Published in final edited form as:
Clin J Oncol Nurs. 2008 October ; 12(5): 759–766. doi:10.1188/08.CJON.759-766.

Symptom Management in Hepatocellular Carcinoma

Virginia Chih-Yi Sun, RN, MSN, ANP and
Senior Research Specialist, Nursing Research & Education, Division of Population Sciences, City of Hope, Duarte, CA

Linda Sarna, RN, DNSc, FAAN, AOCN
Professor, School of Nursing, University of California, Los Angeles, Los Angeles, CA

Abstract

Worldwide, hepatocellular carcinoma (HCC) causes approximately one million deaths every year. Due to advanced stage at diagnosis, HCC carries a five-year survival rate of <5%, if diagnosed with unresectable disease. Incidence for HCC is higher in males and individuals of Asian descent, where viral hepatitis is endemic and a leading cause of HCC. The purpose of this article is to provide an overview of the complexity in symptom management of patients with HCC. The occurrence of multiple symptoms in HCC patients is common, and may include pain, fatigue, weight loss, and obstructive syndromes such as ascites and jaundice. Because of the limitations in the efficacy of current treatment options for HCC, aggressive symptom management is key to preserving physical functioning and QOL in this cancer population. Oncology nurses can play an integral role in symptom management of HCC patients. A multidisciplinary team approach to symptom management of HCC patients is critical due to the multidimensionality of common symptoms in this cancer population.

Introduction

In the United States, an estimated 21,370 new cases of hepatocellular carcinoma (HCC) will be diagnosed, and an estimated 18,410 individuals will die of this cancer in 2007 (Jemal et al., 2008). Worldwide, HCC is the fifth most common of all malignancies and causes approximately one million deaths annually worldwide (McCracken et al., 2007). Incidence of HCC is highest in Africa and Asia, where viral hepatitis is endemic. In the US, HCC occurs more frequently in males and incidence rates in the African American population are twice as high as in Caucasians (Monto & Wright, 2001). HCC is often diagnosed at advanced stages and prognosis is generally poor when the tumor is unresectable. This extremely guarded prognosis is frequently coupled with severe symptom occurrence including pain, fatigue, anorexia, and ascites (Zhu, 2003). This in turn impacts patients' quality of life (QOL) and functional status. The purpose of this article is: 1) to describe the current state of the science on symptom management in HCC; 2) to utilize a clinical case presentation to describe the symptoms experienced by patients with HCC while receiving treatment; and 3) to identify nursing implications for the symptom management of HCC patients.

Epidemiology of HCC

Although uncommon in the United States and most developed countries, epidemiologic studies show that HCC is one of the world's most frequent malignancies. This is partially due to the fact that higher incidence rates are found in some of the most populous regions of the world,

Direct Correspondence to: Virginia Chih-Yi Sun, RN, MSN, ANP, Senior Research Specialist, City of Hope, Nursing Research and Education, Division of Population Sciences, 1500 East Duarte Road, Duarte, CA 91010, Ph: 626/256-HOPE ext. 63122, Fax: 626/301-8941, vsun@coh.org.

including Southeast Asia (i.e. China) and sub-Saharan Africa (Seeff, 2004). Chronic viral hepatitis, a critical risk factor for HCC, is also endemic in these regions. Other common risk factors in HCC include cirrhosis, aflatoxin exposure, alcohol, metabolic disorders such as hereditary hemochromatosis, tobacco, obesity, diabetes, dietary antioxidants, and anabolic steroids (Table 1).(Yu & Yuan, 2004).

The world age-adjusted incidence of HCC is 14.67 per 100,000 population for men and 4.92 for women (Di Bisceglie, 2002). Worldwide, HCC accounted for 5.6% of all human cancers (Bosch, Ribes, Diaz, & Cleries, 2004). The lowest rates are found in developed countries, and the highest in developing countries (Di Bisceglie, 2002). For example, China has the highest incidence rates overall, approaching 35 per 100,000 (Di Bisceglie, 2002). Conversely, incidence rates of HCC in the United States were relatively low (2.1 to 2.5) but within the last 15–20 years a gradual but apparent increase of about 80% in annual incidence rate has occurred (El-Serag & Mason, 1999). Overall, HCC is more common in men and tends to occur earlier in life (20–35 years of age) in countries with the highest incidence (Di Bisceglie, 2002). Mortality rates follow a similar pattern that is consistent with incidence rates, which translates into high lethality. Yearly fatality ratio is approximately one, which indicates that most cases do not survive more than a year (Bosch, Ribes, Diaz, & Cleries, 2004).

Incidence rates in the United States among ethnic groups are lowest in Caucasians, but increasing rates are found in Japanese, African American, Hispanics, Filipino, Chinese, and Korean populations (Bosch, Ribes, Diaz, & Cleries, 2004). Among men, a 1.3- to 10.9-fold excess in HCC mortality is observed in Asian immigrants in North America and Europe (Hanley, Choi, & Holowaty, 1995; Rosenblatt, Weiss, & Schwartz, 1996).

Current Management of HCC

The majority of treatments for HCC (surgical resection, chemoembolization, percutaneous ethanol injection (PEI), radiofrequency ablation, cryosurgery) are palliative in nature and require extensive follow-up patient care. At present, the only potentially curative treatment for HCC is partial hepatectomy, but only 20% are considered surgically resectable (Zhu, 2003). For more advanced and unresectable diseases, overall median survival is about 8 weeks (Leung & Johnson, 2001). Additionally, local recurrence will occur despite curative intent resection (Little & Fong, 2001). Although the perioperative mortality for partial hepatectomy is less than 5% in specialized centers, potential postoperative complications such as portal hypertension and ascites warrant extensive postoperative monitoring (Little & Fong, 2001). Complications associated with other local ablative therapies include hemorrhage, acute cholecystitis, liver infarction, bile duct necrosis, abscess formation, pleural effusions, and acute pancreatitis (Song, Ip, & Fong, 2004).

