Palliative and Supportive Care (2013), **11**, 503–522.
© Cambridge University Press, 2013 1478-9515/13 $20.00
doi:10.1017/S1478951512001137

The promise of clinical interventions for hepatocellular carcinoma from the west to mainland China

MEI BAI, PH.D.C., NANCY R. REYNOLDS, PH.D., C-NP, F.A.A.N., AND
RUTH MCCORKLE, PH.D., F.A.A.N.
School of Nursing, Yale University, New Haven, Connecticut

(RECEIVED July 9, 2012; ACCEPTED August 18, 2012)

ABSTRACT

Objective: Hepatocellular carcinoma (HCC) presents a major health problem with its steadily increasing incidence in Western countries, and persistent high fatality rates worldwide. The well-recognized complexity and toxicity of its treatment as well as inadequate care and limited resources in mainland China exacerbate the difficulty of maintaining quality of remaining life of patients living with this illness. The goal of this comprehensive literature review was to identify promising clinical interventions for improving quality of life (QOL) of people with advanced HCC in mainland China.

Method: A comprehensive literature review was performed in China Academic Journals (CAJ), Cochrane, and PubMed databases. The review was confined to studies of randomized controlled trials (RCT) for adults, in Chinese and English, from 1980 to 2012.

Results: A total of 676 studies in Chinese and 391 studies in English were identified. Eighteen RCTs were selected for the final review, among which three were conducted in mainland China.

Significance of results: Nurse-led home-based comprehensive interventions using a collaborative care approach addressing multiple dimensions of QOL show promise for enhancing clinical outcomes for people with advanced HCC in mainland China. Education and psychosocial support combined with symptom management early in the illness trajectory and ongoing close attention to physical symptoms, emotional distress, as well as spiritual well-being are crucial for maintaining QOL of people with advanced HCC. Telephone monitoring appears to be a feasible way in rural as well as urban areas. Families are advised to be part of overall interventions. It is warranted that promising interventions aiming at improving QOL for advanced cancer patients reported in Western literature be further tested in mainland China.

KEYWORDS: HCC, RCT, QOL, Advanced cancer, Mainland China

INTRODUCTION

Hepatocellular carcinoma (HCC) is one of the most common malignancies in the world. There has been increasing clinical interest in HCC over the past decades because of its increasing incidence in low-risk areas as well as a persistent high fatality rate worldwide (Ferlay et al., 2010). Despite advancement in screening techniques, HCC is frequently diagnosed at an advanced stage with limited treatment options and a dismal prognosis (Teo & Fock, 2001; Sun et al., 2008; Fielding, 2010; Forner et al., 2010). The purpose of this review was to address problems of people diagnosed with advanced HCC in mainland China and to identify promising clinical interventions to improve their quality of life (QOL).

EPIDEMIOLOGY

HCC, the major type of primary liver cancer (PLC) (Wu et al., 2011), represents the fifth most common tumor worldwide and the third most frequent cause of cancer-related death (Sun et al., 2008). The

---

Address correspondence and reprint requests to: Mei Bai, Yale University School of Nursing, 100 Church Street South, PO Box 9740, New Haven, CT 06536-0740. E-mail: mei.bai@yale.edu

incidence of HCC differs in different geographical regions as well as in geo-economic zones within countries (Yuen et al., 2009). Almost 85% of cases of liver cancer occur in Asia, and China alone accounts for 55%, the highest HCC burden worldwide (Parkin et al., 2005; Ferlay et al., 2010). The prognosis of patients with unresectable HCC remains poor, with a median survival of <1 year (Llovet et al., 2008a). According to the recent consensus report of China, HCC is the second most common cause of cancer-related death in this country, exceeded only by lung cancer (Wu et al., 2011).

The major risk factor of HCC in China is hepatitis B virus (HBV) infection followed by hepatitis C virus (HCV) infection, with odds ratios reported to be 12.45 and 4.28, respectively (Yuen et al., 2009). The incidence rate of HCC in China starts to increase from the age of 35–40 years, peaking in the sixth and seventh decades of life for men, possibly later for women. Although it may occur in every adult age stratum, Chinese males have a higher HCC incidence risk than do females (Yuen et al., 2009).

Over the past several decades, the global patterns of HCC have undergone substantial changes, with declining trends reported in Asia and a consistent incidence increase detected in Europe and North America (McGlynn et al., 2001; Allen & Venook, 2004; Yuen et al., 2009). Reasons for both the decreased incidence in high-rate areas and increased incidence in low-rate areas are not fully understood (McGlynn et al., 2001). Some suggest that the increase in low-rate areas may be related to the increased prevalence of HCV infection (McGlynn & London, 2005; Rampone et al., 2009), whereas introduction of universal vaccination for HVB appears to have contributed to the decline in the incidence of Asian countries (Teo & Fock, 2001).

There is no consensus on a given HCC staging system to guide clinical treatment decisions. Because of the complexity of the prognosis of HCC, it is recommended that tumor stage, liver function, and other factors be taken into consideration in clinical treatment decisions, as seen in Barcelona Clinic Liver Cancer (BCLC) staging system (Bruix & Sherman, 2005; Rampone et al., 2009; Forner et al., 2010). This system links five stages with treatment modalities based on published response rates (Forner et al., 2010). For example, patients with very early HCC (stage 0) are optimal candidates for resection, and patients with intermediate HCC (stage B) have been found to benefit from transarterial chemoembolization (TACE). Sorafenib, a multitarget tyrosine kinase inhibitor, was recently confirmed to be a standard of care for people with advanced stage (stage C) disease (Llovet et al., 2008b; Forner et al., 2010, 2012), whereas end-stage (stage D) disease will receive symptomatic treatment. It is important that a specific profile of the patient be examined for personalizing each individual treatment decision, which becomes paramount in complex situations such as unresectable HCC (Llovet et al., 2002; Bruix et al., 2004; Forner et al., 2010).

CONTROVERSIAL TREATMENT OF ADVANCED HCC

TACE was introduced in the 1980s, aiming for tumor necrosis while preserving as much functional liver tissue as possible; it remains one of the most widely used methods of treating unresectable HCC. TACE may improve median survival for 3–4 months (Llovet & Bruix, 2003); this benefit seldom happens in advanced stages because of limited opportunity of complete response and almost unanimous recurrence during this time (Bruix & Llovet, 2002; Bruix & Sherman, 2005; Forner et al., 2010). Repeated embolization in short periods of time may bring serious side effects, known as postembolization syndrome (PES). This syndrome consists of abdominal pain, fever, nausea, vomiting, fatigue, and ileus, accompanied by changes in liver biological indexes. Symptoms are highly heterogeneous in patients, depending upon the disease stage and dose of chemotherapy, as well as the patient's overall health condition. The etiology of PES is not entirely known, but it is thought to be caused by a combination of tissue ischemia and an inflammatory response to chemoembolization (Vogl et al., 2009). It is experienced by 60–90% of patients, lasting from hours to days (Ramsey & Geschwind, 2002; Bruix et al., 2004; Yan & Sellick, 2004; Bruix & Sherman, 2005; Guo, 2005; Llovet et al., 2008a; Sun et al., 2008; Wu et al., 2009; Forner et al., 2010; Oliveri et al., 2011), often resulting in a prolonged postprocedural hospitalization (Vogl et al., 2009).

Increasing clinical as well as research attention has been put on the impact of TACE on QOL. Whereas an overall QOL of patients undergoing TACE did not decline during the first 12 months after treatment (Eltawil et al., 2012), a progressive deterioration of conditions during 24 months of observation was reported for patients after TACE (Toro et al., 2012). Steel and colleagues found that QOL of those who received transcatheter arterial embolization (TAE) or combined with intra-arterial chemotherapy (i.e., TACE) was lower at 3 months than pretreatment, and failed to return to baseline despite transient improvements afterwards (Steel et al., 2006). In addition, patients who lived longer (than median survival) in this study were found to have significantly lower QOL than those who had lived less, likely resulting from greater treatment side effects (Steel et al., 2006).

Although current evidence cannot refute TACE, there is an absence of evidence in support of its benefit to either survival or QOL for patients with unresectable HCC (Lopez et al., 2006; Oliveri et al., 2011). TACE has been suggested to be cautiously used for *intermediate-stage* HCC in selected candidates only (Bruix & Llovet, 2002; Poon et al., 2002; Ramsey & Geschwind, 2002; Llovet & Bruix, 2003; Bruix et al., 2004; Bruix & Sherman, 2005; 2011; Llovet et al., 2008a; Raoul et al., 2011; Forner et al., 2012). Noticeably in China, however, TACE is recognized as the standard therapy for people with advanced HCC without correspondingly more rigorous guidelines for selection of patients or an enhanced postoperative care plan (Teo & Fock, 2001; Wu et al., 2011). Transition from initial treatment to the end of life for these patients often goes unattended and unrecognized.

NEGLECTED TRANSITION TO END-OF-LIFE

A diagnosis of advanced cancer and subsequent treatments overtaxes patient's capacities of dealing with a crisis and usually leads to increased dependence and distressing symptoms (McCorkle et al., 1989; 1998). In mainland China, discussion of palliative treatment decisions between physicians and patients usually happens only once, and on a superficial level, associated with fallacious assumptions of both healthcare providers and patients. Physicians generally assume patients want to prolong life at any cost or pain, believing that they desire a minimum positive treatment effect or tumor response at the expense of all the side-effects (Cella et al., 2002; Ahmed et al., 2004; Hall et al., 2011); patients, on the other hand, trust their physicians to make the right decision, and, therefore, are willing to accept what physicians recommend (Yan & Sellick, 2004; Fu & Zhang, 2007). Consequently, emphasis has been unduly placed on patients' compliance to aggressive treatments (Dong et al., 2009), and palliative care becomes real only at the very end of life.

