

Extrahepatic Bile Ducts

Protocol applies to all invasive carcinomas of the extrahepatic bile ducts. Sarcomas and carcinoid tumors are excluded.

*Protocol revision date: January 2005
Based on AJCC/UICC TNM, 6th edition*

Procedures

- **Local or Segmental Bile Duct Resection**
- **Pancreaticoduodenectomy**

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The College of American Pathologists offers these protocols to assist pathologists in providing clinically useful and relevant information when reporting results of surgical specimen examinations of surgical specimens. The College regards the reporting elements in the "Surgical Pathology Cancer Case Summary (Checklist)" portion of the protocols as essential elements of the pathology report. However, the manner in which these elements are reported is at the discretion of each specific pathologist, taking into account clinician preferences, institutional policies, and individual practice.

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Summary of Changes to Checklist(s)

Protocol revision date: January 2005

No changes have been made to the data elements of the checklist(s) since the January 2004 protocol revision.

Surgical Pathology Cancer Case Summary (Checklist)

*Protocol revision date: January 2005
Applies to invasive carcinomas only
Based on AJCC/UICC TNM, 6th edition*

EXTRAHEPATIC BILE DUCTS: Resection

Patient name:

Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC**Specimen Type**

- Pancreaticoduodenectomy
 Segmental resection of bile ducts(s)
 Choledochal cyst resection
 Other (specify): _____
 Not specified

Tumor Site (check all that apply)

- Right hepatic duct
 Left hepatic duct
 Junction of right and left hepatic ducts
 Cystic duct
 Common bile duct
 Proximal
 Middle
 Distal
 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

Histologic Grade

- Not applicable
 GX: Cannot be assessed
 G1: Well differentiated
 G2: Moderately differentiated
 G3: Poorly differentiated
 G4: Undifferentiated

Pathologic Staging (pTNM)Primary Tumor (pT)

- pTX: Cannot be assessed
 pT0: No evidence of primary tumor
 pTis: Carcinoma in situ
 pT1: Tumor confined to the bile duct histologically
 pT2: Tumor invades beyond the wall of the bile duct
 pT3: Tumor invades the liver, gallbladder, pancreas, and/or unilateral branches of the portal vein (right or left) or hepatic artery (right or left)
 pT4: Tumor invades any of the following: main portal vein or its branches bilaterally, common hepatic artery, or other adjacent structures such as the colon, stomach, duodenum, or abdominal wall

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: _____

* 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.

Margins (check all that apply)

- Cannot be assessed
- Margins uninvolved by invasive carcinoma
 Distance of invasive carcinoma from closest margin: ___ mm
 Specify margin: _____
- Margins involved by invasive carcinoma
 - Proximal bile duct margin
 - Distal bile duct margin
 - Other (specify): _____
- Carcinoma in situ absent at bile duct margin
- Carcinoma in situ present at bile duct margin

***Perineural Invasion**

- * Absent
- * Present
- * Indeterminate

***Venous (Large Vessel) Invasion (V)**

- * Absent
- * Present
- * Indeterminate

***Lymphatic (Small Vessel) Invasion (L)**

- * Absent
- * Present
- * Indeterminate

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

- * None identified
- * Dysplasia
- * Cholangitis
- * Stones
- * Other (specify): _____

***Comment(s)**

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Background Documentation

Protocol revision date: January 2005

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
 - (1) inflammatory bowel disease
 - (2) sclerosing cholangitis
 - (3) choledochal cyst
 - b. Relevant findings (eg, jaundice, serum bilirubin, endoscopic retrograde cholangiopancreatography [ERCP])
 - c. Clinical diagnosis (eg, bile duct obstruction)
 - d. Procedure (eg, brushing, washing, other)
 - e. Operative findings
 - f. Anatomic site(s) of specimen(s) (eg, left/right hepatic ducts, common bile duct)

B. Macroscopic Examination

1. Specimen
 - a. Unfixed/fixed (specify fixative)
 - b. Number of slides received, if applicable
 - c. Quantity and appearance of fluid specimen, if applicable
 - 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. Local or Segmental Bile Duct Resection

