

IV cholangiogram of pancreatic adenocarcinoma

Credit: BSIP/Phototake.

Early Identification of Pancreatic Cancer

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Because of the delayed presentation of definitive signs and symptoms of pancreatic cancer and the anatomic location of the pancreas, pancreatic tumors are rarely detected early. Typically in an advanced stage by the time of presentation, pancreatic cancer is associated with an extremely poor survival rate. It is important for clinicians to maintain an awareness of pancreatic cancer, including patient risk factors, diagnosis through appropriate imaging studies and laboratory testing, clinical presentation, and optimal treatment and management.

In the United States in the year 2012, it has been estimated that some 43,920 patients will receive a new diagnosis of pancreatic cancer, and about 37,390 will die of the disease.¹ Although it represents less than 2% of new cancer diagnoses, pancreatic cancer is the fourth leading cause of cancer-related deaths in both women and men.^{2,3} Because the anatomic location of the pancreas makes the disease difficult to diagnose at an early stage, pancreatic cancer has a median survival of less than six months after diagnosis, and a 4.6% survival rate at 5 years.² The current focus on pancreatic cancer is to improve survival through earlier diagnosis—before the tumor has reached an advanced stage.⁴

The incidence and mortality rates for pancreatic cancer have changed only minimally during the past 30 years. In recent decades, as reported in 2011 by the National Comprehensive Cancer Network (NCCN),⁵ the incidence of pancreatic cancer has increased steadily. Prevalence is greater in men than in women, and African-Americans have an increased incidence of pancreatic cancer, compared with whites. In the United States alone, the approximate medical costs associated with pancreatic cancer in 2006 amounted to nearly \$1.9 billion.⁶

According to data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database,⁷ derived from cases reported from 17 SEER regions between 1975 and 2009, the median patient age for a diagnosis of pancreatic cancer between 2004 and 2008 was 72 years. Prevalence of pancreatic cancer

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TABLE 1
Role of Inherited Factors in Pancreatic Cancer^{2,18,19,20}

Levels of risk (expressed as standard incidence ratios) associated with reported risk factors for pancreatic cancer are shown, in addition to the associated genetic mutations and clinical clues.			
Risk factor	Level of risk	Responsible gene	Clinical clues
Peutz-Jeghers syndrome	132.0	<i>STK11/LKB1</i>	Benign polyps of GI tract; pigmented macules on lips, inner lining of cheeks, hands, and feet
Hereditary pancreatitis	52.0	<i>PRSS1</i>	History of early pancreatic inflammation with no known cause
Cystic fibrosis	31.5	<i>CFTR</i>	History of cystic fibrosis
Hereditary breast/ovarian cancer Carriers of <i>BRCA1</i> Carriers of <i>BRCA2</i>	23.1 5.9 – 6.6	<i>BRCA1</i> <i>BRCA2</i>	History of breast and/or ovarian cancer
Familial atypical multiple mole melanoma syndrome	13.1	<i>CDK2NA/p16</i>	Multiple melanomas, with or without history of pancreatic malignancy
Familial pancreatic cancer	6.4 – 32.0	<i>BRCA2, CDK2NA/p16, STK11, PRSS1</i>	Family history of pancreatic cancer
Hereditary nonpolyposis colorectal cancer syndrome	< 6.0	<i>MLH1</i>	Personal/family history of early colorectal cancer

Abbreviation: GI, gastrointestinal.

Sources: Decker et al. *Gastroenterol Hepatol (N Y)*. 2010²; University of Chicago Medical Center. 2011¹⁸; Pezzilli et al. *Pancreas*. 2003.¹⁹ Hruban et al. *Expert Rev Gastroenterol Hepatol*. 2007.²⁰

was greatest (28.6%) between ages 75 and 84, and age-adjusted incidence was reported at 12.0 per 100,000 men and women per year.⁷

The US median age for pancreatic cancer-associated mortality between 2004 and 2008, as reported by SEER, was 73.⁷ Patients in the 75-to-84 age-group accounted for 30.5% of pancreatic cancer-related deaths. In terms of all patient deaths reported in the US between 2004 and 2008, the overall pancreatic cancer-associated age-adjusted death rate was 10.8 per 100,000 men and women per year.⁷

In most cases, pancreatic cancer has a very unfavorable prognosis. It is estimated that 52% of all patients diagnosed with pancreatic cancer already have distant disease at the time of diagnosis; in 26%, cancer has already metastasized. According to data from the NCCN,⁵ survival rates for pancreatic cancer are 24% at one year after diagnosis, and 5% at five years.