Research with HCC patients has demonstrated worse QOL in terms of physical function, emotional status, and spiritual well-being despite good social and family relationships, in those patients than in people with other cancer sites (Steel et al., 2004; 2006; Yan & Sellick, 2004; Fan et al., 2010). A longitudinal study comparing QOL in two types of hepatobiliary cancers showed that the declining trend of overall spiritual well-being in HCC patients was significantly worse than in patients with pancreatic cancer (Sun et al., 2008). This finding was supported by Yan, who compared liver and other gastrointestinal cancer patients in mainland China, and concluded that QOL of liver cancer patients was significantly the worst (Yan & Sellick, 2004).

There is an absence of evidence of adequate follow-up after TACE treatment in detecting recurrence or QOL maintenance for people with advanced HCC in mainland China. Regardless of higher rates of severe complications after TACE and fast progression of advanced HCC, patients are advised to make a routine follow-up clinical visit 3 months later, which is the next contact with their physicians that patients can expect after discharge. During this period of discontinuous care, distressing symptoms and rapidly deteriorating conditions usually make this disease more and more unmanageable.

LITERATURE IDENTIFICATION

A comprehensive literature review was conducted to identify and analyze promising interventions to enhance the QOL of people with advanced HCC in mainland China throughout the illness trajectory (Corbin & Strauss, 1991; Robinson et al., 1997). Outcomes were chosen to reflect overall QOL, physical, emotional, social, and functional well-being as well as psychological symptoms (such as anxiety and depression), (physical) symptom distress, and enforced social dependency. Spiritual well-being, uncertainty, and posttraumatic growth (Tedeschi & Calhoun, 1996), which are suggested as important for advanced cancer patients but not included in current measures for assessing QOL, were also included as outcomes for this review.

Publications were searched from 1980 to 2012 in the China Academic Journal (CAJ) database using keywords of *liver cancer* and *quality of life* in combination with *randomization* in abstracts. Among the 70 publications identified, 69 studies were excluded because of the pharmaceutical nature of the interventions, the focus on early stage patients, or because they were unacceptable for methodological reasons. Only one study was considered eligible (Guo, 2005).

An extended search in CAJ was then conducted using keywords *quality of life* and *neoplasms* combined with *randomization* in abstracts. Of 676 identified studies, 496 focused on the effect of a drug or clinical technique; 64 targeted patients in the early stage, and 36 were not RCT. In the remaining 80 research articles, methodological issues included a lack of a control group, insufficient details about randomization, and intervention procedures. Three studies (Guo, 2005; Li et al., 2006; Wang et al., 2010) were included for the final review; however, inadequate research design and reporting prevented

Table 1. *Search strategy and results*

Database	Search terms	Identified	Included	Other sources	Total
CAJ	Neoplasms (TI), Liver cancer (TI), Quality of life (TI), Randomization (AB)	676	3	0	3
PubMed[a]	Liver neoplasms (MeSH), Quality of Life (MeSH)	43	2	0	2
	Neoplasms (MeSH), Quality of Life (MeSH), Palliative Care (MeSH), Terminal Care (MeSH), Nursing (subheading), Psychology (subheading), Spirituality (subheading)	348	12	1	13
Total		1067	17	1	18

[a] Limited in randomized controlled trial, adults (≥ 19y), year 1980–2012.
AB, in Abstract; CAJ, China Academic Journals database; TI, in Title; MeSH, Medical Subject Headings.

an accurate evaluation of these interventions (Table 1, Fig. 1).

In order to draw upon evidence of studies from Western countries in addressing QOL for advanced cancer patients potentially generalizable to people with advanced HCC in mainland China, the search was extended to studies conducted outside mainland China. Systematic reviews were searched in the Cochrane database before searching single studies in the PubMed database using the following MeSH terms: *liver neoplasms* and *quality of life*; *neoplasms* and *nursing* (subheading); *palliative care* or *terminal care* and *psychology* (subheading); *neoplasms* and *spirituality.* Limitations were set at RCTs for adults, published between 1980 and 2012 (Table 1). We also hand searched the references of the retrieved articles for further relevant trials.

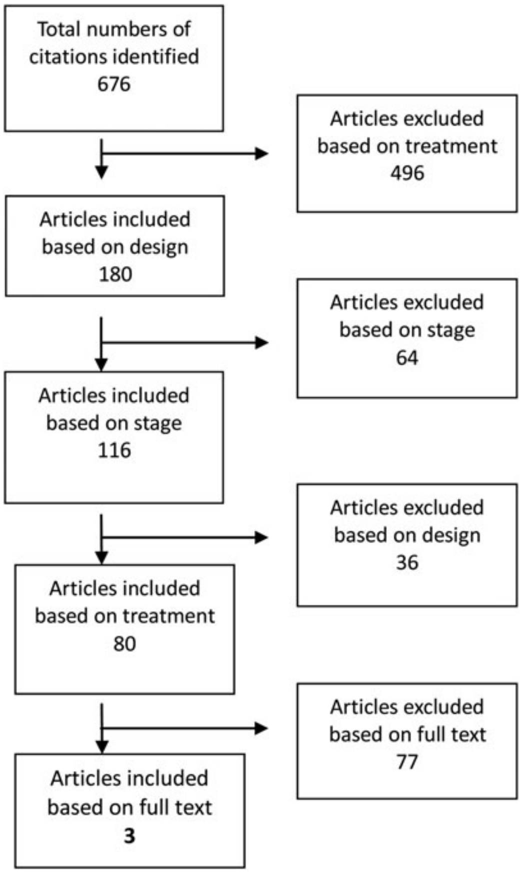

Fig. 1. Flow diagram of the process of data extraction from the China Academic Journals database.

Initial searching found a total of 391 citations; 145 citations were excluded based on design and stage of disease. An additional 160 pharmaceutical interventions targeting survival were discarded. The remaining 86 articles were scrutinized for methodological quality as well as generalizability to HCC patients in mainland China. Fourteen articles were kept for further review. One study (Linn et al., 1982) was identified by hand searching references. Finally, 18 studies (marked by an asterisk) in the reference list were included in the present review, including 3 RCTs conducted in mainland China (Guo, 2005; Li et al., 2006; Wang et al., 2010), 9 in the United States (Linn et al., 1982; McCorkle et al., 1989; Rummans et al., 2006; Steel et al,, 2007; 2011; Bakitas et al., 2009; McCorkle et al., 2009; Breitbart et al., 2010; 2012), 1 each from the United Kingdom (Moore et al., 2002), Norway (Jordhøy et al., 2001), Australia (Hudson et al., 2005), Japan (Ando et al., 2010), and Hong Kong (Lee et al., 2010), respectively. There is also a multisite study across the United States, Canada, and Australia (Chochinov et al., 2011) (Fig. 2).

Overall, outcomes included physiological outcomes (e.g., survival [Linn et al., 1982; Moore et al., 2002; Steel, 2007; Bakitas et al., 2009] or biological indexes [Guo, 2005; Steel et al., 2007; 2011]), healthcare service use and cost effectiveness (McCorkle et al., 1989; Moore et al., 2002; Bakitas et al., 2009), as well as psychosocial outcomes including QOL (Jordhøy et al., 2001; Moore et al., 2002; Guo, 2005; Li et al., 2006; Rummans et al., 2006; Steel et al., 2007; Bakitas et al., 2009; McCorkle et al., 2009; Lee et al., 2010; Wang et al., 2010; Chochinov

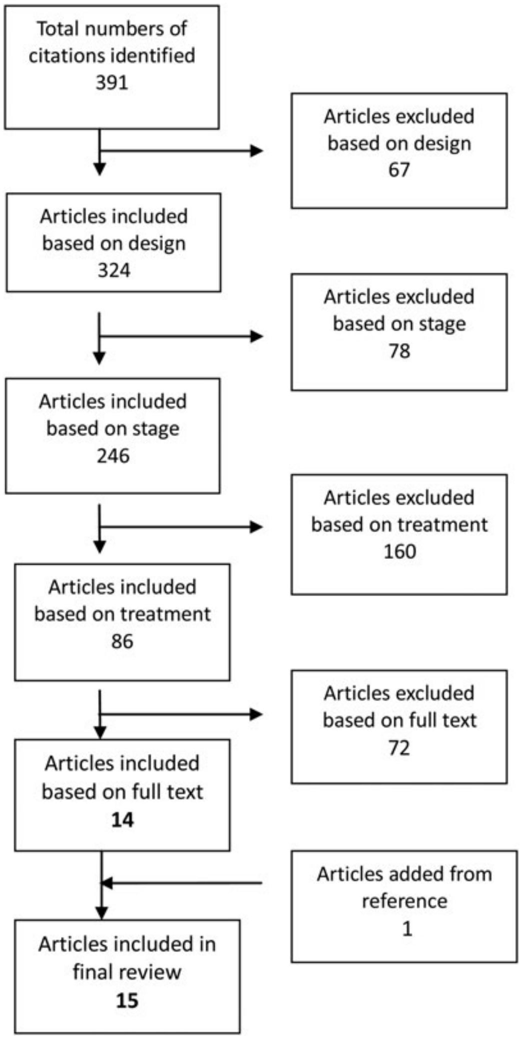

Fig. 2. Flow diagram of the process of data extraction from the PubMed database.

et al., 2011; Breitbart et al., 2012), life satisfaction (Linn et al., 1982), emotional distress (Linn et al., 1982; Hudson et al., 2005; Rummans et al., 2006; Li et al., 2006; Steel et al., 2007; Bakitas et al., 2009; McCorkle et al., 2009; Ando et al., 2010; Breitbart et al., 2010; Chochinov et al., 2011; Breitbart et al., 2012), symptom distress (McCorkle et al., 1989; Rummans et al., 2006; Bakitas et al., 2009; McCorkle et al., 2009; Ando et al., 2010; Chochinov et al., 2011; Breitbart et al., 2012), enforced social dependency (McCorkle et al., 1989; 2009) and disability (Linn et al., 1982), as well as spiritual well-being (Rummans et al., 2006; Ando et al., 2010; Breitbart et al., 2010; 2012; Chochinov et al., 2011), uncertainty (McCorkle et al., 2009), posttraumatic growth (Lee et al., 2010), and dignity (Chochinov et al., 2011). Although the majority of studies focused on patients, two studies included family caregiver outcomes (Hudson et al., 2005; Wang et al., 2010).

