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Cholangiocarcinoma and the Nutrition Care Process

Shelby Herman

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University of North Dakota

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Professor Swanson

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Liver cancer is the second-leading cause of cancer related death worldwide in men after lung cancer and is continually increasing in incidence. Specifically, cholangiocarcinoma (CCA), or bile duct carcinoma, is a malignancy originating in the cholangiocytes of the biliary tree. As the cancer progresses, it impacts many aspects of the patient's life, making it important for registered dietitian nutritionists (RDN) to assist the patient through all aspects of the Nutrition Care Process including nutrition assessment, diagnosis, intervention, monitoring and evaluation, and also referrals. An understanding of the disease is necessary for the RDN to provide competent medical nutrition therapy for their liver cancer patients and this can be done utilizing the Nutrition Care Process.

Definition & Pathophysiology

Adult stem cells are undifferentiated cells with endless replicative potential that can differentiate into specialized cells with the primary role of sustaining the turnover of physiological tissue and tissue repair on varying types of injury. Stem cells are associated with their fast turnover in tissues of the gastrointestinal tract, skin, and bone marrow and are more prone to malignant transformation. These cells are recognized as a source of cancer due to their long lifetime and ability to self-renew.

Cells of a developed liver, however, have a gradual turnover period averaging a hepatocyte life span range of 200 to 300 days (Sia et al., 2017). The body's largest organ, the liver, processes and stores nutrients, produces cholesterol, proteins, clotting factors, lipoproteins to transport cholesterol, bile, and has metabolic functions such as detoxifying carcinogens.

The types of liver cancer are split into hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA), which are further divided into subclasses. HCC, or primary liver

cancer, is the most prevalent form of liver cancer, accounting for 80% of cases. The forms of CCA are classified based on anatomical location with intrahepatic (iCCA), perihilar (pCCA), and distal (dCCA). CCA itself is an epithelial cell malignancy in varying locations of the biliary tree. The most common histological subtype of CCA encountered is adenocarcinoma, or mucus-producing glandular cells of organs. The tumor, node, metastasis (TNM) staging is a classification system used to identify the extent of the tumor, its size, and degree of growth and spread. CCA is not commonly diagnosed until after the cancer has metastasized, meaning that the cancer spreads to nearby organs, such as the liver, lymph nodes, and lungs (Razumilava & Gores, 2014). The late onset of symptoms causes a poor average survival rate at five years of 12% (World, 2015).

Etiology & Epidemiology

Each year in the United States, approximately 5,000 individuals are diagnosed with CCA (DeOliveira et al., 2007). Recent years have shown an unexplained global increase in CCA incidence and mortality. Tumors can occur anywhere along the biliary tree from the peripheral intrahepatic ducts to the intraduodenal bile duct. Men are affected 1.5 times more than women (Shaib Y, 2004). Risk of developing liver cancer increases with age, with the majority of cases diagnosed at age 75 (World, 2015). Cholangiocarcinoma is most prevalent in regions of Eastern Asia due to liver flukes in raw fish. Liver fluke infection is caused by parasites in the water such as *Opisthorchis viverrini, Clonorchis senisis*, and *Opisthorchis felineus,* that can be transmitted to humans through the consumption of raw infected fish. Other risk factors include primary sclerosing cholangitis, biliary stones, chemical carcinogens, alcoholic liver disease, cirrhosis, viral hepatitis, and diabetes.

The case of liver cancer that will be presented is my uncle, who we'll refer to as DB, who was diagnosed with liver cancer at age 55. He experienced fever, weakness, nausea, and vomiting, causing him to need help on his farm as the disease progressed. When I was younger, he would help me plant a large garden at his farm and he would take me for rides on the tractors. At stage IV and receiving treatments, he now has difficulty walking and extreme fatigue. Farm Rescue and dozens of members of the community have come out to support him and help with crops this year.

Nutrition Assessment

The nutrition assessment is the process of collecting and interpreting data related to an individual's food and nutrient intake, lifestyle, and medical history. During each stage of the cancer process, individuals experience the disease differently making it important for the RDN to provide a complete nutritional assessment of the client's health. The Malnutrition Universal Screening Tool (MUST), the Malnutrition Screening Tool (MST), and the Malnutrition Screening Tool for Cancer Patients are useful within the inpatient setting. The RDN should assess energy and protein intake, changes in food and fluid/beverage intake, changes in type, texture, or temperature of food and liquids, use of medical food supplements, food avoidance or intolerances, medications, alternative medicine, and factors affecting access to food.