Treatment options eventually narrow down to palliative care.

Nevertheless, it is important for clinicians to be knowledgeable about pancreatic cancer, with an appreciation for the complexity of this disease. A clinical understanding of patients who are at high risk for pancreatic cancer may afford clinicians the opportunity to identify and treat pancreatic cancer earlier in the disease process.

THE DEVELOPMENT OF PANCREATIC CANCER

The progression from normal ductal epithelium to pancreatic ductal adenocarcinomas occurs through *noninvasive precursor lesions* (usually *pancreatic intraepithelial neoplasias* [PanINs]) that undergo clonally chosen genetic and epigenetic changes in the process.⁸⁻¹⁰ *Intraductal papillary mucinous neoplasms* and *mucinous cystic neoplasms* also play a role in the development of pancreatic cancers.^{8,11,12}

PanINs represent the most commonly identified neoplastic precursor to *invasive ductal adenocarcinomas*,^{8,13} which account for at least 90% of all pancreatic tumors and are considered one of the most lethal among all solid malignancies.¹³⁻¹⁵ PanINs measure less than 5.0 mm in diameter and cannot ordinarily be detected on pancreatic imaging.⁸ PanINs can store somatic genetic changes identified in invasive pancreatic cancers; these changes increase at the same rate that cytologic and architectural atypia develop in the precursor lesions.^{8,10} The genetic and epigenetic variations associated with pancreatic cancer may help explain the rapid progression of the tumor to an advanced stage.⁸

Pancreatic Cancer and Diabetes

The correlation between diabetes mellitus and pancreatic cancer has been acknowledged for many years; patients with type 1 or type 2 diabetes have an increased risk for

TABLE 2
Noninherited risk factors²

Risk factor	Incidence ratio
Chronic pancreatitis	18.5 – 26.3
Diabetes	
Type 1	2.0
Type 2	1.8
Smoking	1.6 – 2.5
Obesity	1.72

Source: Decker et al. *Gastroenterol Hepatol (N Y)*. 2010.²

pancreatic cancer—by 40% to 100% in patients with long-term diabetes.¹⁶ In nearly one-third of patients who develop “late-onset diabetes,” this condition may be an effect (and thus, a “harbinger”¹⁶) of pancreatic cancer. In the recently diagnosed diabetic patient, the risk for pancreatic cancer is increased by four- to sevenfold, and 1% to 2% of patients diagnosed with diabetes at age 50 or older will develop pancreatic cancer within three years.^{16,17}

Pancreatic cancer should not be ruled out in the differential diagnosis in a patient who receives a new diagnosis of diabetes, despite an absence of risk factors for diabetes, after age 70.³

Other Risk Factors for Pancreatic Cancer

Cigarette smoking and family history (ie, at least one first-degree relative affected by the disease) are the predominant risk factors for pancreatic cancer. In addition to smoking, significant avoidable or reversible risk factors include alcohol abuse, obesity, a sedentary lifestyle, a diet high in fats and meats and low in vegetables and folate, and certain environmental exposures (eg, solvents used in dry cleaning, gasoline-related particles, nickel).^{2,4,8} Risk factors that are unavoidable or irreversible include advancing age, male gender, African-American ethnicity, a non-O blood group type, and a history of radiation treatment.^{4,8} Analyses of risk factors for pancreatic cancer appear in Table 1^{2,18-20} (inherited risk factors, page 28) and Table 2² (non-

inherited risk factors).

It has been estimated that 20% to 25% of pancreatic tumors are attributable to cigarette smoking, and individuals who smoke carry more cancer-related genetic mutations than do nonsmokers.^{21,22} Additionally, patients with hereditary pancreatitis who smoke are at double the risk for pancreatic cancer and can develop the disease 20 years earlier than those with the associated genetic mutation who do not smoke.⁴ Among the germline mutations associated with cancer, *BRCA2* mutations have been reported in 12% to 17% of patients with familial pancreatic cancer.²³

As of 2010-2011, the US Preventive Services Task Force²⁴ (USPSTF) recommended against routine screening (ie, abdominal palpation for organomegaly, serologic markers, or ultrasonography) for pancreatic cancer in asymptomatic adults; the USPSTF has not yet reviewed the effectiveness of screening patients with hereditary pancreatitis, even though they

