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Carcinoma of the Appendix Histopathology Reporting Guide

Family/Last name

Given name(s)

Date of birth DD – MM – YYYY

Patient identifiers

Date of request DD – MM – YYYY

Accession/Laboratory number

Elements in **black text** are CORE. Elements in **grey text** are NON-CORE.

SCOPE OF THIS DATASET

CLINICAL INFORMATION (Note 1)

- ◯ Information not provided
- ◯ Information provided (select all that apply)
  - ☐ Appendicitis
  - ☐ Appendiceal mass/tumour
  - ☐ Preoperative therapy, *specify*
  - ☐ Other clinical information, *specify*

OPERATIVE PROCEDURE (Note 2)

- ◯ Not specified
- ◯ Appendicectomy
- ◯ Right colectomy
- ◯ Ileocaecectomy
- ◯ Appendicectomy with partial caecectomy
- ◯ Other, *specify*

TUMOUR SITE (select all that apply) (Note 3)

- ☐ Proximal appendix
- ☐ Distal appendix
- ☐ Entire length of the appendix
- ☐ Other, *specify*

MACROSCOPIC APPEARANCE (select all that apply) (Note 4)

- ☐ Perforation of the appendix
- ☐ Presence of mucin on the surface
- ☐ Other, *specify*

TUMOUR DIMENSIONS (Note 5)

Greatest dimension mm

Additional dimensions mm x mm

- ◯ Cannot be assessed, *specify*

BLOCK IDENTIFICATION KEY (Note 6)

(List overleaf or separately with an indication of the nature and origin of all tissue blocks)

HISTOLOGICAL TUMOUR TYPE (Note 7)

(Value list based on the World Health Organization (WHO) Classification of Tumours of the Digestive System (2019))

- ◯ Appendiceal mucinous neoplasm
- ◯ Adenocarcinoma
- ◯ Mucinous adenocarcinoma
- ◯ Signet ring cell adenocarcinoma
- ◯ Goblet cell adenocarcinoma
- ◯ Small cell neuroendocrine carcinoma
- ◯ Large cell neuroendocrine carcinoma
- ◯ Mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN)
- ◯ Carcinoma, undifferentiated
- ◯ Other, *specify*

HISTOLOGICAL TUMOUR GRADE (Note 8)

- ◯ Not applicable
- ◯ Cannot be assessed
- ◯ G1: Well differentiated
- ◯ G2: Moderately differentiated
- ◯ G3: Poorly differentiated
- ◯ Other, *specify*

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APPENDIX PERFORATION AT OR AWAY FROM TUMOUR (Note 9)

- ◯ Not identified
- ◯ Perforation at tumour
- ◯ Perforation away from tumour

EXTENT OF INVASION (Note 10)

- ◯ Cannot be assessed
- ◯ Tumour confined to mucosa
- ◯ Tumour or mucin extends into submucosa
- ◯ Tumour or mucin extends into muscularis propria
- ◯ Tumour or mucin extends to subserosa
- ◯ Non-mucinous tumour invades visceral peritoneum
- ◯ Acellular mucin on serosal surface
- ◯ Mucin with tumour cells on serosal surface
- ◯ Tumour invades adjacent organ(s)/structure(s)
- ◯ Other, *specify*

LYMPHOVASCULAR INVASION[a] (Note 11)

- ◯ Not identified
- ◯ Indeterminate
- ◯ Present

[a] *Core for all invasive tumours; non-core for low grade mucinous neoplasm (LAMN) and high grade appendiceal mucinous neoplasm (HAMN).*

PERINEURAL INVASION[a] (Note 12)

- ◯ Not identified
- ◯ Indeterminate
- ◯ Present

MARGIN STATUS (Note 13)

- ◯ Cannot be assessed
- ◯ Not involved
  - Distance of tumour from closest margin ____ mm
  - Specify closest margin
- ◯ Involved
  - Specify margin

LYMPH NODE STATUS (Note 14)