Surgical resections of varying degrees remain the gold standard of treatment for HCC. Perioperative mortality for this population can be less than 5% as a result of advances in surgical technologies (Carr, 2004). Although post-surgical recurrence rates have decreased and survival has increased over the last two decades, most patients still have only a 50% 5-year survival rate (Carr, 2004). The most important parameter to be considered in choosing patients for partial hepatectomy is baseline hepatic function (Song, Ip, & Fong, 2004). The most commonly used evaluation tool for patients being considered for partial hepatectomy remains the Child-Pugh-Turcotte grading system (Child & Turcotte, 1964; Pugh et al., 1973) (Table 2). This prognostic tool has been reported to be useful in predicting peri- and post-operative mortality in abdominal surgery patients with cirrhosis (Mansour et al., 1997; Garrison et al., 1984). A numerical score is assigned for a patient in each parameter (albumin, bilirubin, prothrombin time, ascites, encephalopathy), and patients are then categorized into Child A (5–7 points), B (8–11 points), or C (12–15 points), with class C patients presenting with the most abnormalities within each

parameter. Other factors that dictate resectability include absence of extrahepatic lesions, size of residual liver, and expertise of the surgical team (Song, Ip, & Fong, 2004). Perioperative mortality and post-operative morbidity is largely dependent on the presence or absence of cirrhosis. HCC patients with cirrhotic livers have thrombocytopenia, coagulopathy, and varices, which increases the likelihood of operative bleeding. An increasing array of localized semisurgical treatments has become widely accepted. These include percutaneous ethanol injection, radiofrequency ablation, and cryotherapy (Carr, 2004). Local ablative therapies are generally useful in patients with multiple lesions and also as a method to preserve residual liver function when used in combination with surgery. Liver transplantation is a final option for patients with inoperable HCC, but rigorous eligibility criteria must be fulfilled in order for HCC patients to compete for healthy livers.

Transarterial chemoembolization (TACE) is the localized intraarterial delivery of chemotherapeutic agents that are emulsified in an oily medium and combined with embolic material. The rationale behind this type of localized treatment arose from the observation that normal liver tissue receives up to 80% of its blood supply from the portal vein, while liver tumors receive all of its blood supply from the hepatic artery. Hence, it is logical to use the hepatic artery as a means to target liver tumors while preserving normal liver function (Ramsey, Kernagis, Soulen, & Geschwind, 2002). The partial or complete occlusion of the hepatic artery induces tumor necrosis but will not affect normal liver tissue since the blood supply route is different. The goal of chemoembolization treatment is to deliver a highly concentrated dose of chemotherapy directly to the tumor cells. A second objective is to preserve as much functional liver tissue as possible. Significant improvements in long-term survival have been demonstrated, but have yet to be supported by randomized trials. A recent meta-analysis has demonstrated that the four RCTs comparing TACE patients with untreated controls have failed to show an effect on patient survival (Geschwind, Ramsey, Choti, Thuluvath, & Huncharek, 2003). Systemic chemotherapy have been extensively studied in HCC, but few published data have been able to show a response rate of >20% and show no survival benefit when compared with supportive care alone (Carr, 2004).

Selective internal radiation therapy (SIRT) using radiolabeled microspheres is a fairly new therapeutic option for patients with HCC. These microspheres are administered intraarterially, resulting in high radiation doses delivered to the arterial-fed tumors while sparing normal liver parenchyma (Geschwind et al., 2004). One-year survival rate for patients treated with these microspheres are reported to be around 63%. This survival rate is similar to those reported in patients receiving TACE (Geschwind et al., 2004). Side effect profile is similar to those seen in other localized procedures such as TACE, with mild abdominal pain, nausea, and fever being most commonly reported (Popperl, Helmberger, Munzing, Schmid, Jacobs, & Tatsch, 2005).

The search for novel agents in the treatment of HCC has focused on targeted therapies in recent years. One of these agents is sorafenib, an oral multikinase inhibitor of Raf kinase and receptor tyrosine kinases that has been approved for renal cell carcinoma. A phase II study tested the efficacy of sorafenib (400 mg BID) in a population of HCC patients with inoperable disease, no prior systemic treatments, and Child-Pugh class A or B. Results showed that sorafenib had modest efficacy with 33.6% of patients (n=137) achieving stable disease for at least 16 weeks (Abou-Alfa et al., 2006). Median overall survival was 9.2 months (Abou-Alfa et al., 2006). In this study, grade 3 or 4 toxicities included fatigue (9.5%), diarrhea (8%), and hand-foot skin reactions (5.1%) (Abou-Alfa et al., 2006). A subsequent randomized, placebo-controlled phase III study known as the SHARP trial was conducted to evaluate the efficacy and safety of sorafenib (400 mg BID) versus placebo. Inclusion criteria included patients with advanced measurable HCC, no prior systemic treatments, ECOG performance status of 0–2, and Child-Pugh class A. Results suggest that sorafenib was superior in median overall survival (10.7 vs. 7.9 months), which represents a 44% overall survival improvement (Llovet et al., 2007). Most

frequent grade 3 or 4 toxicities included diarrhea (11% vs. 2%), hand-foot skin reactions (8% vs. 1%), and fatigue (10% vs. 15%) (Llovet et al., 2007). The placebo group had higher percentages of fatigue (15% vs. 10%) and bleeding (9% vs. 6%). Although sorafenib was the first agent in decades to have demonstrated statistically significant improvements in survival for advanced HCC patients, some caution needs to be considered. The agent was tested only in patients with Child-Pugh class A and those with high performance status, and therefore would only benefit those patients that fit this category. It is not known whether the agent is efficacious for patients who have lower performance status and higher Child-Pugh scores.

