Pathology Reporting of Colorectal Local Excision Specimens: Recommendations from the International Collaboration on Cancer Reporting (ICCR)

Modern medicine needs clear and adequate communication between different medical specialties. After colonoscopy, patients are risk stratified based on the number, size, and histologic features of resected polyps. Moreover, pathology reporting is the main source of data used for national bowel cancer screening programs, epidemiologic audits, and translational research.[1] It is therefore important that a structured approach to pathology reporting of colorectal polyps is adopted worldwide to capture all necessary information for patient management and to allow the comparison of data between countries.

Structured reporting protocols have been independently developed by multiple organizations around the world to provide high quality and uniform pathology reports.[2–4] In 2011, the International Collaboration on Cancer Reporting (ICCR) was established to coordinate the production of evidence-based pathology reporting datasets developed by a panel of internationally recognized expert pathologists.[5] After the publication of the 5th Edition of the World Health Organization (WHO) Classification of Tumours of the Digestive System in 2019,[6] the ICCR initiated the development of datasets for the structured reporting of pathology data for tumors of the digestive system. This report provides a summary of the ICCR recommendations for the pathology reporting of polyps and early carcinomas in colorectal local excision specimens.

Methods

This dataset has been developed for the reporting of colorectal polypectomies, endoscopic mucosal resections, endoscopic submucosal dissections, endoscopic full thickness resections, transanal minimally invasive surgery specimens, and transanal endoscopic microsurgery specimens. A separate dataset for the reporting of surgical resection specimens for colorectal cancer (CRC) is available at http://www.iccr-cancer.org/datasets/published-datasets/digestive-tract/colorectal.

The process of dataset development by the ICCR is overseen by a Dataset Steering Committee (DSC). The DSC appointed a "Series Champion" (I.D.N.) to coordinate the development of all datasets for the digestive system, and a Chair (C.R.) to oversee production of the colorectal excisional biopsy dataset. An international expert panel was established, including 8 gastrointestinal pathologists, 2 gastroenterologists, and a Project Manager (F.W.), forming the Dataset Authoring Committee (DAC).

The final document includes a set of elements and value lists (responses), followed by an explanatory commentary section (see Supplementary file). Based on literature review and collected evidence, the expert panel categorized each element as core or noncore. Core elements were those considered to be essential in the pathology report and essential for diagnosis, risk stratification, and patient management. In general, core elements had evidentiary support at Level III-2 or above, based on prognostic factors in the National Health and Medical Research Council levels of evidence document.[7] Elements that did not meet these criteria were deemed noncore and considered to be clinically important and appropriate for good practice but not yet validated or used regularly for patient management at the time of dataset development.

The working draft was first developed by the Project Manager after reviewing all published datasets pertaining to colorectal local excision specimens. This draft was edited by the Chair and circulated to the DAC for discussion during a series of teleconferences. After review by the Chair, the draft was recirculated to the DAC for further review and approval. The draft was uploaded to the ICCR website for a period of 2 months for public comment. The documents were reviewed after compilation of all feedback, approved by the DAC, and finally ratified by the DSC. The reporting guide is available at http://www.iccr-cancer.org/datasets/published-datasets/digestive-tract/colorectal-polypectomy.

Recommendations

The list of core and noncore elements is provided in Table 1.[8] Q3

A. Clinical information, endoscopic size, and classification of polyp should be communicated. Q4

Awareness of relevant gastrointestinal disorders, such as a genetic syndrome or inflammatory bowel disease, may influence histologic interpretation.

Polyp size measured during endoscopy is essential for application of surveillance guidelines.

Colorectal polyps can be evaluated on the basis of their endoscopic morphology using the Paris classification or the lateral spreading tumor classification.[9] Direct optical diagnosis of colorectal lesions, using both high-definition white-light and image-enhanced endoscopic techniques, is becoming increasingly used. A discrepancy between optical diagnosis and first histologic impression should prompt the pathologist to order deeper sections.

B. The specimen site, the type of local excision procedure, and the number of polyp(s) submitted in each pathology container must be provided.

Determination of specimen site is based on clinical information provided on the container label, the pathology request form, or the endoscopy report. Any discrepancy should be discussed with the referring clinician.

