After completing this article, the reader should be able to:
- Understand anatomy of the pancreas as well as its exocrine and endocrine functions.
- Compare and contrast the genetic and nongenetic risk factors for pancreatic cancers and acute and chronic pancreatitis.
- List symptoms of duct obstructions, pancreatitis, and pancreatic cancer.
- Describe computed tomography signs of duct obstructions, pancreatitis, and pancreatic cancer.
- Explain staging and prognostic scoring systems for pancreatitis and pancreatic cancer.
- Discuss the roles of contrast-enhanced multidetector computed tomography and other imaging modalities in the diagnosis, staging, and management of pancreatitis and pancreatic cancer.
into the upper duodenum (a C-shaped curve in the upper small intestine) at the major papilla.3,4 The major papilla also is known as the ampulla of Vater, hepatopancreatic ampulla, or hepatopancreatic duct.3,4 Partially digested food, called chyme, moves from the stomach into the duodenum where enzymes break down chyme components for digestion or excretion as waste.

The surface of the pancreas is covered with lobes that contain endocrine cell clusters called islets of Langerhans and clusters of exocrine cells called acini. Acini secrete pancreatic fluids that drain into tiny intralobular ductules and then into the main and accessory pancreatic ducts, through which they reach the duodenum.3,4

The pancreatic blood supply comes from branches of the superior mesenteric, celiac, and splenic arteries (see Figure 1). The pancreas also is surrounded by a regional network of immune system lymph nodes (see Figure 2).

The pancreas is divided into 3 major regions: the pancreatic head, body, and tail.4 The head rests in the curve of the duodenum. It contains the major papilla and a structure known as the uncinate process, which is a wedge-shaped projection.3 The main pancreatic duct passes through the length of the tail and through the body and the head, terminating at the major papilla where it joins with the common bile duct.3,4 The common bile duct originates in the liver and passes through the pancreatic head to deliver bile into the duodenum.3,4 The accessory pancreatic duct usually enters the duodenum slightly above (~2 cm) the major papilla.4

The anatomy of pancreatic ducts can vary considerably between individuals, reflecting prenatal developmental differences.4,5 In the most frequent arrangement of pancreatic ducts, seen in half of patients, the accessory and main ducts communicate. Pancreas divisum is a congenital variant in which the 2 ducts do not fuse to develop a connection. Divisum long was considered a cause of pancreatitis.6 However, despite its marked deviation from typical duct anatomy, pancreas divisum and other anatomic variants of the ducts usually do not affect pancreas function.4

![Figure 1](image1.png)  
**Figure 1.** Gross anatomy of the pancreas, its blood supply, and its relation to other internal organs.

![Figure 2](image2.png)  
**Figure 2.** Lymph node locations surrounding the pancreas.
Endocrine Functions

The pancreas plays a key endocrine role in blood glucose regulation, releasing hormones such as insulin, glucagon, somatostatin (which helps regulate insulin and glucagon secretion), and appetite-suppressing pancreatic polypeptide into the bloodstream. The pancreas’ endocrine tissues are composed of well-vascularized islets of Langerhans, which are situated between exocrine cell acini and are particularly common in the pancreatic tail. The cells of the islets of Langerhans are in close physical association with capillaries, allowing access to the bloodstream, into which they release—and from which they receive—regulatory hormone signals.

The 4 types of cells in the islets of Langerhans are:

- Alpha – secrete glucagon to upregulate glucose levels.
- Beta – secrete insulin to downregulate glucose levels.
- Delta – secrete somatostatin to regulate alpha and beta cell excretion.
- Gamma – secrete the appetite-suppressing hormone pancreatic polypeptide.

Exocrine Functions

The pancreas plays a key role in digestion, producing alkaline bicarbonate ions that neutralize stomach acids and digestive enzymes that are used to break down foods within the small intestine. The exocrine activities of the pancreas are regulated by endocrine hormones at the islets of Langerhans within the pancreas and by hormones secreted in the stomach and duodenum when food arrives in the stomach. These hormones are then delivered to the pancreas in the bloodstream. Pancreatic digestive enzymes include proteases, which break down proteins into amino acids, and lipases, which break down dietary fats. The pancreas also is a source of amylase, which breaks down polysaccharide starches into glucose; amylase also is present in mouth saliva.

These digestive enzymes are powerful and could damage and destroy pancreatic tissues. Therefore, they are produced in an inactive form as proenzymes that carry a protective trypsin inhibitor until they are released into the gastrointestinal tract at the major papilla, at which point they are released from the trypsin and become activated enzymes. (Hereditary childhood-onset pancreatitis appears to be associated with a genetic mutation that prevents trypsin deactivation of digestive enzymes within the pancreas.) Bile that breaks down dietary fats also enters the duodenum at the major papilla.

Pathobiology

The pathobiology of acute and chronic pancreatitis and pancreatic cancer is complex, involving the interaction of genetic-molecular pathways, immune system responses, and toxic insults related to environmental and lifestyle factors. Acute and chronic pancreatitis have overlapping etiologies. Recurring acute pancreatitis can progress to become chronic pancreatitis. In turn, chronic pancreatitis increases the risk of pancreatic cancer, and type 2 diabetes appears to increase the risk of acute and chronic pancreatitis, calculi, and pancreatic cancer.

Biliary and Pancreatic Calculi

Hard and potentially obstructive biliary calculi can develop in the gallbladder, the common bile duct, or the pancreatic ducts. These can range in size from sand-like grains to golf balls. Their chemical constituents can vary but usually include calcium and bilirubin, or cholesterol. Calculi can be classified by anatomy of origin and by their biochemical components. Anatomic classification separates primary gallbladder calculi from secondary gallbladder calculi that have migrated into the common bile duct and primary bile duct calculi. Primary common bile duct calculi are made up mainly of bilirubin, for example, and gallstones are composed of cholesterol. The calculus’ color reflects its chemical composition, with black calculi containing bilirubin and brown calculi (usually found in the common bile duct) containing calcium bilirubinate.

Although biliary calculi are most frequently found in the gallbladder, they also can pass into the bile ducts, where they are sometimes called bile duct stones or secondary gallstones. Calculi also can develop in, and migrate down along, the bile ducts, including the common bile duct, which passes from the liver through the pancreas. In the United States, primary common bile duct calculi occur less often than do gallstones; however, secondary bile duct calculi that initially formed in
the gallbladder are sometimes seen in association with primary gallstones. Common bile duct calculi also occur frequently (70%) among patients who have bile duct calculi. Common bile duct calculi and pancreatic duct calculi can grow to obstruct ducts, contributing to pancreatitis.:

Calculi obstruction of ducts or the major papilla can be asymptomatic but commonly leads to pancreatitis. Without drainage of these structures, patients with this condition often develop jaundice and sometimes fever.

**Acute Pancreatitis**

Pancreatitis refers to the inflammation of the pancreas. It usually is a diffuse disease of the entire pancreas rather than a focal inflammation, except for cases associated with trauma, laceration, and hemorrhage. Acute pancreatitis has a sudden onset of symptoms and represents a potentially life-threatening condition that can be painful; up to 20% of cases are clinically severe and associated with high morbidity and mortality rates. Inflammation occurs when pancreatic enzymes become active before they are delivered into the duodenum, resulting in autodigestion of pancreatic tissues. In up to 80% of cases, acute pancreatitis is not severe and will resolve over time. In severe cases, pancreatic tissue, or the tissue of organs around the pancreas, dies. Complications, primarily infection, associated with this necrosis can be localized or systemic and life threatening. Mild and severe acute pancreatitis were traditionally termed interstitial (edematous) and necrotizing, respectively. More than 80% of deaths related to acute pancreatitis are associated with pancreatic necrosis and infection.

