Pancreatic

Out of the shadows

Home in on this deadly disease to improve patient care.

By Kim McCarron, MS, CRNP

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The American Cancer Society predicts that 46,420 Americans will be diagnosed with pancreatic cancer in 2014 and 39,590 will die from the disease. This means that the incidence nearly equals the mortality. Despite decades of effort, the 5-year survival rate for pancreatic cancer is a dismal 5%. This deadly disease affects both men and women, with 80% of cases arising in the sixth through eighth decades of life. The median age of death is 73.

A diagnosis of pancreatic cancer is extremely difficult for patients and their families to accept because most tumors are detected at an advanced stage of disease with little hope for cure. By knowing the therapeutic and palliative options that are available, you can provide patients and their caregivers with information to help them navigate a challenging course of treatments.

Sizing up the risks

The key modifiable risk factors for pancreatic cancer are obesity and cigarette smoking. Each of these risk factors increases the risk of developing this type of cancer two- to threefold.

Among older adults, new-onset diabetes mellitus may be a sign of pancreatic malignancy. More than a decade of living with type 2 diabetes increases an individual's overall risk by 1.5 times.

Heavy alcohol consumption, defined as more than six drinks per day, is linked to chronic pancreatitis, which elevates the risk of developing a malignancy. Causative dietary factors have been extensively researched. Cured and smoked meats, such as bacon and hot dogs, and foods with nitrosamines contain potentially carcinogenic substances, which may spark cellular changes. Occupational exposure to beta-naphthylamine and benzidine used in dye manufacturing and the rubber

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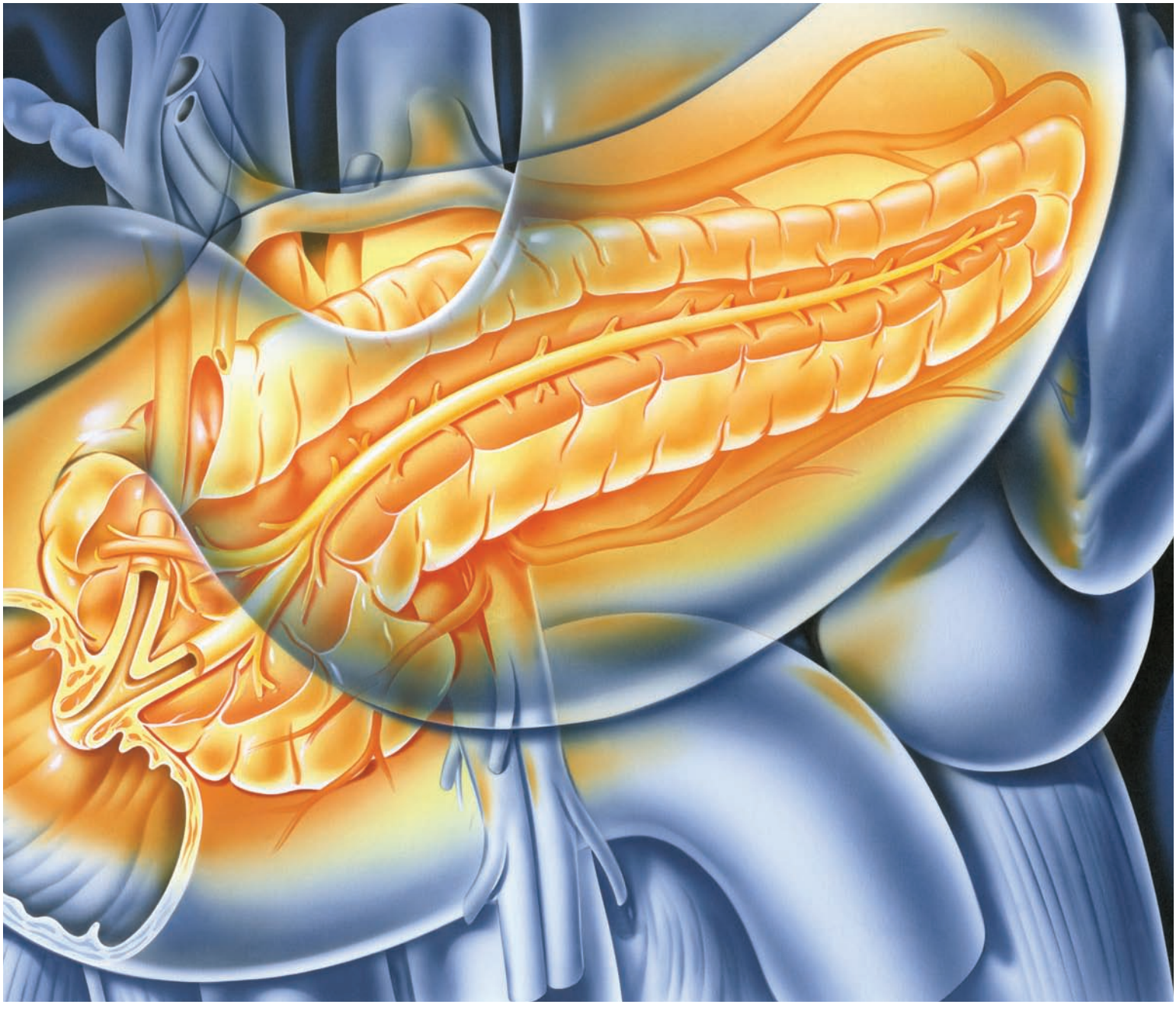