Clinical Case Presentation

Mr. S was an otherwise healthy 67-year-old gentleman who presented with diarrhea and abdominal bloating following a course of antibiotics for treatment of a tooth abscess. He complained of persistent abdominal pain and swelling after completion of antibiotics, and was found to have a liver mass through CT scan and ultrasound. A subsequent biopsy revealed well-differentiated HCC. The tumor was approximately 6 cm. in size and located in the center of the left lobe. At the time of diagnosis, patient was also noted to have moderate ascites. Patient did not have a history of viral hepatitis although his antibody titers were positive on screening. Comorbidities include diabetes that is well-controlled through insulin. He was also noted to have moderate bilateral peripheral edema of the lower extremities. Upon further evaluation, patient has a Child-Pugh C (elevated PT, elevated total bilirubin, lowered albumin, moderate ascites) classification. Although the size and location of the tumor is surgically resectable, the patient's Child's classification makes surgery unsafe. Patient was referred for chemoembolization. Aldactone and Lasix were prescribed for his ascites. He also needed frequent paracentesis. Prior to his illness, Mr. S worked as an insurance agent and was a math major in college. He lives with his wife and has two grown children who are all supportive. Mr. S is a member of the local Greek Orthodox Church, and he reports no history of tobacco, alcohol, or drug use. There was also no family history of hepatitis or HCC.

Mr. S was scheduled for chemoembolization procedure using doxorubicin, mitomycin C, and cisplatin. However, his procedure was considered unsuccessful due to significant intratumoral AV shunting. He tolerated the procedure well with no severe post-embolization syndrome except for mild transient abdominal pain, mild fatigue, and no fevers. Subsequently, his ascites gradually returned, and patient began to experience mild abdominal distention and pain. Liver function tests were also increasing two days post-procedure. After discharge, patient had increasing abdominal distension refractory to medications as well as dyspnea, and paracentesis was performed. Due to decreasing performance status and worsening liver function, patient was not a candidate for further treatment.

Signs, Symptoms, and their Management in HCC

Table 4 provides a detailed list of the common symptoms in HCC and treatment strategies. Patients with HCC are usually asymptomatic during the early stages of disease. Unfortunately, 80% of patients with HCC will be diagnosed with advanced stage disease (Cahill & Braccia, 2004). Between 90–95% of HCC patients will present with the triad of right upper quadrant pain, palpable mass, and weight loss (Bartlett, Carr, & Marsh, 2005). Patients typically present with an enlarged, irregular, and nodular liver. Other physical findings include hepatic bruits (25%), ascites, splenomegaly, jaundice, wasting, and fever. Liver function tests and jaundice may not appear until late in the disease trajectory because of the organ's functional reserve capability (Cahill & Braccia, 2004). Table 3 provides a list of common signs and symptoms in HCC.

HCC patients in the terminal stage of disease may present with a variety of symptoms related to decompensated cirrhosis. These include ascites, variceal bleeding, peripheral edema, and

hepatic encephalopathy (Lin, Wu, Tsai, Lin, Chen, & Hwang, 2004). In a cohort of HCC patients in Taiwan, the most common symptom was abdominal pain (75.5%), which originated from enlarged tumor mass and was characterized as dull visceral pain (Lin, Wu, Tsai, Lin, Chen, & Hwang, 2004). Other common complaints include fatigue or weakness, peripheral edema, cachexia, ascites, dyspnea, anorexia, and vomiting (Lin, Wu, Tsai, Lin, Chen, & Hwang, 2004). Patients diagnosed with HCC were found to have the third highest reported level of psychiatric distress among patients with eight other types of cancer (Zabora, BrintzenhofeSzoc, Curbow, Hooker, & Piantadosi, 2001).

Cancer patients experience a significant number of symptoms as a direct or indirect result of disease, treatment, and comorbidities. Symptoms as experienced by cancer patients are often complex, multifactorial, and challenging to manage. To date, the majority of symptom-related research is focused on a single symptom. However, symptom presentation is not reduced to the experience of a single symptom alone. In fact, this experience includes multiple symptoms, and the relationship between these symptoms, their underlying mechanisms, and impact on patient outcomes are still being explored. Furthermore, it is well-documented that unrelieved symptoms have a negative effect on patient outcomes, including functional status, mood states, and quality of life (QOL) (Miaskowski, 2004).

The concept of symptom clusters has gained incredible momentum in symptom-related research in the past few years. Although the occurrence of multiple symptoms has been studied in the past (Sarna, 1993), it is only recently that this phenomenon was labeled “symptom clusters.” Currently, there are several working definitions for symptom clusters in nursing research. Dodd and colleagues (2001) defines symptom clusters as three or more concurrent symptoms that are related to each other but may not share a common etiology. Kim and colleagues (2005) developed a more comprehensive definition of symptom clusters through a review of symptom clusters research. Symptom clusters consist of 2 or more symptoms that are related to each other and that occur together (Kim, McGuire, Tulman, & Barsevick, 2005). The clusters are composed of stable groups of symptoms, are relatively independent from other clusters, and may uncover specific underlying dimensions of symptoms. Symptoms within a cluster may or may not share a common etiology, and the relationship among symptoms within a cluster is associative rather than causal (Kim, McGuire, Tulman, & Barsevick, 2005).

