

This material is protected by U.S. copyright law. Unauthorized reproduction is prohibited. To purchase quantity reprints, please e-mail reprints@ons.org or to request permission to reproduce multiple copies, please e-mail pubpermissions@ons.org.

Symptom Concerns and Quality of Life in Hepatobiliary Cancers

Virginia Sun, RN, MSN, ANP, Betty Ferrell, RN, PhD, FAAN, Gloria Juarez, RN, PhD,
Lawrence D. Wagman, MD, Yun Yen, MD, PhD, and Vincent Chung, MD

Purpose/Objectives: To describe the symptom concerns of patients with hepatocellular carcinoma (HCC) and pancreatic cancer and explore the effect of symptoms on patients' quality of life (QOL).

Design: Descriptive, longitudinal study.

Setting: Ambulatory clinics of a comprehensive cancer center.

Sample: 45 patients actively receiving treatment for either HCC or pancreatic cancer.

Methods: Patients were followed from baseline for three months, with outcome measures repeated monthly. Outcome measures included the Functional Assessment of Cancer Therapy–Hepatobiliary (FACT-Hep) and the Functional Assessment of Chronic Illness Therapy–Spirituality Subscale (FACIT-Sp-12). Descriptive analysis of demographic, treatment, and symptom data was conducted, followed by two-way repeated measures analysis of variance of FACT-Hep and FACIT-Sp-12 scale scores by diagnosis and treatment type.

Main Research Variables: Symptoms, QOL.

Findings: Overall QOL is poor in patients with hepatobiliary cancer, and this trend continues over time. Symptoms such as abdominal pain, fatigue, weight loss, and poor appetite commonly are reported in this population.

Conclusions: Patients with hepatobiliary cancer suffer from multiple symptoms that may have a negative affect on overall QOL. Specific QOL domains, such as physical and functional well-being, are of particular concern for patients.

Implications for Nursing: The identification of specific symptom and QOL concerns in hepatobiliary cancers will enhance clinical care and aid in the future development of multidisciplinary interventions for this understudied cancer population.

Key Points . . .

- ▶ Patients with hepatobiliary cancers experience high levels of symptom burden because of advanced stages of disease that may affect overall quality of life (QOL).
- ▶ Overall QOL remains poor through treatment, with pain, fatigue, weight loss, and poor appetite of greatest concern to patients.
- ▶ Future research with this understudied cancer population is necessary to determine specific individual, disease, and treatment-related factors that influence overall QOL.

disorders, and fatigue (Zhu, 2003). Multiple symptom occurrences result in a rapid decline in patients' function and quality of life (QOL) and increases morbidity and mortality. Treatment modalities often lead to post-treatment morbidity and symptom burden, with modest or no improvements in survival, particularly for patients with pancreatic cancer. Consequently, patients with hepatobiliary cancers are vulnerable to disease and treatment-related symptoms that may negatively affect overall QOL. Despite these concerns, only a limited number of studies in the literature have addressed symptoms and QOL in patients with HCC. The primary

Virginia Sun, RN, MSN, ANP, is a senior research specialist, Betty Ferrell, RN, PhD, FAAN, is a research scientist, and Gloria Juarez, RN, PhD, is an assistant research scientist, all in the Department of Nursing Research and Education at City of Hope in Duarte, CA; Lawrence D. Wagman, MD, is the executive medical director at St. Joseph's Hospital Cancer Center in Orange, CA; and Yun Yen, MD, PhD, is an associate director of translational research and a professor and staff physician and Vincent Chung, MD, is an assistant professor and staff physician, both in the Department of Medical Oncology and Therapeutics Research at City of Hope. This study was supported by the ONS Foundation 2005 Trish Greene Memorial Grant. (Submitted August 2007. Accepted for publication October 8, 2007.)

Digital Object Identifier: 10.1188/08.ONF.E45-E52

In the United States, an estimated 59,000 new cases of hepatobiliary cancers will be diagnosed in the year 2008, and approximately 52,700 people will die from them (Jemal et al., 2008). The most commonly diagnosed hepatobiliary cancers are hepatocellular carcinoma (HCC) and pancreatic cancer. Worldwide, HCC is the fifth most common of all malignancies and causes approximately one million deaths annually (McCracken et al., 2007). Pancreatic cancer is the 10th leading cause of all new cancer cases for men and the fourth leading cause of death across genders (Jemal et al.). These dismal statistics reflect the reality that hepatobiliary cancers often are diagnosed at advanced stages with poor prognosis and frequently are coupled with severe symptom occurrence, including pain, anorexia, mood

