aromatic amines found in cigarette smoke. Other risk factors include obesity, lack of physical activity, and diabetes mellitus. Studies evaluating the relationship between diet and pancreatic cancer are inconclusive. A Western diet (i.e., high intake of fat and meat, particularly smoked or processed meats) has been linked to the development of pancreatic cancer in many studies. Epidemiologic studies have failed to find a consistent association between alcohol or coffee consumption and the development of pancreatic cancer.

Up to 10% of patients with pancreatic cancer have a family history of the disease, but most cannot be identified with a known genetic disorder. Recognized genetic disorders that predispose to pancreatic cancer include hereditary pancreatitis (*PRSS1* gene), hereditary nonpolyposis colorectal cancer, familial adenomatous polyposis, *BRCA2* germline mutations, Peutz-Jeghers syndrome (*STK11* gene), familial atypical mole melanoma syndrome (*CDKN2A* gene, formerly *MTS1*), ataxia telangiectasia, and the Von Hippel–Lindau syndrome.

Although imaging surveillance of high-risk family cohorts is pursued at some centers, there is no consensus about the optimal methods or frequency of pancreatic cancer screening. Screening has not been shown to improve survival rates.

Pathology

The term *pancreatic cancer* usually refers to ductal adenocarcinoma of the pancreas, representing 85% to 90% of all pancreatic neoplasms. *Exocrine pancreatic neoplasm* is a more inclusive term that includes neoplastic pancreatic ductal and acinar cells and their stem cells and pancreatoblastoma.

More than 95% of malignant neoplasms of the pancreas arise from the exocrine elements. Neoplasms arising from the endocrine pancreas (i.e., islet cell or neuroendocrine tumors) comprise no more than 5% of pancreatic neoplasms. Pancreatic cancers are composed of several distinct elements, including pancreatic cancer cells, tumor stroma, and stem cells. The precursor lesion of pancreatic cancer is pancreatic intraepithelial neoplasia, which progresses from mild dysplasia (PanIN grade 1) to more severe dysplasia (PanIN grades 2 and 3) and eventually to invasive carcinoma.

Clinical Presentation

The clinical manifestations of pancreatic carcinoma may be nonspecific and are often insidious. The tumor has usually reached an advanced stage by the time of diagnosis. Common presenting signs and symptoms of pancreatic cancer include jaundice, weight loss, and abdominal pain. The pain is usually constant, with radiation to the back. Because most cancers begin in the pancreatic head, patients may exhibit obstructive jaundice or a large, palpable gallbladder (i.e., Courvoisier's sign).

Painless jaundice is the most common manifestation in patients with a potentially resectable and curable lesion. Anorexia, nausea, and vomiting may also occur, along with emotional disturbances such as depression. Less common manifestations include superficial thrombophlebitis (i.e., Trousseau's sign), acute pancreatitis, diabetes, ascites, paraneoplastic syndromes (e.g., Cushing's syndrome), hypercalcemia, gastrointestinal bleeding, splenic vein thrombosis, and a palpable abdominal mass.

Diagnosis and Differential Diagnosis

The goal of imaging in the evaluation of suspected pancreatic carcinoma is to establish the diagnosis with a high degree of certainty and to determine resectability in patients who are otherwise candidates for operative resection. The diagnosis of pancreatic cancer is frequently suggested by a pancreatic mass seen on imaging studies. Evidence of a dilated pancreatic duct, hepatic metastases, invasion of vessels, or a dilated common bile duct in the setting of biliary obstruction may also be found. The imaging appearance may be impossible to distinguish from benign causes of pancreatic masses such as focal pancreatitis or autoimmune pancreatitis. Multiphase, multidetector, helical CT is the best initial study to define a mass and assess for liver metastasis or vascular invasion. Compared with CT, MRI, and angiography, EUS is the most accurate diagnostic and staging technique, providing information about tumor location, vascular invasion, and lymph node involvement.

The imaging techniques are highly accurate for recognizing unresectable disease, but they are somewhat limited for identifying resectable disease because occult metastases (<1 cm in diameter) may be on the surface of the liver or peritoneum. Staging laparoscopy is recommended for patients with the highest likelihood of occult metastatic disease: those with tumors of the body or tail of the pancreas who appear to have potentially resectable disease by CT (one half of whom have occult peritoneal metastases), those with large (>3 cm) primary tumors, those for whom imaging suggests occult metastatic disease, and those with a very high initial CA 19-9 level (>1000 units/mL).

The use of tumor markers to diagnose carcinoma of the pancreas has yielded disappointing results. The tumor marker CA 19-9 has a sensitivity of 70% to 80% and a specificity of 85% to 95% for diagnosing selected patients already exhibiting signs and symptoms that suggest pancreatic cancer. However, for early-stage cancers, CA 19-9 has limited sensitivity. Use of CA 19-9 requires the Lewis blood group antigen, which is absent in 5% to 10% of the population. The greatest utility for CA 19-9 is to identify occult metastasis in patients with seemingly resectable tumors, for monitoring patients after apparently curative surgery, and for following those receiving chemotherapy for advanced disease. Rising CA 19-9 levels suggest recurrent disease even in the absence of radiographically detectable lesions.

Unfortunately, only 10% to 20% of carcinomas in the head of the pancreas and rare cancers of the body and tail are resectable for cure. If evaluation is conclusive that a pancreatic tumor is not resectable, the first objective is to confirm the cell type, which can be done accurately by CT- or EUS-guided biopsy.

Treatment

Surgical Resection

The major determinant of operative resectability and long-term survival is vascular invasion or metastatic disease. Although practice varies across institutions, most surgeons consider a pancreatic cancer to be categorically unresectable if there is extrapancreatic involvement, including extensive peripancreatic lymphatic extension, nodal involvement beyond the peripancreatic tissues, or distant metastases (e.g., liver, peritoneum,