

Pancreas (Exocrine)

**Protocol applies to all carcinomas
of the exocrine pancreas.**

*Protocol revision date: January 2004
Based on AJCC/UICC TNM, 6th edition*

Procedures

- **Cytology** (No Accompanying Checklist)
- **Incisional Biopsy** (No Accompanying Checklist)
- **Partial Pancreatectomy**
- **Pancreaticoduodenectomy (Whipple Resection)**

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Surgical Pathology Cancer Case Summary (Checklist)

*Protocol revision date: January 2004
Applies to invasive carcinomas only
Based on AJCC/UICC TNM, 6th edition*

PANCREAS (EXOCRINE): Resection

Patient name:

Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC**Specimen Type**

- Pancreaticoduodenectomy (Whipple resection), partial pancreatectomy
 Pancreaticoduodenectomy (Whipple resection), total pancreatectomy
 Pylorus sparing pancreaticoduodenectomy, partial pancreatectomy
 Pylorus sparing pancreaticoduodenectomy, total pancreatectomy
 Partial pancreatectomy, pancreatic body
 Partial pancreatectomy, pancreatic tail
 Other (specify): _____
 Not specified

Tumor Site (check all that apply)

- Pancreatic head
 Uncinate process
 Pancreatic body
 Pancreatic tail
 Not specified

Tumor Size

Greatest dimension: ___ cm

*Additional dimensions: ___ x ___ cm

 Cannot be determined (see Comment)***Other Organs Resected**

- * None
 * Spleen
 * Gallbladder
 * Other(s) (specify): _____

2

* Data elements **with asterisks** are **not required** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

MICROSCOPIC**Histologic Type**

- Ductal adenocarcinoma
 Mucinous noncystic carcinoma
 Signet-ring cell carcinoma
 Adenosquamous carcinoma
 Undifferentiated (anaplastic) carcinoma
 Undifferentiated carcinoma with osteoclast-like giant cells
 Mixed ductal-endocrine carcinoma
 Serous cystadenocarcinoma
 Mucinous cystadenocarcinoma – invasive
 Invasive papillary-mucinous carcinoma
 Acinar cell carcinoma
 Acinar cell cystadenocarcinoma
 Mixed acinar-endocrine carcinoma
 Other (specify): _____
 Carcinoma, type cannot be determined

Histologic Grade (ductal carcinoma only)

- Not applicable
 GX: Cannot be assessed
 G1: Well differentiated
 G2: Moderately differentiated
 G3: Poorly differentiated
 G4: Undifferentiated
 Other (specify): _____

Pathologic Staging (pTNM)Primary Tumor (pT)

- pTX: Cannot be assessed
 pT0: No evidence of primary tumor
 pTis: Carcinoma in situ
 pT1: Tumor limited to the pancreas, 2 cm or less in greatest dimension
 pT2: Tumor limited to the pancreas, more than 2 cm in greatest dimension
 pT3: Tumor extends beyond the pancreas but without involvement of the celiac axis or the superior mesenteric artery
 pT4: Tumor involves the celiac axis or the superior mesenteric artery

Regional Lymph Nodes (pN)

- pNX: Cannot be assessed
 pN0: No regional lymph node metastasis
 pN1: Regional lymph node metastasis
 N1a: Metastasis in single regional lymph node
 N1b: Metastasis in multiple regional lymph nodes
 Specify: Number examined ____

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Number involved: ____

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Distant Metastasis (pM) pMX: Cannot be assessed pM1: Distant metastasis

*Specify site(s), if known: _____

Margins (check all that apply) Cannot be assessed Margins uninvolved by invasive carcinoma

Distance of invasive carcinoma from closest margin: ____ mm

*Specify margin (if possible): _____

 Carcinoma in situ absent at ductal margins Carcinoma in situ present at common bile duct margin Carcinoma in situ present at pancreatic parenchymal margin Margin(s) involved by invasive carcinoma Posterior retroperitoneal (radial) margin: posterior surface of pancreas Uncinate process margin (non-peritonealized surface of the uncinat process) Distal pancreatic margin Common bile duct margin Proximal pancreatic margin Other (specify): _____***Venous/Lymphatic (Large/Small Vessel) Invasion (V/L)*** Absent* Present* Indeterminate***Perineural Invasion*** Absent* Present***Additional Pathologic Findings (check all that apply)*** None identified* Pancreatic intraepithelial neoplasia (highest grade: PanIN ____)* Chronic pancreatitis* Acute pancreatitis* Other (specify): _____***Comment(s)**

* Data elements **with asterisks** are **not required** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

Background Documentation

Protocol revision date: January 2004

I. Cytologic Material

A. Clinical Information

1. Patient identification
 - a. Name
 - b. Identification Number
 - c. Age (birth date)
 - d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
 - a. Clinical history
 - (1) jaundice
 - (2) pancreatitis
 - (3) previous pancreatic or biliary surgery
 - (4) pseudocyst drainage
 - (5) diabetes mellitus
 - b. Clinical findings (eg, endoscopic retrograde cholangiopancreatography [ERCP] and/or imaging studies)
 - c. Clinical diagnosis
 - d. Procedure (eg, brushing, washing, other)
 - e. Operative findings

B. Macroscopic Examination

1. Specimen
 - a. Unfixed/fixed (specify fixative)
 - b. Number of slides received, if appropriate
 - c. Quantity and appearance of fluid specimen, if appropriate
 - d. Other (eg, cytologic preparation from tissue)
 - e. Results of intraprocedural consultation
2. Material submitted for microscopic evaluation
3. Special studies (specify) (eg, cytochemistry, immunocytochemistry)

C. Microscopic Evaluation

1. Adequacy of specimen (if unsatisfactory for evaluation, specify reason)
2. Tumor, if present (Note **A**)
 - a. Histologic type, if possible (Note **B**)
 - b. Histologic grade, if possible (Note **C**)
 - c. Other features (eg, necrosis)
3. Additional pathologic findings, if present
4. Results/status of special studies (specify)
5. Comments
 - a. Correlation with intraprocedural consultation, as appropriate
 - b. Correlations with other specimens, as appropriate
 - c. Correlation with clinical information, as appropriate

II. Incisional Biopsy**A. Clinical Information**

1. Patient identification
 - a. Name
 - b. Identification Number
 - c. Age (birth date)
 - d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
 - a. Clinical history
 - (1) jaundice
 - (2) pancreatitis
 - (3) previous pancreatic or biliary surgery
 - (4) pseudocyst drainage
 - (5) diabetes mellitus
 - b. Clinical findings (eg, ERCP and/or imaging studies)
 - c. Procedure (eg, ERCP biopsy, wedge biopsy)
 - d. Operative findings
 - e. Anatomic site(s) of specimen(s)

B. Macroscopic Examination

1. Specimen
 - a. Unfixed/fixed (specify fixative)
 - b. Number of pieces
 - c. Largest dimension of each piece
 - d. Results of intraoperative consultation
2. Tissues submitted for microscopic evaluation
 - a. Submit entire specimen
 - b. Frozen section tissue fragment(s) (unless saved for special studies)
3. Special studies (specify) (eg, histochemistry, immunohistochemistry)

