

Protocol for the Examination of Specimens From Patients With Carcinoma of the Ampulla of Vater

Version: AmpullaVater 4.0.0.0

Protocol Posting Date: June 2017

Includes pTNM requirements from the 8th Edition, AJCC Staging Manual

For accreditation purposes, this protocol should be used for the following procedures AND tumor types:

Procedure	Description
Resection	Includes specimens designated ampullectomy and pancreaticoduodenectomy (Whipple Resection)
Tumor Type	Description
Carcinoma	Includes all intra-ampullary, peri-ampullary, and mixed intra- and peri-ampullary carcinomas. Low-grade neuroendocrine tumors (carcinoids) are not included.

This protocol is NOT required for accreditation purposes for the following:

Procedure
Biopsy
Primary resection specimen with no residual cancer (eg, following neoadjuvant therapy)
Cytologic specimens

The following tumor types should NOT be reported using this protocol:

Tumor Type
Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)
Sarcoma (consider the Soft Tissue protocol)

Authors

Sanjay Kakar, MD*; Chanjuan Shi, MD, PhD*; N. Volkan Adsay, MD; Patrick Fitzgibbons, MD; Wendy L. Frankel, MD; Alyssa M. Krasinskas, MD; Timothy Pawlik, MD, PhD; Jean-Nicolas Vauthey, MD; Mary K. Washington, MD, PhD

With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.

** Denotes primary author. All other contributing authors are listed alphabetically*

Accreditation Requirements

This protocol can be utilized for a variety of procedures and tumor types for clinical care purposes. For accreditation purposes, only the definitive primary cancer resection specimen is required to have the core and conditional data elements reported in a synoptic format.

- Core data elements are required in reports to adequately describe appropriate malignancies. For accreditation purposes, essential data elements must be reported in all instances, even if the response is “not applicable” or “cannot be determined.”
- Conditional data elements are only required to be reported if applicable as delineated in the protocol. For instance, the total number of lymph nodes examined must be reported, but only if nodes are present in the specimen.
- Optional data elements are identified with “+” and although not required for CAP accreditation purposes, may be considered for reporting as determined by local practice standards.

The use of this protocol is not required for recurrent tumors or for metastatic tumors that are resected at a different time than the primary tumor. Use of this protocol is also not required for pathology reviews performed at a second institution (ie, secondary consultation, second opinion, or review of outside case at second institution).

Synoptic Reporting

All core and conditionally required data elements outlined on the surgical case summary from this cancer protocol must be displayed in synoptic report format. Synoptic format is defined as:

- Data element: followed by its answer (response), outline format without the paired "Data element: Response" format is NOT considered synoptic.
- The data element must be represented in the report as it is listed in the case summary. The response for any data element may be modified from those listed in the case summary, including “Cannot be determined” if appropriate.
- Each diagnostic parameter pair (Data element: Response) is listed on a separate line or in a tabular format to achieve visual separation. The following exceptions are allowed to be listed on one line:
 - Anatomic site or specimen, laterality, and procedure
 - Pathologic Stage Classification (pTNM) elements
 - Negative margins, as long as all negative margins are specifically enumerated where applicable
- The synoptic portion of the report can appear in the diagnosis section of the pathology report, at the end of the report or in a separate section, but all Data element: Responses must be listed together in one location

Organizations and pathologists may choose to list the required elements in any order, use additional methods in order to enhance or achieve visual separation, or add optional items within the synoptic report. The report may have required elements in a summary format elsewhere in the report IN ADDITION TO but not as replacement for the synoptic report i.e. all required elements must be in the synoptic portion of the report in the format defined above.

CAP Laboratory Accreditation Program Protocol Required Use Date: March 2018*

** Beginning January 1, 2018, the 8th edition AJCC Staging Manual should be used for reporting pTNM.*

CAP Ampulla of Vater Protocol Summary of Changes

The following data elements were modified:

Pathologic Stage Classification (pTNM, AJCC 8th Edition)
Histologic Type
Histologic Grade
Microscopic Tumor Extension
Clinical History

Surgical Pathology Cancer Case Summary

Protocol posting date: June 2017

AMPULLA OF VATER:

Select a single response unless otherwise indicated.