Normal, healthy cells in the body that are susceptible to the effects of these lethal chemotherapeutic agents include those that divide frequently, such as the cells of the bone marrow (red blood cells, white blood cells, and platelets), the epithelial lining of the gastrointestinal tract, and the hair follicles. The most common side effects, therefore, are due to toxicity to these cells and include neutropenia, thrombocytopenia, anemia, diarrhea, mucositis,

and alopecia. Some chemotherapeutic agents are known to cause cardiotoxicity, neurotoxicity, and nephrotoxicity (Nelms, 2016). Cancer cachexia, which is experienced by most patients, is defined as "weight loss, wasting of muscle, loss of appetite, and general debility that can occur during a chronic disease" (Nelms, 2016). As the cancer and treatments progress, patients may need assistance preparing and eating foods.

Symptoms typically do not appear until the cancer has advanced and include abdominal pain and swelling, weight loss, decreased appetite, jaundice, and fever. A common clinical sign is enlargement of the liver. Patients with cancer may experience hypermetabolism and require a higher amount of energy to prevent weight loss. The kilocalorie recommendation for individuals who are slightly hypermetabolic need to gain weight or are anabolic is 30-35 kcal/kg. Additionally, protein requirements are elevated to support cell growth and healing, often falling between 1.5 and 2.5 g/kg of ideal body weight (IBW) per day, but greatly vary among patients (Nelms, 2016).

Nutrition Focused Physical Examination

A nutrition focused physical examination (NFPE) provides an assessment of muscle and fat stores as well as functional status through assessing vital signs, loss of muscle mass, loss of subcutaneous fat, presence of pressure ulcers or wounds, grip strength, and localized or generalized fluid accumulation. Treatment for liver cancer may involve the support of enteral or parenteral nutrition as it progresses. The symptoms of liver cancer will rapidly progress, making it important for the RDN to assess the patient for signs and symptoms of malnutrition or nutrient deficiencies. Conducting frequent NFPE can assist in identifying nutritional deficiencies or alterations in the patient's status. A Functional Assessment of

IADLs and ADLs can be done using the Subjective Global Assessment and handgrip dynamometry.

Client History

The nutrition assessment includes client history which helps to provide the RDN with knowledge surrounding patient history, medical/health/family history, use of complementary/alternative medicine, previous surgeries, and social history. Specifically, for CCA, determine if the patient has a history of cirrhosis, alcoholic liver disease, viral hepatitis, diabetes, or primary sclerosing cholangitis. Liver cancer not only affects the patient but their family and friends as well. Especially as the cancer progresses, it will be important for the patient to have a network in place to help and support them throughout the process.

DB grew up in a rural agricultural region and helped on the farm from a very young age. He eventually took over the family farm and has devoted his life to it. He lives alone and does not have issues with socioeconomic status or food security. After 6 months of fevers, abdominal pain, nausea, vomiting, decreased appetite, weight loss and multiple doctor visits, it was finally concluded that he had liver cancer. Like most farmers, he did have some previous injuries on the farm, including injuries to the knee and surviving a tornado, but no related medical history to the CCA. After one of his flights back after treatment, he ended up in the emergency room with a blood clot in his lung. An additional side effect includes an infected spleen during chemo treatment. For support, DB's sister has been educating herself about liver cancer to provide better care for him and to help him out with doctor visits.

Food and Nutrition Related History

Since cancer and its treatments greatly impact all aspects of a patient's life, it is important that the RDN asks the patient about their appetite, gastrointestinal function, and any other symptoms that may interfere with their ability to maintain adequate nutritional intake through their diet. When meeting with the patient, an RDN should ask about any avoidance of food or complications with eating because it can lead to inadequate intake, especially if frequent. Patients with liver cancer may experience cancer cachexia, nausea, vomiting, anorexia, unintended weight loss, jaundice, upper abdominal pain and swelling, weakness, and fatigue. The diet history will document the patient's intake patterns, food preferences, cultural values, their use of supplements, and alcohol intake. Collecting information on patients is important because not all patients with liver cancer are affected by the same foods and some patients may find that consuming small, frequent meals suits their situation. DB no longer tolerates foods high in sugar but will still try to eat items like candy bars and finds that they do not taste good anymore.

Concerning previous nutrition education and counseling, the RDN should evaluate whether the patient recalls previously learned nutrition education and what the patient has tried. Establish any food allergies or intolerances to determine if the patient has access to resources to purchase and prepare food. To collect additional data, the RDN can suggest a food record or food diary, 24-hour food recall, or a food frequency.