Acute pancreatitis can be caused by a wide array of underlying factors, including heavy alcohol consumption and biliary calculi. It also can be triggered by mumps, infections, surgery, and endoscopy.

Severe acute pancreatitis complications have been described as 2-phased, referring to an early toxicoenzymatic phase that occurs during the first 2 weeks, followed in some cases by a subsequent necrotic infection or septic phase usually emerging 3 weeks or more after onset. When fluids from the inflamed pancreas enter the bloodstream, pancreatic toxemia can ensue, potentially affecting organ function in the heart, lungs, kidneys, and brain. Eventually, without timely and effective intervention, multiple organ failure and death can occur. The emergence of multidrug-resistant infections in severe acute pancreatitis represents an important management challenge.

**Chronic Pancreatitis**

The pathogenesis of chronic pancreatic inflammation is largely unclear. Generally speaking, it appears that chronic inflammation triggers progressive fibrotic scarring and tissue damage. Calculi can exacerbate inflammation and the loss of exocrine and endocrine tissue function when they obstruct the pancreatic ducts. Chronic pancreatitis associated with main pancreatic duct calculi is sometimes called chronic calcific pancreatitis.

Recurring acute pancreatitis sometimes progresses to chronic pancreatitis. A necrosis-fibrosis pathway or sequence has been proposed for this progression, with sequential injuries to pancreatic tissues by alcohol or other insults leading to fibrotic scarring and chronic inflammation. Metabolic insults to pancreatic tissues, particularly in the presence of certain genetic polymorphisms (gene variants), can disrupt trypsin mechanisms and trigger early activation of enzymes within the pancreatic ducts, causing fibrotic scarring that can obstruct ducts. Repeated or chronic immune system activation and inflammation can lead to fibrosis and tissue metaplasia, potentially increasing the risk of tumor formation. Metaplastic pancreatic ducts are associated with pancreatitis and pancreatic cancer.

Among patients with alcoholism, progression from acute to chronic pancreatitis is associated with the number and severity of previous acute attacks. Cessation of alcohol consumption can prevent progression from acute to chronic pancreatitis.

**Pancreatic Cancer**

Almost all pancreatic cancers arise in the organ’s exocrine tissue, and an estimated 70% to 78% of pancreatic tumors occur in the pancreatic head region (see Figure 3). Approximately 11% of pancreatic cancers arise in the pancreatic body region, and 11% arise in the tail region. Because of the likelihood of bile duct obstruction by tumors growing in the
pancreatic head, tumors in this region often become symptomatic at a less advanced stage than is the case with tumors in the pancreatic body or tail.\textsuperscript{22} Pancreatic tumors are frequently inoperable after they have metastasized or have grown around key blood vessels such as the superior mesenteric vein (see Figure 4).

Of the different forms of pancreatic cancer, the most common is pancreatic adenocarcinoma, an aggressive malignancy arising in the organ’s exocrine enzyme-transporting ducts. Adenocarcinoma represents 85% of all pancreatic cancer diagnoses.\textsuperscript{22} It is commonly known as invasive adenocarcinoma or duct cell carcinoma.\textsuperscript{23}

Nonadenocarcinoma pancreatic cancers include the exocrine acinar cell carcinoma of the pancreas, which arises in the cells that produce digestive enzymes rather than in the ductal cells that transport them. Acinar cell carcinomas represent the second most common form of pancreatic cancer but are rare.\textsuperscript{23} Less common forms of exocrine pancreatic cancers include\textsuperscript{23}:

- Adenosquamous carcinoma.
- Cystadenocarcinoma.
- Giant cell carcinoma.
- Mixed type carcinoma (ductal/endocrine or acinar/endocrine).
- Mucinous carcinoma.
- Pancreatoblastoma.
- Papillary cystic neoplasm (Frantz tumor).
- Papillary mucinous carcinoma.
- Signet ring carcinoma.
- Small cell carcinoma.
- Undifferentiated carcinomas.

**Figure 3.** This contrast-enhanced computed tomography (CECT) scan shows a large locally unresectable adenocarcinoma of the pancreatic head (arrow). Note the difference in attenuation between the tumor and the avidly enhancing normal pancreas. Figure used with permission from Darren DD, Brennan MB, Zamboni GA, Raptopoulos VD, Kruskal JB. Comprehensive preoperative assessment of pancreatic adenocarcinoma with 64-section volumetric CT. Radiographics. 2007;27:1656.

**Figure 4.** These CECT images show vascular involvement of a pancreatic tumor. A. Pancreatic mass (arrowhead) causing severe flattening of the superior mesenteric vein (white arrow). Note also the cuff of soft tissue (blue arrows) surrounding the celiac axis. B. The coronal reformatted image depicts the degree of venous deformity and the low-attenuation mass (arrow), which was found to be an unresectable pancreatic tumor. Figure used with permission from Darren DD, Brennan MB, Zamboni GA, Raptopoulos VD, Kruskal JB. Comprehensive preoperative assessment of pancreatic adenocarcinoma with 64-section volumetric CT. Radiographics. 2007;27:1662.
Collectively, ductal pancreatic adenocarcinoma and acinar cell carcinoma make up nearly all of the newly diagnosed pancreatic cancers each year. However, rare neuroendocrine tumors arise in the islet cells and represent 1% or less of pancreatic cancer diagnoses overall. Neuroendocrine tumors are sometimes called islet cell tumors. Neuroendocrine tumors sometimes result from the multiple endocrine neoplasia type-1 (MEN-1) syndrome, which is inherited and can cause cancer of the pancreas, pituitary gland, and parathyroid gland.

Pancreatic Adenocarcinoma

Pancreatic adenocarcinoma tumorigenesis involves the progressive accumulation of genetic mutations in premalignant cysts that evolve over time into malignant tumors. This process is similar to that seen with colon cancer, in which premalignant epithelial polyps become colon tumors. The continuing accumulation of gene mutations during treatment can limit treatment success because it facilitates the acquisition of resistance to particular chemotherapies or targeted anticancer agents.

Nonmalignant pancreatic cysts are important precursors to pancreatic cancer. Such cysts are seen in high rates among whites. Cysts that emerge under conditions of repeated or chronic pancreatic inflammation include intraductal papillary mucinous neoplasms (IPMNs), pancreatic intraepithelial neoplasias (PanIns), and mucinous cystic neoplasms. Under conditions of continued or repeated inflammation and high levels of mutated KRAS gene activity, these cystic lesions can become increasingly dysplastic or disorganized and accumulate additional gene mutations. Over time, they can progress from low-grade type 1 neoplasias into high-grade type 3 precancerous neoplasias, and eventually into malignant adenocarcinoma tumors. This process is sometimes referred to as acinar-to-ductal metaplasia.

KRAS gene mutations affect the progression from precursor, or premalignant, cystic lesions into pancreatic cancers. Both IPMN and PanIn cystic lesions are known to be precursors to pancreatic cancers. IPMN lesions are associated with a 25% overall risk of developing invasive tumors; those found in the main pancreatic duct are the most likely to become cancerous. Although KRAS mutations occur in up to 65% of nonmalignant IPMN cystic lesions, they occur in more than 90% of pancreatic duct adenocarcinoma cancers. More than 90% of PanIn lesions harbor KRAS mutations, possibly rendering them more cancer-prone and dangerous.

In addition to KRAS mutations, pancreatic cancer frequently is associated with other genetic mutations in the tumor-suppressing p16, p53, CDK2NA, and SMAD4 (DPC4) genes. BRCA1 and BRCA2 mutations are well known as risk factors for heritable breast cancer; however, these mutations also increase the risk of pancreatic adenocarcinoma, with BRCA2 mutations more than tripling the risk of this pancreatic malignancy. On average, pancreatic tumor cells harbor 63 genetic mutations in 12 distinct molecular gene pathways. Pancreatic adenocarcinomas harboring SMAD4 (DPC4) mutations are more likely to be aggressively metastatic, meaning they more aggressively spread to regional lymph nodes and distant organs. Tumors with this mutation are associated with shorter patient survival times.