Procedure

- ☐ Ampullectomy
- ☐ Pancreaticoduodenectomy (Whipple resection)
- ☐ Other (specify): _____
- ☐ Not specified

Tumor Site (Note A)

- ☐ Intra-ampullary
 - + ☐ Arising from intra-ampullary papillary-tubular neoplasm (IAPN)
 - + ☐ Ampullary ductal (pancreaticobiliary-type)
- ☐ Peri-ampullary/ampullary duodenal (arising from duodenal surface of the papilla)
- ☐ Intra-ampullary and peri-ampullary (mixed type)
- ☐ Other (specify): _____
- ☐ Cannot be determined
- ☐ Not specified

Tumor Size (Note B)

- Greatest dimension (centimeters): ____ cm
- + Additional dimensions (centimeters): ____ x ____ cm
- ☐ Cannot be determined (explain): _____

Histologic Type (Note C)

- ☐ Adenocarcinoma
- ☐ Adenocarcinoma, pancreaticobiliary type
- ☐ Adenocarcinoma, intestinal type
- ☐ Medullary carcinoma
- ☐ Invasive papillary adenocarcinoma
- ☐ Mucinous adenocarcinoma
- ☐ Clear cell adenocarcinoma
- ☐ Signet-ring cell carcinoma
- ☐ Adenosquamous carcinoma
- ☐ Squamous cell carcinoma
- ☐ Hepatoid adenocarcinoma
- ☐ Large cell neuroendocrine carcinoma
- ☐ Small cell neuroendocrine carcinoma
- ☐ Neuroendocrine carcinoma (poorly differentiated)[#]
- ☐ Undifferentiated carcinoma
- ☐ Undifferentiated carcinoma with osteoclast giant cells
- ☐ Mixed adenoneuroendocrine carcinoma
- ☐ Other histologic type not listed (specify): _____
- ☐ Carcinoma, not otherwise specified

[#] Note: Select this option only if large cell or small cell cannot be determined.

Histologic Grade (Note D)

- ☐ G1: Well differentiated
- ☐ G2: Moderately differentiated
- ☐ G3: Poorly differentiated

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.

- ☐ Other (specify): _____
☐ GX: Cannot be assessed
☐ Not applicable

Tumor Extension (select all that apply)

- ☐ No evidence of primary tumor
☐ Carcinoma in situ/high-grade dysplasia
☐ Tumor limited to ampulla of Vater or sphincter of Oddi
☐ Tumor invades beyond sphincter of Oddi (perisphincteric invasion)
☐ Tumor invades into duodenal submucosa
☐ Tumor invades into muscularis propria of the duodenum
☐ Tumor directly invades pancreas up to 0.5 cm
☐ Tumor extends more than 0.5 cm into pancreas
☐ Tumor extends into peripancreatic soft tissues
☐ Tumor extends into periduodenal tissue
☐ Tumor extends into duodenal serosa
☐ Tumor invades other adjacent organs or structures other than pancreas (specify)[#]: _____
☐ + Tumor involves posterior surface of pancreas
☐ + Tumor involves anterior surface of pancreas
☐ + Tumor involves vascular bed/groove (corresponding to superior mesenteric vein/portal vein)
☐ Cannot be assessed

[#] Adjacent structures may include the stomach, gallbladder, omentum, celiac axis, superior mesenteric artery, common hepatic artery.

Margins (Note E)

Note: Use this section only if all margins are uninvolved and all margins can be assessed.

- ☐ All margins are uninvolved by invasive carcinoma and high-grade intraepithelial neoplasia

Margins examined: _____

Note: Margins for ampullectomy may include deep (radial), duodenal mucosal, pancreatic duct, bile duct, and other margins, while margins for pancreatoduodenectomy (Whipple procedure) may include pancreatic neck/parenchymal, uncinate (retroperitoneal/superior mesenteric artery), bile duct, proximal (gastric or duodenal), distal (duodenal or jejunal), and other margins.