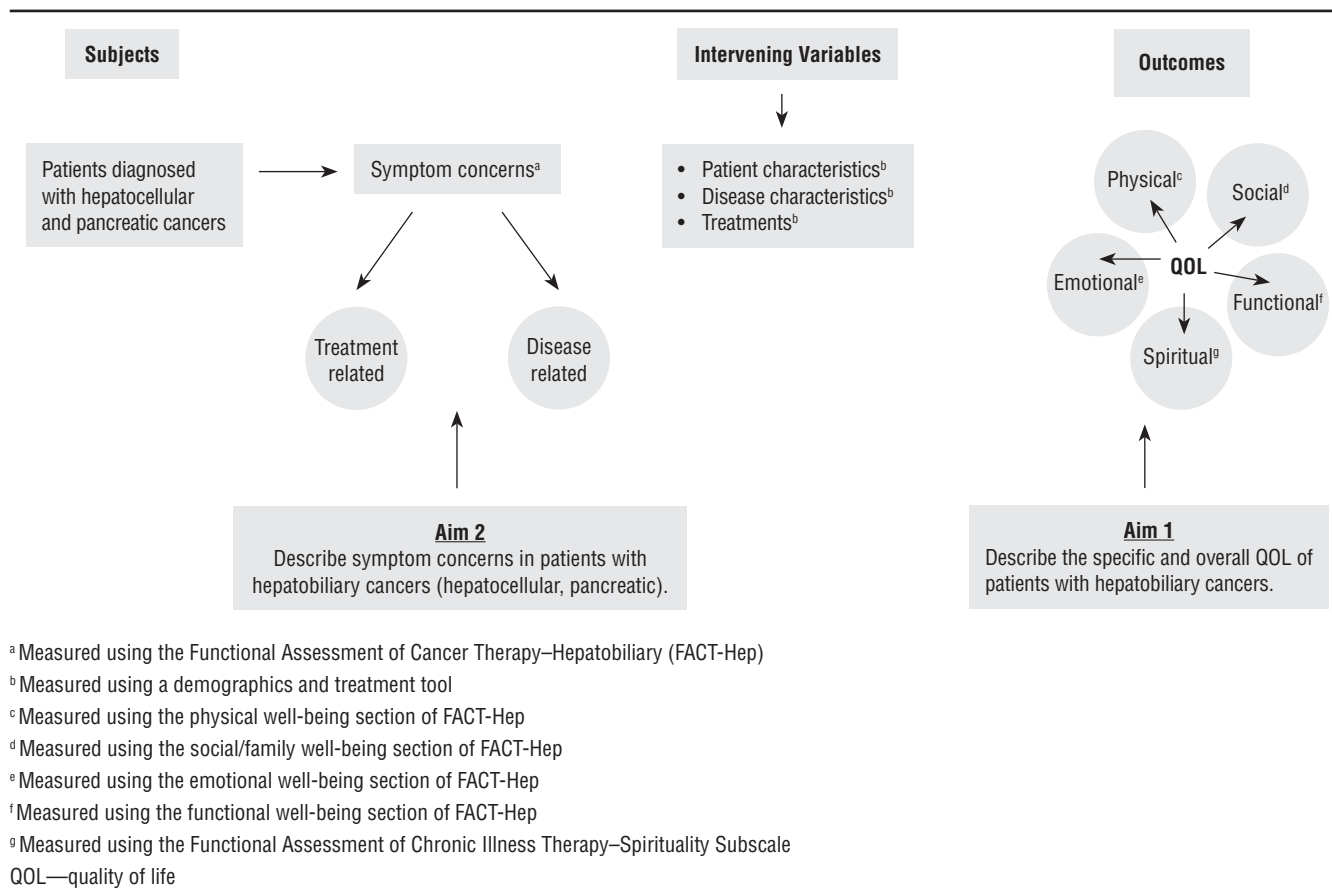


Figure 1. Study Model

purpose of this study was to describe specific symptom concerns and their effect on overall QOL in patients with HCC or pancreatic cancer.

Literature Review

The effect of disease on overall QOL in patients with HCC has been reported in the literature. Overall QOL has been found to be poorer in patients with HCC when compared to a general healthy population (Steel, Chopra, Olek, & Carr, 2007). Perception of QOL in patients with pancreatic cancer was found to be mediated not by symptom burden but rather by coping processes. Patients' perceived threat of symptoms and effectiveness of chosen coping strategies were more important (Fitzsimmons, George, Payne, & Johnson, 1999). Incidence of specific symptoms such as depression is higher in patients diagnosed with HCC (Steel, Geller, Gamblin, Olek, & Carr, 2007) and pancreatic cancer (Carney, Jones, Woolson, Noyes, & Doebbeling, 2003; Kelsen et al., 1995; Passik & Roth, 1999). In addition, psychological distress is found to be higher in patients diagnosed with pancreatic cancer when compared with malignancies in other sites (Zabora, BrintzenhofeSzoc, Curbow, Hooker, & Piantadosi, 2001). Common symptoms of pancreatic cancer include pain (82%), anorexia (64%), early satiety (62%), and weight loss (51%) (Krech & Walsh, 1991). Fatigue, loss of appetite, and impaired sense of overall well-being also have been reported (Labori, Hjermsstad, Wester, Buanes, & Loge, 2006). Sexual functioning was found to be poorer in patients

with HCC when compared to a general healthy population (Steel, Hess, Tunke, Chopra, & Carr, 2005). Reduced QOL in patients with HCC also has been related to factors such as comorbidities, younger age, and sleep disorders and specific symptoms such as pain (Bianchi et al., 2003).

The advancement in technology has yielded new treatment modalities in hepatobiliary cancers, particularly for HCC. Patients with HCC treated with 90-Yttrium microspheres reported better QOL when compared to patients receiving chemotherapy through hepatic arterial infusions (Steel, Baum, & Carr, 2004). Fatigue is common among patients with HCC after transcatheter hepatic arterial chemoembolization (TACE) and stereotactic radiation (Lai et al., 2007; Shun et al., 2005). Factors such as pretreatment fatigue, sleep disturbance, depression, and overall symptom distress predicted fatigue changes after treatment (Lai et al.). Patients who received TACE followed by radiofrequency ablation had significantly higher QOL with better social and functional well-being when compared to patients who received only TACE three months after treatment (Wang et al., 2007). Factors such as liver function, recurrence, complications, and age predicted QOL post-treatment (Wang et al.). With surgical interventions, significant improvements in overall QOL have been reported three months after resection of HCC (Eid et al., 2006; Poon et al., 2001). Assessment of patients treated with major hepatic resection, minor hepatic resection, and hepatic ablation following a diagnosis of HCC found little difference in overall QOL between treatment groups (Eid et al.). Common issues after pancreaticoduodenectomy were related to pancreatic exocrine and endocrine insufficiency, and included

