Cancer system
BNI	British Nursing Index
Brief IPQ	Brief Illness Perception Questionnaire
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CLD	Chronic Liver Disease
CRD	Center for Reviews and Dissemination
CT	Computed Tomography
ECOG	The Eastern Cooperative Oncology Group performance status
EORTC QLQ-HCC18	the European Organization for Research and Treatment of Cancer (EORTC) QLQ-HCC18
EORTC QLQ-C30	European Organization for Research and Treatment for Cancer Quality of Life Questionnaire Core-30
FACT-G	Functional Assessment of Cancer Therapy-Generic
FACT-Hep	Functional Assessment of Cancer Therapy-Hepatobiliary
FHSI	FACT Hepatobiliary Symptom Index
FLIC	Functional Living Index-Cancer
GIVIO	Interdisciplinary Group for Cancer Care Evaluation in Italy
GOT	Glutamic Oxaloacetic Transaminase
GPT	Glutamic Pyruvic Transaminase
GQLI	Gastrointestinal Quality of Life Index
HADS	Hospital Anxiety and Depression Scale
HAI	Hepatic Arterial Infusion
HBV	Hepatitis B Virus
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus
HRQOL	Health-Related Quality of Life
INR	International Normalized Ratio
IPA	Interpretative Phenomenological Analysis
IPQ	Illness Perception Questionnaire
IPQ-R	Illness Perception Questionnaire-Revised version
MID	Minimally Important Difference
NHP	Nottingham Health Profile
PEI	Precutaneous Ethanol Injection

QOL	Quality of Life
QOL-LC	Quality of Life-Liver Cancer
RFA	Radiofrequency Ablation
SF-36	Short-Form 36
SIP	Sickness Impact Profile
SPSS	The Statistical Package for Social Sciences
SRT	Stereotactic Radiation Therapy
TAC	Transarterial Chemotherapy
TACE	Transarterial Chemoembolization
TAE	Transarterial Embolization
TNM system	Tumour, Node, Metastasis system
WHOQOL	World Health Organization Quality of Life Assessment

Chapter 1. Physical Aspects of Hepatocellular Carcinoma

1.1 Abstract

This chapter covered on the physical aspects of hepatocellular carcinoma (HCC), including epidemiology, risk factors, diagnosis and stage, and treatment. In addition, the specific characteristics of HCC in Taiwan are also addressed. HCC is one of the major cancers in Taiwan, around 7,000 patients die from the disease every year. There are demographic and geographic variations in the incidence of HCC. The risk factors include biological, chemical and nutritional factors, especially hepatitis B and C viruses and cirrhosis. There is a lack of consensus about standard staging system and treatment protocols for HCC. In addition, there is a tendency for HCC to be diagnosed at a late stage because of invisible symptoms and reserved liver functions. Although surgical resection or transplantation are curative treatments, most patients who are not eligible for surgery receive local ablative therapy, hepatic artery transcatheter treatment, and systemic treatment.

1.2 Epidemiology

Liver cancer is the sixth most common cancer worldwide in terms of numbers of cases (626,000 or 5.7% of new cancer cases), and it is the third most common cause of death from cancer (598,000) due to the very poor prognosis (Parkin, Bray, Ferlay, & Pisani, 2005). Men are two or three times more often affected than women (El-Serag, 2002). There are geographic variations in HCC (Chen, Yu, & Liaw, 1997), and the largest concentration of patients is in Asia and sub-Saharan Africa (El-Serag, 2002; Parkin et al., 2005), as well as in Taiwan.

In Taiwan, cancer has been the most common cause of death since 1970, and there are steady increases in the numbers of newly diagnosed and deaths of all cancer (see Figures 1.1 and 1.2). HCC is the second most common cancer in Taiwan, and rising incidence and mortality rates of HCC have been reported in last two decades. There were approximately 9,900 new HCC cases and approximately 7,000 people died of HCC in 2005; the numbers of patients who died from HCC is one-fifth of those who died from all cancers (Taiwan Cancer Registry, 2008).

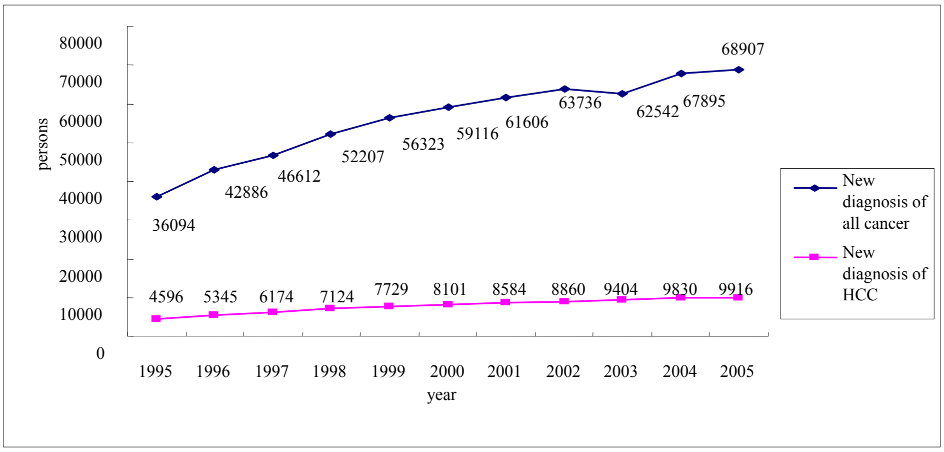

Figure 1.1 Numbers of new diagnosis of all cancer and HCC in Taiwan from 1995 to 2005. Source: Taiwan Cancer Registry, 2008.

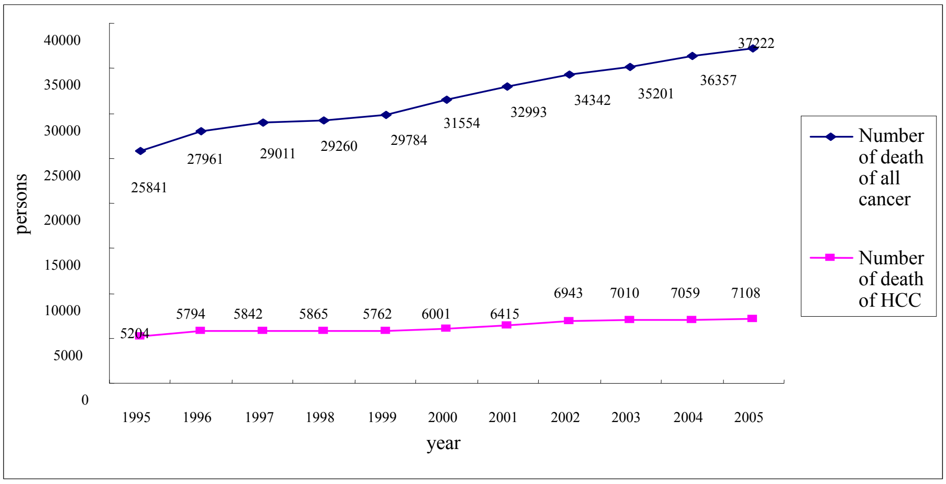

Figure 1.2 Numbers of death of all cancer and HCC in Taiwan from 1995 to 2005. Source: Taiwan Cancer Registry, 2008.

1.3 Risk factors

Hepatic carcinogenesis is a complex process associated with accumulation of genetic and epigenetic changes that run through steps of initiation, promotion and progression (Dominguez-Malagon & Gaytan-Graham, 2001). Based on epidemiological analyses, both ethnic and environmental factors are important determinants of HCC (Chen et al., 1997).

1.3.1 Hepatitis viruses

HCC is commonly the result of chronic viral infection. Hepatitis B virus (HBV) is the most frequent risk factor for HCC. There is a strong positive relation between the prevalence of HBV and HCC, especially in regions with high incidence of HCC (e.g., Taiwan, China, and sub-Saharan Africa) (Llovet, Burroughs, & Bruix, 2003). HBV carriers have a 5- to 15-fold increased risk of HCC compared with the general population (El-Serag, 2002). Hepatitis C virus (HCV) is also associated with a higher risk of developing HCC and HCV carriers have a 17-fold increased risk compared with the HCV negative controls (Donato, Boffetta, & Puoti, 1998). HCV is also associated with increased HCC in the United States and western countries (El-Serag, Davila, Petersen, & McGlynn, 2003). In Asia and Africa, 70% of HCC patients have HBV infection, but only 10-20% in Europe and North America. In contrast, only 20% of HCC patients have HCV infection in Asia and Africa, but 50-70% are affected in Europe and North America (Llovet et al., 2003).

In Taiwan, HBV and HCV are the first and second leading causes of HCC since 1990 (Chen et al., 1997). Overall, the mean age of patients with HBV-related HCC was 53.3 years (SD=13.6), and 65.1 years (SD=9.1) for HCV-related HCC patients. The male/female ratio was 6.4 for HBV-related HCC, while it was 1.7 for HCV-related HCC (Lu et al., 2006). There has been a dramatic decrease in incidence of liver cancer since universal hepatitis B vaccination was introduced in Taiwan (Chang et al., 1997). However, there is increasing tendency of HCV-related HCC (Lu et al., 2006).

1.3.2 Cirrhosis

The most important predisposing factor of HCC is cirrhosis caused by hepatitis viruses, alcohol, or inherited metabolic diseases (Cahill, 2005). Cirrhosis from any causes is the seed-bed of HCC (Schafer & Sorrell, 1999). Most HBV and HCV-related HCC coexist with cirrhosis which is the underlying of the pathologic process of hepatocyte necrosis, chronic inflammation, fibrosis, and scarring that leads to the malignant transformation within the liver (Kew, 1996).

1.3.3 Alcohol consumption

Heavy alcohol drinkers have been found to have a significantly increased HCC risk in most epidemiological studies (Chen et al., 1997). Alcohol could induce cirrhosis and possible malignant change to the hepatocyte (Groen, 1999). Alcohol-related cirrhosis has become the major risk factor of HCC in places where the incidence of chronic viral hepatitis is low (Schafer & Sorrell, 1999).

1.3.4 Chemical substances

There are significant correlations between Aflatoxin exposure and HCC mortality or morbidity (Chen et al., 1997; El-Serag, 2002). Chemicals such as inorganic arsenic, thorotrast, and vinyl chloride increase the risk of HCC. In addition, exogenous and endogenous hormones have been reported to be associated with HCC (Chen et al., 1997).

1.3.5 Genetic and familial tendency

Familial tendency may result from environmental factors such as HBV or genetic factors shared by family members. One study indicated the autosomal recessive gene for HCC in Taiwan (Chen et al., 1997).

The development of HCC is a multistage process with a multifactorial aetiology. In Taiwan, the major pathway of hepatocarinogenesis is through HBV and HCV infection, chronic hepatitis, and liver cirrhosis to HCC. In addition, cigarette smoking, the traditional Chinese vegetarian habit, low vegetable consumption and heavy alcohol drinking may increase the risk of HCC (Chen et al., 1997).

1.4 Symptoms, diagnosis and stage

1.4.1 Symptoms

HCC is insidious in onset and is typically asymptomatic during the early stage (Cahill, 2005). There tends to be a delay in diagnosis due to (1) the lack of symptoms in the early stage; (2) the large size and position of liver behind the costal cartilages, which precludes the tumour from being readily palpable while small; and (3) the large functional reserve of the liver, which delays presentation with functional disturbances r (Lau, 2000). Consequently, HCC is generally diagnosed in the later stages of the disease.

Table 1.1 summarizes the clinical presentations associated with HCC (Bialecki & Di Bisceglie, 2005). Initially, patients present with nonspecific symptoms such as fatigue, weight loss, right upper quadrant pain, or dull ache or pain in the epigastric area (Groen, 1999). When the tumour grows larger, hepatic decompensation becomes common. Ascites and jaundice are typical symptoms, and patients develop tremors, confusion, and encephalopathy while hepatic decompensation worsen (Lau, 2000).

Table 1.1 Clinical presentations in HCC (source: Bialecki & Di Bisceglie, 2005)

Asymptomic	
Liver dysfunction	Ascites
	Jaundice
	Hepatic encephalopathy
	Variceal bleed
Complications of tumour growth	Abdominal pain
	Weight loss
	Cachexia
	Abdominal mass
	Obstructive jaundice
	Tumour rupture
Paraneoplastic syndrome	hypoglycemia
	hypercalcemia
	polycythaemia
	Feminization syndrome
	Diarrhoea
	Cutaneous manifestations
Distant metastasis	

1.4.2 Diagnosis

Percutaneous biopsy provides the definitive diagnosis of hepatic tumours (Groen, 1999). Serum alpha fetoprotein (α-FP) and imaging studies are major methods to diagnose HCC (Cahill & Braccia, 2004). α-FP values that more than 400 ng/ml or a progressive increase in α-FP levels are highly suggestive of HCC (Yu & Keeffe, 2003). Imaging studies that are used to evaluate the size and location of tumours include ultrasonography, computed tomography (CT), magnetic resonance imaging, computed tomographic portogram, hepatic arteriorgraphy, and arteriorgraphically enhanced CT (Groen, 1999).

1.4.3 Stage

The purpose of staging is to accurately categorise patients in order to inform the likely prognosis of disease and most appropriate treatment (Groen, 1999). The most widely used staging systems are the Okuda prognostic staging system (Table 1.2) and the TNM system (tumour, node, metastasis) (Table 1.3) by The American Joint Committee on Cancer (AJCC) (Schafer & Sorrell, 1999).

Table 1.2 Okuda staging system (source: Wildi et al., 2004)

Positive features	Tumour involving >50 per cent of the liver
	Ascites
	Albumin <3 g/dl
	Bilirubin >3 mg/dl
Stage I: No positive features	
Stage II: 1 or 2 positive features	
Stage III: 3 or 4 positive features	

Table 1.3 TNM classification for HCC (source: Wildi et al., 2004)

Pathological staging (pTNM)			
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3	N0	M0
IIIB	T4	N0	M0
IIIC	Any T	N1	M0
Stage IV	Any T	Any N	M1

T definitions	T1: Solitary without vascular invasion
	T2: Solitary tumor with vascular invasion or multinodular >5 cm
	T3: Multinodular > 5 cm or tumor with major vascular invasion
	T4: Tumor with invasion of adjacent organs
N definitions	N0: No regional lymph node metastasis
	N1: Regional lymph node metastasis
M definitions	M0: No distant metastasis
	M1: Distant metastasis

However, there is a lack of consensus in the definition and staging of HCC between different systems (Wildi, Pestalozzi, McCormack, & Clavien, 2004). Most systems fail to link staging to treatment indication, except for Barcelona Clinic Liver Cancer (BCLC) system (Sala, Forner, Varela, & Bruix, 2005) (see Figure 1.3). In Taiwan, AJCC and BCLC are the widely used systems.

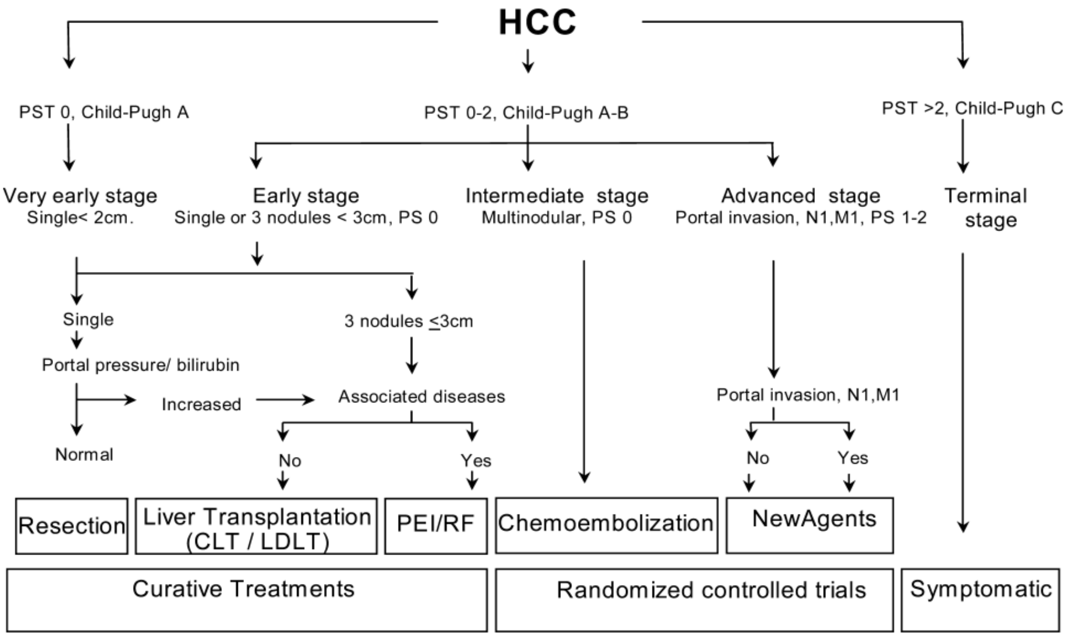

Figure 1.3 Strategy for staging and treatment assignment in patients diagnosed with HCC according to the Barcelona Clinic Liver Cancer (BCLC) system. Source: Bruix & Sherman, 2005.

1.5 Treatment

There are no standard proven treatments for HCC, and the choice of treatment depends on the general condition of the patient, stage of disease, liver function, as well as the treatment protocol and availability of expertise in the individual medical center (Lau, 2000). Treatment options for HCC include surgical and nonsurgical modalities. Surgical therapy is the only potentially curative treatment for HCC, but most patients are not eligible for these procedures by the time of diagnosis. Nonsurgical treatment can prolong survival period and palliate symptoms (Cahill & Braccia, 2004).

Surgical therapy includes resection and liver transplantation. However, only 10-20% of patients are eligible for surgical intervention because of large tumour size and metastases on diagnosis (Groen, 1999). The overall 5-year survival rate of liver resection ranges from 11% to 76% with a median of around 30%; for liver transplantation the rates range from 20% to 36% (Lau, 2000).

For patients with unresectable HCC, treatments include local ablative therapy, hepatic artery transcatheter treatment, and systemic treatment. Precutaneous ethanol injection (PEI) is the most common method of local ablative therapy; ethanol is injected under ultrasound guidance to cause necrosis of tumour (Schafer & Sorrell, 1999). Hepatic artery transcatheter treatment involves (1) transarterial embolization (TAE), embolization of the hepatic artery to induce ischemia of tumour and slow down tumour growth; (2) transaterial chemotherapy (TAC), deliver the chemotherapeutic agents into the hepatic artery to tumour in high concentration; (3) transarterial chemoembolization (TACE), combine TAE and TAC; and (4) transarterial radioembolization, delivery of radioactive isotapes to tumour (Lau, 2000). Systemic treatments that include chemotherapy, immunotherapy, chemoimmunotherapy, hormone therapy, and somatostatin analog, have not been shown to have a proven treatment effect (Lau, 2000).

Based on the BCLC staging system (Figure 1.3), resection is used for patients with very early HCC, radical therapies (resection, liver transplantation or percutaneous treatments) for early HCC, and chemoembolization for intermediate stage. However, patients with advanced HCC may benefit from new agents and patients with terminal HCC receive symptomatic treatment to relieve pain and other symptoms (Sala et al., 2005).

Because of the symptoms, various and repeated treatments, HCC might affect patients' life, for example, they experience pain and other suffering symptoms, regular treatment might mean they can not go to work, if they are exhausted by treatment they will not socialize, and concern about the future may limit what they do, Therefore it is necessary to investigate the impact of HCC, especially quality of life. The next chapter will focus on the issues of quality of life and health-related quality of life.

Chapter 2. Quality of Life and Health-Related Quality of Life

2.1 Abstract

Modern medicine has made significant progress in the screening, diagnosis, and treatments for HCC, but there is debate about the objective of cancer care: should the focus be on the quantity vs. quality of survival? (de Haes & van Knippenberg, 1985). The medical impact of HCC on patients, families, and Taiwan society was shown in Chapter 1. In this chapter, the emphases are on how HCC impacts on quality of life (QOL) of patients, and an additional distinction between QOL and health-related quality of life (HRQOL) is made. The health care system concentrates on QOL and health which are influenced by illness; therefore I used HRQOL through whole thesis. In addition, the characteristics in measurement of HRQOL are discussed, including (1) objectivity vs. subjectivity, (2) generic vs. specific, (3) unidimensional vs. multidimensional, (4) self-report vs. proxy report, (5) reliability, and (6) validity. Subsequently the importance of HRQOL is also addressed.

2.2 QOL and HRQOL

2.2.1 QOL

QOL is taken to refer to amorphous conceptions of the goodness of life (Zautra & Goodhart, 1979). It represents a broad range of human experience about the necessities of life, such as a safe environment, adequate housing, a guaranteed income, respect, love, and freedom that all contribute to an individual’s QOL (Patrick & Erickson, 1993). QOL in a broad concept, encompassing satisfaction about housing, employment, standard of living, marriage, interpersonal relationship, religion, and environment

(Campbell, Converse, & Rogers, 1976). However, the health care system and its providers do not assume responsibility for all these global human concerns, and therefore a distinction is made with HRQOL (Patrick & Erickson, 1993).

2.2.2 HRQOL

In a survey asking health people the five most important things in their lives, health is among the most important valued states (Bowling, 1995). QOL and HRQOL are often used interchangeably to refer the same concept. However, there are differences between the two. As described above, QOL is a broad concept covering all aspects of human life including the economic and environmental aspects of an individual, whereas HRQOL focuses on the effects of illness and treatment (Guyatt et al., 2007). HRQOL is a reflection of the way that individuals perceive and react to their health status and nonmedical aspects of their lives, which include (1) health-related factors, such as physical, functional, emotional, and mental well-being; (2) non-health-related elements, such as job, family, friends, and other life circumstances (Gill & Feinstein, 1994). Regarding health outcomes, most indicators reflect a disease model, but HRQOL provides a comprehensive evaluation encompassing all important aspects of QOL related to health. It has generated a new focus on a broader, more positive concept of health, rather than a narrow, negative focus (disease-based) (Seedhouse, 1986).

A concept of HRQOL is based on a concept of health and QOL, which is influenced by an individual’s experiences, beliefs, expectations, and perceptions (Testa & Simonson, 1996). Health is defined not only the absence of disease or infirmity but also a state of complete physical, mental and social well-being (WHO, 1948). HRQOL is a double-sided concept including positive and negative aspects. The negative aspect is about the disease and dysfunctions, whereas the positive aspect encompasses feelings of mental and physical well-being, full functioning, physical fitness, adjustment and efficiency of mind and body (Bowling, 2001).

HRQOL is a multi-dimensional dynamic concept (Sajid, Tonsi, & Baig, 2008). HRQOL includes multiple components, such as an individual's physical health, psychological state, level of independence, social relationships, and their relationships to salient features of their environment (WHO, 1995). These are health related to the extent they are influenced by illness, injury, and treatment (Patrick & Deyo, 1989). In addition, it is a dynamic concept resulting from past experience, present circumstances, and expectations for the future (Bowling, 2001). Perception and achievement of HRQOL are dependent on not only an individual's physical condition but also preferences and priorities in life (Edlund & Tancredi, 1985). HRQOL can be recognized as a dynamic concept representing individual responses to the physical, mental, and social effects of illness which influence the extent to which personal satisfaction with life circumstances can be achieved, and which allows favourable comparison with others according to the selected criteria (Holmes & Dickerson, 1987). The dimensions of HRQOL encompass consequences for the daily lives of individuals, including health perceptions, functional status, symptoms, and individuals' preferences and values (Clancy & Eisenberg, 1998).

HRQOL is sometimes confused with health status or functional status (Farquhar, 1995). Illness has a pervasive effect that seeps into all areas of life, but HRQOL depends on more than physical health status alone (Guyatt, Feeny, & Patrick, 1993). HRQOL and health status are two distinct constructs. There is no concordance between patient ratings of health status and global HRQOL, for example among patients with poor physical functioning, 43% nevertheless rated HRQOL to be good (Covinsky et al., 1999). Furthermore, patient ratings of their health and global HRQOL seem to be influenced by different factors. Perceived health status was most affected by physical functioning but less by emotional well-being. However, global HRQOL was influenced more by emotional well-being than physical functioning (Smith, Avis, & Assmann, 1999). HRQOL encompasses not only perceived health status but also wide broad of aspects of life.

2.3 The measures issues of HRQOL assessment

In recent years, HRQOL measures have been applied to different diseases, conditions, and populations. However, some criticism has arisen, for example lack of conceptual clarity and measurement feasibility (Hunt, 1997; Rogerson, 1995). It is essential to define and operationalize HRQOL. The field of HRQOL assessment has become more sophisticated and methodologically rigorous (Ferrans, 2007). Eiser and Morse (2001) reviewed HRQOL relevant literatures and provided the performance characteristics for a good measure of HRQOL (see Table 2.1). Although these specifically relate to assessment of HRQOL in children, the key demands are relevant to measurement generally.

Fitzpatrick, Davey, Buxton, and Jones (1998) have also developed criteria for assessing the quality of HRQOL measures, including reliability, validity, precision (measures can distinguish health and illness), responsiveness (measures can detect clinically important changes), acceptability (patients are willing to complete measures), and feasibility (the timing and cost of measures are reasonable). In this section, the important issues of measuring HRQOL were addressed, including (1) objectivity vs. subjectivity, (2) generic vs. specific, (3) unidimensional vs. multidimensional, (4) self-report vs. proxy report, (5) reliability, and (6) validity.

Table 2.1 Performance characteristics for HRQOL measures (Eiser & Morse, 2001)

Performance characteristic
Reliable and valid for the groups of patients for whom it is used
Employ self-report whenever possible
Allow completions by proxy
Brief, easy to administer
Child-centred and developmentally appropriate
The usability of the instrument must be considered (e.g., the language, reading level, and burden to staff); parents and families should be consistent with the stated objectives of the study
Age-corrected, general population norms
Reflect the agreed upon definition of HRQOL
Cover the full spectrum of behaviours thought to contribute to HRQOL (e.g., psychological, physical, social functioning)
Include both generic and subjective assessment
Include a generic core and disease-specific items
Allow for supranormal performance
Cross-culturally compatible
Emphasis health-enhancing aspects of HRQOL

2.3.1 Objectivity vs. subjectivity

HRQOL includes both subjective and objective components (Felce & Perry, 1995; Meeberg, 1993; Muldoon, Barger, Flory, & Manuck, 1998; Testa & Simonson, 1996). Assessment of objective functioning and subjective well-being involve different definitions and methodologies (Muldoon et al., 1998). Subjective well-being has multiple facets, which depends on reactions in multiple physiological and psychological systems (Diener, Suh, Lucas, & Smith, 1999). Subjective assessment includes the individual's perception or appraisal of HRQOL, such as emotional levels, life satisfaction, and well-being (Eiser, 2004b; Testa & Simonson, 1996). Objective functioning is important in defining an individual's degree of health or ability, and individual's subjective perceptions translate the objective functioning into the HRQOL experienced (Testa & Simonson, 1996). Objective assessment focuses on what the individual can do, such as walking or self care ability, and the symptoms, such as pain, fatigue or weakness.

The combination of using HRQOL assessment and objective clinical indicators is popular in evaluating the effectiveness and appropriateness of medical treatments and methods of health services (Enthoven, 2000). HRQOL instruments can be used to assess the ripple effects of disease and symptoms on all aspects of life, not only a narrowly focused measure of the target symptoms (Ferrans, 2007). HRQOL assessment can incorporate these two characteristics.

2.3.2 Generic vs. specific measures

A generic measure is defined as a broad outcome indicator including physical, mental, and social health; but a specific measure is used to assess disease or condition-related attributes (Bowling, 2001). Generic instruments include heath profiles and utility measures (Guyatt et al., 1993). In general, generic HRQOL measures should contain the dimensions of physical, emotional, social functioning, as well as global perceptions of health and well-being (Anderson, Aaronson, & Wilkin, 1993). Generic measures can be used to compare across different types and severities of disease, treatments or interventions, and across demographic and cultural subgroups (Guyatt et al., 1993).

On the other hand, a specific measure focuses on the special area of primary interest, where the instruments may be specific to the disease (e.g., cancer or heart disease), to a population of patients (e.g., children or elderly), to a certain function (e.g., sleeping or eating), or to a problem (e.g., pain) (Guyatt et al., 1993). Disease-specific measures are used to assess a specific population or disease, with the goal of measuring responsiveness or clinically important changes (Guyatt, Bombardier, & Tugwell, 1986; Patrick & Deyo, 1989). Selection of different measures depends on the research objectives, patients' characteristics, and applications of measures in clinical research, practice, or policy analysis (Patrick & Deyo, 1989). It is recommended that generic measures need supplementation with disease-specific measures to address positive and negative clinically important changes (Guyatt et al., 1986; Guyatt et al., 1993).

2.3.3 Unidimensional vs. multidimensional

The results of HRQOL measures can be reported either as a single composite score or as a profile score (Gill & Feinstein, 1994). Unidimensional measures use a single global question to present an overall HRQOL score (Ferrans, 2007). The single item asks patients to evaluate their overall QOL, for example the item in the Functional Assessment of Cancer Therapy-Generic (FACT-G; Cella et al., 1993) is "I am content with the quality of my life right now" and in the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30; Aaronson et al., 1993) is "How would you rate your overall quality of life during the past week?".

However, HRQOL is inherently multidimensional (Muldoon et al., 1998). A domain or dimension refers to the area of behaviours or experience that researchers or physicians are trying to measure (Guyatt et al., 1993). Most HRQOL instruments measure each domain separately, by asking specific questions pertaining to its most important components (Testa & Simonson, 1996). These results can provide a health profile, which measures various aspects of health status, for example physical, psychological, and social functioning (Aaronson, 1988; Gill & Feinstein, 1994; Testa & Simonson, 1996).

2.3.4 Self-report vs. proxy report

The question arises about who should assess HRQOL. Sometimes researchers and physicians obtain HRQOL rating from proxies instead of patients, because of patients' physical conditions and time available. For example, terminally ill patients may be too weak to complete the instrument and children may be too young to understand the meaning of items. Therefore, the views from caregivers or relatives are useful to understand patients' HRQOL. However, the debate here is whether proxy ratings can represent accurately patients' HRQOL.

For example, using the Sickness Impact Profile (Bergner, Bobbitt, Kressel, Pollard, Gilson, Morris et al., 1976) only moderate correlation (*r*=.55) between terminally ill patients (who still could complete the questionnaire) and close relatives, was obtained (McCusker & Stoddard, 1984). The relations between self and proxy reports varies depending on the domains of measurement and the relationships between proxy and patient (Guyatt et al., 1993). Typically, higher correlation is found between self and proxy report in physical functioning, but less in psychosocial aspects (Rothman, Hedrick, Bulcroft, Hickam, & Rubenstein, 1991). In general, it is recommended that HRQOL ratings are obtained from patients directly, and researchers and physicians should limit the inferences based on the ratings from proxies or caregivers (Guyatt et al., 1993; Guyatt et al., 2007).

2.3.5 Reliability

Reliability refers to the stability and equivalence of repeated measures of the same concept (Patrick & Erickson, 1993). A reliable questionnaire is accurate over time (Davies, 2009). Generally, types of reliability for HRQOL measures include internal consistency, test-retest reliability, and inter-rater reliability (Eiser & Morse, 2001).

Internal consistency refers to homogeneity of items, which is the extent to which the items of a domain or scale measure the same concept or construct. Cronbach's alpha is the most widely used statistical test to assess internal consistency (Cronbach, 1951). *Test-retest reliability* refers to the stability of the measure over time, that two sets of scores which are administered on different occasions are positively correlated (Davies, 2009). *Inter-rater reliability* refers to the consistency of measures between different raters, which is normally assessed using the kappa statistic (Cohen, 1968). The minimum level of reliability depends on the type of analysis. In general, reliabilities in the .50-.70 range are acceptable for making comparisons between groups (Ware, 1984).

2.3.6 Validity

Validity is the extent to which a test measures the construct it purports to measure (Lohr et al., 1996), for example the questionnaires are measuring HRQOL rather than some other concept (Eiser & Morse, 2001). Types of validity include content validity, criterion validity, and construct validity. *Content validity* refers to judgments about the extent to which the content of the measure logically includes a full assessment of the characteristics or domains it is intended to measure (Eiser & Morse, 2001). *Criterion validity* is the extent to which a score corresponds to an accurate measure or a gold standard measure. *Construct validity* refers to the extent to which a measure is a good representation of the construct. The types of construct validity include *convergent validity* (a construct is related to (converges on) other constructs that it should also be similar to theoretically) and *discriminant validity* (a construct is not related to another construct which there is no theoretical relationship). Factor analysis, confirmatory factor analysis, and multitrait-multimethod modeling are used for establishing construct validity (Cronbach & Meehl, 1955).

2.4 The importance of HRQOL

HRQOL measures can be used to evaluate different methods of symptom management (Cella et al., 2007) and the effects of treatments (Osoba, 1999), by incorporating with physical indices such as survival rates, response rates, and mortality rates. There are three reasons why researchers and physicians should focus on HRQOL. First, HRQOL is useful to understand patients' point of view about disease and treatment. Second, there is value to understand the normal process of adjustment to cancer and treatment, and by implication, what is abnormal and when intervention is necessary. Third, HRQOL is an important consideration when comparing different treatments and evaluating interventions (Eiser, 2004a; Sajid et al., 2008).

HRQOL measures can be one of several endpoints in clinical trials to help decision-making about the optimal treatment for patients and families (Feld, 1995; Kaasa, 1995; Kiebert, Curran, & Aaronson, 1998; Lipscomb et al., 2004; Roila & Cortesi, 2001). HRQOL measures can help to clarify the tradeoffs between treatments and interventions with major benefits and health-related outcome costs (Guyatt et al., 2007). In particular, if the primary goal of treatment is to improve the way patients are feeling, it is imperative to measure HRQOL directly and use the results in clinical decision-making (Guyatt et al., 2007). More importantly, HRQOL assessment is changing medical care from a disease-centered approach to a patient-centered approach (Osoba, 1999), as well as addressing positive elements of life (Diener et al., 1999).

In summary, assessment of patients' experience about disease and treatment is now commonly agreed to be a central component of health care and healthcare research (Guyatt et al., 2007; Muldoon et al., 1998). HRQOL has become an important endpoint in medical care and clinical trials. Researchers should provide conceptual and operational definitions of HRQOL, as well as the specific domains of measurement (Gill & Feinstein, 1994; Smith, Avis et al., 1999). Moreover, the measures of HRQOL should consider the individual's social and material contexts (Hunt, 1997). The meaning of HRQOL is arguably dependent on the user of the term, their understanding of it, and their position and agenda in the social and political structure (Edlund & Tancredi, 1985).

Based on the literatures reviewed in this chapter, I conclude that HRQOL is an integrative index which combines objective functioning and subjective well-being, and may be presented in health profile or multi-dimensional format. HRQOL rating should be assessed by patients directly. Individuals may simultaneously evaluate all dimensions to formulate the overall judgment; therefore, in the context of chronic disease, HRQOL is the appraisal outcome based on psychological functioning and to a lesser degree on physical functioning (Smith, Avis et al., 1999). It can be used as an outcome measure instead of pathology or underlying disease state (Lydick & Epstein, 1993). Measures of health outcome should incorporate both physical indices and the individual's perspectives as a consequence of adjustment.

In the next chapter, I will review the relevant studies about HRQOL in patients with HCC with aims to understand the HRQOL in this group and to determine the most appropriate measures for my research.

Chapter 3. HRQOL in Patients with HCC: A Systematic Review

3.1 Abstract

Aims: This systematic review was conducted to identify: (1) measures of HRQOL in patients with HCC; (2) differences in HRQOL between patients with HCC, chronic liver disease, and the general population; (3) effects of treatment (liver surgery; hepatic artery transcatheter treatment; and radiotherapy) on HRQOL; (4) relationships between physical variables, symptoms and HRQOL; (5) relationships between demographic characteristics, psychological variables and HRQOL; and (6) effects of psychological interventions on HRQOL.

Methods: HRQOL and HCC relevant keywords were searched in computerized databases, including BNI (1985 to February 2009), CINAHL (1982 to February 2009), Cochrane library (1991 to February 2009), PsychoInfo (1806 to February Week 1 2009), and Pudmed (1950 to February 2009).