- ☐ + Distance of invasive carcinoma from closest margin (millimeters or centimeters): ____ mm or ____ cm
☐ + Specify closest margin: _____

Individual margin reporting required if any margins are involved or margin involvement cannot be assessed

For ampullectomy specimens onlyAmpullectomy Margins

- ☐ Cannot be assessed
☐ Uninvolved by invasive carcinoma
 Distance of invasive carcinoma from closest margin (millimeters or centimeters): ____ mm or ____ cm
☐ + Specify margin
 ☐ + Deep (radial) margin
 ☐ + Duodenal mucosal margin
 ☐ + Other margin (eg, bile duct, pancreatic duct) (specify): _____
☐ Involved by invasive carcinoma
☐ + Specify margin(s)
 ☐ + Deep (radial) margin
 ☐ + Duodenal mucosal margin
 ☐ + Other margin (eg, bile duct, pancreatic duct) (specify): _____

+ Data elements preceded by this symbol are not required for accreditation purposes. These optional elements may be clinically important but are not yet validated or regularly used in patient management.

For pancreaticoduodenal resection specimens onlyPancreatic Neck/Parenchymal Margin

- ☐ Cannot be assessed
- ☐ Uninvolved by invasive carcinoma and pancreatic high-grade intraepithelial neoplasia
 - + Distance of invasive carcinoma from margin (millimeters *or* centimeters): ____ mm *or* ____ cm
- ☐ Uninvolved by invasive carcinoma
 - + Distance of invasive carcinoma from margin (millimeters *or* centimeters): ____ mm *or* ____ cm
- ☐ Involved by invasive carcinoma
- ☐ Involved by pancreatic high-grade intraepithelial neoplasia

Uncinate (Retroperitoneal/Superior Mesenteric Artery) Margin

- ☐ Cannot be assessed
- ☐ Uninvolved by invasive carcinoma
 - + Distance of invasive carcinoma from margin (millimeters *or* centimeters): ____ mm *or* ____ cm
- ☐ Involved by invasive carcinoma

Bile Duct Margin

- ☐ Cannot be assessed
- ☐ Uninvolved by invasive carcinoma and high-grade intraepithelial neoplasia
 - + Distance of invasive carcinoma from margin (millimeters *or* centimeters): ____ mm *or* ____ cm
- ☐ Uninvolved by invasive carcinoma
 - + Distance of invasive carcinoma from margin (millimeters *or* centimeters): ____ mm *or* ____ cm
- ☐ Involved by invasive carcinoma
- ☐ Involved by high-grade intraepithelial neoplasia

Proximal Margin (Gastric or Duodenal)

- ☐ Cannot be assessed
- ☐ Uninvolved by invasive carcinoma and high-grade dysplasia
- ☐ Uninvolved by invasive carcinoma
- ☐ Involved by invasive carcinoma
- ☐ Involved by high-grade dysplasia

Distal Margin (Distal Duodenal or Jejunal)

- ☐ Cannot be assessed
- ☐ Uninvolved by invasive carcinoma and high-grade dysplasia
- ☐ Uninvolved by invasive carcinoma
- ☐ Involved by invasive carcinoma
- ☐ Involved by high-grade dysplasia

Other Margin(s) (required only if applicable)

Specify margin(s): _____

- ☐ Cannot be assessed
- ☐ Uninvolved by invasive carcinoma
- ☐ Involved by invasive carcinoma

Lymphovascular Invasion (Note B)

- ☐ Not identified
- ☐ Present
- ☐ Cannot be determined

+ Perineural Invasion (Note B)

- + ☐ Not identified
- + ☐ Present
- + ☐ Cannot be determined

Regional Lymph Nodes

☐ No lymph nodes submitted or found

Lymph Node Examination (required only if lymph nodes present in specimen)

Number of Lymph Nodes Involved:

☐ Number cannot be determined (explain):

Number of Lymph Nodes Examined:

☐ Number cannot be determined (explain):

Pathologic Stage Classification (pTNM, AJCC 8th Edition) (Note F)

Note: Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. Only the applicable T, N, or M category is required for reporting; their definitions need not be included in the report. The categories (with modifiers when applicable) can be listed on 1 line or more than 1 line.