“may have a higher lifetime risk for developing pancreatic cancer.”²⁴ Screening for pancreatic cancer is usually reserved for patients with a lifetime pancreatic cancer risk of at least 5%; it begins with a genetic analysis to detect mutations associated with pancreatic cancer.^{4,18} Imaging may follow, with the intent to detect precursor lesions or early pancreatic cancers.⁴

CLINICAL PRESENTATION

Clinically silent in its early stages, pancreatic cancer usually presents after the tumor has metastasized to distant organs or has invaded adjacent tissues. Typically, patients with pancreatic cancer have undergone abdominal CT for evaluation of other clinically indicated reasons before receiving this diagnosis.⁸

The presenting symptoms for pancreatic cancer include, but are not limited to, abdominal pain, midback pain, jaundice, loss of appetite and weight loss, floating stools, dyspepsia, nausea, and depression^{5,25} (see Figure

1²⁵ for a detailed analysis of self-reported symptoms in a study of patients with pancreatic cancer). Both deep and superficial venous thrombosis, which are not unusual on presentation, can be an indication of malignant disease.^{8,26} In patients with pancreatic cancer, incidence of thromboembolic disease, in its various manifestations, ranges from 17% to 57%.^{27,28}

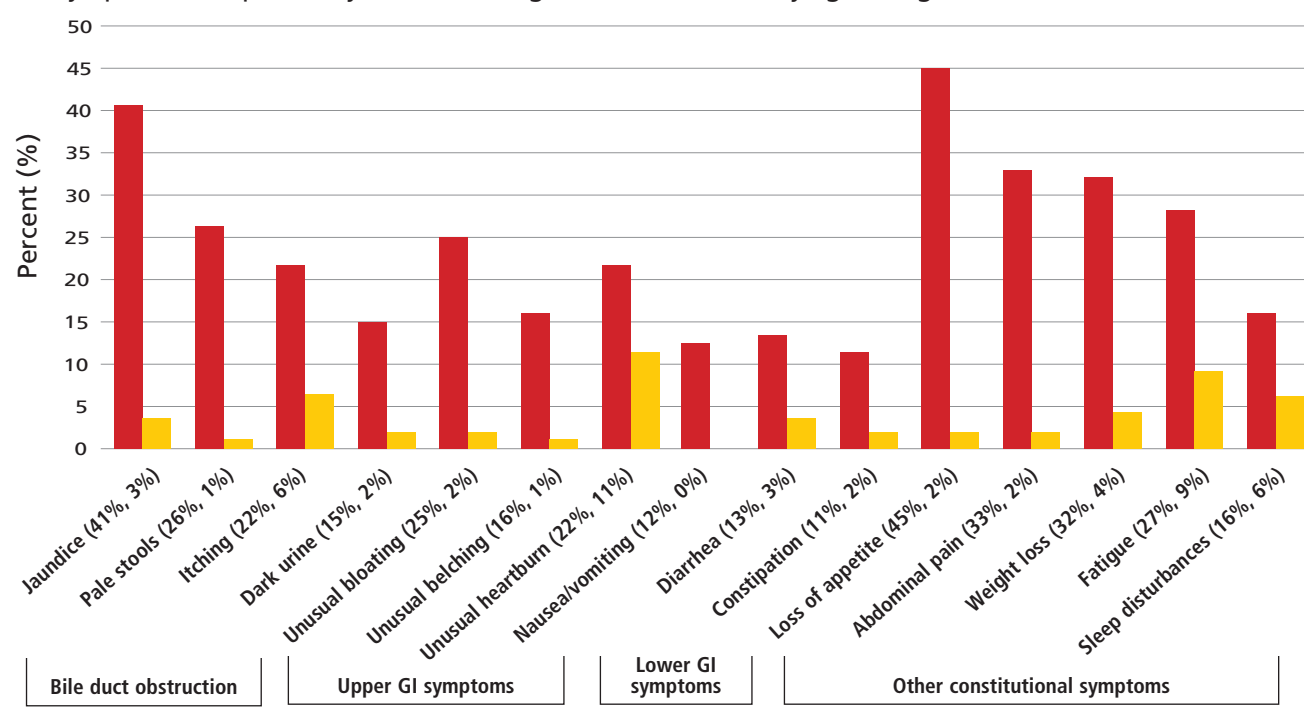
In a 2010 study, Raptis et al²⁹ analyzed data from 355 patients with pancreatic cancer to evaluate whether a specific clinical presentation (abdominal pain, weight loss, jaundice) and delayed timing in referral, diagnosis, and treatment had any impact on the operability, resectability, and/or survival rate associated with pancreatic cancer. The researchers concluded that the time delay between referral and treatment had no significant impact on patient survival.