Epidemiology

The epidemiology of pancreatic disorders is complex and varies between ethnic populations. African Americans suffer rates of pancreatic disease up to 3 times higher than other ethnicities in the United States. However, calculi—a risk factor for pancreatitis—are less prevalent among African Americans than among whites.

Pancreatic diseases are complexly related to one another. For example, type 2 diabetes—an endocrine disorder of the pancreas—is associated with increased risks of pancreatitis, calculi, and pancreatic cancer.

Acute pancreatitis is a leading gastrointestinal cause of hospitalization, with an annual incidence of up to 45 per 100 000 people. Reported rates have increased over the past decade, partly because of improved detection of pancreatic enzymes in patients’ blood. The estimated annual incidence of chronic pancreatitis is much lower at 4 per 100 000 people per year. As with acute pancreatitis, chronic pancreatitis rates and hospitalizations have increased around the world in recent years, possibly because of increasing levels of tobacco smoking and alcohol consumption.
multiple-step etiology, with acute necrotic events triggering obstructive fibrotic scarring and inflammation. In 2014, the United States saw an estimated 46,420 patients newly diagnosed with some form of primary pancreatic cancer, and 39,590 pancreatic cancer patients died. Pancreatic cancer rates increase with age, particularly after age 50 years. Pancreatic cancers rarely are seen before 40 years of age, and the median age at diagnosis is 71 years. Pancreatic adenocarcinoma is a highly lethal type of cancer. Although less common than many other types of cancer, it is the fourth-leading cause of cancer deaths in the United States, representing 7% of cancer deaths overall. Pancreatic cancers typically are diagnosed only after they are advanced, symptomatic, and difficult to treat. More than 90% of patients with pancreatic cancers are diagnosed with metastatic disease. Therefore, the 5-year overall survival rates for patients diagnosed with pancreatic adenocarcinoma is 6% or less; more than half of patients die within 2 years of diagnosis. Pancreatic adenocarcinoma’s dauntingly low survival rate has held for more than 50 years. In contrast, patients diagnosed with the rarer and less aggressive pancreatic neuroendocrine tumors have a 55% overall 5-year survival rate.

**Genetic Factors**

Genetic polymorphisms appear to play a central role in the pathobiology of pancreatic diseases, although these roles are only beginning to be identified and closely studied. For example, KRAS gene activity and mutations are involved in most pancreatic diseases. KRAS gene mutations also might mediate the association of acinar inflammation and pancreatic disease. Candidate gene polymorphisms that might be involved in biliary calculi include ApoB-100 polymorphisms. The total mutational load of pancreatic genomes increases dramatically between normal and chronically or repeatedly inflamed pancreatic tissue, between chronic pancreatitis and pancreatic cancer, and between precancerous intraepithelial neoplasia and pancreatic adenocarcinoma tumors. Certain gene polymorphisms also might increase the risk of acute pancreatitis and the progression of acute to chronic pancreatitis. These include mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, PRSSI, and SPINK1. CFTR mutations affect epithelial cells’ chloride channels in a way that can cause thicker pancreatic exocrine fluids and chronic duct obstruction. PRSSI mutations are seen in hereditary pancreatitis; these mutations lead to a failure to temporarily inactivate digestive enzymes with trypsin while the enzymes are still in the pancreas. SPINK1 mutations similarly disrupt the trypsin inactivation of digestive enzymes, albeit through a different molecular-genetic pathway than does PRSSI. Studies indicate that up to 23% of patients diagnosed with pancreatitis harbor SPINK1 mutations compared with approximately 2% of healthy controls.

Genetic polymorphisms’ influence on pancreatic pathogenesis is not always simple. In most cases, polymorphisms interact with other gene pathways and environmental, dietary, metabolic, and other factors. Regions of the PRSSI, PRSS2, and CLDN2 genes are now understood to play a role in alcohol-related pancreatitis.

**Other Risk Factors**

Authors of a 2014 meta-analysis of data pooled from 51 studies concluded that heavy alcohol consumption, current tobacco use, and obesity are each strongly associated with pancreatic disease risk. Alcohol consumption is a leading causal risk factor for acute and chronic pancreatitis, contributing to up to 67% of chronic pancreatitis diagnoses in North America and up to 95% of cases in the Asia-Pacific region. Tobacco smoking is associated with both acute and chronic pancreatitis, even after alcohol consumption and body mass index are statistically controlled. Cessation of tobacco and alcohol consumption appear to reduce the risk of acute pancreatitis progression and recurrence and to slow progression of chronic pancreatitis.

**Pancreatitis**

In addition to lifestyle risks, acute pancreatitis is associated with calculi, particularly among non–African American patients. Type 2 diabetes, and possibly type 2 diabetes medication, also appear to be associated with an increased risk of acute pancreatitis. Autoimmune disorders appear to increase the risk of both acute and chronic pancreatitis.
associations have been reported for patients with inflammatory bowel disease and systemic lupus erythematosus, for example.\(^{39}\) Autoimmune celiac disease has been estimated to more than double the risk of pancreatitis.\(^{39}\) Autoimmune pancreatitis is infrequent, representing fewer than 5% of pancreatitis diagnoses.\(^{38}\)

Risk factors for chronic pancreatitis are most easily introduced by listing the precipitating risk factor etiologies, which are classified using the TIGAR-O classification system.\(^{17,40}\) Despite a longstanding belief that pancreas divisum is a cause of pancreatitis, the evidence is mixed, and at least one recent study found no association between pancreas divisum and chronic pancreatitis or impaired pancreatic exocrine function.\(^{3}\)

Calculi

Biliary calculi afflicted the people of ancient Egypt and China, as revealed by autopsies of mummies.\(^{46}\) Today, as much as 15% of the U.S. adult population is believed to have biliary calculi, leading to an estimated 622,000 hospitalizations annually.\(^{11}\)

Cirrhosis of the liver and Crohn disease are each strongly correlated with biliary calculi.\(^{44}\) Central obesity (increased abdominal fat) and metabolic syndrome increase the risk of developing biliary and pancreatic duct calculi.\(^{42}\) Common bile duct calculi are a common cause of obstructive acute pancreatitis.\(^{44}\) Because obesity is a risk factor for calculi, it is thought to be a possible cause of the increase in reported pancreatitis rates seen in recent years.\(^{29}\)

African Americans are significantly less likely to develop calculi than are other ethnicities.\(^{4,42}\) In contrast, calculi appear to be more prevalent among Native Americans and Mexican Americans than in other ethnicities, possibly in part because of genetic factors.\(^{4,42}\)

Risk factors also include sex and age. Calculi are unusual in children and are more common in women than in men.\(^{42}\) Risk increases with an increasing number of pregnancies.\(^{42}\) Postmenopausal women tend to face a lower risk of developing calculi than do younger women, but estrogen replacement therapy increases the risk of calculi, suggesting that estrogen plays a role in biliary calculi development.\(^{42}\)

Pancreatic Cancer

Modifiable risk factors for pancreatic cancer include tobacco smoking, obesity, high dietary consumption of animal fats, and type 2 diabetes mellitus.\(^{22}\) Patients with cystic fibrosis or a family history of pancreatic cancer also are at increased risk.\(^{22,23}\) Chronic pancreatitis increases the risk of developing pancreatic cancer, although it is important to note that the overall long-term (20-year) risk of this malignancy is only 5% among patients with chronic pancreatitis.\(^{22,23}\)