industry has also been linked to developing pancreatic cancer.

Men, particularly Black American men, have a slightly higher incidence of pancreatic cancer than women. Ashkenazi Jews, people of Eastern European descent, are more susceptible if they carry the BRCA2 gene. About 4% to 10% of Ashkenazi Jews with pancreatic cancer carry a germline (within the ova or sperm) BRCA2 mutation. Besides the BRCA2 gene, several genes that increase the risk of pancreatic cancer have been identified. Although it's beyond the scope of this article, information on genetic testing and research is readily available. A family history of hereditary nonpolyposis colorectal cancer also elevates the risk.

Go to the head of the pancreas

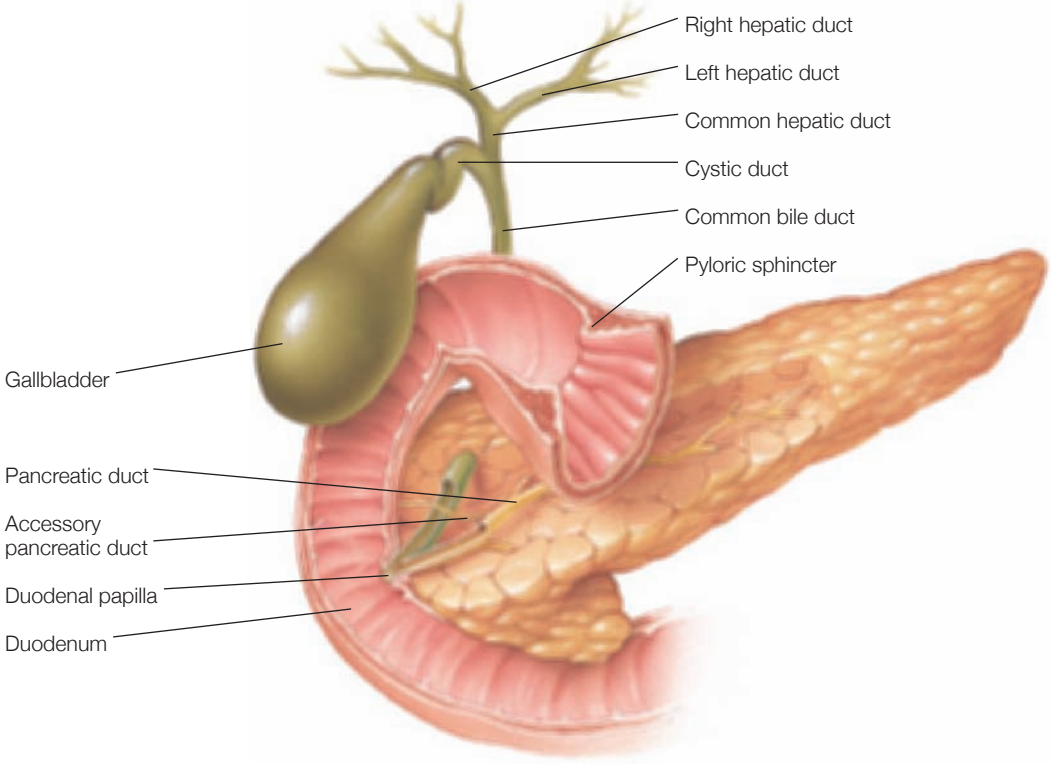
The pancreas has been called "the hermit of the abdomen" because of its protected anatomical location in the retroperitoneal space behind the stomach (see *A closer look at the pancreas*). Stretching horizontally from the duodenum to the spleen, the pancreas is a slender organ with endocrine and exocrine functions:

- the head and uncinate process lie adjacent to the curvature of the duodenum
- the body, which is the midportion of the gland, extends across the abdomen
- the tail lies next to the spleen.

Pancreatic cancer is a solid tumor that invades ductal epithelium. The tumor is classified as adenocarcinoma because it arises from glandular epithelial tissue. As implied, the tumor is firm, but it sends crablike projections of neoplastic cells far beyond the main tumor, invading nerves, lymph nodes, small veins, and adjacent organs.

Be sure to consider anatomy when assessing signs and symptoms because two-thirds

A closer look at the pancreas



of pancreatic cancer occurs in the head of the pancreas, where the common bile duct exits at the ampulla of Vater. When a tumor involving the head of the pancreas obstructs the biliary tract, the patient presents with jaundice resulting from bilirubin pigments staining the skin and sclera, the urine appears darker due to mounting bilirubin, and the stool may be pale from decreased stercobilinogen in the bowel. Pruritus, intense generalized itching, may occur when the bile duct is blocked and bile salts are retained in the circulation.

When cancer arises in the body or tail of the pancreas, the signs and symptoms are often vague and may mimic common gastrointestinal (GI) disorders; the patient doesn't initially present with telltale jaundice because the biliary duct isn't obstructed. Tumors in these regions may grow and invade surrounding tissues before signs and symptoms are recognized as those of a malignancy.

Pain, the most common presenting symptom, may consist of dull or gnawing upper epigastric pain radiating to the middle of the back. It typically worsens at night or after eating and is intensified by lying down. Pain is the result of encroachment of the tumor against adjacent tissues, organs, and nerves, with the back and abdomen being the most common sites of infringement.

Other signs and symptoms include unexplained weight loss; dyspepsia, nausea, and vomiting; fatigue; and increased abdominal girth. Superficial venous thrombophlebitis that's migratory is detected in 10% of patients who have an advanced stage of pancreatic cancer.

Testing, testing, 1-2-3!

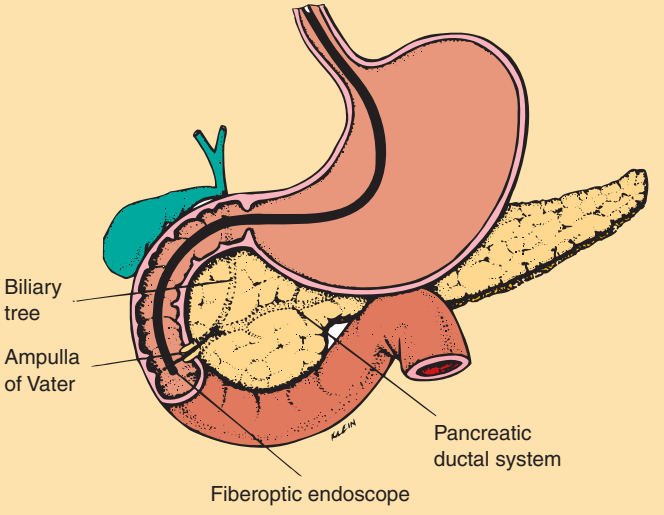
Unfortunately, most patients with localized disease have few signs or symptoms, and no early screening tests can detect pancreatic cancer. As a result, most patients aren't diagnosed until late in the disease after the cancer has metastasized to other organs.

To evaluate suspected pancreatic cancer, endoscopic ultrasound and contrast-enhanced computed tomography (CT) are the imaging procedures of choice. Ultrasound is useful for tumor detection and staging, whereas CT permits cross-sectional visualization of the primary tumor in relation to the surrounding vessels and organs, as does magnetic resonance imaging (MRI), which provides three-dimensional images. CT and MRI have comparable sensitivities and specificities, and both may be used to stage the neoplasm and detect vascular involvement and distant metastases.