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
 - (1) inflammatory bowel disease
 - (2) sclerosing cholangitis
 - (3) choledochal cyst
 - b. Relevant findings (eg, jaundice, serum bilirubin, ERCP)
 - c. Clinical diagnosis (eg, bile duct obstruction)
 - d. Procedure
 - e. Operative findings
 - f. Anatomic site(s) of specimen(s) (eg, left/right hepatic ducts, common duct)

B. Macroscopic Examination

1. Specimen
 - a. Organ(s)/tissue(s) included
 - b. Unfixed/fixed (specify fixative)
 - c. Orientation, if indicated by surgeon
 - d. Previously opened
 - e. Dimensions of bile duct (include thickness of wall)
 - f. External surface of bile duct (color, adhesions, mass)
 - g. Obstruction (partial/complete)
 - h. Stones present (number, type)
 - i. Description of other tissues, as appropriate
 - j. Results of intraoperative consultation
2. Tumor (Note **A**)
 - a. Location
 - (1) origin in bile duct segment
 - (2) origin in choledochal cyst (Note **D**)
 - b. Configuration (Note **E**)
 - c. Size (largest dimension)
 - d. Descriptive features (eg, color, consistency, necrosis)
 - e. Extent of invasion (Note **F**)
3. Additional pathologic findings
4. Margins, as appropriate (Note **G**)
5. Regional lymph nodes
 - a. Location, if possible (Note **F**)
 - b. Number
6. Other organ(s) or structure(s)
 - a. Involved by tumor by direct extension
 - b. Metastatic involvement by tumor
 - c. Additional pathologic findings
7. Tissues submitted for microscopic evaluation
 - a. Carcinoma, including:
 - (1) point of deepest penetration
 - (2) interface with adjacent tissue
 - b. Uninvolved mucosa
 - c. Margins of extrahepatic ducts (Note **G**)
 - d. Other margins, as appropriate (Note **G**)
 - e. All lymph nodes
 - f. Other lesions

- g. Frozen section tissue fragment(s) (unless saved for special studies)
- h. Other tissue(s)/organ(s) (specify) (eg, liver, pancreas, gallbladder, duodenum)
- 7. Special studies (specify) (eg, histochemistry, immunohistochemistry, DNA analysis)

C. Microscopic Evaluation

- 1. Tumor
 - a. Histologic type (Note **B**)
 - b. Histologic grade (Note **C**)
 - c. Extent of invasion (Note **F**)
 - d. Venous/lymphatic vessel invasion
 - e. Perineural invasion (Note **H**)
- 2. Margins (Note **G**)
 - a. Bile duct margins
 - b. Other margins, as appropriate
- 3. Regional lymph nodes
 - a. Number
 - b. Number involved by tumor (Note **F**)
- 4. Additional pathologic findings, if present
 - a. Dysplasia
 - b. Carcinoma in situ
 - c. Sclerosing cholangitis
 - d. Other(s)
- 5. Metastasis to other organ(s) or structure(s) (specify site)
- 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

This protocol applies only to carcinomas arising in the extrahepatic bile ducts (including choledochal cysts) and in the cystic duct. It does not include carcinoid tumors or tumors arising in the ampulla of Vater. More than 98% of the malignant tumors of the extrahepatic bile ducts are carcinomas. They are often associated with a history of ulcerative colitis. Tumors arising within the intrahepatic bile ducts are classified and staged as liver tumors (see Liver protocol).

B. Histologic Type

For consistency in reporting, the histologic classification published by the World Health Organization (WHO), shown below, is recommended.¹ However, this protocol does not preclude the use of other systems of classification or histologic types. By WHO convention, the term “cholangiocarcinoma” is reserved for carcinomas arising in the intrahepatic bile ducts (see Liver protocol). For reporting of carcinoma in situ, the term intraepithelial neoplasia is recommended by the WHO classification.

Some histologic types of extrahepatic bile duct carcinoma are prognostically significant; papillary carcinomas, which are often polypoid on macroscopic examination (see Note **E**, Configuration), have the best prognosis.¹ High-grade tumors such as signet-ring cell

carcinomas, small cell carcinomas, and undifferentiated carcinomas are associated with a poorer prognosis compared to adenocarcinoma.