The exploration of potential symptom clusters is critical to the development of effective symptom management strategies for HCC patients. This understanding is of particular importance in caring for HCC patients with unresectable, metastatic disease. The identification of clusters specific to therapies such as surgery, chemotherapy, and liver-directed therapies will also contribute to the specific symptom management needs of HCC patients based on treatment modalities.

Pain

Pain is one of the most common and distressing symptoms in cancer patients. Abdominal pain is common in hepatocellular carcinoma. This is due primarily to visceral involvement that originates from a primary or metastatic lesion involving the abdominal or pelvic viscera (Mercandante, 2002). Treatment-related pain is also common in HCC patients. In most HCC patients treated with transarterial chemoembolization (TACE), a post-embolization syndrome occurs in 80% to 90% of patients (Ramsey, Kernagis, Soulen, & Geschwind, 2002). This syndrome often includes abdominal pain, ileus, fever, nausea, and vomiting, and it can last from hours to days (Ramsey, Kernagis, Soulen, & Geschwind, 2002). Pain can occur during as well as after TACE, and patients who did not experience distressing levels of pain during the procedure are also vulnerable to post-procedural pain (Lee, Hahn, & Park, 2001).

The treatment of pain in HCC patients begins with a comprehensive assessment of the clinical characteristic of visceral pain. Referred visceral pain in HCC is often found in the right shoulder (Mercadante, 2002). When pain is severe, opioid analgesic remains the gold standard. There are several options for the delivery of opioids (oral, parenteral, transdermal, transmucosal/sublingual, rectal, spinal). Indications in terms of route of administration must be determined based on patient ability to use the specific route, efficacy of the route in delivering adequate analgesia, ease of use for patient and family, associated complications, and cost (Mercadante, 2002). In the setting of visceral pain, NSAIDS have been found to produce a similar analgesic effect to those produced by opioids. They are particularly useful when pain is mild (Mercadante, Casuccio, Agnello, Pumo, Kargar, & Garofalo, 1999).

Fatigue

Another common and distressing symptom in cancer patients is fatigue. HCC patients experience fatigue due to terminal illness as well as fatigue related to treatment modalities. Fatigue is part of the post-embolization syndrome associated with TACE. Patients usually experience mild to moderate levels of fatigue that peaks on the second day after TACE (Shun et al., 2005). Although fatigue level gradually decreases two days post-treatment, level of fatigue is higher than pretreatment six days post-treatment (Shun et al., 2005). The pattern of fatigue in patients undergoing TACE with the chemotherapy Adriamycin is similar to the pattern found following systemic administration of the same agent (Lai et al., 2007).

Fatigue management in HCC patients should begin with an in-depth assessment of the following contributing factors: pain, emotional distress, sleep disturbance, anemia, nutritional deficiencies, deconditioning, and comorbidities (Mock, 2004). Treating these factors as an initial approach may increase the tolerability of fatigue. Pharmacologic interventions are targeted toward the contributing factor associated with fatigue: erythropoietin for chemotherapy-induced anemia, antidepressants when depression is a cause of fatigue, and psychostimulants to increase energy level. There is some evidence in the literature to support the use of methylphenidate in reducing fatigue in advanced cancer (Bruera et al., 2006). There is considerable evidence in the current literature to support the efficacy of nonpharmacologic interventions such as aerobic exercise on fatigue reduction (Schwartz et al., 2003; Courneya et al., 2003; Segal et al., 2003; Mock et al., 1997; Dimeo et al., 1999). Counseling on proper sleep hygiene and energy conservation tips are helpful self-care strategies that patients can utilize at home. A careful review of patients' medications may identify adverse effects that aggravate fatigue.

Anorexia-Cachexia

Weight loss is a frequent problem in cancer patients, including HCC patients. The incidence of weight loss is greater than 54% in most cancer patients and incidence reaches 80% in the terminal stage (Strasser & Bruera, 2002). Cachexia can be separated into primary (metabolic) and secondary (starvation) cachexia. Anorexia is besides weight loss, a leading symptom of the primary metabolic cachexia syndrome, therefore a common term for cancer wasting syndrome is anorexia-cachexia syndrome (Strasser & Bruera, 2002). The diagnosis of ACS is based on simple assessment of weight loss and anorexia, but currently no established tools or guidelines are available to distinguish primary and secondary cachexia. Other parameters, such as hypoalbuminemia, asthenia, chronic nausea, reduced caloric intake, or clinical judgment of reduced muscle and fat mass can serve as additional criteria for the presence of cachexia (Strasser & Bruera, 2002). These criteria can be helpful in HCC patients with relevant fluid retention (ascites, edema) where the extent of weight loss is masked by the accumulation of excess fluid (Strasser, 2000).

The management of anorexia/cachexia syndrome in HCC patients begins with a thorough assessment of potential contributors such as chronic nausea, constipation, early satiety, taste alterations, and depression (Del Fabbro, Dalal, & Bruera, 2006). Pharmacologically, at least 15 RCTs have demonstrated that megestrol acetate (doses ranging from 160 to 1600 mg/day) significantly improves appetite when compared to placebo (Lopez, Roque-Figuls, & Cuchi, 2004). Artificial nutrition such as total parenteral nutrition is frequently used but has not been shown to increase lean body mass (Muscaritoli, Bossola, Aversa, Bellantone, & Rossi Fanelli, 2006). Individualized dietary counseling in recent RCTs in cancer patients is effective in improving patient's food intake, nutritional status, and QOL (Ravasco, Monteiro-Grillo, Vidal, & Camilo, 2005).