Knowledge of the type of procedure may affect specimen handling and pathologic reporting, including the assessment of resection margins. The most commonly used endoscopic resection technique is snare polypectomy, suitable for radical removal of most colorectal polyps.[8] Additional noncore information includes the use of submucosal injection before polypectomy (endoscopic mucosal

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Table 1. Core and Noncore Elements for the Pathology Reporting of Colorectal Local Excision Specimens

Core elements	Noncore elements
•Endoscopic procedure[98]	•Clinical information
•Polyp number	•Use of submucosal injection, electrocautery and type of resection (piecemeal or en bloc)
•Specimen site	•Endoscopic polyp size and classification
•Maximum dimension of intact specimen/polyp	•Aggregated dimensions for fragmented polyps
•Histologic type of polyp	•Maximum dimension of largest piece for fragmented polyps
For specimens with carcinoma only	
•Histologic tumor type	•Precursor polyp/lesion
•Histologic grade of adenocarcinoma	•Maximum width of invasion
•Extent of invasion	•Tumor budding
•Maximum depth of invasion	•Ancillary studies: Mismatch repair (MMR) immunohistochemistry/microsatellite instability (MSI) testing; *BRAF* V600E mutation testing; *MLH1* promoter methylation testing
•Lymphatic and venous invasion	
•Perineural invasion	
•Margin status	
For neuroendocrine neoplasms only	
•Mitotic count and/or Ki-67 proliferation index	
•Neuroendocrine markers for neuroendocrine carcinoma	

resections), the use of electrocautery, and the type of resection (piecemeal or en bloc). En bloc resection allows adequate evaluation of the resection margins in the horizontal as well as in the vertical plane, whereas piecemeal resection precludes a reliable histologic assessment of completeness of excision. Other polypectomy procedures include endoscopic submucosal dissections, transanal endoscopic microsurgery, transanal minimally invasive surgery, and endoscopic full-thickness resections.

Preferably, the retrieved tissue pieces from multiple polypectomy procedures should be placed in separate containers, 1 for each lesion, so that each specimen container will include only 1 polyp for histologic examination. When multiple polyps or an unknown number of polyps are received in a single container, this precludes accurate assessment of the number of polyps received (the number of tissue fragments does not necessarily reflect the number of polyps received after piecemeal resection), histologic classification, and the number of malignant polyps, if carcinoma is identified in more than 1 tissue fragment. If more than 1 polyp is placed in a single container, the number of polyps must be clearly indicated. In this scenario, the pathologist may only be able to provide information on 1 or more polyp histologic types identified in a given specimen, without reliable information on the number of polyps associated with a particular histologic type.

C. The pathologic measurement of large en bloc resection specimens is recorded as part of routine macroscopic examination.

If possible, a photograph should be taken and attached to the pathology report. The maximum diameter of macroscopically visible lesions is recorded. Discordance with endoscopic size may exist and should be discussed with the endoscopist. The measurement of pedunculated polyps does not include the stalk, the measurement of which should be provided separately. For piecemeal resection, a measurement of the aggregated tissue fragments and of the largest piece is recorded as a noncore element. The endoscopic size is used to record polyp size.

D. The histologic classification of polyps follows the latest WHO nomenclature and definition.

Conventional adenomas and serrated polyps comprise the majority of polyps. Conventional adenomas are by definition dysplastic and are subtyped based on the proportion of villous component into tubular, tubulovillous, or villous adenoma. High-grade dysplastic adenomas are characterized by marked architectural changes visible at low magnification, associated with severe cytologic atypia. After the update by the WHO in 2019,[6] the sessile serrated adenoma/polyp is now called sessile serrated lesion. If dysplasia is present, it is reported as sessile serrated lesion with dysplasia. The dysplasia is not graded, because biologically advanced lesions, often with loss of MLH1 expression, may Q5 only show mild morphologic changes.[10] Traditional serrated adenoma is a low-grade dysplastic lesion with ectopic crypt formations, slit-like serration, eosinophilic cytoplasm, and bland palisaded nuclei. Superimposed high-grade dysplasia can occur and should be reported.

Conventional adenomas or serrated polyps may have histologic features that are suspicious but not definite for carcinoma. This can be due to a limited amount of tissue or cautery artefact impeding histologic examination. A common diagnostic challenge is epithelial misplacement of adenomatous glands in the submucosa (also called pseudoinvasion) that can mimic invasive carcinoma. The differentiation from carcinoma may be difficult and sometimes impossible. These cases should have a comment explaining the

