Endoscopic Resection of the Stomach
Histopathology Reporting Guide

<table>
<thead>
<tr>
<th>Family/Last name</th>
<th>Date of birth</th>
<th>DD – MM – YYYY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Given name(s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient identifiers</td>
<td></td>
<td>DD – MM – YYYY</td>
</tr>
<tr>
<td>Accession/Laboratory number</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

- Indicates multi-select values
- Indicates single select values

### SCOPE OF THIS DATASET

#### CLINICAL INFORMATION (select all that apply) *(Note 1)*

- Information not provided
- Relevant biopsy results, specify
- Endoscopic location of the tumour, specify
- Clinical staging, specify level of involvement, distant metastases
- Previous history of gastric cancer, specify
- Previous endoscopic resection (ER), specify
- Previous partial gastrectomy procedure, specify
- History of chronic gastritis, specify
- Other, specify

#### ENDOSCOPIC PROCEDURE *(Note 2)*

- Not specified
- Endoscopic mucosal resection (EMR)
- Endoscopic submucosal dissection (ESD)
- Other, specify

#### SPECIMEN DIMENSIONS *(Note 3)*

- Mucosal area: \( \text{mm} \times \text{mm} \)
- Thickness: \( \text{mm} \)
- Cannot be assessed, specify

#### TUMOUR FOCALITY* *(Note 4)*

- Unifocal
- Multifocal, specify number of tumours in specimen
- Cannot be assessed, specify

* If multiple primary tumours are present, separate datasets should be used to record this and all following elements for each primary tumour.
TUMOUR SITE (select all that apply) (Note 5)
- Not specified
- Cannot be assessed
- Region
  - Upper third
  - Middle third
  - Distal third
- Curvature
  - Greater
  - Lesser
- Wall
  - Anterior
  - Posterior
- Other, specify

TUMOUR DIMENSIONS (Note 6)
Maximum tumour dimension

Additional dimensions

Cannot be assessed, specify

MACROSCOPIC TUMOUR TYPE (Note 7)
(Applicable to early gastric carcinomas)
- Cannot be assessed
- Protruding (type 0-I)
- Superficial (type 0-II)
- Excavated (type 0-III)
- Other, specify

HISTOLOGICAL TUMOUR TYPE (Note 8)
(Value list from the World Health Organization Classification of Tumours of the Gastrointestinal Tract (2019))
- Cannot be assessed
- Tubular adenocarcinoma
- Papillary adenocarcinoma
- Mucinous adenocarcinoma
- Poorly cohesive carcinoma, including signet-ring cell carcinoma and other subtypes
- Mixed adenocarcinoma
- Other histological type/subtype, specify

Lauren classification
(Applicable to adenocarcinomas)
- Intestinal
- Diffuse
- Mixed
- Indeterminate

HISTOLOGICAL TUMOUR GRADE (Note 9)
(Applicable for tubular and papillary adenocarcinomas)
- Not applicable
- GX: Cannot be assessed
- G1: Well differentiated
- G2: Moderately differentiated
- G3: Poorly differentiated, undifferentiated
- Other, specify

TISSUE LAYERS PRESENT (select all that apply) (Note 10)
- Cannot be determined
- Lamina propria
- Muscularis mucosae
- Submucosa
- Muscularis propria

EXTENT OF INVASION (Note 11)
- Cannot be assessed
- No evidence of primary tumour
- Carcinoma in situ (intraepithelial tumour without invasion of the lamina propria, high grade dysplasia)
- Invasion into the lamina propria
- Invasion into the muscularis mucosae
- Invasion into the submucosa, specify depth of invasion
- Invasion into the muscularis propria