C. Microscopic Evaluation

1. Tumor (Note A)
 - a. Histologic type (Note B)
 - b. Histologic grade (Note C)
 - c. Invasion
2. Additional pathologic findings, if present
 - a. Pancreatic intraepithelial neoplasia (PanIN) (Note D)
 - b. Metaplasia
 - c. Pancreatitis
 - d. Other(s)
3. Results/status of special studies (specify)
4. Comments
 - a. Correlation with intraoperative consultation, as appropriate
 - b. Correlation with other specimens, as appropriate
 - c. Correlation with clinical information, as appropriate

III. Partial Pancreatectomy (Distal or Left Pancreatectomy)

A. Clinical Information

1. Patient identification
 - a. Name
 - b. Identification Number
 - c. Age (birth date)
 - d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
 - a. Clinical history
 - (1) jaundice
 - (2) pancreatitis
 - (3) previous pancreatic or biliary surgery
 - (4) pseudocyst drainage
 - (5) diabetes mellitus
 - b. Clinical findings (eg, ERCP and/or imaging studies)
 - c. Clinical diagnosis
 - d. Procedure (eg, distal pancreatectomy, local excision of tumor)
 - e. Operative findings
 - f. Anatomic site(s) of specimen(s)

B. Macroscopic Examination

1. Specimen
 - a. Organs/tissues received (specify)
 - b. Unfixed/fixed (specify fixative)
 - c. Number of pieces
 - d. Dimensions
 - e. Orientation of specimen, if indicated by surgeon
 - f. Results of intraoperative consultation
2. Tumor (Note **A**)
 - a. Location (Note **E**)
 - b. Configuration (Note **F**)
 - c. Dimensions (best estimate) (Note **G**)
 - d. Descriptive features (eg, color, consistency, necrosis, hemorrhage, cavitation)
 - e. Estimated extent of invasion (Note **G**)
 - f. Distance from margins (Note **H**)
 - (1) proximal
 - (2) distal
 - (3) radial (retroperitoneal soft tissue margin closest to deepest tumor penetration)
3. Lesions in noncancerous pancreas
 - a. Pancreatic duct obstruction
 - b. Stones
 - c. Pancreatitis
 - d. Other(s)
4. Regional lymph nodes (identify by location, if possible or if specified by surgeon) (Note **G**)

5. Tissues submitted for microscopic evaluation
 - a. Carcinoma, including:
 - (1) points of deepest penetration of surrounding structures
 - (2) interface with adjacent pancreas
 - (3) interface with adjacent duodenum, if appropriate
 - (4) visceral serosa overlying tumor
 - b. Margins (Note **H**)
 - (1) proximal
 - (2) distal
 - (3) radial (retroperitoneal posterior soft tissue margin closest to deepest tumor penetration)
 - c. All lymph nodes (Note **G**)
 - (1) specify node(s) when marked by surgeon
 - d. Noninvolved pancreas
 - e. Frozen section tissue fragment(s) (unless saved for special studies)
 - f. Other tissue(s)/organ(s)
6. Special studies (specify) (eg, histochemistry, immunohistochemistry, electron microscopy, DNA analysis [specify type])

C. Microscopic Evaluation

1. Tumor (Note **A**)
 - a. Histologic type (Note **B**)
 - b. Histologic grade (Note **C**)
 - c. Extent of invasion (Note **G**)
 - d. Venous/lymphatic vessel invasion (Note **I**)
 - e. Perineural invasion (Note **J**)
2. Margins (Note **H**)
 - a. Proximal
 - b. Posterior pancreatic surface (deep radial margin)
 - c. Distal, if appropriate
3. Peritoneal surface
4. Regional lymph nodes (Note **G**)
 - a. Number
 - b. Number involved by tumor
5. Additional pathologic findings, if present
 - a. Pancreatic intraepithelial neoplasia (PanIN) (Note **D**)
 - b. Metaplasia
 - c. Pancreatitis
 - d. Other(s)
6. Distant metastasis (pM) (specify site)
7. Results/status of special studies (specify)
8. Comments
 - a. Correlation with intraoperative consultation, as appropriate
 - b. Correlation with other specimens, as appropriate
 - c. Correlation with clinical information, as appropriate

IV. Whipple Resection

(Pancreaticoduodenectomy, Partial or Total Pancreatectomy, With or Without Partial Gastrectomy)

A. Clinical Information

1. Identification Number
 - a. Name
 - b. Patient identification
 - c. Age (birth date)
 - d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
 - a. Clinical history
 - (1) jaundice
 - (2) pancreatitis
 - (3) previous pancreatic or biliary surgery
 - (4) pseudocyst drainage
 - (5) diabetes mellitus
 - b. Clinical findings (eg, ERCP and/or imaging studies)
 - c. Clinical diagnosis
 - d. Procedure (eg, pylorus-sparing Whipple resection)
 - e. Operative findings
 - f. Anatomic site(s) of specimen(s)

B. Macroscopic Examination

1. Specimen
 - a. Organs/tissues received (specify)
 - b. Unfixed/fixed (specify fixative)
 - c. Number of pieces
 - d. Dimensions (measure attached tissues individually)
 - e. Orientation of specimen, if indicated by surgeon
 - f. Results of intraoperative consultation
2. Tumor
 - a. Location (Note **E**)
 - b. Configuration (Note **F**)
 - c. Dimensions (best estimate) (Note **G**)
 - d. Descriptive characteristics (eg, color, consistency, necrosis, hemorrhage, cavitation)
 - e. Estimated extent of invasion (Note **G**)
3. Margins (Note **H**)
 - a. Distal pancreas
 - b. Common bile duct
 - c. Posterior pancreatic surface (deep radial margin)
 - d. Proximal (gastric)
 - e. Distal (duodenal)
 - f. Other(s) (eg, uncinate)
4. Regional lymph nodes (Note **G**)
5. Additional pathologic findings, if present
 - a. Common bile duct obstruction
 - b. Pancreatic duct obstruction

- c. Calculi
- d. Pancreatitis
- e. Other(s)
- 6. Tissues submitted for microscopic evaluation
 - a. Carcinoma, including
 - (1) points of deepest penetration of surrounding structures
 - (2) points of deepest penetration of closest margins
 - (3) interface of tumor with adjacent tissues
 - b. Ampulla of Vater (plus accessory papilla if present)
 - c. Margins
 - (1) distal pancreas
 - (2) common bile duct
 - (3) posterior pancreatic surface (deep radial margin)
 - (4) proximal (gastric)
 - (5) distal (duodenal)
 - d. All lymph nodes
 - e. Other lesions (eg, pseudocysts)
 - f. Pancreas uninvolved by tumor
 - g. Frozen section tissue fragment(s) (unless saved for special studies)
 - h. Other tissue(s)/organ(s)
- 7. Special studies (specify) (eg, histochemistry, immunohistochemistry, electron microscopy, DNA analysis [specify type])

C. Microscopic Evaluation

- 1. Tumor (Note **A**)
 - a. Histologic type (Note **B**)
 - b. Histologic grade (Note **C**)
 - c. Extent of invasion (Note **G**)
 - d. Venous/lymphatic vessel invasion (Note **I**)
 - e. Perineural invasion (Note **J**)
- 2. Margins (Note **H**)
 - a. Distal pancreas
 - b. Common bile duct
 - c. Posterior pancreatic surface (deep radial margin)
 - d. Proximal (gastric) (Note **K**)
 - e. Distal (duodenal)
 - f. Other(s)
- 3. Regional lymph nodes (Note **G**)
 - a. Number
 - b. Number with metastases
- 4. Distant metastasis (specify site)
- 5. Additional pathologic findings, if present
 - a. Chronic pancreatitis
 - b. Pancreatic intraepithelial neoplasia (PanIN) (Note **D**)
 - c. Metaplasia
 - d. Other(s)
- 6. Other tissue(s)/organ(s)
- 7. Results/status of special studies (specify)
- 8. Comments
 - a. Correlation with intraoperative consultation, as appropriate