DB has chosen to be part of experimental trials and travels down to a cancer center in Arizona, which means that he has to stay in hotels for weeks at a time. During these times, he has limited food options including restaurants, fast food, a Target within walking distance, and a mini fridge to store foods. When he is at home, DB typically does not cook for himself

but will microwave frozen dinners. He has experienced dramatic changes in food tolerance throughout the progression of cancer and the treatment period, which interferes with his appetite and causes him to skip meals. He stated that some of his favorite foods to eat lately have been potatoes, oatmeal, and pasta dishes. DB also has struggled with drinking water and says it started tasting gross around the time symptoms started presenting. When he does eat, it is large amounts. I remember handing him a pack of crackers and he ate the entire thing and asked if I had any more food. He is thankful that he still has the farm to keep him active whether he's getting calls all day down in Arizona or running equipment in the fields for an hour at a time. This has also kept his strength up because he would rather lay in bed all day than have to get up and walk, but with the farm he's moving frequently.

Anthropometrics

The measurement of body size, weight, and body composition are anthropometric data obtained during the nutrition assessment that can be used to identify goals for nutrition intervention. Monitoring for deviations from the usual body weight (UBW) is used to help identify nutritional risk and disease complications. What commonly occurs with liver cancer is unintentional weight loss, cancer cachexia, and fatigue which can be objectively measured in the anthropometrics. The RDN will evaluate the patient's height, current weight, highest weight, UBW, change in weight, and BMI. The following classify the percentage of weight loss in terms of malnutrition:

Moderate weight loss

- 1-2% in 1 week
- 5% in 1 month

- 7.5% in 3 months
- 10% in 6 months

Severe weight loss

- >2% over 1 week
- >5% over 1 month
- >7.5% over 3 months

These percentage classifications can be used to interpret the significance of weight loss. The BMI of a healthy individual would range from 19-24 kg/m^2. I always remember DB being within a healthy weight range. DB's height is 6'5", current weight 200 pounds, BMI 23.7 kg/m^2, UBW 225, change in body weight 8% in 3 months. About 4 months ago he did drop to 180 pounds but has gained weight since and stated that his weight has fluctuated a lot recently. Healthy body weight for an individual of this height is 187-229lbs. He is within healthy body weight range but has lost a significant amount of muscle. Now, DB is visibly experiencing cachexia, extreme fatigue, and is concerned about how weak he has become. I remember driving him home after a flight while he complained, "I have no butt left and it hurts to sit for long periods of time."

Biochemical Data, Medical Tests, and Procedures

Biochemical data for the nutrition assessment includes laboratory data, tumor markers, scans, tests, and medications. Tumor markers can be utilized to identify presence of disease or response to therapy. The biochemical data available for a patient must be interpreted in the context of the individual patient's disease state. There is no blood test available to diagnose CCA. Elevated liver function markers such as bilirubin (normal range 0.1-1.2 mg/dL),

alkaline phosphatase (44-147 IU), and aminotransferase (<50 U/L) indicate an obstruction, but not necessarily malignancy (Alsaleh et al., 2018). Commonly used serum tumor markers for CCA are carbohydrate antigen (CA)19-9 (<100 U/mL), CA-125 (<46 U/mL), alpha-fetoprotein (10-20 ng/mL), and carcinoembryonic antigen (CEA) (<2.5 ng/mL). These markers are used in conjunction with other diagnostic tools because of their poor ability to diagnose.

Additional methods of detection include high resolution imaging, computed tomography, and magnetic resonance imaging (MRI), which provide more accuracy for detecting CCA than conducting an ultrasound (Alsaleh et al., 2018). Surgical resection is the only curative therapy for CCA. The majority of CCA cases are identified late, not allowing for surgical intervention. The treatment guidelines recommend a combination of Gemcitabine and Cisplatin chemotherapy for cases in which surgery is not an option (Alsaleh et al., 2018.)

Individuals with liver cancer may be at an increased risk of specific vitamin and mineral deficiencies. Those with liver cancer were found to be deficient in vitamin D and studies have suggested a relationship between vitamin D status and the development of cancer. (Schütte et al., 2016). The use of Cisplatin may require supplementation of magnesium, calcium, and potassium. Fat malabsorption occurs in this population due to decreased secretion of bile salts, which may cause a patient to become deficient in fat soluble vitamins A (men-900 ug/RAE., women-700 ug/RAE), D (12- 20 ng/mL), E (15 mg), and K (0.2-3.2 ng/mL). Minerals such as zinc (men-11 mg, women-8 mg), manganese (4–15 µg/L), and copper (70-140 µg/dL) are excreted in the bile. If the bile is not secreted adequately, these minerals may accumulate in the blood. Monitor serum levels of these nutrients to determine if specific foods should be added or avoided, if supplements are necessary, or if changes in

medications need to be considered. DB has been supplementing iron, magnesium, omega-3, thiamin, folate, vitamin B-12, vitamin C, and vitamin E.