Epidemiological studies of pancreatic cancer highlight the potential importance of public health prevention efforts. Researchers who reviewed 117 meta-analyses concluded that two-thirds of major risk factors for pancreatic cancer are modifiable factors such as tobacco use, thereby “affording a unique opportunity for preventing one of our deadliest cancers.”\(^{36}\)

Pancreatic cancer risk also has been connected with Helicobacter pylori infection, idiopathic thrombosis, and ABO group blood types other than O.\(^{22,36}\) In addition, taller adults have a moderately higher risk of developing pancreatic cancer.\(^{36}\)

Type 2 diabetes is an important risk factor for pancreatic cancer, increasing risk by 30% to 200%, according to different studies.\(^{22,10,41}\) Half of patients diagnosed with pancreatic cancer have diabetes; although some studies do not differentiate between type 1 and type 2 diabetes, the association appears to be clear for type 2 rather than type 1 diabetes.\(^{21}\) The association between recently diagnosed diabetes and pancreatic adenocarcinoma is stronger than the long-term risk of this malignancy among people with diabetes, suggesting a possible causal modulation of cancer risk by diabetes disease processes, according to a meta-analysis of data pooled from 88 studies.\(^{43}\) The relationship between diabetes and pancreatic cancer also might be bidirectional, such that diabetes and pancreatic cancer might each increase the risk of the other disease.\(^{29}\) For example, in a small proportion (<1%) of newly onset type 2 diabetes cases, diabetes appears to be caused by pancreatic cancer, and an estimated 40% of patients diagnosed with pancreatic cancer have prior diabetes diagnoses.\(^{29}\)

Diabetes medication also might affect pancreatic cancer epidemiology.\(^{30}\) The diabetes drug metformin has been associated with a reduced risk of pancreatic
cancer, whereas findings about insulin’s role have been inconsistent across studies.\textsuperscript{30,44}

Dietary risk factors have been proposed for pancreatic cancer, although evidence remains weak.\textsuperscript{29} Increased fruit or folate intake appears to reduce the risk of pancreatic cancer,\textsuperscript{30} as does a Mediterranean dietary pattern (consumption of high levels of olive oil, legumes, fruits, and whole grains) when combined with other healthy behaviors like daily physical activity and not smoking.\textsuperscript{29,65}

Other proposed protective factors have included aspirin and tea.\textsuperscript{22} Evidence for aspirin’s benefits have yet to be confirmed.\textsuperscript{22,46} Preliminary in vitro and laboratory animal studies had suggested that green tea or coffee might modulate pancreatic cancer risk, with green tea standing out as a promising chemoprotective agent.\textsuperscript{37,48} However, a meta-analysis of 8 studies found no overall correlation between green tea consumption and pancreatic cancer risk.\textsuperscript{47,48}

Diagnosis and Treatment

Medical imaging plays a critical role in the diagnosis, staging and characterization, treatment planning, and post-treatment monitoring of pancreatic diseases.\textsuperscript{49,50} Although ultrasonography is a noninvasive imaging modality option for initial assessment of acute abdominal pain and to confirm or exclude cholelithiasis (gallstones), CECT is the standard first-line modality for detailed abdominal and pancreatic imaging; it is preferred to confirm diagnoses of pancreatitis and pancreatic cancer.\textsuperscript{10,13,49,50}

CECT helps detect and stage pancreatic cancers.\textsuperscript{49,50} However, CT imaging has important limitations. For example, CT has not yet been shown to reliably detect early duct anatomy changes indicative of chronic pancreatitis or to reliably detect the earliest stages of pancreatic cancer.\textsuperscript{49}

In some situations, other imaging modalities might be more informative. These modalities also are important in diagnostic pancreatic imaging algorithms. Despite relatively low spatial resolution, positron emission tomography (PET)-CT functional imaging with 18-fluorodeoxyglucose is superior to MDCT in detection of pancreatic tumor recurrence after surgery.\textsuperscript{49} PET-CT also allows comprehensive whole-body visualization of the extent of metastatic tumors and, therefore, is potentially useful in staging cancers.\textsuperscript{49} Magnetic resonance (MR) imaging offers better soft-tissue contrast than does CT, and for applications such as detection of suspected small tumors or isoattenuating tumors in the pancreatic head, MR imaging might be superior to CT imaging.\textsuperscript{49} Current diagnostic imaging algorithms for suspected pancreatic tumors recommend initially imaging masses with CECT, but following up with MR imaging if findings from CECT for suspected tumors are ambiguous.\textsuperscript{51}

Computed Tomography

Contrast-enhanced multidetector CT is a standard diagnostic imaging modality for rapidly evaluating patients with abdominal symptoms and suspected pancreatic disease.\textsuperscript{50} The anatomic detail of CECT images and the versatility afforded by contemporary reconstruction and postprocessing software allow detailed differential diagnosis among disorders and etiologies (see Figure 5).

Pancreatic diseases usually affect older adults. Because of the relatively long latency period between irradiation and radiation-associated tumorigenesis, the long-term secondary cancer risk associated with ionizing radiation is relatively low compared with comparable radiation doses delivered to younger patients. Nevertheless, the ALARA (as low as reasonably achievable) principle is a central consideration for ensuring patient protection during any radiographic examination. Observing the ALARA principle means that every patient dose of medical radiation should be the lowest possible to achieve clinical goals. Pancreatic disease management can involve repeated CT examinations. Because of the long-term hazards posed by cumulative doses of ionizing radiation, unnecessary CT examinations should be avoided, and set-up and scan acquisitions should be carefully planned and executed to avoid errors that could require additional imaging examinations.

For pancreatic CECT imaging, the duodenum and stomach usually are distended with a negative oral
contrast medium solution and one cup of water. An intravenous iodinated contrast agent usually is employed to improve image quality and avoid the risk of repeated scanning if noncontrast images offer insufficient detail. The total amount of iodine administered should not exceed 45 g, regardless of concentration or injection rate.

Iodinated contrast bolus tracking allows precisely timed scan delays to ensure acquisition during the intended contrast phase. This involves monitoring the aorta just above the pancreas for enhancement peaks achieving a predefined trigger value (typically, 120-130 HU). The pancreatic phase begins 15 seconds after that trigger value is met. Scan delays also can be timed from the time of contrast agent injection.

CECT acquisition parameters for pancreatic imaging vary between facilities, imaging goals, and MDCT equipment designs and generations. Bolus scan acquisition delay times similarly depend partly on the MDCT equipment involved. Each facility should have written standard operating procedures, and these procedures should be reviewed prior to each examination.

In 2011, Manfredi et al published a protocol for pancreas CECT using MDCT equipment describing a 3-phase scan procedure:

- A precontrast plain CT scan using 10-mm slice collimation is acquired for the upper abdomen.
- A pancreas-phase scan is acquired using 1-mm to 2-mm slice collimation, covering the abdomen from the diaphragm to below the duodenum, during a single breath hold. Scan acquisition of the pancreas (or “late arterial”) phase begins 35 to 40 seconds after intravenous injection of an iodinated contrast agent (125-150 mL bolus injected at a rate of 4-5 mL/s) to allow time for the agent to clear the early arterial phase and reach the pancreatic parenchyma.
- A portal venous-phase scan is acquired of the upper abdomen using 2.5-mm to 5-mm slice collimation. The patient is told to breathe deeply during this scan acquisition, which starts at 70 to 80 seconds after the bolus injection.

The third phase allows visualization of extrapancreatic abnormalities that might help clarify the etiology and extent of pancreatic disease and help identify vein involvement by tumors. CT angiography also can be undertaken to assess pancreatic arteries with an early arterial scan acquisition, with a 20-second delay after contrast injection (see Figure 6).