Results: Thirty-six articles were identified. The results of the review are as follows. (1) The disease-specific concerns include pain, fatigue, nausea, jaundice, weight loss, and body image. (2) Patients with HCC had worse physical, emotional, and functional HRQOL; but better social/family HRQOL compared to the general population. (3) Liver surgery, hepatic artery transcatheter treatment and radiotherapy improved HRQOL. (4) Better liver function, early stage of disease, and no recurrence were positively correlated with better HRQOL; and pain, fatigue, nausea, and performance status were associated with worse HRQOL. (5) HRQOL was negatively correlated with depression, uncertainty, chance health locus of control, and positively with satisfaction with medical services. (6) Psychosocial interventions may reduce negative feelings and enhance HRQOL.

Conclusions: Future work should explore the effects of psychological variables on

HRQOL and the interaction between physical and psychological variables in relation to HRQOL.

3.2 Introduction

Compromised HRQOL has been demonstrated in patients with liver disease such as cirrhosis or hepatitis virus (Marchesini et al., 2001; Spiegel et al., 2005). Patients with HCC would be expected to show impaired HRQOL because of severe symptoms, treatment and side effects, and burden of disease. HRQOL concerns in patients with HCC include generic domains, such as physical symptoms and psychological issues, and others unique to their disease (Heffernan et al., 2002; Weitzner et al., 1995). Therefore, the aims of the systematic review were to determine:

(1) generic, cancer, and liver cancer-specific measures used in current studies to assess HRQOL in patients with HCC;

(2) differences in HRQOL between patients with HCC, patients with chronic liver disease, and the general population;

(3) effects of treatments on HRQOL: liver surgery, hepatic artery transcatheter treatment, and radiotherapy;

(4) relationships between physical variables, symptoms and HRQOL;

(5) relationships between demographic characteristics, psychological variables and HRQOL;

(6) effects of psychological interventions on HRQOL.

3.3 Methods

3.3.1 Methods

The following computerized databases were searched: BNI (British Nursing Index; 1985 to February 2009), CINAHL (Cumulative Index to Nursing and Allied Health Literature; 1982 to February 2009), Cochrane library (1991 to February 2009), PsychoInfo (1806 to February Week 1 2009), and Pubmed (US Library of Medicine and National Institute of Health, 1950 to February 2009). Text word and Thesaurus terms were used to maximize identification of relevant articles. The following keywords were searched using Boolean logic: (1) liver cancer, cancer of liver, hepatic cancer, hepatic neoplasms, liver neoplasms, hepatocellular carcinoma, hepatoma, HCC; (2) quality of life, QOL, health-related quality of life, HRQOL, anxiety, depression, psychological well-being. Additional references cited in retrieved articles or relevant review articles were also obtained.

3.3.2 Inclusion and exclusion criteria

Articles were included which were: (1) published in English or Chinese in a peer reviewed journal; (2) included adults patients (age>18 years) with HCC; (3) focused on HRQOL or relationships between HRQOL and physical or psychological variables; (4) either qualitative or quantitative methodology.

Exclusion criteria were: (1) literature review or case study; (2) samples including children or adolescents only; (3) samples involving heterogeneous populations: including various cancers or liver disease; (4) studies reporting findings not directly relevant to the core concepts of HRQOL; (5) measure of HRQOL based on the Karnofsky performance status scale (Schag, Heinrich, & Ganz, 1984) only.

3.3.3 Review procedure

The systematic review was conducted following recommendations of the Center for Reviews and Dissemination (CRD) (NHS, 2001). The CRD includes 10 phases in three stages, and the details of process are presented in Table 3.1. In Chapter 1 and 2, I reviewed the physical aspects of HCC and the concept of HRQOL, which fulfill requirements of phase 0 in documenting the need for a review to understand HRQOL in patients with HCC. The review processes from phase 1 to 9 are described in Chapter 3.

Table 3.1 The process of systematic review

Stage	Content	Chapter
Stage I	**Plan of the review**	
phase 0	Identification of the need for a review	Ch. 1 & 2
phase 1	Preparation of a proposal for a review	Ch. 3
phase 2	Development of a review protocol	Ch. 3
Stage II	**Conduct of the review**	
phase 3	Identification of research	Ch. 3
phase 4	Selection of studies	Ch. 3
phase 5	Study quality assessment: determine methodological quality, bias, internal validity, and external validity	Ch. 3
phase 6	Data extraction and monitoring progress: extract bibliographic details, descriptions of design, study population, intervention, outcome measures, and results	Ch. 3
phase 7	Data synthesis: integrate results of the target studies, and meta-analyses should be conducted if appropriate	Ch. 3
Stage III	**Reporting and dissemination**	
phase 8	Recommendations	Ch. 3
phase 9	Evidence into practice	Ch. 3

Abstracts were evaluated for relevance and full articles obtained where appropriate. A summary sheet was developed for extracting data. This included (1) aims; (2) methodology: qualitative or quantitative or mixed; longitudinal or cross-sectional; comparison group; randomization; (3) participants; (4) measure of HRQOL, physical and psychological variables; (5) results.

3.4 Results

Two thousand four hundred and twenty-six articles were identified and abstracts obtained. Based on the defined eligibility criteria, 36 articles were selected for review (34 from electronic database searching and 2 from relevant citation). The key search terms are summarized in Table 3.2.

Table 3.2 Key search terms and results

	BNI	CINAHL	Cochrane library	PsychoInfo	Pubmed	Total
1. liver cancer or cancer of liver or hepatic cancer or hepatic neoplasms or liver neoplasms or hepatocellular carcinoma or hepatoma or HCC	13	1956	3129	136	158416	
2. quality of life or QOL or health-related quality of life or HRQOL or anxiety or depression or psychological well-being	7791	78370	46331	224482	431249	
1 and 2	2	76	331	24	2182	**2426**
Target	1	12	5	5	28	**34**
(relevant citation)						**2**

The 36 articles were conducted in Canada (n=1), China (n=7), France (n=2), Hong Kong (n=5), Italy (n=2), Japan (n=3), Nigeria (n=1), Taiwan (n=5), USA (n=9), and one was an international study (Hong Kong, Taiwan, and the UK). Sixteen studies were longitudinal in design. Thirty-three used quantitative methods and three used mixed quantitative and qualitative methods. Four involved a randomized control trial. Of 36 studies, 12 included comparison groups [chronic liver disease (n=5), general population (n=3), different treatments (n=5), and other cancer groups (n=2)]. In addition, two included reports from caregivers and physicians. Summaries of results are presented in Table 3.3.

3.4.1 Aim 1: Measures of HRQOL in patients with HCC

(1) Generic measures

There were four generic HRQOL measures which were used in six studies, including the Short-Form 36 (SF-36; McHorney, Ware, & Raczek, 1993), World Health Organization Quality of Life assessment (WHOQOL; WHO group, 1995, 1998a, 1998b), Nottingham Health Profile (NHP; Hunt, McKenna, McEwen, Williams, & Papp, 1981), and Sickness Impact Profile (SIP; Bergner, Bobbitt, Kressel et al., 1976). The domains of HRQOL assessed, reliability/validity, and references are shown in Table 3.4.

(2) Cancer specific measures

There were five cancer specific HRQOL measures which were used in 24 studies. These included the FACT-G (Cella et al., 1993), EORTC QLQ-C30 (Aaronson et al., 1993), Spitzer QOL index (Spitzer et al., 1981), Interdisciplinary Group for Cancer Care Evaluation in Italy (GIVIO) quality of life questionnaire (The GIVIO Investigators, 1994), and Functional Living Index-Cancer (FLIC; Schipper, Clinch, McMurray, & Levitt, 1984) (see Table 3.4).

Table 3.3 The summary of studies in the review

Author Year Country	Aims	Research design 1. quantitative, qualitative, mixed 2. longitudinal, cross-sectional 3. randomization	Measures	Participants	Age yr (SD or range)	Results
Aim 1: Measures of HRQOL in patients with HCC						
Blazeby et al. 2004 Hong Kong, Taiwan and the UK	To develop a HRQOL questionnaire module in patients with HCC form Europe, Hong Kong and Taiwan.	Mixed Cross-sectional	◆ European Organization for Research and Treatment of Cancer: EORTC-QLQ-HCC18	Phase 1: N=10, health-care professionals N=32, patients Phase 3: N=158 patients	 60 (29-77) 58 (35-83)	◆ Phase 1: generation of HRQOL issues: literature review and semi-structured interview. Phase 2: production of the provisional questionnaire: consultation of the EORTC QOL group item database. Phase 3: pre-testing the questionnaire: testing acceptability and relevance ◆ In phase 1, 29 HRQOL issues were suggested; in phase 2, 22 items were developed; in phase 3, 18 items were formulated. ◆ The scale contains fatigue (3 items), body image (2 items), jaundice (2 items), nutrition (5 items), pain (2 items), fevers (2 items), abdominal swelling (1 item), and sexual interest (1 item).

Heffernan et al. 2002 USA	To develop the instrument to measure HRQOL in patients with hepatobiliary: the Functional Assessment of Cancer Therapy-hepatobiliary (FACT-Hep).	Quantitative Cross-sectional	◆ The Functional Assessment of Cancer Therapy-Generic (FACT-G) ◆ The Functional Assessment of Cancer Therapy-hepatobiliary (FACT-Hep) ◆ The Profile of Mood States–Short Form (POMSSF)	N=30, sample 1 item-generation (HCC: 2) N=51, sample 2 validation (HCC: 10)	64 (10.40, 39-81) 61.50 (9.60, 40-80)	◆ Phase 1: item generation; Phase 2: item reduction; Phase 3: scale construction; Phase 4: initial reliability and validity testing. ◆ The FACT-Hep had 18 items to measure disease-related symptoms and functioning. ◆ The scale had good reliability (Cronbach' α =.72-.93/.82-.94; test-retest=.84-.91) and convergent- divergent validity (high correlation with FACT-G and trial outcome index; no correlation with social desirability)
Steel & Geller et al. 2005a USA	To assess consistency of ratings of HRQOL between patients with HCC, family	Quantitative Longitudinal (baseline, 3, 6, months)	◆ FACT-G & Hep	N=82, patients, caregivers, and physicians	59 (30-86)	◆ The patients' rating of HRQOL improved at three months (higher than baseline) but decreased at six months (lower than baseline). ◆ At baseline, the patients and family were consistent on all subscales except for emotional well-being, but the patients and oncologists were only consistent on physical

	caregivers, and oncologist care providers.					well-being. ◆ At three months, the patients, family, and oncologists were consistent on all subscale except for social/family well-being; at six months, the patients and family were consistent on physical, functional well-being and additional concerns. ◆ The proxies tend to agree with patients on physical and functional well-being, but underestimate on emotional and social/family well-being.
Wan et al. 1998 China	To develop a self-administered HRQOL instrument for patients with liver cancer.	Quantitative Cross-sectional	◆ Quality of life for liver cancer (QOL-LC)	N=105	--	◆ Phase 1: generation of HRQOL issues in patients with liver cancer. Phase 2: selection of items. Phase 3: testing reliability and validity. ◆ The scale includes physical, psychological, symptom/ side effect, and social domains; the test-retest reliability were .76, .96, .71, .80, and the Cronbach'α were .78, .81, .75, .68. ◆ The criterion validity with the functional living index-cancer (FLIC) and SF-36 were .76 and .65.
Yount et al.	To develop and validate a	Quantitative Cross-sectional	◆ FACT-G & Hep	N=95, hepatobiliary		◆ Phase 1: collection the candidate FHSI item. Phase 2: experts selection. Phase 3:

2002 USA	symptom index derived from the FACT-Hep: FACT-Hepatobiliary Symptom Index-8 (FHSI-8).		◆ POMS ◆ Eastern Cooperative Oncology Group Performance Status (ECOG)	cancer experts N=51, hepatobiliary cancer patients (HCC: 10)	61.50 (9.60, 40-80)	psychometric testing. ◆ The Cronbach'α was .79 and test-retest correlation was .86. The FHSI-8 was associated with other subscale of FACT and mood, and patient differentiation by ECOG and treatment. ◆ The eight items included 3 pain, 2 fatigue, nausea, weight loss, and jaundice.
Zhu et al. 2008 China	To evaluate the effectiveness of FACT-Hep Chinese version.	Quantitative Cross-sectional	◆ FACT-G & Hep	N=180	52.34 (10.73)	◆ The Cronbach's α were .42 (social)-.84 and test-retest correlations were .33 (social)-.81. ◆ There were significant differences in the FACT-Hep between different stages or Child-Pugh classes.
Aim 2: Comparison of HRQOL in HCC, chronic liver disease and the general population						
Bianchi et al. 2003 Italy	To assess HRQOL in cirrhotic patients with HCC.	Quantitative Cross-sectional	◆ Short Form-36 (SF-36) ◆ Nottingham Health Profile (NHP)	N=101 N=202, matched patients with cirrhosis	66 (41-87) 66 (41-86)	◆ Compared with normative population, patients with HCC had a significant impairment in energy, sleep, physical mobility, and pain (NHP); and physical functioning, role limitation-physical, bodily pain, general health, role limitation-emotional, vitality, mental health, and social functioning (SF-36).

						◆ Compared with patients with cirrhosis, patients with HCC had more pain and less social isolation (NHP); and more role limitation-physical and bodily pain (SF-36). Patients with HCC had a main impairment in physical component summary instead of mental component summary. ◆ Sleep disorder was strongly related to poor HRQOL, that a third of the patients with HCC (34%) had difficulty in falling asleep, 28% had woken up very early in the morning, and 39% reported waking up several times during the night for problems severely disturbing sleep (muscle cramps, use of diuretics, etc.).
Kondo et al. 2007 Japan	To evaluate the influence of HCC on HRQOL.	Quantitative Cross-sectional	◆ SF-36, Japanese version	N=97, treated successfully with percutaneous ablation therapy N=97, with chronic liver	68.50 (7.80) 68.20 (7.40)	◆ Both patients with chronic liver disease and HCC had low HRQOL than age and sex-matched general population in role limitation-physical, general health, role limitation-emotional, vitality, mental health, and social functioning. ◆ There was no significant difference in all eight subscales of SF-36 between patients with HCC and chronic liver disease. However, patients

				disease without HCC, matched for age and sex		with HCC had a significantly lower physical component summary score than comparison group. ◆ The significant predictors of impaired physical component summary were older age, higher serum bilirubin, and lower serum albumin level; the predictor of impaired mental component summary was lower serum albumin level. ◆ In HCC, liver function predicted HRQOL strongly, but status of HCC (recurrence or not, time period of treatment) did not.
Lee et al. 2007 Taiwan	To evaluate HRQOL in patients with HCC.	Quantitative Cross-sectional	◆ World Health Organization (WHO) QOL-BREF Taiwan version ◆ EORTC-QLQ-C30 ◆ Utility: visual analogue scale and standard gamble method	N=161	61.60 (12.40)	◆ Compared with normative population, the patients with HCC had significant lower HRQOL in physical domain, but higher in environmental domain (adjustment for gender and age). ◆ Duration of HCC more than one year was associated with better HRQOL.

Steel & Chopra et al. 2007a USA	To evaluate the differences in HRQOL between patients with HCC, patients with chronic liver cancer (CLD), and general population.	Quantitative Cross-sectional	◆ FACT-G & Hep	N=83, HCC N=51, CLD N=138, general population	58 (18-83) 54 (32-79) 40 (18-84)	◆ The patients with HCC had worse physical well-being and overall HRQOL than the patients with CLD, and they reported greater weight loss, difficulties digesting food, loss of appetite, and decreased ability to perform usual activities. ◆ The patients with HCC had worse physical, emotional, functional well-being, hepatobiliary symptoms, and overall HRQOL than the general population but they had better social/family well-being. ◆ The patients with CLD had worse physical, functional well-being, hepatobiliary symptoms, and overall HRQOL than the general population, but they had better social/family well-being. ◆ The Child's Pugh score was positively associated with HRQOL.
Aim 3: Effects of treatment on HRQOL						
Boudet et al. 1995 France	To assess HRQOL of cancer patients	Quantitative Cross-sectional	◆ Sickness Impact Profile (SIP) ◆ Side-effects of	N=29, patients grafted for liver tumours	45 (10, 20-62)	◆ The 2-year survival rate of the cancer patients was 34%, lower than the comparison group; 56% of cancer patients retuned to work. ◆ Regarding HRQOL, there was no significant

	receiving orthotopic liver transplantation.		immunosuppression, constraints of follow up (frequency of outpatient visits or readmissions), return to work.	N=111, patients grafted for nonmalignant liver disease		difference between two groups, and 70% of cancer patients claimed to live a normal life after liver transplantation. ◆ There was a high rate of tumour recurrence, and a high mortality in patients with malignant liver disease. However, among the disease-free long-term survivors, the HRQOL of patients transplanted for cancer was similar to that of patients grafted for other indications.
Chen et al. 2004 China	To evaluate the pre- and postoperative HRQOL in patients with liver cancer.	Quantitative Longitudinal (pre-operation, 2,5,10 weeks, 4,6,9 months, 1,1.5,2 years)	◆ Gastrointestinal quality of life index (GQLI)	N=36, liver cancer patients treated surgically	50 (42-72)	◆ The HRQOL was reduced significantly 2-10 weeks after the liver operation, but it recovered gradually. ◆ After operation four months, the HRQOL increased to the preoperative level, and after nine months the HRQOL was higher than that before the operation. ◆ Major hepatectomy (lobectomy and combined segmentectomy) reduced more HRQOL than minor hepatectomy (simple segmentectomy).
Ganageri et al. 2002 Italy	To describe the psychological and social	Mixed Cross-sectional	◆ Quantitative: the Interdisciplinary Group for	N=80, referral for liver transplantation	Median: 54 (inter-quartile	◆ The candidates had a good level of HRQOL assessed by GIVIO and a low prevalence in the personality disorder scales detected by the MMPI.

	conditions of liver transplant candidates and to explore the meaning that these patients attribute to those conditions.		Cancer Care Evaluation in Italy (GIVIO) ◆ The Need Evaluation Questionnaire (NEQ) ◆ the Minnesota Multiphasic Personality Inventory (MMPI) ◆ Structured interview		range: 46-57)	◆ The major need was information about patients' examinations, therapies, and future conditions. ◆ The main support was form spouse or partner, and time spent waiting and possible difficulties after the operation may cause a sort of physical and psychological dependence. ◆ Overall, candidates had more a psychological impact than a physical impact, characterized by anxiety, worry, and irritability.
Poon et al. 2001 Hong Kong	To evaluate the HRQOL of patients undergoing resection of HCC.	Quantitative Longitudinal (before surgery and at 3, 6, 9, 12, 18, 24 months after surgery)	◆ FACT-G	N=66, received hepatic resection N=10, with unresectable HCC and received	52.80 (11, 19-75) 61.10 (8.10, 51-77)	◆ After surgery three months, there were significant improvements in overall HRQOL, physical, emotional, social well-being, and the relationship with physician. The most remarkable improvement was physical well-being. ◆ In patients with unresectable HCC, there was no significant difference in overall HRQOL and sub scales between baseline and three

				TACE		months later. ◆ In the baseline, two groups had similar level of overall HRQOL, but after three months, patients received resection had a significant higher overall HRQOL than the control group. ◆ All post-resection overall HRQOL scores were higher than the scores before resection. The patients received resection were divided into with and without recurrence groups. There was no significant changes in overall HRQOL score of patients without recurrence during 2-years follow up, however, there was a significant decrease in patients with recurrence.
Shun et al. 2008 Taiwan	To explore the changes and factors related to HRQOL in liver cancer patients receiving stereotactic radiation	Quantitative Longitudinal (1 week before SRT and the each week during the first six weeks of SRT: T0-T6)	◆ The functional living index-cancer (FLIC) ◆ Symptom severity scale (SSS) ◆ POMSSF-depression	N=99	62.42 (12.60)	◆ The HRQOL increased slightly but not significantly during SRT, and depression decreased at T3 but increased at T6. However, the symptom severity increased and reached their peaks at T5. ◆ Regarding predictors, patients with poor functional status, more severe levels of depression or symptoms, lower levels of albumin had lower HRQOL.

	therapy (SRT).		subscale ◆ ECOG			◆ Furthermore, when controlling for the effects of depression, functional status, albumin level, and time effect, the most important symptoms to predict changes in HRQOL were fatigue, pain, and nausea.
Steel & Baum et al. 2004 USA	To test the differences in HRQOL and survival between patients with HCC receiving hepatic arterial infusion (HAI) of Cisplatin and 90-Yttrium microspheres.	Quantitative Longitudinal (pre-treatment, 3, 6, 12 months)	◆ FACT-G & Hep	N=14, received 90-Yttrium microspheres N=14, received Cisplatin	56 (18-80) 62 (38-83)	◆ At baseline, the patients received Cisplatin had significant higher functional well-being and HRQOL than the patients received 90-Yttrium microspheres. ◆ At three months, the patients received 90-Yttrium microspheres had significant higher functional well-being and HRQOL. ◆ At six months, the patients received 90-Yttrium microspheres only had significant higher functional well-being. ◆ Patients received different treatments had a similar survival.
Steel & Eton et al. 2006	To test the reliability, sensitivity to	Quantitative Longitudinal (pre-treatment,	◆ FACT-G & Hep ◆ the FACT-	N=158	64 (22-90)	◆ All the measures at three months' follow up were lower than the baseline measures. However, the overall HRQOL, FACT-Hep,

USA	change in biomarkers associated with disease progression and response to treatment, and clinical meaningfulness of the FACT-Hep in patients with hepatobiliary carcinoma.	3, 6 months follow up)	Hepatobiliary Symptom Index (FHSI)			and trial outcome index at six months were significantly higher than these at three months, but not return to the baseline. ◆ The minimally important differences (MIDs) in FACT-Hep for clinically meaningful application: FACT-G subscales = 2-3; FACT-G = 6-7; Hepatobiliary Cancer Subscale = 5-6; FACT-Hep = 8-9; Trial Outcome Index = 7-8; and FHSI = 2-3 points.
Sun et al. 2008 Canada	To describe the symptom concerns of patients with HCC and pancreatic cancer, and to explore the effect of	Quantitative Longitudinal (baseline, 1, 2, 3 months)	◆ FACT-G & Hep ◆ The functional assessment of chronic illness therapy-spirituality subscale (FACIT-Sp-12)	N=22, HCC N=23, pancreatic cancer	59	◆ Patients with HCC had significantly lower scores in overall HRQOL, physical well-being, disease-specific symptoms, and spiritual well-being than patients with pancreatic cancer. ◆ Disease-specific symptoms were highly correlated with physical well-being, functional well-being, and overall FACT-Hep scores. ◆ The spiritual well-being in patients with HCC

	symptoms on HRQOL.					at baseline was significantly higher than the other three time points.
Tanabe et al. 2001 Japan	To explore prognostic factors and HRQOL in patients with tumor recurrence after hepatic resection for HCC.	Quantitative Cross-sectional	◆ The quality of life questionnaire, Japan version	N=188, received curative resection	60.80 (21-80)	◆ 65.43% of patients had recurrence. Unfavorable predictors after recurrence were pTNM Stage III/IV at initial surgery, receiving chemotherapy before initial surgery and presence of extrahepatic recurrence. ◆ The incidence of deteriorated performance status in the repeat resection group was lower than in the TACE group because of better psychological function in patients undergoing resection.
Wang et al. 2005 China	To evaluate the HRQOL of patient with HCC treated with radiofrequency ablation (RFA), and compared with that of patients	Quantitative Cross-sectional	◆ QOL-LC	N=80, RFA N=40, TACE N=40, TACE-RFA	50% patients between 50-70 yrs	◆ The RFA and TACE-RFA groups had significant higher scores in overall HRQOL and symptom/side effect domain than the TACE group. ◆ Age, income, liver function, tumour recurrence, and complication were related to the HRQOL after treatment. ◆ The RFA group had higher 1- 2- 3-years survival rates and less liver function damage, complications, and recurrences than the TACE group.

	treated with TACE or TACE-RFA					
Wang et al. 2007 China	To examine the impact of TACE alone and that of the TACE followed by RFA on HRQOL in patients with HCC.	Quantitative Longitudinal (baseline and 3 months) Randomization	◆ FACT-G	N=40, TACE N=43, TACE-RFA	--	◆ At baseline, there was no difference in HRQOL scores between the TACE group and the TACE-RFA group. At three months, the TACE-RFA group had a significantly higher overall HRQOL, functional, and social/family score. ◆ Child-Pugh Class and tumour recurrence after treatment were significant predictors of post-treatment HRQOL.
Aim 4: Relationships between physical variables, symptoms and HRQOL						
Bonnetain et al. 2008 France	To assess HRQOL as a prognostic factor of overall survival and to determine whether HRQOL	Quantitative Cross-sectional	◆ Spitzer QOL index	N=538	62.64% patients ≧ 65yr	◆ The HRQOL was a strong and independent prognostic factor of overall survival time for patients with HCC following mainly alcohol cirrhosis, and HRQOL can improve the discriminating power of the staging systems. ◆ In order to improve survival time, the therapeutic goal could be to preserve or improve HRQOL by controlling impact of disease on physical and emotional functioning.

	improved three prognostic classifications among patients with HCC.					
Fielding et al. 2007 Hong Kong	To examine whether HRQOL predict survival among Chinese patients with liver and lung cancer.	Quantitative Longitudinal (first outpatient visit and after 1.53 & 1.95 months)	◆ FACT-G ◆ Visual analogue: eating ability, eating appetite, eating enjoyment, self-care ability, and current health perception.	N=176, liver cancer N=358, lung cancer	57.34 (12.76) 64.81 (10.28)	◆ The HRQOL, overall or subscale, did not predict the overall survival in patients with liver cancer. ◆ Less advanced cancer stage and better eating appetite were significantly associated with longer survival in patients with liver cancer.
Lai et al. 2007 Taiwan	To explore the relationship between uncertainty and HRQOL,	Quantitative Cross-sectional	◆ FACT-G & Hep ◆ The Mishel Uncertainty in Illness Scale	N=110	62.07	◆ Regarding uncertainty, the first uncertainties were about the prognosis, future, and symptoms. ◆ There was negative correlation between uncertainty and HRQOL.

	and to find the predictors of HRQOL in patients with liver cancer.					◆ The significant predictors of HRQOL were uncertainty, Child-Pugh classification, pain, and gender that these factors accounted for 44% of variance in HRQOL.
Otegbayo et al. 2005 Nigeria	To evaluate the HRQOL in patients with primary liver cell carcinoma in Nigeria.	Quantitative Cross-sectional	◆ WHOQOL, including body pains, energy and acceptability of bodily appearance	N=34	49.60 (13.40, 23-74)	◆ 70% of patients rated their HRQOL as very poor, poor, neither poor nor good; and 85% were dissatisfied with their health. ◆ 82% of patients reported pain from moderate to extreme extent; and 50% didn't have enough energy to do daily activities; and 61.7% reported their bodily appearance unacceptable to them.
Steel & Hess et al. 2005b USA	To assess the rates of sexual dysfunction in patients with HCC and the relationships between sexual dysfunction and HRQOL.	Quantitative Cross-sectional	◆ FACT-G & Hep ◆ The Sexual Functioning Questionnaire	N=21, HCC N=23, CLD	65 (41-82) 54 (40-79)	◆ Regarding the prevalence of sexual dysfunction in patients with HCC, the rate for hypoactive sexual desire disorder was 5.3%, male erectile disorder was 5.6%, premature ejaculation was 5.6%, and dyspareunia was 5.9%. In patients with CLD, 16% was male erectile disorder and 5% was premature ejaculation and dyspareunia. ◆ Compared with general population, patients with HCC had higher rates in hypoactive

						sexual desire disorder and male erectile disorder, but a lower rate in premature ejaculation. ◆ Compared with patients with CLD, patients with HCC had higher rates in hypoactive sexual desire disorder, sexual aversion disorder, male orgasmic disorder, premature ejaculation, and dyspareunia; but a lower rate in male erectile disorder. ◆ Patients with HCC who reported increased rates of sexual problems had poorer HRQOL, especially in physical well-being.
Ueno et al. 2002 Japan	To explore the risk factors most affecting impaired HRQOL after partial hepatectomy in patients with HCC	Quantitative Cross-sectional	◆ The quality of life questionnaire, Japan version	N=96, received curative resection	60.60 (40-76)	◆ The patients were divided by two groups based on HRQOL score: those with preserved HRQOL and those with impaired HRQOL (cut-point: 22). ◆ The HRQOL after hepatectomy in patients with HCC was impaired in cases of aged patients, treatment for recurrence, and change of the serum cholinesterase level into unfavorable range.
Wong et al.	To assess the impact of	Quantitative Longitudinal	◆ FACT-G ◆ Eating	N=235, liver caner	55.94 (13.53)	◆ Patients with liver cancer reported lower scores in overall HRQOL, physical,

2008 Hong Kong	eating ability on HRQOL in Chinese patients with breast, liver lung, or nasopharyngeal carcinoma.	(baseline and 1.95, 1.57 months)	function: eating ability, eating appetite, eating enjoyment ◆ Pain rating (Visual Analogue) ◆ Depression (single item)	N=250, breast cancer N=334, lung cancer N=242, nasopharyngeal cancer		functional, emotional, eating appetite, and depression than patients with nasopharyngeal cancer. ◆ After controlling for socio-demographic and medical variables, pain, depression, and eating function significantly predicted overall HRQOL, physical, and functional well-being over time (all cancer). ◆ Patients with liver cancer had a slight decreased score in eating appetite, ability, and enjoyment.
Wong et al. 2008 Hong Kong	To examine the longitudinal course of the relationship between patients' satisfaction and HRQOL in Chinese patients with lung and liver	Quantitative Longitudinal (baseline and 1.95, 1.57 months)	◆ FACT-G ◆ The nine-item Chinese patient satisfaction questionnaire (ChPSQ-9) ◆ The cognitive subscale of Medical Interview Satisfaction Scale	N=235, liver cancer N=334, lung cancer	56.61 (12.65) 64.66 (10.60)	◆ There were no differences in HRQOL, patient satisfaction, and psychosocial measures between the two cancer groups. ◆ The MISS-cog didn't predict HRQOL, but all psychosocial factors emerged as covariate of the ChPSQ-9 in predicting HRQOL. After controlling for socio-demographic and psychosocial variables, only ChPSQ-9 predicted HRQOL.

	cancer.		(MISS-cog) ◆ The single item visual analogue to assess eating appetite, optimism, and depression			
Yeo et al. 2006 Hong Kong	To evaluate whether HRQOL is predictive of survival for patients with unresectable HCC.	Quantitative Cross-sectional	◆ EORTC-QLQ-C30	N=233	57 (16-80)	◆ A better score in physical, role, cognitive, social functioning and global HRQOL were significantly correlated with longer survival; a worse score in fatigue, nausea, pain, appetite, and constipation were significantly correlated with shorter survival. ◆ Combining clinical variables and HRQOL in multivariate analysis, advanced staging, high baseline total bilirubin, and worse appetite were independent predictors of shorter survival.
Zhao et al. 2002 China	To evaluate the HRQOL in patients with HCC undergoing	Quantitative Longitudinal (baseline, 1 & 3 months)	◆ QOL-LC	N=175	51.30 (16.6)	◆ The HRQOL at one and three months were significantly higher than that at baseline, especially physical and symptom scale. ◆ The significant predictors of HRQOL included tumour stage, liver function, superselective

	interventional therapy.					catheterization or not, chemoembolization or not, and number of interventional therapy. ◆ Three types of HRQOL change were identified: (1) descending to recovering, (2) constantly ascending, and (3) ascending to descending.
Aim 5: Relationships between demographic characteristics, psychological variables and HRQOL						
Steel & Gamblin et al. 2008 USA	To explore the post-traumatic growth in patients with primary or metastatic hepatobiliary cancer.	Mixed Longitudinal (baseline, 3, 6 months)	◆ FACT-G & Hep ◆ The post-traumatic growth inventory (PTGI) ◆ The Center for epidemiological studies-Depression (CES-D) ◆ Qualitative questions: have you changed your life in any	N=120 N=40, caregivers at 3 months	63 (30-86)	◆ 70% of patients reported positive and negative changes occurring at the time of diagnosis, and 19% reported the changes when they experienced symptoms. ◆ In the qualitative data, patients also reported the changes in health behaviours and the meaning or philosophy of life. ◆ The total and subscale scores of PTGI were not associated with the scores of FACT-Hep and CES-D. ◆ The patients with both positive and negative changes reported poor physical well-being, poor HRQOL, and higher depression than the patients with only negative or no changes.

			way as a result of being diagnosed with cancer? If yes, how?			
Tsai et al. 2007 Taiwan	To explore the HRQOL of liver cancer patients and the factors correlated with the HRQOL.	Quantitative Cross-sectional	◆ The chronic liver disease quality of life questionnaire: physical, emotional, social, and sexual relationship ◆ The chronic liver disease social support questionnaire ◆ The multidimensional health locus of control scale (all self-developed)	N=58	37.9% were 51-60 yrs	◆ The worst aspect of HRQOL was physical well-being and the best aspect was social well-being. ◆ There was a positive correlation between health locus control and HRQOL. ◆ There was no statistically significant correlation between social support and HRQOL.

Aim 6: Effects of psychological interventions on HRQOL						
Guo. 2005 China	To investigate the effects of emotional intervention and Chinese medicated diet therapy on emotion and HRQOL in patients with primary liver carcinoma after hepatic arterial chemo-embolization (HACE).	Quantitative Longitudinal (baseline, 2 months) Randomization	◆ EORTC-QLQ-C30	N=47, intervention group N=47, control group	53 (36-69)	◆ The intervention included psychoeducational course, relaxation training, exercise, and Chinese medicated diet. ◆ After intervention, the liver biological indexes of theintervention group including the levels of glutamic pyruvic transaminase, glutamic oxalacetic transaminase, alkaline phosphatase, lactic dehydrogenase, r-glutamyl transpeptidase, total bilirubin in serum and bile, and direct bilirubin were significantly different from those in the control group. ◆ The symptoms such as tiredness, nausea, emesis, anorexia and general healthy status were significantly improved in the intervention group after treatment than before treatment.
Lin et al. 1998 Taiwan	To investigate the effect of a combination of health education,	Quantitative Longitudinal (baseline, 2, 4, 6, 7 days)	◆ The knowledge questionnaire ◆ The worry inventory ◆ The physical	N=20, experimental group N=20, control	57 (12)	◆ Before experiment, there were no differences in demographic data, knowledge, worry, physical distress, and anxiety. ◆ After experiment, the knowledge score increased and worry score decreased in the

	muscle relaxation, and back massage on reducing stress in patients with HCC received TAE.	Randomization	distress scale ◆ The state-trait anxiety inventory (STAI)	group		experiment group. ◆ After TAE, the experimental group decreased anxiety level but the control group increased. In addition, the experimental group decreased physical distress more rapidly than the control group.
Steel & Nadeau et al. 2007b USA	To evaluate the benefits of individually tailored psychosocial intervention on patients with advanced hepatobiliary carcinoma.	Quantitative Longitudinal (baseline and 3 months) Randomization	◆ FACT-G & Hep ◆ CES-D ◆ STAI	N=14, intervention group N=14, attention-standard of care	67 (39-84)	◆ The patients in the intervention had clinically, but not statistically, significant improvements on symptoms of depression and anxiety, disease-related symptoms and treatment side effects, HRQOL. ◆ The patients in the intervention group also showed modest improvements in peripheral blood leukocytes and survival when compared with the standard of care group.

