

Pancreatic Cancer

Clinical Background

Pancreatic cancer, a common cancer in the U.S., has historically been associated with a high mortality rate.

Epidemiology

- Incidence – 9-10/100,000
- Age – peak incidence in 60s
- Sex – M>F (minimal)
- Ethnicity – 30-40% higher incidence in African Americans

Risk Factors

- Low socioeconomic status
- Male gender
- Tobacco use
- Presence of chronic disease states
 - Chronic pancreatitis
 - Diabetes mellitus
 - Prior cholecystectomy
- Occupational exposures
 - DDT, benzidine, dry cleaning agents, polychlorinated biphenyls (PCBs)
- Genetics
 - Family history of pancreatic cancer
 - Familial syndromes
 - *BRCA1* and *BRCA2* mutations
 - Familial atypical multiple mole melanoma syndrome (FAMMM)
 - Peutz-Jeghers syndrome (PJS)
 - Hereditary nonpolyposis colorectal cancer (HNPCC)
 - Ataxia-telangiectasia syndrome (A-T)
 - Hereditary pancreatitis syndrome
 - Von Hippel-Lindau syndrome (VHL)
 - Li-Fraumeni syndrome (LFS)
 - Familial pancreatic cancer

Pathophysiology

- Tumor is usually ductal adenocarcinoma
 - May also have mucinous cystadenocarcinomic variants
- Uncommon neuroendocrine tumors may also affect the pancreas
 - Insulinoma
 - Glucagonoma
- 70-80% of tumors are located in head of the pancreas
- Tumors may manifest solely as cysts

Clinical Presentation

- No specific early warning symptoms
- Usually abdominal pain and weight loss
- Obstructive jaundice if tumor is at the head of the pancreas

- Late features – ascites, abdominal mass
- If tumors are neuroendocrine in nature, patient may have endocrine syndromes as initial presentation (eg, hypoglycemia)

Diagnosis

- Indications for testing
 - Patient presents with jaundice and pancreatic mass
 - Monitoring for tumor recurrence after surgery
- Laboratory testing
 - CA 19-9 serum antigen testing – sensitivity depends on stage of cancer (70-90% sensitivity and 90% specificity)
 - May be elevated in benign obstructive jaundice, chronic pancreatitis
 - Should be used in conjunction with imaging studies to diagnose pancreatic cancer
 - Limited use as early screening
 - Serial monitoring recommended to assess follow up after potentially curative surgery or response to palliative chemotherapy
 - Other potential markers include MUC-1 antigen (also known as CA15-3 antigen) and carcinoembryonic antigen-related cell adhesion molecule 1 (CEACAM1) – although neither has been sufficiently validated for pancreatic cancer
 - Cystic lesions – fluid concentrations of amylase, carcinoembryonic antigen (CEA), and CA 19-9
 - Levels suggesting a diagnosis of cancer
 - Amylase <250 U/mL
 - CEA >800 ng/mL
 - CA 19-9 >37 U/mL
- Histology
 - Biopsy of tumor with histologic evaluation
 - Fine needle aspiration (FNA) via EUS is initial procedure of choice for diagnosis
- Molecular
 - KRAS2 gene mutation in ductal adenocarcinoma is common
 - FISH detection of aneuploidy for chromosomes 3, 7 and 17 and loss of the 9p21 locus is helpful in establishing the diagnosis of pancreatic ductal carcinoma in cytologic specimens
- Imaging studies
 - Transabdominal ultrasound/CT/MRI
 - Endoscopic retrograde cholangiopancreatography (ERCP) to outline extent of ductal involvement

Screening

- No studies demonstrating efficacy
- Only viable in high-risk patients
- Best screening tool appears to be endoscopic ultrasound

Monitoring

- CA 19-9 – serial monitoring recommended to assess follow-up after potentially curative surgery or response to palliative chemotherapy
 - CEA – less useful in monitoring than CA 19-9

Lab Tests

Indications for Laboratory Testing

Tests generally appear in the order most useful for common clinical situations. For test-specific information, refer to the test number in the ARUP Laboratory Test Directory on the ARUP Web site at www.aruplab.com.

Test Name and Number	Recommended Use	Limitations	Follow Up
Cancer Antigen-GI (CA 19-9) 0080461 Method: Electrochemiluminescent Immunoassay	Diagnose and monitor pancreatic cancer	Cannot be interpreted as absolute evidence of the presence or absence of malignant disease. Results obtained with different methods cannot be used interchangeably	
Cancer Antigen-GI (CA 19-9), Body Fluid 0020746 Method: Electrochemiluminescent Immunoassay	Diagnose and monitor pancreatic cancer	Cannot be interpreted as absolute evidence of the presence or absence of malignant disease. Results obtained with different assay methods or kits cannot be used interchangeably	
Pancreatobiliary FISH 2002461 Method: Fluorescence in situ Hybridization/Automated Image Analysis or Manual Screening	Detect aneuploidy for chromosomes 3, 7, and 17 and loss of the 9p21 locus Use in conjunction with current standard diagnostic procedures as an aid for initial diagnosis of pancreatic cancer	Negative result indicates that none of the numeric chromosomal abnormalities commonly associated with pancreatic carcinoma were identified with specimen; it does not exclude the possibility of pancreatic carcinoma	In the presence of other evidence suggesting pancreatic carcinoma, additional clinical studies should be considered
Amylase, Body Fluid 0020506 Method: Enzymatic	Assist with evaluating pancreatic cysts as benign or malignant		

Immunohistochemistry Stain Offering arup005 Method: Immunohistochemistry	For fixed tissue samples, consultative services as well as immunohistochemical staining for CAM5.2 (LMW), PGP9.5, synaptophysin, EMA, p21 and p27 are available		
---	---	--	--

Additional Tests Available

Test Name and Number	Comments
Carcinoembryonic Antigen, Fluid 0020742 Method: Electrochemiluminescent Immunoassay	Assist with evaluating pancreatic cysts as benign or malignant

Guidelines

Khalid A, Brugge W. ACG practice guidelines for the diagnosis and management of neoplastic pancreatic cysts. *Am J Gastroenterol.* 2007; 102 (10) 2339-2349.