- b. Correlation with other specimens, as appropriate
- c. Correlation with clinical information, as appropriate

Explanatory Notes

A. Tumors

This protocol applies to epithelial tumors of the exocrine pancreas.¹ It excludes endocrine tumors and tumors of the ampulla of Vater. More than 90% to 95% of malignant tumors of the pancreas are exocrine carcinomas.^{1,2} For these tumors, surgical resection remains the only potentially curative approach, and the prognosis is primarily dependent on the anatomic extent of disease.²

B. Histologic Type

A classification of malignant and borderline (uncertain malignant potential) epithelial tumors of the exocrine pancreas recommended by the World Health Organization (WHO) is shown below.³ However, this protocol does not preclude the use of other histologic types or systems of classification.

WHO Classification of Epithelial Tumors of the Exocrine Pancreas

Malignant Tumors

Ductal adenocarcinoma

- Mucinous noncystic carcinoma

- Signet-ring cell carcinoma[#]

- Adenosquamous carcinoma

- Undifferentiated (anaplastic) carcinoma^{##}

- Undifferentiated carcinoma with osteoclast-like giant cells

- Mixed ductal-endocrine carcinoma

Serous cystadenocarcinoma^{###}

Mucinous cystadenocarcinoma^{###}

- Non-invasive

- Invasive

Intraductal papillary-mucinous carcinoma^{###}

- Non-invasive

- Invasive (papillary-mucinous carcinoma)

Acinar cell carcinoma^{###}

- Acinar cell cystadenocarcinoma^{###}

- Mixed acinar-endocrine carcinoma^{###}

Pancreatoblastoma^{###}

Solid pseudopapillary carcinoma^{###}

Others

[#] By convention, signet-ring cell carcinomas are assigned grade 3 (see below).

^{##} By definition, undifferentiated carcinomas are grade 4 (see below).

^{###} These histologic types are not usually graded.

Borderline (Uncertain Malignant Potential)Mucinous cystic neoplasm with moderate dysplasia[#]Intraductal papillary-mucinous neoplasm with moderate dysplasia^{##}Solid-pseudopapillary neoplasm^{##}[#] Cured by complete surgical resection.^{##} Have a favorable prognosis compared to ductal adenocarcinoma.³**C. Histopathologic Grade**For adenocarcinomas, a histologic grade based on the extent of glandular differentiation is suggested as shown below.^{4,5}

Grade X	Cannot be assessed
Grade 1	Well differentiated (greater than 95% of tumor composed of glands)
Grade 2	Moderately differentiated (50% to 95% of tumor composed of glands)
Grade 3	Poorly differentiated (49% or less of tumor composed of glands)

Tumors with no differentiation or minimal differentiation that is discernible only in rare, tiny foci (undifferentiated carcinomas by WHO classification) are categorized as grade 4.

For pancreatic ductal carcinoma, histologic grade has been shown to have prognostic significance, with high grade (grades 3 and 4) being an unfavorable prognostic factor.⁶⁻⁸ In comparisons between the Klöppel grading system and the TNM grading system, no differences in predictive value have been demonstrated.⁸

D. Pancreatic Intraepithelial Neoplasia (PanIN)

Noninvasive dysplastic lesions of the ductal epithelium often are found in the pancreatic parenchyma surrounding ductal adenocarcinoma. These lesions are collectively known as pancreatic intraepithelial neoplasia (PanIN). PanINs have been classified at a National Cancer Institute Think Tank as follows.^{9,10}

Normal	Nonmucinous flattened or cuboidal epithelium without dysplasia
PanIN-1A	Flat mucinous epithelium without dysplasia
PanIN-1B	Papillary mucinous epithelium without dysplasia
PanIN-2	Flat or papillary mucinous epithelium with mild-to-moderate dysplasia (mild-to-moderate nuclear irregularity, hyperchromasia and loss of polarity)
PanIN-3	Flat or papillary mucinous epithelium with severe dysplasia (marked nuclear irregularity, hyperchromasia and loss of polarity), often with cribriforming and intraluminal blebbing (budding off of noncohesive cells)

PanINs are thought to progress from flat to papillary lesions with increasing degrees of dysplasia and increasing numbers of alterations in cancer-associated genes. PanINs are believed to be the precursor lesions of ductal adenocarcinoma of the pancreas. Many of the cytological changes included in the PanIN spectrum are seen in cystic tumors of the pancreas, such as mucinous cystic neoplasms and papillary mucinous neoplasms, but PanINs, by definition, occur in nondilated ducts.

PanIN occurring at the resection margins of an otherwise completely resected malignancy should be noted in the pathology report. In this setting, the biologic significance of low-grade PanINs is unclear, but PanIN-3 is the equivalent of carcinoma in situ.

E. Definition of Location

The anatomic subdivisions defining location of tumors of the pancreas are as follows⁵:

- Tumors of the head of the pancreas are those arising to the right of the left border of the superior mesenteric vein. The uncinate process is part of the head.
- Tumors of the body of the pancreas are those arising between the left border of the superior mesenteric vein and the left border of the aorta.
- Tumors of the tail of the pancreas are those arising between the left border of the aorta and the hilum of the spleen.

F. Tumor Configuration

Major types include intraductal, infiltrative, and circumscribed (if circumscribed: cystic or solid).

G. TNM and Stage Groupings

The TNM Staging System for carcinoma of the exocrine pancreas of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) is recommended and shown below.^{4,5} The postresection prognosis of a patient with pancreatic carcinoma is primarily determined by the anatomic extent of disease as defined by the TNM stage groupings.^{2,5,7,8,11-16}

By AJCC/UICC convention, the designation “T” refers to a primary tumor that has not been previously treated. The symbol “p” refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathologic staging is usually performed after surgical resection of the primary tumor. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumor has been completely removed. If a biopsied tumor is not resected for any reason (eg, when technically unfeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

Primary Tumor[#] (T)

- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- Tis Carcinoma in situ^{##}
- T1 Tumor limited to the pancreas, 2 cm or less in greatest dimension^{###}

- T2 Tumor limited to the pancreas, more than 2 cm in greatest dimension^{###}
- T3 Tumor extends beyond the pancreas but without involvement of the celiac axis or the superior mesenteric artery[^]
- T4 Tumor involves the celiac axis or the superior mesenteric artery (unresectable primary tumor)^{^^}

If more than one tumor is present in the pancreas, the tumor with the highest T category should be classified according to the pT definitions and either the multiplicity (“m”) or the actual number of simultaneous multiple tumors (eg, “3”) should be indicated in parentheses following the T category of the primary tumor (eg, pT3[m] or pT3[2]).¹¹ This applies only to grossly recognizable synchronous primary carcinomas and not to a single grossly detected tumor with multiple separate microscopic foci.¹¹

Multiple synchronous carcinomas of the exocrine pancreas may be¹¹:

- Multiple noninvasive tumors
- Multiple invasive tumors
- Multiple invasive tumors with associated carcinoma in situ
- A single invasive tumor with associated carcinoma in situ

PanIN-3 (see Note **D**) is the equivalent of carcinoma in situ and should be assigned pTis.