Table 3.4 The domains, reliability/validity, and references of the standardized questionnaires used to measure HRQOL in patients with HCC

Title	No. of studies	Domain	Reliability/ validity	Reference
The generic measure				
Short Form 36 (SF-36)	2	Physical health: Physical functioning Role limitation- physical Bodily pain General health Mental health: Role limitation- emotional Vitality Mental health Social functioning	◆ 36 items ◆ Most reliabilities of all subscale>0.8. ◆ Content validity, construct validity (principal component factor analysis), and discriminant validity (groups with different physical/ mental health status and severity) were assessed. ◆ http://www.sf-36.org/	McHorney, Ware, & Raczek, 1993; Ware, 2000; Ware & Sherbourne, 1992
World Health Organization Quality of Life Assessment (WHOQOL)	2	Physical domain Psychological domain Social domain Environmental domain	◆ 100 items; BREF: 28 items ◆ Cronbach's α= .73 -.85; Test-retest reliabilities =.66-.87. ◆ Discriminant validity (healthy and unhealthy individuals) and construct validity (confirmatory factor analysis) were assessed.	WHO group, 1995, 1998a, 1998b; Skevington, Lotfy, & O'Connell, 2004
Nottingham Health Profile (NHP)	1	Part 1: six domains of distress: Energy	◆ Test-retest reliabilities = .77-.85. ◆ Construct validity and criterion-related validity	Anderson, Aaronson, & Wilkin, 1993;

		Sleep Pain Emotional reactions Social isolation Physical mobility. Part 2: disease effects on daily activities: Work Home maintenance Social life Home life Sexual life Hobbies Holidays	(correlation with SF-36 and SIP) were assessed.	Hunt, McKenna, McEwen, Williams, & Papp, 1981
Sickness Impact Profile (SIP)	1	Social interaction Communication Alertness Emotional behaviour Body care Mobility Ambulation Work Eating Sleep	◆ Test-retest reliabilities = .62-.90. ◆ Discriminated validity (dysfunction and severity of illness) and clinical validity (disease specific measures: osteoarthritis, rheumatoid arthritis, and hip replacement) were assessed.	Bergner, Bobbitt, Kressel et al., 1976; Bergner, Bobbitt, Pollard, Martin, & Gilson, 1976; Pollard, Bobbitt, Bergner, Martin, & Gilson, 1976

		Home management Reaction		
The cancer specific measures				
Functional Assessment of Cancer Therapy-generic (FACT-G)	17	Physical well-being Emotional well-being Functional well-being Social and family well-being	◆ 27 items. ◆ Test-retest reliabilities=.72-.92. ◆ Criterion-related validity (correlation with SF-36 and ECOG performance status), convergent and divergent validity (mood, interpersonal support, and social desirability) and discriminant validity (different treatment groups) were assessed. ◆ http://www.facit.org/	Brucker, Yost, Cashy, Webster, & Cella, 2005; Cella et al., 1993; Heffernan et al., 2002; Overcash, Extermann, Parr, Perry, & Balducci, 2001
European Organization for Research and Treatment for Cancer Quality of Life Questionnaire Core-30 (EORTC-QLQ-C30)	4	Five functional scale: physical, role, social, emotional, and cognitive Symptoms: pain, fatigue, nausea/ vomiting, dyspnea, insomnia, appetite loss, constipation, diarrhea Financial impact Global QOL/general health	◆ 30 items. ◆ Cronbach's α =.54-.86. ◆ Construct validity (interscale correlations) and discriminant validities (between different disease, performance status, and health status) were assessed. ◆ http://groups.eortc.be/qol/index.htm	Aaronson et al., 1993; Hjermstad, Fayers, Bjordal, & Kaasa, 1998; King, 1996
Spitzer QOL index	1	Activity Daily life Health perceptions	◆ Observer-based measurement. ◆ Cronbach's α =.74-.84. ◆ Content validity and construct validity (comparing	Anderson et al., 1993; Spitzer et al., 1981

		Social support Behaviour.	physician-rated QOL index) were assessed.	
Interdisciplinary Group for Cancer Care Evaluation in Italy (GIVIO) quality of life questionnaire	1	Satisfaction with life Satisfaction with health Emotional state Cognitive state Functional state Social state Physical symptoms Satisfaction with health care Finally work activities.	◆ For Italian. ◆ Cronbach's α>.70.	The GIVIO Investigators,1994; Mosconi et al., 1998
Functional Living Index-Cancer (FLIC)	1	Physical functioning Mental functioning Social functioning General health/well- being Treatment- related symptoms.	◆ Cronbach's α= .92 -.95. ◆ Construct validity (principal components analysis), convergent/ discriminant validity (between symptoms and anxiety), and criteria- related validity (different nature of diseases and treatment) were assessed.	Schipper, Clinch, McMurray, & Levitt, 1984; Spilker, 1995
The liver cancer specific measures				
FACT-Hepatobiliary (FACT-Hep)*	12	Swelling or cramps in my stomach Losing weight Control of bowels Digest food well Have diarrhea	◆ 18 items, and accompany FACT-G. ◆ Cronbach' α =.72-.93/.82-.94; test-retest=.84-.91. ◆ Convergent- divergent validities (high correlation with FACT-G and trial outcome index; no correlation with social desirability) were assessed.	Heffernan et al., 2002

		Have good appetite Unhappy about change in appearance Back pain Bothered by constipation Fatigued Able to do my usual activities Bothered by jaundice or yellow skin Have fevers Have itching Have change in food tastes Have chills Mouth is dry Discomfort or pain in stomach		
Quality of life scale for patients of liver cancer (QOL-LC)*	3	Physical domain Psychological domain Social domain Symptom/side effect domain: pain in stomach, loss weight, digestive problem, fever, diarrhea	◆ 22 items. ◆ Cronbach's α= .68 -.81; Test-retest reliabilities=.71-.86. ◆ Construct validity (principle component factor analysis) and criteria-related validity (SF-36 and FLIC) were assessed.	Wan et al., 1998
The quality of life questionnaire (JAPAN)	2	Physical function Psychological function Social function Physical sensation	◆ 14 items. ◆ Based on SF-36, NHP, and FLIC.	Gross et al., 1999; Nuruki et al., 1995

		Recognition of the disease		
EORTC QLQ-HCC18*	1	Thirsty Trouble of taste Lost the muscle in arms or legs Abdominal swelling Worry figure of abdomen Worry eyes and skin becoming yellow Feel itch Shoulder pain Abdomen pain Fever Feel cold Worry nutrition Feel full just beginning eating Worry weight too light Vitality is not like anticipate Difficulty finishing things Need to sleep in daytime Influences on sexual life	◆ 18 items, and accompany EORTC QLQ-C30. ◆ The detail of questionnaire development was provided.	Blazeby et al., 2004
FACT Hepatobiliary Symptom Index (FHSI)*	1	Lack of energy Nausea Pain Losing weight	◆ 8 items, extracted from FACT-Hep. ◆ Cronbach’α = 0.79; test-retest reliability= 0.86. ◆ Criteria-related validity (correlation with FACT-Hep) and discriminant validity	Yount et al., 2002

		Pain in back Fatigue Jaundice or yellow color to skin Discomfort or pain in stomach	(differentiation by ECOG and treatment) were assessed.	
Gastrointestinal quality of life index (GQLI)	1	Gastrointestinal Symptoms Emotion function Physical Function Social Function Medical Treatment	◆ Cronbach's α =.75-.91. ◆ Construct validity (factor analysis) and clinical validity (detected different treatment) were assessed.	Eypasch et al., 1995

* the original paper that developed questionnaire was included in the review.

(3) Liver cancer specific measures

There were six liver cancer/disease specific measures shown in Table 3.4. The QOL questionnaire developed in Japan by Nuruki (1995) lacked psychometric information. The Gastrointestinal quality of life index (GQLI; Eypasch et al., 1995) focused on gastrointestinal symptoms instead of HCC symptoms only. Based on this information, it was decided not to use either of these measures in work related to my thesis.

The original articles describing the development of the following four standardized questionnaires [the European Organization for Research and Treatment of Cancer (EORTC) QLQ-HCC18 (Blazeby et al., 2004), the Functional Assessment of Cancer Therapy-Hepatobiliary (FACT-Hep) (Heffernan et al., 2002), the FACT Hepatobiliary Symptom Index (FHSI) (Yount et al., 2002), and the quality of life-liver cancer (QOL-LC) (Wan, Fang, Zhang, Lin, & Lo, 1998)] were included in the review. EORTC QLQ-HCC18 was developed primarily on patients with HCC, assessing fatigue, body image, jaundice, nutrition, pain, fever, sexual interest, and abdominal swelling. However, the FACT-Hep focused on hepatobiliary cancer such as metastatic colorectal cancer, HCC, pancreatic cancer, and cancers of the gallbladder and bile duct. The FHSI was a symptom index which was extracted from FACT-Hep including 8 items (3 pain, 2 fatigue, nausea, weight loss, and jaundice). The QOL-LC was developed for Chinese patients with liver cancer, and the ‘symptom/side effect’ subscale included the disease-specific items.

The FACT-Hep was the most widely used liver cancer specific instrument and was included in 12 of 36 studies. Steel, Eton, Cella, Olek, and Carr (2006) estimated the minimally important difference (MID) for the FACT-Hep to be 8-9 points, and the FHSI was 2-3 points. Steel and colleagues assessed the consistency of the FACT-Hep between patients, caregivers, and physicians. Caregivers were better proxies than physicians; they had adequate estimate of physical, functional, and disease-specific concern, but underestimated emotional and social well-being (Steel, Geller, & Carr, 2005).

3.4.2 Aim 2: Differences in HRQOL between patients with HCC, patients with chronic liver disease, and general population

(1) Comparison with patients with chronic liver disease

Four studies compared HRQOL between patients with HCC and liver disease. Patients with HCC had worse physical well-being and overall HRQOL than patients with chronic liver disease (Bianchi et al., 2003; Kondo et al., 2007; Steel, Chopra, Olek, & Carr, 2007), mainly in pain, loss of appetite and weight, difficulties digesting, and decreased ability to perform usual activities (Bianchi et al., 2003; Steel & Chopra et al., 2007). However, after liver transplantation, there was no significant difference in HRQOL between patients with malignant and nonmalignant liver disease (Boudet et al., 1995).

(2) Comparison with the general population

Three studies compared HRQOL between patients with HCC and the general population. Patients with HCC had lower HRQOL than the general population, especially in physical (Kondo et al., 2007; Lee et al., 2007; Steel & Chopra et al., 2007), psychological (Kondo et al., 2007; Steel & Chopra et al., 2007), functional well-being (Kondo et al., 2007; Steel & Chopra et al., 2007), and hepatobiliary symptoms (This is not surprising given that hepatobiliary symptoms would not be expected among on the general population) (Steel & Chopra et al., 2007). In contrast, patients reported better scores in social/family well-being (Steel & Chopra et al., 2007) and the environment domain of QOL (Lee et al., 2007).

Of 17 studies using the FACT-G & Hep to assess HRQOL, only 10 provided means and standard deviations (Heffernan et al., 2002; Lai, Lin, & Yeh, 2007; Lee et al.,2007; Poon et al., 2001; Steel, Eton, Cella, Olek, & Carr, 2006; Steel, Baum, & Carr, 2004; Steel, Chopra et al., 2007; Steel, Geller, & Carr, 2005; Sun et al., 2008; Wang et al., 2007) (see Table 3.5). The means and standard deviations at baseline were pooled together and compared with the norms for the general population and cancer patients (Brucker, Yost, Cashy, Webster, & Cella, 2005). *t*-tests were used to examine the differences. Patients with HCC had worse physical well-being, *t*(621.2231)=-3.45, *p*<.001, emotional well-being, *t*(544.3254)=-17.52, *p*<.001, functional well-being, *t*(504.3647)=-5.65, *p*<.001, and overall HRQOL, *t*(629.2695)=-4.99, *p*<.001; but had better social/family well-being, *t*(327.6015)=4.19, *p*<.001, than the general population. In addition, patients with HCC had worse emotional well-being, *t*(766.5188)=-14.46, *p*<.001, functional well-being, *t*(748.8241)=-8.01, *p*<.001, social/family well-being t(752.8413)=-8.92, p<.001, and overall HRQOL, *t*(243.2823)=-7.48, *p*<.001, than patients with heterogeneous cancer (Brucker et al., 2005).

Table 3.5 The original and pooled mean (SD) of FACT-G & Hep subscale

	n	PWB	EWB	FWB	SFWB	Hep	Overall	Overall (Hep)
Pooled	798	21.78	16.04	16.79	20.24	47.89	76.49	133.55
		(5.92)	(4.65)	(6.23)	(4.97)	(10.10)	(13.00)	(21.78)
Norm[a]	1075	22.70	19.90	18.50	19.10	--	80.10	--
(GP)		(5.40)	(4.80)	(6.80)	(6.80)		(18.10)	
Norm[a]	2236	21.30	18.70	18.90	22.10	--	80.90	--
(cancer)		(6.00)	(4.50)	(6.80)	(5.30)		(17.00)	

PWB- Physical well-being; EWB- Emotional well-being; FWB- Functional well-being; SFWB- Social/family well-being; Hep- Hepatobiliary concerns; Overall- HRQOL (PWB+EWB+FWB+SFWB); Overall(Hep)- HRQOL (PWB+EWB+FWB+SFWB+Hep); GP- General population. a: data from Brucker et al., 2005.

3.4.3 Aim 3: The effects of treatments on HRQOL: liver surgery, hepatic artery transcatheter treatment, and radiotherapy

(1) Effects of liver surgery on HRQOL

Four studies investigated the effects of liver surgery. Following hepatic resection, HRQOL declined during two-10 week periods after the liver operation, but increased to the preoperative level at three-four months, and was higher than the preoperative level at nine months (Chen et al., 2004; Poon et al., 2001). Significant improvement was found in physical well-being (Poon et al., 2001). Major hepatectomy resulted in more reduced HRQOL than minor hepatectomy (Chen et al., 2004). On the other hand, patients treated with hepatic resection had better HRQOL and were less depressed than patients treated by hepatic arterial infusion (HAI) (Poon et al., 2001; Tanabe et al., 2001). After liver transplantation, there was no significant difference in HRQOL between patients with malignant and nonmalignant liver disease, and 70% of patients with liver cancer claimed to 'live a normal life' (Boudet et al., 1995).

(2) Effects of hepatic artery transcatheter treatment and radiation therapy on HRQOL

Seven studies investigated the effects of the TAE or TACE treatment. The HRQOL in patients who received TAE or TACE was lower at three months than pre-treatment (Steel et al., 2006; Sun et al., 2008), and was higher at six months than at three months, but did not return to baseline (Steel et al., 2006). Patients treated with 90-Yttrium microspheres had better HRQOL than patients who received Cisplatin through hepatic arterial infusion (Steel, Baum, & Carr, 2004). In addition, patients treated with radiofrequency ablation (RFA) or TACE-RFA had better HRQOL than those treated with only TACE (Wang et al., 2005, 2007). On the other hand, HRQOL increased slightly but not significantly during stereotactic radiation therapy (SRT) (Shun et al., 2008).

3.4.4 Aim 4: The relationships between physical variables, symptoms and HRQOL

(1) The relationships between physical variables and HRQOL

Eleven studies explored the relationships between HRQOL and physical variables, including liver function, tumour stage and recurrence. There were significant positive correlations between liver function and HRQOL. Patients with better Child-Pugh classification (Lai, Lin, & Yeh, 2007; Steel & Chopra et al., 2007; Wang et al., 2005, 2007), higher albumin (Kondo et al., 2007; Shun et al., 2008), lower serum bilirubin (Kondo et al., 2007), lower serum cholinesterase (Ueno et al., 2002) had better HRQOL. Patients with advanced stage (Zhao et al., 2002) or tumour recurrence (Chen et al., 2004; Ueno et al., 2002; Wang et al., 2005, 2007) had worse HRQOL. However, there were contrary findings in that tumour mass or hepatocellular failure (Bianchi et al., 2003), and whether or not patients had a HCC recurrence (Kondo et al., 2007), did not predict HRQOL. In addition, patients with duration of HCC more than one year had better HRQOL (Lee et al., 2007).

(2) The relationships between symptoms and HRQOL

Seven studies explored the relationships between HRQOL and symptoms. Severe symptoms were associated with patients' HRQOL including pain (Chen et al., 2004; Lai et al., 2007; Shun et al., 2008; Sun et al., 2008; Wong & Fielding, 2008b), sleep disorder (Bianchi et al., 2003), fatigue (Shun et al., 2008; Sun et al., 2008), nausea (Shun et al., 2008), and sexual problems (Steel, Hess, Tunke, Chopra, & Carr, 2005). In addition, patients who had better performance status (Shun et al., 2008) and eating ability (Wong & Fielding, 2008b) had better HRQOL.

3.4.5 Aim 5: The relationships between demographic characteristics, psychological variables and HRQOL

Regarding demographic characteristics, older age (Chen et al., 2004; Kondo et al., 2007; Ueno et al., 2002), being female (Lai et al., 2007), and lower income (Wang et al., 2005) were associated with worse HRQOL. In contrast, Wang et al. (2005) showed that older patients had better HRQOL.

Five studies explored the relationships between HRQOL and psychological variables. HRQOL was negatively correlated with depression (Shun et al., 2008; Wong & Fielding, 2008b), uncertainty (Lai et al., 2007), and chance health locus of control (Tsai, Chien, Chan, Lin, & Lan, 2007); and was positively correlated with satisfaction about medical services (Wong & Fielding, 2008a).

3.4.6 Aim 6: effects of psychological interventions on HRQOL

Three studies used randomization control trials to investigate the effects of psychological interventions on HRQOL. Guo (2005) randomized 47 patients with primary liver carcinoma to intervention group which received emotional intervention and Chinese medicated diet, and 47 patients to control group who received normal medical care. After two months, patients in the intervention groups had improved liver function and general health status, as well as decreased physical symptoms. Lin, Tsang, and Hwang (1998) randomly assigned 40 patients with HCC to the intervention (n=20) or control group (n=20). The intervention group received health education, muscle relaxation, and back massage; and the control group received routine care. The intervention group showed a greater increase in knowledge scores, a greater decrease in worry scores, and a smaller increase in physical distress scores than the control group. Steel, Nadeau, Olek, and Carr (2007) randomized 14 patients to an intervention group who received education, cognitive behavioural therapy, supportive expressive therapy, and pharmacological intervention; and 14 patients to the control group who received education and attention-standard of care. After three months, the intervention group had clinically significant improvements on depression and anxiety, disease-related symptoms and treatment side effects compared with the control group.

3.5 Discussion

As a result of the systematic review, four generic measures, five cancer specific measures, and six liver cancer specific measures were identified. According to the liver cancer specific questionnaires, the disease-specific concerns include pain, fatigue, nausea, jaundice, weight loss, and body image. A standard measurement instrument with well-established psychometric characteristics and disease specificity is necessary to assess HRQOL in patients with HCC (Poon et al., 2001). The cancer-specific instrument combines a core questionnaire for use in a particular cancer with a module questionnaire which assesses specific issues in cancer patient subgroups (Pallis & Mouzas, 2004). The EORTC QLQ-C30 and the FACT-G are the most widely used instruments in assessing HRQOL of patients with cancer (Pallis & Mouzas, 2004), but these two only measure the general concerns of HRQOL (Aaronson et al., 1993; Cella et al., 1993). They lack the specific measure for patients with HCC, therefore the EORTC and the FACT group developed the liver cancer specific scale. The EORTC QLQ-HCC18 and the FACT-Hep have to accompany the EORTC QLQ-30, FACT-G respectively to measure HRQOL in patients with HCC. Furthermore, the FHSI-8 provides a simple and effective symptom index for clinical application. Both the EORTC QLQ-HCC18 and the FACT-Hep are international instruments and include a Taiwan version, but the EORTC QLQ-HCC18 is specifically focused on HCC patients with clear subdimensions of disease concerns.

Based on this finding, the most appropriate measure of HRQOL for patients with HCC is EORTC QLQ-HCC18 in my thesis.

HRQOL covers all aspects of health and functional status, and it is more informative than medical indices such as survival rate, modality rate, or functional index (Bonnetain et al., 2008). Compared with the general population, patients with HCC have worse HRQOL in physical, emotional, and functional well-being; but they may have better social/family well-being. Compared with heterogeneous adult patients with cancer, they have worse HRQOL in emotional, functional, and social/family well-being. Compared with patients with chronic liver disease, they have worse physical well-being and overall HRQOL.

The present review revealed that patients with HCC have worse HRQOL in physical condition, emotional status, and functional ability, which is consistent with previous reviews (Gutteling, de Man, Busschbach, & Darlington, 2007; Martin, Sheridan, & Younossi, 2002). Conversely, patients with HCC have better social and family relationships, similar to the previous studies (Brucker et al., 2005; Lee et al., 2007; Steel & Chopra et al., 2007). It is possible that family and friends provide more assistance and support for patients after disease. Moreover, patients with HCC have worse HRQOL than patients with chronic liver disease, largely lower in physical aspects. The physical well-being may be impaired due to severe symptoms or treatment side effects, especially pain, loss of appetite, difficulties digesting, and fatigue.

Liver surgery, hepatic artery transcatheter treatment, and radiation therapy can improve patients' HRQOL. HRQOL may decrease from pre-treatment to three months after treatment and increase from three to six months. Patients with better liver function, early stage of disease, and no recurrence have better HRQOL. Severe symptoms such as pain, fatigue, and nausea are negatively correlated with HRQOL, whereas performance status and eating ability positively correlate with HRQOL.

There is a trade-off between benefits and drawbacks of treatment for patients with cancer, and with the goal of improving patients' functions to live the best possible life within the constraint of HCC, HRQOL can be a good outcome to evaluate the cost/benefit of treatment (Wang et al., 2007). Treatment may reduce patients' HRQOL in short-term period but improve HRQOL in longer term. However, the recovery rate varies depending on patients' physical condition and treatment. Various factors may influence the change pattern. The recovery rate of patients treated by surgery is better than those treated by TAE/TACE. The HRQOL in patients treated by surgery improves over that before treatment, but the HRQOL in patients treated with TAE/TACE does not return back to the baseline level. The potential explanation is that patients who receive surgery are at early stage and have better liver function. Liver function is another significant factor associated with HRQOL. Increasing severity of liver disease based on the Child-Pugh classification is strongly correlated with decreased physical component summary scores on the SF-36 (Arguedas, DeLawrence, & McGuire, 2003). In addition, patients with less severe symptoms have better HRQOL. The large-size tumour may compress the adjacent stomach, the gross ascite may cause a feeling of abdominal swelling, hepatic dysfunction may reduce appetite, and the multiple symptoms may lead to poor tolerance to intervention (Yeo et al., 2006).

Apart from medical treatment and physical factors, psychosocial variables also play an important role in determining HRQOL. HRQOL is negatively correlated with depression, uncertainty, chance health locus of control; and positively correlated with satisfaction with medical services. In addition, psychosocial interventions may reduce negative feelings and enhance HRQOL. Patients who feel uncertainty about disease, treatment, and the future, and feel controlled by chance have worse HRQOL (Lai et al., 2007; Tsai et al., 2007). HCC has a great impact on physical health and psychological well-being, even the stigma of death, and patients' anticipated life trajectory is challenged. In addition, satisfaction, especially about doctors and nurses, is strongly related to HRQOL. Satisfaction is based on patients' expectations, medical care that they received, and cultural imperative (Wong & Fielding, 2008a). In the randomization control experiments, the psychological interventions involving psychoeducation, relaxation, and emotional expression were found to improve patients' HRQOL.

In this review, the data pooled together were at baseline in order to minimize the effect of treatment, but there were still other confounding factors, such as liver function, disease stages, or treatments which may influence the differences in HRQOL between patients with HCC and the general population.

Several limitations of this review should be acknowledged. First, the studies varied in terms of the sample (e.g., disease stage, treatment), measurement tool, and country, making simple comparisons difficult. Second, not all the studies provided detailed information regarding means and standard deviations. Third, the norm of FACT (Brucker et al., 2005) is based on the US population and may be different from other countries' norms. Fourth, the dropout rates of some longitudinal studies were high, and therefore the improvement in HRQOL may be overestimated. Fifth, the sample size was small in some studies, especially psychological intervention studies.

In summary, HCC has a negative impact on patients' HRQOL, especially on physical, emotional, and functional well-being, but patients may have better social/family well-being than norms based on the healthy population. Medical variables, such as disease stage, treatment, liver function, and symptoms play an important role in determining HRQOL. Further studies are warranted to understand the effects of psychological variables on HRQOL, the interaction between physical variables and psychological variables, and to explore the factors that may enhance patients' HRQOL and adjustment. However, only a few of the studies focused on the psychosocial variables. I propose therefore to explore the influences of both physical and psychosocial variables on HRQOL.

Although I wanted to recruit either qualitative or quantitative methodology, but no qualitative study with good quality was founded. Three studies stated that they used both research methods but only used some open-ended questions and lacked a rigid qualitative methodology. In addition, the previous studies used the standardized questionnaires that may ignore the specific characteristics and cultural differences in patients with HCC in Taiwan. Hence, I decided to use a mixed methods approach, combining qualitative and quantitative methodology, to gain a broad understanding of the HRQOL and adjustment in patients with HCC. In the next chapter, general considerations of mixed methods research will be discussed.

Chapter 4. Mixed Method Research

4.1 Abstract

The results of Chapter 3 revealed that most previous studies used standardized measures and focused on the effects of physical variables. There were very little studies given link to patients' perceptions and the role of psychological variables; in order to gain a broader understanding about the HRQOL and process of adjustment in patients with HCC, a mixed methods approach would be most appropriate. At first, I concentrated on the definition of mixed methods research and compared the differences between qualitative and quantitative methods; and then I described how to conduct a mixed methods research, including characteristics and typologies, as well as data combination. Finally I described the research design of my thesis.

4.2 What is a mixed methods research

In recent years, mixed methods research has become popular in various fields and been accepted as a rigorous and legitimate research design (Tashakkori & Teddie, 2003). However, there are major differences in philosophical worldview and rationales of proponents of qualitative and quantitative methodology and these need consideration.

4.2.1 Definition

Mixed methods research began in the 1950s when Campbell developed the multitrait and multimethod matrix for validation of psychological traits (Campbell & Fisker, 1959); and following two decades of development, mixed methods research has concrete theoretical foundation and practical guidelines, and has been accepted as the third research paradigm (quantitative approach, qualitative approach, and mixed methods research approach) (Creswell & Plano Clark, 2007; Johnson & Onwuegbuzie, 2004). It is defined as research which combines elements of qualitative and quantitative research methods for the broad purposes of breadth and depth of understanding and corroboration (Johnson, Onwuegbuzie, & Turner, 2007). The combination of qualitative and quantitative methods may occur at different stages of the research process, such as formulation of research questions, sampling, data collection, data analysis, and result interpretation (Bryman, 2006).

Mixed methods research not only expands the research toolbox, but also provides the opportunity for synthesis of research traditions and methods which is beyond the scope of any single technique (Borkan, 2004). When using both qualitative method and quantitative method in a single study, two questions may arise: the first is the conflicts between different philosophical assumptions of knowledge, and the other is a technical problem (Morgan, 1998). In order to solve the first question, the comparisons between qualitative and quantitative methods will be conducted and a theoretical framework will be provided. The second problem will be discussed in the next section.

4.2.2 The comparisons between qualitative and quantitative approaches

Disputes between qualitative and quantitative researchers have been apparent for a long period. The basic differences between two methods are summarised in Table 4.1 and include seven points.

Table 4.1 The comparisons between qualitative method, quantitative method, and mixed methods research

	Quantitative method	Qualitative method	Mixed method
Philosophical worldviews	Postpositivism	Constructivism	Pragmatism
Purposes	To ask for an exploration of the central phenomenon or concept in a study	To find out about the relationships among variables, ex. cause-and-effect or predictive relationships	The integrated question to answer both quantitative and qualitative questions
Specific methods	Observation Interviews Groups Documents photographic	Experiment Quasi-experiment Correlation study Survey	Both qualitative and quantitative methods
Data analysis	Text or image analysis To identify the themes and meanings	Numerical statistical analysis To reject hypothesis or not	Data transformation and data integration
The role of researcher	Interpret the meanings of data actively, and aware personal value or status may influence the results	Keep objectivity and remove bias	Both qualitative and quantitative positions
Quality of research	Reliability Validity Generalizability	Credibility Dependability Transferability Confirmability	Both qualitative and quantitative criteria
Strengths	To describe phenomenon in rich detail, such as contextual factors and dynamic process	To control the confounding factors To test hypothesis or theory, and to generalize the results	To combine numeric and narrative data, and provide qualitative and quantitative approaches strength
Weaknesses	Difficulties to test hypothesis or theory, and to generalize the results Researchers' bias	Difficulties to application for specific situation or context	Practical difficulties, e.g., Time and money consuming Methodological problems, e.g., paradigm mixing, data transformation, and conflicting data

(1) Philosophical worldviews

The philosophical worldview can be seen as a basic set of beliefs that guide action (Guba & Lincoln, 2005). It is a general orientation about the world and the nature of research and knowledge that researchers hold (Creswell, 2009). The worldview includes ontology (view of reality), epistemology (view of knowing and the relationship between knower and to-be-known), methodology (view of research process), and axiology (view of what is valuable) (Creswell & Plano Clark, 2007; Guba & Lincoln, 2005). Post-positivism, which is usually associated with the quantitative method, asserts that social science should be objective, and treats social phenomena as determination which causes probably determine effects or outcomes (Johnson & Onwuegbuzie, 2004). Objective reality exists out there in the world, and numerical measures of study are developed in this philosophy (Creswell, 2009). In contrast, constructivism, associated with qualitative method, contends that multiple-constructed realities exist whereby individuals seek understanding of the world. They then construct subjective meanings of their experience, and the individual's subjective view is the only source of reality (Johnson & Onwuegbuzie, 2004).

(2) Research purposes

Qualitative and quantitative methods deal with different research questions. The questions typically employed in a qualitative study are to explore the specific phenomenon and to understand the meaning that individuals give to the phenomenon inductively. On the other hand, the central questions in quantitative study are to test whether the relationship between various factors exists as well as to test a theory deductively (Creswell, 2009; Creswell & Plano Clark, 2007).

(3) Research methods

In general, qualitative study asks open-ended questions while quantitative study asks closed-ended questions. Qualitative method collects audio-visual materials from observation, interview (individual or group), documents, or photographs. Quantitative method collects numeric data from various designs such as experiment, quasi-experiment, correlation study, or survey.

(4) Data analysis

Qualitative method is to identify the significant themes and meanings for providing depth description of phenomenon. Quantitative method uses statistical analysis to test the hypothesis and confirm the numerical relationships (Creswell, 2009).

(5) The role of Researchers

In qualitative method, researchers play an active role to interpret results and they have to aware of the influences of personal values or background on the analysis process. However, in quantitative method, researchers have to keep a detached position to report results objectively (Creswell & Plano Clark, 2007).

(6) Criteria for assessing the quality of research

In qualitative method, researchers have to demonstrate the trustworthiness of work, in terms of whether the findings represent a credible interpretation from original data (credibility), whether similar findings can be identified in similar contexts (dependability), whether findings can be produced in different contexts (transferability), and whether other similar researchers have similar findings (confirmability) (Denzin & Lincoln, 1994; Lyons, 1999). On the other hand, in quantitative method, researchers need to provide information concerning the stability of measures (reliability), the accuracy of measures (validity), and the generalizability of findings across different settings (generalizability) (Lyons, 1999).

(7) Strength and weaknesses

Qualitative method provides a rich description about target phenomenon or formulates a theory, including contextual factors and dynamic process. But it is difficult to test a hypothesis or theory and generalize the results. In addition, the researchers' bias would influence the qualitative results. On the contrary, quantitative method can test a hypothesis or theory, but the results may be too general to apply in specific situation (Johnson & Onwuegbuzie, 2004).

4.2.3 The philosophical worldview of mixed methods approach

In spite of the differences between the two research approaches, qualitative and quantitative approaches should not be taken as entirely distinct. There can be quantitative components in qualitative study, and vice versa. For example, the important themes in qualitative study may be based on the frequency of events, and the categories of variables in quantitative study should be based on the meaning of the categories. Therefore, the approaches can be viewed as a continuum with the qualitative approach anchored at one pole and the quantitative anchored at the other pole, and mixed methods approach covering the middle area (Johnson et al., 2007).

Both qualitative and quantitative methods are empirical methods to explore the world/truth and to answer research questions. In the research process, both types of methodologists carry out studies to describe their data, formulate possible arguments from data, and construct theories to explain or predict phenomena (Sechrest & Sidana, 1995). The commonalities among qualitative and quantitative methods provide the foundations for combining two approaches (Reichardt & Rallis, 1994). Thus, qualitative and quantitative methods are not incompatible but should be seen as complementary (Malterud, 2001). Mixed methods research should use a philosophy and method which fit together the logistic provided by qualitative and quantitative approaches into a workable solution (Johnson & Onwuegbuzie, 2004).

Regarding the philosophical worldview, pragmatism provides a potential foundation for mixed methods research (Tashakkori & Teddie, 2003). Pragmatism states truth value is to be determined by the experiences or practical consequences of belief in or use of the expression in the world (Murphy, 1990). It focuses on the consequences of research, as well as on the primary importance of the questions asked rather than the methods. It is pluralistic and addressed on practice and "what works" (Creswell & Plano Clark, 2007).

4.2.4 The rationales of mixed methods approach

Mixed methods research uses both qualitative and quantitative methods in a study, and the philosophical worldview is to get useful and practice knowledge for research questions. In spite of this, there are some challenges, such as the time- and money-intensive nature of collecting and analyzing both text and numeric data, and requirement for researchers to have both qualitative and quantitative skills. However, a mixed methods approach has multiple sources of data and integrations of analysis, and uses the strengths of one method to enhance the performance of the other (Morgan, 1998). It can provide a complete picture of phenomena as well as in-depth knowledge of participants' perspectives (see Table 4.1 the strengths and weaknesses of mixed methods research) (Creswell, 2009; Creswell & Plano Clark, 2007; Morgan-Ellis et al., 2006).

There are five major purposes in conducting mixed methods research,: (1) *triangulation:* convergence, corroboration, correspondence of results form the different methods; (2) *complementary:* elaboration, enhancement, illustration, clarification of the results from one method with the other; (3) *development:* using the result from one method to inform the other method; (4) *initiation:* exploratory discovery of contradiction, new perspectives, or recasting of questions; (5) *expansion:* extends the breadth and range of inquiry (Greene, Caracelli, & Graham, 1989).

4.3 How to conduct a mixed methods research

The philosophical worldview and rationales of mixed methods research were discussed in the above section. In this section, the characteristics and typologies, and data combination will be addressed.

4.3.1 The characteristics and typologies

The recognition of characteristics and typologies in mixed methods research can help researchers to design their studies. The various types of typologies have been identified (Creswell & Plano Clark, 2007). The basic characteristics of typologies include (1) timing, (2) weighting, (3) mixing, and (4) theorizing (Creswell, 2009).

(1) Timing: concurrent vs. sequential.

Timing refers to the order of data collection; whether the qualitative and quantitative data are collected sequentially or concurrently (Bryman, 2006; Creswell, Fetters, & Ivankova, 2004; Greene et al., 1989; Morgan, 1998). In a sequential design, the data from one method serves as a basis for the other data collection and analysis; in a concurrent design, both types of data are collected at the same time and are merged together in analysis and interpretation stages (Creswell et al., 2004). The key point is how to connect the two types of information for maximizing their contributions to the overall research (Morgan, 1998).

(2) Weighting: equal vs. unequal.

Weighting refers to the priority of data with the emphasis on quantitative data, qualitative data, or an equal priority between the two types (Bryman, 2006; Creswell et al., 2004; Greene et al., 1989; Morgan, 1998). It is determined by researchers, the research questions, and the audience for the research (Creswell, 2009). The key point is how to make the combination of analysis and results in a coherent fashion (Morse, 1991).