TNM Descriptors (required only if applicable) (select all that apply)

☐ m (multiple primary tumors)

☐ r (recurrent)

☐ y (posttreatment)

Primary Tumor (pT)

☐ pTX: Primary tumor cannot be assessed

☐ pT0: No evidence of primary tumor

☐ pTis: Carcinoma in situ

☐ pT1: Tumor limited to ampulla of Vater or sphincter of Oddi or tumor invades beyond the sphincter of Oddi (perisphincteric invasion) and/or into the duodenal submucosa

☐ pT1a: Tumor limited to ampulla of Vater or sphincter of Oddi

☐ pT1b: Tumor invades beyond the sphincter of Oddi (perisphincteric invasion) and/or into the duodenal submucosa

☐ pT2: Tumor invades into the muscularis propria of the duodenum

☐ pT3: Tumor directly invades the pancreas (up to 0.5 cm) or tumor extends more than 0.5 cm into the pancreas, or extends into peripancreatic or periduodenal tissue or duodenal serosa without involvement of the celiac axis or superior mesenteric artery

☐ pT3a: Tumor directly invades the pancreas (up to 0.5 cm)

☐ pT3b: Tumor extends more than 0.5 cm into the pancreas, or extends into peripancreatic tissue or periduodenal tissue or duodenal serosa without involvement of the celiac axis or superior mesenteric artery

☐ pT4: Tumor involves the celiac axis, superior mesenteric artery, and/or common hepatic artery, irrespective of size

Regional Lymph Nodes (pN)

☐ pNX: Regional lymph nodes cannot be assessed

☐ pN0: No regional lymph node metastasis

☐ pN1: Metastasis to one to three regional lymph nodes

☐ pN2: Metastasis to four or more regional lymph nodes

Distant Metastasis (pM) (required only if confirmed pathologically in this case)

☐ pM1: Distant metastasis

Specify site(s), if known:

+ Additional Pathologic Findings (select all that apply) (Note G)

+ ☐ None identified

+ ☐ Dysplasia/adenoma

+ ☐ Other (specify):

+ Ancillary Studies (Note G)

+ Specify: _____

+ ___ Not performed

+ Comment(s)

Explanatory Notes

A. Anatomical Considerations

The ampulla of Vater is a complex structure that usually represents the confluence of the distal common bile duct and main pancreatic duct (Figure 1). In some individuals the ampulla includes only the distal common bile duct, with the pancreatic duct entering the duodenum elsewhere. The ampulla traverses the duodenal wall and opens into the duodenal lumen through a small mucosal elevation, the duodenal papilla (papilla of Vater) (Figure 1). The ampulla is lined by pancreaticobiliary type ductal epithelium, whereas the duodenal papilla is covered by small intestinal epithelium. The sphincter of Oddi is part of the ampulla and consists of smooth muscle fibers that surround the distal end of the merged ducts.

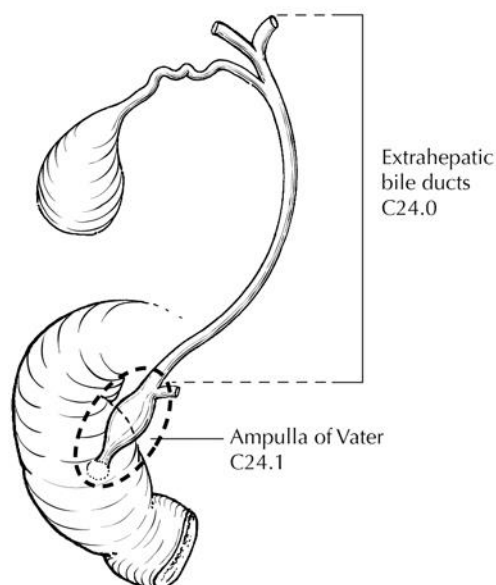


Figure 1. Anatomy of the ampulla of Vater. From Greene et al.²⁵ Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the *AJCC Cancer Staging Atlas* (2006) published by Springer Science and Business Media LLC, www.springerlink.com.

Tumors of the ampulla of Vater may arise in the ampulla (intra-ampullary type) or on the duodenal surface of the papilla (peri-ampullary type),¹ or may involve both the intra-ampullary and peri-ampullary regions (mixed type). Thus, ampullary tumors may show biliary and/or intestinal features. The origin of the tumor may be difficult, and occasionally impossible, to determine; the differential diagnosis includes carcinoma of the distal common bile duct, main pancreatic duct, and duodenum. Tumors may be exophytic or ulcerated.

