# **Ampulla of Vater**

# Protocol applies to all intra-ampullary, peri-ampullary, and mixed intra- and peri-ampullary carcinomas.

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

# Procedures

- Cytology (No Accompanying Checklist)
- Incisional Biopsy (No Accompanying Checklist)
- Ampullectomy
- 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, 6<sup>th</sup> edition

# **AMPULLA OF VATER: Ampullectomy**

Patient name: Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

### MACROSCOPIC

### **Tumor Site**

- \_\_\_\_ Intra-ampullary
- \_\_\_\_ Peri-ampullary
- \_\_\_\_ Junction of ampullary and duodenal mucosa
- \_\_\_\_ Not specified

### MICROSCOPIC

### Histologic Type

- \_\_\_\_ Adenocarcinoma (not otherwise characterized)
- \_\_\_\_ Papillary adenocarcinoma
- \_\_\_\_ Adenocarcinoma, intestinal type
- \_\_\_\_ Adenocarcinoma, gastric foveolar type
- \_\_\_\_ Mucinous adenocarcinoma
- \_\_\_\_ Clear cell adenocarcinoma
- \_\_\_\_ Signet-ring cell carcinoma
- \_\_\_\_ Adenosquamous carcinoma
- \_\_\_\_ Other (specify): \_
- \_\_\_\_ Carcinoma, type cannot be determined

### **Histologic Grade**

- \_\_\_\_ Not applicable (histologic type not usually graded)
- \_\_\_\_ GX: Cannot be assessed
- \_\_\_\_ G1: Well differentiated
- \_\_\_\_ G2: Moderately differentiated
- \_\_\_\_ G3: Poorly differentiated
- \_\_\_\_ G4: Undifferentiated
- \_\_\_ Other (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.

### **Digestive System • Ampulla of Vater**

# **CAP** Approved

# **Tumor Size**

Specify: cm Cannot be determined (see Comment)

# Pathologic Staging (pTNM)

### Primary Tumor (pT)

- \_\_\_\_ pTis: Carcinoma in situ
- \_\_\_\_pT1: Tumor limited to ampulla of Vater or sphincter of Oddi
- pT2: Tumor invades duodenal wall

### Margins (check all that apply)

- Not applicable
- \_\_\_\_ Cannot be assessed
- \_\_\_\_ Uninvolved by invasive carcinoma
  - Specify distance of invasive carcinoma to closest margin: \_\_\_\_mm
  - \_\_\_\_ Uninvolved by carcinoma in situ/adenoma
  - Involved by carcinoma in situ/adenoma
- Involved by invasive carcinoma

### \*Additional Pathologic Findings (check all that apply)

- None identified
- \*\_\_\_\_ Dysplasia/adenoma \*\_\_\_\_ Ampullitis
- Adenomyosis
- \*\_\_\_\_ 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.

# Surgical Pathology Cancer Case Summary (Checklist)

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

# **AMPULLA OF VATER: Whipple Resection**

Patient name: Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

### MACROSCOPIC

### **Specimen Type**

- \_\_\_\_ Pancreaticoduodenectomy
- \_\_\_\_ Pancreaticoduodenectomy (pylorus sparing)
- \_\_\_\_ Other (specify): \_\_\_\_\_
- \_\_\_\_ Not specified

### Tumor Site (check all that apply)

- \_\_\_\_ Intra-ampullary
- \_\_\_\_ Peri-ampullary
- \_\_\_\_\_ Junction of ampullary and duodenal mucosa
- \_\_\_\_ Not specified

### Tumor Size

Greatest dimension: \_\_\_\_ cm \*Additional dimensions: \_\_\_\_x\_\_\_ cm

\_\_\_\_ Cannot be determined (see Comment)

### MICROSCOPIC

### **Histologic Type**

- \_\_\_\_ Adenocarcinoma (not otherwise characterized)
- \_\_\_\_ Papillary adenocarcinoma
- \_\_\_\_ Adenocarcinoma, intestinal type
- \_\_\_\_ Adenocarcinoma, gastric foveolar type
- \_\_\_\_ Mucinous adenocarcinoma
- \_\_\_\_ Clear cell adenocarcinoma
- \_\_\_\_ Signet-ring cell carcinoma
- \_\_\_\_ Adenosquamous carcinoma
- \_\_\_\_ Other (specify):
- \_\_\_\_ Carcinoma, type cannot be determined

\* 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.