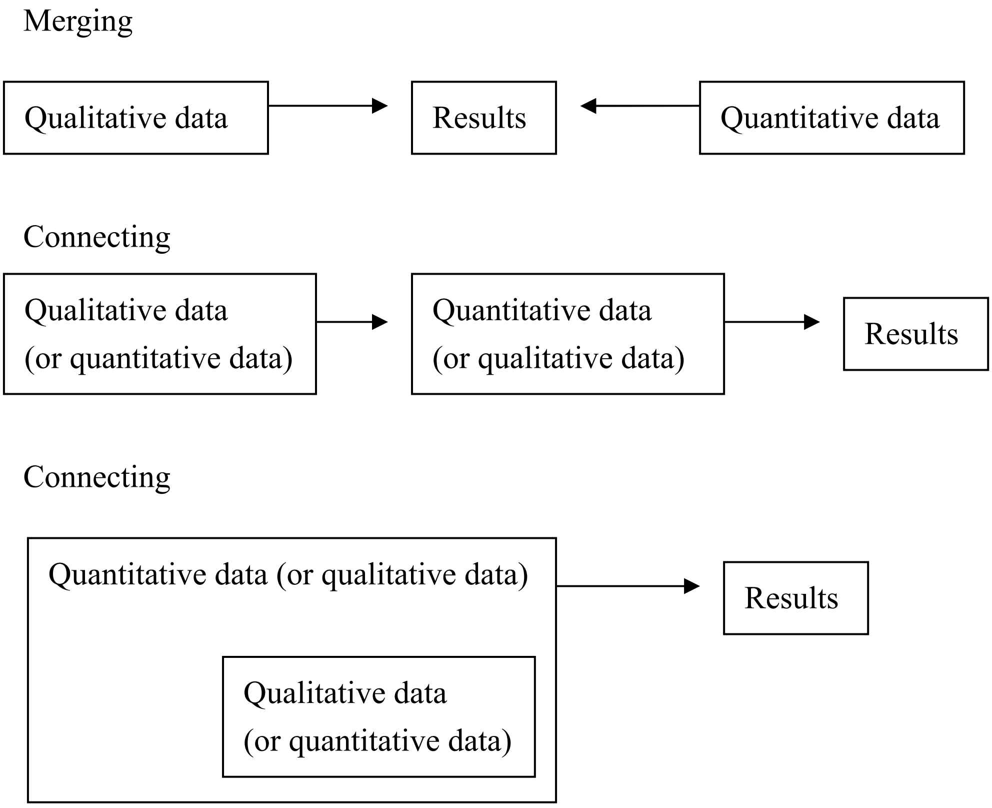

Figure 4.1 The ways of mixing (From Creswell & Plano Clark, 2007)

(3) Mixing: merging vs. connecting vs. embedding.

Mixing refers to the ways of combining two types of data (Bryman, 2006; Creswell, 2009; Creswell & Plano Clark, 2007). Two basic questions need to be considered: *when* and *how* does mixing occur? (Creswell, 2009) Mixing can occur at data collection, data analysis, and data interpretation, or all of three phases (Creswell, 2009). There are three ways in which mixing can occur: merging, transforming one set of data into the other form and combining both together; connecting, using one type of data in the first phase as the basis for the second phase; embedding, using one type of data as a supportive role for the other data (see Figure 4.1) (Creswell, 2009; Creswell & Plano Clark, 2007).

(4) Theorizing: explicit vs. implicit.

Theorizing refers to whether a theoretical perspective or framework guides the research design (Creswell, 2009). Generally, researchers have an explicit theory which guides their studies.

Creswell (2009) combined the purposes and characteristics of mixed methods research, to identify the four major types of mixed methods design: (1) the triangulation design (convergence model, data transformation model, validating quantitative data model, and multilevel model), (2) the embedded design (experimental model and embedded correlational model), (3) the explanatory design (follow-up explanations model and participants selection model), and (4) the exploratory design (instrument development model and taxonomy development model). He suggested researchers should select a design which best matches their research questions (Creswell & Plano Clark, 2007).

4.3.2 Data combination

The mixed methods research process includes eight steps: determine the research question; determine whether a mixed methods design is appropriate; select the mixed method design that matches the research question; collect the data; analyze the data; interpret the data; legitimate the data; and draw conclusion and write the report

(Johnson & Onwuegbuzie, 2004). It is a complex and dynamic process, after setting purposes and research questions, the next steps can vary in order, iteration, or be revised when needed (Johnstone, 2004).

Data combination is based on research questions, research design, and the nature of data. Although qualitative and quantitative data can be combined at different stages of research, most occur at the analysis and interpretation stages (Niglas, 2004). There are three levels of integration: at the lowest level, qualitative and quantitative research are conducted separately and the essential components only are combined; at the middle level, the two types of research are conducted in the same study but the integration is not specified; and at the highest level, the integration occurs throughout the whole research process, from design through analysis and integration (Greene et al., 1989; Mortenson & Oliffe, 2009).

Onwuegbuzie and Teddie (2003) described seven basic phases regarding the data analysis process, including data reduction, data display, data transformation, data correlation, data consolidation, data comparison, and data integration. Researchers identify the main dimensions of qualitative data and significant results of quantitative data, and describe both results in visual materials, such as matrices, charts, diagrams, tables, or graphs. Then the data are transformed into the other form. Quantitative data are converted into narrative data which can be analyzed qualitatively (qualitized), and qualitative data are converted into numerical data and analyzed in statistics (quantitized) (Caracelli & Greene, 1993; Tashakkori & Teddie, 1998). In the next phase, qualitative data are correlated with the quantitized data, and quantitative data with qualitized data; and consolidated variables or data sets are created based on the combinations. In addition, data comparison can be conducted between qualitative and quantitative data sources. In the final phase, two types of data are integrated into a coherent whole or two separate sets (qualitative and quantitative) of coherent wholes (Onwuegbuzie & Teddie, 2003).

Furthermore, mixed methods research design influences the data analysis. In concurrent triangulation design, qualitative and quantitative data are analyzed separately and are merged together. Researchers can transform one type of data to make the qualitative and quantitative datasets comparable, or compare the data without transformation in a discussion or a matrix (Creswell & Plano Clark, 2007). On the other hand, in sequential explanatory or exploratory design, researchers have to consider what information in the early stage is important and useful for the next stage. When qualitative study is conducted first, the codes and themes, significant statements, and potential models are important for the next quantitative study; when quantitative study is conducted first, the significant-nonsignificant results, demographic characteristics, comparison groups, and extreme cases should be considered (Creswell & Plano Clark, 2007).

The final issue is about validity. Combining qualitative and quantitative data may raise potential validity problems. Researchers should consider the reliability and validity issues in qualitative and quantitative approaches, but also assess the trustworthiness of both data combinations and interpretations (Onwuegbuzie & Johnson, 2004, 2006). Researchers have to ensure consistency among the research purposes, the questions, and the methods they use, as well as the legitimacy or applicability of the results (Newman, Ridenour, Newman, & DeMarco Jr, 2003).

4.4 The research design of thesis

In the systematic review described in Chapter 3, it was concluded that most previous research used quantitative methods with standardized instruments and focused on the effects of physical factors on the HRQOL in patients with HCC. However, treatment and physical factors cannot totally explain the HRQOL and quantitative method by itself cannot explore the potentially important variables which may influence patients' adjustment. A mixed methods research design may be useful to gain in-depth knowledge of the adjustment process from patients' perspectives and to test the physical and psychological factors that influence patients' HRQOL.

Table 4.2 The characteristics of thesis

Characteristics	Content
Rationale for mixing	Both qualitative and quantitative data are used to gain comprehensiveness of phenomenon, and triangulation of result
Forms of data collection	
Qualitative	Semi-structured interview
Quantitative	Standardized instruments
Analytical procedure	
Qualitative	Interpretative phenomenological analysis
Quantitative	Descriptive statistics, correlations, and regressions
Characteristics of design	
Timing	Concurrent: qualitative + quantitative
Weighting	Equal
Mixing	Analysis and reports of results
Type of design model	Triangulation

The overall objective of this mixed methods research is to understand the HRQOL and adjustment of patients with HCC in Taiwan. The details of the research design based on Creswell's criteria are presented in Table 4.2 (Creswell et al., 2004). A concurrent triangulation design will be conducted. Two studies will be conducted.

In the qualitative study, semi-structured interviews will be used to collect data and be analyzed using Interpretative Phenomenological Analysis (Smith, 1996; Smith, Flowers, & Larkin, 2009). In a parallel study, standardized instruments will be used to measure the relationships between HRQOL, depression and anxiety, and other psychological variables, including illness perceptions, coping strategies, and social support, as well as physical variables, including disease stage, treatment, liver function, and performance status. Qualitative and quantitative data will first be analyzed separately, and merged together including (1) transforming and relating the data, (2) comparing the results in discussion. The process of integration is shown in Figure 4.2.

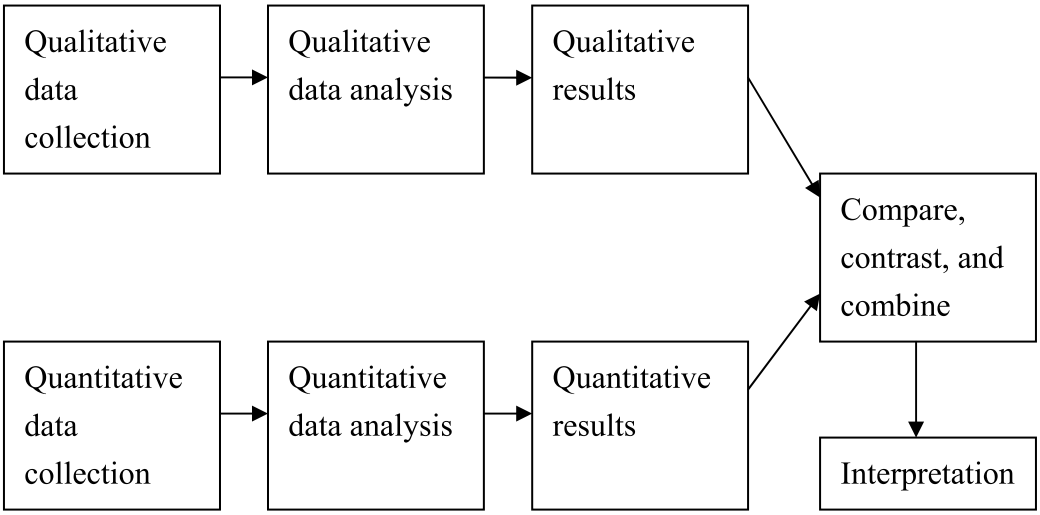

Figure 4.2 The process of analysis and integration

Chapter 5. Illness Experience in Patients with HCC: An Interpretative Phenomenological Analysis Study

5.1 Abstract

Aims: HCC is common in Asia and previous research shows patients with HCC report compromised HRQOL mainly in physical and psychological dimensions. However, most past research used standardized instruments to measure HRQOL and lacked qualitative in-depth information. In order to determine more precisely the effect of HCC in Taiwan we conducted a qualitative study to explore patients' experience of the illness journey, and significant factors which they see may influence their HRQOL and adjustment.

Methods: Patients with HCC in Taiwan (n=33) undergoing one or more of three treatments (surgery, TAE/TACE, and chemotherapy). They were classified according to one of four stages of disease severity (I to IV). A semi-structured interview was developed to collect data. Interview guides included illness experience, the strategies used to deal with the disease, and the significant concerns in their current life. Data were analyzed using Interpretative Phenomenological Analysis (IPA), and an introduction of IPA was also included in this chapter

Results: Four main themes were identified: (1) *the impact of disease*: physical symptoms, psychological reactions, social relationship, daily activities and life aspect, and positive change; (2) *the illness perceptions*: consequence, timeline, control, and perceived causal factor; (3) *information needs*: medical information and non-medical information; and (4) *coping strategies*: problem-oriented and emotion-oriented coping strategies for disease-related and life-related problems.

Conclusions: A preliminary model of illness adjustment was developed. The findings

have clinical implications for future care of patients with HCC and for development of culturally sensitive measures.

5.2 Introduction

HCC is common in Asia and has wide impact on patients and families. The results of the systematic review (Chapter 3) suggested that a limitation or previous work was the reliance on standardized instruments to measure HRQOL and these measures tend to be US based and may not be appropriate for work in other cultures. In addition, quantitative measures cannot gain a comprehensive picture of patients' illness journey. We therefore conducted a qualitative study.

In the traditional view, psychology is seen as 'hard science' where a positivist quantitative research paradigm has a predominant role. In health psychology, the quantitative method has considerable strengths, for example to test the impact of disease or the effects of intervention. However, it has some limitations, including lack of in-depth information and ease of implementation in clinical practice (Jones, 1995). Nowadays the qualitative method is important in health psychology to explore the meanings of health and illness experience (Chamberlain, Stephens, & Lyons, 1997; Mays & Pope, 1995).

The results of the systematic review tell us little about the illness journey including how patients cope with HCC, interpret the illness, and adjust to new life after diagnosis. Therefore, the aims of this study were to: (1) describe the impact of HCC on HRQOL, (2) explore the adjustment process, and (3) identify the significant factors which help patients' adjustment.

5.3 Interpretative phenomenological analysis

Interpretative phenomenological analysis (IPA) was used as a guide to conduct this research. IPA has been developed as a specific technique for qualitative health psychology (Smith, 1996; Smith, Flowers, & Larkin, 2009; Smith & Osborn, 2008), and the aims of IPA are to explore how individuals are making sense of their personal and social world, and how they are gaining meaning from particular experiences or events (Smith & Osborn, 2008). In this section the basic components of IPA were introduced including theoretical foundations, research questions, sampling, data collection, analysis strategies, and quality of research.

5.3.1 Theoretical foundations

IPA attempts to get close to the individuals' personal world, an 'insider's perspective' (Conrad, 1987). There are two theoretical foundations of IPA: phenomenology and symbolic interactionism (Smith, 1996). *Phenomenology* is a philosophical approach that studies human experience. It focuses on the individual's lived experience, and tries to explore the individual's personal perception or account of an object or event instead of to produce an objective statement of the object or event itself (Smith, 1996; Smith & Osborn, 2008). *Symbolic interactionism*, which was influenced by pragmatism, focuses on how persons are interpreting and sense-making. It argues that a central concern of social scientists is to explore the meanings individuals ascribe to events, but those meanings are only obtained through a process of interpretation (Smith, 1996; Smith & Osborn, 2008). In other words, meanings are in, and a result of, social interactions (Smith, Flowers, & Osborn, 1997).

Humans, as self-interpreting beings, tend to interpret objects or events actively, and make sense of their experiences actively (Smith & Eatough, 2006). IPA draws attention to not only individual's thinking concerning objects or events (outcomes) but also the ways of sense-making (processes). It emphasises cognitive, linguistic, affective, and physical components; and assumes a chain of connection between people's talking, their thinking, and emotional state (Smith, 1996; Smith & Osborn, 2008). However, there is a dual interpretation process. Individuals are trying to interpret and make sense of their experiences and world, and the researcher is trying to make sense of participants' process of sense-making (Smith & Osborn, 2008). From this view, IPA assumes that research is a dynamic process with an active role for the researcher in the process (Smith & Eatough, 2006).

IPA has been widely applied in health psychology (Brocki & Wearden, 2006). Health psychologists are concerned with patients' perception and interpretation of their illness and bodily experience, and how they gain meanings (Leventhal, Nerenz, & Steele, 1984). Health psychology makes assumptions about (1) the existence of real and discrete bodies, and (2) individuals' thinking about their bodies can be expressed by their talk. IPA can realize the gap between objective physical conditions and subjective perceptions of their bodies (Smith, 1996). IPA can be used to determine the beliefs that patients have about their bodies and illness, the speech that they use to talk about their bodies and illness, and their response to their illness (Smith, Jarman, & Osborn, 1999). It can explore meanings and contexts to understand the complexity of phenomenon (Brocki & Wearden, 2006).

5.3.2 Research questions

IPA is useful to approach phenomenon with complexity, process, or novelty (Smith & Osborn, 2008). It focuses on individuals' lived experiences and with how they are making sense of experiences in a particular context. The key questions are concerned with participants' perceptions or view, and how they formulate perceptions and views (Smith & Eatough, 2006; Smith et al., 2009).

5.3.3 Sampling

IPA tries to find a homogeneous sample, and uses purposive sampling instead of theoretical sampling (Brocki & Wearden, 2006; Smith & Osborn, 2008). There is no recommended sample size. In past studies, the numbers of participants varied from one to 48 (Brocki & Wearden, 2006), but six to eight is often considered appropriate (Smith & Eatough, 2006). In general, sample size of an IPA study depends on the degree of commitment to the case study level of analysis, the richness of the individual case, and the practical restrictions that the researcher is working under (Smith & Osborn, 2008).

5.3.4 Data collection

Qualitative methods of data collection are appropriate for an IPA study, such as interview, focus group, personal accounts, or diaries; but the best and the most popular way is through the semi-structured interview. The advantages of the semi-structured interview are flexibility in that researchers can follow up novel avenues resulting in richness of data (Smith & Osborn, 2008). Semi-structured interviews are guided by the following principles: researchers need to establish rapport with participants; the order of questions is less important; researchers are free to probe interesting topics that arise; and the interview can follow participants' interests or concerns (Smith, 1995).

Before starting the interview, researchers should design an interview schedule. The steps for producing an interview schedule include: (1) determine the overall issues to be tackled in the interview; (2) set up the issues in appropriate sequence, researchers have to think what is the most logical order to address these issues and what is the most sensitive issue; (3) think of appropriate questions related to each issue; and (4) design possible probes and prompts which can facilitate participants to talk more (Smith, 1995). In general, the interview starts with general and non-specific questions and moves to specific-level and sensitive questions. In addition, audio record is necessary so that researchers can concentrate on the interview and have detailed information of whole interview.

5.3.5 Analysis strategies

Meaning is central and the aim is to understand the content and complexity of those meanings in IPA, therefore, researchers have to get inside participants' psychological worlds (Smith & Osborn, 2008). The analysis is an iterative process: (1) Reading and re-reading: researchers have to read and re-read the transcripts several times and be familiar with the contents. (2) Initial noting: researchers use one margin to write down the first impressions, such as descriptive, linguistic, and conceptual comments. (3) Developing emergent themes: researchers use the other margin to write down the themes which emerge from the original data. The themes have a slightly higher level of abstraction and invoke psychological terminology. (4) Searching for connections across emergent themes: researchers can explore and innovate in terms of organizing the analysis through abstraction, polarization, contextualization, numeration, function, to bring themes together. (5) Moving to the next case: researchers can use a master list of themes from the first case or create a new list. (6) Looking for patterns across cases: after analysis of all cases, the final results can show how themes are nested within super-ordinate themes and illustrate the meanings, contents, and examples of each theme (Smith et al., 2009).

The above steps are a suggestion for analysis methods rather than prescriptions. Analysis is a cyclical process, the temporary results from each step will force researchers to think the focus and directions of study; in addition, IPA involves personal interpretative process and researchers have to distinguish what the participants' said and their interpretation (Smith et al., 1999).

5.3.6 Quality of research

Three levels of interpretation (phenomenological, metaphorical, and theoretical) have been identified, and IPA should move beyond the text to a more interpretative and psychological level, but still contrast a grounded IPA reading which is based on participants' accounts (Smith, 2004). Researchers have to demonstrate the quality of research. There are four principles. The first is sensitivity and context, that researchers can demonstrate an appreciation of the rationale for adoption of IPA, the interactional nature of data collection within the interview situation, and the match of data and analysis process. The second is commitment and rigour. Commitment means researchers show the degree of attentiveness to participants during data collection. Rigour refers to the thoroughness of the research such as the appropriateness of the sample to the question, the quality of interview, and the completeness of the analysis. The third is transparency and coherence. Transparency refers to the fact that researchers have to describe clearly each stage of research process in the write-up, and coherence refers the fitness between question, data collection, analysis, and writing. The last is impact and importance regarding whether the research tells readers something interesting, important or useful (Yardley, 2000).

In summary, IPA pays attention to the cognitive, linguistic, and affective components of human beings, and addresses the meanings and the process of interpretation and sense-making. It is useful to make a specific statement about individuals rather that a general claim for the research group. The IPA method is flexible but also with practical guides. It has been widely used in health psychology; therefore IPA was used in my thesis.

5.4 Methods

5.4.1 Participants

Thirty-three adult patients with HCC were recruited. They had undergone at least one of three treatments (surgery, TAE/ TACE, and chemotherapy) and were categorized into four stages of disease depending on severity (I to IV). These ratings were made by staff in two medical teaching hospitals in Taiwan. Inclusion criteria were: (1) diagnosis of HCC confirmed by histopathological examination of either surgical samples or needle biopsy specimens, by typical image pictures plus a serum level of *a*-FP higher than 400 ng/mL, or by more than two typical image pictures; (2) age 18 years or older; (3) speak Chinese or Taiwanese. Patients with a history of suicidal ideation or psychosis were excluded.

5.4.2 Data collection

(1) Procedure

Ethics approvals were obtained from the Department of Psychology, University of Sheffield and two participating hospitals in Taiwan (National Taiwan University Hospital and Chi-Mei Medical Center, Liou Ying). Medical staff identified the patients who met the inclusion criteria, and the researcher approached potential patients to provide an oral explanation and give them detailed information sheets. Patients were encouraged to ask any questions about the research and reassured about the voluntary nature of participation. They were also informed that whether or not they participated would not influence their treatment or care, and that they had the right to withdraw at any time without any explanations. Patients signed a consent form when they were willing to participate in the research. The interviews were conducted in Taiwanese or Chinese, and the author translated the results into English when writing the report.

(2) Interview

A semi-structured interview was used to collected data, and the interview guides were set up in advance (Smith, 1995). These included:

(i) Would you please describe your experience about illness briefly, about the whole process?
    (*Prompts:* since feeling uncomfortable, being told the diagnosis, receiving treatments, knowing the progress of disease).
(ii) What are the influences or impact of disease on your life?
    (*Prompts:* physical, psychological, social, and other domains).
(iii) How do you deal/cope with the impact?
    (*Prompts:* specific coping strategies, resources including internal and external, which factors are the most important).
(iv) Are there any significant concerns in current life?
(v) Are you satisfied with your adjustment to illness? What are other significant factors which may influence your adjustment but we didn't mention above?
(vi) Is there anything you want to stress or mention?

(3) Measures

The demographic data included gender and age; and medical data included ECOG score (The Eastern Cooperative Oncology Group performance status score) (Oken et al., 1982), AJCC stage of HCC, time since diagnosis, and the most recent treatment were also collected from medical notes.

5.4.3 Analysis

Interviews were audiotaped and transcribed verbatim, and IPA was used to analyze data (Smith, 1996; Smith et al., 2009; Smith & Osborn, 2008). The transcript was read and re-read, the comments and initial themes were written down. Through analytic reading, the preliminary themes were identified and the relationships between themes were structured. Comparisons across different conditions: disease stages, treatments, and time since diagnosis were conducted. A list of master themes was produced. After analysis of all transcripts, the final list was shaped. Atlas. ti 5.0 was used to assist the process of analysis.

In order to enhance validity, the second coder who is a senior nurse with a Masters degree in oncology analyzed transcripts independently, and the two coders discussed their coding to increase the consistency and coherence of the analysis (Yardley, 2008).

5.5 Results

The demographic characteristics of patients are presented in Table 5.1. The mean age of patients was 54.24 years (SD=12.73, range from 31 to 76 years). Two thirds were male and most patients had good performance status (ECOG=1 & 2). The mean time since diagnosis was 31.36 months (SD=29.48, range from 1 to 93 months); 30.30% were assessed at stage III, and 39.40% received surgery. The mean time of interview was 58.79 minutes (SD=30.40, range from 21 to 127 minutes).

Four main themes were identified from interview data, including (1) the impact of disease on patients' lives, (2) illness perceptions, (3) information needs, and (4) coping strategies. A conceptual model of adjustment was then developed.

Table 5.1 The demographic and disease characteristics of patients (n=33)

Variables	Frequency (%)
Age (yrs)	
Mean=54.24 (SD=12.73), range=31-76	
Gender	
Male	22 (66.66%)
Female	11 (33.33%)
ECOG	
1	16 (48.49%)
2	10 (30.30%)
3	5 (15.15%)
4	2 (6.06%)
AJCC stage	
1	8 (24.24%)
2	7 (21.21%)
3	10 (30.30%)
4	3 (9.10%)
Missing	5 (15.15%)
Time since diagnosis (months)	
Mean=31.36 (SD=29.48), range=1-93	
Most recent treatment	
Surgery	13 (39.40%)
TAE/TACE	10 (30.30%)
Chemotherapy/ drug therapy	10 (30.30%)

5.5.1 The impact of disease on patient's life

The disease had widespread impact for patients' lives (see Table 5.2). Physical symptoms including liver-specific symptoms, such as jaundice, digestive problem, flatulence; and general symptoms, such as sleep problems, fatigue, lack of physical vigour, and weakness were recorded. Psychological reactions to the disease included cognitive, emotional, and behavioural components.

> *Cognition:* at beginning I was afraid a lot…in the past cancer is related to death, when I will die… people who had such severe disease may have a maggot in their

> head, I don't know how many years I can live. (P26)
>
> *Emotion:* ha, three years ago, three years ago I couldn't laugh at all, everyday I was depressed, and my temperament was bad, very bad. (P10)
>
> *Behaviour:* maybe because of hepatic coma, I blamed the nurse, I shouted to my wife, but actually I couldn't recognize anyone. So they moved me to the single room. I could remember these, they told me these when I was clear. (P10)

In social relationships, the impact involved patients and family members, caregivers and other family members, as well as patients and friends. In addition, caregivers and family members were also influenced by the disease. There were tense between patients, caregivers, and other family members because of treatment decisions, care responsibility, and emotional stress.

> *Patients and family members:* having such a body, it is very difficult to maintain a family, to take care of other families. … and this time the result of examination is not clear, I have to come back after 2 weeks, how do I talk to them? If I tell them I have to receive examination again, they will definitely worry these 2 weeks. (P17)
>
> *Caregivers and other family members:* she (wife) stays here all day and knows all situations. But my parents found some Chinese herb that they hear someone said it can cure liver cancer, and they wanted me to try. However, she didn't want and worried the Chinese herb may influence the treatment. (P2)
>
> *Patients and friends:* I don't like tell my disease to other people, only some close friends know. And I don't let them come to hospital, I don't want to cause their burden…I don't want to let them see me... (P1)

There were wide influences on daily activities, for example patients had to stop work temporally or quit work, received treatment and came back to hospitals regularly, and could not travel far. All of above influences put a halt to patients' lives or a sense that life was totally changed by the disease.

> I never experience three months so longer so slowly. Before the disease, I was busy in my job, my studying, but now suddenly my life was stopped and the disease changed the direction of my life. (P32)

Table 5.2 The impact of disease

Dimension	Description	Example
Physical symptoms	The uncomfortable symptoms which caused by disease, but there are varieties between disease stages and treatments.	*Liver-specific symptoms:* constipation, diarrhea, digestive problem, excrete problem, feel full just beginning eating, flatulence, hepatic coma, internal hemorrhage, *General symptoms:* dry mouth, fatigue, fever, itch, jaundice, lack of physical vigour, loss appetite, loss weight, muscular pain in shoulder, pain, pant, sleep, trouble tasting, vertigo, vomiting, weakness
Psychological reaction	The psychological responses to illness, including cognition, emotion, and behaviour.	*Cognition:* a knot in one's heart, body image, can't escape from death, close death, have a maggot in my head, loss of faith, loss of living willing *Emotion:* anger (to him/herself; medical staff), regret, anxiety (in general life and before physical examination), bad mood, depression/depressive mood, fear, feel inferior, frustration, helplessness, hopelessness, initial panic, initial shock, irritable, numb, sensitive or arousal easily, uncertainty, unhappy, uselessness, worry *Behaviour:* move restlessly
Social relationship	The influences of disease on social relationships between patients, family members, and friends.	*Patients and family:* can't maintain family role, conflicts between patient and family, worry about family *Caregivers and family:* conflict between family members, increase family's burden *Patients and friends:* reduce of social activity, withdraw from social interaction
Daily activities and life aspects	The influences of disease on daily activities and life aspects.	*Daily activities:* can't work, economic burden, can't go far away, can't stay at home, regular follow-up, regular treatment, inconvenient in hospital, social stress *Life aspects:* change life direction, collapse of life, life stop!, stop or change life plan
Positive change	Positive changes induced by the disease	Help others, be a volunteer, be a example for others (for quit bad habits), health life style, rearrange life priority and schedule, better family relationship, be optimism or magnanimous or open-minded, accept him/herself, live here and now

On the other hand, the disease caused some positive changes. For example patients may rearrange their priorities in life, develop healthy habits and quit bad habits, want to help others (e.g. use themselves as examples for others quitting bad habits), and be optimistic or open-minded.

> It is obviously a good transition. Except for less income, but it is good for my family, to spend more time with my children, to do a lot of what they like, it is positive. (P16)

5.5.2 Illness perceptions

How do patients perceive their disease, HCC? Four components of illness perceptions were identified, including consequences, timeline, perceived causal factors, and control (see Table 5.3). *Consequences* were influenced by several factors, including physical symptoms, psychological burden, and self-care or working ability. Patients described the consequences as various levels, from mild to severe.

> It is a huge stress, I don't expect it (disease), but I have to stand it. Now I can't stand anymore, so my life becomes collapsed. (P32)
>
> Because the recovery of surgery is quite good, so far my physical condition is okay, so it (disease) is not a big deal. (P15)

Unlike of the different consequences, there was consistency in timeline perception, that this disease is a chronic disease and needs long-term treatment.

> I thought everything was done when the tumour was taken by resection at the first diagnosis. But now (recurrence), it is not easy to be cured, it will prolong a long period. (P4)

Perceived causal factors included early stage liver disease (HBV, HCV, and cirrhosis), alcohol, life style (stay up late, irregular life schedule, and overdraft of physical vigour), family history, and stress.

> *HBV:* I don’t think this question (why I got HCC), but I think why I got HBV, I think that. When I got HBV, it is so easy to get HCC. (P4)
>
> *Drinking:* why? It is my deserved. When I was young, didn’t know the bad influence, just drunk wine frequently. (P11)
>
> *Stress:* I thought the cancer is related to our emotion. I lived with my parents-in-law, they treated me well, but there is always pressure for me, it is not easy. (P26)

Feelings of control centered on two dimensions, curability and controllability. A majority of patients did not think their disease could be cured. However, controllable feelings related to treatments, physical condition, and personal interpretation.

> *Curable:* I asked the doctor if this disease can be cured. He said frankly, just receiving treatments (TAE) repeatedly until can not do anything, if you take care of your liver well, maybe it can prolong your life. (P13)
>
> *Controllable:* when it relapsed, I thought: it happens again, now it is bad, it is not easy to be treated. (P4)
>
> *Controllable:* I am not afraid, because I know there are always treatments, surgery, TAE. Even until you cannot receive TAE, there is still liver transplantation. (P25)

In addition, knowledge of disease, stereotype of disease, and personal illness experience may formulate patients’ illness perceptions.

> *Knowledge of disease:* At beginning, I was not afraid, but when she (patients’ wife who was nurse before) explain the disease to me; I realized it is a critical disease, I started to be afraid. (P20)
>
> *Stereotype of disease:* I knew, I knew it is HCC at the beginning of diagnosis. It is the “national disease” (major disease in our country). And cancer, everyone is afraid of cancer. (P7)
>
> *Illness experience:* When I had abdominal distention and jaundice, I knew the situation got worse. This disease, if the abdomen becomes bigger, it is a bad sign. (P13)

Table 5.3 Illness perceptions about HCC

Illness perceptions	Description	Example
Consequence	An integrative evaluation about the level of disease impact on life	Various levels of perceived consequences and impact, from mild to severe
Timeline	A perception about the time period of disease.	A majority of patients perceived HCC as a long-term and chronic disease.
Causal factor	Potential factors that patients thought the factors cause the disease, mainly early stage liver disease (HBV, HCV, cirrhosis), alcohol, life style, family history, and stress.	Alcohol drinking, early stage liver diseases, chemical substance, food, life style, family history, working stress, life stress, personality
Control	A feeling that whether patients can control the disease, including curable and controllable.	Curable or not Controllable or not

5.5.3 Information needs

When the disease was diagnosed, a series of questions and thoughts arose. These involved medical information and non-medical information. The details of questions are presented in Table 5.4.

> When the doctor told me this diagnosis…DONG…a lot of thoughts…a lot of questions arose, about cancer this problem, what will happen if I receive surgery, how many years I can live, and such as and such as. (P26)

Table 5.4 Information needs

Category	Questions
Medical information	What factors cause HCC?
	What reason causes the specific symptom? How to manage symptom?
	What are the benefits and side effects of treatments, examination, and medicine? The effects of medicine on liver (whether increase the burden of liver)
	The meaning of medical index, such as GOT (Glutamic Oxaloacetic Transaminase), GPT (Glutamic Pyruvic Transaminase), α-FP, 5 years survival rate.
	How to take care their liver? Do they need to take medicine? How to follow-up? Do they need to take any examination in a certain period?
	How about the disease prognosis? Whether recurrence? What will happen in the future?
Non medical information	How to adjust the disease including patients and families, and how to make mood stable or happy.
	Life schedule? What they can eat? What can't eat? What can do, and what can't?
	The interaction between physical and psychological aspects
	When they can return to work and normal life?
	Recovery, and am I normal?
	What resource can help me, such as cancer or disease association
	Want to know other patients' situation (to make comparisons)

5.5.4 Coping strategies

We identified both problem- and/or emotion-oriented coping strategies. The problem-oriented coping involved patients taking direct action to the stressor itself, while the emotion-oriented coping involved patients trying to manage their emotional responses to the stressor. The disease may raise multiple problems rather than a single stressor; the usage of coping strategies depends on different stressors. There were two kinds of stressors: disease-focused and life-focused (see Table 5.5).

Focusing on disease itself, different problem-oriented coping strategies were used at different stages. At the beginning patients would react to disease immediately, for example searching information, find a famous/good doctor, make plans for treatment and worst situations; after acute stage, patients may rearrange their life, for example do exercise, eat healthy and light food, go to bed early, and quit bad habits.

> Coping with the disease? Only life style, eat light food, go to bed early, regular life schedule. That's all, nothing special, but don't increase liver's burden. (P2)

Emotion-oriented coping involves a dynamic transition process. Patients illustrated the attitude confronting the disease, for example face and deal with the problem, get along with tumour, let it be, let nature take its course; or don't keep it (disease or tumour) in mind, distraction, change thoughts using positive thinking, social comparison; or stand it, suppression, get used to it. In addition, talking to someone who can understand or sharing experience with other patients is also a good coping strategy.

> *Get along with tumour:* only let it be. Now that it came to my body, just like a friend live in my body, no matter it is a good friend or bad friend, let it stay. (P3)
>
> *Let nature take its course:* let nature take its course. It means you should do right things in the right moment, depend on your physical condition. If the doctor said you should receive treatment, then you just receive; if not, then you should let it go. (P4)
>
> *Positive thinking:* I wouldn't think that I didn't drinking, smoking, and staying up late, then why I got this disease. I thought just because I didn't have such bad habits, so I still preserved well liver function. In addition the tumour in a good location, so I could receive resection. (P30)
>
> *Social comparison:* of course I am afraid; however we still have to face this problem. So many people get cancer, two of my friends who also got liver cancer at the same year as me passed away. It is bonus from God that I live longer. (P13)
>
> *Suppression:* no, I don't have any good way to against this disease, too many times (TAE treatments), it breaks down my faith. I only can stand it by myself. (P17)

Patients tried to develop a healthy life style, separate disease and life, make simple life, and find something to do (e.g. interesting or habits) as problem-oriented coping. On the other hand, patients did not treat themselves as patients and kept life going, separate disease and life, found the meaning of life, sought for religious belief, and lived here and now.

> As what I told you before, in psychological aspect I don’t treat myself as a patient, but in behavioural aspect, eating, sleeping such as, I have to treat myself as a patient and take these carefully. (P29)

Table 5.5 Coping strategies

	Problem-oriented	Emotion-oriented
Focus on disease	Accept the fact Knowledge is power, understand the effects of medicine, search for information, health speech Rearrange life schedule, diet, exercise/chi kung, sit in meditation, go to bed early, quit bad habits Think and make the plan for the worst situation, dying preparation Treatment, immediately react to disease, find a right doctor, alternative prescription, new clinical trial, search other medical resources	Blog, record illness experience, share experience with others Crying Distraction, don't keep it in mind, let it be Get along with tumour Give hope Let nature take its course Positive thinking, change thought Separate attitude and behaviours, separate physical and psychological aspects Social comparison Suppression, stand it, used to it, get used to the symptom
Focus on life	Depend on partner Have something to do, interesting Keep normal life Keep social interaction Keep the original role Simple life To be independent	Don't give myself too much stress, don't have too much desires Find the meaning of life Humor I don't treat myself as a patient Keep faith Keep going Live here and now Religious belief, spiritual group Separate disease from life

5.6 Discussion

Through integrating the findings, a preliminary model of adjustment was developed to summarize the relationships between illness perceptions, coping, and adjustment outcomes shown in Figure 5.1. Adjustment to HCC is a dynamic process and many variables may influence this process. The variation of physical condition, personal characteristics, and social support are important antecedent factors. The above three factors may contribute to patients' illness perceptions and coping strategies. In addition the adjustment outcome is constantly changing rather than a fixed result.