RESULTS

The outcomes of RCTs in the oncology literature depend upon the quality of the study design and the timing of the cancer trajectory, as well as a number of moderating factors (Rehse & Pukrop, 2003). To fully understand the intervention effects and extract evidence imbedded, studies are reported with an emphasis on critical evaluation and synthesis of the current empirical evidence of promising clinical interventions on QOL and other psychosocial variables taking into account various influencing factors (Tables 2 and 3).

OUTCOMES REPORTED IN REVIEWED STUDIES

QOL

QOL is examined in 10 of the 18 RCTs, using either generic (McCorkle et al., 2009; Lee et al., 2010; Chochinov et al., 2011), cancer-specific (Jordhøy et al., 2001; Moore et al., 2002; Guo, 2005; Li et al., 2006; Rummans et al., 2006; Wang et al., 2010), or site-specific QOL instruments (Steel et al., 2007) or palliative care specific instruments (Bakitas et al., 2009; Breitbart et al., 2012). All but one (Chochinov et al., 2011) of these studies used multidimensional QOL measures. Among these studies, five focused on specific cancer sites of liver (Guo, 2005; Steel et al., 2007), lung (Moore et al., 2002), gynecological system (McCorkle et al., 2009), and colorectal system (Lee et al., 2010). Three of these interventions were psychotherapy based using meaning-centered therapy (Breitbart et al., 2012), the Eastern body–mind–spirit model (Lee et al., 2010) or dignity therapy (Chochinov et al., 2011), whereas the others used a comprehensive approach integrating multiple self and family management components addressing QOL.

Intervention effects on QOL among groups were demonstrated in four studies (Rummans et al., 2006; Bakitas et al., 2009; McCorkle et al., 2009; Breitbart et al., 2012). Among them, one study on a sample of predominantly ovarian cancer patients revealed impact for the subgroup who received additional psychological intervention but not for the full sample (McCorkle et al., 2009); two trials showed impact for post-intervention but not for the follow-up time (Rummans et al., 2006; Breitbart et al., 2012). The tailored psychosocial pilot intervention for the United States HCC patients suggested feasibility and possible clinical significance (Steel et al., 2007), whereas the experiment conducted with HCC patients after TACE in mainland China showed impact on general health status only (Guo, 2005). One

Table 2. *Summary of studies*

Study	Population & setting	Measures	Intervention delivery	Intervention components	Control components	Key findings	Grade[a]
Guo, 2005 China	N=94; HCC patients after TACE; two waves; inpatient	EORTC-QLQ-C30	Emotional education intervention by physician; daily (diet) and weekly (education) 2 months	Education, relaxation training, functional exercise, Chinese medicated diet	Usual care; tertiary hospital;l urban	Physical symptoms decreased (p <0.05), liver function ($p < 0.01$) and general health status ($p <. 005$) improved.	IIB
Li et al., 2006 China	$N = 76$; terminal elder cancer patients and families; two waves; palliative care units	Quality of life scale[b], social support scale[b], HADS	Comprehensive team intervention by surgeons, physicians and nurses; daily; 1 month	Death education, pain relief, psychosocial support, nutritional and other palliative therapies	Usual care; tertiary hospital; urban	Quality of life (<0.05), social support (<0.01) improved, depression (<0.01) and anxiety (<0.05) decreased.	IIB
Wang et al., 2010 China	$N = 184$; cancer patients and their families; two waves; home	*Patients:* EORTC QLQ-C30; *Caregivers*: SF-36	Comprehensive intervention by general practitioners and nurses; biweekly or every month; 6 months	Symptom monitoring, pain management, nutritional & psychological support	Usual care; tertiary hospital; urban	Quality of life of both patients (<0.01) and their caregivers (<0.01) improved.	IIB
Linn et al., 1982 U.S	$N = 120$ (50% lung cancer); end stage cancer; all male. six waves: baseline, 1, 3, 6, 9, and 12 months; home	POMS; Sherwood's self-esteem scale; Cantril's life satisfaction scale; Srole's alienation scale; Rotter's loss of control scale; Rapid Disability Rating Scale	Weekly therapist-led psychosocial counseling; 12 months	Develop trust relationship, reduce denial but maintain hope. Stress feelings of control, encourage meaningful activities. Listen to the patient reminisce to reinforce accomplishments, develop a sense of meaning of one's life, and provide a basis for increased self-esteem and life satisfaction. Simply listening, understanding, and sometimes only sitting quietly with the patient were elements of treatment.	Regular medical therapy	Quality of life variables including depression, self-esteem, life satisfaction, alienation and locus of control showed greater improvement in the intervention group by 3 months ($p < 0.001$), and this positive change was maintained for those who lived for 12 months ($p < 0.001$). Functional status (on disability) did not show significant changes. Same pattern occurred for lung cancer patients subgroup.	IIA
McCorkle et al., 1989 U.S.	$N = 166$; lung cancer ($\geq$stage II), 2 months after diagnosis; four waves: at 6 week intervals for > 6 months; home	SDS; McGill-Melzack Pain questionnaire; ESDS; general health rating index	Home care by specialized oncology home care nurses or standardized interdisciplinary team versus office care by physician	Nursing care in symptom management, cancer treatments and appropriate referral or team work	Traditional treatment by physician	Increased symptom distress ($p = 0.03$) and social dependency ($p = 0.02$) occurred later in the intervention group, reported health perception was worse	IIA

						($p < 0.05$) in the intervention group throughout the study.	
Jordhøy et al., 2001 Norway	Cluster randomized trial; $N = 434$; advanced/end stage cancer; seven waves, 6 months; palliative care unit & home	EORTC; IES	Multidisciplinary palliative care program led by general practitioner and community nurse versus conventional care at hospital and community levels; 4 months	Systematic assessment of psychological, social, and spiritual needs	Palliative care service in conventional care is generally good in Norway; staff in the intervention group were inexperienced at the time of the study	No QOL variables in the intervention group showed difference from baseline to 6 months in comparison with the control.	IIA
Moore et al., 2002 U.K.	$N = 203$; lung cancer (60% advanced stage); four waves; home & outpatient	EORTC	Clinical nurse specialist led collaborative care, monthly telephone or clinic assessment; 12 months	Assessment monthly over the telephone or in a nurse-led clinic to identify signs of disease progression, symptoms warranting intervention, or serious complications. Intervention focused on providing information and support and coordinating input from other agencies or services. Additional contacts with nurse were available without an appointment.	Conventional care consisted of routine outpatient appointments (one postoperative appointment, then appointments at 2 or 3 month intervals) for medical assessment and investigations to monitor disease progression	Intervention group showed less severe dyspnea at 3 months ($p = 0.03$) and better emotional functioning ($p = 0.03$), less peripheral neuropathy ($p = 0.05$) at 12 months. Although no differences were seen in rates of progression, nurses recorded symptomatic progression sooner than the physicians ($p = 0.01$).	IIA
Hudson et al., 2005 Australia	$N = 106$; family caregivers of advanced cancer patients admitted to a home-based palliative care service; three waves (baseline, 5 weeks from baseline and 8 weeks following patient's death); home	Preparedness, competence and rewards of caregiving scales; HADS, self-efficacy scale	Nurse-delivered psycho-educational intervention to caregivers: two home visits and one telephone follow-up between visits; guidebook for easy access to written information and audiotape; 8 weeks	Providing information and support; teaching skills; promoting self-care, enhancing meaning	Standard home-based palliative care service: multidisciplinary health professionals including nurses, social workers, volunteers, and bereavement counselors. Access to 24-hour phone advice and emergency visits from nurses in addition to prescheduled home visits.	No intervention effects were identified with respect to preparedness to care, self-efficacy, competence, and anxiety. However research indicates that nurse-delivered psycho-educational intervention can increase caregiver rewards in challenging circumstances.	IIB
Rummans et al., 2006 U.S	$N = 103$; advanced cancer patients undergoing radiation therapy; four waves: baseline, week 4 (end of	LASAs; Spitzer QOL Uniscale; SDS; POMS(SF); FACIT-Sp-12	Psychiatrist or psychologist led, structured multidisciplinary intervention of eight 90-minute sessions versus standard	Education, physical therapy, coping skills training, emotional management and support, meaning enhancement	Interaction with oncologists, referrals to specialists when indicated, and opportunities for receiving support through a range of	Higher overall QOL (mean 72.8 vs. 64.1, $p = 0.047$) as well as spiritual well-being (mean 92.9 vs. 83.9, $p = 0.003$) was observed in the	IIA

Continued

Table 2. *Continued*

Study	Population & setting	Measures	Intervention delivery	Intervention components	Control components	Key findings	Grade[a]
	intervention), week 8, and week 27; outpatient		medical care as recommended by patient's radiation oncologist; 3 days per week over 3 weeks		outside agencies including the American Cancer Society support group	intervention group at week 4. The improvement of overall QOL (score change 3 vs. −9, ES = 0.13, $p = 0.009$) was greater in intervention group at week 4. Over the remaining 5 months at week 8 or 27, no difference was observed: QOL maintained in the intervention group whereas control group returned to baseline. Physical (score change 0.4 vs. −10, $p = .022$), emotional (2.8 vs. −5.4, $p = 0.046$), and social well-being ($p < 0.05$) showed improvements from baseline to week 4, whereas control declined. Symptom distress with SDS, spiritual well-being or emotional distress with POMS did not reveal difference between groups.	
Steel et al., 2007 U.S.	Pilot RCT; $N = 28$ hepatobiliary cancer (23 HCC) under or between treatment (cisplatin et al); two waves: baseline and 3-month follow-up; outpatient & home	FACT-Hep; CES-D; STAI leukocytes	Individually tailored psychosocial education and therapy; in- person sessions or counseling over phone; 3 months	One or a combination of education, CBT, supportive-expressive therapy, and intensified pharmacological monitoring were employed to treat problems of individual patients.	Attention-standard of care (usual education regarding the treatment and medication; ongoing phone contact with nurse coordinator over the course of treatment)	Intervention group showed improved overall QOL (score change 17 vs. 11, ES = 0.29) and emotional well-being (score change 18 vs. 13), depressive symptoms (−12 vs. −1) and state anxiety (−16 vs. −3). No statistical significance was observed.	IIA
Bakitas et al., 2009 U.S.	$N = 322$, people with advanced cancer; baseline, 1 month, and every 3	FACIT-Pal; ESAS; CES-D	Advanced nurse practitioner-administered telephone-based	Problem solving, advance care planning, family and healthcare team	Patients were allowed to use all oncology and supportive services without restrictions	Higher quality of life (ES = 0.18, $p = 0.02$) and lower depressed mood ($p = 0.02$) were	IIA