Table 1. Demographics and Disease Characteristics

| Variable | Hepatocellular Carcinoma (N = 22) | | Pancreatic (N = 23) | |
|----------------------------------|-----------------------------------|----|---------------------|-----|
| | n | % | n | % |
| Gender | | | | |
| Male | 16 | 72 | 13 | 56 |
| Female | 6 | 28 | 10 | 44 |
| Ethnicity | | | | |
| Caucasian | 8 | 36 | 15 | 65 |
| Asian | 6 | 27 | 4 | 17 |
| Hispanic | 6 | 27 | 2 | 9 |
| African American | 1 | 5 | 1 | 4 |
| Native American | 1 | 5 | — | — |
| Other | — | — | 1 | 4 |
| Education | | | | |
| High school or less | 13 | 59 | 3 | 13 |
| College | 6 | 27 | 11 | 48 |
| Graduate | 3 | 14 | 9 | 39 |
| Marital status | | | | |
| Married | 14 | 64 | 18 | 78 |
| Not married | 8 | 36 | 5 | 22 |
| Religion | | | | |
| Catholic | 10 | 46 | 7 | 30 |
| Protestant | 4 | 18 | 6 | 26 |
| Other | 6 | 27 | 6 | 26 |
| None | 2 | 9 | 4 | 17 |
| Employment status | | | | |
| Employed | 4 | 18 | 8 | 35 |
| Retired | 11 | 50 | 8 | 35 |
| Other | 7 | 32 | 7 | 30 |
| Stage of disease | | | | |
| I–III | 7 | 33 | 10 | 46 |
| IV | 14 | 67 | 12 | 55 |
| Treatment | | | | |
| Surgery | 10 | 46 | — | — |
| Chemotherapy | 6 | 27 | 23 | 100 |
| Chemoembolization | 6 | 27 | — | — |
| Previous surgery | | | | |
| Yes | 9 | 41 | 14 | 64 |
| No | 13 | 59 | 8 | 36 |
| Previous chemotherapy | | | | |
| Yes | 7 | 32 | 14 | 67 |
| No | 15 | 68 | 7 | 33 |
| Previous radiation | | | | |
| Yes | 1 | 5 | 5 | 22 |
| No | 20 | 95 | 18 | 78 |
| Comorbidities^a | | | | |
| Diabetes | 4 | 25 | 8 | 67 |
| Hepatitis | 9 | 56 | — | — |
| Liver cirrhosis | 8 | 50 | 1 | 8 |

^a Data are presented for pertinent items only.

Note. Because of missing data, not all n values total the sample size. Also, because of rounding, not all percentages total 100.

weight loss, abdominal pain, fatigue, foul-smelling stools, and diabetes (Huang et al., 2000).

The effect of QOL on survival in patients with hepatobiliary cancers has been explored; this area is of interest because cur-

rent treatment modalities for hepatobiliary cancers, particularly pancreatic cancer, produce very modest survival benefits. Specific domains of QOL, such as physical and functional status, predicted longer survival in patients with unresectable HCC (Yeo et al., 2006). In the same cohort, lower appetite scores, advanced stages of disease, and higher liver dysfunction all independently predicted shorter survival (Yeo et al.). Better global QOL and family functioning were significantly associated with survival in a cohort of patients with pancreatic cancer, even after controlling for stage at diagnosis (Lis, Gupta, & Grutsch, 2006). In pancreatic cancer, patients who initially had jaundice had shorter intervals between symptom onset and first medical treatment, thereby leading to a significantly better prognosis (Watanabe et al., 2004). Conversely, patients who initially had back pain had a significantly worse prognosis. (Watanabe et al.). The level of depression, however, did not predict survival among patients with pancreatic cancer (Sheibani-Rad & Velanovich, 2006).

Finally, two studies addressed the needs of family caregivers of patients with hepatobiliary cancer. Coleman et al. (2005) found that family members were more likely than patients to access a pancreatic, cancer-specific Web site chat room for information and support. Questions posted on the Web site focused on end-of-life issues and symptoms, and pain was the most commonly cited symptom. In a separate study, Nolan et al. (2006) found that a large number of postings by family members on the same Web site addressed spirituality, and many family members returned to the site and posted information after the death of their loved ones.

Overall, the current literature clearly has documented that QOL is an important issue in hepatobiliary cancer, and individual, disease, and treatment-related factors can mediate or moderate patients' perceptions of QOL. Although the importance of QOL to patients with hepatobiliary cancer has been supported, additional research is warranted to clarify the specific components of QOL in this understudied cancer population. The current study attempted to address the following questions: What are the specific domains (physical, social, emotional, functional, spiritual) and overall QOL for patients receiving active treatment for hepatobiliary cancer? What are the specific symptom concerns for these patients related to their disease and treatments?

Conceptual Framework

Figure 1 presents the study model. This model is based on QOL research conducted at a National Cancer Institute–designated comprehensive cancer center since the mid-1980s (Ersek, Ferrell, Dow, & Melancon, 1997; Ferrell, Grant, Padilla, Vemuri, & Rhiner, 1991; Ferrell, Dow, Leigh, Ly & Gulasekaram, 1995; Ferrell et al., 1996; Ferrell, Grant, Funk, Otis-Green, & Garcia, 1997a, 1997b, 1998;). The model demonstrates that subjects (in this case, patients with HCC and pancreatic cancer) are expected to experience symptoms that are disease and treatment related. These symptoms may influence QOL across physical, social, emotional, functional, and spiritual domains. Other intervening variables that may affect QOL outcomes included patient characteristics, disease characteristics, treatment modality, and comorbidities. Study aims were listed under the corresponding sections in the model. Measures used to collect data on pertinent variables and outcomes were noted within each corresponding section of the model.

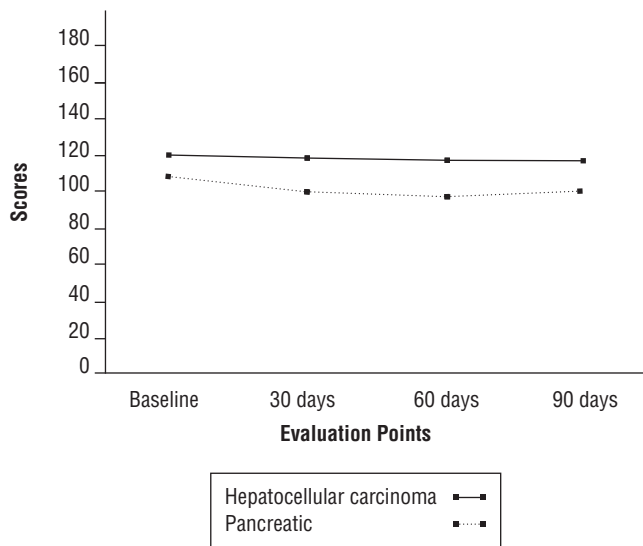


Figure 2. Overall Quality of Life (Functional Assessment of Cancer Therapy–Hepatobiliary)

Methods

Procedure

Approval from an institutional review board was obtained prior to study initiation. Research nurses approached patients who met eligibility criteria during regularly scheduled clinic visits. Written informed consent was obtained from patients prior to participation in the study. Participants provided demographic and disease data at baseline along with other outcome measures to assess symptoms and overall QOL across the six domains in the study model. All outcome measures were repeated monthly after baseline for a total of three months.