PHYSICAL EXAMINATION

Abdominal pain is the presenting complaint in about half of all

FIGURE 1
Symptoms of pancreatic cancer²⁵

In a population-based study of pancreatic cancer in the San Francisco Bay area, Holly et al²⁵ compared incidence of symptoms as reported by 120 patients with the disease (red bars), compared with incidence of symptoms as reported by 180 controls (gold bars), matched by age and gender.



Reprinted from *Clin Gastroenterol Hepatol*, 2004;2(6). Holly et al. Signs and symptoms of pancreatic cancer: a population-based case-control study in the San Francisco Bay area, page 513.²⁵ Copyright (2004), with permission from Elsevier.

Case Patient: Woman, 66, with Left-side Abdominal Pain and Weight Loss^{33,34}

An African-American woman, age 66, presented with a 5-month history of continuous abdominal pain. She reported nausea without vomiting, whether or not she had eaten recently, and denied any associated contributing factors (ie, constipation, diarrhea, bloody stools). She described the abdominal pain as cramping in nature and generalized to the left side of her abdomen; she rated the pain at 7 on a 10-point pain scale. Increased activity, she noted, aggravated her symptoms.

The patient reported a lack of appetite as a result of her abdominal pain and a weight loss of about 10 lb over the previous 2 months. Additionally, intermittent low back pain, which she described as a “pulling” sensation, had begun during the previous 2 to 3 months, although she denied any injury or trauma to explain this.

Observation revealed a patient with a nonjaundiced appearance. The abdominal exam revealed a soft and round, nondistended abdomen with no hepatosplenomegaly and no ascites. Marked tenderness of the epigastric region was noted, as well as left-side pain with no fluid wave.

The patient was referred to a gastroenterologist for further evaluation of her abdominal pain and appropriate treatment. Eventually, after multiple diagnostic tests (see “Noteworthy Findings From Diagnostic Studies,” below), abdominal/pelvic CT findings led to a diagnosis of locally advanced pancreatic cancer.

Further imaging was performed to determine the

staging of the pancreatic mass. Endoscopic ultrasonography revealed three enlarged peripancreatic lymph nodes and cholelithiasis; concern for malignant involvement was raised as a result of these and other endosonographic criteria.^{33,34} Results of biopsy of the three enlarged lymph nodes were positive for malignancy, consistent with adenocarcinoma (tumor staging, T4 N1 MX).

Noteworthy Findings from Diagnostic Studies

Laboratory results

The only abnormal finding was blood urea nitrogen (BUN), which measured low at 6.0 mg/dL (normal range, 7.0 to 20.0 mg/dL).

Imaging

- *Colonoscopy.* Diffuse diverticulosis, left- greater than right-sided. Internal and external hemorrhoids. Two hyperplastic sigmoid polyps.
- *Abdominal ultrasound.* Poorly visualized liver. Underlying liver lesion cannot be excluded. No gallstones detected. Thickening of pericholecystic fluid with an unremarkable pancreas.
- *Abdominal/pelvic CT.* Nonspecific mass encasing the superior mesenteric artery. Differential considerations include inflammatory tissue relative to vasculitis versus an infiltrative surrounding mass, such as a sarcoma/lymphoma. No other significant finding (eg, adenopathy).
- *Pelvic ultrasound.* Markedly limited, uterus surgically absent, ovaries not seen.
- *Upper endoscopy.* Numerous erosions, some measuring 6 mm to 7 mm, located in the antrum and the distal body of the stomach. Linear erosions, duodenitis, normal-appearing esophagus.

nosis should include a malignant obstruction of the common bile duct, gastric cancer, cholangitis, cholelithiasis, choledolithiasis, cholecystitis, a choledochal cyst, duodenal or gastric ulcers, and acute or chronic pancreatitis.³ Additionally, conditions whose symptoms can mimic those of pancreatic cancer include abdominal aortic aneurysm, intestinal ischemia, and stricture of the bile duct. Symptoms associated with pancreatic ductal adenocarcinoma may also occur in patients with tumors of the bile duct, pancreatic lymphoma, gastric lymphoma, ampullary carcinoma, or hepatocellular carcinoma.³