**Acute Pancreatitis**

Clinical symptoms of acute pancreatitis usually include rapid-onset, steady, and intense pain in the abdomen that radiates to the patient’s back. Pain onset is commonly accompanied by nausea, vomiting, and low-grade fever. Jaundice can indicate bile duct or major papilla obstruction, which can occur in association with acute or chronic pancreatitis.

Acute pancreatitis can represent a medical emergency, as can other conditions with similar clinical presentations. Prompt differential diagnosis is necessary to confirm pancreatitis and rule out such alternative diagnoses as perforated peptic ulcer, gallbladder inflammation, gastrointestinal obstruction,
appendicitis, and intestinal or myocardial (inferior wall) infarction.

In cases of acute pancreatitis, lab tests typically reveal increased levels of pancreatic amylase and lipase; elevated amylase is a preferred method for acute pancreatitis diagnosis.12-13 Onset of acute pancreatitis is defined as the time of onset of abdominal pain; the time since onset should be noted in patients’ medical records when tests and imaging are undertaken.53

Using the revised Atlanta classification system, diagnosis of acute pancreatitis involves confirming at least 2 of the following53:

- Abdominal pain or “acute onset of a persistent, severe, epigastric pain often radiating to the back.”
- Serum lipase or amylase activity concentrations at least 3 times greater than the upper limit of normal.
- Diagnostic imaging findings consistent with acute pancreatitis, obtained using CECT, transabdominal ultrasonography, or MR imaging.

When pain and elevated serum lipase or amylase are confirmed, a diagnosis of acute pancreatitis might be made prior to imaging.53 However, imaging must be undertaken for diagnosis if a patient presents with pain suggestive of acute pancreatitis but without elevated lipase or amylase levels.13

When enzyme-containing pancreatic fluids escape into general circulation, complications can be severe and include early shock, infection, multiple organ failure, enzyme damage to lung tissue, and systemic inflammation.12 Intra-abdominal hypertension and abdominal compartment syndrome commonly occur in severe acute pancreatitis and can lead to hemorrhage, severe edema, and intestinal obstruction.14 Late complications can include potentially painful scar tissue-lined pockets of pancreatic fluids called pseudocysts that might bleed, rupture, or obstruct ducts.55,56 Acute bleeding also can indicate retroperitoneal hemorrhage or pseudoaneurysms, which can be confirmed with follow-up CT imaging.13

**Acute Pancreatitis Computed Tomography**

CECT is the standard imaging examination for diagnosing, assessing, and monitoring patients with suspected acute pancreatitis.10 CT imaging also is used to assess prognosis and plan treatments.13 Serial or repeated MDCT examinations allow close monitoring of the progression of acute pancreatitis and timely detection of potentially life-threatening complications.10

CT examinations have been incorporated into the revised Atlanta classification system’s 3 criteria for diagnosis of acute pancreatitis, partly because CT images can reveal anatomic defects and irregularities with sufficient detail to allow for the differentiation of pancreatitis from other disorders that have similar signs and symptoms.10

MDCT imaging of acute pancreatitis can involve a 3-phase or a biphasic acquisition protocol (see Table).17 Postacquisition reconstruction of 2-D axial images or images in other planes, as needed, is possible with any standard MDCT workstation.10 In CECT, healthy pancreas tissue has uniform morphologic texture and exhibits homogeneous CT enhancement of 100 HU to 150 HU.10,57 Acute pancreatitis is associated with enlargement of the pancreas and CT enhancement heterogeneities, with the degree of inflammatory edema correlating with the degree of enhancement heterogeneity.10

Acute accumulations of enzyme-containing pancreatic fluids might appear within or close to the

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**Figure 6.** A pancreatic CT angiograph showing a large mass (arrows) arising from the pancreatic neck and invading the stomach (arrowhead), representing a T3 tumor that does not involve the celiac axis or superior mesenteric artery. This tumor was associated with distant metastases and deemed unresectable. Reprinted with permission from Darren DD, Brennan MB, Zamboni GA, Raptopoulos VD, Kruskal JB. Comprehensive preoperative assessment of pancreatic adenocarcinoma with 64-section volumetric CT. Radiographics. 2007;27:1659.
If a fluid accumulation does not resolve, it could develop into an encapsulated acute pseudocyst or pancreatic abscess. A pseudocyst will appear on CECT images as a discrete, low-attenuation area with a thin but well-defined wall. Pancreatic abscesses usually occur 4 weeks or later after onset of symptoms and appear on CECT images as discrete pus accumulations with a thick, irregular wall in contrast to pseudocysts’ thin and well-defined walls.

CT images also are important in identifying the cause or etiology of confirmed cases of acute pancreatitis, such as gallstones or pancreatic calculi, and in identifying extra-pancreatic findings associated with acute pancreatitis, such as liver or gallbladder inflammation (which appear as enhanced regions on CECT). Usually, CECT cannot differentiate sterile from infected necrosis. However, the presence of small air bubbles is a sign of infection. CT-guided percutaneous fine-needle aspiration of necrotic fluids allows for laboratory culture testing for bacterial or fungal infection.

Predicting the clinical severity of acute pancreatitis is possible using clinical and imaging criteria. Pleural effusion on a plain chest radiograph is predictive of severe acute pancreatitis. The condition is seen in only 8.6% of patients with mild pancreatitis, whereas in severe cases, pleural effusion is seen in 84% of patients.

The CT Severity Index (CTSI) facilitates radiologic assessment of acute pancreatitis, associated fluid accumulations, and pancreatic necrosis. CTSI scores are based on observer assessments of 5 pancreatic anatomy observations and the percentage of pancreas that appears necrotic in reviews of CECT pancreas images.

CT finding:
- Score 0 – normal pancreas (Grade A).
- Score 1 – pancreatic enlargement (Grade B).
- Score 2 – pancreatic inflammation or peripancreatic fat changes (Grade C).
- Score 3 – single collection of peripancreatic fluid (Grade D).
- Score 4 – two or more collections of pancreatic fluid or retroperitoneal air (Grade E).

**Table**

<table>
<thead>
<tr>
<th>MDCT Parameters for Acute Pancreatitis Biphasic Imaging</th>
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<tr>
<td>Vascular Phase (40-45 s)</td>
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Pancreatic necrosis:
- Score 0 – no necrosis noted.
- Score 2 – < 30% necrosis.
- Score 4 – 30% to 50% necrosis.
- Score 6 – > 50% necrosis.

To calculate the CTSI score, the numerical scores for CT findings (grades) and percent of necrosis are summed. Scores of 0 to 3 are predictive of mild acute pancreatitis, with a 3% risk of mortality, whereas scores of 7 to 10 are predictive of severe cases and are associated with 17% mortality. CT scores higher than 5 are associated with an increased likelihood of surgical necrosectomy. The accuracy of CTSI staging of pancreatitis depends on administration of an intravenous contrast agent, and CTSI should not be undertaken with plain radiographic images.

In rare cases, pancreatitis affects only one segment or region of the pancreas, often the head. This is an indication of biliary obstruction–associated pancreatitis and usually is associated with recurrent and mild acute episodes.

Prognostic Scoring and Classification of Acute Pancreatitis

Predicting the clinical course of acute pancreatitis can be challenging, and severe acute pancreatitis is associated with high morbidity and mortality rates. Therefore, prognostic risk-stratification systems have been devised using clinical variables to differentiate patients with severe cases who require immediate and aggressive medical intervention and monitoring from those with nonsevere cases. Each system has its strengths and weaknesses.

Single biochemical-marker systems have been proposed, including hematocrit, creatinine and blood urea nitrogen, and C-reactive protein levels. Produced by the liver, C-reactive protein is an inflammatory biomarker of acute pancreatitis. It sometimes is used to help differentiate between mild and severe acute pancreatitis.