Sample and Setting

Study participants were recruited from the medical and surgical oncology ambulatory care clinics at an NCI-designated comprehensive cancer center. Eligibility criteria included a diagnosis of HCC or pancreatic cancer, at least age 18, and ability to understand English. The eligibility criteria were intended to maximize study accrual and to allow the investigators to collect as much information as possible to describe this understudied cancer population.

Outcome Measures

Investigators developed a demographic and treatment data tool to compile information on each participant at baseline. Demographic information such as age, ethnicity, education level, religious affiliation, marital status, living situation, employment status, and annual income were collected using this tool. The tool also was designed to capture key disease and treatment variables of importance in describing the sample population and for analysis of influencing variables.

The **Functional Assessment of Cancer Therapy—Hepatobiliary (FACT-Hep)** is a cancer-specific version of the Functional Assessment of Chronic Illness Therapy (FACIT) measurement system (Cella, 2005). The FACT-Hep is developed specifically for use in patients with hepatobiliary cancers. It contains the original FACT-General (FACT-G)

scales that include a 27-item compilation of general questions divided into four primary QOL domains: physical, social/family, emotional, and functional well-being. An additional 18 questions that assess symptom and QOL concerns pertinent to patients with hepatobiliary cancer were included. All the disease-specific QOL tools in the FACT system include the original FACT-G as well as a disease-specific subscale. All items are scored from 0–4, with higher overall and subscale scores indicating better QOL. Cronbach alpha was 0.94 and test-retest reliability of 0.90 has been reported (Heffernan et al., 2002). Alpha coefficients for the subscales ranged from 0.72 for the social/family domain to 0.84 for the functional domain; these alphas improved at retest (Heffernan et al.).

The **FACIT-Spirituality Subscale (FACIT-Sp-12)** (Peterman, Fitchett, Brady, Hernandez, & Cella, 2002) assesses the spiritual well-being of patients living with a chronic illness. It measures a sense of meaning and peace, and also assesses the role of faith in illness. The tool contains 12 items scored at a range of 0–4, with higher overall and subscale scores indicating better quality of life. Items are divided into two subscales: meaning/peace and faith. Cronbach alpha for the FACIT-Sp-12 was 0.87, and subscale coefficients ranged from 0.81 for the meaning/peace domain to 0.88 for the faith domain (Peterman et al.). A separate tool was chosen to measure spirituality, primarily because the overall QOL tool for the study did not contain a measure of this domain.

Data Analysis

The specific aims of this study were accomplished primarily through quantitative methods, which included a descriptive, longitudinal design to describe symptoms and QOL in patients with hepatobiliary cancers. The Power Analysis and Sample Size software was used to compute power and sample size requirements that called for testing relationships using Pearson correlations between QOL subscale scores and symptom scores. This required calculating five Pearson correlations at each of four time periods, or a total of 20 correlation coefficients. Because of inflation of alpha created by conducting multiple statistical tests, a conservative alpha of 0.01 was selected. A sample size of 42 subjects provided 80% power to detect a difference between null correlation of 0.0 and alteration correlation of 0.5 using a two-sided Fisher's two-tailed test at 0.01 significance level.

Analysis included tabulation of standard summary statistics of demographic characteristics, disease/treatment characteristics, and all scores at each time point. In addition, descriptive statistics for individual QOL items, domain scores, symptom subscale scores, and total QOL scores were computed for each evaluation period. Pearson correlation coefficients between the symptom score and each of the QOL scale scores were computed for all four evaluation periods. Mean scores for each QOL and the symptom scores were plotted in a multiple line graph during the four evaluation periods to detect trends over time. Descriptive analysis of demographic, treatment, and symptom data was conducted, followed by two-way repeated measures analysis of variance (ANOVA) of FACT-Hep and FACIT-Sp-12 scale scores by diagnosis and type of treatment.

Results

A total of 45 participants were accrued to the study and had complete data that was evaluable. The mean age of these participants was 59 years, and 64% were male. This is comparable to

Table 2. Quality of Life (QOL) Scores by Diagnoses Over Time

| Time | QOL Subscale | | | | | | | | | | | |
|--------------------------|--------------------------|-----|------------------------|-----|---------------------------|-----|----------------------------|-----|--|------|------------------------------|------|
| | Physical (Range 0–28) | | Social (Range 0–28) | | Emotional (Range 0–24) | | Functional (Range 0–28) | | Disease-Specific Symptoms (Range 0–72) | | Overall QOL (Range 0–180) | |
| | \bar{X} | SD | \bar{X} | SD | \bar{X} | SD | \bar{X} | SD | \bar{X} | SD | \bar{X} | SD |
| Baseline | | | | | | | | | | | | |
| Hepatocellular carcinoma | 14.9 | 6.6 | 22.1 | 4.7 | 14.8 | 5.5 | 13.5 | 4.9 | 45.3 | 10.6 | 110.6 | 23.1 |
| Pancreatic | 16.9 | 6.8 | 23.1 | 3.8 | 14.4 | 6.3 | 13.9 | 6.7 | 49.5 | 11.8 | 118.0 | 28.9 |
| One month | | | | | | | | | | | | |
| Hepatocellular carcinoma | 9.2 | 6.0 | 22.2 | 5.2 | 12.6 | 5.9 | 14.4 | 5.7 | 42.8 | 11.8 | 101.4 | 23.4 |
| Pancreatic | 13.4 | 7.4 | 24.4 | 3.0 | 14.0 | 6.3 | 15.2 | 7.2 | 48.8 | 11.6 | 116.0 | 28.6 |
| Two months | | | | | | | | | | | | |
| Hepatocellular carcinoma | 8.9 | 5.7 | 22.4 | 6.5 | 11.7 | 5.5 | 13.9 | 4.2 | 41.2 | 10.2 | 98.2 | 21.5 |
| Pancreatic | 12.1 | 7.8 | 24.9 | 3.0 | 12.8 | 5.8 | 16.7 | 4.8 | 48.8 | 10.5 | 115.5 | 27.1 |
| Three months | | | | | | | | | | | | |
| Hepatocellular carcinoma | 9.0 | 5.6 | 22.0 | 6.3 | 11.8 | 5.8 | 14.6 | 3.8 | 42.9 | 8.8 | 100.3 | 16.9 |
| Pancreatic | 12.5 | 8.1 | 23.9 | 4.1 | 13.4 | 6.3 | 16.4 | 4.8 | 48.2 | 10.8 | 114.6 | 28.4 |