LABORATORY WORKUP

Testing should include a complete metabolic panel, lipase, amylase, and a complete blood count with differential. These will reveal abnormalities in the total bilirubin and/or liver enzymes, and possible elevation of lipase and/or amylase, which could indicate acute, chronic, or hereditary pancreatitis—all of which are implicated in pancreatic cancer.^{2,35-37}

No distinct tumor markers for pancreatic cancer have yet been identified. Though low in specificity for pancreatic cancer, the serum marker *cancer antigen 19-9* (CA 19-9) is elevated in most patients when pancreatic cancer is diagnosed.³⁸ Also, postsurgical levels of CA 19-9 are effective in evaluating patients’ response to neoadjuvant therapy and determining patient prognosis.³⁹

DIAGNOSTIC IMAGING

Because it is noninvasive and relatively inexpensive, abdominal ultrasound (US) is often used first to investigate abdominal pain or jaundice; results suggestive of pancreatic cancer might include low echoic mass or dilatation of the pancreatic duct or of the common bile duct.⁴⁰ However, conventional US is only 50% to 70% accurate for a diagnosis of pancreatic tumor.^{40,41}

In many trials of imaging options for early detection and

adult patients who seek primary care.^{30,31} This presentation is contestable in both primary care and specialty practice, such as gastroenterology, because it is usually a benign symptom; it can also be an indication of serious acute pathology³² (see “Case Patient”^{33,34} in box above).

In the study by Raptis et al,²⁹ abdominal pain was the symptom with which patients affected by pancreatic cancer most commonly presented to primary care. Thus, it is important for the clinician to perform a thorough abdominal exam—inspection, auscultation, percussion, light touch, and deep palpation—on any patient with such symptoms. Deep palpation is specifically

sensitive, since it can sometimes help the provider feel the abdominal organs, especially if they are enlarged. Opioids may be given if needed while the assessment proceeds.³⁰

Other key points to include in the physical exam of a patient presenting with abdominal pain are vital signs, observation for jaundice (which in one study was reported in 41% of patients with pancreatic cancer²⁵), chest auscultation and percussion, examination of the rectal, pelvic, and genitourinary regions, and an evaluation of mental status.³¹⁻³³

Abnormal findings can help guide clinical decision making and treatment planning. It should be emphasized, however, that tu-

mors of the pancreas can be difficult to detect and diagnose because of the anatomic location of the pancreas and the disease’s insidious properties.^{4,14}

Differential Diagnosis

It is critical to explore the many differential diagnoses for abdominal pain; the history and physical examination should guide the evaluation. Characterizing the pain according to location, chronology, severity, aggravating and alleviating factors, and associated symptoms can be most helpful. Pregnancy should be excluded in all women of childbearing age who present with abdominal pain.^{30,31}

When pancreatic cancer is suspected, the differential diag-

staging of pancreatic cancer, *endoscopic US* (EUS) has been deemed an effective modality for defining local T and N staging and for evaluating the potential for vascular involvement; CT has been pronounced effective for defining distant metastasis.²³ For an algorithm detailing evaluation of the patient with a suspected pancreatic tumor, see Figure 2.²³

All patients with suspected pancreatic cancer should be evaluated initially using CT or MRI.⁵ *Multidetector row CT* (MDR-CT) is the most commonly used imaging modality for the detection and staging of pancreatic carcinoma.²³ On contrast-enhanced CT, pancreatic adenocarcinoma commonly appears as a low-density area. EUS-guided fine-needle aspiration is an appropriate option for making a diagnosis with tissue samples.^{3,23,40} Triphasic pancreatic protocol CT provides about 90% accuracy for predicting resectability of a pancreatic tumor; EUS is comparably effective.^{3,5}

MR cholangiopancreatography (MRCP) is a useful tool for visualizing the pancreas and the bile duct, while *endoscopic retrograde cholangiopancreatography* (ERCP) combines endoscopy and x-ray to visualize the pancreas and biliary tree.^{18,42} In one prospective, controlled study comparing these two modalities, MRCP and ERCP had 84% and 70% sensitivity, respectively, and 97% and 94% specificity, respectively, for diagnosis of pancreatic cancer (in cases actually diagnosed by histologic findings following surgical or fine-needle biopsy).⁴² Although ERCP makes it possible to obtain cytology and histology samples and to perform biliary stenting in patients with obstructive jaundice, it can miss tumors in the uncinus process, the accessory duct, and the tail of the pancreas.^{23,40}