### **CAP** Approved

### **Histologic Grade**

- \_\_\_\_ 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 ampulla of Vater or sphincter of Oddi
- \_\_\_\_ pT2: Tumor invades duodenal wall
- \_\_\_\_ pT3: Tumor invades pancreas
- \_\_\_\_ pT4: Tumor invades peripancreatic soft tissues or other adjacent organs or structures

Regional Lymph Nodes (pN)

- \_\_\_\_ pNX: Cannot be assessed
- \_\_\_\_ pN0: No regional lymph node metastasis
- \_\_\_\_ pN1: Regional lymph node metastasis
- Specify: Number examined: \_\_\_\_ Number involved: \_\_\_\_

#### 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 pancreatic duct margin
    - \_\_\_\_ Carcinoma in situ present at pancreatic duct margin
    - \_\_\_\_ Carcinoma in situ absent at common bile duct margin
  - \_\_\_\_ Carcinoma in situ present at common bile duct margin
  - \_ Margins involved by invasive carcinoma
    - Specify location(s) (if possible): \_\_\_\_\_
- \_\_\_\_ Not applicable
- \* 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.

### **CAP** Approved

### \*Venous/Lymphatic (Large/Small Vessel) Invasion (V/L)

- Absent
- Present
- Indeterminate

#### \*Perineural Invasion

- Absent
- Present

#### \*Additional Pathologic Findings (check all that apply)

- None identified
- \_\_\_\_ Dysplasia/adenoma
- \_\_\_\_ Ampullitis
- \_\_\_ Adenomyosis
- \*\_\_\_\_ Chronic pancreatitis \*\_\_\_\_ Acute pancreatitis
- \_\_ Gastritis
- \*\_\_\_\_ 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. Relevant history (eg, pancreatitis, familial adenomatous polyposis syndrome)
    - b. Relevant findings (eg, endoscopic, endoscopic retrograde cholangiopancreatography [ERCP], and/or imaging studies)
    - c. Clinical diagnosis
    - d. Procedure (eg, brushing, washing, other)
    - e. Operative findings
    - f. Anatomic site(s) of specimen(s)

# **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. Correlation 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

# For Information Only

- c. Age (birth date)
- d. Sex
- 2. Responsible physician(s)
- 3. Date of procedure
- 4. Other clinical information
  - a. Relevant history (eg, pancreatitis, familial adenomatous polyposis syndrome)
  - b. Relevant findings (eg, endoscopic, ERCP, and/or imaging studies)
  - c. Clinical diagnosis
  - d. Procedure (eg, endoscopic biopsy, ERCP biopsy)
  - e. Operative findings
  - f. 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. Submit entire specimen and 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. Duodenitis
  - b. Adenoma
  - c. Other
- 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.** Ampullectomy

# 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. Relevant history (eg, pancreatitis, familial adenomatous polyposis syndrome)
  - b. Relevant findings (eg, endoscopic, ERCP, and/or imaging studies)

- c. Clinical diagnosis
- d. Procedure
- e. Operative findings
- f. Anatomic site(s) of specimen(s)

### **B.** Macroscopic Examination

- 1. Specimen
  - a. Organ(s)/tissue(s) included (specify)
  - b. Unfixed/fixed (specify fixative)
  - c. Number of pieces
  - d. Dimensions (3)
  - e. Orientation, if indicated by surgeon
  - f. Results of intraoperative consultation
- 2. Tumor, if visible
  - a. Location
  - b. Configuration
  - c. Size (Note D)
  - d. Descriptive features (eg, color, consistency, necrosis, hemorrhage)
  - e. Distance from margin of resection
- 3. Tissues submitted for microscopic evaluation
  - a. Submit entire specimen, include margin
  - b. Frozen section tissue fragment(s) (unless saved for special studies)
- 4. Special studies (specify) (eg, histochemistry, immunohistochemistry, electron microscopy)

### C. Microscopic Evaluation

- 1. Tumor (Note A)
  - a. Histologic type (Note **B**)
  - b. Histologic grade (Note **C**)
  - c. Extent of invasion (Note D)
  - d. Venous/lymphatic vessel invasion (Note E)
  - e. Perineural invasion (Note F)
- 2. Margins, as appropriate
- 3. Additional pathologic findings, if present
- 4. Results/status of special studies (specify)
- 5. 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 Complete, With or Without Partial Gastrectomy)

### 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. Relevant history (eg, pancreatitis, familial adenomatous polyposis syndrome)
  - b. Relevant findings (eg, endoscopic, ERCP, and/or imaging studies)
  - c. Clinical diagnosis
  - d. Procedure (eg, gastroduodenal pancreatectomy, partial or complete)
  - e. Operative findings
  - f. Anatomic site(s) of specimen(s)