the general hepatobiliary cancer population, where incidences are higher in men and older age (Jemal et al., 2008). The sample included 51% Caucasian, 22% Asian, 18% Hispanic, and 4% African American participants. More than half of the Hispanic and Asian participants in the study were diagnosed with HCC, whereas most Caucasian participants were diagnosed with pancreatic cancer. Seventy percent of participants were married and reported living with either a spouse or children. The majority of participants (65%) had a college education or graduate degree, and 36% had an educational level of high school or less. Participants diagnosed with HCC were more likely to have an educational level of high school or less, whereas patients diagnosed with pancreatic cancer were more likely to have a college or graduate level education. Most participants (42%) were retired, and 27% were disabled as a result of their cancer diagnosis.

In terms of disease-specific variables, the study sample included 22 patients with HCC and 23 patients with pancreatic cancer. The majority of participants had stage III (26%) or IV (61%) disease at the time of accrual; 82% had been diagnosed recently, and 13% had recurrent disease. More than half of patients had undergone some type of surgery for their cancer. Forty-six percent of those who had previous surgery were in the HCC group. Having a diagnosis of pancreatic cancer was associated significantly with previous chemotherapy. Almost 30% of participants reported having diabetes, and 20% reported being diagnosed with hepatitis. Complete demographic data by diagnosis is provided in Table 1.

Quality of Life

Descriptive statistics were computed for each of the five QOL domains (physical, social, emotional, functional, and spiritual) and hepatobiliary subscale. Repeated measures ANOVA by diagnosis were conducted. Baseline overall QOL scores were low in the HCC and pancreatic cancer groups. Over time, overall QOL scores continued to decrease, with an exception in the HCC group at three-month evaluation, where overall scores increased. The increase, however, was not statistically significant, and overall QOL score changes were not statistically significant over time with one exception: Baseline QOL was higher when compared to the other three

evaluation periods ($p = 0.048$). A plot of overall QOL scores over time can be found in Figure 2.

In terms of subscale scores, results indicate that baseline QOL for physical well-being was significantly higher than at one, two, and three months ($p < 0.001$), whereas baseline emotional well-being was significantly higher than two and three months ($p = 0.033$). No significant differences over time were found in the social and functional well-being domains. At baseline, across the four subscales of the FACT-Hep, scores were highest for social well-being ($\bar{X} = 22.6$, $SD = 4.3$). Conversely, scores were lowest for functional well-being ($\bar{X} = 13.7$, $SD = 5.9$). At the three-month evaluation, social well-being remained highest ($\bar{X} = 22.9$, $SD = 5.3$) and physical well-being was lowest ($\bar{X} = 10.8$, $SD = 7.1$). Overall QOL scores and subscale scores are provided in Table 2.

Pearson's correlations between the disease-specific symptom subscale and each of the QOL subscale scores were computed for all four evaluations, including baseline. Results at baseline suggest that symptoms were highly correlated with physical well-being (0.72), functional well-being (0.73), and overall FACT-Hep scores (0.93). Correlations at baseline among symptoms and emotional well-being (0.51), spirituality (0.54), and social/family well-being (0.17) were moderate to low. These correlational trends were found across time for the physical well-being domain and overall FACT-Hep scores. Table 3 provides Pearson's correlations among symptoms and QOL across study time points.

Spirituality

No significant differences were found over time or by group in relation to overall spirituality; however, a significant interaction between group and time was found in the meaning/peace subscale of the FACIT-Sp-12. Results suggest that spiritual well-being in the pancreatic cancer group was significantly higher than the HCC group at the three-month evaluation, and within the HCC group, baseline spiritual well-being was significantly higher when compared to the other three evaluation time points ($p < 0.05$). No significant differences over time or by diagnosis were found in the faith

Table 3. Pearson's Correlations Between Symptoms and Quality of Life Over Time

| Variable | Coefficients |
|--------------------------|--------------|
| Baseline | |
| Physical well-being | 0.72* |
| Social/family well-being | 0.17 |
| Emotional well-being | 0.51 |
| Functional well-being | 0.74* |
| Spirituality | 0.54 |
| FACT-Hep score | 0.93* |
| One month | |
| Physical well-being | 0.76* |
| Social/family well-being | 0.07 |
| Emotional well-being | 0.44 |
| Functional well-being | 0.64 |
| Spirituality | 0.35 |
| FACT-Hep score | 0.91* |
| Two months | |
| Physical well-being | 0.75* |
| Social/family well-being | 0.23 |
| Emotional well-being | 0.49 |
| Functional well-being | 0.54 |
| Spirituality | 0.31 |
| FACT-Hep score | 0.88* |
| Three months | |
| Physical well-being | 0.67 |
| Social/family well-being | 0.12 |
| Emotional well-being | 0.31 |
| Functional well-being | 0.36 |
| Spirituality | 0.27 |
| FACT-Hep score | 0.78* |

* p < 0.01

FACT-Hep—Functional Assessment of Cancer Therapy–Hepatobiliary

subscale scores. Table 4 provides overall spirituality and subscale scores for the FACIT-Sp-12.

Disease-Specific Symptom Subscale

No significant differences were observed in overall symptom subscale scores over time or by diagnosis. In the HCC group, the overall symptom subscale score decreased over time from baseline, one-, and two-month evaluations, but was increased at three months. For the pancreatic cancer group, overall scores stabilized between one month and two months and then decreased by the three-month evaluation. These changes were not statistically significant.