Endoscopic ultrasound uses fine-needle aspiration to obtain tissue samples to determine the pathology of the neoplasm; the results influence chemotherapy treatment choices. Endoscopic retrograde cholangiopancreatography (ERCP) is indicated when biliary drainage is obstructed; a stent may be placed to permit flow and drainage of bile into the small bowel (see *Picturing ECRP*). In magnetic retrograde cholangiopancreatography, no contrast dye is used because bile and fluids act as the media to provide clear images of the bile duct and pancreas.

Cancer antigen 19-9 (CA19-9), a protein marker found in pancreatic tissue, may be

Picturing ECRP



elevated in benign biliary, hepatic, and pancreatic disorders. The normal value of CA19-9 is less than 37 U/mL. Lower serum levels at the time of cancer diagnosis are associated with early pathologic stages and more favorable outcomes. In 5% of the population, this marker doesn't rise in the face of pancreatic cancer, even when the tumor burden is large, because these patients lack an enzyme needed to produce CA19-9. Although CA19-9 isn't recommended as a screening test for pancreatic cancer, it may be used to monitor disease progression. A decrease in serial CA19-9 after surgery or chemotherapy reflects better survival rates.

TNM staging of pancreatic cancer

Primary tumor (T)	
TX	Primary tumor can't be assessed
TO	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor limited to pancreas, 2 cm or less in diameter
T2	Tumor limited to pancreas, more than 2 cm in greatest diameter
T3	Tumor expands beyond pancreas but without involvement of the celiac axis or the superior mesenteric artery
T4	Tumor involves the celiac axis or the superior mesenteric artery
Regional lymph nodes (N)	
NX	Regional lymph nodes can't be assessed
NO	No regional lymph node metastasis
N1	Regional lymph node metastasis
Distant metastases (M)	
MO	No distant metastasis
M1	Distant metastasis
Stage grouping	
Stage 0	Tis NO MO
Stage IA	T1 NO MO
Stage IB	T2 NO MO
Stage IIA	T3 NO MO
Stage IIB	T1 N1 MO T2 N1 MO T3 N1 MO
Stage III	T4 Any N MO
Stage IV	Any T Any N M1

Source: National Comprehensive Cancer Network. Clinical practice guidelines for pancreatic adenocarcinoma. http://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf.

Setting the stage

The standard staging system for pancreatic cancer is the TNM classification (see *TNM staging of pancreatic cancer*). The staging workup focuses on measuring the tumor mass in centimeters, defining the relationship of the tumor to large vessels, and identifying regional lymph node involvement and the presence of metastatic disease.

"T" designates the location and size of the tumor and ranges from "T0," where there's no evidence of primary tumor, to "T4," in which the tumor has grown substantially, invaded vascular structures, and isn't surgically resectable. "N" assesses regional lymph node involvement. The categories are "NX," in which the lymph nodes can't be assessed; "N0," where there's no evidence of regional lymph node involvement; and "N1," which signifies regional lymph node metastasis. "M" indicates distant metastasis; the primary sites to which pancreatic cancer spreads are the liver, peritoneum, and lungs.

Zero in on treatment choices

Fewer than 20% of patients are candidates for surgery, which is the only curative option if it can be performed early in the disease process when the tumor is still localized. The type of surgical procedure depends on the location of the tumor, with most involving the head of the pancreas.

In the Whipple procedure, the surgeon removes the head of the pancreas, the uncinate process, the duodenum, the proximal 20 to 30 cm of the jejunum, the gallbladder, 40% of the stomach, and the associated regional lymph nodes (see *Picturing the Whipple procedure*). The remaining portion of the stomach and the body and tail of the pancreas, including the common bile duct, are anastomosed to the jejunum.

Removal of the entire pancreas, or total pancreatectomy, is indicated when a large portion of the gland is involved. Patients who've had this procedure require lifelong insulin and pancreatic enzyme replacement therapy.

If the tumor has developed in the body or tail of the pancreas, these sections may be removed, as well as the spleen in some cases. This is called a distal pancreatectomy with splenectomy, which may be performed using a laparoscope to minimize complications.