Obstructive Syndromes

Jaundice presents in 19% to 40% of patients with HCC at the time of diagnosis and usually occurs in later stages (Qin & Tang, 2003). Only 1–12% of HCC patients present with obstructive jaundice as the initial clinical symptom (Lai & Lau, 2006). Obstructive jaundice occurs secondary to diffuse tumor invasion of the liver parenchyma or progressive liver failure. Intraductal tumor growth may occur in the common hepatic duct and/or common bile duct causing obstructive jaundice (Qin & Tang, 2003). Jaundice is not necessarily a harbinger of advanced disease nor a contraindication for aggressive treatment such as surgery.

The management of obstructive jaundice in HCC patients can be achieved using percutaneous drainage or the placement of a biliary stent. Cholestatic pruritus associated with obstructive jaundice can be managed using cholestyramine to decrease the enterohepatic circulation of bile acids (Jones & Bergasa, 2000). Other self-care measures include the use of emollients to maintain skin moisture and the use of mild and fragrant free soaps to prevent skin irritation that may further exacerbate pruritus (Cherny, 2002).

The accumulation of ascites is a result of an imbalance in the normal state of influx and efflux of fluid from the peritoneal cavity. This decreased rate of efflux may occur as a result of lymphatic blockage from tumor invasion (Keen & Fallon, 2002). Symptoms related to ascites include increased intra-abdominal pressure, abdominal wall discomfort, dyspnea, anorexia, early satiety, nausea and vomiting, esophageal reflux, pain, and peripheral edema (Keen & Fallon, 2002).

Diuretics remain the gold standard in management of ascites in cancer patients. The rates of response to diuretics range from 38% to 86% (Gough & Balderson, 1993; Greenway, Johnson, & Williams, 1982). A potassium-sparing diuretic in combination with a loop diuretic is helpful in the treatment of ascites secondary to hepatic cirrhosis (Keen & Fallon, 2002). Abdominal paracentesis remain the most commonly used procedure for the management of ascites. This procedure affords quick symptomatic relief and is useful in HCC patients when diurectics are either ineffective or requires a significant lag period prior to efficacy.

Managing the Side Effects of Sorafenib

As shown in pivotal clinical trials for HCC, common side effects from sorafenib include fatigue, diarrhea, and hand-foot skin reactions. The drug should be taken on an empty stomach 1 hour before meals or 2 hours after (Woods, 2006). For management of fatigue, encourage open-communication between patients and providers regarding the assessment and follow-up of fatigue. Patients should be encouraged to stay as active as possible, and to maintain a balanced diet with adequate fluid intake. Detailed assessment of baseline bowel habits and stool consistencies will aid in the selection of proper treatment for diarrhea. If needed, loperamide (Imodium) or diphenoxylate (Lomotil) can be initiated on a prn basis. Dermatologic reactions associated with sorafenib include dry skin, rash, pruritus, blistering, desquamation,

and calluses (Woods, 2006). Areas of hyperkeratosis are commonly found in the soles of the feet, which may result in thick calluses (Woods, 2006). Although there is no empirical evidence to support the use of topical ointments to control dermatologic toxicities, anecdotal reports suggest that they may be helpful in minimizing the effects of skin reactions. Patients can be advised to use non-fragrant lotions and soaps, and to maintain skin moisture. In more severe cases, treatment interruption or dose reductions are warranted, but discontinuation of treatment is rare (Woods, 2006).

Nursing Implications

HCC is a leading cause of cancer-related mortality worldwide. This is primarily related to the high incidence of unresectable, metastatic disease within this cancer population, which inevitably leads to poor prognosis. Therefore, aggressive symptom management of disease- and treatment-related symptoms is particularly critical in preserving the functional status and QOL in HCC patients with unresectable, advanced disease. Oncology nurses can impact the care of HCC patients through several methods. First, nurses should become familiar with the established guidelines for the management of common cancer-related symptoms such as pain, fatigue, and weight loss. These guidelines are largely based on evidence presented in the current literature, and they should be used as tools to aid in developing individualized strategies for symptom management based on patient preferences, physical status, and disease condition. In addition, nurses can provide counseling and education for HCC patients on disease- and treatment-related symptoms commonly seen in this cancer population. Finally, nurses can bridge the communication of symptoms between patients and clinicians through advocacy and thorough symptom assessment of HCC patients. Early identification of symptom burden can facilitate the prompt referral of HCC patients to experts in supportive care services (nutrition, rehab, pain specialist) for symptom control.

The complex interplay of physical, psychological, social, spiritual, existential, medical, financial and social burdens experienced by those facing HCC make it imperative that an integrative team approach be used. Quality symptom management can best be delivered in a collaborative environment that integrates the skills of medicine, nursing and supportive care professionals. The interdisciplinary model of care encourages collaboration, and members of the team working proactively to care for the symptom needs of patients. Furthermore, an interdisciplinary model of care provides an opportunity to administer tailored interventions of symptom management, since the model is completely driven by the needs of patients individually rather as a group.

Conclusions

There is considerable evidence pointing to the symptom burden experienced by HCC patients. While much of the current literature addresses single symptoms in isolation, there is an important and relevant need to assess and manage multiple symptoms in HCC. Symptom management and relief is a relevant topic in the discipline of nursing, and nurses are ideally positioned to impact patient outcomes through effective clinical assessment and management of cancer-related symptoms. It is imperative for nurses to foster collaborative, multidisciplinary methods of symptom management to impact physical functioning and QOL in HCC.

At a Glance

1. Symptoms are common and potentially distressing in hepatocellular carcinoma (HCC) due to advanced disease and guarded prognosis.

