COLLEGE of AMERICAN PATHOLOGISTS

Protocol for the Examination of Specimens From Patients With Carcinoma of the Appendix

Version: Appendix 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
Excision	Includes specimens designated appendectomy with or without segmental resection (right hemicolectomy)
Tumor Type	**Description**
Carcinoma	Includes adenocarcinoma (and variants), goblet cell carcinoid, mucinous neoplasms, small cell and large cell (poorly differentiated) neuroendocrine carcinoma

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
Well-differentiated neuroendocrine tumors (consider the Appendix NET protocol)
Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)
Gastrointestinal stromal tumor (GIST) (consider the GIST protocol)
Non-GIST sarcoma (consider the Soft Tissue protocol)

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

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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 Appendix Protocol Summary of Changes

The following data elements were modified:
Pathologic Stage Classification (pTNM, AJCC 8th Edition)
Histologic Type
Microscopic Tumor Extension
Tumor Deposits

The following data element was deleted:
Clinical History

Surgical Pathology Cancer Case Summary

Protocol posting date: June 2017

APPENDIX:

Select a single response unless otherwise indicated.

Procedure (Note A)
___ Appendectomy
___ Appendectomy and right colectomy
___ Other (specify): _____

+ Tumor Site (select all that apply) (Note B)
+ ___ Proximal half of appendix
    + ___ Base of appendix involved by tumor
    + ___ Base of appendix uninvolved by tumor
    + ___ Involvement of base of appendix cannot be assessed
+ ___ Distal half of appendix
+ ___ Diffusely involving appendix
+ ___ Appendix, not otherwise specified
+ ___ Other (specify): _____

Tumor Size
Greatest dimension (centimeters): ___ cm
+ Additional dimensions (centimeters): ___ x ___ cm
___ Cannot be determined (explain): _____

Histologic Type (Note C)
___ Adenocarcinoma
___ Mucinous adenocarcinoma
___ Low-grade appendiceal mucinous neoplasm
___ High-grade appendiceal mucinous neoplasm
___ Signet-ring cell carcinoma
___ Goblet cell carcinoid
___ Mixed goblet cell carcinoid-adenocarcinoma (adenocarcinoma ex goblet cell carcinoid)
___ Large cell neuroendocrine carcinoma
___ Small cell neuroendocrine carcinoma
___ Neuroendocrine carcinoma (poorly differentiated)[#]
___ Mixed adenoneuroendocrine carcinoma
___ Medullary carcinoma
___ Adenosquamous carcinoma
___ Undifferentiated carcinoma
___ Other histologic type not listed (specify): _____
___ Carcinoma, type cannot be determined (explain): _____

[#] *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
___ Other (specify): _____
___ GX: Cannot be assessed
___ Not applicable

Tumor Extension (select all that apply)
___ No evidence of primary tumor
___ Tumor invades lamina propria or muscularis mucosa
___ Tumor invades submucosa
___ Tumor invades muscularis propria
___ Acellular mucin invades subserosa or mesoappendix but does not extend to the serosal surface
___ Tumor invades through the muscularis propria into the subserosa or mesoappendix but does not extend to the serosal surface
___ Acellular mucin invades the visceral peritoneum (serosa)
___ Tumor invades the visceral peritoneum (serosa)
___ Tumor directly invades adjacent organs or structures (specify): _____
___ Cannot be assessed

Margins (Note E)

Proximal Margin (select all that apply)
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
___ Involved by invasive carcinoma
___ Involved by high-grade dysplasia
___ Uninvolved by appendiceal mucinous neoplasm
___ Involved by low-grade appendiceal mucinous neoplasm
___ Involved by high-grade appendiceal mucinous neoplasm
___ Involved by acellular mucin

Mesenteric Margin (required only if applicable) (select all that apply)
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
+ Distance of invasive carcinoma from closest mesenteric margin (millimeters *or* centimeters):
___ mm *or* ___ cm
___ Involved by invasive carcinoma
___ Uninvolved by appendiceal mucinous neoplasm
___ Involved by low-grade appendiceal mucinous neoplasm
___ Involved by high-grade appendiceal mucinous neoplasm
___ Involved by acellular mucin