- ◯ No nodes submitted or found

Number of lymph nodes examined

- ◯ Not involved
- ◯ Involved
  - Number of involved lymph nodes
  - ◯ Number cannot be determined

TUMOUR DEPOSITS[a] (Note 15)

- ◯ Cannot be assessed
- ◯ Not identified
- ◯ Present
  - Number of tumour deposits
  - ◯ Number cannot be determined

ADDITIONAL FINDINGS (select all that apply) (Note 16)

- ☐ None identified
- ☐ Appendicitis
- ☐ Ulcerative colitis
- ☐ Crohn disease
- ☐ Diverticulosis
- ☐ Neuroendocrine tumour
- ☐ Other, *specify*

ANCILLARY STUDIES (Note 17)

Neuroendocrine carcinomas only

- ◯ Not applicable

Neuroendocrine markers

- ◯ Not performed

Select at least two of the following

- ☐ Synaptophysin
- ☐ Chromogranin-A
- ☐ INSM1

Ki-67 proliferation index ____ %

- ◯ Not performed

p53

- ◯ Not performed
- ◯ Abnormal, *specify*
- ◯ Wildtype pattern

Mismatch repair (MMR) immunohistochemistry

- ◯ Proficient
- ◯ Equivocal
- ◯ Deficient, *specify*

Rb1

- ◯ Retained ◯ Deficient

Low molecular weight cytokeratin(s)

- ◯ Positive ◯ Negative

ANCILLARY STUDIES (Note 17) **continued**

Other tumours

- ◯ Not performed
- ◯ Performed (select all that apply)
  - ☐ MMR immunohistochemistry[b]
    - ◯ Proficient
    - ◯ Equivocal
    - ◯ Deficient, *specify*
  - ☐ Microsatellite instability (MSI) testing[b]
  - ☐ Other, *record test(s), methodology and result(s)*

Representative blocks for ancillary studies, *specify those blocks best representing tumour and/or normal tissue for further study*

[b] *Core for invasive carcinoma only.*

PERITONEAL METASTASES (Note 18)

- ◯ Not identified
- ◯ Present
  - ◯ Acellular mucin only
  - ◯ Mucin with mucinous neoplastic cells, *specify grade*
  - ◯ Metastatic adenocarcinoma, non-mucinous
  - ◯ Goblet cell adenocarcinoma

NON-PERITONEAL METASTASES (Note 19)

- ◯ Not known
- ◯ Present, *specify site(s)*

PATHOLOGICAL STAGING (UICC TNM 9th edition)[c] (Note 20)

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

- ☐ m - multiple primary tumours
- ☐ y - post-therapy
- ☐ r - recurrent

Primary tumour (pT)

- ◯ TX[d] Primary tumour cannot be assessed
- ◯ T0 No evidence of primary tumour
- ◯ Tis Carcinoma in situ: intraepithelial or invasion of lamina propria
- ◯ Tis (LAMN)[e] Low grade appendiceal mucinous neoplasm confined to the muscularis propria; acellular mucin or mucinous epithelium may invade into the muscularis propria
- ◯ T1 Tumour invades submucosa[f]
- ◯ T2 Tumour invades muscularis propria[f]
- ◯ T3 Tumour invades subserosa or mesoappendix
- ◯ T4 Tumour perforates visceral peritoneum, including mucinous peritoneal tumour or acellular mucin on the serosa of the appendix or mesoappendix and/or directly invades other organs or structures[g]
  - ◯ T4a Tumour perforates visceral peritoneum, including mucinous peritoneal tumour or acellular mucin on the serosa of the appendix or mesoappendix
  - ◯ T4b Tumour directly invades other organs or structures

Regional lymph nodes (pN)

- ◯ NX[d] Regional lymph nodes cannot be assessed
- ◯ N0 No regional lymph node metastasis
- ◯ N1 Metastasis in 1-3 regional lymph nodes
  - ◯ N1a Metastasis in 1 regional lymph node
  - ◯ N1b Metastases in 2-3 regional lymph nodes
  - ◯ N1c Tumour deposit(s), i.e., satellites,[h] in the subserosa, or in non-peritonealised pericolic or peri-rectal soft tissue *without* regional lymph node metastasis
- ◯ N2 Metastasis in 4 or more regional lymph nodes