	months until death or study completion; home & outpatient; rural		intensive curriculum (four weekly sessions), and ongoing assessment and coaching (at least monthly contact); 3 years	communication strategies, symptom management and crisis prevention, and timely referral to palliative care and hospice resources	including referral to the institutions' interdisciplinary palliative care service. Medical Center site in rural area with an advanced illness coordinated care program.	achieved in the intervention group longitudinally for the total sample as well as the subsample who died. Symptom intensity was not significantly different between groups.	
McCorkle et al., 2009 U.S.	$N = 145$; gynecological cancer (73% were newly diagnosed), advanced stage (66%); four waves: baseline (24–48 h after surgery), 1, 3, and 6 months post-surgery; home	SF-12; CES-D; MUIS; SDS; EDT	Tailored specialized care by an oncology APN with eight home visits, seven calls, three clinical visits, plus specialized psychiatric assessment for subgroup with higher distress versus attention control by research assistant with eight contacts; 6 months	Symptom management and monitoring, emotional support, education, decision-making facilitation, referrals, direct care	Symptom management toolkit; usual care by oncologist; tertiary cancer center	Total sample showed less uncertainty (unadjusted $ES = 0.134$, $p = 0.0006$) in the APN intervention group. Subgroup who received additional PCLN intervention showed improved QOL ($p \leq 0.0001$) as well as less symptom distress ($p < 0.0001$) and uncertainty ($p = 0.0181$) than attention control group. Depressive symptoms did not reveal difference.	IIA
Ando et al., 2010 Japan	$N = 68$; cancer patients; two waves; palliative care units	FACIT-Sp-12; HADS; numerical rating scales for pain, physical symptoms and psychological suffering	Short-term life-review psychotherapy (30–60 min each) by trained interviewers; two sessions, over 1 week for each session.	Asking patient for life review questions; encouraging patient to feel continuity of self from the past to the present, to accept life completion and to be satisfied with life; making album for patient;	General support in addition to usual medical treatment, with no particular psychotherapy	Spiritual well-being ($p < 0.001$) and psychological distress (anxiety and depression) ($p < 0.001$) showed greater improvement in the intervention group. Pain, psychological suffering and physical symptoms did not differ between groups.	IIA
Breibart et al., 2010 U.S	$N = 90$; advanced cancer patients; three waves: pre- and post-intervention (T1, T2), 2 months after intervention (T3)	FACIT-Sp-12; HADS	Psychiatrist or clinical psychologist led 8-week meaning-centered group psychotherapy (MCGP) versus clinical psychologist or licensed social worker led supportive group psychotherapy	helping patients with advanced cancer sustain or enhance a sense of meaning, peace, and purpose in their lives even as they approach the end of life, focusing around eight themes related to meaning and advanced cancer	Encouraging patients to share concerns related to the cancer diagnosis and treatment, to describe their experiences and emotions related to these experiences, voice problems that they have in coping with cancer, and offer	Overall spiritual well-being ($p < 0.0001$) as well as meaning/peace ($p < 0.0001$) and faith ($p = 0.02$ at T2; 0.006 at T3) increased post-intervention (T2) and in 2 months follow-up (T3) in the intervention group	IIA

Continued

Table 2. *Continued*

Study	Population & setting	Measures	Intervention delivery	Intervention components	Control components	Key findings	Grade^{a}
			(SGP); both eight sessions.		support and advice to other group members	with effect sizes at T3 greater. Anxiety/depression showed improvement at T3 in the intervention group ($p = 0.02$). The improvement for overall spiritual well-being ($p = 0.009$) as well as meaning/peace ($p = 0.03$) at T2 was greater for intervention group. Anxiety/depression did not differ between groups at either T2 or T3.	
Lee et al., 2010 Hong Kong	$N = 166$; advanced colorectal cancer patients; Five waves: baseline, immediately after intervention, 4 months, 8 months, and 12 months post intervention. Hospital	SF-36; CECS; PTG	Psychosocial intervention, meet weekly for 5 weeks, 3 h per session	In-depth sharing, emotional expression, meditation, and physical exercise.	Both groups received educational materials on colorectal cancer.	Significant difference was found for PTG improvement between groups ($p = 0.000$), which remained significant 4 months after intervention. No other variables showed intervention effect.	IIB
Chochnov et al., 2011 Multisite: U.S., Canada, Australia	$N = 441$; terminally ill patients (94% cancer); two waves: pre-post 3 group design; home or hospital	Two-item QOL scale; FACIT-Sp-12; patient dignity inventory; ESAS HADS; survey	Psychologist, psychiatrist or palliative care nurse led dignity therapy, meet twice for 60 min. and 30 min. respectively over 7-10 days	Tailored dignity psychotherapy, targeting what might enhance a sense of meaning, purpose, continued sense of self, and overall sense of dignity.	Control 1: nurse-led client-centered care (supportive psychotherapeutic) focusing on illness, associated symptoms, and their distress. Control 2: standard palliative care with access to the complete range of palliative-care-support services that were available to all study patients, including specialist palliative care physicians and nurses social workers, chaplains, and psychologists or psychiatrists.	Intervention revealed no significant difference among groups for primary outcomes: QOL, spiritual well-being, symptom distress, dignity, anxiety or depression. Secondary outcomes suggested better end-of-life experience in the intervention group compared with the other two control groups.	IIA

Steel et al., 2011 U.S.	Pilot RCT; $N = 226$ HCC under or between treatment; Data started prior to the patients' first treatment and every 2 months for the first year, then every 6 months for another 2 years or until death; outpatient & home	FACT-Hep; FACT-Fatigue	Collaborative care intervention in person led by psychologists, through phone or website versus enhanced usual care	Face to face visits each time patient had treatment, at least two telephone follow-up contacts; access to a specifically designed website including educational information, a self-management area, journaling, a chat room, an audiovisual library, peer support, and other resources	Routine medical care from the nurse coordinator and attending physician; a binder with educational information; brief intervention for those with significant distress or severe pain.	Collaborative care intervention is feasible. No results are available.	IIA
Breitbart et al., 2012 U.S.	$N = 120$; advanced cancer patients; three waves: pre- and post-intervention (T1, T2), 2 months after intervention (T3); outpatient clinic	FACIT-Sp-12; MSAS; MQOL; HADS	Psychologist-led 7-week individual meaning-centered psychotherapy (IMCP) versus 7-week licensed massage therapist-led therapeutic massage (TM)	Assist patients with advanced cancer in sustaining or enhancing a sense of meaning, peace, and purpose in their lives as they face limitations caused by progression of disease and treatment.	Manipulation of the soft tissue of the whole body or particular areas of the body.	Greater improvement was shown in IMCP for spiritual well-being ($p < 0.001$) as well as meaning/ peace ($p = 0.003$) and faith subscale ($p = 0.03$), overall QOL (adjusted $ES = 0.27$, $p = 0.013$), number of physical symptoms endorsed ($p < 0.001$), and physical symptom distress ($p < 0.001$). No significant differences were found between groups in anxiety or depression changes. No difference was found at 2-month follow-up between groups.	IIA

---

[a] Stetler's level and quality of evidence. Level conveys rating per type of research, level I= Meta analysis of multiple controlled studies; level II= individual experimental study. Quality for any level ranges from A to D, and reflects basic scientific credibility of the overall study. Quality evaluation details please refer to Table 3.

[b] Developed in China.

APN, advanced practice nurse; BDI, Beck Depression Inventory; CBT, cognitive behavioral therapy; CECS, the Courtauld Emotional Control Scale; CES-D, Center for Epidemiological Studies Depression Scale; EDT, Emotional Distress Thermometer; EORTC, the European Organization for Research and Treatment of Cancers; effect size (ES), the Enforced Social Dependency Scale (ESDS), Edmonton Symptom Assessment Scale; ESDS, FACT-Hep, the Functional Assessment of Cancer Therapy—Hepatobiliary; FACIT-Pal, Functional Assessment of Chronic Illness Therapy for Palliative Care; FACIT-Sp-12, the 12 item Functional Assessment of Chronic Illness Therapy–Spiritual Well-Being; HADS, the Hospital Anxiety and Depression Scale; HCC, hepatocellular carcinoma; IES, Impact of Event Scale; LASAs, Linear Analog Scales of Assessment; McGill Quality of Life Questionnaire (MQOL), Memorial Symptom Assessment Scale (MSAS), MUIS, the Mishel Uncertainty in Illness Scale; PCLN, psychiatric consultation–liaison nurse; POMS, Profile of Mood States; POMS (SF), Profile of Mood States (Short Form); PTGI, the posttraumatic Growth Inventory; QLQ-30 RCT, randomized controlled trial; SF-36, 36-item short form health survey; SDS, Symptom Distress Scale; STAI, the State Trait Anxiety Index; TACE, transarterial chemoembolization.