Other Margin(s) (required only if applicable)
Specify margin(s): _____
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
___ Involved by invasive carcinoma

Lymphovascular Invasion (select all that apply) (Note F)
___ Not identified
___ Present
___ Cannot be determined

Tumor Deposits (Note G)
___ Not identified
___ Present
___ Specify number of deposits: ____
___ Number of tumor deposits cannot be determined (explain): _____
___ Cannot be determined

+ Perineural Invasion (Note H)
+ ___ Not identified

+ ___ Present
+ ___ Cannot be determined

Regional Lymph Nodes

___ No lymph nodes submitted or found

Lymph Node Examination (required only if lymph nodes are present in the 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 I)

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 (intramucosal carcinoma; invasion of the lamina propria or extension into but not through the muscularis mucosae)
___ pTis(LAMN): Low-grade appendiceal mucinous neoplasm confined by the muscularis propria. Acellular mucin or mucinous epithelium may invade into the muscularis propria. T1 and T2 are not applicable to LAMN. Acellular mucin or mucinous epithelium that extends into the subserosa or serosa should be classified as T3 or T4a, respectively.
___ pT1: Tumor invades the submucosa (through the muscularis mucosa but not into the muscularis propria)
___ pT2: Tumor invades the muscularis propria
___ pT3: Tumor invades through the muscularis propria into the subserosa or mesoappendix
___ pT4: Tumor invades the visceral peritoneum, including the acellular mucin or mucinous epithelium involving the serosa of the appendix or mesoappendix, and/or directly invades adjacent organs or structures
___ pT4a: Tumor invades through the visceral peritoneum, including the acellular mucin or mucinous epithelium involving the serosa of the appendix or serosa of the mesoappendix
___ pT4b: Tumor directly invades or adheres to adjacent organs or structures

Regional Lymph Nodes (pN)
___ pNX: Regional lymph nodes cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: One to three regional lymph nodes are positive (tumor in lymph nodes measuring ≥0.2 mm), or any number of tumor deposits is present, and all identifiable lymph nodes are negative
___ pN1a: One regional lymph node is positive
___ pN1b: Two or three regional lymph nodes are positive
___ pN1c: No regional lymph nodes are positive, but there are tumor deposits in the subserosa or mesentery
___ pN2: Four or more regional lymph nodes are positive

Distant Metastasis (pM) (required only if confirmed pathologically in this case)
___ pM1: Distant metastasis
___ pM1a: Intraperitoneal acellular mucin, without identifiable tumor cells in the disseminated peritoneal mucinous deposits[#]
___ pM1b: Intraperitoneal metastasis only, including peritoneal mucinous deposits containing tumor cells
___ pM1c: Metastasis to sites other than peritoneum
Specify site(s), if known: _____

[#] *Note: For specimens containing acellular mucin without identifiable tumor cells, efforts should be made to obtain additional tissue for thorough histologic examination to evaluate for cellularity.*

+ Additional Pathologic Findings (select all that apply) (Note J)
+ ___ None identified
+ ___ Appendicitis
+ ___ Perforation, not at tumor
+ ___ Ulcerative colitis
+ ___ Crohn disease
+ ___ Diverticulosis
+ ___ Other (specify): _____

+ Ancillary Studies (Note K)
+ Specify: _____
+ ___ Not performed

+ Comment(s)

Explanatory Notes

A. Anatomic Site

Tumors located at the base of the appendix must be distinguished from cecal carcinomas extending into the appendix, a distinction based primarily on a careful gross examination of the specimen with determination of the location of the bulk of the tumor. Microscopic examination may reveal a precursor lesion, and its location may indicate the primary site of origin.

B. Tumor Location

Appendiceal tumors located in the base of the appendix may cause obstruction of the lumen early in their course, resulting in acute appendicitis and their early recognition, with a resultant better prognosis compared to tumors located either in the colon or distal appendix.

C. Histologic Type

For consistency in reporting, the histologic classification of appendiceal carcinomas proposed by the World Health Organization (WHO) is recommended.[1] However, this protocol does not preclude the use of other systems of classification or histologic types.