Distant metastasis (pM)

- ◯ M1 Distant metastasis microscopically confirmed
  - ◯ M1a Intraperitoneal acellular mucin only
  - ◯ M1b Intraperitoneal metastasis only, including mucinous epithelium
  - ◯ M1c Non-peritoneal metastasis

[c] *Reproduced with permission. Source: UICC TNM Classification of Malignant Tumours, 9th Edition, eds by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, Elizabeth Van Eycken. 2025, Publisher Wiley (incorporating any errata published up until 21st January 2026).*

[d] *TX and NX should be used only if absolutely necessary.*

[e] *The Tis(LAMN) category does not apply to HAMNs; HAMN are staged using the appendiceal adenocarcinoma T categories.*

[f] *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.*

[g] *Direct invasion in T4 includes invasion of other intestinal segments by way of the serosa, e.g., invasion of ileum. Tumour that is adherent to other organs or structures, macroscopically, is classified cT4b. However, if no tumour is present in the adhesion, microscopically, the classification should be pT1, 2 or 3.*

[h] *Tumour deposits (TDs) represent discrete tumour nodules of any shape, contour or size in peri-rectal and peri-colonic fat, away from the leading edge of the tumour, within the lymph drainage area of the primary carcinoma. TDs can originate from different histological structures, including lymph nodes, vessels and nerves. Therefore, TDs may contain foci of extramural vascular invasion (EMVI) and perineural invasion (PNI). The feature distinguishing a TD from EMVI and PNI is the presence of unequivocal tumour extension from the vessel or nerve into the surrounding fat or fibroconnective tissue. When tumour outgrowth from EMVI and/or PNI is present, the diagnosis of TDs and EMVI/PNI should be denoted separately in the report. If the tumour involves an identifiable lymph node, it is considered as lymph node metastasis and not as TDs even if the tumour extends into the perinodal fat.*

Definitions

CORE elements

CORE elements are those which are essential for the clinical management, staging or prognosis of the cancer. These elements will either have evidentiary support at Level III-2 or above (based on prognostic factors in the National Health and Medical Research Council (NHMRC) levels of evidence[1]). In rare circumstances, where level III-2 evidence is not available an element may be made a CORE element where there is unanimous agreement by the Dataset Authoring Committee (DAC). An appropriate staging system, e.g., Pathological TNM staging, would normally be included as a CORE element.

Molecular and immunohistochemical testing is a growing feature of cancer reporting. However, in many parts of the world this type of testing is limited by the available resources. In order to encourage the global adoption of ancillary tests for patient benefit, International Collaboration on Cancer Reporting (ICCR) includes the most relevant ancillary testing in ICCR Datasets as CORE elements, especially when they are necessary for the diagnosis. Where the technical capability does not yet exist, laboratories may consider temporarily using these data elements as NON-CORE items.

The summation of all CORE elements is considered to be the minimum reporting standard for a specific cancer.

NON-CORE elements

NON-CORE elements are those which are unanimously agreed should be included in the dataset but are not supported by level III-2 evidence. These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.

Key information other than that which is essential for clinical management, staging or prognosis of the cancer such as macroscopic observations and interpretation, which are fundamental to the histological diagnosis and conclusion e.g., macroscopic tumour details, may be included as either CORE or NON-CORE elements by consensus of DAC.

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Scope

The dataset has been developed for the pathological reporting of carcinomas and mucinous neoplasms of the appendix. It includes specimens designated appendectomy with or without segmental resection. Biopsy specimens are excluded. Neuroendocrine carcinomas (NEC) and mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN) are included. Well differentiated neuroendocrine tumours and non-epithelial malignancies are not included.

NOTE: PRIOR TO PUBLICATION THE DATASET CONTENT WILL BE UPDATED TO REFLECT WHO 6TH EDITION.