Table 3. *Study quality evaluation*

Study randomization		Equivalence at baseline	Intervention details	Control details	Attrition[a]	Statistics	Generalization to HCC in China
Guo, 2005 China	0.5	0.5 (no demo & clinic data presented)	1	0	0	0.5 (no between-group difference analysis)	HCC after TACE
Li et al., 2006 China	0.5 (odd and even number method)	0.5 (no clinical information)	0.5	0	Unclear	0.5 (cross-sectional only; no control of confounders)	Not clear, as no description of clinic characteristics besides stage and site
Wang et al., 2010 China	1	0.5 (no stage information)	0.5	0	5.98%	0.5 (no within-group difference analysis)	Not clear, no description of clinic characteristics
Linn et al., 1982 U.S	1	0.5 (demo or clinical baseline not balanced)	1	0.5 (not clear whether usual care counseling possibility)	107/120	1	Male terminal cancer patients, prognosis within 12 months
McCorkle et al., 1989 U.S.	0.5	0.5 (clinical variables were not balanced)	0.5	0.5	66%	1 (adjusted for baseline imbalance)	Poor diagnosis, under treatments, increased symptoms, newly diagnosed
Jordhøy et al., 2001 Norway	1	0.5 (outcome variables were not compared)	1	1	91%	1	Advanced cancer of prognosis of 2-9 months
Moore et al., 2002 U.K.	0.5	1	1	1	70%	1	60% advanced lung cancer patients; not clear about treatment.
Hudson et al., 2005 Australia	1	0.5 (outcome measures not provided)	1	1	79/106	1	Caregivers of incurable cancer admitted to palliative service at home
Rummans et al.,2006 U.S	0.5	1	1	1	20%	1	Advanced cancer patients undergoing radiation treatments
Steel et al., 2007 U.S.	0.5	1	1	1	50%	1	HCC on chemotherapy
Bakitas et al., 2009 U.S.	0.5	1	1	1	154/322	1	Advanced cancer, not clear about treatment.
McCorkle et al., 2009 U.S.	1	0.5 (outcome measures not balanced)	1	0.5 (usual care not in detail)	22/145	1	Majority (66%) of patients were advanced stage, with poor prognosis, but with exclusively women.
Ando et al., 2010 Japan	1	0.5 (outcome measures not provided)	1	1	Not provided	1	Incurable cancer patients in palliative care unit. Not clear about prognosis or treatment.
Breitbart et al., 2010 U.S	0.5	1	1	1	Not provided (29 finished all sessions)	1	Advanced cancer, ambulatory

Lee et al., 2010 Hong Kong	1	1	0.5	0.5	45/166	1	Majority had advanced cancer, treatment information was not provided.
Chochnov et al., 2011 Multi-site	1	0.5 (outcome variables at baseline not provided)	1	1	115/441	1	Various cancer site of terminal stage; treatment information not clear.
Steel et al., 2011 U.S.	**1**	NA	1	1	NA	NA	HCC on treatments
Breitbart et al., 2012 U.S	1	1	1	1	44% (66% finished all sessions)	1	Advanced cancer, ambulatory, KPS > 50. Not clear if patients were undergoing distressing treatments.

Studies were rated on randomization, equivalence at baseline, intervention details, control details, and statistics.
0 = not done, 0.5 = not clear, 1 = clearly explained.
[a] Attrition here refers to measurement attrition and was calculated based on the people who were lost to follow-up regardless of treatment.
HCC, hepatocellular carcinoma; KPS, Karnofsky Performance Status; TACE, transarterial chemoembolization.

study with advanced lung cancer patients in the United Kingdom showed significant results for specific symptoms and emotional well-being but not overall QOL (Moore et al., 2002). Three studies failed to show any benefits on QOL in comparison with controls (Jordhøy et al., 2001; Lee et al., 2010; Chochinov et al., 2011).

Emotional Distress

Eleven of the 18 RCTs specifically examined emotional distress (Linn et al., 1982; Hudson et al., 2005; Li et al., 2006; Rummans et al., 2006; Steel et al., 2007; Bakitas et al., 2009; McCorkle et al., 2009; Ando et al., 2010; Breitbart et al., 2010; 2012; Chochinov et al., 2011) and 4 revealed intervention effects on either anxiety or depressed mood (Linn et al., 1982; Li et al., 2006; Bakitas et al., 2009; Ando et al., 2010), observation time ranging from 2 weeks (Ando et al., 2010) to 3 years (Bakitas et al., 2009). It is noted in one multidisciplinary intervention (Rummans et al., 2006) for advanced cancer patients undergoing radiation treatment that whereas intervention showed benefit on emotional well-being with the Linear Analog Scales of Assessment Scale (LASAs) (Locke et al., 2007), emotional distress on the Profile of Mood States Scale (POMS) (Baker et al., 2002) did not reveal significant difference among randomized groups.

Symptom Distress

Seven studies specifically assessed physical symptoms, using the symptom distress scale (SDS) (McCorkle & Young, 1978; McCorkle et al., 1989; 2009; Rummans et al., 2006) or symptom severity measures (Bakitas et al., 2009; Ando et al., 2010; Chochinov et al., 2011; Breitbart et al., 2012) with varied findings. In one study with advanced stage lung cancer patients, McCorkle and colleagues (1989) demonstrated the impact of nurse-led home care intervention on symptom distress ($p = 0.03$) over the 6 month study period. In this study, general health and functioning also showed statistically significant difference among groups. In another longitudinal study testing nurse-administered telephone-based intervention for advanced cancer patients in rural areas, the intervention showed impact of higher QOL ($p = 0.02$) and lower depressed mood ($p = 0.02$) but not diminished symptom intensity (Bakitas et al., 2009). One psychologist-led 7 week individual meaning-centered psychotherapy (IMCP) revealed an effect post-intervention in comparison with 7 week licensed massage ($p < 0.001$), which did not hold at 2 month follow-up (Breitbart et al., 2012). Rummans and colleagues in their structured comprehensive intervention for advanced cancer patients, demonstrated intervention effect on symptom reduction with the LASAs, but not the SDS (Rummans et al., 2006).

Spiritual Well-Being

It has been criticized that spiritual well-being is not routinely assessed in QOL, although it takes on an important role for people with advanced cancer. Among the 18 trials, 5 examined spiritual well-being on the 12 item Functional Assessment of Chronic Illness Therapy–Spiritual Well-Being (FACIT-Sp-12) (Peterman et al., 2002) as primary outcomes. Among them, one multisite study using dignity therapy for terminally ill patients, of whom the majority were diagnosed with late stage cancer, failed to reveal significant difference between groups (Chochinov et al., 2011), whereas the majority of studies showed only short-term impact (Rummans et al., 2006; Ando et al., 2010; Breitbart et al., 2010; 2012). For example, in two psychologist-led meaning-centered therapies for advanced cancer patients at the group and individual levels, respectively, immediate impact on patients' spiritual well-being ($p = 0.009$, Breitbart et al., 2010; $p < 0.001$, Breitbart et al., 2012) as well as the Meaning/Peace subscale ($p = 0.03$, Breitbart et al., 2010; $p = 0.003$, Breitbart et al., 2012) was shown at post-intervention; however, intervention effect ceased to be significant during the 2 month follow-up. Noticeably, despite control condition variance as well as slight difference in the duration of the intervention and sample size in these two studies, significant difference was reported among randomized groups in patients' spiritual well-being but not emotional distress.

In the structured multidisciplinary study for advanced cancer patients undergoing radiotherapy, spiritual well-being as well as overall QOL revealed significant difference only at week 4, which was the end of treatment (Rummans et al., 2006). During the subsequent 5 months, whereas the intervention group maintained this level, spiritual well-being as well as QOL in the control group gradually returned to baseline. It is important to note that in this trial, the beneficial effect on the spiritual well-being from baseline to week 4 using repeated measures analysis of variance failed to reveal difference on either the LASAs or the FACIT-Sp-12.

Uncertainty and posttraumatic growth (PTG) were also extensively studied variables for people with advanced cancer. In one 6 month nurse-led home intervention for improving post-surgery outcomes of predominantly ovarian cancer patients, uncertainty showed unequivocal intervention impact between the intervention and the enhanced control groups (McCorkle et al., 2009). One 5 week psychotherapy intervention conducted in Hong Kong with advanced colorectal cancer patients demonstrated maintained intervention effect on posttraumatic growth (PTG) for 4 months (Lee et al., 2010).

Family Caregivers

Cancer is a disease affecting not only the person diagnosed but also the families, who are often not adequately prepared to handle the physical and emotional needs that are inherent in cancer management (Stehlin & Beach, 1966; McCorkle & Pasacreta, 2001). In this review, one study examined the impact of interventions on family caregivers (Wang et al., 2010), and one specifically designed the intervention for family caregivers (Hudson et al., 2005). Hudson and colleagues examined a psycho-educational intervention for family caregivers of patients dying of cancer at home in Australia. Although caregivers who received the intervention reported a significantly more positive experience than those who received standard care, indicating that it is possible to increase caregiver rewards in the midst of negative circumstances, no intervention effects were identified with respect to psychosocial variables. This might be associated with potential selection bias during recruitment resulting in unexpectedly highly functioning caregivers, disclosed by the researchers.

FACTORS POTENTIALLY INFLUENCING OUTCOMES

Intervention Delivery Mode

The majority of the interventions in this review were led by psychologists or psychiatrists (Linn et al., 1982; Rummans et al., 2006; Steel et al., 2007; 2011; Ando et al., 2010; Breitbart et al., 2010; 2012; Chochinov et al., 2011), whereas eight interventions were led by nurses (McCorkle et al., 1989; 2009; Moore et al., 2002; Hudson et al., 2005; Bakitas et al., 2009), physicians and nurses (Jordhøy et al., 2001; Wang et al., 2010), or a physician alone (Guo, 2005). Interventions were delivered on an individual basis (Linn et al., 1982; McCorkle et al., 1989; 2009; Moore et al., 2002; Steel et al., 2007; 2011; Bakitas et al., 2009; Ando et al., 2010; Wang et al., 2010; Breitbart et al., 2012), in group settings (Guo, 2005; Rummans et al., 2006; Breitbart et al., 2010; Lee et al., 2010; Chochinov et al., 2011), or cluster levels (Jordhøy et al., 2001). It is also important to note that the majority of studies were home based (Linn et al., 1982; McCorkle et al., 1989; 2009; Moore et al., 2002; Hudson et al., 2005), telephone based (Bakitas et al., 2009), or combined home visits and telephone calls (Hudson et al., 2005; McCorkle et al., 2009). Telephone calls were also used in conjunction with interventions in outpatient settings (Moore et al., 2002; Steel et al., 2007; 2011).