B. Non-TNM Prognostic Factors

Although not included in the TNM staging system for tumors of the ampulla of Vater, tumor size has been shown to have independent prognostic significance for local recurrence.² In some series, pancreatic invasion, not tumor size, appears to be the more important prognostic factor.³

Lymphovascular invasion⁴ and perineural invasion⁵ have also been shown to be adverse prognostic factors.

C. Histologic Type

This protocol uses 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 gallbladder and extrahepatic bile ducts published by the World Health Organization (WHO) that is applicable to the ampulla of Vater is as follows⁶:

WHO Classification of Ampullary Carcinoma

Adenocarcinoma (not otherwise characterized)

Adenocarcinoma, pancreaticobiliary type^a

Adenocarcinoma, intestinal type[#]
 Invasive papillary adenocarcinoma^{##}
 Medullary carcinoma
 Mucinous adenocarcinoma
 Clear cell adenocarcinoma
 Signet-ring cell carcinoma
 Adenosquamous carcinoma
 Squamous cell carcinoma
 Hepatoid carcinoma
 High-grade neuroendocrine carcinoma
 Large cell neuroendocrine carcinoma
 Small cell neuroendocrine carcinoma
 Undifferentiated carcinoma
 Undifferentiated carcinoma with osteoclast giant cells
 Mixed adenoneuroendocrine carcinoma

[#] The pancreaticobiliary-type adenocarcinomas are more aggressive compared to the intestinal type.⁷ Since morphologic distinction can be challenging, immunohistochemistry has been advocated to make this distinction as the histologic subtype (intestinal vs pancreaticobiliary) can help in the choice of adjuvant therapy.⁸⁻¹⁰ Intestinal-type tumors are typically positive for CK20 or CDX2 or MUC2 with negative MUC1, or are positive for CK20, CDX2, and MUC2, irrespective of the MUC1 staining. Pancreatobiliary-type tumors are positive for MUC1 and negative for CDX2 and MUC2, irrespective of CK20 staining.⁹ This panel was able to classify 92% of cases in 1 study.⁹ A two-tiered approach has also been advocated based on which all tumors with pancreaticobiliary histology, MUC1 positivity and CDX2 negativity are classified as pancreaticobiliary, while the rest are considered as intestinal-type.^{10,11} Most mucinous adenocarcinomas exhibit intestinal subtype.

^{##} Pre-invasive mass forming ampullary neoplasms are similar to their pancreatic and bile duct counterparts and the term “intra-ampullary papillary-tubular neoplasm” (IAPN) has been proposed for these tumors.¹² These can be associated with an invasive component (invasive papillary adenocarcinoma by WHO terminology). IAPN with invasive component have a favorable outcome compared to other invasive ampullary carcinomas.¹²

D. Histologic Grade

For nonpapillary 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 [#] (49% or less of tumor composed of glands)

Poor differentiation has been shown to be an adverse prognostic factor on univariate analysis in some, but not all, series.^{2,13}

Signet-ring cell carcinomas are assigned grade 3 by convention. Undifferentiated carcinomas lack morphologic and immunohistochemical evidence of glandular, squamous, or neuroendocrine differentiation. This grading scheme is not applicable to poorly differentiated neuroendocrine carcinomas.

E. Margins

Local recurrence from invasive carcinoma in the region of the pancreatic head, including ampullary cancers invading the pancreas, most often occurs at the uncinate margin (retroperitoneal or superior mesenteric artery margin) of the pancreatic head. Because this is a critical margin, inking the uncinate margin and submitting sections through the tumor at its closest approach to this margin is recommended. Complete en face sections of the pancreatic neck/parenchymal resection margin and the resection margin of the common bile duct should also be taken. Microscopically positive margins of resection (R1) have been shown to have an adverse impact on prognosis in ampullary carcinoma.¹⁴

F. Pathologic Stage Classification

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.¹ The postresection 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.

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 infeasible) 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.

TNM Descriptors

For identification of special cases of TNM or pTNM classifications, the “m” suffix and “y” and “r” 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 after 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 before 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.