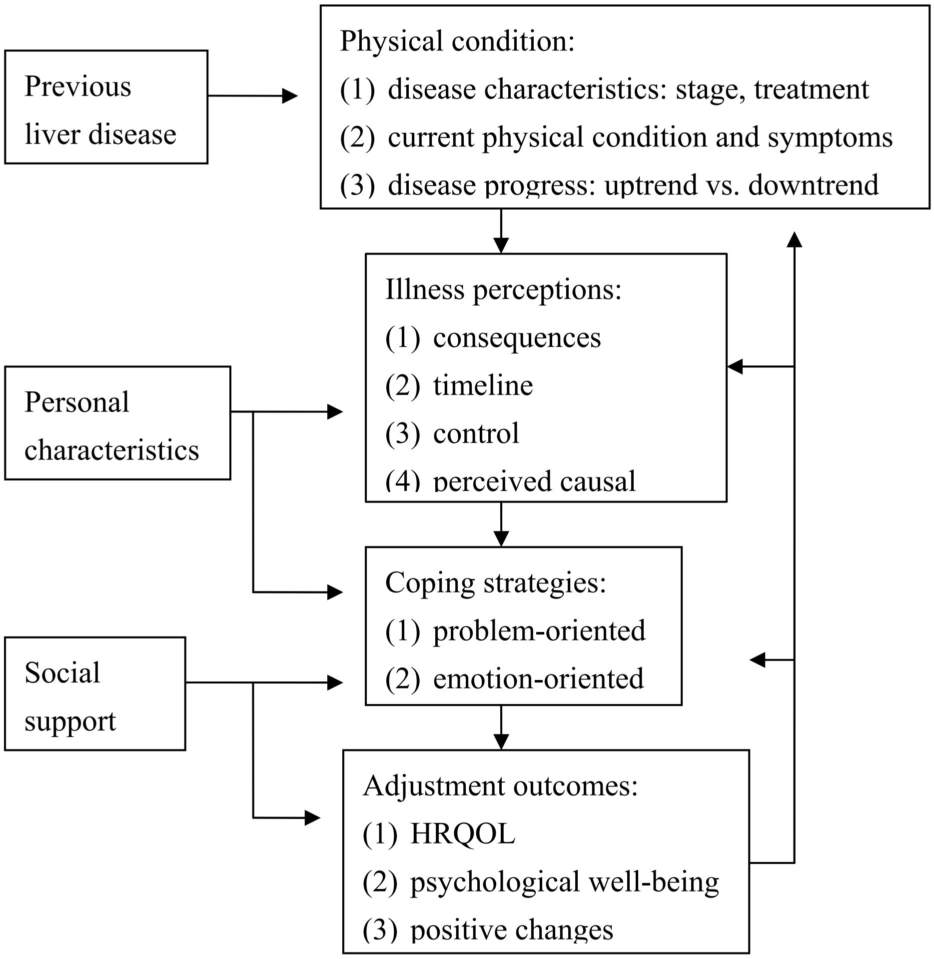

Figure 5.1 The adjustment model in patients with HCC

Previous liver disease. Previous liver disease, including hepatitis or cirrhosis, would influence the illness experience and perceptions. Some patients realized they were high risk patients and anticipated that one day the liver disease would progress to liver cancer. In addition, they may have relevant knowledge about liver disease and liver cancer, which was helpful for adjustment. Female patients (because of low prevalence) or patients without previous liver disease (e.g., HBV, HCV, or cirrhosis) may ask the question “why me, why I got HCC?”.

Physical condition. Physical condition played an important role in formulating patients’ adjustment. The components of physical condition included disease characteristics, current physical condition and symptoms, and disease progress. Patients with different stages and treatments had diverse experience. For example, patients with surgery came back to hospitals regularly to receive image and blood examination; however patients with TAE/TACE had higher level of threat of recurrence and most of them received several TAE/TACE repeatedly, and patients with drug therapy have to receive treatment more frequently.

Based on the time since diagnosis and progress of disease three stages: acute, remission, and advanced can be described. Each stage has different tasks. In the acute stage when disease was just diagnosed, patients and family tried to find efficacious and effective treatment. In the remission stage when physical condition was stable, they had to rearrange their life to a new balance. In the advanced stage when the disease recurrence and physical condition gets worse, they would receive treatment repeatedly and bear more psychological impact than at earlier stages.

Current physical condition and symptoms also inform illness experience. Patients with better performance status, independent self-care ability, and mild symptoms have less stress and burden. Patients did not want to increase burden on caregivers or family, and rely on others’ help. Furthermore, uptrend or downtrend disease progress also influenced illness perceptions and adjustment. If the physical condition was stable or progress was uptrend, then patients had positive evaluation of disease outcome and had faith to cope with disease.

> *Uptrend:* in these two years everyone (both patient and family) is relieved, we don't think HCC so much, much better than the first year. Now the physical condition is quit stable, and the results of physical examinations are all in the normal range. (P15)
>
> *Downtrend:* there is no improvement. If you said it can be cured, then I can stand the suffering treatment (TAE) and side effect. However, it is impossible (to be cued), and becomes worse after each treatment, just like gets close the death… (P13)

Physical symptom is the first consideration which can cause suffering experiences and formulate illness perceptions. However, physical symptom is only one antecedent factor. Patients who had the same physical condition may not have the same illness perceptions and adjustment outcomes. Patients integrate information about their current physical conditions, personal illness experience, and social stereotype to formulate illness perceptions. Patients' personal characteristics, social support, illness perceptions, and coping may contribute to the outcomes of disease adjustment.

Personal characteristics. When facing disease or other threats, personal characteristics can influence their cognitive evaluation (e.g., illness perceptions) or behavioural response (e.g., coping behaviours). Personal characteristics can be taken as internal resources and may modify patients' illness perceptions and the choice of coping strategies. The important personal characteristics that patients mentioned in the interview included optimism, anxiety, and flexibility. Optimistic patients tended to use positive thinking or focused on the positive aspects of disease, but anxious patients may think the worst situations. Flexibility meant patients can modify their cognitive thoughts or behaviours to cope with disease flexibly. However, personal characteristics may be also influenced by the disease; it is a stable rather than constant variable. Long-term illness experience may change patients' personal trait, such as positive changes.

> *Optimism:* yes, you can say I am an optimism guy, we have to face the problem, can't escape it. Now that you all have to face this, why not choose a happy attitude or in a positive way. (P15)
>
> *Anxious:* it is like to be sentenced by the doctor when he told me the diagnosis… (be sentenced)…yes, I sometimes use words so strongly, maybe it is about my personality, I always think the worst situations, negative aspects of events, very pessimistic. (P30)
>
> *Flexibility:* you have to rearrange your life and your attitude to disease and life. Like me, I can't continue work that time, but 50 years old is the best time, I was in manage level, I still had to give up. If you can do that then try your best, if not, you only can accept it.

Social support. Social support, for example tangible and emotional support from families, was an important resource that helped patients to deal with the disease. . The sources of social support included partners, family members, and friends, but mainly the first two. Social support, as an external resource, can provide patients with assistance in dealing with the demands of disease. However, there were tensions between patients and families or friends. Most patients did not want to increase their family's burden. They may reduce their social interactions with unfamiliar friends because of feeling inferior or perceiving that they are being judged by others. Whether to supplement medical treatment with Chinese herbal medicine was also an important issue about treatment decisions. In addition, social relationship is an important motivation for patients to overcome the disease. Patients didn't want to let their relatives or friends disappoint, so they tried hard to against the disease.

> Haha, my friends asked me how I could stand up from such a big disease. Because I had a lot of support, my sons, their supports, provided information, be with me. A lot of relatives and friends encouraged me, supported me. Through these, I could face the disease. (P24)

Furthermore, cultural background influenced the disease process and had interactions with patients' adjustment. For example, family members were deeply involved the treatment decisions and care plans. In some extreme examples, adult sons or daughters would make decisions for elderly parents. However it cannot be denied that this cultural background provides strong support, no matter whether tangible or emotional, for patients to cope with this severe disease.

Illness perceptions. Illness perceptions and coping reactions can be linked between physical condition and adjustment outcome. Physical condition or symptoms, knowledge of disease, and social stereotype of disease formulated patients' illness perceptions. A majority of patients perceive HCC as a chronic disease with great threat, but the consequence of disease may depend on the disturbance of performance status, symptoms, and daily life.

Coping strategies. Based on illness perceptions, patients tried to make efforts to cope with the demands caused by the disease. Focusing on current symptoms, patients found suitable doctors and appropriate treatments; focusing on causal factors, patients rearrange their life schedule, quit bad habits, and develop healthy habits; focusing on timeline, patients learn to accept the disease and get along with the tumour. On the other hand, the outcome of coping also regulated their illness perceptions. Successful experience enhances the feeling of control. For example, patients maintained healthy life style because they realized it could reduce burden on the liver and might be helpful for preventing recurrence. Unsuccessful experience made them modify their coping or illness experience. They recognized the disease as a chronic and high threatening disease because of recurrence and repeatedly treatment, and they might try to use emotion-oriented coping to accept the disease and regulate their emotional responses.

Adjustment outcomes. Regarding the outcome of disease, comprehensive indices were necessary to evaluate patients' adjustment rather than a physical index. HRQOL was a suitable index that combines objective and subjective measures. In addition, psychological well-being can focus on psychological aspects only, including negative feeling, such as anxiety, depression, or uncertainty; as well as positive feeling, such as peaceful, happiness, or satisfaction. Finally, positive change was a potential index which can help patients to cope with disease and get along with the tumour.

The disease has wide impact on not only physical symptoms but also psychosocial and daily aspects. The findings support that earlier views that the measures of HRQOL for patients with HCC should incorporate generic and disease-specific aspects (Blazeby et al., 2004; Heffernan et al., 2002), and the assessment should cover multiple aspects of life. On the other hand, it is also important to note the positive change in that the disease may bring the positive effects on personal growth or family relationships (Steel, Gamblin, & Carr, 2008).

The findings supported previous research in that illness perceptions can play important roles in the relationship between illness and adjustment outcome (Hagger & Orbell, 2003; Leventhal et al., 1984) and relate to coping strategies. In addition, the use of coping strategies depends on illness perceptions, personal characteristics and stressors. Patients search relevant information and try to figure out the potential causal factors and effective interventions for the disease. For example alcohol drinking, fatty food, and staying up late are negative factors which increase liver's burden, and patients will change bad habits and develop healthy habits and life style. However, multiple factors cause the disease and most of the time patients cannot recognize which factor is the exactly causal factor, and the disease cannot be cured in a short period. Emotion-oriented coping is an essential coping strategy that patients have to learn in the illness trajectory. Most patients stress that they learn to face the disease and take the essential reaction, however if the disease progress worse, they have to accept the situation and let it take the nature course.

The adjustment outcomes would feedback to illness perceptions and coping strategies, and patients would change their illness perceptions and modify coping strategies based on the outcome. Patients deal with the demands of disease until achieving a balanced status, and when the variation in physical or internal conditions, they will try to achieve a new balance status.

This study used a qualitative method to explore HCC patients' illness perceptions and adjustment process. The impact of disease, illness perceptions, information needs, and coping strategies were identified, and a preliminary model of adjustment was developed. The findings have some implications for clinical care. First, health professionals should deliver appropriate information to meet patients and family's needs. Second, a family can be taken as a unit so that health professionals educate the whole family about how to take care of patients, and assist family interaction. Third, health professionals can help patients to identify their illness perceptions and find individuals' coping strategies, in addition to amend strategies following different stages and physical conditions. This study illustrated a preliminary model of adjustment in patients with HCC based on qualitative data, and the future study is to use quantitative technique to establish the statistic relationships between illness perceptions, coping, and adjustment.

Chapter 6. Quantitative Study. Part I: The Impact of HCC

6.1 Abstract

Aims: In Chapter 5 the themes developed from qualitative data included the impact of HCC, information needs, how patients perceived the illness and how they coped with HCC. The aims of this quantitative study were to explore the impact of HCC by determining: (1) differences in HRQOL between patients with HCC and the general population, and patients with liver cancer; (2) the prevalence of anxiety, depression, and emotional distress; and (3) perceptions of HCC using a standardized measure.

Methods: Participants were 286 patients with HCC, and data collection included (1) *adjustment outcomes*: HRQOL, anxiety and depression; (2) *psychological variables*: illness perceptions, coping, and social support; and (3) *demographic and physical variables*: demographic information, disease and treatment characteristics (stage, treatment, Child-Pugh stage, and time since diagnosis), and current physical conditions (ECOG, α-FP, T-bilirubin, Albumin, GOT (Glutamate Oxaloacetate Transaminase), GPT (Glutamic Pyruvic Transaminase), INR (International Normalized Ratio), and Platelet).

Results: Patients with HCC had worse global HRQOL, physical, role, cognitive, and social functioning; but better emotional functioning than the general population. The prevalence of clinical anxiety, depression and emotional distress in patients with HCC was 11.27%, 25.44%, and 20.14% respectively. The most severe problems in HRQOL included trouble doing strenuous activities, sleeping in daytime, and lack of vitality. The perceived causal factors of HCC included HBV and HCV, drinking alcohol, and fatigue.

Conclusions: HCC was associated with adverse physical and psychological impact on patients' HRQOL. Based on these findings, an integrative adjustment model will be described in the next chapter.

6.2 Introduction

As discussed in Chapters 1 and 3, HCC has a wide impact on society, patients, and their families and, as with all cancer patients, issues of adjustment and HRQOL are paramount. Improved survival rates and awareness of the potential problems associated with treatment means there is a growing emphasis on psychological well-being and adaptation when facing cancer or chronic illness (Folkman & Greer, 2000). The results of a systematic review (Chapter 3) highlighted that HCC had considerable adverse consequences for physical and psychological aspects of HRQOL. Furthermore, this review indicated that although treatment and physical variables are important, psychological variables also play an important role in determining HRQOL and adjustment outcomes (Fan, Eiser, & Ho, 2010).

Based on patient interviews, the work in Chapter 5 described the range of variables that may influence the dynamic process of adjustment between patients' perceptions of the disease, their efforts to cope with the disease and related demands, and adjustment outcomes. In this chapter the influences of HCC on HRQOL, illness perceptions, and coping strategies will be explored further through quantitative work, using standardized measures with a representative sample.

A key theme identified in the interviews was patients' perceptions of the illness and these ideas have been more formally described previously by Leventhal, Nerenz, and Steele (1984). According to the Common Sense Model (see Figure 6.1), patients actively process (for example understand and interpret) information related to their health status or illness. Patients develop two parallel-processing pathways, involving cognitive representations and emotional responses to their illness. Based on these representations, patients plan and implement coping behaviours to manage the problems. After that, patients evaluate the results of coping in terms of whether the desired goals have been achieved. As a result of feedback from illness outcomes or appraisal of coping, patients modify their illness representations and coping behaviours. This processing system is hierarchically organized (Leventhal et al., 1984).

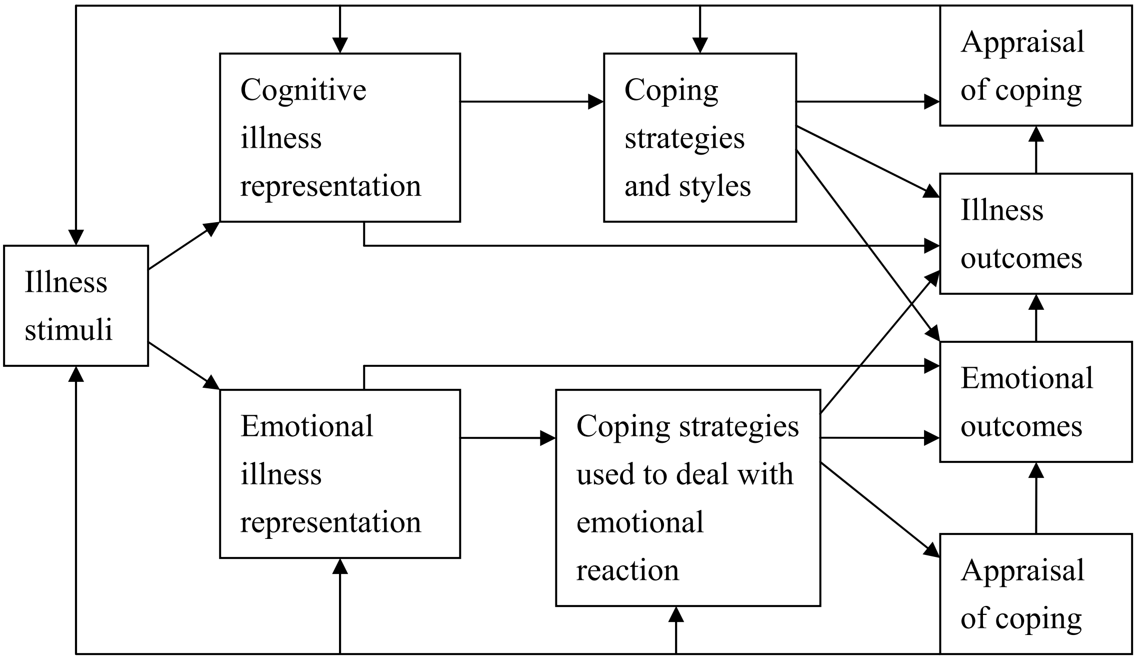

Figure 6.1 Common Sense Model of illness representations (Source: Hagger & Orbell, 2003; Leventhal et al., 1984)

Illness representations are important in the process of adjustment to chronic disease (Leventhal et al., 1984; Weinman & Petrie, 1997). As originally described, there are five components of illness representations, including (1) *identity* about the label or nature of their conditions, (2) *causal* belief about the causes of their disease, (3) *timeline* about the duration of their disease, (4) *consequences* about the impact of disease on one's life, and (5) *cure* beliefs about whether their disease is amenable to cure or control (Skelton & Croyle, 1991; Weinman, Petrie, Moss-Morris, & Horne, 1996; Weinman, 1996).

Illness representations can be assessed with a standardized instrument, the Illness Perception Questionnaire (IPQ), which includes five subscales: identity, cause, timeline, consequences, and control/cure (Weinman et al., 1996). In order to improve the internal consistency of control/cure and timeline subscales, as well as to address a greater construction of illness perceptions, a revised version of IPQ (IPQ-R) was developed. This includes 11 scales: timeline acute/chronic, timeline cyclical, consequences, personal control, treatment control, illness coherence, emotional representations, and causal beliefs about the contribution of psychological factors, behavioural risk factors, immunity, and accident or chance (Moss-Morris et al., 2002). For clinical application and rapid screening, the brief IPQ was developed incorporating nine items including cognitive representation, emotional representation, understanding of illness, and causal factors (Broadbent, Petrie, Main, & Weinman, 2006).

The importance of illness perceptions has been identified in diverse diseases, such as chronic fatigue syndrome (Moss-Morris, Petrie, & Weinman, 1996), heart disease (Broadbent, Ellis, Gamble, & Petrie, 2006; French, Lewin, Watson, & Thompson, 2005), Huntington's disease (Kaptein et al., 2006), as well as cancers (Rozema, Vollink, & Lechner, 2009; Scharloo et al., 2005). A meta-analysis conducted by Hagger and Orbell (2003) supported hypothesized relationships between illness cognitions, coping behaviours, and psychological outcomes across different diseases. When patients perceived their disease as controllable, they tended to use cognitive strategies such as re-appraisal and problem-oriented coping. In addition, better adjustment outcomes, for example psychological well-being, were related to lower perceived consequences and illness identity.

In addition to these perceptions, coping involves both cognitive and behavioural efforts to manage the external or internal demands that are appraised as taxing or exceeding the resources of the person (Lazarus & Folkman, 1984). In general, there are two kinds of coping behaviours: *problem-oriented coping* aims to manage the stressor or solve the problem, and *emotion-oriented coping* aims to regulate the emotional response which is induced by the stressor. Past studies have shown that coping strategies are related to adjustment in cancer patients. For example, psychosocial adaptation has been found to be positively related to support and self-control rather than denial (Heim, Valach, & Schaffner, 1997). Emotional coping strategies, such as focusing on the positive aspects and distancing were associated with less emotional distress, but avoidance was associated with more emotional distress (Dunkel-Schetter, Feinstein, Taylor, & Falke, 1992). Positive re-appraisal and actively processing emotions has been found to be associated with better adaptation (Stanton, Danoff-Burg, & Huggins, 2002). The interaction of problem-oriented coping and perceived control has been found to be a significant predictor of lower anxiety/depression that patients perceived high control and used problem-oriented coping had lowest anxiety/depression symptoms (Osowiecki & Compas, 1998). In addition, patients may use different ways to cope with different cancer-related stressors. Future research need to focus on the connection between the stress (De Faye, Wilson, Chater, Viola, & Hall, 2006), appraisal, and coping processes (Thomsen, Rydahl-Hansen, & Wagner, 2010).

The main purposes of this quantitative study (Chapter 6 and 7) were to explore the HRQOL in patients with HCC and to identify the significant variables that may influence their adjustment process, specifically based on the Common Sense Model of illness perceptions and coping theory. Adjustment outcomes were HRQOL, anxiety, and depression; and predictive variables included demographic and physical variables (disease and treatment characteristics, and current physical conditions), and psychological variables (illness perceptions, coping, and social support). The details of variables are presented in Figure 6.2.

Specific aims were to explore HRQOL in patients with HCC by determining: (1) differences in HRQOL between patients with HCC and the general population, and patients with liver cancer; (2) the prevalence of anxiety, depression, and emotional distress; and (3) perceptions of HCC.

Demographic information

Physical variables:
(1) disease and treatment characteristics
(2) current physical conditions

Psychological variables:
(1) illness perceptions
(2) coping strategies
(3) social support

Adjustment outcomes:
(1) EORTC: global HRQOL and sub-scales
(2) HADS: Anxiety, depression, and emotional distress

Figure 6.2 The categories of variables in this study

6.3 Method

6.3.1 Participants and procedures

Adult patients with HCC were recruited from two medical teaching hospitals in Taiwan. Inclusion criteria were: (1) diagnosis of HCC stages (I to IV), undergoing surgery, TAE/TACE, and chemotherapy; (2) age 18 years or older; and (3) able to speak Chinese or Taiwanese. Patients with a history of suicidal ideation or psychosis were excluded.

Ethics approvals were obtained from the Department of Psychology, University of Sheffield and both participating hospitals in Taiwan (National Taiwan University Hospital and Chi-Mei Medical Center, Liou Ying). Medical staff identified patients who met the inclusion criteria, and the researcher approached the potential patients to provide a verbal explanation and give them detailed information sheets. Patients signed a consent form if they were willing to participate in the research. Questionnaires were administered in the clinic or inpatient wards. If participants could not finish questionnaires in one session because of their physical condition, data collection was administered over more than one session but within one week.

6.3.2 Measures

Three categories of variables in this quantitative study included: (1) Demographic and physical variables, (2) adjustment outcomes, and (3) psychological variables (see Figure 6.2).

(1) Demographic and physical variables

Demographic data were obtained from patients' reports. Disease characteristics and current physical conditions were obtained from medical charts.

(i) Demographic information included gender, age, job, education level, marital status, and whether they needed a caregiver and who provided care.

(ii) Disease characteristics included stage of HCC based on AJCC (Schafer & Sorrell, 1999) and BCLC (Bruix & Sherman, 2005) stage, most recent treatment, Child-Pugh stage, diagnosis date, past treatment history.

(iii) Current physical conditions included ECOG performance status score (Oken et al., 1982), and physical examinations: including α-FP, T-bilirubin, Albumin, GOT (Glutamate Oxaloacetate Transaminase), GPT (Glutamic Pyruvic Transaminase), Platelet, and INR (International Normalized Ratio).

(2) Adjustment outcomes

(i) HRQOL. The EORTC QLQ-C30 was used to evaluate patients' cancer specific HRQOL. This incorporates five functional scales: physical (five items), role (two items), emotional (four items), cognitive (two items) and social (two items) functioning; three symptoms scales: pain (two items), fatigue (three items), nausea/vomiting (two items); and six single items (dyspnoea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties); as well as a global HRQOL (two items) assessment. (EORTC website: http://groups.eortc.be/qol/) (Aaronson et al., 1993; Fayers et al., 2001). In

addition, the EORTC QLQ-HCC18 was used to measure disease-specific HRQOL in patients with HCC, including fatigue (three items), body image (two items), jaundice (two items), nutrition (five items), pain (two items), fever (two items), sexual interest (one item) and abdominal swelling (one item) (Blazeby et al., 2004).

The EORTC QLQ-C30 and HCC-18 can be scored to yield three scores:

(1) *global HRQOL score*: two items concerning global HRQOL;

(2) *functioning score*: five subscales: physical, role, emotional, cognitive, and social functioning; and

(3) *symptom score*: all symptom items in EORTC QLQ-C30 and HCC18 were combined to reduce the number of dependent variables.

A high score on the functional scale or global HRQOL indicates high level of functioning and good HRQOL, and high scores on symptom scale indicates worse symptoms. The scale has been translated into Chinese, with demonstrated reliability and validity (Chie, Yang, Hsu, & Yang, 2004).

(ii) Anxiety and depression. Anxiety and depression were measured by the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). The 14 items comprise *anxiety* (7 items; e.g., “I feel tense or wound up”) and *depression* (7 items; e.g., “I can laugh and see the funny side of things”) scales. Responses are made using 4-point Likert scales and scored to yield sum scores for each of these two scales. A score of 0 to 7 for either subscale is regarded as being in the normal range, 8 to 10 being suggestive of the presence of the respective state, and 11 or higher indicating probable presence ('caseness') of the mood disorder. In addition, a total HADS score of 15 or above has been defined as *emotional distress* (Strong et al., 2007). The HADS has been found to perform well in assessing the symptom severity and caseness of anxiety disorders and depression in primary care patients (Bjelland, Dahl, Haug, & Neckelmann, 2002).

(3) Psychological variables

(i) Illness perceptions. The Brief Illness Perception Questionnaire is a nine item questionnaire (Brief IPQ) (Broadbent, Petrie et al., 2006) yielding three scores: *cognitive representations* (five items: consequences, timeline, personal control, treatment control, and identity), *emotional representations* (two items: concerns and emotions), *illness comprehensibility* (one item: understanding). Responses are made on 10-point Likert scales; and one item about *causal representation* is assessed by an open-ended question (IPQ website: http://www.uib.no/ipq/). Higher scores indicate more negative illness perceptions. The test-retest reliabilities of all items range from .48 to .70, and the discriminant validity has been found to be good (Broadbent, Petrie et al., 2006) and Brief IPQ has been translated into Chinese.

(ii) Coping. Coping strategies were assessed using the Jalowiec coping scale, which is based on Lazarus and Folkman’s coping theory (Jalowiec & Powers, 1981). It contains 40 items to assess *emotion-orientation coping* (25 items; e.g., “worried about the problem”, “seek comfort or help from family or friends”) and *problem-orientation coping* (15 items; e.g., “tried to find out the information about the disease and treatment”, “actively try to change the situation”). Patients are asked to rate the frequency of using coping strategies on 4-point scales (0=never, 3=always) (Jalowiec, Murphy, & Powers, 1984). The questionnaire has been translated into multiple languages including Chinese, and has good reliability and validity (Jalowiec, 2003).

(iii) Social support. The 15-item Inventory of Social Support Behaviour (Barrera, 1981; Barrera & Ainlay, 1983) was used to assess patients’ perceptions of the amount of social support, including *tangible assistance* (six items; e.g., “did some activity together to help you get your mind off things”), *emotional support* (four items; e.g., “listened to

you talk about your private feelings”), and *informational and appraisal support* (five items; e.g., “gave you some information on how to cope with disease”). Items are scored on 4 point response scales (1=not at all to 4=always) and higher scores indicate better social support. In addition, one open-ended item is used to assess the source of social support. The Cronbach’s α of the total scale is .88 (Barrera, 1981; Barrera & Ainlay, 1983). The questionnaire has been translated into Chinese and has good reliability and validity (Tseng, 1999).

6.3.3 Statistical analysis

Descriptive statistics were used for all variables (frequency, mean, standard deviation, and range). Scales were scored according to guidelines in relevant publications or on websites. One sample *t*-tests were used to examine the differences in HRQOL between patients with HCC and the general population; as well as patients with liver cancer. The Statistical Package for Social Sciences (SPSS) windows version 16.0 was used for all statistical analyses.

6.4 Results

6.4.1 Demographic and medical characteristics

A total of 298 patients were contacted but 12 refused to participate because they felt uncomfortable, did not have time or they did not want to. Thus, 286 patients were recruited and details of demographic and medical information are presented in Tables 6.1 and 6.2. The mean age of patients was 59.85 years (SD=12.16), and 76.22% were males. Just over half of the patients (65.38%) stated they could take care of themselves without caregivers. Mean time since diagnosis was 28.70 months (SD=26.43). In addition, 117 (40.91%) patients received surgery and 108 (37.76%) were in stage 1 of AJCC.

Table 6.1 Demographic data n=286

Variables	Frequency (%)
Age (yrs)	
Mean=59.85 (SD=12.16), range=25.46-84.81	
Gender	
Male	218(76.22)
Female	68(23.78)
Education	
Elementary school	112(39.16)
Junior high school	52(18.18)
Senior high school	54(18.88)
Undergraduate	59(20.63)
Postgraduate	9(3.15)
Marital status	
Single	15(5.24)
Married/ Living with partner	258(90.21)
Divorced/ Separated	8(2.80)
Widowed	5(1.75)
Religion	
General religion	64(22.38)
Buddhism	86(30.07)
Taoism	26(9.09)
Christian	9(3.15)
Catholic	2(0.70)
None	91(31.82)
Other	8(2.80)
Job	
Full time	52(18.18)
Part time	23(8.04)
None	211(73.78)
Main caregiver	
Self	187(65.38)
Husband/Wife	55(19.23)
Son/Daughter	35(12.24)
Father/Mother	3(1.05)
Other relatives/ Friend	1(0.35)
Other	5(1.75)

Table 6.2 Disease and medical information n=286

Variables	Frequency (%)
Time since diagnosis (months)	
Mean=28.70 (SD=26.43), range =0.07-121.20	
Most recent treatment	
Surgery	117(40.91)
TAE/TACE	96(33.57)
Drug therapy	73(25.52)
ECOG	
0	147(51.40)
1	77(26.92)
2	38(13.29)
3	20(6.99)
4	4(1.40)
AJCC stage	
Stage 1	108(37.76)
Stage 2	65(22.73)
Stage 3	87(30.42)
Stage 4	12(4.20)
Missing	14(4.90)
BCLC stage	
Stage A	25(8.74)
Stage B	34(11.89)
Stage C	10(3.50)
Stage D	3(1.05)
Missing	214(74.83)
Child-Pugh stage	
Stage A	224(78.32)
Stage B	42(14.69)
Stage C	16(5.59)
Missing	4(1.40)
Chronic disease	
HBV	184(64.34)
HCV	85(29.72)
Diabetes	48(16.78)
Hypertension	81(28.32)
Chronic obstructive pulmonary disease	1(0.35)
Kidney disease	3(1.05)

Medical examination	
α-FP (normal range: <20)	Normal: 168(58.74)
	Abnormal: 87(30.42)
	Missing: 31(10.84)
T-bilirubin (normal range: 0.2-1.2)	Normal: 158(55.24)
	Abnormal: 109(38.11)
	Missing: 19(6.64)
Albumin (normal range: 3.5-5.0)	Normal: 40(13.99)
	Abnormal: 32(11.19)
	Missing: 214(74.83)
GOT (normal range: ♀<31, ♂<37)	Normal: 92(32.17)
	Abnormal: 167(58.39)
	Missing: 27(9.44)
GPT (normal range: ♀<31, ♂<41)	Normal: 113(39.51)
	Abnormal: 170(59.44)
	Missing: 3(1.05)
Platelet (normal range: 120-320)	Normal: 165(57.69)
	Abnormal: 101(35.31)
	Missing: 20(6.99)
INR (normal range: 0.8-1.2)	Normal: 48(16.78)
	Abnormal: 10(3.50)
	Missing: 228(79.72)

6.4.2 Psychometric characteristics of standardized measures

The means, standard deviations, and Cronbach’s α for subscales in EORTC, HADS, Brief IPQ, coping scale, and inventory of social support behaviour are presented in Table 6.3. These subscales will be used in hierarchical regression analyses in the next chapter.

Table 6.3 Psychometric characteristics of standardized measures

Subscales	Mean (SD)	Cronbach's α
EORTC (range: 0-100)		
Global HRQOL	50.76(20.19)	.77
Physical functioning	78.18(21.43)	.84
Role functioning	70.98(32.34)	.95
Emotional functioning	80.97(17.88)	.66
Cognitive functioning	83.97(17.17)	.51
Social functioning	81.29(24.87)	.90
Symptom	16.89(12.53)	.88
HADS		
Anxiety (range: 0-21)	3.64 (2.91)	.74
Depression (range: 0-21)	4.81 (3.99)	.84
Emotional distress (range: 0-42)	8.46 (6.31)	.87
Brief IPQ (range: 0-10)		
Cognitive representation	5.07(3.05)	.78
Emotional representation*	5.76(2.15)	.56
Understanding	7.95(2.23)	--
Coping scale		
Problem-oriented coping (range: 0-45)	9.85(7.57)	.87
Emotion-oriented coping (range: 0-75)	13.67(5.31)	.52
Inventory of social support behaviour		
Tangible support (range: 6-24)	15.59(3.73)	.85
Emotional support (range: 4-16)	11.52(2.37)	.85
Informational and appraisal support (range: 5-20)	14.06(2.60)	.74

-- single item

* only two items

6.4.3 Aim 1: Differences in HRQOL between patients with HCC and the general population, and patients with liver cancer

Student's *t*-test was used to compare with a norm of general population (n=5087-7722, depended on different scales) (Scott et al., 2008), patients with HCC had worse global HRQOL, *t*(287.8297)=-16.71, *p*<.001, physical, *t*(288.2039)=-9.03, *p*<.001, role, *t*(292.3532)=-7.09, *p*<.001, cognitive, *t*(287.0386)=-2.05, *p*<.05, social, *t*(289.3312)=-4.16, *p*<.001, functioning; but better emotional functioning, *t*(287.2006)=4.29, *p*<.001 than the general population.

Student's *t*-test was used to compare with a norm of patients with liver/bile/pancreas cancer (n=244-739, depended on different scales) (Scott et al., 2008), patients with HCC had worse global HRQOL, *t*(254.6401)=-3.40, *p*<.001; but better physical, *t*(66.51761)=1.96, *p*<.05, role, *t*(2758.2318)=2.56, *p*<.001, emotional, *t*(230.6749)=7.89, *p*<.001, cognitive, *t*(241.3337)=3.75, *p*<.001, and social functioning, *t*(249.3544)=6.53, *p*<.001.

6.4.4 Aim 2: The prevalence of anxiety, depression, and emotional distress in patients with HCC

As shown in Table 6.4, 9.51% patients showed symptoms of mild anxiety and 1.76% had severe anxiety; and 13.42 % had mild depression and 12.02% had severe depression. In addition, 20.4% patients scored above the cut-off for emotional distress.

Compared with a norm of general population (n=1792, Crawford, Henry, Crombie, & Taylor, 2001), patients with HCC had lower levels of anxiety, *t*(281.8747)=-12.91, *p*<.01, and emotional distress, *t*(284.3488)=-3.41, *p*<.01; but had higher levels of depression, *t*(284.7096)=4.58, *p*<.01.