LYMPHOVASCULAR INVASION (Note 12)
- Not identified
- Present

MARGIN STATUS (select all that apply) (Note 13)
(Applicable for gastric carcinomas)
- Invasive carcinoma
  - Mucosal margin
    - Cannot be assessed
    - Not involved by invasive carcinoma
    - Distance of tumour from closest margin
    - Involved by invasive carcinoma
  - Deep margin
    - Cannot be assessed
    - Not involved by invasive carcinoma
    - Distance of tumour from closest margin
    - Involved by invasive carcinoma
- High grade dysplasia
  - Cannot be assessed
  - Not involved by high grade dysplasia
  - Distance of high grade dysplasia from closest margin
  - Involved by high grade dysplasia
- Low grade dysplasia
  - Cannot be assessed
  - Not involved by low grade dysplasia
  - Involved by low grade dysplasia

TUMOUR SITE
- Not specified
- Cannot be assessed
- Region
  - Upper third
  - Middle third
  - Distal third
- Curvature
  - Greater
  - Lesser
- Wall
  - Anterior
  - Posterior
- Other, specify

TUMOUR DIMENSIONS
Maximum tumour dimension

Additional dimensions

Cannot be assessed, specify

MACROSCOPIC TUMOUR TYPE
(Applicable to early gastric carcinomas)
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- Protruding (type 0-I)
- Superficial (type 0-II)
- Excavated (type 0-III)
- Other, specify

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- Lamina propria
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(Applicable for gastric carcinomas)
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  - Mucosal margin
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    - Distance of tumour from closest margin
    - Involved by invasive carcinoma
  - Deep margin
    - Cannot be assessed
    - Not involved by invasive carcinoma
    - Distance of tumour from closest margin
    - Involved by invasive carcinoma
- High grade dysplasia
  - Cannot be assessed
  - Not involved by high grade dysplasia
  - Distance of high grade dysplasia from closest margin
  - Involved by high grade dysplasia
- Low grade dysplasia
  - Cannot be assessed
  - Not involved by low grade dysplasia
  - Involved by low grade dysplasia

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ANCILLARY STUDIES (Note 15)

For neuroendocrine neoplasms only

☐ Not applicable

☐ Neuroendocrine markers (chromogranin A, synaptophysin, other), specify test(s) performed and result(s) if available

Ki-67 proliferation index  %

☐ Not performed

☐ Performed, specify

PATHOLOGICAL STAGING (UICC TNM 8th edition) (Note 16)
(Applicable to specimens with sufficient tissue layers present)

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

☐ m - multiple primary tumours

☐ r - recurrent

Primary tumour (pT)

☐ TX Primary tumour cannot be assessed

☐ Tis Carcinoma in situ: intraepithelial tumour without invasion of the lamina propria, high grade dysplasia

☐ T1 Tumour invades lamina propria, muscularis mucosae, or submucosa

☐ T1a Tumour invades lamina propria or muscularis mucosae

☐ T1b Tumour invades submucosa

☐ T2 Tumour invades muscularis propria

Scope

The dataset has been developed for the pathology reporting of endoscopic resection (ER) specimens of the stomach. Surgically resected specimens are covered in a separate dataset.

Carcinomas involving the oesophagogastric junction (OGJ) with their epicentre >20 millimetres (mm) into the proximal stomach and cardia cancers that do not involve the OGJ are included. These criteria are set by the World Health Organization (WHO) and define the diagnosis “gastric cancer”. A dataset for oesophageal carcinomas is available for tumours not meeting these criteria.

Neuroendocrine carcinomas (NECs) and mixed neuroendocrine-non-neuroendocrine neoplasms (MiNENs) (with the exception of mixed adenoma and well differentiated neuroendocrine tumours (NETs)) are included in this dataset.

Well differentiated NETs, non-epithelial malignancies, and secondary tumours are excluded from this dataset.

Note 1 – Clinical information (Non-core)

Clinical information can be provided by the clinician in the endoscopy report or the pathology request form. Patient medical records may be another source of information if accessible.

Relevant biopsy results include the presence of carcinoma, dysplasia, intestinal metaplasia, etc. Endoscopic tumour location or information on the tumour location as reported by the clinicians are important guides to determine the tumour epicentre.