Tumor size has been shown to have independent prognostic significance.^{2,7,13,17-23}

[^] For T3, extension beyond the pancreas may include invasion of soft tissues adjacent to the pancreas, the common bile duct, and/or duodenum (including the ampulla of Vater). Specifically, peripancreatic tissues include the surrounding retroperitoneal fat (retroperitoneal soft tissue), including mesentery (mesenteric fat), mesocolon, greater and lesser omentum, and peritoneum.^{5,11} Involvement of the peripancreatic soft tissues has been shown to have independent prognostic significance as an adverse factor.^{14,20,22-26}

^{^^} Invasion of the portal vein also has been shown to have independent prognostic significance as an adverse factor.^{14,20,27,28}

Regional Lymph Nodes (N)[#]

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis^{##}
- N1 Regional lymph node metastasis^{###}
- N1a Metastasis in a single regional lymph node[^]
- N1b Metastasis in multiple regional lymph nodes

The regional nodes may be subdivided as follows:

- Superior Lymph nodes superior to head and body of pancreas.
- Inferior Lymph nodes inferior to head and body of pancreas.
- Anterior Anterior pancreaticoduodenal, pyloric, and proximal mesenteric lymph nodes.
- Posterior Posterior pancreaticoduodenal, common bile duct or pericholedochal, and proximal mesenteric nodes.

Splenic (For tumors in body and tail only) nodes of the splenic hilum and tail of pancreas.

The following lymph nodes are also considered regional: hepatic artery nodes, infrapyloric nodes (for tumors in head only), subpyloric nodes (for tumors in head only), celiac nodes (for tumors in head only), superior mesenteric nodes, pancreaticolieno (for tumors in body and tail only), splenic nodes (for tumors in body and tail only), retroperitoneal nodes, and lateral aortic nodes. Tumor involvement of other nodal groups is considered distant metastasis.

Regional Lymph Nodes (pN0): Isolated Tumor Cells

Isolated tumor cells (ITCs) are single cells or small clusters of cells not more than 0.2 mm in greatest dimension. Lymph nodes or distant sites with ITCs found by either histologic examination, immunohistochemistry, or nonmorphologic techniques (eg, flow cytometry, DNA analysis, polymerase chain reaction [PCR] amplification of a specific tumor marker) should be classified as N0 or M0, respectively. Specific denotation of the assigned N category is suggested as follows for cases in which ITCs are the only evidence of possible metastatic disease.^{11,29}

- pN0 No regional lymph node metastasis histologically, no examination for isolated tumor cells (ITCs)
- pN0(i-) No regional lymph node metastasis histologically, negative morphologic (any morphologic technique, including hematoxylin-eosin and immunohistochemistry) findings for ITCs
- pN0(i+) No regional lymph node metastasis histologically, positive morphologic (any morphologic technique, including hematoxylin-eosin and immunohistochemistry) findings for ITCs
- pN0(mol-) No regional lymph node metastasis histologically, negative nonmorphologic (molecular) findings for ITCs
- pN0(mol+) No regional lymph node metastasis histologically, positive nonmorphologic (molecular) findings for ITCs

The presence of lymph node metastases has been shown to have independent prognostic significance as an adverse factor.^{7,8,18,20,27,28,30-32}

^ Rationale: prognostic differences between N1a and N1b have been defined as follows.¹²

	2-Year (% ± SE)	5-Year (% ± SE)	Median Survival (Months)
pN1a	51 ± 17%	30 ± 16%	19.5
pN1b	18 ± 7%	0%	6.1

The difference between pN1a and pN1b is statistically significant (p<0.01).

Distant Metastasis (M)

- MX Distant metastasis cannot be assessed
- M0 No distant metastasis

M1 Distant metastasis[#]

[#] Peritoneal seeding or ascitic peritoneal fluid containing cytologic evidence of malignancy is considered M1.¹¹ Positive peritoneal cytology in patients without ascites is also considered M1 because the data suggest that this finding predicts a short survival.⁵

Stage Groupings

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

TNM Descriptors

For identification of special cases of TNM or pTNM classifications, the “m” suffix and “y,” “r,” and “a” prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The “m” suffix indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

The “y” prefix indicates those cases in which classification is performed during or following initial multimodality therapy (ie, neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a “y” prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The “y” categorization is not an estimate of tumor prior to multimodality therapy (ie, before initiation of neoadjuvant therapy).

The “r” prefix indicates a recurrent tumor when staged after a documented disease-free interval, and is identified by the “r” prefix: rTNM.

The “a” prefix designates the stage determined at autopsy: aTNM.

Additional Descriptors

Residual Tumor (R)

Tumor remaining in a patient after therapy with curative intent (eg, surgical resection for cure) is categorized by a system known as R classification, shown below.³³

RX	Presence of residual tumor cannot be assessed
R0	No residual tumor
R1	Microscopic residual tumor
R2	Macroscopic residual tumor

For the surgeon, the R classification may be useful to indicate the known or assumed status of the completeness of a surgical excision. For the pathologist, the R classification is relevant to the status of the margins of a surgical resection specimen. That is, tumor involving the resection margin on pathologic examination may be assumed to correspond to residual tumor in the patient and may be classified as macroscopic or microscopic according to the findings at the specimen margin(s).

Vessel Invasion

By AJCC/UICC convention, vessel invasion (lymphatic or venous) does not affect the T category indicating local extent of tumor unless specifically included in the definition of a T category. In all other cases, lymphatic and venous invasion by tumor are coded separately as follows.

Lymphatic Vessel Invasion (L)

LX Lymphatic vessel invasion cannot be assessed
 L0 No lymphatic vessel invasion
 L1 Lymphatic vessel invasion

Venous Invasion (V)

VX Venous invasion cannot be assessed
 V0 No venous invasion
 V1 Microscopic venous invasion
 V2 Macroscopic venous invasion

H. Margins

Most local recurrences of invasive pancreatic adenocarcinoma arise in the pancreatic bed corresponding to the deep radial posterior margin of the pancreas. Since this a critical margin, the AJCC and this protocol recommend inking the posterior surface of the pancreas and, if applicable to the specimen, the non-peritonealized surface of the uncinate process (the uncinate margin) and submitting sections through the tumor at its closest approach to this margin.⁵

When dealing with an intraductal tumor, the distal resection margin, the common bile duct margin (Whipple resection) or the proximal resection margin of the pancreas (distal pancreatectomy) are the most critical. Complete *en face* sections through the pancreatic margin and the common bile duct margin should be taken.

I. Venous/Lymphatic Vessel Invasion

Venous/lymphatic (small vessel) invasion has been shown to be an adverse prognostic factor.²⁴

J. Perineural Invasion

Perineural invasion has been shown to be an adverse prognostic factor.^{20,32}

K. Other Evaluation

In addition to the examination of other tissues/organs that are part of pancreaticoduodenectomy specimens, pathologic evaluation may also include examination of the gastric antrum for gastritis (eg, *Helicobacter pylori* gastritis or

chemical gastritis) and the duodenum for duodenitis, peptic ulcer disease, and ampullitis.