Table 6.4 The prevalence of anxiety, depression, and emotional distress

	Cut-off point	%
Anxiety	Mild: 8 ≦HADS-A≦10	9.51
	Severe: 11≦HADS-A	1.76
Depression	Mild: 8 ≦HADS-D≦10	13.42
	Severe: 11≦HADS-D	12.02
Emotional distress	15≦HADS-A +HADS-D	20.14

6.4.5 Aim 3: Perceptions of HCC

The means and standard deviations for each item (range from 0 to 10) in brief IPQ are presented in Table 6.5. Highest scores in understanding and timeline indicated that patients had high level of illness understanding and thought that the disease would continue to a long period. Lowest scores in identity and treatment control indicated that patients experienced few symptoms, but treatment could not help their disease.

Table 6.5 The mean (SD) of Brief IPQ items

Variables	Mean (SD)
Consequences	5.48(3.12)
Timeline	7.54(2.04)
Personal control	5.54(2.60)
Treatment control	3.41(2.00)
Identity	3.35(2.72)
Concern	6.73(2.17)
Understanding	7.95(2.23)
Emotional response	4.80(2.95)

Perceived causal factors are listed in Table 6.6. Patients were most likely to report the causes of their disease to be liver diseases especially HBV (36.01%), health-related behaviours (drinking, 14.69%; staying up late, 6.64%; irregular life schedule, e.g., eating or sleeping not on time, 4.5%; or diet and food, e.g., not fresh or can food, 4.20%), stress-relevant factors (negative emotion, 3.15%; or heavy-load or high stress level of working, 5.24%), fatigue (6.99%), genetic and family tendency (5.94%).

Table 6.6 The perceived causes of HCC

Factors	N(%)	Factors	N(%)
Liver diseases		**Health-related behaviours**	
HBV	103(36.01)	Drinking	42(14.69)
HCV	31(10.84)	Stay up late/ sleep	19(6.64)
Hepatitis (non specific)	6 (2.10)	Irregular life schedule	13(4.55)
Cirrhosis, fatty liver	2 (.70)	Diet and food	12(4.20)
		Bad life habits	6(2.10)
Stress-relevant factor		Smoking	5(1.75)
Stress	10(3.50)	Didn't take care of body	5(1.75)
Emotion	9(3.15)	No health examination	4(1.40)
Working	15(5.24)		
		Genetic or family tendency	17(5.94)
Fatigue	20(6.99)	Other	25(8.74)

6.5 Discussion

In this chapter quantitative data were used to explore the impact of HCC, focusing on HRQOL and negative emotional feelings; as well as patients' reactions to HCC, focusing on illness perceptions and coping behaviours. Patients in this study had worse global HRQOL, physical, role, cognitive, and social functioning; but better emotional functioning than the general populations. The disease influenced patients' daily activities, disturbed sleep, the need to take a rest in daytime, as well as decreased vitality or feeling tired (Bianchi et al., 2003). The prevalence of anxiety, depression and emotional distress in patients with HCC was 11.27%, 25.44%, and 20.14% respectively. In addition patients with HCC had higher levels of depression than the general population.

HCC impacted widely on patients' HRQOL. Similar to previous studies (Kondo et al., 2007; Lee et al., 2007; Steel, Chopra et al., 2007), patients with HCC had worse HRQOL but better emotional functioning than general population. However, HCC may cause negative feelings in patients (Huang & Lin, 2009) as, based on the HADS, more than one-fifth of patients with HCC experienced emotional distress. The finding that these patients reported better emotional functioning than the general population needs careful explanation. Considering the results of the EORTC and HADS scores, the inconsistent results might arise for several reasons. First, it is possible that, the emotional functioning subscale in EORTC includes only general items (e.g., did you worry, did you feel depressed?) but the HADS includes more specific and detailed items resulting in more psychological problems being detected. Second, when patients adjusted to the disease, they may experience positive growth/changes from the illness experience. However, health professionals should focus on a certain groups of patients who might have emotional problems, especially depression.

Patients interpreted the disease as having broad consequences, long-term timeline, and low treatment control. In addition, patients reported high level of understanding about HCC. They reported that the factors which impaired liver function or increased burden on the liver would induce HCC, included HBV, HCV, drinking alcohol, or fatigue. There were socio-cultural reasons that patients believed these factors would cause their HCC. For example, there is a high prevalence of HBV and HCV in Taiwan, and people believed that alcohol and fatigue could damage their liver.

A limitation should be noted that the norms for EORTC are from Western countries (Austria, Denmark, Germany, Norway, and US), and the differences in social-cultural background may compromise the comparisons. For example, Taiwan patients may have self-report bias that under-response the psychosocial items, especially only few items about psychological issues in EORTC. This chapter only described the physical and psychological impact of HCC, illness perceptions, and coping behaviours. Further regression analyses will be conducted in the next chapter to test the relationships between physical, psychological variables and adjustment outcomes.

Chapter 7. Quantitative Study. Part II: The Role of Illness Perceptions and Coping in HRQOL and Adjustment in Patients with HCC

7.1 Abstract

Aims: This quantitative study builds on the data presented in Chapter 6 to establish a model of the relationships between illness perceptions, coping, and adjustment outcomes derived from the Common Sense Model (Leventhal et al., 1984) in patients with HCC. Using the data described in Chapter 6, we aimed to determine: (1) relationships between demographic and physical variables and the EORTC and HADS scores, as well as illness perceptions; (2) relationships between psychological variables and the EORTC and HADS scores; (3) significant physical and psychological predictors of the EORTC and HADS scores; and (4) mediation effects of illness perceptions and coping.

Methods: Participants, data collection, measures, and procedures were described in Chapter 6. Correlation and hierarchical regression analyses were used to investigate the relationships between variables.

Results: Demographic and physical variables explained significant amounts of variance in the EORTC (global HRQOL and all subscales; R^2=.17-.62) and HADS scores (anxiety, depression, and emotional distress; R^2=.26-.36). Psychological variables (illness perceptions, coping, and social support) also explained significant amounts of variance in the EORTC (R^2=.09-.50) and HADS scores (R^2=.42-.52). The significant physical predictors of EORTC and HADS scores were ECOG and α-FP; and the significant psychological predictors were cognitive and emotional representations. In addition, illness perceptions explained an additional 2.90%-33.12% of the variance in the EORTC and HADS scores after controlling for ECOG and α-FP. In testing mediation, cognitive representations mediated the effects of ECOG on all EORTC and HADS scores; and problem-oriented coping only mediated the effects of cognitive representations on global HRQOL, depression, and emotional distress.

Conclusions: The results suggest that cognitive and emotional illness representations mediate the relationships between physical variables and adjustment outcomes. Other potential pathways of adjustment are also discussed.

7.2 Introduction

In this chapter, the data described previously are used to test the relationships between adjustment outcomes (EORTC: global HRQOL and all subscales; and HADS: anxiety, depression, and emotional distress), demographic and physical variables (demographic information, disease characteristics, and current physical conditions), and psychological variables (illness perceptions, coping, and social support) (see Figure 7.1). The aims were to determine:

(1) relationships between demographic and physical variables and the EORTC and HADS scores, as well as illness perceptions;

(2) relationships between psychological variables and the EORTC and HADS scores;

(3) significant physical and psychological predictors of the EORTC and HADS scores; and

(4) mediation effects of illness perceptions and coping.

Based on the Common Sense Model (Leventhal et al., 1984; Weinman & Petrie, 1997), it was hypothesized that physical variables would influence adjustment outcomes, but that their influences may be through illness perceptions and coping. Illness perceptions might mediate the effects of physical variables on the EORTC and HADS scores, and coping might mediate the effects of illness perceptions on the EORTC and

HADS scores.

Demographic information:
gender, age, job, education level, marital status, whether they need a caregiver and who provided care, and whether they know their diagnosis

Physical variables:
(1) *disease and treatment characteristics:* stage of HCC, most recent treatment, Child-Pugh stage, diagnosis date, and past treatment history
(2) *current physical condition:* ECOG, α-FP, T-bilirubin, Albumin, GOT, GPT, Platelet, and INR

Psychological variables:
(1) *illness perceptions*: cognitive and emotional representations, and understanding
(2) *coping strategies*: problem- oriented coping and emotion-oriented coping
(3) *social support*: tangible assistance, emotional support, and information and appraisal support

Adjustment outcomes:
(1) *EORTC scores:* global HRQOL; physical, role, emotional, cognitive, social functioning; and symptom scales
(2) *HADS scores:* anxiety, depression, and emotional distress

Figure 7.1The categories of variables in this study

7.3 Methods

The participants, standardized questionnaires, and research procedures were the same as Chapter 6.

7.3.1 Screening of variables

The basic assumptions of multivariate analysis were first examined including normal distribution, multicollinearity, and outliers (Field, 2005). The physical examinations (current physical conditions: α-FP, T-bilirubin, Albumin, GOT, GPT, Platelet, and INR) had extreme outliers and were not normally distributed; therefore, dichotomous variables (normal vs. abnormal) were used in the regression analyses. Other categorical variables (treatments, stages, ECOG, and Child-Pugh) were transformed into dummy variables. Descriptive statistics were used for all variables (frequency, mean, standard deviation, and correlation). Spearman's correlation was used to determine the relationships between categorical variables and the EORTC, HADS scores; Pearson's correlation was used to test the relationships between the EORTC, HADS scores and illness perceptions, coping and social support. Variables (Albumin and INR) that had too many missing data were not entered in the regression analysis.

7.3.2 Statistical analysis

Aim 1. First, MANOVAs were conducted to test differences in the EORTC and HADS scores between patients (1) at different stages, and (2) who received different treatments. Second, demographic and physical variables were used to predict the EORTC and HADS scores, as well as illness perceptions by hierarchical regressions.

Aim 2. Hierarchical regressions were used to predict the EORTC and HADS scores from illness perceptions, coping, and social support.

Aim 3. Both physical and psychological variables were entered in hierarchical regressions to predict the EORTC and HADS scores. We investigated the influences of coping and social support on the relationships between illness perceptions and the EORTC and HADS scores, when controlling the effects of demographic and physical variables.

Aim 4. The mediation effects of illness perceptions on relationships between the physical variables and EORTC, HADS scores; and coping on relationships between illness perceptions and EORTC, HADS scores were tested according to the methods by

Preacher and Hayes (2008).

7.4 Results

Correlations between the EORTC, HADS scores and illness perceptions, coping, and social support are presented in Table 7.1. Cognitive and emotional representations were negatively correlated with global HRQOL, physical, role, emotional, cognitive, social functioning; but positively correlated with symptoms, anxiety, depression, and emotional distress. Problem-oriented coping was positively correlated to global HRQOL, physical, role, emotional, cognitive, social functioning; but negatively related to symptoms, anxiety, depression, and emotional distress. Emotion-oriented coping was negatively correlated to global HRQOL and social functioning, but positively correlated to symptoms, anxiety, and emotional distress. Considering social support, tangible support was positively correlated to global HRQOL and social functioning, but negatively correlated with depression and emotional distress. Emotional support, and informational and appraisal support were positively correlated with global HRQOL, but negatively correlated with depression.

Table 7.1 The correlations between EORTC, HADS, illness perceptions, coping, and social support

	HRQOL	PF	RF	EF	CF	SF	SY	HADS_ A	HADS_ D	ED	IP_CO	IP_EM	IP_UN	CO_PR	CO_EM	SS_TA	SS_EM
PF	.52**																
RF	.52**	.81**															
EF	.54**	.33**	.30**														
CF	.27**	.38**	.34**	.24**													
SF	.60**	.60**	.59**	.45**	.28**												
SY	-.63**	-.66**	-.66**	-.55**	-.32**	-.56**											
HADS_A	-.59**	-.37**	-.38**	-.60**	-.14*	-.49**	.54**										
HADS_D	-.69**	-.53**	-.53**	-.51**	-.31**	-.65**	.64**	.66**									
ED	-.71**	-.50**	-.51**	-.60**	-.26**	-.64**	.65**	.88**	.94**								
IP_CO	-.67**	-.50**	-.56**	-.52**	-.26**	-.60**	.65**	.53**	.65**	.66**							
IP_EM	-.51**	-.26**	-.29**	-.63**	-.12*	-.45**	.45**	.59**	.53**	.61**	.62**						
IP_UN	.12*	.32**	.27**	.08	.15*	.13*	-.16**	-.13*	-.17**	-.17**	-.13*	-.08					
CO_PR	.23**	.17**	.16*	.17**	.15*	.13*	-.11	-.05	-.25**	-.18**	-.16*	-.03	.29**				
CO_EM	-.16**	-.06	-.08	-.09	.02	-.15*	.19**	.22**	.10	.17**	.16*	.17**	.05	.27**			
SS_TA	.19**	.01	.05	.11	.09	.14*	-.06	-.09	-.21**	-.17**	-.14*	-.02	.05	.34**	.16*		
SS_EM	.15*	.02	.02	.07	.08	.09	-.00	-.01	-.15*	-.10	-.05	.03	.01	.36**	.19**	.80**	
SS_IN	.12*	.00	.03	.09	.07	.11	-.01	-.03	-.14*	-.10	-.08	.03	.05	.33**	.13*	.81**	.80**

*: *p*<.05; **: *p*<.01

HRQOL: global HRQOL; PF: physical functioning; RF: role functioning; EF: emotional functioning; CF: cognitive functioning; SF: social functioning; SY: symptom; HADS_A: anxiety in HADS; HADS_D: depression in HADS; ED: emotional distress in HADS; IP_CO: cognitive representation of illness perceptions; IP_EM: emotional representation of illness perceptions; IP_UN: understanding of illness; CO_PR: problem-oriented coping; CO_EM: emotion-oriented coping; SS_TA: tangible assistance of social support; SS_EM: emotional support of social support; SS_IN: informational and appraisal support of social support.

7.4.1 Aim 1: Relationships between demographic and physical variables and the EORTC and HADS scores, as well as illness perceptions

(1) Differences in the EORTC and HADS scores by disease stage

Because of the small sample size in stage 4 (n=12), stages 3 and 4 were combined. The overall MANOVA test was significant, *F*(48, 488)=2.14, *p*<.001. Patients in stages 3 & 4 had worse global HRQOL, *F*(2, 266)=12.28, *p*<.001, physical functioning, *F*(2, 266)=7.76, *p*=.001, role functioning, *F*(2, 266)=11.40, *p*<.001, emotional functioning, *F*(2, 266)=5.70, *p*=.004, social functioning, *F*(2, 266)=15.20, *p*<.001; higher levels of anxiety, *F*(2, 266)=4.37, *p*=.014, depression, *F*(2, 266)=13.09, *p*<.001, and emotional distress, *F*(2, 266)=10.35, *p*=.001, than patients in stages 1 or 2. Patients in stages 3 & 4 also had higher symptom score, *F*(2, 266)=6.14, *p*=.002, more fatigue, *F*(2, 266)=5.02, *p*=.007, nausea and vomiting, *F*(2, 266)=5.33, *p*=.005, appetite loss, *F*(2, 266)=4.28, *p*=.015, nutritional problems, *F*(2, 266)=12.60, *p*<.001, and abdominal swelling, *F*(2, 266)=11.40, *p*<.001; and worse body image, *F*(2, 266)=5.40, *p*=.005, than patients in stages 1 or 2.

(2) Differences in the EORTC and HADS scores by treatment

The overall MANOVA test was significant, *F*(48, 516)=3.22, *p*<.001, indicating that there were significant differences in the EORTC and HADS scores between the surgery, TAE/TACE, and drug therapy groups. Patients who received surgery or TAE/TACE had better physical functioning, *F*(2, 280)=26.08, *p*<.001, role functioning, *F*(2, 280)=28.59, *p*<.001, emotional functioning, *F*(2, 280)=8.72, *p*<.001, cognitive functioning, *F*(2, 280)=8.83, *p*<.001; and less severe symptoms, *F*(2, 280)=16.48, *p*<.001, and anxiety, *F*(2, 280)=3.60, *p*=.029, than patients who received drug therapy. Patients who received surgery had the highest level of global HRQOL, *F*(2, 280)=28.94, *p*<.001, social functioning, *F*(2, 280)=25.99, *p*<.001, as well as the lowest levels of depression, *F*(2, 280)=22.13, *p*<.001, and emotional distress, *F*(2, 280)=14.44, *p*<.001.

(3) Predictors of the EORTC and HADS scores depending on demographic and physical variables

(i) EORTC scores

Hierarchical regressions were conducted with demographic data (gender and age) entered in the first block; disease characteristics (stages, treatments, child-Pugh stages, and time since diagnosis) were entered in the second block; and current physical conditions (α-FP, T-bilirubin, GOT, GPT, and Platelet) were entered in the third block. Again because of small sample size; stages 3 and 4 were combined, as well as ECOG 3 and 4. The dependent variables were all EORTC scores: global HRQOL, five functioning scores, and symptom.

Demographic characteristics only explained between 0.53%-6.03% of the variance in EORTC scores. Entering the disease characteristics at step 2 produced large and significant increments in the amounts of variance explained in the EORTC scores, from 7.95%-24.39%. Current physical conditions entered at step 3 explained an additional significant 6.23%-33.57% of the variance in all EORTC scores, except for cognitive functioning. The highest amounts of variance were explained in physical functioning (R^2=.62, *p*<.001), role functioning (R^2=.56, *p*<.001), and symptom (R^2=.45, *p*<.001), which were all relevant to physical components.

Considering the specific predictors, patients who had better performance status (ECOG=0 or 1) had better global HRQOL and five functioning scales, and less symptom score than those with poorer performance status (ECOG=3 & 4). In addition, patients with normal α-FP level had better physical, role, social functioning, and less severe symptoms than those with abnormal α-FP level. A summary of these regression analyses is presented in Table 7.2.

(ii) HADS scores

A similar analysis strategy was used to predict the HADS scores: anxiety, depression, and emotional distress (see Table 7.3). Demographic characteristics only explained between 0.32%-2.70% of the variance in anxiety, depression, and emotional distress. Entering the disease characteristics at step 2 produced large and significant increments in the amounts of variance explained in anxiety, depression, and emotional distress, from 10.66%-21.73%. Current physical conditions entered at step 3 explained an additional 11.96%-15.35% of the variance in anxiety, depression, and emotional distress. Considering the specific predictors, patients with good performance status or normal α-FP level had lower levels of anxiety, depression, and emotional distress.

(4) Predictors of illness perceptions depending on demographic and physical variables

Demographic characteristics, disease characteristics and current physical conditions were entered in hierarchical regressions in a sequence to investigate whether demographic and physical variables predicted illness perceptions. Disease characteristics significantly explained 22.81% of the variance in cognitive representation, 13.99% of the variance in emotional representation, and 8.05% of the variance in illness understanding. Current physical conditions explained an additional 5.97%-16.87% of the variance in three variables. Patients who were older, received surgery, had better performance status (ECOG=0) and normal α-FP level perceived HCC as less negative cognitive representation. A longer period of disease was associated with higher levels of understanding (see Table 7.4).

Table 7.2 Summary of regression analyses: demographic and physical variables predicting the EORTC scores (standardized beta values, R^2, and ΔR^2)

DV	HRQOL	PF	RF	EF	CF	SF	SY
Step 1							
Gender	-.06	-.15*	-.07	-.13	-.13*	.05	.17*
Age	-.03	-.17**	-.10	.04	-.09	.12	-.03
Step 2							
Gender	-.07	-.15*	-.08	-.12	-.12	.05	.16**
Age	-.07	-.21**	-.16**	.02	-.09	.08	.00
Stage 1	.12*	.08	.09	.07	.03	.12	-.03
Stage 2	.18*	.08	.11	.15*	-.01	.14*	-.12
Child 1	.23	.26*	.22*	.16	.14	.40**	-.39**
Child 2	.09	.09	.11	-.02	.01	.20*	-.14
Treat 1	.27**	.27**	.27**	.13	.20*	.24**	-.18
Treat 2	.05	.23**	.29**	.09	.22*	.09	-.10
T_diag	.15*	.14*	.18**	.03	-.07	.09	-.09
Step 3							
Gender	-.02	-.09*	-.01	-.09	-.10	.09	.11*
Age	.04	-.05	.01	.11	-.04	.18**	-.14*
Stage 1	.04	-.01	-.01	.03	.03	.04	.06
Stage 2	.11	-.02	.00	.11	-.02	.06	-.02
Child 1	.06	-.04	-.06	.04	.06	.22*	-.11
Child 2	-.01	-.07	-.04	-.10	-.01	.10	.02
Treat 1	.08	-.07	-.08	.02	.05	.01	.09
Treat 2	-.09	-.08	-.01	.01	.09	-.08	.11
T_diag	.06	.01	.03	-.06	-.08	.00	.05
ECOG 1	.61**	1.23**	1.11**	.37*	.53**	.70**	-.94**
ECOG 2	.35**	.75**	.56**	.15	.36**	.41**	-.49**
ECOG 3	.15	.34**	.23**	.06	.26**	.19*	-.27**
α-FP	.10	.12*	.14*	-.00	.01	.17**	-.13*
T-bil	-.01	.03	.04	.02	-.07	.02	-.11*
GOT	.13	-.01	-.03	.19*	.06	.02	-.05
GPT	-.02	-.02	-.02	-.06	-.11	.01	-.02
Plate	-.10	-.13**	-.07	-.11	.06	-.06	.14*
1 $\Delta R^2(F)$	.01(.62)	.06(7.43)**	.02(2.23)	.02(1.97)	.03(3.50)*	.02(2.27)	.03(3.33)*
2 $\Delta R^2(F)$	.24(9.58)**	.22(9.56)**	.23(9.70)**	.10(3.63)**	.08(2.88)**	.24(10.38)**	.19(7.74)**
3 $\Delta R^2(F)$	.13(4.97)**	.34(20.92)**	.31(17.46)**	.07(2.42)*	.06(1.59)	.14(5.11)**	.23(11.62)**
$R^2(F)$	.37(6.94)**	.62(18.44)**	.56(15.06)**	.19(2.97)**	.17(2.41)**	.41(7.69)**	.45(10.50)**

*: $p<.05$; **: $p<.01$

Dependent variables: HRQOL: global HRQOL; PF: physical functioning; RF: role functioning; EF: emotional functioning; CF: cognitive functioning; SF: social functioning; SY: symptom.

Independent variables: gender: male (1) vs. female (2); stage 1: stage 1 in AJCC (1) vs. other stage (0); stage 2: stage 2 in AJCC (1) vs. other stage (0); child 1: Child-Pugh stage A (1) vs. other (0); child 2: Child-Pugh stage B (1) vs. other (0); treat 1: surgery (1) vs. other treatments(0); treat 2: TAE/TACE (1) vs. others (0); T_diag: time since diagnosis; ECOG 1: ECOG 0 (1) vs. other ECOG (0); ECOG 2: ECOG 1 (1) vs. other ECOG (0); ECOG 3: ECOG 2 (1) vs. other ECOG (0); T-bil: T-bilirubin; plate: platelet. α-FP, T-bil, GOT, GPT, plate: normal=1 vs. abnormal=0.

Table7.3 Summary of regression analyses: demographic and physical variables predicting the HADS scores (standardized beta values, R^2, and ΔR^2)

DV	Anxiety	Depression	Emotional distress
Step 1			
Gender	.14*	.05	.10
Age	-.12	-.03	-.07
Step 2			
Gender	.15*	.06	.10
Age	-.067	.01	-.02
Stage 1	-.08	-.15	-.13
Stage 2	-.17*	-.17*	-.18*
Child 1	-.30*	-.36**	-.36**
Child 2	-.13	-.17	-.17
Treat 1	.07	-.18	-.08
Treat 2	.14	-.03	.05
T_diag	-.19**	-.12	-.16**
Step 3			
Gender	.11	.03	.07
Age	-.15*	-.07	-.11
Stage 1	-.02	-.06	-.04
Stage 2	-.10	-.10	-.11
Child 1	-.14	-.16	-.17
Child 2	-.02	-.06	-.05
Treat 1	.22*	.03	.12
Treat 2	.27**	.13	.21*
T_diag	-.09	-.04	-.06
ECOG 1	-.51**	-.63**	-.64**
ECOG 2	-.24*	-.38**	-.36**
ECOG 3	-.15	-.20*	-.20*
α-FP	-.17*	-.24**	-.23**
T-bil	-.05	-.08	-.07
GOT	-.09	-.06	-.08
GPT	.04	.08	.07
Plate	.17*	.06	.12
1 $\Delta R^2(F)$	.03(3.24)*	.00(.37)	.01(1.43)
2 $\Delta R^2(F)$	.11(3.97)**	.22(8.48)**	.19(7.29)**
3 $\Delta R^2(F)$	.12(3.95)**	.14(5.48)**	.15(5.90)**
$R^2(F)$	.26(4.12)**	.36(6.68)**	.35(6.53)**

*: $p<.05$; **: $p<.01$

Independent variables: gender: male (1) vs. female (2); stage 1: stage 1 in AJCC (1) vs. other stage (0); stage 2: stage 2 in AJCC (1) vs. other stage (0); child 1: Child-Pugh stage A (1) vs. other (0); child 2: Child-Pugh stage B (1) vs. other (0); treat 1: surgery (1) vs. other treatments(0); treat 2: TAE/TACE (1) vs. others (0); T_diag: time since diagnosis; ECOG 1: ECOG 0 (1) vs. other ECOG (0); ECOG 2: ECOG 1 (1) vs. other ECOG (0); ECOG 3: ECOG 2 (1) vs. other ECOG (0); T-bil: T-bilirubin; plate: platelet. α-FP, T-bil, GOT, GPT, plate: normal=1 vs. abnormal=0.

There was the possibility of suppressor variable effects in this table that age was significant related to time since diagnosis (r=.15) and ECOG score (performance status, r=-.24), and physical variables may correlated with each other. These effects may influence the interpretations of this result.

Table 7.4 Summary of regression analyses: demographic and physical variables predicting illness perceptions (standardized beta values, R^2, and ΔR^2)

DV	IP_CO	IP_EM	IP_UN
Step 1			
Gender	.02	.07	-.11
Age	-.08	-.06	-.11
Step 2			
Gender	.03	.09	-.14*
Age	-.06	-.04	-.14*
Stage 1	-.03	-.07	.06
Stage 2	-.10	-.08	.02
Child 1	-.14	-.06	-.15
Child 2	-.08	-.05	-.13
Treat 1	-.38**	-.23*	.09
Treat 2	-.12	-.03	.09
T_diag	-.20**	-.22**	.23**
Step 3			
Gender	-.02	.06	-.11
Age	-.15*	-.10	-.13
Stage 1	.09	-.00	.03
Stage 2	.00	-.02	-.00
Child 1	.05	.03	-.15
Child 2	.03	.02	-.15
Treat 1	-.19*	-.14	.02
Treat 2	-.02	-.01	-.02
T_diag	-.08	-.13	.20**
ECOG 1	-.44**	-.11	.31*
ECOG 2	-.19	.07	.25*
ECOG 3	-.02	.10	.22*
α-FP	-.27**	-.10	.20**
T-bil	-.07	-.06	-.13*
GOT	-.07	-.09	.02
GPT	-.01	.01	.00
Plate	.09	.05	-.15**
1 $\Delta R^2(F)$	.01(.66)	.01(.87)	.03(3.93)*
2 $\Delta R^2(F)$	.23(9.50)**	.14(5.21)**	.08(2.91)**
3 $\Delta R^2(F)$	.17(7.85)**	.06(2.13)*	.08(2.21)**
$R^2(F)$	.40(8.68)**	.21(3.35)**	.19(2.73)**

*: $p<.05$; **: $p<.01$

Dependent variables: IP_CO: cognitive representation of illness perceptions; IP_EM: emotional representation of illness perceptions; IP_UN: understanding of illness.

Independent variables: gender: male (1) vs. female (2); stage 1: stage 1 in AJCC (1) vs. other stage (0); stage 2: stage 2 in AJCC (1) vs. other stage (0); child 1: Child-Pugh stage A (1) vs. other (0); child 2: Child-Pugh stage B (1) vs. other (0); treat 1: surgery (1) vs. other treatments(0); treat 2: TAE/TACE (1) vs. others (0); T_diag: time since diagnosis; ECOG 1: ECOG 0 (1) vs. other ECOG (0); ECOG 2: ECOG 1 (1) vs. other ECOG (0); ECOG 3: ECOG 2 (1) vs. other ECOG (0); T-bil: T-bilirubin; plate: platelet. α-FP, T-bil, GOT, GPT, plate: normal=1 vs. abnormal=0.

7.4.2 Aim 2: Relationships between psychological variables and the EORTC and HADS scores

(i) EORTC scores

The psychological variables included illness perceptions (cognitive representation, emotional representation, and understanding) entered at the first step, coping (problem-oriented and emotion-oriented) entered at the second step, and social support (tangible assistance, emotional support, and informational and appraisal support) entered at the third step.

The three kinds of variables explained significant amounts of variance in all EORTC scores from 9.42% to 49.93%. Illness perceptions explained significant amounts of variance in all EORTC scores (ΔR^2=.09-.42, p<.01); however, only cognitive representation was a consistent predictor for all EORTC scores. Coping produced a significant increment in the amount of variance explained for global HRQOL (ΔR^2=.03, p=.002) and emotional functioning (ΔR^2=.01, p=.048). Three subscales of social support failed to produce significant increments in the variance explained in all EORTC scores (see Table 7.5).

(ii) HADS scores

A similar analysis as described above was used to predict anxiety, depression, and emotional distress. Illness perceptions explained significant amounts of variance in HADS scores from 39.69% to 50.43%; coping explained amounts of variance from 1.18% to 2.04%, only significant for depression (ΔR^2=.02, p=.009); social support explained amounts of variance from 0.46% to 0.975%, all non-significant. Cognitive (B=.23-.47, p<.001) and emotional (B=.22-.41, p<.001) representations were always significant for anxiety, depression, and emotional distress, even when entering the variables of coping and social support (see Table 7.6).

Table 7.5 Summary of regression analysis: psychological variables predicting the EORTC scores (standardized beta values, R^2, and ΔR^2)

DV	HRQOL	PF	RF	EF	CF	SF	SY
Step 1							
IP_CO	-.57**	-.51**	-.58**	-.21**	-.29**	-.51**	.60**
IP_EM	-.16**	.07	.08	-.50**	.07	-.13*	.07
IP_UN	.04	.26**	.20**	.01	.12	.05	-.08
Step 2							
IP_CO	-.52**	-.51**	-.57**	-.18**	-.28**	-.49**	.59**
IP_EM	-.16**	.07	.08	-.51**	.06	-.13*	.06
IP_UN	-.00	.26**	.19**	-.02	.10	.04	-.08
CO_PR	.17**	.02	.02	.13*	.07	.05	-.01
CO_EM	-.10*	-.01	-.02	-.01	.03	-.07	.09
Step 3							
IP_CO	-.52**	-.52**	-.58**	-.18**	-.28**	-.48**	.59**
IP_EM	-.16**	.08	.08	-.52**	.06	-.14*	.06
IP_UN	.01	.26**	.19**	-.02	.11	.05	-.08
CO_PR	.13*	.03	.03	.12*	.06	.02	-.02
CO_EM	-.11*	-.01	-.02	-.01	.02	-.08	.09
SS_TA	.06	-.14	-.07	-.02	.01	.03	-.02
SS_EM	.13	.14	.04	-.03	.06	.01	-.01
SS_IN	-.09	-.06	-.01	.09	-.04	.05	.05
1 $\Delta R^2(F)$	.46(70.05)**	.32(37.94)**	.35(43.87)**	.43(60.64)**	.09(7.74)**	.37(47.39)**	.44(63.27)**
2 $\Delta R^2(F)$	.03(6.19)**	.00(.04)	.00(.12)	.01(3.08)*	.01(.80)	.01(1.00)	.01(1.57)
3 $\Delta R^2(F)$	.01(1.79)	.01(1.37)	.00(.31)	.00(.47)	.00(.15)	.00(.75)	.00(.15)
$R^2(F)$	.50(29.88)**	.33(14.70)**	.35(16.34)**	.44(23.92)*	.09(3.12)**	.38(18.25)*	.45(24.03)*

*: $p<.05$; **: $p<.01$

Dependent variables: HRQOL: global HRQOL; PF: physical functioning; RF: role functioning; EF: emotional functioning; CF: cognitive functioning; SF: social functioning; SY: symptom.

Independent variables: IP_CO: cognitive representation of illness perceptions; IP_EM: emotional representation of illness perceptions; IP_UN: understanding of illness; CO_PR: problem-oriented coping; CO_EM: emotion-oriented coping; SS_TA: tangible assistance of social support; SS_EM: emotional support of social support; SS_IN: informational and appraisal support of social support.

Table 7.6 Summary of regression analyses: psychological variables predicting the HADS scores (standardized beta values, R^2, and ΔR^2)

DV	Anxiety	Depression	Emotional distress
Step 1			
IP_CO	.26**	.51**	.45**
IP_EM	.43**	.20**	.33**
IP_UN	-.07	-.09	-.09
Step 2			
IP_CO	.25**	.48**	.42**
IP_EM	.41**	.22**	.33**
IP_UN	-.07	-.05	-.06
CO_PR	-.01	-.16**	-.11*
CO_EM	.12*	.03	.08
Step 3			
IP_CO	.23**	.47**	.40**
IP_EM	.41**	.22**	.33**
IP_UN	-.07	-.06	-.07
CO_PR	.003	-.12*	-.08
CO_EM	.13*	.04	.09
SS_TA	-.11	-.08	-.10
SS_EM	.03	-.07	-.03
SS_IN	.02	.04	.04
1 $\Delta R^2(F)$	.40(53.75)**	.46(68.38)**	.50(83.07)**
2 $\Delta R^2(F)$	.01(2.78)	.02(4.72)**	.01(2.96)
3 $\Delta R^2(F)$	.01(.63)	.01(1.52)	.01(1.32)
$R^2(F)$	.42(21.68)**	.49(28.35)**	.52(33.01)**

*: p<.05; **: p<.01

Independent variables: IP_CO: cognitive representation of illness perceptions; IP_EM: emotional representation of illness perceptions; IP_UN: understanding of illness; CO_PR: problem-oriented coping; CO_EM: emotion-oriented coping; SS_TA: tangible support of social support; SS_EM: emotional support of social support; SS_IN: informational and appraisal support of social support.

7.4.3 Aim 3: Significant physical and psychological predictors of the EORTC and HADS scores

In order to reduce the number of physical variables to be included in the regression analyses, only ECOG and α-FP, which were consistent predictors for all EORTC and HADS scores (see Table 7.2 & 7.3), were entered in the first block. Illness perceptions were entered in the second block, and coping and social support in the third block.

(i) EORTC scores

ECOG and α-FP explained 12.56%-58.39% of the variance in all EORTC scores (*ps*<.01). Illness perceptions explained an additional, and significant 4.39%-33.12% of the variance in all EORTC scores except for cognitive functioning (ΔR^2=.03, *p*=.054). However, coping and social support explained an additional significant 3.64% of the variance in global HRQOL, but failed to explain significant additional amounts of variance in five functioning scores and symptom (see Table 7.7).

ECOG, cognitive and emotional representations, and problem-oriented and emotion-oriented coping were significant predictors of global HRQOL. Better performance status, less negative cognitive and emotional representations, more problem-oriented coping and less emotion-oriented coping were associated with better global HRQOL. ECOG was still a significant predictor when entering illness perceptions, coping, and social support. In addition, cognitive and emotional representations were still significant predictors when entering coping and social support. It indicated that ECOG and cognitive and emotional representations may play more important roles than other predictor variables.

ECOG and cognitive representations were significant predictors for all EORTC scores. In addition, α-FP was associated with emotional functioning; emotional representation was associated with global HRQOL, role, emotional, and social functioning negatively; understanding related to physical functioning positively; problem-oriented coping was associated with global HRQOL and emotional functioning positively; emotion-oriented coping was associated with global HRQOL negatively; and emotional support related to physical functioning positively.