WHO Classification of Carcinoma of the Extrahepatic Bile Ducts

- Adenocarcinoma
- Papillary adenocarcinoma[#]
- Adenocarcinoma, intestinal type
- Adenocarcinoma, gastric foveolar type
- Mucinous adenocarcinoma
- Clear cell adenocarcinoma[#]
- Signet-ring cell carcinoma^{##}
- Adenosquamous carcinoma
- Squamous cell carcinoma
- Small cell carcinoma^{###}
- Large cell neuroendocrine carcinoma
- Undifferentiated carcinoma^{###}
- Biliary cystadenocarcinoma

[#] These histologic types are not usually graded (see below).

^{##} By convention, signet-ring cell carcinomas are assigned grade 3 (see below).

^{###} Small cell carcinomas and undifferentiated (histologic type) carcinomas are assigned grade 4 (see below).

C. Histologic Grade

For adenocarcinomas, a quantitative grading system based on the proportion of gland formation within the tumor is suggested¹ and shown below.

- Grade X Grade 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 (less than 50% of tumor composed of glands)

Definitions corresponding to the above histologic grades are as follows.

- Grade 1 Composed entirely of glands or has less than 5% solid or cord-like growth patterns
- Grade 2 Has from 6% to 49% solid or cord-like growth patterns
- Grade 3 Has 50% to 100% solid or cord-like growth patterns

For squamous cell carcinomas, a rare tumor type in the extrahepatic bile ducts, a suggested grading system is shown below. If there are variations in the differentiation within the tumor, the highest (least favorable) grade is recorded.

- Grade X Grade cannot be assessed
- Grade 1 Well differentiated
- Grade 2 Moderately differentiated
- Grade 3 Poorly differentiated

Note: 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.

D. Choledochal Cyst

Carcinomas may arise in choledochal cysts (congenital cystic dilatation or duplications) of the bile duct. Histologically, they are classified in the same way as those arising in the gallbladder or bile ducts. Stones may be found in these cysts. If carcinoma in situ is found on initial microscopic sections, then multiple additional sections should be examined to exclude invasive cancer in other areas of the cyst.

E Configuration

Configuration includes polypoid, nodular, diffusely infiltrating, or combined features. Polypoid tumors, which often prove to be papillary carcinomas on microscopic examination, have a better prognosis and should be specifically reported.^{1,2}

F. TNM and Stage Groupings

The TNM staging system for malignant tumors of the extrahepatic bile ducts of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) is recommended by the protocol and shown below.^{3,4} The staging system also applies to tumors arising in choledochal cysts.

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 confined to the bile duct histologically |
| T2 | Tumor invades beyond the wall of the bile duct |
| T3 | Tumor invades the liver, gallbladder, pancreas, and/or unilateral branches of the portal vein (right or left) or hepatic artery (right or left) |
| T4 | Tumor invades any of the following: main portal vein or its branches bilaterally, common hepatic artery, or other adjacent structures such as the colon, stomach, duodenum, or abdominal wall |

Regional Lymph Nodes (N)

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

Distant Metastasis (M)

- MX 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 | 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,⁵ 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

G. Margins

It is important to evaluate carefully all surgical margins, including an assessment of vascular (lymphatic and blood vessel) and perineural invasion. Local recurrence is often related to residual tumor located in the proximal or distal surgical margins of the bile duct or from tumor located along the dissected soft tissue margin in the portal area.⁶ Local recurrence (usually at the surgical margins) is most common with carcinomas arising in the hepatic duct(s).

In addition, malignant tumors of the extrahepatic bile ducts are often multifocal.⁷ Therefore, microscopic foci of carcinoma or intraepithelial neoplasia may be found at the margin(s) even though the main tumor mass has been resected. In some cases it may be difficult to evaluate margins on frozen section preparations because of inflammation and reactive atypia of the surface epithelium or within the intramural mucous glands. If surgical margins are free of carcinoma, the distance between the closest margin and the tumor edge should be measured.

Since 5% of patients with bile duct carcinoma have synchronous carcinomas of the gallbladder, examination of the entire surgical specimen including the gallbladder is advised.

H. Perineural and Lymphatic Invasion

Perineural and lymphatic invasion are common in extrahepatic bile duct carcinomas. They should be specifically evaluated since they are associated with adverse outcome.^{1,8-10} Perineural invasion is also useful for distinguishing carcinoma from primary sclerosing cholangitis.

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