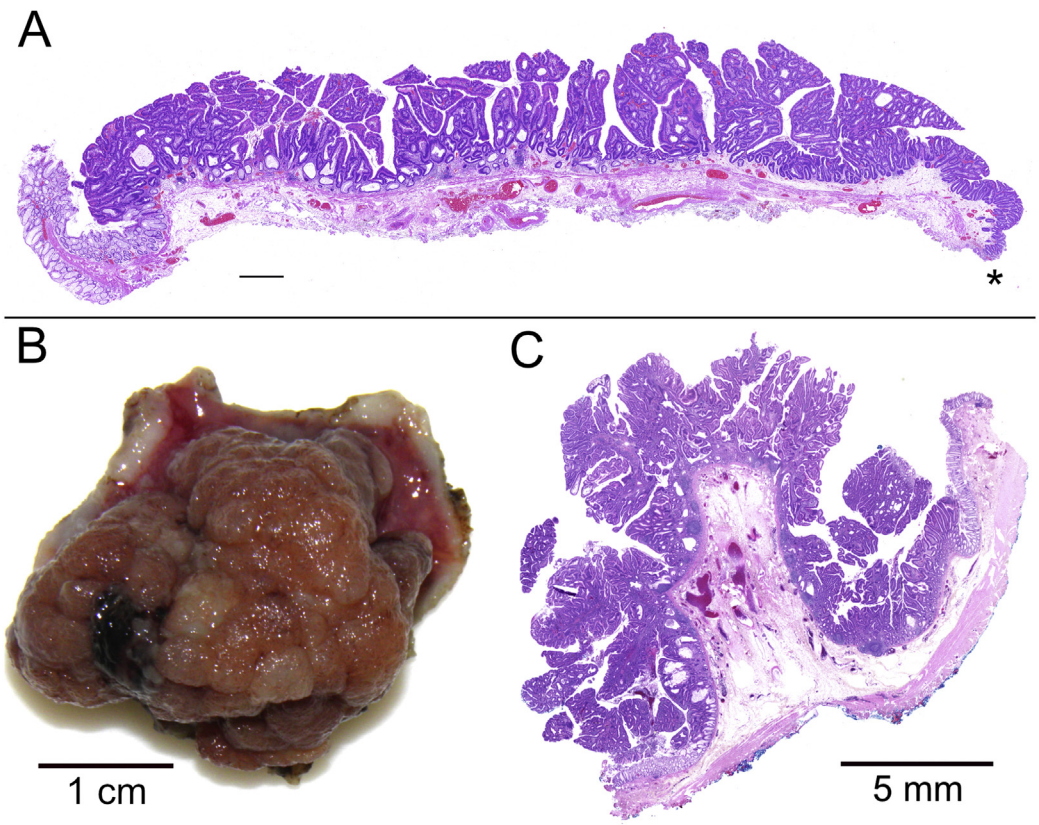

Figure 1. (*A*) Endoscopic submucosal dissection specimen of a large traditional serrated adenoma of the rectum involving the lateral margin (*) (hematoxylin and eosin-stained section, scale bar = 1 mm). (*B and C*) Transanal minimally invasive surgery specimen of a large rectal tubulovillous adenoma with high-grade dysplasia and clear margins.

diagnostic difficulties and be discussed in a multidisciplinary meeting. Consultation with other pathologists or an expert panel for consensus opinion is recommended.

E. For specimens with carcinoma, the latest WHO classification for histologic types and grading is used.

Most carcinomas in malignant polyps and en bloc resection specimens are adenocarcinomas "not otherwise specified." Other carcinoma subtypes include mucinous adenocarcinoma, signet-ring cell carcinoma, medullary carcinoma, serrated adenocarcinoma, micropapillary adenocarcinoma, and adenoma-like adenocarcinoma. If identified, the precursor lesion from which the carcinoma arose can be recorded as a noncore element.

Grading only applies to adenocarcinoma not otherwise specified and mucinous adenocarcinoma. A 2-tiered system dividing adenocarcinoma into low-grade (well and moderately differentiated) and high-grade (poorly differentiated and undifferentiated) categories is recommended because it is more prognostically relevant than a 3- or 4-tiered system.[11] Grading is based on the degree of gland formation in the least differentiated component of the tumor, not on the predominant pattern in the overall volume of tumor.[6] Tumor buds and poorly differentiated clusters, mostly found at the invasive front of the carcinoma, are not included in the histologic grading.

A note on the clinical behavior of nongraded carcinoma subtypes can be added: high-grade for signet-ring cell, micropapillary, and serrated adenocarcinoma; low-grade for medullary carcinoma and adenoma-like adenocarcinoma. Tumor mismatch repair (MMR) status is likely to affect the clinical behavior of some histologic types, including mucinous adenocarcinoma. However, histologic grading is superior to MMR status for prognostication of mucinous adenocarcinomas.[12]

F. Neuroendocrine neoplasms are classified according to the latest WHO classification.

Neuroendocrine neoplasms are classified into neuroendocrine tumors, small cell, and large cell neuroendocrine carcinomas. The proliferation activity of all neuroendocrine neoplasms must be assessed using the mitotic count (per 2 mm^2) and/or the Ki-67 proliferation index.[13] If a pure or mixed neuroendocrine carcinomas is suspected on morphology, immunohistochemistry is required to confirm neuroendocrine differentiation, usually applying synaptophysin and chromogranin A.

G. For specimens with carcinoma, the extent of invasion into the bowel wall (pT category) and the depth of invasion in millimeters are recorded.