2. Aggressive symptom management using an interdisciplinary model is key to maintaining quality of life (QOL) in HCC patients and should be initiated at diagnosis.
3. Oncology nurses must be aware of the impact of multiple symptoms in HCC patients.

Acknowledgments

Supported by an NIH/NINR Predoctoral Fellowship (T32 NR007077)

References

Bartlett, DL.; Carr, BI.; Marsh, JW. Cancer of the liver. In: DeVita, J.; Vincent, T.; Hellman, S.; Rosenberg, SA., editors. Cancer: Principles & practice of oncology. 7th ed.. Philadelphia: Lippincott Williams & Wilkins; 2005. p. 986-1008.

Bosch FX, Ribes J, Diaz M, Cleries R. Primary liver cancer: Worldwide incidence and trends. Gastroenterology 2004;127:S5–S16. [PubMed: 15508102]

Bruera E, Valero V, Driver L, Shen L, Willey J, Zhang T, et al. Patient-controlled methylphenidate for cancer fatigue: a double-blind, randomized, placebo-controlled trial. Journal of Clinical Oncology 2006;24(13):2073–2078. [PubMed: 16648508]

Cahill BA, Braccia D. Current treatment for hepatocellular carcinoma. Clin J Oncol Nurs 2004;8(4):393–399. [PubMed: 15354926]

Carr BI. Hepatocellular carcinoma: Current management and future trends. Gastroenterology 2004;127:S218–S224. [PubMed: 15508087]

Cherny, NI. Jaundice in gastrointestinal malignancy. In: Ripamonti, C.; Bruera, E., editors. Gastrointestinal symptoms in advanced cancer patients. New York: Oxford University Press, Inc; 2002. p. 291-298.

Child, C.; Turcotte, J. Surgery and portal hypertension. In: Child, C., editor. The liver and portal hypertension. Philadelphia: Saunders; 1964. p. 50-62.

Courneya KS, Mackey JR, Bell GJ, Jones LW, Field CJ, Fairey AS. Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: Cardiopulmonary and quality of life outcomes. J Clin Oncol 2003;21(9):1660–1668. [PubMed: 12721239]

Del Fabbro E, Dalal S, Bruera E. Symptom control in palliative care--part ii: Cachexia/anorexia and fatigue. J Palliat Med 2006;9(2):409–421. [PubMed: 16629571]

Di Bisceglie AM. Epidemiology and clinical presentation of hepatocellular carcinoma. J Vasc Interv Radiol 2002;13(9 Pt 2):S169–S171. [PubMed: 12354833]

Dimeo FC, Stieglitz RD, Novelli-Fischer U, Fetscher S, Keul J. Effects of physical activity on the fatigue and psychologic status of cancer patients during chemotherapy. Cancer 1999;85(10):2273–2277. [PubMed: 10326708]

Dodd MJ, Miaskowski C, Paul SM. Symptom clusters and their effect on the functional status of patients with cancer. Oncol Nurs Forum 2001;28(3):465–470. [PubMed: 11338755]

El-Serag HB, Mason AC. Rising incidence of hepatocellular carcinoma in the united states. N Engl J Med 1999;340(10):745–750. [PubMed: 10072408]

Garrison RN, Cryer HM, Howard DA, et al. Clarification of risk factors for abdominal operations in patients with hepatic cirrhosis. Ann Surg 1984;199:648–655. [PubMed: 6732310]

Geschwind JF, Ramsey DE, Choti MA, Thuluvath PJ, Huncharek MS. Chemoembolization of hepatocellular carcinoma: Results of a metaanalysis. Am J Clin Oncol 2003;26(4):344–349. [PubMed: 12902882]

Geschwind JF, Salem R, Carr BI, Soulen MC, Thurston KG, Goin KA, et al. Yttrium-90 microspheres for the treatment of hepatocellular carcinoma. Gastroenterology 2004;127:S194–S205. [PubMed: 15508085]

Gough IR, Balderson GA. Malignant ascites. A comparison of peritoneovenous shunting and nonoperative management. Cancer 1993;71(7):2377–2382. [PubMed: 7680947]

Greenway B, Johnson PJ, Williams R. Control of malignant ascites with spironolactone. Br J Surg 1982;69(8):441–442. [PubMed: 7049306]

Hanley AJ, Choi BC, Holowaty EJ. Cancer mortality among chinese migrants: A review. Int J Epidemiol 1995;24(2):255–265. [PubMed: 7635584]

Hwang SJ, Tong MJ, Lai PP, Ko ES, Co RL, Chien D, et al. Evaluation of hepatitis b and c viral markers: Clinical significance in asian and caucasian patients with hepatocellular carcinoma in the united states of america. J Gastroenterol Hepatol 1996;11(10):949–954. [PubMed: 8912133]

Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. CA Cancer J Clin 2007;57 (1):43–66. [PubMed: 17237035]

Jones EA, Bergasa NV. Evolving concepts of the pathogenesis and treatment of the pruritus of cholestasis. Can J Gastroenterol 2000;14(1):33–40. [PubMed: 10655025]

Kadry, Z.; Furukawa, H.; Todo, S.; Clavien, AP. Assessment of liver function and mass in cirrhotic and noncirrhotic livers. In: Clavien, PA.; Fong, Y.; Lyerly, H.; Morse, MA.; Venook, AP., editors. Malignant liver tumors: current and emerging therapies. 2nd edition. Sudbury, MA: Jones and Bartlett; 2004.

Keen, J.; Fallon, M. Malignant ascites. In: Ripamonti, C.; Bruera, E., editors. Gastrointestinal symptoms in advanced cancer patients. New York: Oxford University Press, Inc; 2002. p. 279-290.