(ii) HADS scores

ECOG and α-FP explained 14.79%-31.43% of the variance in anxiety, depression, and emotional distress. Illness perceptions explained an additional, and significant, 20.19%-26.44% of the variance. Coping and social support only explained an additional 2.98% of the variance in depression significantly. Patients who had better performance status, less negative cognitive and emotional representations, had less anxiety, depression, and emotional distress. In addition, emotion-oriented coping was related to anxiety positively (see Table 7.8).

Table 7.7 Summary of regression analysis: physical and psychological variables predicting the EORTC scores (standardized beta values, R^2, and ΔR^2)

DV	HRQOL	PF	RF	EF	CF	SF	SY
Step 1							
ECOG 1	.73**	1.18**	1.03**	.50**	.65**	.76**	-.91**
ECOG 2	.39**	.71**	.52**	.25*	.44**	.48**	-.50**
ECOG 3	.15	.31**	.20**	.09	.29**	.23**	-.27**
α-FP	.15*	.07	.09	.03	.00	.22**	-.12*
Step 2							
ECOG 1	.486**	1.03**	.87**	.29**	.53**	.58**	-.68**
ECOG 2	.31**	.63**	.43**	.23*	.38**	.43**	-.41**
ECOG 3	.16*	.27**	.17**	.14	.27**	.24**	-.28**
α-FP	-.02	-.02	-.01	-.11	-.07	.10	.04
IP_CO	-.45**	-.23**	-.32**	-.20**	-.21*	-.33**	.46**
IP_EM	-.16**	.06	.09	-.51**	.05	-.15*	.08
IP_UN	-.01	.14**	.09*	.00	.08	-.02	-.01
Step 3							
ECOG 1	.49**	1.04**	.87**	.28**	.53**	.59**	-.68**
ECOG 2	.31**	.65**	.44**	.21*	.38**	.43**	-.43**
ECOG 3	.19**	.28**	.17*	.15	.28**	.25**	-.29**
α-FP	-.02	-.02	-.00	-.12*	-.07	.10	.04
IP_CO	-.40**	-.25**	-.32**	-.18*	-.20*	-.31**	.45**
IP_EM	-.17**	.07	.09*	-.53**	.04	-.15*	.07
IP_UN	-.03	.16**	.10	-.03	.07	-.02	-.02
CO_PR	.11*	-.05	-.04	.12*	.05	-.02	.01
CO_EM	-.11*	.01	.01	-.02	.01	-.07	.09
SS_TA	.08	-.11	-.03	-.03	.02	.05	-.04
SS_EM	.13	.16*	.03	-.01	.08	.03	-.02
SS_IN	-.09	-.05	.02	.09	-.05	.04	.05
1 $\Delta R^2(F)$	.31(25.80)**	.58(79.98)**	.54(67.40)**	.13(8.19)**	.13(8.47)**	.33(27.59)**	.38(35.10)**
2 $\Delta R^2(F)$	.21(33.78)**	.04(8.84)**	.06(10.65)**	.33(27.03)**	.03(2.59)	.14(18.70)**	.17(29.21)**
3 $\Delta R^2(F)$	.04(3.66)**	.01(1.07)	.00(.16)	.02(16.54)	.01(.40)	.01(1.13)	.01(.87)
$R^2(F)$	.56(23.51)**	.64(32.12)**	.60(27.52)**	.47(25.12)**	.17(3.65)**	.47(16.53)**	.56(23.64)**

*: $p<.05$; **: $p<.01$

Dependent variables: HRQOL: global HRQOL; PF: physical functioning; RF: role functioning; EF: emotional functioning; CF: cognitive functioning; SF: social functioning; SY: symptom.

Independent variables: ECOG 1: ECOG 0 (1) vs. other ECOG (0); ECOG 2: ECOG 1 (1) vs. other ECOG (0); ECOG 3: ECOG 2 (1) vs. other ECOG (0); IP_CO: cognitive representation of illness perceptions; IP_EM: emotional representation of illness perceptions; IP_UN: understanding of illness; CO_PR: problem-oriented coping; CO_EM: emotion-oriented coping; SS_TA: tangible assistance of social support; SS_EM: emotional support of social support; SS_IN: informational and appraisal support of social support.

Table 7.8 Summary of regression analyses: physical and psychological variables predicting the HADS scores (standardized beta values, R^2, and ΔR^2)

DV	Anxiety	Depression	Emotional distress
Step 1			
ECOG 1	-.44**	-.69**	-.65**
ECOG 2	-.20	-.42**	-.36**
ECOG 3	-.11	-.21*	-.19*
α-FP	-.17*	-.26**	-.24**
Step 2			
ECOG 1	-.23*	-.46**	-.40**
ECOG 2	-.17	-.35**	-.31**
ECOG 3	-.15	-.22**	-.21**
α-FP	-.03	-.10	-.08
IP_CO	.21**	.37**	.33**
IP_EM	.43**	.22**	.34**
IP_UN	-.04	-.03	-.04
Step 3			
ECOG 1	-.24*	-.46**	-.41**
ECOG 2	-.18	-.34**	-.31**
ECOG 3	-.16*	-.24**	-.23**
α-FP	-.03	-.10	-.08
IP_CO	.18*	.33**	.29**
IP_EM	.42**	.24**	.35**
IP_UN	-.05	-.00	-.02
CO_PR	.01	-.09	-.06
CO_EM	.13*	.04	.09
SS_TA	-.12	-.10	-.12
SS_EM	.03	-.08	-.04
SS_IN	.03	.06	.05
1 $\Delta R^2(F)$	.15(9.89)**	.31(26.12)**	.29(22.69)**
2 $\Delta R^2(F)$	.26(33.53)**	.20(31.30)**	.26(43.97)**
3 $\Delta R^2(F)$	.02(1.54)	.03(2.89)*	.02(2.14)
$R^2(F)$	.43(13.89)*	.55(22.05)**	.57(24.30)**

*: p<.05; **: p<.01

Independent variables: ECOG 1: ECOG 0 (1) vs. other ECOG (0); ECOG 2: ECOG 1 (1) vs. other ECOG (0); ECOG 3: ECOG 2 (1) vs. other ECOG (0); IP_CO: cognitive representation of illness perceptions; IP_EM: emotional representation of illness perceptions; IP_UN: understanding of illness; CO_PR: problem-oriented coping; CO_EM: emotion-oriented coping; SS_TA: tangible assistance of social support; SS_EM: emotional support of social support; SS_IN: informational and appraisal support of social support.

7.4.4 Aim 4: Mediation effects of illness perceptions and coping

In this section, the mediating effects of illness perceptions and coping were tested: (1) whether illness perceptions mediated relationships between ECOG and the EORTC and HADS scores; (2) whether coping mediated relationships between cognitive representation and the EORTC and HADS scores; and (3) whether coping mediated relationships between emotional representation and global HRQOL, emotional functioning, anxiety, depression, and emotional distress.

(1) The mediation effects of illness perceptions on the relationships between ECOG and the EORTC, HADS scores

(i) EORTC scores

The mediation analyses described by Preacher and Hayes (2008) were used to test whether illness perceptions mediated the relationships between ECOG and the EORTC scores. In Tables 7.2 and 7.7, ECOG was a significant predictor across all EORTC scores; therefore ECOG was entered as the independent variable. The two illness perceptions scores (cognitive and emotional representations) were entered as potential mediators, and all EORTC scores were used as dependent variables (see Figure 7.2).

When global HRQOL was the dependent variable, the paths from ECOG to cognitive representation, *B*=4.65, *SE*=.50, *p*<.001, and to emotional representation, *B*=1.33, *SE*=.26, *p*<.001, were both significant. The direct effects of cognitive representation, *B*=-.97, *SE*=.13, *p*<.001, and emotional representation, *B*=-.74, *SE*=.25, *p*=.003, on global HRQOL were also significant. The effect of ECOG on global HRQOL, *B*=-11.04, *SE*=1.07, *p*<.001, though reduced, was still significant when controlling for cognitive and emotional representations, *B*=-5.56, *SE*=1.01, *p*<.001, suggesting partial mediation. Using bootstrapping procedures, the total mediated effect was found to be significant, *B*=-5.52, *SE*=.71, *CI*=-4.26 to -7.12. Inspection of the individual mediators showed that both cognitive representation, *B*=-4.54, *SE*=.76, *CI*=-3.09 to -6.10, and emotional representation, *B*=-.98, *SE*=.44, *CI*=-.35 to -2.26, mediated the effect of ECOG on global HRQOL.

The same procedure was applied to other EORTC scores, and the results are summarized in Table 7.9. The total mediation effects (both cognitive and emotional representation) were significant for all EORTC scores. Cognitive representation was a significant mediator across all EORTC scores, whereas emotional representation was a significant mediator for global HRQOL, emotional functioning, and social functioning.

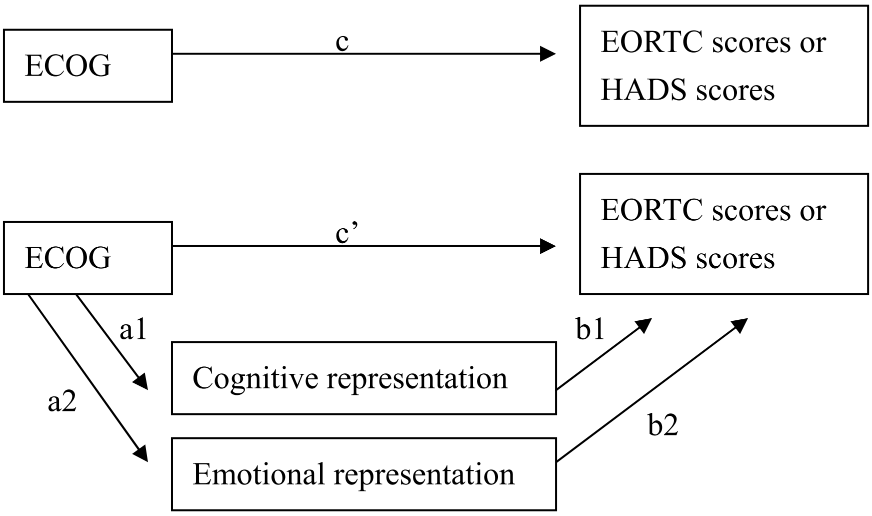

Figure 7.2 To test the mediation effects of illness perceptions on the relationships between ECOG and the EORTC, HADS scores

Table 7.9 Summary of mediation testing: illness perceptions on the relationships between ECOG and the EORTC scores

		HRQOL	PF	RF	EF	CF	SF	SY
Pathway								
c	*B*	-11.04	-16.15	-23.82	-5.84	-5.64	-12.57	7.38
	SE	1.07**	.84**	1.39**	1.06**	.99**	1.28**	.63**
c’	*B*	-5.56	-14.37	-19.46	-1.54	-4.47	-7.13	4.34
	SE	1.01**	.94**	1.50**	.97	1.12**	1.29**	.61**
Indirect effects								
Total	*B*	-5.52	-1.77	-4.32	-4.35	-1.16	-5.44	3.07
(b1+b2)	*SE*	.71	.46	.90	.71	.55	.79	.43
	CIs	-7.12	-2.80	-6.38	-5.84	-2.34	-7.02	2.23
		-4.26*	-.96*	-2.77*	-2.92*	-.06*	-3.99*	3.89*
b1	*B*	-4.54	-2.19	-5.10	-1.55	-1.50	-4.43	2.78
	SE	.76	.60	1.10	.65	.67	.86	.49
	CIs	-6.10	-3.58	-7.65	-2.85	-3.12	-6.21	1.91
		-3.09*	-1.21*	-3.42*	-.35*	-.30*	-2.77*	3.81*
b2	*B*	-.98	.42	.78	-2.81	.34	-1.01	.29
	SE	.44	.33	.54	.64	.41	.50	.24
	CIs	-2.26	-.18	-.12	-4.09	-.44	-2.13	-.17
		-.35*	1.19	2.08	-1.50*	1.13	-.17*	.82

*p<.05, **p<.01

Dependent variable: HRQOL: global HRQOL; PF: physical functioning; RF: role functioning; EF: emotional functioning; CF: cognitive functioning; SF: social functioning; SY: symptom.

Pathway: c: the direct effect of ECOG on EORTC scores; c’: the direct effect of ECOG on EORTC scores controlling cognitive and emotional representations; b1+b2: the indirect effect of ECOG on EORTC scores through cognitive and emotional representations; b1: the indirect effect of ECOG on EORTC scores through cognitive representation; b2: the indirect effect of ECOG on EORTC scores through emotional representations.

(ii) HADS scores

The same procedure was applied to the HADS scores, ECOG was entered as the independent variable; cognitive and emotional representations were potential mediators; and anxiety, depression, and emotional distress were dependent variables (Figure 7.2). The results are summarized in Table 7.10. The total mediation effects (both cognitive and emotional representations) were significant for anxiety, depression, and emotional distress. Considering the individual mediators, both cognitive and emotional representations were significant mediators for anxiety, depression, and emotional distress.

Table 7.10 Summary of mediation testing: illness perceptions on the relationships between ECOG and the HADS scores

		Anxiety	Depression	Emotional distress
Pathway				
c	*B*	1.01	2.05	3.06
	SE	.17**	.21**	.34**
c’	*B*	.32	.99	1.30
	SE	.16*	.20**	.31**
Indirect effect				
Total	*B*	.69	1.07	1.76
(b1+b2)	*SE*	.12	.15	.26
	CIs	.47	.76	1.25
		.93*	1.35*	2.25*
b1	*B*	.31	.81	1.13
	SE	.11	.16	.24
	CIs	.13	.53	.71
		.56*	1.18*	1.62*
b2	*B*	.38	.25	.62
	SE	.09	.09	.15
	CIs	.22	.10	.38
		.56*	.46*	1.00*

*p<.05, **p<.01

Pathway: c: the direct effect of ECOG on HADS scores; c’: the direct effect of ECOG on HADS scores controlling cognitive and emotional representations; b1+b2: the indirect effect of ECOG on HADS scores through cognitive and emotional representations; b1: the indirect effect of ECOG on HADS scores through cognitive representation; b2: the indirect effect of ECOG on HADS scores through emotional representations.

(2) The mediation effects of coping on the relationships between cognitive representation and the EORTC, HADS scores

(i) EORTC scores

Cognitive representation was entered as the independent variable, problem-oriented and emotion-oriented coping were the potential mediators, and all EORTC scores were dependent variables (see Figure 7.3). When global HRQOL was the dependent variable, the paths from cognitive representation to problem-oriented coping, *B*=-.13, *SE*=.05, *p*=.011, and to emotion-oriented coping, *B*=.09, *SE*=.04, *p*=.013, were both significant. The direct effects of problem-oriented coping, *B*=.43, *SE*=.13, *p*=.001, and emotion-oriented coping, *B*=-.42, *SE*=.19, *p*=.027, on global HRQOL were also significant. The effect of cognitive representation on global HRQOL, *B*=-1.42, *SE*=.10, *p*<.001, was reduced, but was still significant when controlling problem-oriented and emotion-oriented coping, *B*=-1.32, *SE*=.10, *p*<.001. Using bootstrapping procedures, the total mediated effect was found to be significant, *B*=-.10, *SE*=.04, *CI*=-.17 to -.03. Inspection of the individual mediator showed that both problem-oriented coping, *B*=-.06, *SE*=.03, *CI*=-.13 to -.01, and emotion-oriented coping, *B*=-.04, *SE*=.02, *CI*=-.10 to -.002, mediated the effect of cognitive representation on global HRQOL.

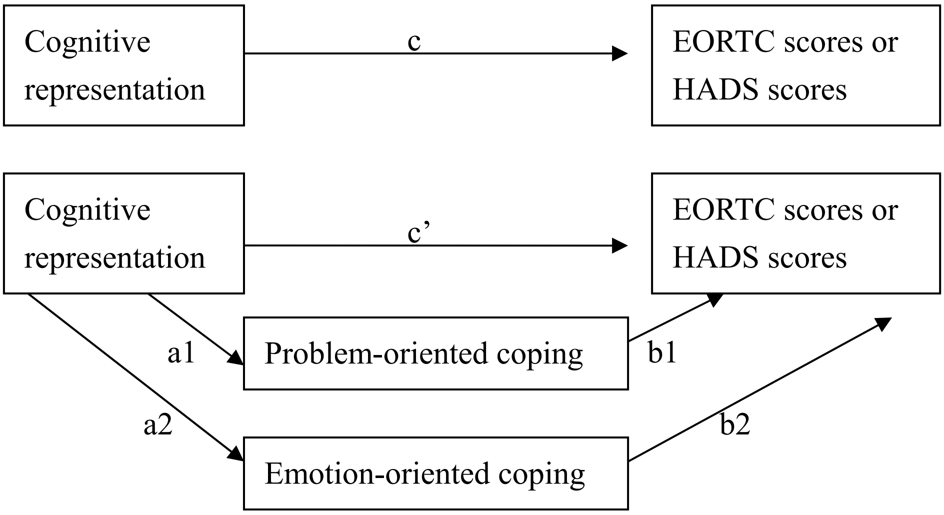

Figure 7.3 To test the mediation effects of coping on the relationships between cognitive representation and the EORTC, HADS scores

Further analyses indicated that problem-oriented and emotion-oriented coping did not mediate the effects of cognitive representation on the five functioning scores and symptom (see Table 7.11).

Table 7.11 Summary of mediation testing: coping strategies on the relationships between cognitive representation and the EORTC scores

		HRQOL	PF	RF	EF	CF	SF	SY
Pathway								
c	*B*	-1.42	-1.08	-1.89	-.99	-.48	-1.46	.86
	SE	.10**	.11**	.17**	.10**	.10**	.12**	.06**
c’	*B*	-1.32	-1.05	-1.84	-.95	-.46	-1.41	.84
	SE	.10**	.12**	.18**	.11**	.11**	.13**	.07**
Indirect effects								
Total	*B*	-.10	-.03	-.05	-.04	-.02	-.05	.03
(b1+b2)	*SE*	.04	.03	.06	.03	.03	.03	.02
	CIs	-.17	-.09	-.17	-.10	-.08	-.12	-.01
		-.03*	.03	.05	.01	05	.01	.07
b1	*B*	-.06	-.03	-.04	-.03	-.03	-.02	.01
	SE	.03	.02	.03	.02	.02	.02	.01
	CIs	-.13	-.08	-.12	-.07	-.07	-.06	-.02
		-.01*	.01	.01	-.0002	.01	.02	.03
b2	*B*	-.04	.00	-.01	-.01	.01	-.03	.02
	SE	.02	.02	.04	.02	.02	.02	.01
	CIs	-.10	-.04	-.10	-.07	-.02	-.11	.0004
		-.002*	.04	.07	.01	.06	.002	.06

*p<.05, **p<.01

Dependent variable: HRQOL: global HRQOL; PF: physical functioning; RF: role functioning; EF: emotional functioning; CF: cognitive functioning; SF: social functioning; SY: symptom.

Pathway: c: the direct effect of cognitive representation on EORTC scores; c’: the direct effect of cognitive representation on EORTC scores controlling problem- and emotion-oriented coping; b1+b2: the indirect effect of cognitive representation on EORTC scores through problem- and emotion-oriented coping; b1: the indirect effect of cognitive representation on EORTC scores through problem-oriented coping; b2: the indirect effect of cognitive representation on EORTC scores through emotion-oriented coping.

(ii) HADS scores

Cognitive representation was entered as the independent variable; problem-oriented and emotion-oriented coping were the potential mediators; and anxiety, depression, and emotional distress were dependent variables (Figure 7.3). The analyses indicated that problem-oriented coping mediated the effects of cognitive representation on depression and emotional distress; and emotion-oriented coping mediated the effects of cognitive representation on anxiety (see Table 7.12).

Table 7.12 Summary of mediation testing: coping strategies on the relationships between cognitive representation and the HADS scores

		Anxiety	Depression	Emotional Distress
Pathway				
c	*B*	.16	.27	.43
	SE	.02**	.02**	.03**
c’	*B*	.15	.26	.41
	SE	.02**	.02**	.03**
Indirect effect				
Total	*B*	.01	.01	.02
(b1+b2)	*SE*	.01	.01	.01
	CIs	-.001	.003	.004
		.02	.03*	.04*
b1	*B*	.0006	.01	.01
	SE	.0002	.00	.01
	CIs	-.005	.002	.0001
		.01	.02*	.03*
b2	*B*	.01	.00	.01
	SE	.004	.00	.01
	CIs	.001	-.004	-.0001
		.02*	.01	.03

*p<.05, **p<.01

Pathway: c: the direct effect of cognitive representation on HADS scores; c’: the direct effect of cognitive representation on HADS scores controlling problem- and emotion-oriented coping; b1+b2: the indirect effect of cognitive representation on HADS scores through problem- and emotion-oriented coping; b1: the indirect effect of cognitive representation on HADS scores through problem-oriented coping; b2: the indirect effect of cognitive representation on HADS scores through emotion-oriented coping.

(3) The mediation effects of coping on the relationships between emotional representation and global HRQOL, emotional functioning, anxiety, depression, and emotional distress

Next, the mediation analyses were conducted to test whether coping mediated the effects of emotional representation on psychological aspects of adjustment outcomes, including global HRQOL, emotional functioning, anxiety, depression, and emotional distress. Emotional representation was entered as the independent variable, the potential mediators were problem-oriented and emotion-oriented coping, and psychological aspects of adjustment outcomes were the dependent variables (Figure 7.4).

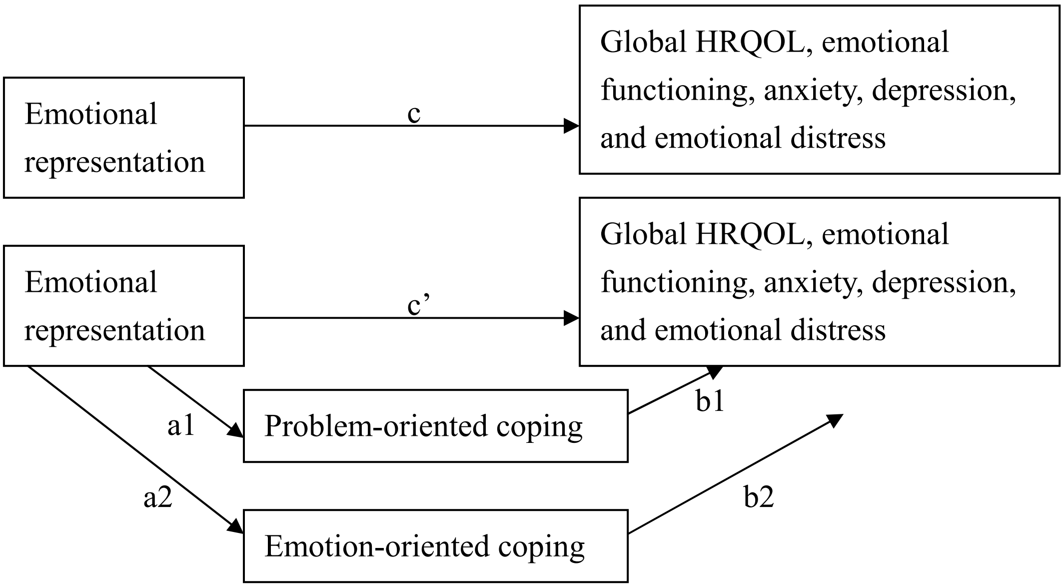

Figure 7.4 To test the mediation effects of coping on the relationships between emotional representation and psychological aspects of adjustment outcomes

When global HRQOL was dependent variable, the path from emotional representation to emotion-oriented coping, *B*=.21, *SE*=.08, *p*=.006, was significant, but the path to problem-oriented coping, *B*=-.05, *SE*=.11, *p*=.632, was not. The direct effects of problem-oriented coping, *B*=.68, *SE*=.15, *p*<.001, and emotion-oriented coping,

Table 7.13 Summary of mediation testing: coping strategies on the relationships between emotional representation and psychological aspects of adjustment outcomes

		Global HRQOL	Emotional functioning	Anxiety	Depression	Emotional distress
Pathway						
c	*B*	-2.28	-2.55	.37	.45	.82
	SE	.25**	.19**	.03**	.05**	.07**
c’	*B*	-2.12	-2.52	.35	.44	.79
	SE	.24**	.19**	.03**	.05**	.07**
Indirect effects						
Total	*B*	-.16	-.03	.02	.02	.04
(b1+b2)	*SE*	.09	.05	.01	.02	.02
	CIs	-.34	-.15	.01	-.01	.0005
		.004	.06	.04*	.05	.09*
b1	*B*	-.04	-.01	.00	.01	.01
	SE	.07	.04	.00	.01	.02
	CIs	-.19	-.10	-.004	-.02	-.02
		.10	.05	.01	.03	.04
b2	*B*	-.12	-.02	.02	.01	.03
	SE	.06	.04	.01	.01	.02
	CIs	-.27	-.11	.003	-.003	.01
		-.02*	.05	.04*	.04	.07*

*p<.05, **p<.01

Pathway: c: the direct effect of emotional representation on psychological aspects of adjustment outcomes; c’: the direct effect of emotional representation on psychological aspects of adjustment outcomes controlling problem- and emotion-oriented coping; b1+b2: the indirect effect of emotional representation on psychological aspects of adjustment outcomes through problem- and emotion-oriented coping; b1: the indirect effect of emotional representation on psychological aspects of adjustment outcomes through problem-oriented coping; b2: the indirect effect of emotional representation on psychological aspects of adjustment outcomes through emotion-oriented coping.

B=-.57, *SE*=.21, *p*=.007, on global HRQOL were also significant. The effect of emotional representation on global HRQOL, *B*=-2.28, *SE*=.25, *p*<.001, was reduced, but was still significant when controlling for problem-oriented and emotion-oriented coping, *B*=-2.12, *SE*=.24, *p*<.001. Using bootstrapping procedures, the total mediated effect was found to be non-significant, *B*=-.16, *SE*=.09, *CI*=-.34 to .004. However, inspection of the individual mediators showed that emotion-oriented coping, *B*=-.12, *SE*=.06, *CI*=-.27 to -.02, mediated the effect of emotional representation on global HRQOL, but problem-oriented coping, *B*=-.04, *SE*=.07, *CI*=-.19 to .10, did not.

In summary, emotion-oriented coping mediated the effects of emotional representation on global HRQOL, *B*=-.12, *SE*=.06, *CI*=-.27 to -.02, anxiety, *B*=.02, *SE*=.01, *CI*=.003 to .04, and emotional distress, *B*=.03, *SE*=.02, *CI*=.01 to .07. However, problem-oriented coping did not mediate the relationships between emotional representation and psychological aspects of adjustment outcomes (see Table 7.13).

7.5 Discussion

Table 7.14 The summary of potential pathways of adjustment

Pathways
1. Physical variables → EORTC and HADS scores
2. ECOG → Cognitive representation → EORTC and HADS scores
3. ECOG → Emotional representation → Global HRQOL, emotional functioning, social functioning, anxiety, depression, emotional distress
4. Cognitive representation → Problem-oriented coping → Global HRQOL, depression, emotional distress
5. Cognitive representation → Emotion-oriented coping → Global HRQOL, anxiety
6. Emotional representation → Emotion-oriented coping → Global HRQOL, anxiety, emotional distress

This quantitative study explored the effects of physical variables, illness perceptions, coping, and social support on the EORTC and HADS scores in patients with HCC.

Multiple pathways and factors are likely to influence the process of adjustment (see Table 7.14).

As shown in pathway 1, physical variables are the first important variables that contribute to all components of HRQOL, as well as anxiety and depression. Patients who received surgery tended to report the best HRQOL in both physical and psychological aspects and, as would be expected, patients with early stage disease also had better adjustment outcomes than those in later stages. Patients needed to have better physical conditions (e.g., small size of tumour, better liver function) to receive surgery. As disease progresses or metastases, patients' physical conditions get worse.

Physical variables explained the largest amount of variance in all EORTC and HADS scores; and physical variables remained significant after entering psychological variables. In addition, mediation testing also revealed the direct effect of performance status (ECOG score) on all EORTC and HADS scores. Better physical conditions and performance status were associated with better HRQOL, especially physical aspects (e.g., physical functioning, role functioning, and symptoms), and less negative feelings.

In addition, the significant predictors of physical variables were ECOG and α-FP. ECOG is an index of performance status that includes the levels of independence and activities: patients with better performance status have better self-care, less uncomfortable symptoms, and do not need caregivers' help. Poorer performance status indicates worse physical conditions and need for others care, resulting in patients having worse adjustment. α-FP is a screening index for HCC. When the index is out of normal range, it indicates tumour existence or recurrence and patients tend to have worse HRQOL.

Furthermore, disease characteristics and current physical conditions also shaped patients' illness perceptions. Patients who were older, had good performance status, underwent surgery, and had normal level of α-FP perceived their disease as less negative cognitive representation (e.g., less severe and felt more the disease was more controllable). Better physical conditions were associated with a more positive cognitive representation and less negative emotional representation of disease.

As shown in pathway 2 and 3, illness perceptions are the second important factor that contributes to patients' adjustment outcomes. The results supported previous results that illness perceptions could mediate the relationships between physical variables and adjustment outcomes (Hagger & Orbell, 2003). Cognitive representation mediated the relationships between performance status and all components of HRQOL, as well as anxiety and depression. Emotional representation also had mediating effects, but limited to the psychological aspects of adjustment outcomes, including global HRQOL, emotional functioning, social functioning, anxiety, depression, emotional distress. Physical variables may influence patients' cognitive perceptions about their disease, which then influence adjustment outcomes. Patients who perceived more negative emotional representation from HCC had worse global HRQOL, emotional, and social functioning, and higher levels of anxiety, depression, and emotional distress.

Pathway 4, 5, and 6 showed that coping mediated the relationships between illness perceptions and psychological aspects of adjustment outcomes, rather than physical aspects of HRQOL, such as physical, role, cognitive functioning, or symptoms. Problem-oriented coping mediated the relationships between cognitive representation and global HRQOL, depression, emotional distress. Similar mediation effects for emotion-oriented coping were founded on the relationships between cognitive representation and global HRQOL and anxiety, and emotion-oriented coping mediated the relationships between emotional representation and global HRQOL, anxiety, and emotional distress.

The results revealed that the use of problem-oriented coping strategies was associated with increased HRQOL and emotional functioning, and decreased depression. Patients who perceived their disease to be more severe had worse HRQOL and higher levels of depression, but using problem-oriented coping strategies buffered this negative effect of cognitive representation on global HRQOL and depression. However, the use of emotion-oriented coping was associated with higher levels of anxiety that patients who used more emotion-oriented coping had higher level of anxiety.

The present study used quantitative methods to examine multi-components of adjustment outcomes, to identify both physical and psychological predictors of adjustment outcomes, and to examine the theoretical fitness of the Common Sense Model, addressing the importance of illness perceptions and coping. Patients who received surgery or who were at early stages of disease had better adjustment outcomes than those who received drug therapy or were at advanced stages. In addition, the significant physical predictors were performance status and α-FP. The most significant psychological predictors were cognitive and emotional representations. The results supported the mediation effects of illness perceptions on the relationships between physical conditions and adjustment outcomes, as well as the mediation effects of coping on the relationships between illness perceptions and psychological aspects of adjustment outcomes. In the next chapter, the interpretations, combinations, and comparisons of qualitative and quantitative results, as well as methodology considerations will be conducted.

Chapter 8. Discussion

8.1 Abstract

Adjustment to cancer is a long-term trajectory, and many factors can influence the process. This whole thesis was based on assumptions from the Common Sense Model (Leventhal et al., 1984) using both qualitative and quantitative methodology. In this final chapter, a summary of findings are presented followed by establishment of an adjustment model which integrates quantitative and qualitative results. The adjustment model includes multiple pathways predict adjustment outcomes: physical variables had a direct effect on adjustment outcomes; and illness perceptions mediated the relationships between physical variables and adjustment outcomes, and coping mediated the relationships between illness perceptions and adjustment outcomes. Third, methodological considerations involving the integration of qualitative and quantitative results, and quantitative issues were addressed. Finally, clinical implications based on the adjustment model are made for improving the quality of care.

8.2 Summary of findings

The overall purpose of this thesis was to explore the impact of HCC on patients' HRQOL, to identify the significant predictors of HRQOL and adjustment outcomes, and to construct an adjustment model for patients with HCC.

In a systematic review (Chapter 3), patients with HCC were shown to have worse physical, psychological, and functional well-being than the general population. This was supported by empirical findings in Chapter 6 that showed that patients had worse global HRQOL, physical, role, cognitive, social functioning; and more severe symptoms than the general population. In addition, the HADS results showed that patients with HCC had higher levels of depression than the general population, and more than one-fifth patients had emotional distress. Therefore, HCC is associated with both physical and psychological impact on patients' life

In Chapter 3, different treatments, liver function, symptoms (e.g., pain, fatigue, and nausea), performance status, and negative feelings (e.g., depression, uncertainty, and chance health locus of control) were associated with HRQOL. The results of regression analyses in Chapter 7 also showed the significant physical predictors were ECOG and α-FP; and the psychological predictors were cognitive and emotional illness representations.

Furthermore, the hierarchical regression and mediation analyses showed the multiple pathways of adjustment. The qualitative results also provided rich contextual and dynamic information about how patients perceived HCC, how they coped with and adjusted to the disease, and the significant factors which may influence their adjustment. In the next section, both quantitative and qualitative results will be integrated for constructing an adjustment model.

8.3 Toward an integrated model

Based on the findings of the research described, an integrated model of adjustment in patients with HCC was developed (see Figure 8.1) and is described below.

8.3.1 Role of quantitative findings

The quantitative results suggested some modification to the Common Sense Model and highlighted the multiple pathways of adjustment.

We found pathways to adjustment outcomes were mediated by Illness perceptions and coping: from physical variables to illness perceptions and then adjustment outcomes (not through coping); or from illness perceptions to coping, and then to psychological aspects of adjustment outcomes. However, there was still another pathway: from physical variables to adjustment outcomes directly.

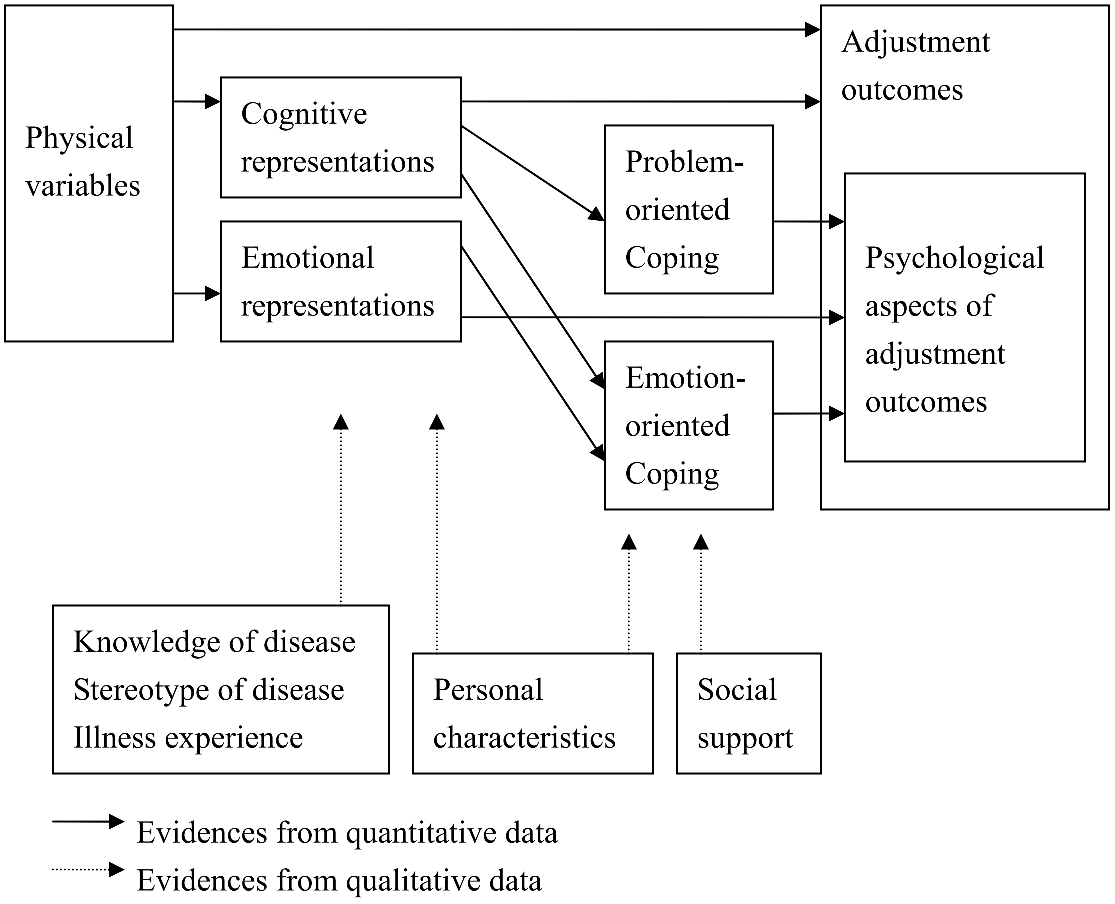

Figure 8.1 Adjustment model in patients with HCC

First, physical variables had a direct influence on all adjustment outcomes. Similar to previous research, physical conditions and symptoms were the main stressor, and poor performance status and greater symptom distress were associated with worse adjustment (Ponto, Ellington, Mellon, & Beck, 2010; Shun et al., 2008). In addition, physical variables were positively associated with illness perceptions.