T Category Considerations

For ampullary carcinomas, carcinoma in situ (pTis) as a staging term includes cancer cells confined within the glandular basement membrane (high-grade dysplasia). The term carcinoma in situ is not widely applied to glandular neoplastic lesions in the gastrointestinal tract but is retained for tumor registry reporting purposes as specified by law in many states. Noninvasive ampullary carcinomas with a papillary growth pattern (intra-ampullary papillary-tubular neoplasms) are classified as pTis. The revised T categories in the AJCC 8th edition address the discrepancies in the previous definitions and correlate better with outcome.^{15,16}

T categories are illustrated in Figures 2-5.

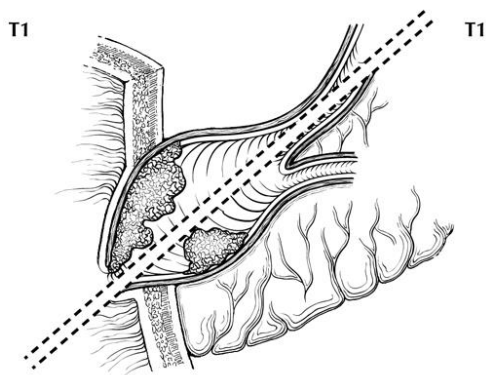


Figure 2. T1a tumors are limited to the ampulla of Vater (below the dotted line) or sphincter of Oddi (above the dotted line). From Greene et al.²⁵ Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the *AJCC Cancer Staging Atlas* (2006) published by Springer Science and Business Media LLC, www.springerlink.com.

T2

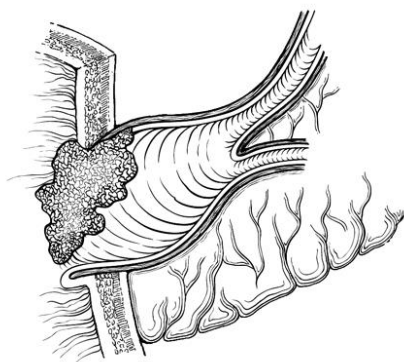


Figure 3. T1b tumors invade beyond the sphincter of Oddi or into duodenal submucosa. From Greene et al.²⁵ Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the *AJCC Cancer Staging Atlas* (2006) published by Springer Science and Business Media LLC, www.springerlink.com.

T3

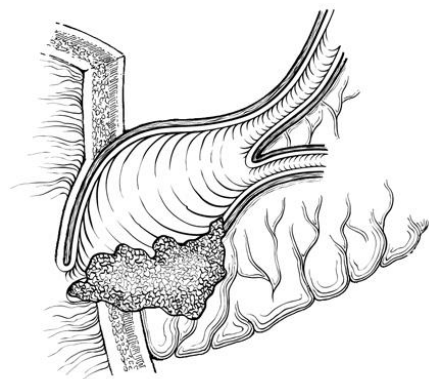


Figure 4. T3a tumors directly invade pancreas up to 0.5 cm. From Greene et al.²⁵ Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the *AJCC Cancer Staging Atlas* (2006) published by Springer Science and Business Media LLC, www.springerlink.com.

T4

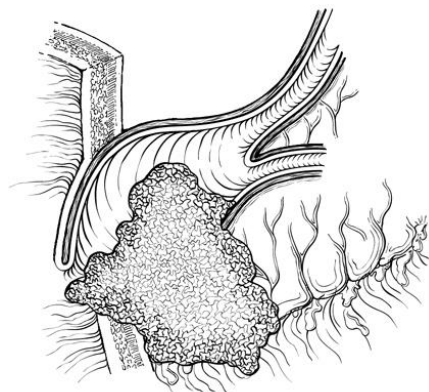


Figure 5. T3b tumors extend more than 0.5 cm into pancreas, peripancreatic fat (shown) or duodenal serosa. From Greene et al.²⁵ Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the *AJCC Cancer Staging Atlas* (2006) published by Springer Science and Business Media LLC, www.springerlink.com.

N Category Considerations

Regional lymph node metastases have been shown to have independent significance as an adverse prognostic factor in multiple series.^{2,17,18} Evaluation of a minimum of 12 lymph nodes in Whipple resections is recommended for optimal staging.^{15,19,20}

The regional nodes (Figure 6) include peripancreatic lymph nodes as well as lymph nodes along hepatic artery and portal vein.