The common medications prescribed for liver cancer and chemotherapy treatments have side effects that impact the patient's daily living and ability to consume food.

- Cisplatin is an alkylating agent chemotherapy that alters DNA structure by misreading DNA code, initiating breaks in the DNA molecule, cross-linking DNA strands. This can cause bone marrow suppression, nausea, vomiting, stomatitis, alopecia, gonadal suppression, and renal toxicity.
- Gemcitabine (Gemzar) is a cytotoxic chemotherapy that has numerous side effects including fever, headache, sore mouth, difficulty moving and swallowing, nausea, vomiting, sore throat, lack of appetite, and low white blood cell count.

In the experimental trials, DB is receiving treatment from a combination of Cisplatin and Gemcitabine. He had a port placed in the right side of his chest to prepare him for treatment. DB said he has experienced neuropathy, very low white blood cell count, and his vision is worsening due to the Cisplatin. This has been upsetting for him because he is concerned with having lasting side effects.

Nutrition Diagnosis

Nutrition diagnoses will vary based on the primary tumor site, extent of tumor burden, and treatment modality and individual nutrition assessment. Possible diagnoses include increased nutrient needs, inadequate oral intake, malnutrition, inadequate fluid intake, altered GI function, swallowing and/or biting/chewing difficulty, unintended weight loss, impaired ability to prepare foods/meals, or malnutrition. Possible PES statements include the following:

- Inadequate oral intake related to lack of appetite as evidenced by poor appetite and 2% weight loss over 2 weeks.
- Increased fluid needs related to sweat loss from fever as evidenced by dehydration and poor skin turgor.
- Severe malnutrition related to loss of appetite as evidenced by unintentional weight loss of 8% in 3 months and severe depletion of muscle and fat mass.
- Food-medication interaction related to use of Gemcitabine and Cisplatin as evidenced by dry mouth, diarrhea, and loss of appetite.
- Impaired ability to prepare foods/meals related to cancer treatments as evidenced by reduced mobility, fatigue, and decreased intake of less than 75% of estimated energy needs.

Possible Interventions

Nutrition intervention occurs in two stages a planning stage and an implementation stage. There are four categories to consider during planning and implementation of the nutrition intervention: nutrition education, nutrition counseling, food and nutrient delivery, and coordination of care.

For DB's case of CCA, I would choose all four of these. Possible interventions for patients with liver cancer include:

- Cancer induced nausea and vomiting (CINV) is often experienced by patients undergoing chemotherapy which may originate from radiation, anticipatory, and chemotherapy. Patients are often prescribed antiemetics to control the nausea and vomiting which should be taken 30-45 minutes before a meal.

- For emesis, eat a small, low-fat meal in the morning of the treatment and avoid fried, greasy, and favorite foods for several days following.
- Early satiety due to delayed gastric emptying is improved with small, frequent meals that are nutrient dense. Beverages should also be nutrient dense and consumed prior to or between meals to avoid the feeling of fullness.
- Follow guidelines for the prevention and treatment of mouth sores associated with mucositis. Additionally, a patient may eat soft, nonfibrous, nonacidic foods, and avoid hot foods. High-calorie, high-protein shakes or nutritional supplements may be beneficial.
- Patients with diarrhea should be encouraged to drink small amounts of fluid frequently, avoid large amounts of fruit juice, and use antidiarrheal medications as prescribed.
- Chemotherapeutic agents, specifically cisplatin, cause dysgeusia. Individuals may prefer use plastic utensils instead of metal ones to avoid a metallic taste in their mouth. Meats are often not tolerated and high-protein foods are encouraged.
- Patients lacking taste should be encouraged to use more highly spiced and flavorful foods.
- In those experiencing xerostomia, sugar-free gum may increase the flow of saliva in the mouth.
- Home delivered meals through a delivery system such as Meals on Wheels.
- Motivational interviewing to assist with shifts in lifestyle.

- Exercise to help increase appetite in those with anorexia. At least 30 minutes of physical activity a day is recommended, but any amount during treatment is beneficial.

Prior to DB starting the experimental trials he drank Essiac Tea because a friend had researched and heard that this tea would help with appetite for cancer patients. He still makes sure to drink this tea at least once a day. His weight fluctuates within a range of 5-10 pounds, but has not significantly changed in recent months.

Nutrition Monitoring & Evaluation.