WHO Classification of Appendiceal Carcinoma

Adenocarcinoma
Mucinous adenocarcinoma
Low-grade appendiceal mucinous neoplasm[#]
*High-grade appendiceal mucinous neoplasm[#]
Signet-ring cell carcinoma
Medullary carcinoma
Adenosquamous carcinoma
Goblet cell carcinoid[##]
*Mixed goblet cell carcinoid-adenocarcinoma or adenocarcinoma ex goblet cell carcinoid[##]
Mixed adenoneuroendocrine carcinoma[##]
Poorly differentiated neuroendocrine carcinoma
Large cell neuroendocrine carcinoma
Small cell neuroendocrine carcinoma
Undifferentiated carcinoma

* These subtypes are not included in the WHO 2010 classification but are included in the AJCC 8th edition.

Some studies have shown that mucinous carcinomas in the appendix have a better prognosis than nonmucinous adenocarcinomas[2,3] and are less likely to demonstrate lymphatic or hematogenous spread.[2,4]

The distinction between a carcinoma that is cystic and one that is not cystic has not been shown to be of biologic significance. Therefore, the prefix “cyst” is a descriptive term rather than a clinically significant characteristic of appendiceal carcinomas.

[#] This protocol is applicable to low-grade (or high-grade) appendiceal mucinous neoplasms as well as invasive carcinomas. Low-grade appendiceal mucinous neoplasm (LAMN) is considered a low-grade carcinoma. Adenomatous proliferation with an intact muscularis mucosa is considered an appendiceal adenoma.[1] Tumors with obliteration of muscularis mucosa in which the adenomatous epithelium rests on fibrous tissue or tumors with nondestructive mural or peritoneal involvement qualify for the diagnosis of LAMN.[1] Tumors with destructive invasion and desmoplasia are classified as invasive adenocarcinoma. Both LAMN and invasive carcinomas should be staged as per this protocol.[1] If the histologic features qualify for LAMN, the histologic type in the tumor synoptic should be selected as LAMN even if there is peritoneal involvement. High-grade appendiceal neoplasms (HAMNs) are rare tumors that resemble LAMN in lacking destructive invasion, but show high-grade cytologic features. This term is not part of the current WHO terminology, but has been recommended in a recent consensus publication and has been included in the AJCC 8th edition.[5]

One of the most critical prognostic factors in mucinous appendiceal neoplasms is the presence or absence of mucinous epithelial cells in extra-appendiceal mucin.[6-9] Hence the presence or absence of epithelial cells in mucin should be clearly noted in the surgical pathology report.

[##] Goblet cell carcinoids (GCC) have a less favorable prognosis than pure appendiceal neuroendocrine tumors and should be staged using the TNM system for appendiceal carcinoma, whereas well differentiated neuroendocrine tumors of the appendix should be staged using the TNM system for appendiceal neuroendocrine tumors. Some tumors show a combination of GCC and adenocarcinoma (conventional, mucinous, or signet-ring cell type). These mixed GCC-adenocarcinomas have been referred to as *adenoneuroendocrine carcinoma* in the WHO 2010 classification.[1] This term can create the mistaken impression of a component of poorly differentiated neuroendocrine carcinoma, which is treated differently from GCC or adenocarcinoma. Hence it is preferable to use the term *adenoneuroendocrine carcinoma* for tumors showing a combination of adenocarcinoma and a poorly differentiated neuroendocrine carcinoma. Tumors showing a combination of GCC and adenocarcinoma, are better designated as *mixed goblet cell carcinoid-adenocarcinoma* or *adenocarcinoma ex goblet cell carcinoid.*[10,11] The behavior of these mixed tumors may be more aggressive compared to pure GCC.[11]

D. Histologic Grade

Although rigorous criteria for grading have not been applied, histologic grade has been shown to be a prognostic factor in several series of appendiceal carcinoma.[12-17]

Nonmucinous tumors: These tumors are graded as well differentiated (G1, >95% gland formation), moderately differentiated (G2, 50-95% gland formation), and poorly differentiated (G3, <50% gland formation).