References

1. Solcia E, Capella C, Klöppel G. *Tumors of the Pancreas. Atlas of Tumor Pathology*. 3rd series, Fascicle 20. Washington, DC: Armed Forces Institute of Pathology; 1997.
2. Roder JD, Ott K. Cancer of the pancreas. In: Gospodarowicz MK, Henson DE, Hutter RVP, O'Sullivan B, Sobin LH, Wittekind C, eds. *Prognostic Factors in Cancer*. New York: Wiley-Liss; 2001:333-347.
3. Klöppel G, Hruban RH, Longnecker DS, Adler G, Kern SE, Partanen TJ. Carcinoma of the pancreas. In: Hamilton SR, Aaltonen LA, eds. *World Health Organization Classification of Tumours. Pathology and Genetics. Tumours of the Digestive System*. Lyon: IARC Press; 2000:219-251.
4. Sobin LH, Wittekind C, eds. *UICC TNM Classification of Malignant Tumours*. 6th ed. New York: Wiley-Liss; 2002.
5. Greene FL, Page DL, Fleming ID, et al. eds. *AJCC Cancer Staging Manual*. 6th ed. New York: Springer; 2002.
6. Klöppel G, Lindenthal G, von Bülow M, Kern HF. Histological and fine structural features of pancreatic ductal adenocarcinoma in relation to growth and prognosis: studies in xenografted tumours and clinico-histopathological correlation in a series of 75 cases. *Histopathology*. 1985;9:841-856.
7. Böttger TC, Störkel S, Wellek S, Störkel M, Junginger T. Factors influencing survival after resection of pancreatic cancer. *Cancer*. 1994;73:63-73.
8. Giulianotti PC, Boggi U, Fornaciari G, et al. Prognostic value of histological grading in ductal adenocarcinoma of the pancreas: Klöppel vs TNM grading. *Int J Pancreatol*. 1995;17:279-289.
9. Hruban RH, Adsay VN, Albores-Saavedra J, et al. Pancreatic intraepithelial neoplasia: a new nomenclature and classification system for pancreatic duct lesions. *Am J Surg Pathol*. 2001;25:579-586.
10. Klein WM, Hruban RH, Klein-Szanto AJP, Wilenz RE. Direct correlation between proliferative activity and dysplasia in pancreatic intraepithelial neoplasia (PanIN): additional evidence for a recently proposed model of progression. *Mod Pathol*. 2002;15:441-447.
11. Wittekind C, Henson DE, Hutter RVP, Sobin LH, eds. *TNM Supplement. A Commentary on Uniform Use*. 2nd ed. New York: Wiley-Liss; 2001.
12. Hermanek P. Staging of exocrine pancreatic carcinoma. *Eur J Surg Oncol*. 1991;17:167-172.
13. Böttger T, Zech WW, Sorger K, Junginger T. Relevant factors in the prognosis of ductal pancreatic carcinoma. *Acta Chir Scand*. 1990;156:781-788.
14. Tsunoda T, Ura K, Eto T, Matsumoto T, Tsuchiya R. UICC and Japanese Stage Classifications for carcinoma of the pancreas. *Int J Pancreatol*. 1991;8:205-214.
15. Eskelinen M, Lipponen P. A review of prognostic factors in human pancreatic adenocarcinoma. *Cancer Detect Prevent*. 1992;16:287-295.
16. Bakkevold KE, Kambesta B. Staging of carcinoma of the pancreas and ampulla of Vater. *Int J Pancreatol*. 1995;17:249-259.
17. Allison DC, Bose KK, Hruban RH, et al. Pancreatic cancer cell DNA content correlates with long-term survival after pancreaticoduodenectomy. *Ann Surg*. 1991;214:648-656.

18. Geer RJ, Brennan MF. Prognostic indicators for survival after resection of pancreatic adenocarcinoma. *Am J Surg*. 1993;165:68-73.
19. Baumel H, Huguier M, Manderscheid JC, Fabre JM, Houry S, Fagot H. Results of resection for cancer of the exocrine pancreas: a study from the French Association of Surgery. *Br J Surg*. 1994;81:102-107.
20. Griffanti-Bartoli F, Arnone GB, Ceppa P, Ravera G, Carrabetta S, Civalleri D. Malignant tumors in the head of the pancreas and the periampullary region, diagnostic and prognostic aspects. *Anticancer Res*. 1994;14:657-666.
21. Fortner JG, Klimstra DS, Senie TR, Maclean BJ. Tumor size is the primary prognosticator for pancreatic cancer after regional pancreatectomy. *Ann Surg*. 1996;223:147-153.
22. Yeo CJ, Cameron JL, Lillemoe KD, et al. Pancreaticoduodenectomy for cancer of the head of the pancreas. *Ann Surg*. 1995;221:721-723.
23. Tsuchiya R, Oribe T, Noda T. Size of the tumor and other factors influencing prognosis of carcinoma of the head of the pancreas. *Am J Gastroenterol*. 1985;80:459-462.
24. Tannapfel A, Wittekind C, Hunefeld G. Ductal adenocarcinoma of the pancreas. *Int J Pancreatol*. 1992;12:145-152.
25. Nagakawa T, Konishi T, Ueno K, et al. The results and problems of extensive radical surgery for carcinoma of the head of the pancreas. *Jpn J Surg*. 1991;21:262-267.
26. Manabe T, Ohshio G, Baba N, Tobe T. Factors influencing prognosis and indications for curative pancreatectomy for ductal adenocarcinoma of the head of the pancreas. *Int J Pancreatol*. 1990;7:1871-1893.
27. Manabe T, Miyashita T, Ohshio G, et al. Small carcinoma of the pancreas. *Cancer*. 1988;62:135-141.
28. Manabe T, Tobe T. Progress in the diagnosis and treatment of pancreatic cancer: the Tokyo University experience. *Hepatogastroenterology*. 1989;36:431-436.
29. Singletary SE, Greene FL, Sobin LH. Classification of isolated tumor cells: clarification of the 6th edition of the American Joint Committee on Cancer Staging Manual. *Cancer*. 2003;90(12):2740-2741.
30. Tsuchiya R, Noda T, Harada N, et al. Collective review of small carcinomas of the pancreas. *Ann Surg*. 1986;203:77-81.
31. Reber HA. Lymph-node involvement as a prognostic factor in pancreatic cancer. *Int J Pancreatol*. 1990;7:125-127.
32. Nagakawa T, Mori K, Nakano T, et al. Perineural invasion of carcinoma of the pancreas and biliary tract. *Br J Surg*. 1993;80:619-621.
33. Wittekind C, Compton CC, Greene FL, Sobin LH. Residual tumor classification revisited. *Cancer*. 2002;94:2511-2516.

Bibliography

Ductal Carcinoma

- Allema JH, Reinders ME, van Gulik TM, et al. Prognostic factors for survival after pancreaticoduodenectomy for patients with carcinoma of the pancreatic head region. *Cancer*. 1995;75:2069-2076.
- Cohen JR, Kuchta N, Geller N, Shires GT, Dineen P. Pancreaticoduodenectomy: a 40-year experience. *Ann Surg*. 1982;195:608-617.
- Cubilla AL, Fortner J, Fitzgerald PJ. Lymph-node involvement of the head of the pancreas area. *Cancer*. 1978;41:880-887.