Multiple tumours may occur in the stomach and previous history of cancer or cancer treatment is relevant. In addition, a number of conditions, including previous partial gastrectomy for a benign disease and chronic atrophic gastritis, are risk factors for gastric cancer.

Note 2 – Endoscopic procedure (Core)

Endoscopic resection, including endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD), is recommended for selected early gastric carcinomas. En bloc resection may be necessary to obtain precise pathological diagnosis. EMR cannot be used to resect lesions larger than 15 mm in one piece, and piecemeal resections are potentially associated with risk of local recurrence. Therefore, for larger lesions, ESD is the better option. The European Society of Gastrointestinal Endoscopy (ESGE), American Gastroenterological Association (AGA) and Japanese Gastric Cancer Association (JGCA) recommend ESD as the treatment of choice for most gastric superficial neoplastic lesions. The standard criteria for ER are 1) T1a, 2) well/moderately differentiated, 3) ≤2 centimetres (cm), 4) non-ulcerated, and 5) no lymphovascular invasion (also see National Comprehensive Cancer Network (NCCN) guidelines for gastric cancer). Extended criteria for ESD include: 1) moderately and well differentiated intramucosal carcinoma with no ulcer, size ≥2 cm; 2) moderately and well differentiated intramucosal carcinomas, with ulcer, size ≤3 cm; 3) moderately and well differentiated...
carcinomas with early submucosal invasion (SM1) ≤500 micrometres (μm), with no ulcer and size ≤3 cm; and 4) poorly differentiated intramucosal carcinoma ≤2 cm, with no ulcer. Reliable long-term results have not been established for the extended criteria.¹ Table 1 shows therapeutic recommendations for endoscopic treatment of gastric cancer from the 2018 JGCA treatment guidelines.⁵ Based on pathological examination of the ER specimens, patients are managed with either endoscopic surveillance or surgery.

**Table 1: Therapeutic recommendations for endoscopic treatment of gastric cancer based on histopathologic examination of endoscopically resected specimens, from the 2018 Japanese Gastric Cancer Association (JGCA) treatment guidelines.**

<table>
<thead>
<tr>
<th>Endoscopic treatment (EMR/ESD)</th>
<th>Differentiateda</th>
<th>Undifferentiateda</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertical/deep margin (−)</td>
<td>Vertical/deep margin (−)</td>
<td></td>
</tr>
<tr>
<td>Lymphovascular infiltration (−)</td>
<td>Horizontal/lateral margin (−)</td>
<td></td>
</tr>
<tr>
<td>Any of following:</td>
<td>Lymphovascular infiltration (−)</td>
<td></td>
</tr>
<tr>
<td>• Intramucosal without ulcer, any size</td>
<td>Intramucosal without ulcer, diameter ≤2 cm</td>
<td></td>
</tr>
<tr>
<td>• Intramucosal with ulcer, diameter ≤3 cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Submucosal, diameter ≤3 cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Follow-upb</td>
<td>Surgery</td>
<td></td>
</tr>
</tbody>
</table>

EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection.  
¹According to the Nakamura classification;⁶ see Table 3 for the corresponding 2017 JGCA and 2019 WHO classifications.  

**Note 3 – Specimen dimensions (Core)**

There is no official agreement or recommendation on how specimens should be measured and whether they should be measured fresh or after formalin fixation. However, the Stomach ER Dataset Authoring Committee recommended that the reporting of specimen dimensions should be a Core element.

↑ Back
Note 4 – Tumour focality (Core)

While multifocal gastric carcinomas are rare, they should be documented. If multiple primary tumours are present, separate datasets should be used to describe each primary tumour.