Individual item responses were explored for the symptom subscale. This was undertaken to obtain symptom-specific data embedded within the overall QOL assessment. Particular attention was given to specific symptoms such as pain, fatigue, weight loss, and mood states because these are common in hepatobiliary cancer. Overall, symptom scores were high for weight loss, appetite, fatigue, ability to perform usual activities, and abdominal pain and tended to worsen over time. Individual item scores for the symptom subscale are provided in Table 5.

Discussion

In this study, we identified a cancer population with mainly advanced disease, which is typical for a tertiary cancer

center. Study sample was diverse, with 44% of participants being non-Caucasian. Baseline QOL, as expected, was low across both diagnoses. This trend continued over time, with the exception of a slight increase in the HCC group at three months that was not statistically significant. Because 46% of HCC patients were treated with surgery in this study, this finding is consistent with previous studies that suggest recovery of QOL in patients with HCC at three-months after surgery (Eid et al., 2006; Poon et al., 2001). Another finding was a trend for worsening of physical and emotional well-being over time that was statistically significant; however, the decline was not statistically significant for social and functional well-being, which is interesting given that a parallel decline in function should be expected with decreasing physical well-being. The finding suggests that other factors may be involved in overall perceived functional status in patients with cancer receiving active treatment and further exploration is warranted.

Recent studies have emphasized the importance of assessing spirituality in patients with advanced disease, and results have found that spiritual support is associated with better QOL (Balboni et al., 2007). Overall spirituality scores were high across both groups. Significant differences were found in the meaning/peace subscale, where the pancreatic cancer group scored higher at three months compared to the HCC group. A significant trend of decline also was observed in overall spirituality in the HCC group. These results warrant further exploration because spirituality is the least understood domain of QOL in patients with cancer, regardless of diagnosis.

Previous studies have found that multiple symptom burden in patients with hepatobiliary cancer is common (Kelsen et al., 1995; Krech & Walsh, 1991; Steel, Geller, et al., 2007). Predictably, participants in this study had many symptom-related concerns. Overall, scores for the symptom subscale were low for both diagnoses. Again, a trend was found in the HCC group, with a slight improvement in overall symptom concern at three months that was not statistically significant. The finding is probably related to a similar improvement in overall QOL shown at three months for this group, which might indicate that decreased symptom burden resulted in recovery of QOL. Analysis of individual item responses in

Table 4. Spirituality Scores by Diagnosis Over Time

| Time | Meaning/Peace Subscale (Range = 0–32) | | Faith Subscale (Range = 0–16) | |
|--------------------------|---------------------------------------|-----|-------------------------------|-----|
| | \bar{X} | SD | \bar{X} | SD |
| Baseline | | | | |
| Hepatocellular carcinoma | 24.7 | 5.3 | 10.2 | 4.1 |
| Pancreatic | 23.5 | 6.2 | 12.3 | 4.5 |
| One month | | | | |
| Hepatocellular carcinoma | 22.1 | 4.1 | 10.7 | 4.7 |
| Pancreatic | 24.3 | 6.5 | 11.4 | 4.2 |
| Two months | | | | |
| Hepatocellular carcinoma | 21.1 | 4.6 | 10.0 | 4.8 |
| Pancreatic | 24.3 | 5.2 | 11.0 | 3.9 |
| Three months | | | | |
| Hepatocellular carcinoma | 20.9 | 5.7 | 9.6 | 5.4 |
| Pancreatic | 24.2 | 5.2 | 10.7 | 4.3 |

Table 5. Individual Symptom Item Scores Over Time

| Variable | Baseline | | One Month | | Two Months | | Three Months | |
|-------------------------------------|-----------|------|-----------|------|------------|------|--------------|------|
| | \bar{X} | SD | \bar{X} | SD | \bar{X} | SD | \bar{X} | SD |
| Swelling or cramps in my stomach | 2.20 | 1.40 | 1.90 | 1.30 | 1.60 | 1.30 | 1.70 | 1.30 |
| Losing weight | 1.80 | 1.40 | 1.60 | 1.40 | 1.30 | 1.30 | 1.20 | 1.30 |
| Control of bowels | 3.20 | 1.20 | 3.10 | 1.10 | 3.10 | 1.10 | 3.20 | 1.10 |
| Digest food well | 3.00 | 1.10 | 3.00 | 1.20 | 3.00 | 1.00 | 3.20 | 1.10 |
| Have diarrhea | 3.50 | 0.92 | 3.50 | 1.00 | 3.50 | 0.94 | 3.50 | 0.97 |
| Have good appetite | 1.90 | 1.10 | 1.60 | 1.10 | 1.60 | 1.10 | 1.40 | 1.10 |
| Unhappy about change in appearance | 2.90 | 1.30 | 2.90 | 1.30 | 3.00 | 0.94 | 3.10 | 1.10 |
| Back pain | 2.50 | 1.10 | 2.60 | 1.20 | 2.70 | 1.10 | 2.80 | 1.00 |
| Bothered by constipation | 3.10 | 1.00 | 3.20 | 1.10 | 3.10 | 0.93 | 3.20 | 0.81 |
| Fatigued | 1.30 | 1.20 | 0.80 | 0.87 | 0.80 | 1.00 | 0.80 | 1.10 |
| Able to do my usual activities | 1.80 | 1.10 | 1.50 | 1.00 | 1.80 | 1.10 | 1.60 | 0.93 |
| Bothered by jaundice or yellow skin | 3.30 | 1.10 | 3.10 | 1.00 | 2.80 | 1.20 | 2.90 | 1.10 |
| Have fevers | 3.50 | 0.76 | 3.20 | 0.98 | 3.10 | 1.00 | 3.10 | 1.10 |
| Have itching | 3.10 | 1.20 | 3.10 | 1.20 | 2.90 | 1.10 | 2.90 | 1.20 |
| Have change in food tastes | 2.30 | 1.40 | 2.70 | 1.40 | 2.10 | 1.10 | 2.70 | 1.20 |
| Have chills | 3.10 | 1.10 | 3.30 | 1.00 | 3.20 | 1.00 | 3.40 | 0.91 |
| Mouth is dry. | 3.00 | 1.00 | 2.80 | 1.20 | 3.00 | 0.95 | 3.00 | 1.10 |
| Discomfort or pain in stomach | 1.90 | 1.30 | 1.90 | 1.30 | 1.70 | 1.10 | 1.80 | 1.10 |

Note. Range = 0–4, with higher scores indicating better quality of life

the symptom subscale revealed that, as expected, participants reported high levels of concern for weight loss, appetite, fatigue, and abdominal pain. This finding is consistent with previous studies and underscores the importance of aggressive symptom management for patients with hepatobiliary cancer.