The consequences of surgery

In patients who undergo the Whipple procedure, mortality has improved substantially over the decades and is now less than 2% in high-volume medical centers. The Whipple procedure is the most common surgical treatment, with a 5-year survival rate of 20% when the patient opts not to undergo adjuvant chemotherapy as opposed to 30% when the recommended chemotherapy is completed. Morbidity, which remains between 30% and 45%, is still a health-related challenge.

The most common post-op complication is delayed gastric emptying, which may require placement of a jejunostomy tube. Other common complications include wound infections, pancreatic fistulas, abdominal abscesses, cholangitis, bile leaks, and sepsis.

As a result of surgery or obstruction of the pancreatic duct, fewer pancreatic enzymes are produced and patients report steatorrhea (fatty stools), excessive flatulence following meals, abdominal cramping, and weight loss. Pancreatic enzymes, a mixture of lipases, amylases, and proteases prepared from hog pancreas, are supplied in time-release capsules designed to dissolve in the jejunum. Patients must take the enzyme with every meal and snack, and never chew, crush, or retain capsules in the mouth because doing so may cause tissue irritation with resulting ulceration. Because these enzymes contain high levels of purines, they may pose a risk to patients with gout or hyperuricemia (increased levels of serum uric acid).

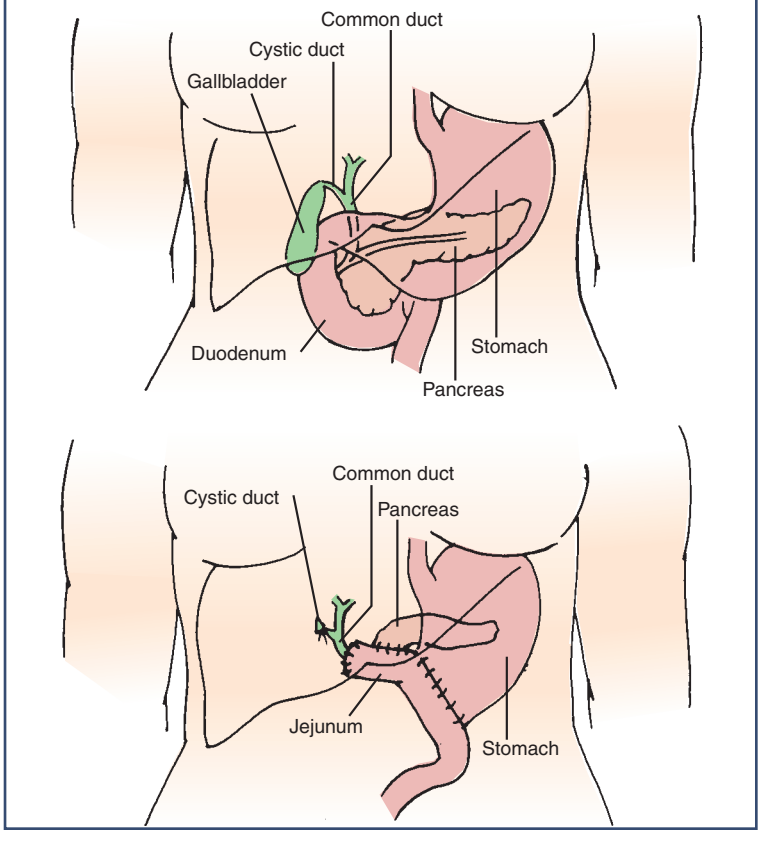
Other approaches to treatment

Because most patients aren't surgical candidates, chemotherapy alone or in combination with radiation therapy may be used to improve survival by reducing the tumor burden. This combined approach is also used for patients who've undergone surgery; for these patients, it's initiated 4 to 8 weeks after recovery.

The National Comprehensive Cancer Network's (NCCN) Clinical Practice Guidelines for Pancreatic Adenocarcinoma is a complete guide for treatment from early- to late-stage cancer. Multiple recommendations for chemotherapy include cisplatin, 5-fluorouracil, and gemcitabine. Chemotherapy is given in cycles of treatment days followed by time to let the body recover. Cycles are 14-, 21-, or 28-days long, and the objective is to kill cancer cells in various growth phases.

Targeted therapy is directed against certain parts of the cell and the signals needed for a

Picturing the Whipple procedure



did you know?