Note 5 – Tumour site (Core)

The stomach is divided into the cardia, fundus, body, antrum and pylorus, but these regions are difficult to define macroscopically, which is especially true for the cardia and fundus. The JGCA guidelines divide the stomach into upper third, middle third and distal third by the lines connecting the trisected points on the lesser and greater curvatures (Figure 1).\(^8\) Primary gastric cancer located in the upper third of the stomach, especially at the OGJ/cardia, are reported to be more aggressive and associated with a poor prognosis.\(^9\)

![Figure 1: The stomach can be divided into 3 portions: upper third (U), middle third (M) and distal third (L).](image)

The OGJ is defined as the border between the oesophageal and gastric muscles, irrespective of the type of epithelial lining of the oesophagus. However, it can be challenging to determine the exact location of the OGJ, especially in individuals with conditions affecting OGJ landmarks. Four methods have been proposed to locate the OGJ anatomically (see also JGCA guidelines):\(^8-10\)

1. The distal end of the longitudinal palisading small vessels in the lower oesophagus. It can be seen endoscopically as well as microscopically and is commonly used by Japanese pathologists. However, it can be obscured by inflammation.
2. The horizontal level of the angle of His (defined as starting from the peritoneal reflection of the stomach onto the diaphragm), as shown by barium meal examination. It can be altered by hiatal hernia or tumour invasion.

3. The proximal end of the gastric longitudinal mucosal folds, which is the most commonly used definition by endoscopists in Western countries. However, it can be obscured by the presence of gastric mucosal atrophy (i.e., post chemoradiation therapy and atrophic gastritis) or a large gastric mass.

4. The level of the macroscopic calibre changes of the resected oesophagus and stomach.

The current recommendation is to use the proximal end of the gastric longitudinal mucosal folds as the landmark for the OGJ. If it cannot be identified, use the distal end of the longitudinal palisading small vessels.

The Siewert classification categorises OGJ cancer into Siewert type I (tumours with their epicentre located 1-5 cm above the OGJ), type II (tumour epicentre located from 1 cm above to 2 cm below the OGJ) and type III (tumour epicentre located from 2 cm - 5 cm below the OGJ). The Siewert classification, the proximal end of the gastric longitudinal mucosa folds is used as pragmatic reference for the endoscopic cardia/OGJ (zero point). The current Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC) 8th edition Staging System definition of gastric cancer includes those tumours involving the OGJ but with the epicentre >2 cm into the proximal stomach and cardia cancer without involvement of the OGJ (Figure 2). Therefore, all Siewert type III and some Siewert type II tumours are classified as gastric cancer based on the UICC/AJCC 8th edition Staging Systems.

Figure 2: (A) Oesophagogastric junction (OGJ) tumours with their epicentre located >2 cm into the proximal stomach are staged as stomach cancers. (B) Cardia cancers not involving the OGJ are staged as stomach cancers. (C) Tumours involving the OGJ with their epicenter <2 cm into the proximal stomach are staged as esophageal cancer. Used with permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging Manual, Eighth Edition (2016) published by Springer Science+Business Media.
Note 6 – Tumour dimensions (Core & Non-core)

For early gastric cancer, the tumour dimension is usually measured microscopically. However, when the tumour size is large, macroscopic mapping of the entire tumour and a thorough pathologic examination may be necessary.

If multiple primary tumours are present, separate datasets should be used to record each primary tumour.

↑ Back

Note 7 – Macroscopic tumour type (Non-core)

Early gastric carcinoma is defined as an invasive carcinoma involving only the mucosa (T1a) or submucosa (T1b). Growth patterns of early gastric carcinoma are classified into type 0-I (protruding), type 0-II (superficial), and type 0-III (excavated). Type 0-II tumours are further divided into type 0-IIa (superficial, elevated), type 0-IIb (superficial, flat) and type 0-IIc (superficial depressed) (Figure 3, Table 2). Early gastric carcinomas are usually small, and their macroscopic tumour types may only be accurately assessed by endoscopists.

| Table 2: Subclassification of early (type 0) gastric cancer. 