Second, the influence of physical variables may be mediated by illness perceptions. Physical variables may shape a patient's illness perceptions, which in turn influence adjustment outcomes. For example, deteriorating physical conditions made patients perceive that their disease became worse, and the perceptions, both cognitive and emotional representations, may decrease patients' HRQOL and increase negative feelings. Cognitive representation could moderate the effects of physical variables on both physical and psychological components of adjustment outcomes, but emotional representation only mediates the influences on psychological components of adjustment outcomes. The findings are similar to those made in a previous meta-analytic review (Hagger & Orbell, 2003), the importance of illness perceptions were also found in various cancers, such as head and neck squamous cell carcinoma (Scharloo et al., 2010), breast cancer (Rozema et al., 2009), gynaecological cancer (Gould, Brown, & Bramwell, 2010), and prostate cancer (Traeger et al., 2009; Wootten et al., 2007). Illness perceptions about timeline, identity, or consequences were negatively associated with HRQOL or psychological well-being in above studies. The quantitative results in Chapter 5 also revealed the process, whereby physical conditions or symptoms shaped patients' interpretations about the disease, and then the interpretations influenced adjustment.

Third, the mediation effects of coping also occurred between illness perceptions and psychological aspects of adjustment outcomes, such as emotion functioning in HRQOL, anxiety, depression, or emotional distress. Patients who perceived their disease as worse used less problem-oriented coping, which in turn related to worse psychological outcomes. In addition, perceptions about emotional impact only influenced psychological outcomes through emotional-oriented coping instead of problem-oriented coping. More emotional impact was associated with more emotional-oriented coping, which in turn determined worse psychological outcomes.

In previous studies, coping is one of most important variables. For example, denial and avoidant coping mediated the relationships cognitive representations and negative mood in gynaecological cancer (Gould et al., 2010); or emotion-oriented coping mediated the relationships between dyadic adjustment and mood disturbance in prostate cancer (Wootten et al., 2007). However, in women with breast cancer, the role of coping was not significantly associated with perceived physical and mental health (Rozema et al., 2009). In this thesis, the role of coping was not as important as illness perceptions, and the mediation effects occurred partially between illness perceptions and psychological aspects of adjustment outcomes. The potential explanations include the possibility of multiple components of coping, and various factors may influence the use of coping strategies (Thomsen et al., 2010; Wattebot O'Brien & Moorey, 2010), not only illness perceptions. The second is the different characteristics of adjustment outcomes. For example, coping explained more variance in psychological or emotional functioning than physical or cognitive functioning. Coping has the potential to influence the psychological well-being rather than physical well-being or symptoms.

The regression analyses showed the positive effects of problem-oriented coping but negative effects of emotion-oriented coping on adjustment outcomes, similar to the previous review (Wattebot O'Brien & Moorey, 2010). In addition, some coping strategies were found to be associated with better adjustment in cancer patients, such as acceptance (Bussell & Naus, 2010; Shapiro, McCue, Heyman, Dey, & Haller, 2010), humour (Shapiro et al., 2010), positive reappraisal, and good reengagement (Schroevers, Kraaij, & Garnefski, 2010); but self-blame (Bussell & Naus, 2010), avoiding, or self-distraction (Schroevers et al., 2010) were related to worse adjustment. However, the qualitative results in Chapter 5 highlighted the individual differences and situation differences which may influence the use of coping strategies. For example, an elderly patient with low education level would rely on their children and doctors to make the treatment decision. Perhaps when the huge stress (e.g., in the early stage of diagnosis) was more than patients can tolerate, they would use avoiding strategies. Therefore, more evidence is needed to investigate the effects of specific coping on specific situations.

8.3.2 Role of qualitative findings

The quantitative results (Chapter 5) extended our understanding of illness perceptions. Potential factors which contribute to illness perceptions include not only physical variables (or stressor/stimuli) but also knowledge of disease, stereotype of disease, and illness experience. Knowledge of disease included information about disease and treatment, for example causal factors, treatment methods, prognosis, and side effects. When they were diagnosed as HCC, most patients find relevant information or ask doctors, and it helped them to form a concept of HCC. Stereotype of disease also shaped illness perceptions. In this social-cultural background, high prevalence of HBV and death stigma of cancer, it was inevitable to be fearful and have worries. Illness experience had two phases, first was previous liver disease before diagnosis and the other was from diagnosis until now. When patients had previous experience about hepatitis or cirrhosis, they may anticipate one day the disease may progress until HCC. This helped them dealing with the relevant medical problems. Furthermore, the adjustment outcomes since diagnosis until now would feedback to their illness perceptions. If they could handle the disease and adjust well, illness perceptions would be positive and have less negative impact.

Personal characteristics influenced cognitive evaluations (e.g., illness perceptions) and behavioural responses (e.g., coping behaviours) to the disease. For example, a nervous patient might interpret the disease as very severe but an optimistic patient might not. Except for evaluation of the stressor (disease), patients may use the coping methods which they were familiar with.

In contrast to previous studies which showed the positive relationships between social support and psychological well-being (Pinquart & Frohlich, 2009; Schroevers, Ranchor, & Sanderman, 2003), and the interaction effects of social support and coping on emotional well-being (Kim, Han, Shaw, Mctavish, & Gustafson, 2010) in cancer patients, regression results in Chapter 7 showed social support was not a significant predictor when controlling for physical variables and illness perceptions. Maybe other variables (physical variables and illness perceptions) play a more important role than social support in the adjustment process. But in qualitative interviews, patients expressed that social support could be taken as an external resource to deal with the demanding from the disease, and provide emotional support. In addition, support from families and friends would change depending on disease progress and physical conditions (Pinquart, Hoffken, Silbereisen, & Wedding, 2007). When patients' conditions were stable or did not receive regular treatment, then the tangible support would decrease, not as much as the beginning of diagnosis or treatment.

8.4 Methodological issues

8.4.1 Integrating qualitative and quantitative methodologies

A mixed methods design including quantitative and qualitative studies was used in this thesis. The two kinds of data were collected at the same time but analyzed separately. The key issue was how to combine or integrate the two kinds of results for improving the validity of the study and reducing the weakness of each methodology.

It is inevitable that there are interferences/interactions between two kinds of methodological process. For participants, the sequences of data collection may influence patients' response. Patients' ratings to items in standardized questionnaires might be affected when they received interview first. For researchers, in analysis process, one kind of data would influence the other, especially qualitative analysis. If researchers already know the results of quantitative analyses, then the qualitative analysis may be biased because of preconceived ideas.

In order to reduce these possible interferences, patients who participated in both studies were asked to complete standardized questionnaires first, and then received an interview. In this way we hoped to reduce the influence of the interview on questionnaire responses. In analyses, qualitative data were analyzed first and then quantitative data. A senior oncology nurse who was not involved in the quantitative data collection also helped to analyze qualitative data to enhance the validity of study.

The combinations and comparisons of qualitative and quantitative results occurred in the interpretation levels. First, the relationships between physical variables, illness perceptions, coping, and adjustment outcomes were based on the quantitative results. The analyses in section 7.4.4 could clarify and modify the model obtained from qualitative results (Figure 5.1), and provide strong statistical evidences to generalize the results to other patients with HCC. Second, qualitative results could provide rich information about the context, dynamic changes, or specific items. For example, quantitative results revealed the importance of illness perceptions in adjustment process, and qualitative results highlighted which factors shaped illness perceptions and how illness perceptions influenced adjustment outcomes. In addition, qualitative results provided disease-specific and cultural-specific coping strategies in Taiwan society. Third, it is essential to investigate the differences between qualitative and quantitative results. For example, quantitative results showed that social support was not a significant predictors when physical variables, illness perceptions, and coping entering in the regression analyses. In contrast, qualitative results highlighted social support was an important resource in coping with the disease. The role of social support in adjustment process needs further studies to identify.

8.4.2 Specific method issues in quantitative study

Some methodological considerations about the quantitative study should be noticed and future studies need to be addressed.

First is the choice of standardized measures. From the initial literature review (Chapter 2), it was concluded that any comprehensive assessment of HRQOL should incorporate both generic and disease-specific measures. In Chapter 3, both FACT and EORTC groups provide cancer-specific and Hepatobiliary/HCC specific measures which are widely used and have good psychometric characteristics, and were translated into Chinese. Especially the development of EORTC HCC18 also recruited Taiwan patients with HCC, and it is appropriate for this thesis.

Second, the norms of EORTC QLQ-C30 and HADS (Chapter 6) which were used to compare the differences in HRQOL between patients with HCC and the general population are from western countries, but the patients in this study were from Taiwan. The socio-cultural background is a potential confounding factor, and the norm from the same country or society is necessary.

Third, in order to reduce patient burden, the short form Brief IPQ and coping questionnaire were used in this study. The Cronbach's α of emotional representation in Brief IPQ and emotion-oriented coping were not good enough. The possible explanations were that emotional representation only has two items and emotion-oriented coping includes various meanings of items. For example, seeking family support and blaming others are categorized in emotion-oriented coping, but may cause different effects. The detailed measure of coping behaviours would facilitate measurement of additional coping behaviours such as escape-avoidance, distancing, self-controlling, seeking social support, accepting responsibility, planful problem-solving, or positive reappraisal (Jalowiec, 2003). However the greater burden on patients in completing longer questionnaires needs to be considered.

On the other hand, qualitative results showed that the disease-specific or cultural-specific coping (e.g., diet, quit bad habits, develop health life style, or seek religious belief), which were not measured in standardized questionnaire, may be important for patients' adjustment. It is possible that coping questionnaires could be developed that included these disease-specific or cultural-specific items.

Fourth, the sample size was big enough to run regression analyses in quantitative study. The author also rechecked after patients completed the standardized measures for reducing the missing data. However, there were a lot of missing data in physical variables which were obtained form medical charts, for example Albumin and INR. Therefore these data could not be entered in the regression analyses.

Fifth, a cross-sectional correlation design was used to investigate the HRQOL and adjustment in patients with HCC; a longitudinal design is essential to investigate the long-term changes in adjustment outcomes and psychological variables, such as illness perceptions, coping, and social support. The variations of these variables may depend on the changes of physical conditions or life events.

In addition, the relationships between illness perceptions, coping, and adjustment outcomes were based on regression analyses. Although the relationships implied the directions between variables, it still lacks consolidated evidence to support cause-and-effect relationships. Experimental or quasi-experimental designs are essential to establish the cause-and-effect relationships. For example, interventions focusing on illness perceptions and coping using randomized controlled trial could be conducted to test whether these interventions can improve patients' HRQOL and psychological well-being.

8.5 Clinical implications

Some suggestions about clinical services can be made based on the adjustment model (Figure 8.1) which could potentially improve patients' care. First the results emphasise the importance of conducting a comprehensive assessment about patients' HRQOL, including physical functioning, psychological well-being, as well as positive changes after disease. Focus on medical outcomes alone does not reflect the whole way in which HCC affects the individual. Second it is important to consider the effectiveness of treatment to remove tumour and reduce uncomfortable symptoms. The data suggest that recovery/uptrend of physical conditions may have direct effects to improve HRQOL and psychological well-being. Patients in qualitative interviews mentioned that improvement of physical conditions made them have hope and believe they can overcome the disease.

Third the results suggest healthcare professionals should provide appropriate information for patients and families to satisfy their needs (see Table 5.4). It is clear from analyses of interviews that patients and families wanted to find out what happened and what was wrong with their body, and whether any factors caused or precipitated the disease, especially in the early stages of diagnosis. However, the data also suggested there are individual differences in information needs. Some patients tried to gain a feeling of control through understanding all situations, but others may just find a doctor who can be trusted and follow the doctor's treatments and suggestions.

Fourth, assessment of patients' illness perceptions about their disease and conditions may be useful in clinical care. This will enable decisions to be made about the accuracy of their illness perceptions and importance of modifying the perceptions. Through assessment of illness perceptions, patients and healthcare professionals can work together to find out the effective ways to promote adjustment to the disease.

Fifth, patients applied the coping strategies, both problem-oriented and emotion-oriented coping, to overcome the demands of the disease. Based on feedback from the coping strategies, they can continue to use or modify the strategies. More emotional impact was associated with more use of emotional-oriented coping, which in turn determined worse psychological outcomes (Table 7.9). However, in the analyses there was no evidence to suggest the use of emotion-oriented coping resulted in decreased psychological components of HRQOL or psychological well-being. Health professionals can help patients to evaluate multiple factors, such as the stressor, resources, and the expectancy of effect, for finding the better strategies.

Sixth, although the role of social support is not clear, it is still likely that family support is crucial in helping patients' adjustment, particularly in the transition phases of disease, such as diagnosis, disease deterioration, and terminal stage. More culturally sensitive measures of social support may be needed for further work in this area.

The strengths of this thesis were incorporation of both physical and psychological variables, as well as both qualitative and quantitative methodology. In addition, multiple variables, all subcomponents of HRQOL, anxiety, depression, and emotional distress, were used as adjustment outcomes. Despite the huge amount of work that has considered cancer patients experiences, it has almost all been based in the US or Western Europe. This research described here has made a very significant contribution to our understanding of how cancer affects patients in Taiwan. Also of significance was the focus on HCC, in contrast to much previous work that has focused on cancers more prevalent in the west (e.g., breast, lung cancer). For the future, more work that looks at both the similarities and differences in how patients cope with cancer in different health care systems may contribute to a broader understanding of the patient experience generally.

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Appendices

1. Questionnaires (English and Chinese versions):
    - Demographic information
    - Medical information
    - Brief IPQ
    - EORTC-QLQ-C30 & HCC18
    - HADS
    - Coping Scale
    - Social Support Inventory
2. Consent form
3. Publication

Appendix 1: Questionnaires (English and Chinese versions)

Demographic information

1. Chart No.:
2. Sex: ☐①Male ☐②Female
3. Date of birth: ☐☐☐☐/☐☐/☐☐
4. Education: ☐①Elementary school ☐②Junior high school
   ☐③Senior high school ☐④Undergraduate ☐⑤Postgraduate
5. Marital status: ☐①Single ☐②Married/Living with partner
   ☐③Divorced/Separated ☐④Widowed
6. Religion: ☐①Buddhism ☐②Taoism ☐③Christian ☐④Catholic
   ☐⑤General religion ☐⑥None
7. Job: ☐①Full time ☐②Part time ☐③None
8. Do you need other's care: ☐①Yes ☐②No
9. If yes, the main caregiver is: ☐①Father/Mother ☐②Husband/Wife
   ☐③Son/Daughter ☐④Friend ☐⑤Other

Medical information

1. Date of diagnosis：☐☐☐☐/☐☐/☐☐
2. Chronic disease：☐①none ☐②HBV ☐③HCV ☐④Diabetes
   ☐⑤Hypertension ☐⑥COPD ☐⑦Kidney disease
3. ECOG: ☐①1 ☐②2 ☐③3 ☐④4
4. AJCC stage：☐①stage 1 ☐②stage 2 ☐③stage 3 ☐④stage 4
5. BCLC stage：☐①stage A ☐②stage B ☐③stage C ☐④stage D
6. Child-Pugh stage：☐①stage A ☐②stage B ☐③stage C
7. Exam ：☐①α-FP:__________ng/mL ☐②T-bilirubin:__________mg/dL
   ☐③Albumin:__________g/dL ☐④GOT:__________U/L
   ☐⑤GPT:__________U/L ☐⑥Platelet:__________/L
   ☐⑦INR:__________
8. Most recent treatment: ☐① Surgery ☐②TAE/TACE ☐③Drug therapy
9. Date of most recent treatment: ☐☐☐☐/☐☐/☐☐
10. Past treatment (Multiple choice)
    ☐①None
    ☐②Surgery: ☐☐☐☐/☐☐/☐☐
    ☐③TAE/TACE: ☐☐☐☐/☐☐/☐☐
    ☐④Drug therapy: ☐☐☐☐/☐☐/☐☐

Section A. Brief Illness Perception Questionnaire

For the following questions, please circle the number that best corresponds to your views:

How much does your illness affect your life

Not affect at all	0	1	2	3	4	5	6	7	8	9	10	Severely affects my life

How long do you think your illness will continue?

a very short time	0	1	2	3	4	5	6	7	8	9	10	forever

How much control do you feel you have over your illness?

Absolutely no control	0	1	2	3	4	5	6	7	8	9	10	extreme amount of control

How much do you think your treatment can help your illness?

not at all	0	1	2	3	4	5	6	7	8	9	10	Extremely helpful

How much do you experience symptoms from your illness?

no symptoms at all	0	1	2	3	4	5	6	7	8	9	10	many severe symptoms

How concerned are you about your illness?

not at all concerned	0	1	2	3	4	5	6	7	8	9	10	Extremely concerned

How well do you feel you understand your illness?

don’t understand at all	0	1	2	3	4	5	6	7	8	9	10	Understand very clearly

How much does your illness affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?)

not at all affected emotionally	0	1	2	3	4	5	6	7	8	9	10	Extremely affected emotionally

Please list in rank-order the three most important factors that you believe caused your illness. The most important causes for me:-

(1)____________________ (2)__________________ (3)__________________

Section B. EORTC-QLQ-C30 & HCC-18

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no “right” or “wrong” answers. The information that you provide will remain strictly confidential.

		Not at all	A little	Quit a bit	Very much
1.	1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2.	Do you have any trouble taking a long walk?	1	2	3	4
3.	Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4.	Do you need to stay in bed or a chair during the day?	1	2	3	4
5.	Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4
During the past week					
6.	Were you limited in doing either your work or other daily activities?	1	2	3	4
7.	Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8.	Were you short of breath?	1	2	3	4
9.	Have you had pain?	1	2	3	4
10.	Did you need to rest?	1	2	3	4
11.	Have you had trouble sleeping?	1	2	3	4
12.	Have you felt weak?	1	2	3	4
13.	Have you lacked appetite?	1	2	3	4
14.	Have you felt nauseated?	1	2	3	4
15.	Have you vomited?	1	2	3	4
16.	Have you been constipated?	1	2	3	4
17.	Have you had diarrhea?	1	2	3	4
18.	Were you tired?	1	2	3	4
19.	Did pain interfere with your daily activities?	1	2	3	4
20.	Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21.	Did you feel tense?	1	2	3	4
22.	Did you worry?	1	2	3	4
23.	Did you feel irritable?	1	2	3	4
24.	Did you feel depressed?	1	2	3	4

25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your <u>family</u> life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your <u>social</u> activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall <u>health</u> during the past week?

Very poor 1 2 3 4 5 6 7 Excellent

30. How would you rate your overall <u>quality of life</u> during the past week?

Very poor 1 2 3 4 5 6 7 Excellent

EORTC-HCC-18

During the past week	Not at all	A little	Quit a bit	Very much
31. Did you feel thirsty?	1	2	3	4
32. Have you had trouble of taste?	1	2	3	4
33. Have you had lost the muscle of arms or legs?	1	2	3	4
34. Have you had abdomen swelling?	1	2	3	4
35. Have you worried about the figure of abdomen?	1	2	3	4
36. Have you worried the eyes and skin becoming yellow?	1	2	3	4
37. Did you feel itch?	1	2	3	4
38. Did you have shoulder pain?	1	2	3	4
39. Did you have abdomen pain?	1	2	3	4
40. Did you have fever?	1	2	3	4
41. Did you feel cold?	1	2	3	4
42. Did you worry to get enough nutrition?	1	2	3	4
43. Did you feel full just beginning eating?	1	2	3	4
44. Did you worry your weight too light?	1	2	3	4
45. Did you feel the vitality which is not like what you anticipate?	1	2	3	4
46. Have you had difficulty finishing things?	1	2	3	4
47. Did you need to sleep in daytime?	1	2	3	4
During the past four weeks				
48. Did disease or treatment have influences on your sexual life?	1	2	3	4

Section C. Hospital Anxiety and Depression Scale

Doctors are aware that emotions play an important part in most illnesses. If your doctor knows about these feelings he will be able to help you more. This questionnaire is designed to help your doctor to know you feel. Read each item and underline the reply which comes closest to how you have been feeling in the past week. Don't take too long over your replies; your immediate reaction to each item will probably be nore accurate than a long thought out response.

---

1. I feel tense or wound up
   ☐①Most of the time ☐②A lot of the time
   ☐③From time to time, occasionally ☐④Not at all
2. I still enjoy the things I used to enjoy
   ☐①Definitely as much ☐②Not quite so much ☐③Only a little
   ☐④Hardly at all
3. I get a sort of frightened feeling as if something awful is about to happen
   ☐①Very definitely and quite badly ☐②Yes, but not too badly
   ☐③A little, but it doesn't worry me ☐④Not at all
4. I can laugh and see the funny side of things
   ☐①As much as I always could ☐②Not quite so much now
   ☐③Definitely not so much now ☐④Not at all
5. Worrying thoughts go through my mind
   ☐①A great deal of the time ☐②A lot of time
   ☐③From time to time but not too often ☐④Only occasionally
6. I feel cheerful
   ☐①Not at all ☐②Not often ☐③Sometimes ☐④Most of time
7. I can sit at ease and feel relaxed
   ☐①Definitely ☐②Usually ☐③Not often ☐④Not at all
8. I feel as if I am slowed down
   ☐①Nearly all the time ☐②Very often ☐③Sometimes ☐④Not at all
9. I get a sort of frightened feeling like 'butterflies' in the stomach
   ☐①Not at all ☐②Occasionally ☐③Quite often ☐④Very often
10. I have lost interest in my appearance
    ☐①Definitely ☐②I don't take so much care as I should
    ☐③I may not take quite as much care ☐④I take just as much as ever
11. I feel restless as if I have to be on the move
    ☐①Very much indeed ☐②Quite a lot ☐③Not very much ☐④Not at all
12. I look forward with enjoyment to things
    ☐①As much as ever I did ☐②Rather less than I used to /

☐③Definitely less than I used to ☐④Hardly at all

13. I get sudden feelings of panic

☐①Very often indeed ☐②Quite often ☐③Not very often ☐④Not at all

14. I can enjoy a good book or radio or TV program

☐①Often ☐②Sometimes ☐③Not often ☐④Very seldom

Section D. Coping scale

The Jaloweic coping scale includes 40 items and yields two scores: problem-oriented coping and emotion-oriented coping. The author does not permit to put the full text of scale on thesis; therefore I do not show this scale.

Section E. Social support inventory

The frequency of getting support from others in past one month.

	Not at all	sometimes	often	always
1. Listened to you talk about your private feeling	1	2	3	4
2. Expressed interest and concern in your well-being	1	2	3	4
3. Let you know that he/she will always be around if you need assistance	1	2	3	4
4. Joked and kidded to try to cheer you up	1	2	3	4
5. Agreed that what you want to do is right	1	2	3	4
6. Someone encouraged you when physical condition improved	1	2	3	4
7. Expressed esteem or respect for a competency or personal quality of yours	1	2	3	4
8. Gave you information about disease	1	2	3	4
9. Gave you information and provided assistance about daily care	1	2	3	4
10. Reminded me to take medicine and come back to hospital	1	2	3	4
11. Assisted you in setting a goal for future	1	2	3	4
12. Suggested some action that you can take to release stress	1	2	3	4
13. Took care of you and helped you to deal with daily life events	1	2	3	4
14. Did some activity together to help you get your mind off things	1	2	3	4
15. Provided financial support	1	2	3	4
16. Please give the two person who help most:				

Section A. 疾病知覺 Brief Illness Perception Questionnaire

請在標度的某個數字上畫圈，以表明您同意或不同意下列每個說法的堅決程度：

1. 您的疾病對您生活的影響有多大？

毫無影響 0 1 2 3 4 5 6 7 8 9 10 嚴重影響我的生活

2. 您認為您的疾病將持續多長時間？

很短時間 0 1 2 3 4 5 6 7 8 9 10 永遠

3. 您感覺您能在多大程度上控制住您的疾病？

絕對不能控制 0 1 2 3 4 5 6 7 8 9 10 極大的控制力

4. 您認為您接受的治療（藥丸等）能在多大程度上對疾病有所幫助？

毫無幫助 0 1 2 3 4 5 6 7 8 9 10 極其有幫助

5. 您經受疾病引起的症狀的程度有多大？

毫無症狀 0 1 2 3 4 5 6 7 8 9 10 許多嚴重的症狀

6. 您有多關切您的疾病？

毫不關切 0 1 2 3 4 5 6 7 8 9 10 極其關切

7. 您感覺您在多大程度上瞭解自己的疾病？

毫不瞭解 0 1 2 3 4 5 6 7 8 9 10 很清楚地瞭解

8. 疾病在多大程度上影響您的情緒？比如它是否讓您生氣、害怕、沮喪或憂鬱？

毫無情緒上的影響 0 1 2 3 4 5 6 7 8 9 10 情緒上極其受影響

9. 請按照次序列出三個最重要的因素，您相信這三個因素導致了您的疾病。

對我來說最重要的病因是：

(1)____________________ (2)__________________ (3)__________________

Section B.生活品質 EORTC-QLQ-C30 & HCC-18

我們很希望瞭解有關您和您的健康狀況。請您親自回答以下所有的問題，圈選最合適於您的答案。

	完全沒有	有一點	相當多	非常多
29. 您從事一些費力的活動，如攜帶重的購物袋或手提箱，是否有困難？	1	2	3	4
30. 您從事長距離步行，是否有困難？	1	2	3	4
31. 您在戶外從事短距離步行，是否有困難？	1	2	3	4
32. 您在白天是否需要待在床上或椅子上？	1	2	3	4
33. 您進食、穿衣、洗澡或上廁所需要別人幫助嗎？	1	2	3	4
在過去一星期內（過去七天內）				
34. 您在從事工作或日常活動上是否受到限制？	1	2	3	4
35. 您在從事嗜好或休閒活動上是否受到限制？	1	2	3	4

36. 您呼吸會喘嗎？	1	2	3	4
37. 您曾感到疼痛嗎？	1	2	3	4
38. 您需要休息嗎？	1	2	3	4
39. 您睡眠曾有困難嗎？	1	2	3	4
40. 您曾感到虛弱嗎？	1	2	3	4
41. 您曾缺乏食慾嗎？	1	2	3	4
42. 您曾感到噁心嗎？	1	2	3	4
43. 您曾嘔吐嗎？	1	2	3	4
44. 您曾便秘嗎？	1	2	3	4
45. 您曾腹瀉嗎？	1	2	3	4
46. 您疲倦嗎？	1	2	3	4
47. 疼痛干擾您的日常活動嗎？	1	2	3	4
48. 您曾否難將注意力集中在一些事情上，如看報紙或看電視？	1	2	3	4
49. 您覺得緊張嗎？	1	2	3	4
50. 您感到憂慮嗎？	1	2	3	4
51. 您覺得容易發怒嗎？	1	2	3	4
52. 您覺得情緒低落嗎？	1	2	3	4
53. 您曾感到記憶困難嗎？	1	2	3	4
54. 您的身體狀況或醫療過程是否曾干擾您的家庭生活？	1	2	3	4
55. 您的身體狀況或醫療過程是否曾干擾您的社交活動？	1	2	3	4
56. 您的身體狀況或醫療過程是否曾造成您財務上的困難？	1	2	3	4

以下問題，請在1 到7 之間圈選最適合您的答案。

29. 您如何評定過去一星期內（過去七天內）您整體的健康？

非常差 1 2 3 4 5 6 7 極好

30. 您如何評定過去一星期內（過去七天內）您整體的生活品質？

非常差 1 2 3 4 5 6 7 極好

在過去一星期內（過去七天內）	完全沒有	有一點	相當多	非常多
49. 您覺得口渴嗎？	1	2	3	4
50. 您曾有味覺方面的問題嗎？	1	2	3	4
51. 您曾有手臂或腿部肌肉消瘦的情形嗎？	1	2	3	4
52. 您曾有腹部腫脹嗎？	1	2	3	4
53. 您曾為您腹部的外觀而煩惱嗎？	1	2	3	4
54. 您曾為您皮膚或眼睛變黃（黃疸）而煩惱嗎？	1	2	3	4
55. 您曾覺得癢嗎？	1	2	3	4

56. 您曾有肩膀疼痛嗎？	1	2	3	4
57. 您曾有腹部疼痛嗎？	1	2	3	4
58. 您曾發燒嗎？	1	2	3	4
59. 您曾畏寒嗎？	1	2	3	4
60. 您曾為能否得到足夠的營養而擔心嗎？	1	2	3	4
61. 您曾經剛剛進食很快就覺得飽了嗎？	1	2	3	4
62. 您曾擔心自己體重過輕嗎？	1	2	3	4
63. 您曾感到不如預期的有活力嗎？	1	2	3	4
64. 您曾發覺要完成所做的事會有困難嗎？	1	2	3	4
65. 您曾需要在白天睡覺嗎？	1	2	3	4
在過去四星期內	1	2	3	4
66. 疾病或治療曾對您的性生活有任何影響嗎？				

Section C.焦慮與憂鬱 Hospital Anxiety and Depression Scale

此部分主要了解您的感受，包括 14 個感受敘述，每個敘述有 4 個選擇，請仔細閱讀每個敘述並勾選最能表示您過去一週的感受之選項，請不要花太多時間思考，您的立即反應可能比長時間思考後的反應來得正確。

1.______我覺得緊張或神經緊繃

(1)總是如此　(2)經常如此　(3)偶爾如此　(4)一點也不會

2.______我仍喜歡過去我喜歡的事物

(1)和過去一樣喜歡　(2)不像過去那樣喜歡　(3)只有一點喜歡　(4)幾乎都不喜歡

3.______我有一種可怕的感覺，好像有什麼不好的事情即將發生

(1)這感覺很確定且很強烈　(2)有這感覺但不是很強烈　(3)有一點但不令我擔心
(4)一點也沒有

4.______我可以大笑並感受到事情有趣的一面

(1)如同過去一樣　(2)不像過去那樣　(3)確實比過去少　(4)一點也沒辦法

5.______我心裡有些擔憂的想法

(1)總是如此　(2)經常如此　(3)有時會有，但並不頻繁　(4)只是偶爾會有

6.______我覺得開心或愉快

(1)經常覺得　(2)有時覺得　(3)不常覺得　(4)一點也不覺得

7.______我可以舒服的坐著並覺得很放鬆

(1)的確如此　(2)經常如此　(3)不常如此　(4)一點也沒辦法

8.______我覺得自己的生活步調好像慢了下來

(1)總是如此　(2)經常如此　(3)有時如此　(4)一點也不會

9.______我有一種可怕的感覺，就好像胃裡有東西在動

(1)總是覺得　(2)經常覺得　(3)偶爾覺得　(4)一點也不會

10.______我已不在關心自己的外表

(1)的確如此 (2)我沒有應該有的關心 (3)我不太關心 (4)我和過去一樣關心

11._____我覺得坐立不安，好像我非得不停的動不可

(1)的確總是如此 (2)經常如此 (3)不太會這樣 (4)一點也不會

12._____我對事物感到期待或有希望

(1)和過去一樣 (2)比過去少些 (3)比過去少多了 (4)幾乎沒有這種期待

13._____我突然覺得恐慌

(1)總是如此 (2)經常如此 (3)不常如此 (4)一點也不會

14._____我可以欣賞或沉浸於一本書或好的廣播/電視節目

(1)總是如此 (2)有時如此 (3)不常如此 (4)極少如此

Section E.社會支持 Social support inventory

本量表是想要了解您目前生活中，來自週圍他人所提供給您的支持與協助的情形，根據您平時的感覺、想法，每個問題勾選最適合的選項。

1 分：沒有獲得支持 2 分：偶爾獲得支持

3 分：經常獲得支持 4 分：總是獲得支持

	沒有獲得支持	偶爾獲得支持	經常獲得支持	總是獲得支持
17. 有人可以傾聽我訴說心中的想法及感受	1	2	3	4
18. 有人會關心我的健康狀態	1	2	3	4
19. 在不如意的情況下，有人可以安慰陪伴我、度過困境	1	2	3	4
20. 沮喪時，有人會鼓勵我，振作起來繼續生活下去	1	2	3	4
21. 有人可以支持我所做的決定	1	2	3	4
22. 身體狀況改善時，有人會稱讚、鼓勵我	1	2	3	4
23. 有人能重視我或尊重我的意見	1	2	3	4
24. 有關疾病方面的問題，有人會與我討論並提供我意見	1	2	3	4
25. 有關生活方面的照顧,有人會提供我意見並實際幫助我	1	2	3	4
26. 有人會提醒我按時服藥，定期到醫院檢查	1	2	3	4
27. 有人可以和我一起討論並擬定未來的目標計劃	1	2	3	4
28. 有人可以提供我一些壓力紓解的方式	1	2	3	4
29. 生病時，有人可以照顧我或幫助我處理日常事務	1	2	3	4
30. 有人可以陪伴我一起做活動，使我不去想自己的困境	1	2	3	4
31. 如果我需要經濟支援，有人可以提供	1	2	3	4
32. 請針對以上題目至少列出兩位幫助您最多的人：	(1)			
	(2)			

Appendix 2: Consent Form

Dear Sir/Madam:

The study is to explore HCC patients' quality of life and the significant factors. The questionnaires assess the factors that impact on your illness experiences, quality of life and coping strategies. The results may be used to help medical staff understand your needs and improve clinical care.

Please read the following questions and tick the answer that best describes your experiences. Remember there are no right or wrong answer. Please try not to leave out any questions. Thank you.

Data Protection Act

In accordance with the Data Protection Act, we have to ask you to sign the following declaration. You can be quite sure that all the information we collect will be used only for the purposes of research and kept confidential to the research team itself: it will not be released to anybody else.

> *I agree to allow the university to provide the research team with my name, contact details, grades and other information about my course of study. I also agree that this information, and the data collected from me, may be held and processed by the team for the purposes of research.*

Sign: ______________________________________ Date:_____________

Appendix 3: Publication

Papers:

Fan, S. Y., Hu, W. Y., & Chiu, T. Y. (2008). Ethical issues of psychological research in the context of end-of-life. *Taiwan Journal of Hospice Palliative Care,13*(4), 471-483.

Fan, S. Y., & Eiser, C. (2009). Body image of children and adolescents with cancer: A systematic review. *Body Image, 6,* 247-256.

Fan, S. Y., Eiser, C., & Ho, M. C. (2010). Health-related quality of life in patients with hepatocellular carcinoma: A systematic review. *Clinical Gastroenterology and Hepatology, 8*(7), 559-564, e1-10.

Book chapter:

Fan, S. Y. (in press). Health-related quality of life in patients with liver cancer. In. Liver Cancer: Causes, Diagnosis and Treatment. NOVA science publishers.

Poster:

Fan, S. Y. (2010). An investigation of inpatient referrals to a clinical psychologist in a hospital-based palliative care. The Second National Cancer Conference: Hull, UK.

Hou, Y. C., Hu, S. E., & **Fan, S. Y.** (2010). Clinical psychologists in hospice palliative care: experience and reflection from Taiwan. The 4th Asian Congress of Health Psychology: Taipei, Taiwan.