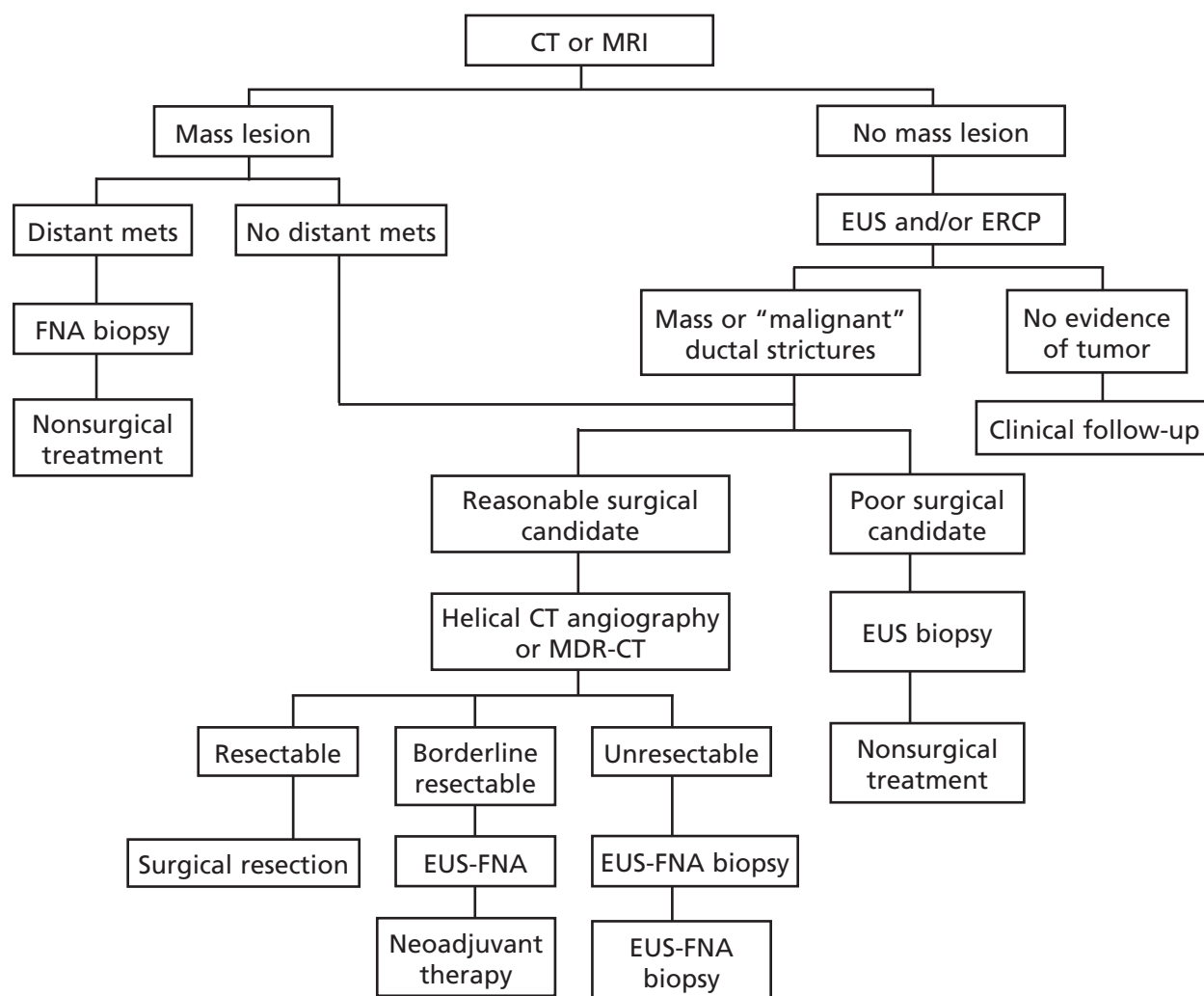
Tumor Staging for Pancreatic Cancer

Pancreatic tumors can develop from various pancreatic cell lines;

FIGURE 2

Diagnostic approach to the patient with suspected pancreatic cancer²³

Patients experiencing pain, weight loss, and jaundice should be evaluated as shown.



Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; mets, metastases; EUS, endoscopic ultrasonography; ERCP, endoscopic retrograde cholangiopancreatography; FNA, fine-needle aspiration; MDR-CT, multi-detector row CT.

Adapted with permission from: Fernández-Del Castillo C, Jimenez RE. Epidemiology and risk factors for exocrine pancreatic cancer (2011).²³ In: UpToDate, Basow DS (Ed), UpToDate, Waltham, MA, 2012. Copyright © 2012 UpToDate, Inc. For more information, visit www.uptodate.com.

they are defined by appearance, hormonal function, and origin cell type.⁴³ The staging system for pancreatic exocrine cancer continues to evolve.^{44,45} In the seventh edition of the American Joint Committee on Cancer's *AJCC Staging Manual* (2011),⁴⁴ the AJCC bases the preoperative clinical staging of pancreatic cancer on the results of high-quality cross-sectional imaging, through which local resectability and the absence or presence of distant disease are determined^{44,45} (see Table 3,^{44,45} page 32).

Clinical staging categories for the pancreatic tumor are:

- Resectable
- Borderline resectable

- Locally advanced, and
- Metastatic disease.⁸

The significance of tumor staging extending past *resectable* versus *unresectable* is currently unknown, as treatment has had little effect on survival. Cancers involving the pancreas are typically described according to the location of involvement within the organ: the head, the body, the tail, or the uncinus process.⁸

Confirming the presence of ductal adenocarcinoma by histology and cytology is essential; long-term survival may be increased in patients treated for other forms of pancreatic cancer (eg, ampullary or periampullary carcinomas; mucinous cystad-

enocarcinomas) or even benign lesions.¹⁵

TREATMENT AND MANAGEMENT

One reliable evidence-based clinical resource is the NCCN publication *Clinical Guidelines in Oncology for Pancreatic Adenocarcinoma*.⁵ A multidisciplinary approach to resectable or borderline resectable pancreatic cancer is the best management strategy and should involve a consulting gastroenterologist, a primary care provider, a surgeon, a medical oncologist, and a radiation oncologist, if one is needed.^{5,8,46} In patients with locally advanced or metastatic pancreatic cancer, a

TABLE 3
Current Tumor–Node–Metastasis Staging for Pancreatic Cancer^{44,45}

The American Joint Committee on Cancer,⁴⁴ in the seventh edition of its staging manual, recommends preoperative staging of pancreatic cancer using the following definitions, anatomic stages, and prognostic subgroups:

Primary tumor (T):

TX	Cannot be assessed
T0	No evidence thereof
Tis	Carcinoma in situ ¹ (including PanINIII classification)
T1	Limited to the pancreas, ≤ 2 cm at greatest dimension
T2	Limited to the pancreas, > 2 cm at greatest dimension
T3	Extends beyond pancreas but neither celiac axis nor superior mesenteric artery involved
T4	Involves celiac axis or superior mesenteric artery (ie, is unresectable)

Regional lymph nodes (N):

NX	Cannot be assessed
N0	No metastasis
N1	Metastasis present

Distant metastasis (M):

M0	None present
M1	Present

Anatomic stages/prognostic subgroups

Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T1	N1	M0
	T2	N1	M0
	T3	N1	M0
Stage III	T4	Any N	M0
Stage IV	Any T	Any N	M1

Sources: Edge et al, eds. *AJCC Staging Manual*. 2011⁴⁴; Katz et al. *CA Cancer J Clin*. 2008.⁴⁵

complete evaluation by a palliative care team is indicated.²⁶

Surgery

Currently, the only known curative therapy for pancreatic cancer is surgical resection of the tumor and its surrounding tissue.⁴⁷ The anatomic location and position of the tumor will guide the choice among surgical options:

- *Classic pancreaticoduodenectomy* (the Whipple procedure), recommended for tumors involving the head, neck, and uncinate process of the pancreas
- *Pylorus-preserving pancreaticoduodenectomy* (resection of the head, neck, uncinate pro-

cess, and transection of the duodenum)

- *Extended or radical pancreaticoduodenectomy* (treatment, as for periampullary malignancies, that may involve resection of the head, neck, and uncinate process of the pancreas; the duodenum, gastric antrum and pylorus, common bile duct, and gallbladder; extensive dissection of retroperitoneal tissue and lymph nodes; possible vascular resection)
- *Total pancreaticoduodenectomy*, an option to treat a multicentric tumor or diffuse carcinoma of the entire gland; and
- *Distal pancreatectomy*, for ade-

nocarcinomas in the body and tail of the pancreas.^{14,48-50}

In patients with borderline resectable pancreatic cancer, the risk for positive surgical margins is high because tumors are likely to be involved with adjacent tissue (eg, nerve plexus, portal vein).^{46,51} This risk can be reduced, and prognosis improved, through neoadjuvant treatment regimens that combine gemcitabine-based chemotherapy and chemoradiotherapy.⁵¹