Appendiceal mucinous tumors have been graded as low or high grade based on cytologic features in the WHO 2010 scheme. For mucinous tumors involving the peritoneum, the AJCC recommends a 3-tier grading scheme as the prognostic significance of three groups has been shown in multiple studies for mucinous tumors involving the peritoneum. The proposed 3-tier grading scheme by AJCC is modified from Davison et al[16] and is based on cytologic features, tumor cellularity, and presence of signet-ring component. The grade of the appendiceal and peritoneal tumors is concordant in most instances, but some cases may show discordant grades in the appendix and peritoneum. In case of discordance of grades, the highest grade should be assigned to the tumor for staging (see note I).

Table: Three-Tier Grading Scheme Recommended by AJCC[18]
(based on scheme proposed by Davison et el[16])

Well-differentiated (G1)	Low-grade cytologic atypia, no signet-ring cells. Tumors involving peritoneum show acellular mucin or low cellularity (typically <20%) and lack infiltrative invasion of the peritoneum or other organs are considered G1.
Moderately differentiated (G2)	Mix of low- and high-grade cytologic atypia or diffuse high-grade cytologic atypia, no signet-ring cells.
Poorly differentiated (G3)	High-grade cytologic atypia, usually with signet-ring cell component.

In the appendix, G1 tumors usually lack typical features of invasion and are classified as LAMNs. In the peritoneum, G1 tumors may involve peritoneal surface or organs with a pushing front without desmoplasia, and lack infiltrative invasion. Perineural invasion and lymphovascular invasion are not seen. G1 tumors with peritoneal involvement have been variously termed as LAMN with peritoneal involvement, low-grade mucinous carcinoma peritonei and disseminated peritoneal adenomucinosis (DPAM). In cancer protocols, the histologic type of these tumors is best recorded as LAMN. G2 mucinous tumors in the appendix may correspond to high-grade mucinous appendiceal neoplasms (HAMN) or mucinous adenocarcinomas with destructive invasion and associated desmoplasia. The latter often shows complex architecture, such as cribriform glandular spaces and complex papillary structures. G3 mucinous tumors in the appendix are high-grade, invasive tumors that usually have a signet ring cell component. With extra-appendiceal spread, G2 and G3 tumors can show invasion (with desmoplasia) into the peritoneum or other organs, perineural invasion, and lymphovascular invasion. Most mucinous G2 and G3 tumors with peritoneal involvement would correspond to terms such as high-grade mucinous carcinoma peritoneii and peritoneal mucinous adenocarcinoma.

By convention, signet-ring cell carcinomas are grade 3. The above grading schemes are not applicable to poorly differentiated neuroendocrine carcinoma and goblet cell carcinoid. Tumors with no differentiation (undifferentiated carcinomas) are categorized as grade 4 in the WHO 2010 classification, but G4 is not included in the AJCC 8th edition.

E. Margins
Margins in a simple appendectomy specimen include the proximal and, in some cases, radial margin. It is recommended that the proximal margin on a simple appendectomy specimen be taken en face in order to evaluate the entire appendiceal mucosa and muscularis circumferentially. In the vast majority of cases, the appendix is entirely peritonealized, and the mesenteric resection margin represents the radial margin. The closest distance between the invasive carcinoma and this margin should be measured. Even retrocecal appendices are usually invested by peritoneum but have adhered to the posterior cecum, either because of inflammation or tumor. Exceptionally, a retrocecal appendix may be retroperitoneal, in which case the nonperitonealized surface is the radial resection margin. The distance between the invasive carcinoma and this margin should be measured.

In right hemicolectomy specimens, the ileal and colonic margins are the proximal and distal margins, respectively. The distance between the tumor and the ileal and colonic margins should be measured, and these margins are considered to be grossly negative if they are greater than 5 cm from the tumor.

F. Lymph-Vascular Invasion
Lymph-vascular invasion (LVI) includes small vessel (lymphatic or vascular) invasion and large vessel (venous) invasion. The prognostic significance of lymph-vascular invasion has not been widely studied in appendiceal carcinoma. However, given their significance in colorectal carcinoma, this feature should be reported in all cases.