Criteria of the American Joint Committee on Cancer[14] and the Union for International Cancer Control[15] are applied with the exception of pT in situ. Given the negligible metastatic

potential of colorectal neoplasms with invasion confined to the lamina propria, including those with a poorly differentiated and signet ring cell morphology,[16] these should be classified under the category "noninvasive neoplasia/high-grade dysplasia." A comment in the pathology report should address the findings, and discussion in a multidisciplinary meeting is recommended.

The depth of invasion is reported as the maximum thickness of invasive carcinoma measured in millimeters from the deepest part of the tumor to the lower aspect of the muscularis mucosae or the surface of the lesion if the muscularis mucosa is obscured (ulcerated lesion, marked disruption of the muscularis mucosa). This requires well-oriented sections perpendicular to the surface. A cutoff of 1 mm is used in most prediction models with invasive carcinomas measuring ≥1 mm associated with a significant increased risk of lymph node metastasis.[17] The maximum width of the invasive front is reported as a noncore element.[17]

For pedunculated malignant polyps, the junction between the adenoma and the stalk (level 2 Haggitt's line) is sometimes used as the upper limit of measurement. Carcinomas limited to the head of the polyp, above the baseline ("head invasion"), carry 0% risk of lymph node metastasis if no lymphovascular invasion is present.[18]

H. For specimens with carcinoma, lymphovascular invasion and perineural invasion are reported.

Lymphovascular invasion is divided into 2 groups according to the type of vessel involved: small vessel for lymphatics, capillaries or postcapillary venules, and large vessel for venous invasion. Small vessel invasion is associated with lymph node metastatic disease and is an independent indicator of adverse outcome.[19] In malignant polyps, lymphatic invasion often prompts surgery. Identification of venous invasion may require multiple levels in tissue blocks and the application of elastic stain. Intramural venous invasion is an adverse prognostic factor, but the evidence is much weaker than for extramural venous invasion.[20]

Perineural invasion is extremely rare in malignant polyps but can be identified in full-thickness resection specimens and is associated with poor outcome, particularly in stage II disease.[21]

I. For specimens with carcinoma, the reporting of tumor budding is recommended.

There is increasing evidence that tumor budding is an independent adverse prognostic factor in CRC. It is considered a noncore element, pending the emergence of further evidence of reproducibility of assessment and clinical significance. If reported, tumor budding is scored using a 3-tiered system: low (0–4 buds), intermediate (5–9 buds), and high (≥10 buds) scores.[22]

J. The histologic assessment of margin status is reported for en bloc resection specimens.

An involved (positive) deep resection margin is a predictor for adverse outcome, specifically, local recurrence rather than lymph node or distal metastasis if no other adverse histologic features are present. Pathologists must report the deep margin as either involved if carcinoma cells are present directly at the margin (or outer aspect of the diathermy zone) or record the clearance distance to the nearest 0.1 mm between the deep margin and the closest invasive carcinoma. Most studies have considered a clearance of <1 mm as a positive deep margin, without providing more precise measurement.[23]

Lateral margin is less critical for patient management and a noncore element. A positive lateral margin does not influence local recurrence rate. If possible, the component of the malignant polyp present at the margin (carcinoma or benign precursor polyp) should be specified.

K. For specimens with carcinoma, MMR testing is recommended.

Testing carcinoma for MMR protein deficiency is performed for Lynch syndrome screening and provides therapeutic decision information for patient management. *BRAF* mutation testing and *MLH1* promoter methylation analysis are performed to help distinguish sporadic MLH1-deficient CRCs from Lynch syndrome-associated tumors. Among several strategies, testing all CRC patients or those aged <70 years have been recommended by several international jurisdictions.[24] MMR testing is currently considered as noncore.

Conclusion

Pathology reporting is evolving from a narrative report to a structured report with checklists of essential parameters critical for patient management. For cancer resection specimens, the implementation of synoptic reporting resulted in higher rates of completeness and overall improved quality of pathology reports.[25] In these recommendations from the ICCR, we have discussed a list of essential (core) items that should be part of a structured approach to the pathology reporting colorectal local excision specimens. Standardization of reporting incorporating key endoscopic features and histologic findings will facilitate application of surveillance colonoscopy guidelines and patient management. It is hoped that harmonization of the reporting of colorectal polyps and early carcinomas by pathologists worldwide will facilitate international benchmarking, data sharing and multi-institutional collaborative studies.

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Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2021.04.066.

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C.R. and I.D.N. supervised the study. C.R. and F.W. acquired data and drafted the manuscript. All authors, including additional authors from the Dataset Authoring Committee, contributed to analysis and interpretation of data and to critical revision of the manuscript for important intellectual content.

Conflicts of interest

The authors disclose no conflicts.

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