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Note 1 – Clinical information (Core and Non-core)

Clinical information can be provided by the clinician on the pathology request form. Pathologists can search for additional information from previous pathology reports, if any, or accessible medical records. Whether the patient presented with abdominal pain/appendicitis or with features clinically concerning for an underlying mass should be recorded. It is worth noting that many appendiceal tumours can present with symptoms of appendicitis, particularly appendiceal mucinous neoplasms and goblet cell adenocarcinoma, although a significant number present with features concerning for neoplasm.[2-6] In fact, presentation as appendicitis correlates with better prognosis in patients with goblet cell adenocarcinoma.[7,8] The mimics of mucinous neoplasm such as interval appendectomy specimens, post-inflammatory mucosal hyperplasia and appendiceal diverticular disease most often present with features of appendicitis or treated appendicitis, and only rarely does the surgeon raise concern for neoplasia, whereas appendiceal mucinous neoplasms often present with a clinical concern for underlying tumour.[9-12]

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Note 2 – Operative procedure (Core)

The operative procedure pertains to the appendix primary tumour; additional specimens that are submitted, such as spleen or peritoneal sampling/debulking in patients with disseminated disease, are separately recorded and described according to their nature. The type of specimen in appendiceal neoplasia affects the likelihood of an involved surgical resection margin.[13,14] Furthermore, the nature of the operative procedure has been shown in several studies to have prognostic importance in mucinous and non-mucinous adenocarcinomas of the appendix, with right hemicolectomy being superior to appendectomy,[14-20] although some studies showed no significant difference in survival in patients with high stage tumours or well differentiated tumours.[20,21] Right hemicolectomy has also shown to improve survival compared to appendectomy in Stage II goblet cell adenocarcinoma.[13,14] However, one study showed no survival advantage to right hemicolectomy in goblet cell adenocarcinoma.[22]

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Note 3 – Tumour site (Non-core)

Location of the tumour along the appendix may affect the clinical presentation; for example, an early paper on appendiceal adenocarcinoma described tumours at the base of the appendix presenting with symptoms of appendicitis.[23] However, in a review of published cases before 1956, another group of authors found no correlation between tumour location and the co-existence of acute appendicitis.[24] Tumours that involve the base may be more likely to involve the margin in appendectomy specimens than tumours that involve the distal half of the appendix. However, location of the tumour along the appendix has not been shown to affect prognosis, independent of the stage of the tumour.[25,26]

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Note 4 – Macroscopic appearance (Non-core)

The macroscopic appearance of the tumour should be recorded, particularly gross perforation and the presence or absence of mucinous tumour on the appendiceal serosal surface. In patients with appendiceal mucinous neoplasms, rupture of the appendix confers a risk of developing pseudomyxoma peritonei.[27] Other macroscopic features such as cystic change, solid areas, polypoid lesions, infiltrative type lesions, or thickening of the appendix may be noted. In some cases, the tumour may not be grossly evident.

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Note 5 – Tumour dimensions (Core and Non-core)

Recording tumour size, based on a combination of macroscopic and microscopic assessment, allows correlation with pre-operative imaging and surgical assessments. Assessment of tumour dimensions should, if possible, exclude any inflammatory component. No prognostic significance has been attached to tumour size for appendiceal cancer and size does not directly influence tumour staging.[4] In one study of non-mucinous adenocarcinomas, tumour size less than 20 millimetres (mm) had a statistically significantly lower risk of having lymph node metastases on univariate analysis but not on multivariate analysis.[15] Goblet cell adenocarcinoma is notorious for being grossly inapparent and difficult to measure; not surprisingly, studies show no correlation between size and prognosis in patients with goblet cell adenocarcinoma.[2,3]

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Note 6 – Block identification key (Non-core)

The origin/designation of all tissue blocks should be recorded. This information should ideally be documented in the final pathology report and is particularly important when further internal or external review arises. The reviewer needs to have unequivocal description of the origin of each block in order to provide an informed specialist opinion. If this information is not included in the final pathology report, it should be available on the laboratory computer system and relayed to the reviewing pathologist. It is highly encouraged to have a digital image (photograph) of the specimen and record of the key of the tumour blocks.