| Type 0-I (protruding): Polyplloid lesions, protruding >3 mm |
| Type 0-IIa (superficial elevated): Slightly elevated lesions protruding <3 mm |
| Type 0-IIb (superficial flat): Tumours without elevation or depression |
| Type 0-IIc (superficial depressed): Slightly depressed lesions |
| Type 0-III (excavated): Lesions with a deep depression |


Note 8 – Histological tumour type (Core and Non-core)

Several classification schemes have been used for subtyping gastric carcinomas histologically, including the Lauren, Nakamura, JGCA, WHO (Table 3) and Ming classifications. For consistency in reporting, the WHO histological classification of gastric carcinomas is recommended (Table 3 and 4). The Lauren classification is also widely used for gastric adenocarcinomas. In the Lauren classification, gastric adenocarcinomas are simply divided into two histological subtypes - intestinal type and diffuse type. Gastric carcinomas that do not fit into one of the two are placed into the mixed or indeterminate categories. The Lauren classification provides a simplified categorisation of common types of gastric carcinoma and may offer a better understanding of their biology and behaviour compared to the WHO classification. However, unlike the WHO classification, the Lauren classification cannot be applied to a variety of rare histologic subtypes.
### Table 3: Comparison of the Lauren, Nakamura, Japanese Gastric Cancer Association (JGCA) and World Health Organization (WHO) classification of gastric cancer.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal</td>
<td>Differentiated</td>
<td>Papillary</td>
<td>Papillary</td>
</tr>
<tr>
<td></td>
<td></td>
<td>pap</td>
<td>Tubular, well differentiated</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tubular 1, well differentiated: tub1</td>
<td>Tubular, moderately differentiated</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tubular 2, moderately differentiated: tub2</td>
<td>Tubular, moderately differentiated</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>Undifferentiated</td>
<td>Poorly 1 (solid type): por1</td>
<td>Tubular (solid), poorly differentiated</td>
</tr>
<tr>
<td>Diffuse</td>
<td>Undifferentiated</td>
<td>Signet-ring cell: sig</td>
<td>Poorly cohesive, signet-ring cell phenotype</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Poorly 2 (non-solid type): por2</td>
<td>Poorly cohesive, other cell types</td>
</tr>
<tr>
<td>Intestinal/diffuse/indeterminate</td>
<td>Differentiated/un differentiated</td>
<td>Mucinous</td>
<td>Mucinous</td>
</tr>
<tr>
<td>Mixed</td>
<td>Not defined</td>
<td>Description according to the proportion (e.g., por2&gt;sign&gt;tub2)</td>
<td>Mixed</td>
</tr>
<tr>
<td>Not defined</td>
<td>Not defined</td>
<td>Special type: Adenosquamous carcinoma</td>
<td>Other histological subtypes: Adenosquamous carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Squamous cell carcinoma</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Undifferentiated carcinoma</td>
<td>Undifferentiated carcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Carcinoma with lymphoid stroma</td>
<td>Carcinoma with lymphoid stroma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hepatoid adenocarcinoma</td>
<td>Hepatoid adenocarcinoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adenocarcinoma with enteroblastic differentiation</td>
<td>Adenocarcinoma with enteroblastic differentiation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adenocarcinoma of fundic gland type</td>
<td>Adenocarcinoma of fundic gland type</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other histological subtypes: Adenosquamous carcinoma</td>
<td>Micropapillary adenocarcinoma</td>
</tr>
</tbody>
</table>