Locker GY, Hamilton S, Harris J, Jessup JM, Kemeny N, Macdonald JS, Somerfield MR, Hayes DF, Bast RC Jr. ASCO 2006 update of recommendations for the use of tumor markers in gastrointestinal cancer. *J Clin Oncol.* 2006; 24 (33) 5313-5327.

Tumor Markers in Pancreatic Ductal Adenocarcinoma. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines And Recommendations For Use Of Tumor Markers In The Clinic. [Accessed: 27 Apr 2009]

General References

Canto MI. Strategies for screening for pancreatic adenocarcinoma in high-risk patients. *Semin Oncol.* 2007; 34 (4) 295-302.

Chari ST. Detecting early pancreatic cancer: problems and prospects. *Semin Oncol.* 2007; 34 (4) 284-294.

Francis IR. Pancreatic adenocarcinoma: diagnosis and staging using multidetector-row computed tomography (MDCT) and magnetic resonance imaging (MRI). *Cancer Imaging.* 2007; 7 Spec No A S160-S165.

Goggins M. Identifying molecular markers for the early detection of pancreatic neoplasia. *Semin Oncol.* 2007; 34 (4) 303-310.

Goonetilleke KS, Siriwardena AK. Systematic review of carbohydrate antigen (CA 19-9) as a biochemical marker in the diagnosis of pancreatic cancer. *Eur J Surg Oncol.* 2007; 33 (3) 266-270.

Grote T, Logsdon CD. Progress on molecular markers of pancreatic cancer. *Curr Opin Gastroenterol.* 2007; 23 (5) 508-514.

Katz MH, Mortenson MM, Wang H, Hwang R, Tamm EP, Staerckel G, Lee JH, Evans DB, Fleming JB. Diagnosis and management of cystic neoplasms of the pancreas: an evidence-based approach. *J Am Coll Surg.* 2008; 207 (1) 106-120.

Klimstra DS, Pitman MB, Hruban RH. An algorithmic approach to the diagnosis of pancreatic neoplasms. *Arch Pathol Lab Med.* 2009; 133 (3) 454-464.

Maitra A, Hruban RH. Pancreatic cancer. *Annu Rev Pathol.* 2008; 3 157-188.

Pappas S, Federle MP, Lokshin AE, Zeh HJ III. Early detection and staging of adenocarcinoma of the pancreas. *Gastroenterol Clin North Am.* 2007; 36 (2) 413-29, x.

Schneider G, Hamacher R, Eser S, Friess H, Schmid RM, Saur D. Molecular biology of pancreatic cancer--new aspects and targets. *Anticancer Res.* 2008; 28 (3A) 1541-1550.

Shi C, Daniels JA, Hruban RH. Molecular characterization of pancreatic neoplasms. *Adv Anat Pathol.* 2008; 15 (4) 185-195.

Shi C, Hruban RH, Klein AP. Familial pancreatic cancer. *Arch Pathol Lab Med.* 2009; 133 (3) 365-374.

Tempero M, Arnoletti JP, Ben-Josef E, Bhargava P, Casper ES, Kim P, Malafa MP, Nakakura EK, Shibata S, Talamonti M, Wang H, Willett C. Pancreatic adenocarcinoma. *Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw.* 2007; 5 (10) 998-1033.

van der Waaij LA, van Dullemen HM, Porte RJ. Cyst fluid analysis in the differential diagnosis of pancreatic cystic lesions: a pooled analysis. *Gastrointest Endosc.* 2005; 62 (3) 383-389.

References from the ARUP Institute for Clinical and Experimental Pathology®

Awadallah NS, Shroyer KR, Langer DA, Torkko KC, Chen YK, Bentz JS, Papkoff J, Liu W, Nash SR, Shah RJ. Detection of B7-H4 and p53 in pancreatic cancer: potential role as a cytological diagnostic adjunct. *Pancreas.* 2008; 36 (2) 200-206.

La'ulu SL, Roberts WL. Performance characteristics of five automated CA 19-9 assays. *Am J Clin Pathol.* 2007; 127 (3) 436-440.

Layfield LJ, Bentz J. Giant-cell containing neoplasms of the pancreas: an aspiration cytology study. *Diagn Cytopathol.* 2008; 36 (4) 238-244.

Willmore-Payne C, Volmar KE, Huening MA, Holden JA, Layfield LJ. Molecular diagnostic testing as an adjunct to morphologic evaluation of pancreatic ductal system brushings: potential augmentation for diagnostic sensitivity. *Diagn Cytopathol.* 2007; 35 (4) 218-224.

Reviewed by

Layfield, Lester, MD. Fine-Needle Aspiration Services and Molecular Diagnostics at ARUP Laboratories; Professor and Division Head, Anatomic Pathology, University of Utah

Roberts, William L., MD, PhD. Medical Director, Automated Core Laboratory at ARUP Laboratories; Professor of Pathology, University of Utah

Related Content

Glucagonoma

Hyperinsulinemic Hypoglycemia

Insulinoma

Melanoma

Multiple Endocrine Neoplasias - MEN

Pancreatic Neuroendocrine Tumors - NET

Pancreatitis, Acute

Pancreatitis, Autoimmune

Somatostatinoma

Tumor Markers

Vasoactive Intestinal Polypeptide Secreting Tumor - VIPoma

Comprehensive Review: August 2009

Last Update: November 2009