Recording the origin/designation of tissue blocks also facilitates retrieval of blocks for further immunohistochemical or molecular analysis, research studies, or clinical trials.

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Note 7 – Histological tumour type (Core)

Histologic type is a major determinant of tumour biology, prognosis, and patient management.[28] All carcinomas and mucinous neoplasms of the appendix should be classified based on the 5th edition World Health Organization (WHO) Classification of Digestive System Tumours, 2019.[28] Appendiceal mucinous neoplasms generally do not metastasise to lymph nodes, and therefore right hemicolectomy is generally not required. However, they frequently metastasise to the peritoneal cavity where peritoneum-directed therapy becomes relevant. Among invasive adenocarcinomas, mucinous adenocarcinoma generally has a better prognosis than non-mucinous adenocarcinoma.[6,29] In some studies, this difference is only among Stage IV

tumours.[30,31] A study of patients with appendiceal tumours and peritoneal metastases found that histologic tumour type was associated with prognosis on multivariable analysis, with non-mucinous adenocarcinoma having a worse prognosis than appendiceal mucinous neoplasms.[32] Among non-mucinous adenocarcinomas, signet ring cell carcinomas often present at higher tumour stage and are associated with a worse outcome than non-signet ring cell carcinomas.[30,33] Conversely, non-signet ring cell morphology is a lower risk for lymph node metastases than signet ring cell morphology.[15]

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Note 8 – Histological tumour grade (Core)

Tumour grade has been shown across many studies to affect the likelihood of lymph node involvement as well as prognosis. In one study, univariate analysis showed that tumour grade is significantly associated with overall and disease specific survival in primary appendiceal adenocarcinoma and goblet cell adenocarcinoma.[6] Among appendiceal non-mucinous adenocarcinomas, poor and undifferentiated carcinomas conferred high risk for lymph node metastases compared to well or moderately differentiated tumours and showed worse disease specific survival.[15,34] In other studies of mucinous and non-mucinous adenocarcinoma, tumour grade correlates with overall survival and disease specific survival,[16] including among Stage IV tumours.[30] In goblet cell adenocarcinoma, tumour grade correlates with prognosis, regardless of the classification system.[8,35-38] In patients with goblet cell adenocarcinoma, grade may be an important prognostic factor in terms of survival, but the data are limited.[39]

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Note 9 – Appendix perforation at or away from tumour (Non-core)

Perforation of the appendix at, or away from, tumour incorporates both macroscopic and microscopic examination. Perforation of an appendiceal adenocarcinoma at the site of the tumour has been shown to be a poor prognostic finding, compared to perforation distal to the tumour.[25] In patients with appendiceal cancer and appendicitis, rupture of the appendix (presumably due to appendicitis rather than tumour) did not affect survival.[18] In appendiceal mucinous neoplasms, perforation away from the tumour has not been specifically studied; perforation of the appendix confers risk of pseudomyxoma peritonei by allowing mucin and neoplastic cells to escape,[27] and that risk can be further estimated by the identification of mucin and/or neoplastic mucinous epithelial cells on the appendiceal serosa or beyond.[40-42] In goblet cell adenocarcinoma, one study found perforation of the appendix to be prognostically significant on univariate but not multivariate analysis.[36]

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Note 10 – Extent of invasion (Core)

Appendiceal mucinous neoplasms that are confined to the appendix (low grade mucinous neoplasm (LAMN)/high grade appendiceal mucinous neoplasm (HAMN)), with an intact appendiceal serosa, have been shown across several studies to be cured by appendectomy in the vast majority of cases.[42-44] However, exceptional cases of peritoneal recurrence have been reported in patients with tumours apparently confined to the appendix (i.e., neither mucin nor neoplastic cells outside the appendix).[45] In cases with perforation of the appendiceal serosa, the presence of acellular mucin on the serosa is associated with a low risk of