- Edis AJ, Kiernan PD, Taylor WF. Attempted curative resection of ductal carcinoma of the pancreas: review of Mayo Clinic experience 1951-1975. *Mayo Clin Proc.* 1980;55:531-536.
- Eskelinen M, Lipponen P, Marin S, et al. Prognostic factors in human pancreatic cancer, with special reference to quantitative histology. *Scand J Gastroenterol.* 1991;26:483-490.
- Forrest JF, Longmire WP. Carcinoma of the pancreas and periampullary region: a study of 279 patients. *Ann Surg.* 1979;189:129-138.
- Kellokumpu-Lehtinen P, Huovinen R, Tuominen J. Pancreatic cancer: evaluation of prognostic factors and treatment results. *Acta Oncol.* 1989;28:481-484.
- Manabe T, Ohshio G, Baba N, et al. Radical pancreatectomy for ductal cell carcinoma of the head of the pancreas. *Cancer.* 1989;64:1132-1137.
- Nitecki SS, Sarr MG, Colby TV, van Heerden JA. Long-term survival after resection for ductal adenocarcinoma of the pancreas: is it really improving? *Ann Surg.* 1995;221:59-66.
- Nix GA, Dubbelman C, Wilson JHP, Schutte HE, Jeekel J, Postema RR. Prognostic implications of tumor diameter in carcinoma of the head of the pancreas. *Cancer.* 1991;67:529-535.
- Reber HA, Ashley SW, McFadden D. Curative treatment for pancreatic neoplasms. *Surg Clin North Am.* 1995;75:905-912.
- Takahashi S, Ogata Y, Tsuzuki T. Combined resection of the pancreas and portal vein for pancreatic cancer. *Br J Surg.* 1994;81:1190-1193.
- Trapnell JE. Staging of cancer of the pancreas. *Int J Pancreatol.* 1990;7:109-116.
- Tryka AF, Brooks JR. Histopathology in the evaluation of total pancreatectomy for ductal carcinoma. *Ann Surg.* 1979;190:373-379.
- Tyler DS, Evans DB. Reoperative pancreaticoduodenectomy. *Ann Surg.* 1994;219:211-221.
- Wade TP, El-Ghazzawy AG, Virgo KS, Johnson FE. The Whipple resection for cancer in US Department of Veterans Affairs hospitals. *Ann Surg.* 1995;221:241-248.
- Warshaw AL, Fernandez-del Castillo C. Pancreatic carcinoma. *N Engl J Med.* 1992;326:455-465.
- Watanapa P, Williamson RCN. Resection of the pancreatic head with or without gastrectomy. *World J Surg.* 1995;19:403-409.
- Winek T, Hamre D, Mozell E, Vetto RM. Prognostic factors for survival after pancreaticoduodenectomy for malignant disease. *Am J Surg.* 1990;159:454-456.
- Yamaguchi K, Nishihara K, Kolodziejczyk P, Tsuneyoshi M. Long survivors after pancreaticoduodenectomy for pancreas head carcinoma. *Aust NZ J Surg.* 1992;62:545-549.

Solid-pseudopapillary Carcinoma and Solid-pseudopapillary Tumor

- Boor P, Swanson M. Papillary-cystic neoplasm of the pancreas. *Am J Surg Pathol.* 1979;3:69-75.
- Huntrakoon, M. Oncocytic carcinoma of the pancreas. *Cancer.* 1983;51:332-336.
- Kamei K, Funabiki T, Ochiai M, et al. Three cases of solid and cystic tumor of the pancreas. *Int J Pancreatol.* 1991;10:269-278.
- Kloppel G, Morohoshi T, John HD, et al. Solid and cystic acinar cell tumor of the pancreas: a tumour in young women with favourable prognosis. *Virchows Arch [Pathol Anat].* 1981;392:171-183.

- Lack EE, Levey R, Cassady JR, et al. Tumors of the exocrine pancreas in children and adolescents: a clinical and pathologic study of eighteen cases. *Am J Surg Pathol.* 1983;7:319-327.
- Lee W-Y, Tzeng C-C, Jin Y-T, et al. Papillary cystic tumor of the pancreas: a case indistinguishable from oncocytic carcinoma. *Pancreas.* 1993;8:127-132.
- Matsunou H, Konishi F. Papillary-cystic neoplasm of the pancreas: a clinicopathologic study concerning the tumor aging and malignancy of nine cases. *Cancer.* 1990;65:283-291.
- Matsunou H, Konishi F, Yamamichi N, et al. Solid, infiltrating variety of papillary cystic neoplasm of the pancreas. *Cancer.* 1990; 65:2747-2757.
- Morohoshi T, Kanda M, Horie A, et al. Immunocytochemical markers of uncommon pancreatic tumors: acinar cell carcinoma, pancreato-blastoma, and solid cystic (papillary-cystic) tumor. *Cancer.* 1987;59:739-747.
- Morrison DM, Jewell LD, McCaughey WTE, et al. Papillary cystic tumor of the pancreas. *Arch Pathol Lab Med.* 1984;108(9):723-727.
- Nishihara K, Nagoshi M, Tsuneyoshi M, et al. Papillary cystic tumors of the pancreas: assessment of their malignant potential. *Cancer.* 1993;71:82-92.
- Nishihara K, Tsuneyoshi M. Papillary cystic tumors of the pancreas: an analysis by nuclear morphometry. *Virchows Arch [Pathol Anat].* 1993;422:211-217.
- Pettinato G, Manivel JC, Ravetto C, et al. Papillary cystic tumor of the pancreas: a clinicopathologic study of 20 cases with cytologic, immunohistochemical, ultrastructural and flow cytometric observations, and a review of the literature. *Am J Clin Pathol.* 1992;98:478-488.
- Sclafani LM, Reuter VE, Coit DG, et al. The malignant nature of papillary and cystic neoplasm of the pancreas. *Cancer.* 1991;68:153-158.
- Stommer P, Kraus J, Stolte M, et al. Solid and cystic pancreatic tumors: clinical, histochemical and electron microscopic features in 10 cases. *Cancer.* 1991;67:1635-1641.
- Ueda N, Nagakawa T, Ohta T, et al. Clinicopathological studies on solid and cystic tumors of the pancreas. *Gastroenterol Jpn.* 1991;26:497-502.
- Yamaguchi K, Hirakata R, Kitamura K. Papillary cystic neoplasm of the pancreas: radiological and pathological characteristics in 11 cases. *Br J Surg.* 1990;77:1000-1003.

Pancreatoblastoma

- Grosfeld JL, Vane DW, Rescorla FJ, et al. Pancreatic tumors in childhood: analysis of 13 cases. *J Pediatr Surg.* 1990;25:1057-1062.
- Horie A, Haratake J, Jimi A, et al. Pancreatoblastoma in Japan, with differential diagnosis from papillary cystic tumor (ductuloacinar adenoma) of the pancreas. *Acta Pathol Jpn.* 1987;37:47-63.
- Isaki M, Suzuki T, Koizumi Y, et al. Alpha-fetoprotein-producing pancreatoblastoma: a case report. *Cancer.* 1986;57:1833-1835.
- Jaksic T, Yaman M, Thorner P, et al. A 20-year review of pediatric pancreatic tumors. *J Pediatr Surg.* 1992;27:1315-1317.
- Lack E. Primary tumors of the exocrine pancreas: classification, overview, and recent contributions by immunohistochemistry and electron microscopy. *Am J Surg Pathol.* 1989;13(suppl 1):66-89.