The approach to monitoring and evaluating a patient should be based on the nutrition diagnoses and interventions implemented. Nutrition intervention domains will be reassessed for effectiveness and revised as appropriate. Typically, weight and weight change will be measured, caloric and protein intakes determined, and components of the NFPE are reassessed for any changes or risk of malnutrition. The RDN will determine their tolerance to the diet and identify any changes in symptoms. At the follow-up visit, food and nutrition-related education can be evaluated to determine how the patient is receiving the information and if they have applied any concepts. Patients who have completed treatment for a malignancy may modify goals including eat mostly plant-based foods, which are low in energy density, remain physically active, and maintain a healthy weight.

Monitoring DB is unique due to the experimental trial and COVID precautions. Being that he is immunocompromised and has already experienced a blood clot from flying, traveling for treatment has been risky, especially with the threat of COVID-19. He communicates through telehealth with members of his care team that are out-of-state. He is fortunate to be financially

stable because the experimental trials are not covered by insurance. He has not met with a dietitian because his intake has been adequate recently but plans to if his health begins to decline.

Prevention & Conclusion

The American Institute for Cancer Research Guidelines for Cancer Prevention has established prevention measures for clinicians to recommend to their patients include: being at the lower end of the healthy BMI range, getting 30 minutes of physical activity per day, avoiding sugary drinks, limiting the intake of energy dense foods and red or processed meats, eating a variety of fruits, vegetables, whole grains, and legumes, and limiting alcoholic beverages. Strong evidence suggests that drinking 1-2 cups of coffee each day decreases the risk of liver cancer (World, 2015). Additionally, the intake of alcoholic beverages to 2 a day for men and 1 for women is shown to reduce the risk of liver diseases and liver cancer. Of individuals with chronic hepatitis C, 1-4% develop liver cancer (World, 2015). The RDN has a crucial role of handling dietary choices and nutritional status of a patient throughout the treatment of cancer because many patients are at increased nutritional risk.

I found researching this type of cancer and the NCP to very interesting, especially because DB is still in the process of treatment. This project also helped me to learn more about how cancer overall is approached from a dietetic standpoint since the treatment of liver cancer does not significantly vary from the treatment of other types of cancer.

References

Alsaleh, M., Leftley, Z., Barbera, T. A., Sithithaworn, P., Khuntikeo, N., Loilome, W., Yongvanit, P., Cox, I. J., Chamodol, N., Syms, R. R., Andrews, R. H., & Taylor-Robinson, S. D. (2018). Cholangiocarcinoma: a guide for the nonspecialist. *International journal of general medicine*, *12*, 13–23. https://doi.org/10.2147/IJGM.S186854

Bémeur, C., Desjardins, P., & Butterworth, R. F. (2010). Role of nutrition in the management of hepatic encephalopathy in end-stage liver failure. *Journal of nutrition and metabolism*, *2010*, 489823. https://doi.org/10.1155/2010/489823

DeOliveira, M. L., Cunningham, S. C., Cameron, J. L., Kamangar, F., Winter, J. M., Lillemoe, K. D., Choti, M. A., Yeo, C. J., & Schulick, R. D. (2007). Cholangiocarcinoma: thirty-one-year experience with 564 patients at a single institution. *Annals of surgery*, *245*(5), 755–762. https://doi-org.ezproxylr.med.und.edu/10.1097/01.sla.0000251366.62632.d3

Nelms, M., Sucher, P.K., Lacey, K. (2016). Nutrition Therapy and Pathophysiology. Boston, MA: Cengage Learning pg. 702-720.

Razumilava, N., & Gores, G. J. (2014). Cholangiocarcinoma. *Lancet (London, England)*, *383*(9935), 2168–2179. https://doi-org.ezproxylr.med.und.edu/10.1016/S0140-6736(13)61903-0

Schütte, K., Schulz, C., & Malfertheiner, P. (2016). Nutrition and Hepatocellular Cancer. *Gastrointestinal tumors*, *2*(4), 188–194. https://doi.org/10.1159/000441822

Shaib Y, El-Serag HB. The epidemiology of cholangiocarcinoma. Semin Liver Dis. 2004 May;24(2):115-25. doi: 10.1055/s-2004-828889. PMID: 15192785.

Sia, D., Villanueva, A., Friedman, S. L., & Llovet, J. M. (2017). Liver Cancer Cell of Origin, Molecular Class, and Effects on Patient Prognosis. *Gastroenterology*, *152*(4), 745–761.

https://doi-org.ezproxylr.med.und.edu/10.1053/j.gastro.2016.11.048

World Cancer Research Fund International/American Institute for Cancer Research. Continuous Update Project Report: Diet, Nutrition, Physical Activity and Liver Cancer. 2015. Retrieved from: wcrf.org/sites/default/files/Liver-Cancer-2015-Report.pdf. Accessed October 8, 2020.