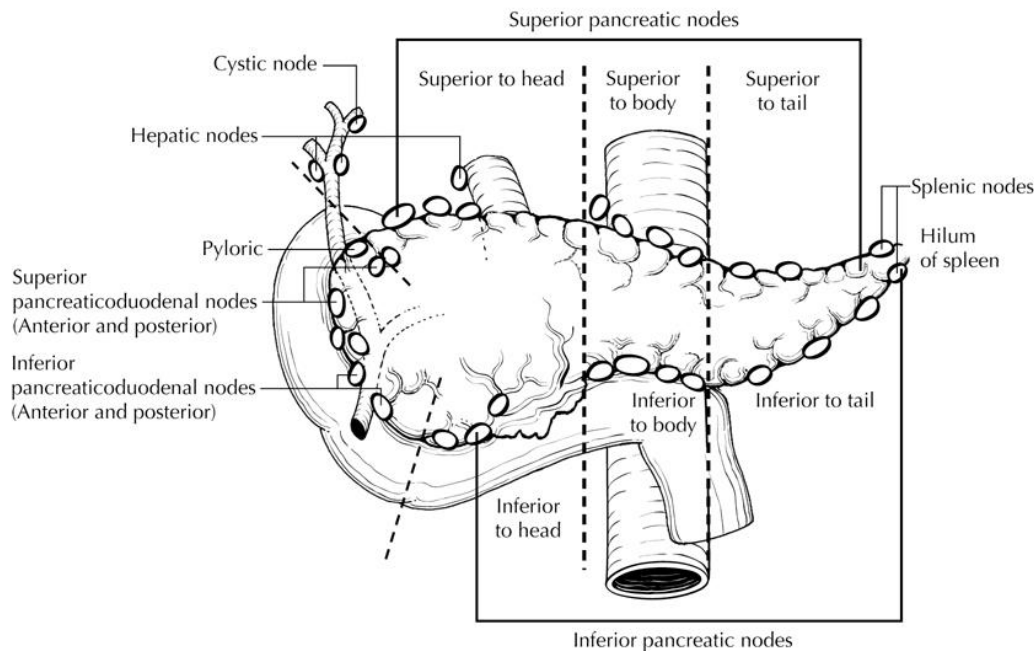


Figure 6. Regional lymph nodes of the ampulla of Vater. From Greene et al.²⁵ Used with permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the *AJCC Cancer Staging Atlas* (2006) published by Springer Science and Business Media LLC, www.springerlink.com.

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.¹

Routine assessment of regional lymph nodes is limited to conventional pathologic techniques (gross assessment and histologic examination), and data are currently insufficient to recommend special measures to detect micrometastasis or isolated tumor cells. Thus, neither multiple levels of paraffin blocks nor the use of special/ancillary techniques such as immunohistochemistry are recommended for routine examination of regional lymph nodes.

Stage Groupings

Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
	T2	N0	M0
Stage IIA	T3a	N0	M0
Stage IIB	T3b	N0	M0
Stage IIIA	T1a	N1	M0
	T1b	N1	M0
	T2	N1	M0
	T3a	N1	M0
	T3b	N1	M0
Stage IIIB	T4	Any N	M0
	Any T	N2	M0
Stage IV	Any T	Any N	M1

Vessel Invasion

By AJCC/UICC convention, vessel invasion (small vessel or venous) does not affect the T category indicating local extent of tumor unless specifically included in the definition of a T category.

G. Additional Pathologic Findings and Ancillary studies

Ampullary adenomas are common in patients with familial adenomatous polyposis coli, and such patients are at increased risk for ampullary adenocarcinomas. Estimated lifetime incidence is roughly 12% for ampullary carcinoma in this population.¹⁹

Ampullary adenocarcinoma can occur in patients with Lynch syndrome. Absence of DNA mismatch repair (MMR) proteins by immunohistochemistry has been described in 5-10% of ampullary adenocarcinomas.²²⁻²⁴ These tumors tend to be of the intestinal type. Histologic features associated with microsatellite instability (MSI) such as tumor-infiltrating lymphocytes and mucinous subtype may be present, but the association is not as strong as in colorectal adenocarcinomas.²⁴ Currently, there are no formal recommendations for MMR or MSI testing in ampullary adenocarcinoma, but this practice has been adopted in some centers.

References

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