Kim HJ, McGuire DB, Tulman L, Barsevick AM. Symptom clusters: Concept analysis and clinical implications for cancer nursing. Cancer Nurs 2005;28(4):270–282. quiz 283-274. [PubMed: 16046888]

Lai EC, Lau WY. Hepatocellular carcinoma presenting with obstructive jaundice. ANZ J Surg 2006;76 (7):631–636. [PubMed: 16813631]

Lai YH, Shun SC, Hsiao YL, Chiou JF, Wei LL, Tsai JT, et al. Fatigue experiences in hepatocellular carcinoma patients during six weeks of stereotactic radiotherapy. Oncologist 2007;12(2):221–230. [PubMed: 17296818]

Lee SH, Hahn ST, Park SH. Intraarterial lidocaine administration for relief of pain resulting from transarterial chemoembolization of hepatocellular carcinoma: Its effectiveness and optimal timing of administration. Cardiovasc Intervent Radiol 2001;24(6):368–371. [PubMed: 11907741]

Leung TW, Johnson PJ. Systemic therapy for hepatocellular carcinoma. Semin Oncol 2001;28(5):514–520. [PubMed: 11685744]

Lin MH, Wu PY, Tsai ST, Lin CL, Chen TW, Hwang SJ. Hospice palliative care for patients with hepatocellular carcinoma in taiwan. Palliat Med 2004;18(2):93–99. [PubMed: 15046405]

Little SA, Fong Y. Hepatocellular carcinoma: Current surgical management. Semin Oncol 2001;28(5): 474–486. [PubMed: 11685740]

Lopez A, Roque Figuls M, Cuchi G. Systematic review of megestrol acetate in the treatment of anorexia-cachexia syndrome. Journal of Pain and Symptom Management 2004;27:360–369. [PubMed: 15050664]

Mansour A, Watson W, Shayani V, et al. Abdominal operations in patients with liver cirrhosis: still a major surgical challenge. Surgery 1997;122:730–736. [PubMed: 9347849]

Marrero JA, Fontana RJ, Fu S, Conjeevaram HS, Su GL, Lok AS. Alcohol, tobacco and obesity are synergistic risk factors for hepatocellular carcinoma. J Hepatol 2005;42(2):218–224. [PubMed: 15664247]

McCracken M, Olsen M, Chen MS Jr, Jemal A, Thun M, Cokkinides V, et al. Cancer incidence, mortality, and associated risk factors among Asian Americans of Chinese, Filipino, Vietnamese, Korean, and Japanese ethnicities. CA A Cancer Journal for Clinicians 2007;57(4):190–205. [PubMed: 17626117]

Mercadante, S. Abdominal pain. In: Ripamonti, C.; Bruera, E., editors. Gastrointestinal symptoms in advanced cancer patients. New York: Oxford University Press, Inc; 2002. p. 223-234.

Mercadante S, Casuccio A, Agnello A, Pumo S, Kargar J, Garofalo S. Analgesic effects of nonsteroidal anti-inflammatory drugs in cancer pain due to somatic or visceral mechanisms. J Pain Symptom Manage 1999;17(5):351–356. [PubMed: 10355213]

Miaskowski C, Dodd M, Lee K. Symptom clusters: The new frontier in symptom management research. J Natl Cancer Inst Monogr 2004;(32):17–21. [PubMed: 15263036]

Mock V. Evidence-based treatment for cancer-related fatigue. J Natl Cancer Inst Monogr 2004;(32):112–118. [PubMed: 15263051]

Mock V, Dow KH, Meares CJ, Grimm PM, Dienemann JA, Haisfield-Wolfe ME, et al. Effects of exercise on fatigue, physical functioning, and emotional distress during radiation therapy for breast cancer. Oncol Nurs Forum 1997;24(6):991–1000. [PubMed: 9243585]

Monto A, Wright TL. The epidemiology and prevention of hepatocellular carcinoma. Semin Oncol 2001;28(5):441–449. [PubMed: 11685737]

Muscaritoli M, Bossola M, Aversa Z, Bellantone R, Rossi Fanelli F. Prevention and treatment of cancer cachexia: New insights into an old problem. Eur J Cancer 2006;42(1):31–41. [PubMed: 16314085]

Poon RT, Fan ST, Yu WC, Lam BK, Chan FY, Wong J. A prospective longitudinal study of quality of life after resection of hepatocellular carcinoma. Arch Surg 2001;136(6):693–699. [PubMed: 11387012]

Popperl G, Helmberger T, Munzing W, Schmid R, Jacobs TF, Tatsch K. Selective internal radiation therapy with sir-spheres in patients with nonresectable liver tumors. Cancer Biother Radiopharm 2005;20(2):200–208. [PubMed: 15869456]

Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. Br J Surg 1973;60(8):646–649. [PubMed: 4541913]

Qin LX, Tang ZY. Hepatocellular carcinoma with obstructive jaundice: Diagnosis, treatment and prognosis. World J Gastroenterol 2003;9(3):385–391. [PubMed: 12632482]

Ramsey DE, Kernagis LY, Soulen MC, Geschwind JF. Chemoembolization of hepatocellular carcinoma. J Vasc Interv Radiol 2002;13(9 Pt 2):S211–S221. [PubMed: 12354839]

Ravasco P, Monteiro-Grillo I, Vidal PM, Camilo ME. Dietary counseling improves patient outcomes: A prospective, randomized, controlled trial in colorectal cancer patients undergoing radiotherapy. J Clin Oncol 2005;23(7):1431–1438. [PubMed: 15684319]