# B. Macroscopic Examination

- 1. Specimen
  - a. Organ(s)/tissue(s) included (specify)
  - b. Unfixed/fixed (specify fixative)
  - c. Number of pieces
  - d. Dimensions (measure attached tissues individually)
  - e. Orientation, if indicated by surgeon
  - f. Results of intraoperative consultation
- 2. Tumor
  - a. Location
  - b. Configuration
  - c. Size (Note D)
  - d. Descriptive features (eg, color, consistency, necrosis, hemorrhage)
  - e. Estimated extent of invasion (Note D)
- 3. Margins (Note G)
- 4. Regional lymph nodes (Note **D**)
- 5. Additional pathologic findings, if present
  - a. Common bile duct obstruction
  - b. Pancreatic duct obstruction
  - c. Pancreatitis
  - d. Other
- 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. Accessory papilla, if present
  - c. Margins
    - (1) distal pancreas
    - (2) common bile duct
    - (3) posterior pancreatic surface (deep radial margin)
    - (4) proximal (gastric or duodenal)
    - (5) distal (duodenal)
  - d. All lymph nodes (Note D)
    - (1) regional
    - (2) nonregional
  - e. Other lesions (eg, pseudocysts)
  - f. Pancreas uninvolved by tumor
  - g. Other tissue(s)/organ(s)
  - h. Frozen section tissue fragment(s) (unless saved for special studies)

7. Special studies (specify) (eg, histochemistry, immunohistochemistry, electron microscopy)

# C. Microscopic Evaluation

- 1. Tumor (Note A)
  - a. Histologic type (Note B)
  - b. Histologic grade (Note **C**)
  - c. Extent of invasion (Note D)
  - d. Venous/lymphatic vessel invasion (Note E)
  - e. Perineural invasion (Note F)
- 2. Margins (Note G)
  - a. Distal pancreas
  - b. Common bile duct
  - c. Posterior pancreatic surface (deep radial margin)
  - d. Proximal (gastric)
  - e. Distal (duodenal)
- 3. Regional lymph nodes (Note D)
  - a. Number
  - b. Number with metastases
  - 4. Distant metastasis (specify site)
- 5. Additional pathologic findings, if present
  - a. Chronic pancreatitis
  - b. Dysplasia
  - c. Metaplasia
  - d. Helicobacter pylori gastritis (Note H)
  - e. Other
- 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. Application

The ampulla of Vater is a complex structure that represents the confluence of the distal common bile duct and main pancreatic duct, which traverses the duodenal wall and opens into the duodenal lumen through a small mucosal elevation, the duodenal papilla. Tumors of the ampulla of Vater include tumors arising in the ampulla (intraampullary type), tumors arising on the ampulla (peri-ampullary type), and tumors arising at the junction of the mucosa of the ampulla with that of the papilla or involving both the intra-ampullary and peri-ampullary region of the duodenum (mixed type). Thus, tumors of the ampulla of Vater may show biliary and/or intestinal features. Tumors may be exophytic or ulcerated. The origin of the tumor may be difficult, and occasionally impossible, to determine. This protocol applies to all primary carcinomas of the ampulla of Vater including those showing focal endocrine differentiation, but it does not apply to carcinoid tumors, gastrointestinal stromal tumors, or lymphomas.<sup>1,2</sup>

### B. Histologic Type

This protocol applies to the following histologic classification but does not preclude the use of other histologic types or systems of classification. A modified classification of carcinomas of the extrahepatic bile ducts published by the World Health Organization (WHO) that is applicable to the ampulla of Vater is as follows.<sup>3</sup>

### WHO Classification of Ampullary Carcinoma<sup>#</sup>

Adenocarcinoma Papillary adenocarcinoma<sup>#</sup> Adenocarcinoma, intestinal type Adenocarcinoma, gastric foveolar type Mucinous adenocarcinoma Clear cell adenocarcinoma Signet-ring cell carcinoma<sup>##</sup> Adenosquamous carcinoma Squamous cell carcinoma Small cell carcinoma<sup>###</sup> Large cell neuroendocrine carcinoma Undifferentiated carcinoma<sup>###</sup> Biliary cystadenocarcinoma

The term "carcinoma, NOS (not otherwise specified)" is not part of the WHO classification.

