

HIGHLIGHT ARTICLE

Quality of Life in Patients with Pancreatic Cancer

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Summary

Pancreatic cancer is a rapidly fatal disease with palliation often serving as the main goal of treatment. The end of life is often marked by severe symptoms and poor quality of life (QoL). Several studies presented at the 2012 ASCO Gastrointestinal Cancers Symposium addressed the importance of symptom identification and management for patients with pancreatic cancer: 1) a study evaluating the correlation between patient-reported symptoms, disease burden and treatment duration in patients with advanced pancreatic cancer undergoing gemcitabine-based chemotherapy (Abstract #370); 2) a Japanese study found that patients without worsening of pain or sleep symptoms at one month of chemotherapy had higher frequency of disease control (Abstract #195); and 3) a study showed that fear of cancer recurrence is a substantial problem following resection and should be targeted (Abstract #289). The authors summarize the findings and discuss the importance of QoL in these patients. The results of these studies may facilitate in identifying symptom changes as predictive markers, and improving care and QoL for patients with this devastating disease.

Pancreatic Cancer and Quality of Life

Pancreatic cancer is the fourth leading cause of cancer death in the United States. Its prognosis remains poor despite advances in surgery, radiation therapy, and chemotherapy [1]. As pancreatic cancer often presents insidiously, the majority of patients are not diagnosed until they have advanced or metastatic disease. For the 20% of patients who can undergo curative resection, even with clear margins, the 5-year survival rate is only 10-25%. Therefore, much of pancreatic cancer management is aimed at palliation of symptoms. Common symptoms include pain, fatigue, malabsorption, cachexia, obstruction (both intestinal and biliary), and thromboembolism. Though treatment with surgery, radiation, and chemotherapy may help to improve morbidity, the toxicities from treatments can also add to the symptom profile, which should always be taken into consideration. For example, when gemcitabine was approved in the mid 1990s it showed only a modest survival benefit; however, 23.8% of patients showed improvement in terms of clinical benefit response (which takes into account pain,

weight, and performance status) [2]. Supportive management of symptoms must be initiated early and aggressively to ensure patient comfort [3].

In addition to evaluating methods for symptom management, there has been interest as to how identification of symptoms may aid in prognostication. Several studies have shown that baseline quality of life (QoL) measures are associated with survival in pancreatic cancer [4, 5]. Bernard *et al.* [6] observed that baseline patient-rated pain and tiredness were predictors of survival, though less significant than CA 19-9 tumor marker levels. Though only some of these studies have shown statistical significance, these measures may help to provide additional information to guide patient care. Tumor markers may benefit from supplementation by measures of QoL which can additionally take into consideration the patient's perception of their situation as a whole (including both pathophysiological and emotional wellbeing).

What Did We Learn at the 2012 ASCO Gastrointestinal Cancers Symposium?

Here, we review a few of the studies presented at the 2012 ASCO Gastrointestinal Cancers Symposium that address symptom identification and how they may help improve pancreatic cancer management.

Identification of Common Symptoms in Patients with Advanced Pancreatic Cancer Undergoing Gemcitabine-Based Chemotherapy (Abstract #370 [7])

Wang *et al.* evaluated the correlation between patient-reported symptoms, disease burden and treatment

<p>Key words Palliative Care; Pancreatic Neoplasms; Quality of Life Abbreviations MDASI: M.D. Anderson Symptom Inventory; QoL: quality of life Correspondence Muhammad Wasif Saif Division of Hematology and Oncology; Columbia University Medical Center; 177 Fort Washington Ave. 6GN-435; New York, NY 10032; USA Phone: +1-212.305.0592; Fax: +1-212.305.6762 E-mail: mws2138@columbia.edu</p>

Table 1. Patient-reported symptoms in patients with advanced pancreatic cancer undergoing gemcitabine-based chemotherapy (Wang *et al.*, Abstract #370 [7]).

Study methods	Patient rated symptoms weekly during chemotherapy, then every two weeks by using MDASI.
No. of patients	100
Patients characteristics	Median age: 65 years Gender: 50% female
Treatment	Gemcitabine-based chemotherapy for advanced pancreatic cancer 87 patients with no prior treatment 32 patients received opioids for severe pain
Results	Three most severe MDASI symptoms at baseline: fatigue, lack of appetite, and pain Poor performance status and opioid use were related to severity of above baseline symptoms Patients who ended treatment early (before 9 weeks) reported more severe symptoms, including worse pain at baseline, more persistent fatigue and lack of appetite than those at more than 26 weeks Lack of appetite improved over time for patients receiving gemcitabine-based therapy; however, pain and fatigue tended to worsen over the course of the study

MDASI: MD Anderson Symptom Inventory

duration in patients with advanced pancreatic cancer undergoing gemcitabine-based chemotherapy [7]. They evaluated 100 patients undergoing chemotherapy with the MD Anderson Symptom Inventory (MDASI) (Table 1). Common symptoms include pain, fatigue, and loss of appetite. Of particular interest, is that patients who ended treatment earlier (before 9 weeks) suffered more pain at baseline and had persistently worse symptoms. The authors suggest that more severe symptoms reported by patients may be associated with greater disease burden, and a higher likelihood to stop treatment earlier.