Rosenblatt KA, Weiss NS, Schwartz SM. Liver cancer in asian migrants to the united states and their descendants. Cancer Causes Control 1996;7(3):345–350. [PubMed: 8734828]

Sarna L. Correlates of symptom distress in women with lung cancer. Cancer Pract 1993;1(1):21–28. [PubMed: 8324526]

Schwartz AL, Mori M, Gao R, Nail LM, King ME. Exercise reduces daily fatigue in women with breast cancer receiving chemotherapy. Med Sci Sports Exerc 2001;33(5):718–723. [PubMed: 11323538]

Seeff LB. Introduction: The burden of hepatocellular carcinoma. Gastroenterology 2004;127(5 Suppl 1):S1–S4. [PubMed: 15508071]

Segal RJ, Reid RD, Courneya KS, Malone SC, Parliament MB, Scott CG, et al. Resistance exercise in men receiving androgen deprivation therapy for prostate cancer. J Clin Oncol 2003;21(9):1653–1659. [PubMed: 12721238]

Shun SC, Lai YH, Jing TT, Jeng C, Lee FY, Hu LS, et al. Fatigue patterns and correlates in male liver cancer patients receiving transcatheter hepatic arterial chemoembolization. Support Care Cancer 2005;13(5):311–317. [PubMed: 15611851]

Song TJ, Ip EW, Fong Y. Hepatocellular carcinoma: Current surgical management. Gastroenterology 2004;127:S248–S260. [PubMed: 15508091]

Strasser F. Impact of fluid retention on evaluation of cancer cachexia. Supplement to Supportive Care in Cancer 2000;8(3):249.

Strasser, F.; Bruera, E. Cancer anorexia/cachexia syndrome: Epidemiology, pathogenesis, and assessment. In: Ripamonti, C.; Bruera, E., editors. Gastrointestinal symptoms in advanced cancer patients. New York: Oxford University Press, Inc; 2002. p. 39-80.

Yu MC, Yuan JM. Environmental factors and risk for hepatocellular carcinoma. Gastroenterology 2004;127:S72–S78. [PubMed: 15508106]

Zabora J, BrintzenhofeSzoc K, Curbow B, Hooker C, Piantadosi S. The prevalence of psychological distress by cancer site. Psychooncology 2001;10(1):19–28. [PubMed: 11180574]

Zhu AX. Hepatocellular carcinoma: Are we making progress? Cancer Invest 2003;21(3):418–428. [PubMed: 12901288]

Table 1

Risk Factors of Pancreatic Cancer[8]

Smoking
Genetics (familial pancreatic cancer, BRCA-2)
Age
Diabetes Mellitus
Pancreatitis
Dietary carcinogens
Obesity

Table 2

Child-Pugh Classification

Points	1	2	3
Albumin	>35	30–35	<30
Bilirubin	<50	50–75	>75
Prothrombin time	>60	40–60	<40
Ascites	None	Mild	Tense
Encephalopathy	None	I–II	III–IV
Child-Pugh grade: sum of individual points for the above 5 variables. A: 5–6; B: 7–9; C: 10–15			

Source: Kadry, Z., Furukawa, H., Todo, S., & Clavien, A.P. (2004). Assessment of liver function and mass in cirrhotic and noncirrhotic livers. In P.A. Clavien, Y. Fong, H. Lyerly, M.A. Morse, A.P. Venook (Eds.), *Malignant liver tumors: current and emerging therapies, 2nd edition.* Sudbury, MA: Jones and Bartlett.

Table 3

Commons Signs and Symptoms of HCC

Right upper quadrant pain
Palpable liver mass
Nodular liver
Weight loss
Hepatic bruits
Ascites
Pruritus
Splenomegaly
Jaundice
Fever
Peripheral edema
Nausea and vomiting
Asthenia
Early satiety

Source: Di Bisceglie, A. M. (2002). Epidemiology and clinical presentation of hepatocellular carcinoma. *J Vasc Interv Radiol*, *13*(9 Pt 2), S169–171.

Table 4

Management of common symptoms in HCC

Symptom	Treatment
Abdominal pain	• Opioid analgesics (moderate to severe) • NSAIDS (mild)
Fatigue	Treatment of contributing factors, if indicated: • Anemia (erythropoietin) • Antidepressants (depression) • Sleep disturbance • Nutritional deficiencies • Deconditioning (exercise) • Decreased energy level (psychostimulants)
Anorexia/cachexia	Treatment of contributing factors, if indicated: • Chronic nausea (antiemetics) • Constipation (laxatives) • Antidepressants (depression) Pharmacologic: • Megestrol acetate Others: • Artificial nutrition • Dietary counseling
Ascites	Pharmacologic: • Diuretics (potassium-sparing + loop) Procedural: • Paracentesis
Jaundice secondary to biliary obstruction	• Percutaneous drainage • Biliary stent For cholestatic pruritus: • Cholestyramine • Self-care measures (emollients, perfume-free soaps)

Source: NCCN Clinical Guidelines for Adult Cancer Pain, V.1.2006 ; NCCN Clinical Guidelines for Cancer-Related Fatigue, V.2.2007; Del Fabbro, E., Dalal, S., & Bruera, E. (2006). Symptom control in palliative care--part ii: Cachexia/anorexia and fatigue. *J Palliat Med, 9*(2), 409–421; Greenway, B., Johnson, P. J., & Williams, R. (1982). Control of malignant ascites with spironolactone. *Br J Surg, 69*(8), 441–442; Jones, E. A., & Bergasa, N. V. (2000). Evolving concepts of the pathogenesis and treatment of the pruritus of cholestasis. *Can J Gastroenterol, 14*(1), 33–40.