Promising interventions to improve multiple QOL dimensions were found to be individually based and/or individually tailored, with few exceptions. For example, Ando and colleagues (2010) examined the efficacy of a short-term life review for the enhancement of spiritual well-being of 68 terminally ill Japanese cancer patients. Results showed significant improvement in both spiritual well-being and psychological scores in the intervention arm ($p < 0.001$), indicating this short-term life review is effective and clinically relevant in improving spiritual well-being of terminally ill cancer patients and alleviating their psychosocial distress. Future research is warranted to examine whether the benefit of this life review interview to spiritual well-being could transfer to more dimensions of QOL for people with advanced cancer. On the contrary, one experiment conducted in Hong Kong, China, with 166 advanced colorectal inpatient cancer participants used group sessions of psychotherapy and this study found benefit only for PTG ($p = 0.000$), with no differentiation on QOL among groups (Lee et al., 2010).

Rummans and colleagues (2006) conducted a structured intervention containing eight 90-minute sessions for advanced cancer patients during radiotherapy with intervention effect shown at the end of treatment (also the end of 4 weeks of radiotherapy). Whereas the main body of the intervention was based on group sessions led by a psychiatrist or psychologist, further support from multidisciplinary team was on an individual level. Another study with HCC after TACE in mainland China used group sessions for weekly psychoeducational intervention; however, the Chinese medicated diet was individually tailored (Guo, 2005). Similarly, in a multisite dignity psychotherapy, sessions were designed at the group level; however, the content was individually tailored, accommodating the participant's preferences and choices (Chochinov et al., 2011). This study failed to show intervention effect among groups on dignity, spiritual well-being, or QOL, potentially attributed to the competing control groups.

Timing of Interventions

Timing of interventions for advanced cancer patients varied, ranging from during the perioperative period (Moore et al., 2002; Guo, 2005; McCorkle et al., 2009), to while undergoing or between radiation or chemotherapies (Rummans et al., 2006; Steel et al., 2007; 2011), to while receiving end-of-life palliative care service (Linn et al., 1982; Jordhøy et al., 2001; Li et al., 2006; Bakitas et al., 2009; Ando et al., 2010; Chochinov et al., 2011), whereas the time frame with respect to diagnosis was only clearly documented in two studies (McCorkle et al., 1989; Bakitas et al., 2009).

Intervention Type and Components

Six of the 18 RCTs selected a single component of psychosocial methods such as psychotherapy (Ando et al., 2010; Lee et al., 2010), counseling (Linn et al., 1982), dignity therapy (Chochinov et al., 2011), or meaning-based logotherapy (Breitbart et al., 2010; 2012), whereas the others used a comprehensive approach containing clinical assessments, complication monitoring, teaching self-management skills, and coordinating resources for patients' ongoing needs as well as treatment decision-making assistance and direct care (McCorkle et al., 1989; 2009; Jordhøy et al., 2001; Moore et al., 2002; Guo, 2005; Hudson et al., 2005; Li et al., 2006; Steel et al., 2007; 2011;Bakitas et al., 2009; Wang et al., 2010).

The pilot trial with HCC patients in the United States reported by Steel and colleagues (2007) deserves to be mentioned. In this individually tailored intervention, a combination of education, cognitive-behavioral therapy, and supportive-expressive therapy was delivered either in person or via phone (depending upon whether patients were undergoing treatments or were between treatments) to 28 hepatobiliary participants (among them 23 were HCC patients). Clinically although not statistically significant improvements of symptoms of depression and anxiety, and disease-related symptoms were shown for people randomized to the intervention arm who reported a minimally important difference (MID) (Cella et al., 2002) for emotional well-being, albeit with decrements in physical and functional well-being. However, the control group receiving only education also showed MID.

Education as the basic level of a psychosocial intervention (Cunningham, 2002; Rehse & Pukrop, 2003) has been integrated in most studies to improve patients' and families' outcomes across acute (Guo, 2005), unstable (Rummans et al., 2006), downward (McCorkle et al., 1989; 2009; Moore et al., 2002; Steel et al., 2007; 2011; Bakitas et al., 2009), and dying phases (Hudson et al., 2005; Li et al., 2006). However, one remarkable characteristic of nurse-led interventions (McCorkle et al., 1989; 2009; Moore et al., 2002; Hudson et al., 2005; Bakitas et al., 2009) that emerged in this review for advanced cancer patients was symptom management.

Wang and colleagues (2010) reported home care services in mainland China for cancer patients and their families. The intervention consisted of symptom monitoring, pain management, functional rehabilitation, nutritional guidance, and psychological as well as social support to both patients and families. Significant differences were found in patients' fatigue, nausea and vomiting, somnipathy, anepithymia, constipation, diarrhea, and overall QOL in comparison with the control group ($p < 0.01$); better QOL was also reported in families ($p < 0.01$). Results however have to be interpreted with caution because of insufficient details of the randomization process.

McCorkle and colleagues (1989) examined the effect of comprehensive home nursing service early in lung cancer patients' trajectory on distressing symptoms, functional status, health perceptions, and psychosocial concerns. Their intervention involved nursing care in symptom management, cancer coordination, appropriate referral, and team building. Results showed that home nursing care groups run by either oncology nurse specialists or interdisciplinary teams had less distress ($p = 0.03$) and greater independence 6 weeks longer ($p = 0.02$) albeit worse health perceptions ($p < 0.05$) than traditional care groups provided by physicians; no differences in pain, mood disturbance, or concerns were found between the intervention and control groups. This indicates that home nursing care may assist patients with forestalling distress from symptoms, maintaining longer independence, and holding realistic health perceptions congruent with their physical conditions.

This nurse-led comprehensive home care intervention was further tested in a sample of postsurgical women with gynecological cancers (McCorkle et al., 2009). In addition to clinical assessments, complication monitoring, teaching self-management skills, and coordinating resources by advanced practice nurse (APN) for patients' ongoing needs, a consultative psychiatric liaison nurse was added for additional psychological support. Results showed that the intervention group, particularly the subgroup receiving the tailored psychological support had less uncertainty, ($p = 0.02$) less symptom distress ($p < 0.0001$) and better QOL ($p \leq 0.0001$), which demonstrated the effects of this tailored intervention based on the standard nursing intervention protocol (SNIP) in improving QOL outcomes for people with advanced cancer (McCorkle et al., 2000).

Concerns about the lack of continuity of care for postoperative cancer patients were also revealed in the study by Moore and colleagues (2002). This study assessed the effectiveness of nurse-led follow-up for lung cancer patients who had completed initial treatment in comparison with conventional medical follow up in the United Kingdom. Clinical nurse specialists provided information and support monthly over the phone or in a clinic, and coordinated with other agencies or services. Compared with conventional medical follow-up, the intervention arm achieved less severe dyspnea at 3 months ($p = 0.03$), better emotional functioning ($p = 0.03$), and less peripheral neuropathy at 12 months ($p = 0.05$).

Bakitas and colleagues (2009) tested the effectiveness of APN-administered telephone-based intensive and ongoing assessment and coaching to 322 advanced cancer patients living in rural areas. Specifically, the intervention included symptom management, advance directive planning and treatment decision making, with an emphasis on communicating during anticancer treatments. The intervention also involved teaching patients and families to improve coping and problem-solving skills. This 3 year study revealed an intervention effect on improved QOL (the Functional Assessment of Chronic Illness Therapy for Palliative Care or FACIT-Pal, $p = 0.02$) (Lyons et al., 2009) and lower depressed mood (Center for Epidemiological Studies Depression Scale or CES-D, $p = 0.02$) (Okun et al., 1996). Symptom intensity measured with the Edmonton Symptom Assessment Scale (ESAS) (Bruera et al., 1991) was not significantly different between groups.

Control Condition

It is important to point out that intervention effect is context dependent, and results of intervention have to be interpreted in light of the context in which they were obtained, as changes in setting or point in time or a more homogeneous sample might produce different findings (Jordhøy et al., 2001).

The study conducted in Norway assessing the impact of multidisciplinary palliative care interventions at hospital and community levels to advanced cancer patients included systematic assessment of multiple domains of QOL by trained staff and coordinated follow-up by general practitioners and community nurses, but no significant difference was found in comparison with standard care (Jordhøy et al., 2001).

Li and colleagues (2006) conducted a 1 month comprehensive team intervention by surgeons, physicians, and nurses for 76 terminally ill cancer patients and their families in palliative care units of mainland China. The intervention included death education, pain relief, psychosocial support, and nutritional and other palliative therapies; the control group received usual care and was described as "[holistic care];" however, no criteria or necessary specific details were provided for the control condition. Although QOL and other indexes showed significant differences between groups ($p < 0.05$), it is difficult to interpret the results in comparison with the control group, could be identified to determine how it differed from those receiving usual care.

Only one non-pharmaceutical intervention for people diagnosed with HCC in mainland China designed by Guo (2005) deserves to be mentioned. This experiment involved an emotional intervention combined with Chinese medicated diet after TACE, while patients remained in the hospital. Specifically, patients were taught about treatments they were receiving, prognosis of the disease, relaxation via music, or meditation; Chinese medicated diet contained traditional Chinese medicine, tailored to the individual's physical condition, adjuvant with the treatments. After 2 months, the intervention arm showed significantly improved symptoms of fatigue, nausea, emesis, anorexia, and overall QOL ($p < 0.05$) as well as liver biological indexes ($p < 0.01$).

The results of this study have to be viewed with caution. First, the author who administered the interventions and also assessed the outcomes was not blinded to group assignment. Second, details about randomization and intervention procedures as well as effort of eliminating possible confounding factors were unable to be identified, making it difficult to interpret the results. Furthermore, as the time length of hospitalization after TACE in mainland China varied but generally within ≤ 2 weeks, making translating this 2 month intervention into practice problematic.

LIMITATIONS

Several limitations of this review should be noted. First, studies were reviewed based on CONSORT guidelines for randomized controlled trials (Boutron et al., 2008; Schulz et al., 2010) and graded using Stetler's level and quality of evidence (Stetler et al., 1998); evidence might have been further strengthened if all the reviewed studies had provided effect size and power analysis. In addition, the studies reviewed varied in sample homogeneity and attrition rates, as well as instruments selected for targeted outcomes, making interpretation of findings and comparison among studies difficult, if even possible.