Symptoms as Predictors of Disease Control (Abstract #195 [8])

A Japanese study by Kuwahara *et al* aimed to determine symptom changes that could predict disease control [8]. The study included 87 patients with treatment naïve, unresectable pancreatic tumors. The patients received gemcitabine monotherapy (n=42), gemcitabine-based chemotherapies (n=41), or S-1 monotherapy (n=4). The patient's symptoms were scored using a Japanese modified version of the MDASI prior to initiation of treatment and one month

later. The tumor responses were assessed using the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.0. They found that patients without worsening of pain or sleep symptoms had higher frequency of disease control, though this only reached significance for sleep disturbance (P=0.004).

This is consistent with the theory of Wang *et al.* [7] that diminished pain on presentation may be indicative of small tumor burden. This study is a helpful complement to ongoing research evaluating the utilization of symptoms as prognostic signs for treatment success and mortality. Gemcitabine has appeared in many studies to improve pain control, but there has been considerable debate as to its impact on overall QoL measures. Romanus *et al.* addressed this discrepancy, and their results suggest that this may, in part, be due to the use of different tools measuring QoL [9]; therefore, addressing specific symptoms like pain may provide more appropriate reproducibility.

Fear of Cancer Recurrence (Abstract #289 [10])

The symptoms suffered by patients, however, are not only physical in nature, but can also play heavily on their emotional wellbeing. Fear of cancer recurrence

Table 2. Fear of cancer recurrence and quality of life (QoL) following resection of pancreatic and periampullary cancers (Petzel *et al.*, Abstract #289 [10]).

Study methods	Cross-sectional study. Instruments: - Fear of cancer recurrence: Fear of Recurrence Inventory - QoL: Functional Assessment of Cancer Therapy-Hepatobiliary Questionnaire - Psychosocial distress: Hospital Anxiety and Depression Scale
No. of patients	188
Patients characteristics	Patients received potentially curative surgery 1991-2011 for non-recurrent: - Pancreatic ductal adenocarcinoma, 39% - Periampullary adenocarcinoma, 29% - Pancreatic neuroendocrine tumor, 32%
Results	Median fear of cancer recurrence severity score: - Adenocarcinoma, 55% - Periampullary adenocarcinoma, 51% - Pancreatic neuroendocrine tumor, 63% Factors associated with lower fear of cancer recurrence: older age, male gender, periampullary adenocarcinoma, negative lymph nodes, longer interval since operation Factors associated with higher fear of cancer recurrence: anxiety, depression, and depressed QoL

has been a stressor studied extensively in cancers with better long-term prognosis, such as breast, prostate, and colon cancer [11]. Petzel *et al.* [10] evaluated this concern in 188 patients who underwent potentially curative surgery for non-recurrent pancreatic ductal adenocarcinoma, periampullary adenocarcinoma, or pancreatic neuroendocrine tumors (Table 2). All three histologic types had rates of fear of cancer recurrence greater than 50%.

Though these patients are considered successes in a field with such high mortality, this study demonstrates that other symptomatic targets, including those of psychosocial etiology, should be further addressed to provide better support for our patients.

Discussion

Due to pancreatic cancer's dismal prognosis, much of management is focused upon palliation and symptom management, and the decision to treat a patient with more aggressive maneuvers must always take into account the impact upon a patient's QoL. However, these three studies present how identification of these symptoms may also change treatment adherence, disease prognosis, or emotional wellbeing. Wang *et al.* [7] showed a correlation between self-reported pain and early termination of treatment. Though a causal relationship cannot be specifically identified, it is possible that these symptoms either identify a more at-risk population for early drop out, a population that requires better targeting of pain control, or a subgroup with higher disease burden that is less likely to attain disease control. The last theory is particularly consistent with Kuwahara *et al.* [8] who found that patients with disease control had greater improvement of pain and sleep disturbance scores; suggesting that patient symptoms might be utilized in addition to other markers as indicators of treatment success. The abstract of Petzel *et al.* [10] also highlighted how other stressors, such as fear of cancer recurrence, anxiety, and depression are also part of QoL measures, and that causes of emotional anxiety must also be taken into consideration when attempting to provide the best care for a patient.

Therefore, when evaluating patients in the clinic setting it will be important to evaluate the patient as a whole and to seek the patients' self-perception of their symptoms. Patients and their families will be best served by a multidisciplinary team, where oncologist,

radiation oncologist, surgeon, nutritionist, psychiatrist and others work together to create a plan which provides comprehensive support for the patient. In the future, this can help improve treatment, adherence, and with future studies, may identify prognostic factors that will better prepare patients and physicians for the natural course of their disease.

Conflict of interest The authors have no potential conflicts of interest

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