G. Tumor Deposits
A tumor focus in the periappendiceal fat or mesoappendix, but without identifiable lymph node tissue or vascular structure, is considered a tumor deposit. If the vessel wall or its remnant is identified (H&E, elastic, or any other stain), it should be classified as vascular (venous) invasion, and not as tumor deposit. Similarly, a tumor focus is present in or around a large nerve, should be classified as perineural invasion and not as tumor deposit. Size and shape of the tumor focus are not relevant for classification as a tumor deposit. The presence of tumor deposits in the absence of any regional node involvement is categorized as N1c, irrespective of T category. The significance of tumor deposits has not been specifically examined in appendiceal tumors. In view of the established prognostic significance of tumor deposits in colorectal cancer, this feature has been adopted into the AJCC staging scheme for the appendix.[18]

H. Perineural Invasion
The prognostic significance of perineural invasion has not been widely studied in appendiceal carcinomas. Based on limited studies[16] and its prognostic significance in colorectal cancer, its presence or absence should be recorded for appendiceal carcinomas.

I. Pathologic Stage Classification
A revised TNM staging system has been developed by the American Joint Committee on Cancer (AJCC) for the 8th edition of the *AJCC Cancer Staging Manual.*[18] This system also incorporates tumor grade to subclassify stage IV tumors.

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 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.

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

T Category Considerations
When confined to muscularis propria, LAMN is classified as Tis (LAMN) as there is no significant risk of extra-appendiceal spread, and designated as T3 or T4a if it extends beyond muscularis propria. Acellular mucin involving the serosal surface is considered as T4a, due to a small risk of peritoneal recurrence. In some instances, acellular mucin may be seen on the serosal surface due to “carryover” related to specimen handling or sectioning artifact. In these instances, mucin dissection into the stroma and tissue reaction such as inflammation, mesothelial hyperplasia and neovascularization can help in this distinction.

N Category Considerations
The regional lymph nodes for the appendix include the anterior cecal, posterior cecal, ileocolic, and right colic lymph nodes.

The presence of lymph node metastasis is relatively rare in appendiceal carcinoma[16] but is an adverse prognostic finding.[2] Among patients with high-stage disease (peritoneal spread of appendiceal carcinoma), lymph node status appears to have less impact on overall survival.[4,19]

M Category Considerations
Seeding of peritoneum or abdominal organs is considered distant metastasis. Extensive sampling should be performed before using the designation of M1a. Peritoneal mucinous deposits containing tumor cells should be staged as M1b and are grouped based on tumor grade as stage IVA (mucinous G1 tumors) or stage IVB (nonmucinous G1 and all G2/G3/G4 tumors). The highest grade is used in case if there is a discordance in tumor between the appendix and peritoneum. Peritoneal implants involving abdominopelvic organs, such as the serosa of the small or large bowel and the surfaces of the ovary, spleen, or liver, should be classified as M1b, even if the implants demonstrate infiltration of underlying tissue. M1c designation is used for metastasis to nonperitoneal sites.

Stage Groupings

Stage 0	Tis	N0	M0	
	Tis (LAMN)	N0	M0	
Stage I	T1	N0	M0	
	T2	N0	M0	
Stage IIA	T3	N0	M0	
IIB	T4a	N0	M0	
IIC	T4b	N0	M0	
Stage IIIA	T1	N1	M0	
	T2	N1	M0	
IIIB	T3	N1	M0	
	T4	N1	M0	
	Any T	N2	M0	
Stage IVA	Any T	N0	M1a	
IVA	Any T	Any N	M1b	G1
IVB	Any T	Any N	M1b	GX, G2, G3, or G4
Stage IVC	Any T	Any N	M1c	Any G

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).

J. Additional Pathologic Findings
Appendiceal perforation may be an adverse prognostic factor, but its adverse significance as an independent prognostic is not well established.[4,20,21]

Diverticula are a common finding in the appendix and may represent a route of egress for mucin in cases of LAMN.[7] Ruptured diverticula can show extraappendiceal mucin with or without epithelium and should not be mistaken for LAMN.[22]

Appendiceal adenocarcinomas have been reported in the setting of inflammatory bowel disease, although causation has not been established.[23]

Well-differentiated neuroendocrine tumors (typical carcinoid tumor) of any size should be reported using the CAP protocol for neuroendocrine tumors of the appendix.

K. Ancillary Studies
A minority of appendiceal carcinomas show high levels of microsatellite instability, but MSI testing is not currently recommended as standard of care for these tumors.[24,25]

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