Another limitation was associated with the unique challenge imposed by the specific population of interest. Studies for HCC in mainland China are underrepresented in this review because of a general lack of critical details required for reporting of RCT (Boutron et al., 2008), which precluded appraisal of studies on HCC in more detail. The setting was uniformly selected in tertiary, academic hospitals or urban communities, making generalization of findings with respect to rural areas questionable. For intervention components, few studies provided sufficient description of the procedure for tailoring the interventions to individual participants; for controls, there was generally no description of the care that the control group received, and regarding the intervention group, the number of sessions, timing of each session, duration of each session, duration of each main component of each session, and overall duration of the intervention were seldom described. In clinical practice in mainland China, social workers, chaplains, and psychologists are seldom involved, and the training needed for the professionals implementing the trials was not documented in either intervention or control groups.

Because of scant evidence for people diagnosed with advanced HCC in mainland China, we have extended our searching to advanced cancer patients in general as well as rigorously designed studies that show promise in the West. This evidence derived from the West might be argued to be not generalizable to a population in another country. It is important to note, however, that this generalization limitation poses challenges not for the current review alone; effective translation of research evidence outside the original setting is always a concern (Kirchhoff, 2004). Intervention effectiveness is not only associated with population and setting, but also the interaction of the intervention with subjects and context; and the latter can be hard to control even for studies conducted within the same culture and the same type of healthcare systems.

Finally, despite the comprehensive inclusion of PubMed and CAJ, search using these two databases may not be exhaustive for retrieving studies from the Western and Chinese literature, and further expansion is warranted.

CONCLUSIONS

HCC remains one of the most highly lethal cancers in the world. Ongoing close attention to the unique physiological and psychosocial concerns is crucial for the remaining QOL of people with advanced HCC throughout their cancer trajectory. Timely assessment and evaluation of symptoms present a particular challenge for people with HCC in mainland China, as the lack of standardization in treatment methodology and patient selection of TACE (Raoul et al., 2011) exacerbates the need of intensified monitoring of patients after this treatment. Moreover, most people are treated at tertiary care centers where they visit infrequently and travel long distances for evaluation and treatment, and this may have further restrained access to already limited resources.

In mainland China, in spite of the necessity of intensive follow-up for postoperative cancer patients after discharge (McCorkle et al., 2000), effort has been largely limited to the perioperative period during hospitalization, and people with advanced

HCC are confronted with a quickly progressive disease, limited treatment options, and inadequate care. Most patients enter a downward and dying phase soon after being discharged from the hospital. The time from discharge to the end of life is neglected. This review confirms and extends the findings of earlier work that education and psychosocial support combined with symptom management early in the illness trajectory may improve multiple domains of QOL for these patients. Nurse-led home-based comprehensive intervention delivered for postoperative follow-up either by telephone or face-to-face contact is most promising to improve QOL for people with advanced cancer in general and HCC in particular. The complex interplay of physical, psychological, social, and spiritual burdens experienced by these patients makes it paramount that interventions be designed using a collaborative care approach and conducted with the aim of providing comprehensive care to address multiple dimensions of QOL (Milone-Nuzzo & McCorkle, 2001; Sun et al., 2008; Zimmermann et al., 2008; Fielding, 2010).

One of the challenges for researchers in Eastern countries is how to appreciate and use evidence from the West. This generalization gap in geographic borderlines should not be overemphasized, as culture is only one of all those factors that could modify the intervention effect and there is no clear evidence of the impact of culture in determination of the intervention effect. There is little evidence, however, that strategies working well in Western countries will be as effective in mainland China, especially when insufficient data prevent making reasonable comparisons between the East and West (Wu et al., 2009). It is, therefore, warranted that promising clinical interventions aimed to improve quality of life for advanced cancer patients reported in Western literature be further tested in mainland China.

ACKNOWLEDGMENT

This study was supported by a grant from the National Institutes of Health (NIH) and the National Institutes of Nursing Research (NINR) through the Research Project Grant (R01) (Grant number NR011872, to Dr. McCorkle).

REFERENCES

Ahmed, N., Ahmedzai, S., Vora, V., et al. (2004). Supportive care for patients with gastrointestinal cancer (Review). *Cochrane Database of Systematic Reviews*, *3*, CD003445.

Allen, J. & Venook, A. (2004). Hepatocellular carcinoma: Epidemic and treatment. *Current Oncology Reports*, *6*, 177–183.

*Ando, M., Morita, T., Akechi, T., et al. (2010). Efficacy of short-term life-review interviews on the spiritual well-being of terminally ill cancer patients. *Journal of Pain and Symptom Management*, *39*, 993–1002.

Baker, F., Denniston, M., Zabora, J., et al. (2002). A POMS short form for cancer patients: psychometric and structural evaluation. *Psycho-oncology*, *11*, 273–281.

*Bakitas, M., Lyons, K.D., Hegel, M.T. et al. (2009). Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer: The project ENABLE II randomized controlled trial. *Journal of the American Medical Association*, *302*, 741–749.

Boutron, I., Moher, D., Altman, D.G., et al. (2008). Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. *Annals of Internal Medicine*, *148*, 295–309.

*Breitbart, W., Poppito, S., Rosenfeld, B., et al. (2012). Pilot randomized controlled trial of individual meaning-centered psychotherapy for patients with advanced cancer. *Journal of Clinical Oncology*, *30*, 1304–1309.

*Breitbart, W., Rosenfeld, B., Gibson, C. et al. (2010). Meaning-centered group psychotherapy for patients with advanced cancer: a pilot randomized controlled trial. *Psycho-oncology*, *19*, 21–28.

Bruera, E., Kuehn, N., Miller, M., et al. (1991). The Edmonton Symptom Assessment System (ESAS): a simple method for the assessment of palliative care patients. *Journal of Palliative Care*, *7*, 6–9.

Bruix, J. & Llovet, J. (2002). Prognostic prediction and treatment strategy in hepatocellular carcinoma. *Hepatology*, *35*, 519–524.

Bruix, J., Sala, M. & Llovet, J.M. (2004). Chemoembolization for hepatocellular carcinoma. *Gastroenterology*, *127*, S179–188.

Bruix, J. & Sherman, M. (2005). Management of hepatocellular carcinoma. *Hepatology*, *42*, 1208–1236.

Bruix, J. & Sherman, M. (2011). Management of hepatocellular carcinoma: An update. *Hepatology*, *53*, 1020–1022.

Cella, D., Hahn, E.A. & Dineen, K. (2002). Meaningful change in cancer-specific quality of life scores: differences between improvement and worsening. *Quality of Life Research*, *11*, 207–221.

*Chochinov, H.M., Kristjanson, L.J., Breitbart, W., et al. (2011). Effect of dignity therapy on distress and end–of-life experience in terminally ill patients: a randomised controlled trial. *Lancet Oncology*, *12*, 753–762.

Corbin, J.M. & Strauss, A. (1991). A nursing model for chronic illness management based upon the trajectory framework. *Scholarly Inquiry for Nursing Practice*, *5*, 155–174.

Cunningham, A.J. (2002). Group psychological therapy: An integral part of care for cancer patients. *Integrative Cancer Therapies*, *1*, 67–75.

Dong, G.L., Shen, M.Y., Shen, J., et al. (2009). Investigation and analysis on therapeutic compliance and its influential factors in hepatocellular carcinoma patients with transarterial chemoembolization [in Chinese]. *Nursing Journal of Chinese PLA*, *26*, 30–32.

Eltawil, K.M., Berry, R., Abdolell, M., et al. (2012). Quality of life and survival analysis of patients undergoing transarterial chemoembolization for primary hepatic malignancies: A prospective cohort study. *HPB (Oxford)*, *14*, 341–350.

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

Ferlay, J., Shin, H., Bray, F., et al. (2010). Estimates of worldwide burden of cancer in 2008: Globocan 2008. *International Journal of Cancer*, *127*, 2893–2917.

Fielding, R. (2010). Hepatobiliary cancer. In *Psycho-oncology*. Holland, J.C., Breitbart, P.B., Jacobsen, M.S., et al. (eds.), pp. 146–151. New York: Oxford University Press.

Forner, A., Llovet, J.M. & Bruix, J. (2012). Chemoembolization for intermediate HCC: Is there proof of survival benefit? *Journal of Hepatology*, *56*, 984–986.

Forner, A., Reig, M., de Lope, C., et al. (2010). Current strategy for staging and treatment: The BCLC update and future prospects. *Seminars in Liver Disease*, *30*, 61–74.

Fu, X.X. & Zhang, Y.C. (2007). Hospice in the perspective of anthropology. *Journal of Social Sciences*, *9*, 115–123.

*Guo, Y.M. (2005). Effects of emotional intervention and Chinese medicated diet in improving the quality of life in patients with liver cancer after chemotherapy [in Chinese]. *Chinese Journal of Clinical Rehabilitation*, *9*, 30–31.

Hall, S., Kolliakou, A., Petkova, H., et al. (2011). Interventions for improving palliative care for older people living in nursing care homes (Review). *Cochrane Database of Systematic Reviews*, *16*, CD007132.

*Hudson, P.L., Aranda, S. & Hayman–White, K. (2005). A psycho-educational intervention for family caregivers of patients receiving palliative care: A randomized controlled trial. *Journal of Pain and Symptom Management*, *30*, 329–341.

*Jordhøy, M.S., Fayers, P., Loge, J.H., et al. (2001). Quality of life in palliative cancer care. *Journal of Clinical Oncology*, *19*, 3884–3894.

Kirchhoff, K. T. (2004). State of the science of translational research: from demonstration projects to intervention testing. *Worldviews on Evidence-Based Nursing*, *1*, S6–12.

*Lee, A.M., Ho, J.W. & Chan, C.L. (2010). Efficacy of psychosocial intervention in improving quality of life and psychological well-being of Chinese patients with colorectal cancer: A randomised controlled trial, *Hong Kong Medical Journal*, *16*, 20–24.

*Li, Y.Q., Zhang, M.X., Fu, G.X., et al. (2006). Effect of hospice care on the quality of life and psychological state of aged dying inpatients (in Chinese). *Journal of Central South University (Med Sci)*, *31*, 538–542.