- Morohoshi T, Sagawa F, Mitsuya T. Pancreatoblastoma with marked elevation of serum alpha-fetoprotein: an autopsy case report with immunocytochemical study. *Virchows Arch [Pathol Anat]*. 1990;416:265-270.
- Ohaki Y, Misugi K, Fukuda J, et al. Immunohistochemical study of pancreatoblastoma. *Acta Pathol Jpn*. 1987;37:1581-1590.
- Ohaki Y, Misugi K, Sasaki Y, et al. Pancreatic carcinoma in childhood: report of an autopsy case and a review of the literature. *Acta Pathol Jpn*. 1985;35:1543-1554.
- Silverman JF, Holbrook CT, Pories WJ, et al. Fine needle aspiration cytology of pancreatoblastoma with immunocytochemical and ultrastructural studies. *Acta Cytol*. 1990;35:632-640.

Acinar Cell Carcinoma and Acinar Cell Cystadenocarcinoma

- Cantrell BB, Cubilla AL, Erlandson RA, et al. Acinar cell cystadenocarcinoma of human pancreas. *Cancer*. 1981;47:410-416.
- di Sant'Agnese P. Acinar cell carcinoma of the pancreas. *Ultrastruct Pathol*. 1991;15:573-577.
- Hseuh C, Kuo T. Acinar cell carcinoma of the pancreas: report of two cases with complex histomorphologic features causing diagnostic problems. *Int J Pancreatol*. 1992;12(3):305-313.
- Itoh T, Kishi K, Tojo M, et al. Acinar cell carcinoma of the pancreas with elevated serum alpha-fetoprotein levels: a case report and a review of 28 cases reported in Japan. *Gastroenterol Jpn*. 1992;27:785-791.
- Klimstra DS, Heffess CS, Oertel JE, Rosai J. Acinar cell carcinoma of the pancreas: a clinicopathologic study of 28 cases. *Am J Surg Pathol*. 1992;16:815-837.
- Nojima T, Kojima T, Kato H, et al. Alpha-fetoprotein-producing acinar cell carcinoma of the pancreas. *Hum Pathol*. 1992;23:828-830.
- Stamm B, Burger H, Hollinger A. Acinar cell cystadenocarcinoma of the pancreas. *Cancer*. 1987;60:2542-2547.
- Webb JN. Acinar cell neoplasms of the exocrine pancreas. *J Clin Pathol*. 1977;30:103-112.

Osteoclast-like Giant-Cell Tumor

- Alguacil-Garcia A, Weiland LH. The histologic spectrum, prognosis, and histogenesis of the sarcomatoid carcinoma of the pancreas. *Cancer*. 1977;39:1181-1189.
- Berendt RC, Shnitka TK, Wiens E, et al. The osteoclast-type giant-cell tumor of pancreas. *Arch Pathol Lab Med*. 1987;111:43-48.
- Dworak O, Wittekind C, Koerfgen HP, et al. Osteoclastic giant-cell tumor of the pancreas: an immunohistological study and review of the literature. *Pathol Res Pract*. 1993;189:228-231.
- Fischer HP, Altmannsberger M, Kracht J. Osteoclast-type giant-cell tumor of the pancreas. *Virchows Arch [Pathol Anat]*. 1988;412:247-253.
- Goldberg RD, Michelassi F, Montag AG. Osteoclast-like giant-cell tumor of the pancreas: immunotypic similarity to giant-cell tumor of bone. *Hum Pathol*. 1991;22:618-622.
- Jalloh SS. Giant-cell tumour (osteoclastoma) of the pancreas: an epithelial tumour probably of acinar origin. *J Clin Pathol*. 1983;36:1171-1175.
- Lewandowski KB, Weston L, Dickersin GR, et al. Giant-cell tumor of the pancreas of mixed osteoclastic and pleomorphic cell type: evidence for a histogenetic relationship and mesenchymal derivation. *Hum Pathol*. 1990;21:1184-1187.

- Mentes A, Yuce G. Osteoclastic giant-cell tumor of the pancreas associated with mucinous cystadenoma. *Eur J Surg Oncol.* 1993;19:84-86.
- Posen JA. Giant-cell tumor of the pancreas of the osteoclastic type associated with a mucous secreting cystadenocarcinoma. *Hum Pathol.* 1981;12:944-947.
- Reyes CV, Crain S, Wang T. Pleomorphic giant-cell carcinoma of the pancreas: a review of nine cases. *J Surg Oncol.* 1980;15:345-348.
- Silverman JF, Dabbs DJ, Finley JL, et al. Fine-needle aspiration biopsy of pleomorphic (giant cell) carcinoma of the pancreas: cytologic, immunocytochemical and ultrastructural findings. *Am J Clin Pathol.* 1988;89:714-720.
- Suster S, Phillips M, Robinson MJ. Malignant fibrous histiocytoma (giant-cell type) of the pancreas: a distinctive variant of osteoclast-type giant-cell tumor of the pancreas. *Cancer.* 1989;64:2303-2308.
- Tschang TP, Garza-Garza R, Kissane JM. Pleomorphic carcinoma of the pancreas: an analysis of 15 cases. *Cancer.* 1977;39:2114-2126.

Mucinous Non-cystic Carcinoma

- Chen J, Baithum SI. Morphological study of 391 cases of exocrine pancreatic tumours with special reference to the classification of exocrine pancreatic carcinoma. *J Pathol.* 1985;146:17-29.

Undifferentiated (Anaplastic) Carcinoma

- Ackerman NB, Aust JC, Bredenberg CE, et al. Problems in differentiating between pancreatic lymphoma and anaplastic carcinoma and their management. *Ann Surg.* 1976;184:705-708.

Adenosquamous Carcinoma

- Ishikawa O, Matsui Y, Aoki I, et al. Adenosquamous carcinoma of the pancreas: a clinicopathologic study and report of three cases. *Cancer.* 1980;46:1192-1196.
- Motojima K, Tomioka T, Kohara N, et al. Immunohistochemical characteristics of adenosquamous carcinoma of the pancreas. *J Surg Oncol.* 1992;49:58-62.
- Yamaguchi K, Enjoji M. Adenosquamous carcinoma of the pancreas: a clinicopathologic study. *J Surg Oncol.* 1991;47:109-116.

Mucinous Cystic Tumor

- Albores-Saavedra J, Angeles-Angeles A, Nadji M, et al. Mucinous cystadenoma of the pancreas: morphologic and immunocytochemical observations. *Am J Surg Pathol.* 1987;11:11-20.
- Albores-Saavedra J, Gould EW, Angeles-Angeles A, et al. Cystic tumors of the pancreas. *Pathol Annu.* 1990;25(pt 2):19-50.
- Alles AJ, Warshaw AL, Southern JF, et al. Cyst fluid CA 72-4 (TAG 72) in the differential diagnosis of pancreatic cysts: a new marker to distinguish malignant from benign pancreatic neoplasms and pseudocysts. *Ann Surg.* 1994;219:131-134.
- Ayella AS, Howard JM, Grotzinger PJ. Cystadenoma and cystadenocarcinoma of the pancreas. *Am J Surg.* 1962;103:242-246.
- Becker WF, Welsh RA, Pratt HS. Cystadenoma and cystadenocarcinoma of the pancreas. *Ann Surg.* 1964;161:854-860.