<sup>#</sup> Ampullary tumors of the papillary histologic type have been shown to have a favorable prognosis compared to tumors of non-papillary histologic types.<sup>4,5</sup>

<sup>##</sup> Signet-ring cell carcinomas are, by convention, classified as poorly differentiated (grade 3/4) adenocarcinomas, and poor differentiation has been shown to be an adverse prognostic factor for ampullary carcinomas (see below).<sup>5,6</sup>

<sup>###</sup> Small cell carcinomas and undifferentiated (histologic type) carcinomas are assigned grade 4 (see below).

### C. Histologic Grade

For non-papillary adenocarcinomas, the following grading system is suggested:

- GX Grade cannot be assessed
- G1 Well differentiated (greater than 95% of tumor composed of glands)
- G2 Moderately differentiated (50% to 95% of tumor composed of glands)
- G3 Poorly differentiated<sup>#</sup> (49% or less of tumor composed of glands)

<sup>#</sup>Poor differentiation has been shown to be an adverse prognostic factor.<sup>5,6</sup>

Grade 4 carcinomas include both undifferentiated carcinomas (histologic type) and small cell carcinoma (high-grade neuroendocrine carcinomas) in the WHO classification (see above).

# D. TNM and Stage Groupings

The TNM staging system for tumors of the ampulla of Vater of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) is recommended and shown below.<sup>1,7</sup> The post-resection prognosis of a patient with ampullary carcinoma is primarily determined by the anatomic extent of disease as defined by the TNM classification and stage groupings.<sup>6-11</sup>

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)<sup>#</sup>

- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- Tis Carcinoma in situ
- T1 Tumor limited to the ampulla of Vater or sphincter of Oddi<sup>##</sup>
- T2 Tumor invades the duodenal wall
- T3 Tumor invades pancreas
- T4 Tumor invades peripancreatic soft tissues or other adjacent organs or structures

<sup>#</sup> Although tumor size is not included in the TNM staging system for tumors of the ampulla of Vater, it has been shown to have independent prognostic significance as follows<sup>12</sup>:

Tumor Size	5-Year Survival Rate (% <u>+</u> SE)	
Less than 2.5 cm	65%	
2.5 cm or more	20%	

The difference is statistically significant (p=0.039).

<sup>##</sup> Invasion of the muscle of the sphincter of Oddi has been shown to be an adverse prognostic factor.<sup>5</sup>

### Regional Lymph Nodes (N)<sup>#</sup>

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Regional lymph node metastasis

<sup>#</sup> Regional lymph node metastases have been shown to have independent significance as an adverse prognostic factor.<sup>4,6,8,12</sup>

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

The following lymph nodes are also considered regional: hepatic artery nodes, infrapyloric nodes, subpyloric nodes, celiac nodes, superior mesenteric nodes, retroperitoneal nodes, and lateral aortic nodes. Tumor involvement of other nodal groups is considered distant metastasis. Anatomic division of regional lymph nodes is not necessary, but separately submitted lymph nodes should be reported as submitted.<sup>1</sup>

### 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.<sup>13,14</sup>

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

### **Distant Metastasis (M)**

- MX Presence of distant metastasis cannot be assessed
- M0 No distant metastasis
- M1 Distant metastasis

### Stage Groupings

-			
Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
Stage IIA	Т3	N0	M0
Stage IIB	T1	N1	M0
•	T2	N1	M0
	Т3	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.

<u>The "m" suffix</u> indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

<u>The "y" prefix</u> 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).

<u>The "r" prefix</u> 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.

- 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

### E. Venous/Lymphatic Invasion

Lymph and small blood vessel invasion has been shown to be an adverse prognostic factor.<sup>5,10</sup>

# F. Perineural Invasion

Perineural infiltration by tumor has been shown to be an adverse prognostic factor.<sup>5</sup>

### G. Margins

Local recurrence from invasive carcinoma in the region of the pancreatic head most often occurs at the posterior margin of the pancreatic head. Since this is a critical margin, the protocol recommends inking the posterior retroperitoneal surface of the pancreas and submitting sections through the tumor at its closest approach to this margin. Local recurrence from intraductal tumor, however, is most likely to occur at a ductal resection margin (ie, the main pancreatic duct and/or the common bile duct margin). Thus, complete en face sections through the distal pancreatic margin (representing the distal margin of the main pancreatic duct) and the margin of the common bile duct should also be taken. Involvement of resection margins has been shown to be an adverse prognostic factor.<sup>6,15</sup>

### H. Other Evaluation

Sections of gastric antrum may be evaluated for gastritis (eg, *Helicobacter pylori* gastritis, chemical gastritis).

# References

- 1. Greene FL, Page DL, Fleming ID, et al, eds. *AJCC Cancer Staging Manual.* 6<sup>th</sup> ed. New York: Springer; 2002.
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