The word *pancreas* originates from a Greek word meaning "all flesh."

tumor to develop and keep growing. Therapy may target specific enzymes needed for cancer cell growth; induce apoptosis, causing the cancer cell to die; or interfere with angiogenesis (the ability of cancer cells to form new blood vessels). Erlotinib, a targeted therapy that acts on the epidermal growth factor receptor, interferes with a growth signal that's sent from the cell membrane to its nucleus. It has been approved for treatment of pancreatic cancer and is among a new group of pharmaceuticals used to treat cancer.

Chemotherapeutic agents are among the most toxic to tissue with a high growth fraction. These are tissues with few cells in the "resting" phase. The bone marrow, GI epithelial cells, hair follicles, and sperm-forming cells are particularly vulnerable to the effects of chemotherapy.

Bone marrow suppression reduces the number of neutrophils, making the patient vulnerable to infection; decreases platelets, increasing bruising and bleeding risk; and depresses red blood cell production, leading to anemia. For the digestive tract, nursing interventions focus on stomatitis, inflammation of the oral mucosa, and thrush resulting from fungal overgrowth, as well as diarrhea, impairment of nutrients, and electrolyte abnormalities. Because nausea and vomiting are common adverse reactions, chemotherapeutic agents are rated according to their emetic potential. Effective drugs used in combination for pretreatment antiemesis include dexamethasone, aprepitant, and ondansetron.

Before beginning external radiation treatment, the patient will undergo simulation, a process that determines the exact treatment field, the shape of the radiation beams, and the dosage needed. Three types of external beam radiation therapy are used to treat pancreatic cancer: 3D-conformal radiation therapy; intensity–modulated radiation therapy (based on tumor thickness); and stereotactic ablative radiotherapy, in which high doses of gamma rays are delivered within a short timeframe.

Ink marks on the skin are used to aim radiation beams at the tumor. Take care not to remove these marks during bathing. Use lukewarm water and advise the patient to pat the skin dry and avoid deodorant soaps, antiperspirants, perfumes, cosmetics, and talcum powder. Soft, loose cotton clothing is more comfortable against the skin, and local irritation may be soothed with lotion containing vitamin E or aloe. Remind the patient not to apply any lotion before radiation treatment because it can increase the amount of heat absorbed by the dermis.

Patients who've been treated with chemotherapy, radiation, and/or surgery may have a constellation of signs and symptoms arise secondary to these therapies, including cramping and diarrhea, anemia, fever and chills, alopecia, muscle wasting, and depression.

Managing pain

Pain is the main factor limiting quality of life. As the disease progresses, so does the severity of discomfort. Opioids are the mainstay of pharmacologic therapy, ranging from short-acting to sustained-release morphine or oxycodone. Common adverse reactions of opioids include sedation, constipation, pruritus, nausea, and testosterone suppression in those on long-term therapy. Constipation is commonly managed with stool softeners or bowel motility-promoting agents; the peripheral mu-opioid receptor antagonist methylnaltrexone is effective for treating opioid-induced constipation.

When pain isn't controlled with opioids, a celiac plexus block may be performed. Recall that a plexus is a network of intersecting nerves, and coalescence of the greater and lesser splanchnic nerves in the vicinity of the celiac trunk form the celiac plexus. This network of nerves provides visceral innervation from the pancreas and its surrounding structures. The

on the web

Johns Hopkins Pancreas Multidisciplinary Cancer Clinic:
http://pathology.jhu.edu/pc/mdc/index.php

NCCN Guidelines for Patients:
http://www.nccn.org/patients/guidelines/pancreatic/index.html

celiac plexus block uses 50% to 100% ethyl alcohol, which causes neurolysis (nerve fiber degeneration) that interrupts the transmission of sensory nerve signals, resulting in pain relief for 70% to 90% of patients.

If the patient is in the advanced stages of pancreatic cancer, referral to hospice care is warranted.

Out of the shadows

Because most patients with pancreatic cancer are diagnosed when it's at an advanced stage, are burdened with multiple signs and symptoms, and have a poor prognosis, the care plan requires a sensitive team approach. The complex interplay of physical, psychological, spiritual, social, financial, and medical factors requires a collaborative environment to integrate the skills of nursing, medicine, social services, physical therapy, pharmacy, and supportive and palliative care. ■

Learn more about it

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