- Compagno J, Oertel JE. Mucinous cystic neoplasms of the pancreas with overt and latent malignancy (cystadenocarcinoma and cystadenoma). *Am J Clin Pathol.* 1978;69:573-580.
- Corbally MT, McAnena OJ, Urmacher C, et al. Pancreatic cystadenoma: a clinicopathologic study. *Arch Surg.* 1989;124:1271-1274.
- Friedman AC, Lichtenstein JE, Dachman AH. Cystic neoplasms of the pancreas: radiological-pathological correlation. *Radiology.* 1983;149:45-50.
- Hodgkinson DJ, ReMine WH, Weiland LH. Pancreatic cystadenoma: a clinicopathologic study of 45 cases. *Arch Surg.* 1978;113:512-519.
- Hyde GL, Davis JB, McMillin RD, et al. Mucinous cystic neoplasm of the pancreas with latent malignancy. *Am Surg.* 1984;50:225-229.
- Katoh H, Rossi RL, Braasch JW, et al. Cystadenoma and cystadenocarcinoma of the pancreas. *Hepatogastroenterology.* 1989;36:424-430.
- Lewandrowski KB, Southern JF, Pins MR, et al. Cyst fluid analysis in the differential diagnosis of pancreatic cysts: a comparison of pseudocysts, serous cystadenomas, mucinous cystic neoplasms and mucinous cystadenocarcinoma. *Ann Surg.* 1993;217:41-47.
- Lewandrowski KB, Warshaw AL, Compton CC, et al. Variability in cyst fluid carcinoembryonic antigen level, fluid viscosity, amylase content, and cytology among multiple loculi of a pancreatic mucinous cystic neoplasm. *Am J Clin Pathol.* 1994;100:425-427.
- Rubin D, Warshaw AL, Southern JF, et al. Cyst fluid CA 15-3 concentration differentiates pancreatic mucinous cystadenocarcinomas from benign pancreatic cysts. *Surgery.* 1994;115:52-55.
- Sachs JR, Deren JL, Sohn M, et al. Mucinous cystadenoma: pitfalls of differential diagnosis. *Am J Gastroenterol.* 1989;84:811-816.
- Talamini MA, Pitt HA, Hruban RH, et al. Spectrum of cystic tumors of the pancreas. *Am J Surg.* 1992;163:117-124.
- Tatsuta M, Iishi H, Ichii M, et al. Values of carcinoembryonic antigen, elastase 1, and carbohydrate antigen determinant in aspirated pancreatic cystic fluid in the diagnosis of cysts of the pancreas. *Cancer.* 1986;57:1836-1839.
- Yamaguchi K, Enjoji M. Cystic neoplasms of the pancreas. *Gastroenterology.* 1987;92:1934-1943.
- Warshaw AL, Compton CC, Lewandrowski KB, et al. Cystic tumors of the pancreas: new clinical, radiologic, and pathologic observations in 67 patients. *Ann Surg.* 1990;212:432-443.
- Warshaw AL, Rutledge PL. Cystic tumors mistaken for pancreatic pseudocysts. *Ann Surg.* 1987;205:393-398.
- Yu HC, Shetty J. Mucinous cystic neoplasm of the pancreas with high carcinoembryonic antigen. *Arch Pathol Lab Med.* 1985;109:375-377.

Intraductal Papillary-Mucinous Tumor

- Bastid C, Bernard JP, Sarles H, et al. Mucinous ductal ectasia of the pancreas: a premalignant disease and a cause of obstructive pancreatitis. *Pancreas.* 1991;6:15-22.
- Conley CR, Scheithauer BW, van Heerden JA, et al. Diffuse intraductal papillary adenocarcinoma of the pancreas. *Ann Surg.* 1987;205:246-249.

- Ferrari BT, O'Halloran RL, Longmire WP, et al. Atypical papillary hyperplasia of the pancreatic duct mimicking obstructing pancreatic carcinoma. *N Engl J Med*. 1979;301:531-532.
- Furukawa T, Takahashi T, Kobari M, et al. The mucus-hypersecreting tumor of the pancreas: development and extension visualized by three-dimensional computerized mapping. *Cancer*. 1992;70:1505-1513.
- Itai Y, Ohhashi K, Nagai H, et al. "Ductectatic" mucinous cystadenoma and cystadenocarcinoma of the pancreas. *Radiology*. 1986;161:697-700.
- Kawarada Y, Yano T, Yamamoto T, et al. Intraductal mucin-producing tumors of the pancreas. *Am J Gastroenterol*. 1992;87:634-638.
- Kloppel G, Bommer G, Ryckert K, et al. Intraductal proliferation in the pancreas and its relationship to human and experimental carcinogenesis. *Virchows Arch [Pathol Anat]*. 1980;387:221-233.
- Kozuka S, Sassa R, Taki T, et al. Relation of pancreatic duct hyperplasia to carcinoma. *Cancer*. 1979;43:1418-1428.
- Milchgrub S, Campuzano M, Casillas J, et al. Intraductal carcinoma of the pancreas. *Cancer*. 1992;69:651-656.
- Morohoshi T, Kanda M, Asanuma K, et al. Intraductal papillary neoplasms of the pancreas: a clinicopathologic study of six patients. *Cancer*. 1989;64:1329-1335.
- Nagai E, Takashi T, Chijiwa K, Tanaka M, Tsuneyoshi M. Intraductal papillary mucinous neoplasms of the pancreas associated with so-called "mucinous ductal ectasia." *Am J Surg Pathol*. 1995;19:576-589.
- Nishihara K, Fukuda T, Tsuneyoshi M, Kominami T, Maeda S, Saku M. Intraductal papillary neoplasm of the pancreas. *Cancer*. 1993;72:689-696.
- Obara T, Saitoh Y, Maguchi H, et al. Multicentric development of a pancreatic intraductal carcinoma through atypical papillary hyperplasia. *Hum Pathol*. 1992;23:82-85.
- Oertel JE. The pancreas: nonneoplastic alterations. *Am J Surg Pathol*. 1989;13(suppl 1):50-65.
- Rickaert F, Cremer M, Deviere J, et al. Intraductal mucin-hypersecreting neoplasms of the pancreas: a clinicopathologic study of eight patients. *Gastroenterology*. 1991;101:512-519.
- Santini D, Campione O, Salerno A, et al. Intraductal papillary-mucinous neoplasm of the pancreas. *Arch Pathol Lab Med*. 1995;119:209-213.
- Tian F, Myles J, Howard JM. Mucinous pancreatic ductal ectasia of latent malignancy: an emerging clinicopathologic entity. *Surgery*. 1992;111:109-113.
- Yamada M, Kozuka S, Yamao K, et al. Mucin-producing tumor of the pancreas. *Cancer*. 1991;68:159-168.
- Yoshida J, Ozaki H, Yamamoto J, et al. Adenocarcinoma and concomitant intraductal papillary adenoma in the pancreas. *Jpn J Clin Oncol*. 1991;21:453-456.