Limitations of the present study included the small sample size. Findings from the study cannot be generalized. Although ethnic minority participation was fairly high in this study, the small sample size precluded determination of statistical differences by ethnicity. The present pilot study originally was not designed to analyze comparisons across ethnicity. Although important demographic and disease data were collected, analysis based on factors such as age and type of treatment cannot be conducted because of the small sample size. Another limitation is the heterogeneity of a sample population with two different cancer diagnoses. The combining of the two diagnoses was undertaken to maximize study accrual. This strategy limited the number of participants accrued into each diagnosis group, which, in turn, prohibited generalizations of study results because of the small sample size in each diagnosis group.

Implications for Nursing Practice and Research

The findings of this study provide preliminary insight into the QOL of patients with hepatobiliary cancers. Results suggest that this understudied cancer population is burdened with low QOL and multiple symptom concerns. Although these findings were expected and validated results from previous studies conducted in this population, it is frustrating to find that research with this understudied cancer population remains minimal. Nurses caring for patients with hepatobiliary cancer must be aware of the QOL and symptom concerns and advocate for aggressive symptom management for this vulnerable cancer population.

Nurse researchers are in an ideal position to advance the scientific knowledge of the symptoms experience and QOL of patients with hepatobiliary cancers. Several important areas of interest warrant further exploration. First, future research with this cancer population should explore the diagnoses separately. The category of hepatobiliary cancers includes several different and, perhaps, distinct diagnoses. Therefore, a more homogeneous sample allows for the potential to derive more meaningful findings specific to patient and family needs based on diagnosis. Second, given that patients with hepatobiliary cancers are burdened by multiple symptoms, explorations of other symptom-related factors affecting QOL, such as distress, may assist in determining effective symptom management for this cancer population. Effective symptom management is particularly important given that current treatment modalities for hepatobiliary cancers produce minimal or no survival benefit. In this situation, aggressive symptom management is paramount. Third, future research exploring QOL in this population must include spirituality as a moderator of overall QOL. Finally, factors such as symptom and illness perceptions must be explored to fully comprehend the meaning of QOL for patients with hepatobiliary cancer.

In conclusion, the present study suggests that hepatobiliary cancer is associated with multiple symptoms burden and diminished QOL. The decline in QOL continues through treatment and disease progression. Through research, further understanding of the symptom experience of patients with hepatobiliary cancer will aid in the development of effective nursing interventions to improve the QOL of this understudied cancer population.

The authors gratefully acknowledge Gwen Uman, RN, PhD, at Vital Research, LLC, for her assistance in statistical design and analysis, and Michelle Duff, DPT, director of Patient and Liaison Services and Medical Affairs at the Pancreatic Cancer Network for her role as external consultant for this study.

Author Contact: Virginia Sun, RN, MSN, ANP, can be reached at vsun@coh.org, with copy to editor at ONFEditor@ons.org.