*Linn, M.W., Linn, B.S. & Harris, R. (1982). Effects of counseling for late stage cancer patients. *Cancer*, *49*, 1049–1055.

Llovet, J.M. & Bruix, J. (2003). Systematic review of randomized trials for unresectable hepatocellular carcinoma: Chemoembolization improves survival. *Hepatology*, *37*, 429–442.

Llovet, J.M., Di-Bisceglie, A.M., Bruix, J., et al. (2008a). Design and endpoints of clinical trials in hepatocellular carcinoma. *Journal of the National Cancer Institute*, *100*, 698–711.

Llovet, J.M., Real, M. & Montaña, X. (2002). Arterial embolisation or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: A randomised controlled trial. *Lancet*, *359*, 1734–1739.

Llovet, J.M., Ricci, S., Mazzaferro, V., et al. (2008b). Sorafenib in advanced hepatocellular carcinoma. *The New England Journal of Medicine*, *359*, 378–390.

Locke, D.E.C., Decker, P.A., Sloan, J.A. et al. (2007). Validation of single-item linear analog scale assessment of quality of life in neuro-oncology patients. *Journal of Pain and Symptom Management*, *34*, 628–638.

Lopez, P.M., Villanueva, A. & Llovet, J.M. (2006). Systematic review: Evidence-based management of hepatocellular carcinoma—An updated analysis of randomized controlled trials. *Alimentary Pharmacology &Therapeutics*, *23*, 1535–1547.

Lyons, K.D., Bakitas, M., Hegel, M.T., et al. (2009). Reliability and validity of the Functional Assessment of Chronic Illness Therapy-Palliative care (FACIT-Pal) scale. *Journal of Pain and Symptom Management*, *37*, 23–32.

*McCorkle, R., Benoliel, J.Q., Donaldson, G., et al. (1989). A randomized clinical trial of home nursing care for lung cancer patients. *Cancer*, *64*, 1375–1382.

*McCorkle, R., Dowd, M., Ercolano, E., et al. (2009). Effects of a nursing intervention on quality of life outcomes in pust-surgical women with gynecological cancers. *Psycho-oncology*, *18*, 62–70.

McCorkle, R., Hughes, L. & Robinson, L. (1998). Nursing interventions for newly diagnosed older cancer patients facing terminal illness. *Journal of Palliative Care*, *14*, 39–45.

McCorkle, R. & Pasacreta, V. (2001). Enhancing caregiver outcomes in palliative care. *Cancer Control*, *8*, 36–45.

McCorkle, R., Strumpf, N.E., Nuamah, I.F., et al. (2000). A specialized home care intervention improves survival among older post-surgical cancer patients. *Journal of the American Geriatrics Society*, *48*, 1707–1713.

McCorkle, R. & Young, K. (1978). Development of a symptom distress scale. *Cancer Nursing*, *1*, 373–378.

McGlynn, K.A. & London, W.T. (2005). Epidemiology and natural history of hepatocellular carcinoma. *Best Practice & Research. Clinical Gastroenterology*, *19*, 3–23.

McGlynn, K.A., Tsao, L., Hsing, A.W., et al. (2001). International trends and patterns of primary liver cancer. *International Journal of Cancer*, *94*, 290–296.

Milone-Nuzzo, P. & McCorkle, R. (2001). Home care. In *Textbook of Palliative Nursing*. Ferrell, B. R. & Coyle, N. (eds.), pp. 543–555. New York: Oxford University Press.

*Moore, S., Coner, J., Haviland, J., et al. (2002). Nurse led follow up and conventional medical follow up in management of patients with lung cancer: randomized trial. *British Medical Journal*, *325*, 1145–1151.

Oliveri, R.S., Wetterslev, J. & Gluud, C. (2011). Transarterial (chemo) embolisation for unresectable hepatocellular carcinoma (Review). *Cochrane Database of Systematic Reviews*, *16*, CD004787.

Okun, A., Stein, R.E., Bauman, L.J., et al. (1996). Content validity of the Psychiatric Symptom Index, CES-Depression Scale, and State-Trait Anxiety Inventory from the perspective of DSM-IV. *Psychological Reports*, *79*, 1059–1069.

Parkin, D., Bray, F., Ferly, J., et al. (2005). Global cancer statistics, 2002. *CA: A Cancer Journal for Clinicians*, *55*, 74–108.

Peterman, A.H., Fitchett, G., Brady, M.J., et al. (2002). Measuring spiritual well-being in people with cancer: The Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being Scale (FACIT-Sp). *Annals of Behavioral Medicine*, *24*, 49–58.

Poon, R.T., Fan, S.T., Tsang, F.H., et al. (2002). Locoregional therapies for hepatocellular carcinoma: a critical review from the surgeon's perspective. *Annals of Surgery*, *235*, 466–486.

Rampone, B., Schiavone, B., Martino, A., et al. (2009). Current management strategy of hepatocellular carcinoma. *World Journal of Gastroenterology*, *15*, 3210–3216.

Ramsey, D.E. & Geschwind, J.F. (2002). Chemoembolization of hepatocellular carcinoma—what to tell the skeptics: Review and meta-analysis. *Techniques in Vascular and Interventional Radiology*, *5*, 122–126.

Raoul, J.L., Sangro, B., Forner, A., et al. (2011). Evolving strategies for the management of intermediate-stage hepatocellular carcinoma: Available evidence and expert opinion on the use of transarterial chemoembolization. *Cancer Treatment Reviews*, *37*, 212–220.

Rehse, B. & Pukrop, R. (2003). Effects of psychosocial interventions on quality of life in adult cancer patients: meta analysis of 37 published controlled outcome studies. *Patient Education and Counseling*, *50*, 179–186.

Robinson, L., Nuamah, I.F., Cooley, M.E., et al. (1997). A test of the fit between the Corbin and Strauss trajectory model and care provided to older patients after cancer surgery. *Holistic Nursing Practice*, *12*, 36–47.

*Rummans, T.A., Clark, M.M., Sloan, J.A. et al. (2006). Impacting quality of life for patients with advanced cancer with a structured multidisciplinary intervention: A randomized controlled trial. *Journal of Clinical Oncology*, *24*, 635–642.

Schulz, K.F., Altman, D.G. & Moher, D. (2010). CONSORT 2010 Statement: Updated Guidelines for Reporting Parallel Group Randomized Trials. *Annals of Internal Medicine*, *152*, 726–732.

Steel, J., Baum, A. & Carr, B. (2004). Quality of life in patients diagnosed with primary hepatocellular carcinoma: Hepatic arterial infusion of Cisplatin versus 90-Yttrium microspheres (Therasphere). *Psycho-oncology*, *13* 73–79.

Steel, J.L., Eton, D.T., Cella, D., et al. (2006). Clinically meaningful changes in health-related quality of life in patients diagnosed with hepatobiliary carcinoma. *Annals of Oncology*, *17*, 304–312.

*Steel, J., Geller, D.A., Tsung, A., et al. (2011). Randomized controlled trial of a collaborative care intervention to manage cancer-related symptoms: lessons learned. *Clinical Trials*, *8*, 298–310.

*Steel, J.L., Nadeau, K., Olek, M., et al. (2007). Preliminary results of an individually tailored psychosocial intervention for patients with advanced hepatobiliary carcinoma. *Journal of Psychosocial Oncology*, *25*, 19–42.

Stehlin, J.S. & Beach, K.H. (1966). Psychological aspects of cancer therapy. *Journal of American Medical Association*, *197*, 100–104.

Stetler, C.B., Morsi, D., Rucki, S., et al. (1998). Utilization-focused integrative reviews in a nursing service. *Applied Nursing Research*, *11*, 195–206.

Sun, V., Ferrell, B., Juarez, G., et al. (2008). Symptom concerns and quality of life in hepatobiliary cancers. *Oncology Nursing Forum*, *35*, E45–E52.

Tedeschi, R.G. & Calhoun, L.G. (1996). The posttraumatic growth inventory: Measuring the positive legacy of trauma. *Journal of Traumatic Stress*, *9*, 455–471.

Teo, E.K. &, Fock, K.M. (2001). Hepatocellular carcinoma: an Asian perspective. *Digestive Diseases*, *19*, 263–268.

Toro, A., Pulvirenti, E., Palermo, F., et al. (2012). Health-related quality of life in patients with hepatocellular carcinoma after hepatic resection, transcatheter arterial chemoembolization, radiofrequency ablation or no treatment. *Surgical Oncology*, *21*, e23–30.

Vogl, T.J., Naguib, N.N., Nour-Eldin, N.E., et al. (2009). Review on transarterial chemoembolization in hepatocellular carcinoma: palliative, combined, neoadjuvant, bridging, and symptomatic indications. *European Journal of Radiology*, *72*, 505–516.

*Wang, J.F., Zhou, J.H. & Ma, X.Q. (2010). Community nursing intervention mode for tumor patients [in Chinese]. *Nursing Journal of Chinese PLA*, *27*, 881–884, 906.

Wu, M.C., Tang, Z.Y., Sun, Y., et al. (2011). Guideline for standardized treatment of primary liver cancer [in Chinese]. *Chinese Clinical Oncology*, *16*, 929–946.

Wu, P., Dugoua, J.J., Eyawo, O., et al. (2009). Traditional Chinese medicines in the treatment of hepatocellular cancers: a systematic review and meta-analysis. *Journal of Experimental & Clinical Cancer Research*, *28*, 112–124.

Yan, H. & Sellick, K. (2004). Symptoms, psychological distress, social support, and quality of life of Chinese patients newly diagnosed with gastrointestinal cancer. *Cancer Nursing*, *27*, 389–399.

Yuen, M.F., Hou, J.L., Chutaputti, A., et al. (2009). Hepatocellular carcinoma in the Asia pacific region. *Journal of Gastroenterology and Hepatology*, *24*, 346–353.

Zimmermann, C., Riechelmann, R., Krzyzanowska, M., et al. (2008). Effectiveness of specialized palliative care: a systematic review. *Journal of the American Medical Association*, *299*, 1698–1709.