Palliative Chemotherapy

The stated purpose of palliative therapy, according to the NCCN,⁵ is to optimize quality of life by relieving cancer-related pain and other symptoms associated with biliary obstruction or gastric outlet obstruction. For patients with locally advanced, resectable or metastatic disease, NCCN recommendations (category 1 or 2A) for appropriate first-line therapy include:

- Gemcitabine, standard infusion (ie, 1,000 mg/m² over 30 min, once per week for three weeks every 28 days), though not considered effective for certain pancreatic carcinomas⁸
- Gemcitabine plus cisplatin
- Gemcitabine plus erlotinib
- Gemcitabine plus capecitabine.^{5,52-55}

In 2011, researchers in France reported results of a phase III trial comparing gemcitabine with the combination chemotherapy regimen FOLFIRINOX (oxaliplatin, irinotecan, fluorouracil, and leucovorin). According to Conroy et al,⁵⁶ patients randomized to receive FOLFIRINOX experienced a survival advantage (median progression-free survival,

than patients in the gemcitabine group.^{5,56}

NCCN-recommended second-line therapies include gemcitabine monotherapy (for patients who have not previously received this agent); capecitabine monotherapy; 5-fluorouracil combined with leucovorin and oxaliplatin; or oxaliplatin plus capecitabine.^{5,57,58}

FOLLOW-UP

The primary care provider should initiate supportive care at the time the patient receives a diagnosis of pancreatic cancer, including information about prognosis and treatment options (particularly palliative care).⁸ The clinician should continue to follow the patient's clinical course throughout treatment for advanced disease. Pain management should be a priority, particularly identifying and addressing its precise cause.²⁶

As with other cancers, pancreatic cancer poses a considerable risk for recurrence after surgical resection and/or chemoradiation. Ongoing follow-up physical exams, routine laboratory studies (including screening for CA 19-9 every one to three months), and imaging studies should be ordered and results reviewed periodically (for example, CT at least every six months).²³

Anticipatory Guidance for At-Risk Patients

Counseling patients at high risk for pancreatic cancer, targeting prevention and early detection, is key to reducing the incidence of this lethal disease. It is important to educate patients regarding the risk factors associated with

pancreatic cancer—particularly smoking, the most reversible risk factor for pancreatic cancer.⁴ Patients who present with chronic pancreatitis and who consume excessive amounts of alcohol should be warned about the association between chronic pancreatitis and pancreatic cancer.^{4,8}

►PRIMARY POINT

Neoadjuvant treatment regimens combining chemotherapy and chemoradiotherapy may reduce the risk for positive surgical margins in patients who undergo surgery for borderline resectable pancreatic cancer.

6.4 months vs 3.3 months) and delayed degradation of quality of life, but they were more likely to experience toxicity (eg, febrile neutropenia, thrombocytopenia)

Counseling should also focus on healthy eating, with a diet high in fruits and vegetables, routine physical activity, weight management, and an increased dietary intake of vitamin D (> 600 IU/d).^{24,59}

Genetic counseling and testing options should be explored with at-risk patients and their families. These patients should be advised to seek immediate medical attention for abdominal pain, unexplained weight loss, and/or jaundice, and to return for further evaluation if symptoms persist despite initial treatment.⁵⁹

The greater the clinician's clinical understanding of the various pancreatic syndromes and their management, the better prepared he or she will be to evaluate each patient's genetic risk and to provide high-quality clinical care.

CONCLUSION

Making a diagnosis of pancreatic cancer early enough to make effective treatment possible continues to challenge both researchers and clinicians. Current treatment modalities are not sufficiently effective, as evidenced by the high mortality rate associated with pancreatic cancer. Until clinical research provides increased insight into detecting this lethal disease and generating more effective therapies, it is up to the primary care clinician to routinely explore the family and social history of at-risk patients and to recognize the risk factors and symptomatology associated with pancreatic cancer. Early detection, followed by the most effective treatment options available, may lead to a more hopeful prognosis. **CR**

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