Clinical severity assessment instruments used in cases of acute pancreatitis include the revised Atlanta classification system, Ranson Criteria for Pancreatitis Mortality, the 12-item Acute Physiology and Chronic Health Evaluation (APACHE II) system, the Modified Glasgow (Imrie’s) Severity Criteria, and radiologic imaging-based or imaging/clinical-based scoring systems like the CTSI. Some of these systems have been modified from their original form to address the recently recognized prognostic significance of organ dysfunction outside of the pancreas, which might be even more important than infection status in predicting mortality. One example is the revised Atlanta classification system, which classifies cases of acute pancreatitis as mild, moderate, or severe:
- Mild – no organ failure, no local or systemic complications.
- Moderate – transient (< 48 hours) organ function disruption (organ failure), local or systemic complications, or both.
- Severe – persistent (> 48 hours) organ dysfunction (organ failure).

Organ failure is defined as shock (systolic blood pressure < 90 mm Hg), pulmonary insufficiency (PaO₂ ≤ 60 mm Hg), renal failure (serum creatinine > 2 mg/dL following rehydration), or gastrointestinal bleeding (exceeding 500 mL in 24 hours). Under the revised Atlanta classification system, persistent organ failure also can be assessed using the modified Marshall score, which quantifies organ dysfunction of the lungs, heart, circulatory system, and kidneys. Assessed within 72 hours of hospitalization, the Marshall score compares well to the APACHE II score in predicting patient death. The alternative sequential organ failure assessment score also is used 48 hours after symptom onset to assess organ failure; it has a sensitivity of 86% and a specificity of 79% for predicting patient death, which is comparable to the Marshall score’s accuracy.

A separate severity classification system for acute pancreatitis called determinant-based classification has been promulgated. This system adds a “critical” classification to the risk-assessment categories of mild, moderate, and severe acute pancreatitis:
- Mild – no necrosis of pancreatic tissue and no organ dysfunction.
- Moderate – sterile (uninfected) necrosis of pancreas tissue, transient (< 48 hours) systemic organ dysfunction, or both.
- Severe – infected necrosis of the pancreas or persistent (> 48 hours) systemic organ dysfunction.
- Critical – infected necrosis of pancreas tissue and persistent (> 48 hours) systemic organ dysfunction.
Managing Acute Pancreatitis

Patients experiencing pancreatic necrosis must be monitored for persisting organ failure, shock, and pancreatic or systemic infection. They might be hospitalized for as long as 6 months. Aggressive fluid resuscitation, long considered necessary for treating severe acute pancreatitis, can worsen patients’ outcomes. Patients should be monitored for intra-abdominal hypertension.

Acute pancreatitis complications include clinical evidence of heart, lung, or kidney dysfunction (usually within 2-3 days of onset); infection; abscesses and pseudocysts; and metabolic disorders leading to coagulopathy, hyperglycemia, diabetes or diabetic coma, hypocalcemia, thrombosis, or bleeding. Pancreatic necrosis affects up to 10% of patients and can become infected or remain sterile. Necrotic pancreatitis-associated infections can become systemic, and systemic infections might become drug resistant if antibiotics are overused; therefore, prophylactic antibiotic therapy should not be undertaken. Percutaneous draining is undertaken for pancreatitis-associated infection; if the procedure is ineffective and abdominal organs begin to fail, surgery is indicated.

Overall, less aggressive management offers better patient outcomes compared with more aggressive interventions. Thus, early surgery should be avoided if possible. Pancreatic necrosis should be managed with percutaneous drainage when possible. Fine-needle aspiration allows fluid collection for confirmation of infected necrotic tissue in the pancreas or adjacent organs. This allows for detection of drug-resistant infections and avoidance of unnecessary antibiotic treatment when tissue is determined not to be infected.

Open surgery is associated with high morbidity and mortality rates and should be avoided if possible. Endoscopic and interventional radiologic approaches for drainage and debridement of necrotic tissue might be undertaken, but open abdominal surgery (necrosectomy) is sometimes necessary. Multiple endoscopic necrosectomy procedures can remove fluid accumulations and tissue necrosis and appear to be associated with a lower risk of postprocedural complications than open surgery. Another alternative to open surgery is minimally invasive retroperitoneal pancreatic necrosectomy, which involves CT-guided placement of a percutaneous drain. Acute pancreatitis progression and recurrence can be slowed by tobacco and alcohol cessation. Patients diagnosed with pancreatitis should be informed of cessation program resources and told that refraining from tobacco and alcohol use can help improve their prognosis.

Chronic Pancreatitis

Chronic pancreatitis is sustained pancreatic inflammation that has caused progressive and permanent loss of organ function. Clinical presentations for chronic pancreatitis involve abdominal pain in up to 85% of patients, associated with severe epigastric pain, or pain of the left or right quadrant of the abdomen radiating to the back. Patients often adopt a stooped posture because of abdominal pain. Chronic pancreatitis pain might involve either constant and severe pain or repeated episodes of pain lasting up to several weeks followed by intervening periods of respite. Chronic pancreatitis etiologies are classified using the TIGAR-O system (see Box). Chronic pancreatitis is associated with progressive symptoms stemming from long-term inflammation and accumulated fibrotic scarring that diminishes endocrine and exocrine tissue function. Therefore, complications can include malnutrition and weight loss caused by the loss of exocrine tissue.

Box
The TIGAR-O System to Categorize Risk Factors for Developing Chronic Pancreatitis

- Toxic-metabolic – alcohol, tobacco, hyperlipidemia, chronic renal failure, toxins like organotin compounds, and medication abuse (primarily involving the pain medication phenacetin, which was banned in the United States in 1983).
- Idiopathic – tropical calcific pancreatitis, fibrocalculous pancreatic diabetes.
- Genetic – dominant-allele disorders.
- Autoimmune – isolated autoimmune chronic pancreatitis, autoimmune disease syndrome-associated pancreatitis.
- Recurring and severe acute pancreatitis progression – postnecrotic, recurrent acute pancreatitis, ischemic vascular disease, postirradiation.
- Obstructive – duct obstruction by tumor, post-traumatic pancreatic duct scarring.
function and type 3c pancreatic diabetes caused by the loss of endocrine tissue function. Pancreatic enzyme insufficiency can cause malnutrition via impaired gut digestion and absorption, a sign of advanced chronic pancreatitis-associated loss of exocrine tissue. Fatty or oily loose stool is evidence of lipase insufficiency.

Chronic pancreatitis also can cause osteoporosis because of the low vitamin D levels resulting from impaired fat absorption; this affects an estimated 25% of patients. Other complications include:

- Pancreatic duct calculi and pseudocysts.
- Bile duct obstructions.
- Fibrotic scarring of the duodenum.
- Bleeding in the gastrointestinal tract.
- Pancreatic fistula (pancreatic fluid leaking).
- Lung damage.
- Pleural effusion.
- Pancreatic cancer.

Calculi and pseudocysts that obstruct ducts can act as feedback mechanisms, worsening pancreatic inflammation and loss of endocrine and exocrine function. Biliary and pancreatic calculi commonly are discovered in the course of diagnostic workups for pancreatitis or pancreatic cancer. Endoscopic removal has limited success for pancreatic duct calculi, but even incomplete removal and relief of intraductal pressure can ease a patient’s pain. Extracorporeal shockwave lithotripsy can fragment remaining calculi from pancreatic and biliary ducts after endoscopic procedures, allowing natural passage into the gut or removal in follow-up endoscopy. When endoscopy approaches fail—or when pancreatic cancer also is suspected—calculi can be removed surgically via operations such as pancreato-duodenectomy, which is the most common technique for removing pancreatic tumors.