recurrence, whereas neoplastic cells in mucin on the serosa confers high risk of recurrence as pseudomyxoma peritonei.[4,40,42] Therefore, it is imperative that pathologists report the presence of mucin on the appendiceal serosa, and distinguish between acellular mucin and cellular mucin. Both scenarios are designated as pT4a, and therefore pathologic T stage is insufficient to convey this important information. When an appendix contains a non-mucinous tumour and shows distal perforation due to appendicitis or obstruction, it may be appropriate to stage the tumour based on its extent of invasion separately from the serosal mucin, if that serosal mucin can be attributed to obstruction. In appendiceal mucinous tumours (LAMN/HAMN), it may be impossible to determine if neoplastic cells escaped into the peritoneum whenever there is serosal mucin, and it is appropriate to stage the tumour based on the spread of mucin as pT4a.

Among adenocarcinomas, one study of non-mucinous adenocarcinoma showed that T stage (T1 versus >T1) was independently associated with the risk of lymph node metastasis.[15] T stage also correlates with overall survival, progression free survival, and disease specific survival in appendiceal adenocarcinoma.[6,16,34] Similarly, T stage has been shown to correlate with the likelihood of lymph node metastasis in goblet cell adenocarcinoma[13] and to correlate with progression free survival and overall survival.[6,22] In other studies, T stage did not correlate with prognosis; patients with Stage IV disease had a worse prognosis than patients with Stage I to III.[7,8]

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Note 11 – Lymphovascular invasion (Core)

Lymphovascular invasion is not an expected finding in appendiceal mucinous neoplasms, but its presence has been shown to be an adverse prognostic finding in appendiceal adenocarcinoma.[20,29] Furthermore, the presence of lymphovascular invasion predicts lymph node involvement in appendiceal mucinous and non-mucinous adenocarcinoma, including goblet cell adenocarcinoma.[2,15,46,47] Some studies showed lymphovascular invasion was significant on univariate analysis, although it was no longer significant on multivariate analysis.[8,36,48] In one study of patients with Stage I to III disease, lymphovascular invasion did not predict recurrence.[7]

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Note 12 – Perineural invasion (Core)

Perineural invasion is highly unlikely in appendiceal mucinous neoplasms. In contrast, it is commonly present in goblet cell adenocarcinomas. In goblet cell adenocarcinoma, perineural invasion has been shown to be a negative prognostic factor, at least on univariate analysis.[2,8,48] However, in a study on goblet cell adenocarcinomas, perineural invasion did not predict recurrence in patients with Stage I-III disease.[7] Another large series of goblet cell adenocarcinomas found no prognostic difference in patients with and without perineural invasion.[36]

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Note 13 – Margin status (Core)

The margins of an appendectomy specimen include the proximal transection margin and, when it can be identified, the mesenteric margin; however, the status of the proximal transection margin is usually the margin of interest. Acellular mucin at the proximal margin should be reported but not classified as a positive margin. Most studies that have examined the outcome of appendiceal mucinous tumours with proximal margin involvement have concluded that tumours that involve the appendiceal margin will not recur and additional resection specimens do not show residual tumour.[4,41,44,49-51] One study found that a positive margin was associated with increased frequency of disease recurrence or death, although confounding factors such as perforation were not considered.[52] In the setting of either invasive adenocarcinoma or goblet cell adenocarcinoma, involvement of the proximal appendiceal margin warrants consideration of additional resection.

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Note 14 – Lymph node status (Core)

The likelihood of lymph node involvement differs based on tumour type, stage, and tumour grade. Appendiceal mucinous neoplasms are unlikely to show lymph node involvement.[32,53] Well-differentiated mucinous adenocarcinoma has a low likelihood of lymph node involvement whereas high-grade mucinous adenocarcinoma and signet ring cell carcinomas have higher likelihood of lymph node involvement.[53-55] Tumour T stage also correlates with the likelihood of nodal metastases.[53,55] This understanding may inform the extent of surgical resection as well as the number of lymph nodes considered adequate for appropriate pathologist stage. Finding fewer than 10 lymph nodes in a right colectomy specimen has been reported to correlate with reduced overall survival for patients with appendiceal adenocarcinoma, presumably due to missed occult metastases,[54] whereas finding fewer than 12 was associated with worse prognosis in a study by Xie et al (2016).[56] In appendiceal adenocarcinoma, including mucinous adenocarcinoma, signet ring cell carcinoma, and goblet cell adenocarcinoma, lymph node involvement has been shown to be an adverse prognostic finding.[13,20,29,34,53,55]