References

- Balboni, T.A., Vanderwerker, L.C., Block, S.D., Paulk, M.E., Lathan, C.S., Peteet, J.R., et al. (2007). Religiousness and spiritual support among advanced cancer patients and associations with end-of-life treatment preferences and quality of life. *Journal of Clinical Oncology*, 25(5), 555–560.
- Bianchi, G., Loguercio, C., Sgarbi, D., Abbiati, R., Brunetti, N., De Simone, T., et al. (2003). Reduced quality of life of patients with hepatocellular carcinoma. *Digestive and Liver Diseases*, 35(1), 46–54.
- Carney, C.P., Jones, L., Woolson, R.F., Noyes, R., Jr., & Doebbeling, B.N. (2003). Relationship between depression and pancreatic cancer in the general population. *Psychosomatic Medicine*, 65(5), 884–888.
- Cella, D. (2005). Quality of life outcomes: Measurement and intervention. *Journal of Supportive Oncology*, 3(2), 133–134.
- Coleman, J., Olsen, S.J., Sauter, P.K., Baker, D., Hodgins, M.B., Stanfield, C., et al. (2005). The effect of a frequently asked questions module on a pancreatic cancer Web site patient/family chat room. *Cancer Nursing*, 28(6), 460–468.
- Eid, S., Stromberg, A.J., Ames, S., Ellis, S., McMasters, K.M., & Martin, R.C. (2006). Assessment of symptom experience in patients undergoing hepatic resection or ablation. *Cancer*, 107(11), 2715–2722.
- Ersek, M., Ferrell, B.R., Dow, K.H., & Melancon, C.H. (1997). Quality of life in women with ovarian cancer. *Western Journal of Nursing Research*, 19(3), 334–350.
- Ferrell, B., Grant, M., Padilla, G., Vemuri, S., & Rhiner, M. (1991). The experience of pain and perceptions of quality of life: Validation of a conceptual model. *Hospice Journal*, 7(3), 9–24.
- Ferrell, B.R., Dow, K. H., Leigh, S., Ly, J., & Gulasekaram, P. (1995). Quality of life in long-term cancer survivors. *Oncology Nursing Forum*, 22(6), 915–922.
- Ferrell, B.R., Grant, M., Funk, B., Garcia, N., Otis-Green, S., & Schaffner, M.L. (1996). Quality of life in breast cancer. *Cancer Practice*, 4(6), 331–340.
- Ferrell, B.R., Grant, M., Funk, B., Otis-Green, S., & Garcia, N. (1997a). Quality of life in breast cancer. Part I: Physical and social well-being. *Cancer Nursing*, 20(6), 398–408.
- Ferrell, B.R., Grant, M.M., Funk, B., Otis-Green, S., & Garcia, N. (1997b). Quality of life in breast cancer survivors as identified by focus groups. *Psycho-Oncology*, 6(1), 13–23.
- Ferrell, B.R., Grant, M.M., Funk, B.M., Otis-Green, S.A., & Garcia, N.J. (1998). Quality of life in breast cancer survivors: implications for developing support services. *Oncology Nursing Forum*, 25(5), 887–895.
- Fitzsimmons, D., George, S., Payne, S., & Johnson, C.D. (1999). Differences in perception of quality-of-life issues between health professionals and patients with pancreatic cancer. *Psycho-Oncology*, 8(2), 135–143.
- Heffernan, N., Cella, D., Webster, K., Odom, L., Martone, M., Passik, S., et al. (2002). Measuring health-related quality of life in patients with hepatobiliary cancers: The Functional Assessment of Cancer Therapy-Hepatobiliary questionnaire. *Journal of Clinical Oncology*, 20(9), 2229–2239.
- Huang, J.J., Yeo, C.J., Sohn, T.A., Lillemoe, K.D., Sauter, P.K., Coleman, J., et al. (2000). Quality of life and outcomes after pancreaticoduodenectomy. *Annals of Surgery*, 231(6), 890–898.
- Jemal, A., Siegel, R., Ward, E., Murray, T., Xu, J., & Thun, M.J. (2008). *Cancer statistics 2008*. Retrieved April 14, 2008, from <http://www.cancer.org/downloads/STT/2008CAFFfinalsecured.pdf>
- Kelsen, D.P., Portenoy, R.K., Thaler, H.T., Niedzwiecki, D., Passik, S.D., Tao, Y., et al. (1995). Pain and depression in patients with newly diagnosed pancreas cancer. *Journal of Clinical Oncology*, 13(3), 748–755.
- Krech, R.L., & Walsh, D. (1991). Symptoms of pancreatic cancer. *Journal of Pain and Symptom Management*, 6(6), 360–367.
- Labori, K.J., Hjermsstad, M.J., Wester, T., Buanes, T., & Loge, J.H. (2006). Symptom profiles and palliative care in advanced pancreatic cancer: A prospective study. *Supportive Care in Cancer*, 14(11), 1126–1133.
- Lai, Y.H., Shun, S.C., Hsiao, Y.L., Chiou, J.F., Wei, L.L., Tsai, J.T., et al. (2007). Fatigue experiences in hepatocellular carcinoma patients during six weeks of stereotactic radiotherapy. *Oncologist*, 12(2), 221–230.
- Lis, C.G., Gupta, D., & Grutsch, J.F. (2006). Patient satisfaction with quality of life as a predictor of survival in pancreatic cancer. *International Journal of Gastrointestinal Cancer*, 37(1), 35–44.
- McCracken, M., Olsen, M., Chen, M.S., Jr., Jemal, A., Thun, M., Cokkinides, V., et al. (2007). Cancer incidence, mortality, and associated risk factors among Asian Americans of Chinese, Filipino, Vietnamese, Korean, and Japanese ethnicities. *CA: A Cancer Journal for Clinicians*, 57(4), 190–205.
- Nolan, M.T., Hodgins, M.B., Olsen, S.J., Coleman, J., Sauter, P.K., Baker, D., et al. (2006). Spiritual issues of family members in a pancreatic cancer chat room. *Oncology Nursing Forum*, 33(2), 239–244.
- Passik, S.D., & Roth, A.J. (1999). Anxiety symptoms and panic attacks preceding pancreatic cancer diagnosis. *Psycho-Oncology*, 8(3), 268–272.
- Peterman, A.H., Fitchett, G., Brady, M.J., Hernandez, L., & Cella, D. (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(1), 49–58.
- Poon, R.T., Fan, S.T., Yu, W.C., Lam, B.K., Chan, F.Y., & Wong, J. (2001). A prospective longitudinal study of quality of life after resection of hepatocellular carcinoma. *Archives of Surgery*, 136(6), 693–699.
- Sheibani-Rad, S., & Velanovich, V. (2006). Effects of depression on the survival of pancreatic adenocarcinoma. *Pancreas*, 32(1), 58–61.
- Shun, S.C., Lai, Y.H., Jing, T.T., Jeng, C., Lee, F.Y., Hu, L.S., et al. (2005). Fatigue patterns and correlates in male liver cancer patients receiving transcatheter hepatic arterial chemoembolization. *Supportive Care in Cancer*, 13(5), 311–317.
- 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(2), 73–79.
- Steel, J., Hess, S.A., Tunke, L., Chopra, K., & Carr, B.I. (2005). Sexual functioning in patients with hepatocellular carcinoma. *Cancer*, 104(10), 2234–2243.
- Steel, J.L., Chopra, K., Olek, M.C., & Carr, B.I. (2007). Health-related quality of life: Hepatocellular carcinoma, chronic liver disease, and the general population. *Quality of Life Research*, 16(2), 203–215.
- Steel, J.L., Geller, D.A., Gamblin, T.C., Olek, M.C., & Carr, B.I. (2007). Depression, immunity, and survival in patients with hepatobiliary carcinoma. *Journal of Clinical Oncology*, 25(17), 2397–2405.
- Wang, Y.B., Chen, M.H., Yan, K., Yang, W., Dai, Y., & Yin, S.S. (2007). Quality of life after radiofrequency ablation combined with transcatheter arterial chemoembolization for hepatocellular carcinoma: Comparison with transcatheter arterial chemoembolization alone. *Quality of Life Research*, 16(3), 389–397.
- Watanabe, I., Sasaki, S., Konishi, M., Nakagohri, T., Inoue, K., Oda, T., et al. (2004). Onset symptoms and tumor locations as prognostic factors of pancreatic cancer. *Pancreas*, 28(2), 160–165.
- Yeo, W., Mo, F.K., Koh, J., Chan, A.T., Leung, T., Hui, P., et al. (2006). Quality of life is predictive of survival in patients with unresectable hepatocellular carcinoma. *Annals of Oncology*, 17(7), 1083–1089.
- Zabora, J., BrintzenhofeSzoc, K., Curbow, B., Hooker, C., & Piantadosi, S. (2001). The prevalence of psychological distress by cancer site. *Psycho-Oncology*, 10(1), 19–28.
- Zhu, A.X. (2003). Hepatocellular carcinoma: Are we making progress? *Cancer Investigation*, 21(3), 418–428.