Treatment of chronic pancreatitis focuses on management of complications, supportive therapy for abdominal pain (including alcohol and tobacco abstinence), administration of nonsteroidal anti-inflammatory drugs, and management of maldigestion. As with acute pancreatitis, smoking and alcohol cessation might slow the progression of disease, and patients should be provided with resources to help change their behavior.

Pseudocysts are a common complication of pancreatitis. They are pancreatic fluid-filled cysts contained by fibrotic tissue that appear to result from downstream duct obstructions and are evidenced by upstream ductal dilatation. Pseudocysts can be associated with increased pain, vomiting, and duct obstructions, and they can be treated with endoscopic drainage. When bile duct obstruction or damage leads to jaundice, endoscopic or surgical decompression is indicated. Administration of exogenous pancreatic enzymes can improve maldigestion resulting from impaired pancreas exocrine function. When weight loss is pronounced, pancreatic cancer (which is associated with chronic pancreatitis) might be responsible. Lung damage, pleural effusion, and shortness of breath are indications for pulmonary imaging and consideration of endoscopic stent placement.

Chronic Pancreatitis Computed Tomography

CT imaging is useful for confirming chronic pancreatitis, detecting its complications, and identifying duct obstructions. Chronic pancreatitis usually causes the pancreas to atrophy, thereby appearing progressively smaller. Pancreatic duct calculi and other pancreatic calcifications are common throughout chronic pancreatitis-affected pancreas tissues and can obstruct ducts. Calcifications are identified easily as hyperdense foci that frequently are rounded when small or irregular when larger. Calcifi can be seen readily even in nonenhanced CT imaging but can be confused with splenic artery calcifications when iodinated contrasts are not administered.

CT images of chronic pancreatitis reveal an atrophic pancreas and dilatation of the main pancreatic duct and, not infrequently, obstructions contributing to duct dilatation and pancreatic inflammation. As previously noted for acute pancreatitis, CT imaging can detect complications such as pseudocysts, which occur in 25% of patients with chronic pancreatitis. Pseudoaneurysms also can occur in the pancreatic, duodenal, and splenic arteries.

Pancreatic Cancer

Typically, precursor cystic lesions and early-stage pancreatic cancers are asymptomatic. These malignancies tend to be diagnosed only after they have progressed to advanced stages and have already spread to
Common clinical signs and symptoms of pancreatic cancers include:

- Abdominal pain.
- Back pain.
- Nausea.
- Vomiting.
- Diarrhea.
- Anorexia and weight loss.
- Physical weakness.
- Dark urine.
- Itching.
- Type 2 diabetes.

Clinical signs and symptoms can vary depending on where the tumor is located in the pancreas. For example, jaundice is commonly associated with tumor obstruction of bile ducts passing through the pancreatic head and is less common when tumors occur in the pancreatic body or tail regions. Tumors in the pancreatic head tend to become symptomatic at an earlier stage than do tumors in the pancreatic body or tail.

Other signs include hepatomegaly, right upper quadrant abdominal mass, and cachexia (muscle wasting). Cachexia is common but is not strongly associated with cancer stage or tumor burden. Large pancreatic tumors can encroach on the duodenum and stomach, obstructing the gastrointestinal tract and leading to nausea and loss of appetite.

Pancreatic adenocarcinoma typically metastasizes to the liver, abdomen, and lungs. Pancreatic cancer testing is indicated for any patient aged older than 50 years newly diagnosed with diabetes and any of the signs or symptoms described above. Imaging and blood tests are undertaken and often initially include transabdominal ultrasonography, a complete blood count, and liver enzyme and bilirubin tests. Endoscopic biopsy with ultrasonography allows confirmation and pathologic testing of the tumor.

Diagnostic CECT imaging of pancreatic ductal adenocarcinoma is useful in confirming the presence of tumors, staging cancer (documenting tumor locations, sizes, and involvements with other organs and tissues), and monitoring patients and restaging cancers after treatment.

Biphasic pancreatic CECT is sensitive for diagnostic and staging imaging of adenocarcinoma, as well as for detection of metastatic tumors beyond the pancreas (e.g., liver). The portal venous-phase scan acquisition image offers good visualization of veins and peripancreatic organs such as the liver that might harbor metastatic pancreatic tumors.

Adenocarcinoma tumors are visualized as low-enhancement regions that contrast with the enhancing normal tissues of the pancreas, making CECT an excellent modality for diagnostic imaging of these malignancies (see Figure 3). However, in approximately 10% of tumors, pancreatic adenocarcinomas are isodense with surrounding nonmalignant pancreatic tissue. Therefore, images must be reviewed for evidence of duct or blood vessel encroachment or cutoff by tumors that are not otherwise evident (see Figure 5). Postprocessing techniques such as maximum intensity projections can improve visualization of duct and vascular deformation and dilatation, indirectly revealing the presence of isodense tumors.

Current diagnostic imaging algorithms for suspected pancreatic tumors recommend initially imaging pancreatic masses with CECT, but following up with MR or endoscopic ultrasound and biopsy if a suspected tumor is not visualized on the CT image. If CECT does detect pancreatic cancer, endoscopic ultrasound and biopsy are performed for pathologic confirmation as well as staging and assessment of tumor resectability.

Adenocarcinomas of the uncinate process have distinct patterns from those of adenocarcinoma tumors elsewhere in the pancreatic head region. These include significantly less frequent pancreatic duct and common bile duct dilatation and significantly more frequent mesenteric artery encasement by tumors in the uncinate process.

Premalignant cystic neoplasms are at high risk of progressing to pancreatic adenocarcinoma tumors. Premalignant cystic neoplasms like intraductal papillary mucinous neoplasms (IPMNs) and mucinous cystic neoplasms can be detected in diagnostic imaging examinations, but high-risk pancreatic intraductal neoplasm (PanIN) cysts are commonly missed. Small cysts of any
type can be difficult to characterize and might be mistaken for pseudocysts, although a cystic wall is usually readily detectable in pseudocysts and is absent in IPMNs.\(^5\) IPMNs can cause CECT-detectable dilatation of the main pancreatic duct and bulging of the major papilla.\(^4\)

**Staging Pancreatic Cancer**

Treatment options depend on tumor location and tumor, node, and metastases (TNM) stage.\(^2\,^7\) The National Comprehensive Cancer Network regularly updates guidelines for pancreatic tumor staging.\(^7\,^5\) CT imaging plays a central role in the staging and assessment of surgical resectability of pancreatic tumors.\(^2\) Tumors also are restaged after systemic therapy.\(^7\)

**Managing Pancreatic Cancer**

Most patients diagnosed with pancreatic cancer already have metastatic disease. For these patients, supportive care is emphasized, and fluorouracil and gemcitabine-based chemotherapy regimens might be administered to modestly prolong the patient’s survival time.\(^2\,^1\,^2\) A combination chemotherapy regimen of fluorouracil, irinotecan, oxaliplatin, and leucovorin (FOLFIRINOX) is emerging as a standard option for metastatic pancreatic cancer.\(^2\,^2\,^4\,^7\) When localized, nonmetastatic tumors are unresectable, radiation therapy or a combination of chemotherapy with gemcitabine and radiation therapy often is administered.\(^2\) Generally, T4-grade tumors are not resectable, but T1, T2, and T3 tumors are sometimes resectable.\(^2\,^4\,^7\)

Vascular involvement is a key determinant of tumor resectability.\(^2\) Closely assessing tumor involvement of the celiac and superior mesenteric arteries and veins, the portal vein, and hepatic artery are crucial steps in determining tumor resectability.\(^2\) Tumors without any arterial or superior mesenteric or portal vein involvement might be resectable. Tumors not eligible for surgery include those involving metastatic disease, including lymph nodes distant to the pancreas, or tumors that encase the superior mesenteric artery or celiac axis (\(> 180^\circ\)).\(^7\) Resection also is not an option when tumor involvement or occlusion of major veins renders vascular reconstruction impossible.\(^7\)