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Note 15 – Tumour deposits (Core)

Tumour deposits have not been studied in appendiceal adenocarcinoma, but they should be reported given their established significance in colorectal adenocarcinoma. Tumour deposits are less relevant in appendiceal mucinous neoplasms or mucinous adenocarcinomas, since the distinction between a tumour deposit and mucinous carcinoma peritonei is ambiguous. In those settings, discontinuous mucinous tumour deposits should be interpreted as peritoneal dissemination of a mucinous tumour and infiltration of the underlying connective tissue.

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Note 16 – Additional findings (Non-core)

The presence of other pathologic findings in the appendix may be recorded. Additional mucosal lesions such as sessile serrated lesion, conventional colorectal type adenoma, or mucinous adenoma may be included under 'other'. Since it is difficult in the appendix to distinguish sessile serrated lesion from mucosal hyperplasia secondary to obstructing tumours, and given the small size of the appendix, it is unusual to have a benign polyp separate from the invasive tumour and its precursor. In cases of goblet cell adenocarcinoma, in which a conventional precursor is generally not present, overlying mucosal benign polyps may be noted, although it is challenging to discriminate mucosal obstructive changes from sessile serrated lesions or even low-grade appendiceal mucinous neoplasms.

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Note 17 – Ancillary studies (Core and Non-core)

Mismatch repair (MMR) immunohistochemistry and/or microsatellite instability (MSI) testing should be performed on all invasive carcinomas, although MMR deficiency in appendiceal adenocarcinoma is rare.[57-59] RAS, GNAS, and TP53 are frequently mutated in appendiceal adenocarcinoma and have shown prognostic significance in some studies.[60] In patients with peritoneal metastases, molecular studies for RAS, GNAS, and TP53 may be useful for patient prognostication and management, and should be considered.[61,62]

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Note 18 – Peritoneal metastases (Core)

Peritoneal metastasis is a common mode of spread of appendiceal malignancies. The presence or absence of mucin with or without tumour cells is essential to appropriately manage patients with these malignancies. The presence of acellular mucin in the peritoneal cavity has been shown to carry a lower risk for progressive disease compared to cellular mucinous tumour deposits, and to have a better prognosis than cellular mucin deposits.[32,63-65] In contrast, the presence of mucinous epithelial cells within peritoneal mucin is a progressive disease, and the peritoneal tumour grade has prognostic value in that setting.[63,66-70] In cases in which the peritoneal tumour grade and the primary tumour grade are discordant, both tumour grades should be recorded; in this setting, the grade of the peritoneal tumour correlates with prognosis.[71,72]

Patients with non-mucinous adenocarcinoma or goblet cell adenocarcinoma who develop peritoneal metastases have a relatively poor prognosis.[39] One study showed no difference in overall survival in patients with peritoneal metastases of non-mucinous adenocarcinoma and goblet cell adenocarcinoma.[32]

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Note 19 – Non-peritoneal metastases (Core and Non-core)

Data regarding the significance of non-peritoneal metastases is limited, but the consensus of the DAC was that reporting the presence of non-peritoneal metastases should be a core element. The reporting of the sites where present is non-core.

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Note 20 – Pathological staging (Core)

The pathologic stage should be assessed according to the 9th edition of the Union for International Cancer Control (UICC)/8th edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual as it provides critical information for patient management and prognosis.[73,74] In SEER data, Stage IV appendiceal adenocarcinoma is associated with worse prognosis.[75] In goblet cell adenocarcinoma, distant spread is associated with a worse prognosis compared to local or regional disease.[22]

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