Resection of tumors in the pancreatic head or neck can involve open surgery (pancreatoduodenectomy), distal pancreatectomy, or laparoscopic surgery to remove tumors of the pancreatic body or tail, or minimally invasive resections.\(^2\) Tumor resection usually is accompanied by adjuvant or neoadjuvant (presurgery) administration of chemotherapy and radiation therapy to kill remaining tumor cells in the surgical margins or in lymph node tissue.\(^2\) For example, FOLFIRINOX, gemcitabine, and paclitaxel albumin-stabilized nanoparticle formulation (nab-paclitaxel) are becoming more widely used as adjuvant therapies.\(^2\) Adjuvant immunotherapies also are undergoing clinical trial investigations.\(^2\)

**Conclusion**

CECT plays a central role in the diagnostic imaging, disease staging, and monitoring of patients with pancreatitis and pancreatic cancer. As the contributions to pancreatic disease of molecular-genetic pathways become better understood, it might become possible to develop better prognostic biomarkers and targeted, etiology-specific therapeutic agents, reducing morbidity and improving survival rates associated with pancreatitis and pancreatic cancer.\(^1\) Genetic biomarker tests that can reveal tumors harboring SMAD4 mutations might allow for better risk-stratification of patients to personalize treatment plans.\(^2\)

Some researchers expect routine genetic testing to soon become central to the management of pancreatic diseases.\(^1\) The development of increasingly sophisticated diagnostic imaging techniques and serum tumor biomarkers might help realize the longstanding goal of detecting premalignant lesions and more readily curable early-stage pancreatic tumors.\(^7\) Indeed, although the role of CECT in cancer screening for early detection of adenocarcinoma is controversial, the detection of very early-stage tumors should become increasingly feasible as MDCT designs and postprocessing algorithms improve.\(^7\)

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References


Directed Reading Quiz

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Read the preceding Directed Reading and choose the answer that is most correct based on the article.

1. Which of the following statements regarding the pancreas is false?
   a. The pancreas helps regulate blood glucose levels.
   b. The pancreas was first tentatively identified by the ancient Egyptians.
   c. The pancreas is essentially a glandular network of ducts.
   d. The pancreas is heavily vascularized.

2. The pancreatic blood supply comes from branches of all of the following arteries except the ______ artery.
   a. femoral
   b. mesenteric
   c. celiac
   d. splenic

3. The main pancreatic duct passes through which regions of the pancreas?
   1. head
   2. body
   3. tail
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

4. The pancreas’ endocrine tissues are particularly common in which pancreatic region?
   a. body
   b. head
   c. tail
   d. uncinate process

continued on next page
5. Type 2 diabetes appears to increase the risk of which of the following?
   1. acute pancreatitis
   2. chronic pancreatitis
   3. pancreatic cancer
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

6. Which of the following is associated with calculi obstruction and undrained obstruction of the ducts or the major papilla?
   1. pancreatitis
   2. jaundice
   3. fever
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

7. Which of the following can cause acute pancreatitis?
   1. pancreatic divisum
   2. heavy alcohol consumption
   3. mumps
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

8. A necrotic infection or septic phase usually emerges in how many weeks after onset of severe acute pancreatitis?
   a. 1
   b. 2
   c. 3
   d. 4

9. Metabolic insults to pancreatic tissues, particularly in the presence of certain genetic polymorphisms (gene variants), can disrupt _______ mechanisms and trigger early activation of enzymes.
   a. amylase
   b. trypsin
   c. insulin
   d. KRAS

10. Metaplastic pancreatic ducts are associated with pancreatic cancer but not with pancreatitis.
    a. true
    b. false

11. Pancreatic adenocarcinomas arise in the organ’s:
    a. islet cells.
    b. ducts.
    c. tail.
    d. uncinate process.

12. Ductal pancreatic adenocarcinoma and _______ carcinoma together make up nearly all of the pancreatic malignancies newly diagnosed each year.
    a. acinar cell
    b. neuroendocrine
    c. adenosquamous
    d. mucinous

13. Neuroendocrine tumors sometimes result from the multiple endocrine neoplasia type-1 (MEN-1) syndrome, which is inherited and also is associated with cancers of the:
    a. thyroid.
    b. pituitary.
    c. adrenals.
    d. tonsils.
14. Under conditions of continued or repeated inflammation and high levels of ______ activity, cystic lesions become increasing dysplastic.
   a. amylase
   b. trypsin
   c. insulin
   d. mutated KRAS gene

15. ______ people suffer a lower rate of calculi but higher rates of pancreatic disease overall.
   a. African American
   b. White
   c. Mexican American
   d. Asian American

16. Which of the following gene polymorphisms might increase the risk of progression from acute to chronic pancreatitis?
   1. CFTR
   2. PRSS1
   3. SPINK1

   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

17. Which of the following appears to reduce the risk of pancreatic cancer?
   a. coffee
   b. green tea
   c. fruit
   d. aspirin

18. Which imaging modality is superior to multidetector computed tomography (MDCT) in detection of pancreatic tumor recurrence after surgery?
   a. positron emission tomography (PET)-CT functional imaging with 18-fluorodeoxyglucose
   b. single-photon emission computed tomography (SPECT)
   c. magnetic resonance (MR) imaging
   d. transabdominal ultrasonography (US)

19. Total iodine administration for contrast-enhanced computed tomography (CECT) should not exceed ______ g, regardless of concentration or injection rate.
   a. 25
   b. 35
   c. 45
   d. 55

20. Which imaging modalities’ findings are included in the revised Atlanta classification system’s diagnostic criteria to confirm acute pancreatitis?
   1. CECT
   2. PET-CT
   3. transabdominal US

   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

21. ______ commonly occur(s) in severe acute pancreatitis and can lead to hemorrhage and intestinal obstruction.
   a. Intra-abdominal hypertension
   b. Biliary duct rupture
   c. Pseudocysts
   d. Pleural effusion

continued on next page
22. On pancreatic CECT images, healthy pancreas tissue exhibits CT enhancement values of 100 HU to ______ HU.
   a. 120
   b. 130
   c. 140
   d. 150

23. Pleural effusion on ______ can predict a patient’s eventual diagnosis with severe acute pancreatitis.
   a. a plain chest radiograph
   b. MR imaging
   c. MDCT
   d. SPECT

24. A Computed Tomography Severity Index (CTSI) score higher than ______ is associated with an increased risk of surgical necrosectomy.
   a. 2
   b. 3
   c. 4
   d. 5

25. ______ categories describe the severity of acute pancreatitis.
   1. Acute Physiology and Chronic Health Evaluation (APACHE-II)
   2. TIGAR-O
   3. CTSI
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

26. Some clinical severity assessment instruments have been modified from their original forms to address the recently recognized prognostic significance of:
   a. infection status.
   b. ethnicity.
   c. organ dysfunction outside of the pancreas.
   d. C-reactive protein.

27. Pancreatic necrosis should be managed with ______ if possible.
   a. surgery
   b. percutaneous drainage
   c. prophylactic antibiotics
   d. fluid resuscitation

28. ______ appear to result from downstream duct obstructions and are evidenced by upstream ductal dilatation.
   a. Aneurysms
   b. Pancreatic intraepithelial neoplasms
   c. Pseudocysts
   d. Fistulas

29. To which of the following does pancreatic adenocarcinoma typically metastasize?
   1. liver
   2. brain
   3. lungs
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

30. In approximately ______% of tumors, pancreatic adenocarcinomas are isoattenuating with surrounding nonmalignant pancreatic tissue.
   a. 10
   b. 20
   c. 30
   d. 40