**Table 4: World Health Organization (WHO) histological classification of gastric carcinomas.**

<table>
<thead>
<tr>
<th>Tumour type</th>
<th>Histologic features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adenocarcinoma, main histologic types</strong></td>
<td></td>
</tr>
<tr>
<td>Tubular adenocarcinoma</td>
<td>Most common subtype; composed of dilated or slit-like branching tubules of variable diameter or acinar structures</td>
</tr>
<tr>
<td>Papillary adenocarcinoma</td>
<td>Exophytic growth pattern and most commonly well differentiated; composed of elongated finger-like processes lined by columnar or cuboidal cells supported by fibrovascular cores</td>
</tr>
<tr>
<td>Poorly cohesive carcinoma, including signet ring cell carcinoma and other subtypes</td>
<td>Accounting for 20-54% of gastric cancers; composed of neoplastic cells that are isolated or arranged in small aggregates without well-formed glands; either signet-ring cell type (composed predominantly or exclusively of signet-ring cells) or non-signet ring cell type with marked desmoplasia</td>
</tr>
<tr>
<td>Mucinous adenocarcinoma</td>
<td>Composed of malignant epithelium and extracellular mucin pools (mucin pools &gt;50% of the tumour area)</td>
</tr>
<tr>
<td>Mixed adenocarcinoma</td>
<td>Composed of signet ring cell/poorly cohesive component and one or more other distinct histological components such as tubular/papillary carcinoma</td>
</tr>
<tr>
<td><strong>Adenocarcinoma, other histological subtypes</strong></td>
<td></td>
</tr>
<tr>
<td>Gastric (adeno)carcinoma with lymphoid stroma</td>
<td>Characterised by irregular sheets, trabeculae, ill-defined tubules or syncytia of polygonal cells embedded within a prominent lymphocytic infiltrate, with intraepithelial lymphocytes; frequently associated with Epstein-Barr virus (EBV) infection; less commonly associated with microsatellite instability or DNA mismatch repair deficiency</td>
</tr>
<tr>
<td>Hepatoid adenocarcinoma and related entities</td>
<td>Composed of large polygonal eosinophilic hepatocyte-like neoplastic cells with AFP expression; other AFP-producing carcinomas including well differentiated papillary/tubular-type adenocarcinoma with clear cytoplasm, adenocarcinoma with enteroblastic differentiation and yolk-sac tumour-like carcinoma.</td>
</tr>
<tr>
<td>Micropapillary adenocarcinoma</td>
<td>Composed of micropapillary component (10-90% of the tumour area) and tubular/papillary adenocarcinoma</td>
</tr>
<tr>
<td>Gastric adenocarcinoma of fundic-gland type</td>
<td>Likely develop from oxyntic gland adenoma with oxyntic gland differentiation; include chief-cell predominant (most common), parietal cell-predominant, and mixed phenotype</td>
</tr>
<tr>
<td>Rare histological subtypes</td>
<td>Mucoepidermoid carcinoma, paneth cell carcinoma, and parietal cell carcinoma</td>
</tr>
<tr>
<td><strong>Gastric squamous cell carcinoma</strong></td>
<td>Only composed of squamous cell carcinoma with no other histological component after thorough sampling</td>
</tr>
<tr>
<td><strong>Gastric adenosquamous cell carcinoma</strong></td>
<td>Admixture of adenocarcinoma and squamous cell carcinoma with the squamous cell component ≥25%</td>
</tr>
<tr>
<td><strong>Gastric undifferentiated (anaplastic) carcinoma</strong></td>
<td>Composed of diffuse sheets of anaplastic, large to medium size polygonal cells, with frequent pleomorphic tumour giant cells; other morphologies that may be seen include rhabdoid cell, sarcomatoid pleomorphic pattern, undifferentiated carcinoma with osteoclast-like giant cells, carcinoma with lymphoepithelioma-like feature, and a glandular component</td>
</tr>
<tr>
<td><strong>Gastroblastoma</strong></td>
<td>Composed of uniform spindle cells and uniform epithelial cells</td>
</tr>
</tbody>
</table>
A high incidence of intragastric recurrence is observed in certain histological subtypes including undifferentiated carcinoma and mixed adenocarcinoma with both signet ring cell carcinoma and poorly differentiated adenocarcinoma. Close endoscopic surveillance is required for these patients.

**Note 9 – Histological tumour grade (Core)**

The three-tiered system, applicable for tubular and papillary adenocarcinomas, is recommended by the UICC\(^{12}\)/AJCC\(^{13}\) 8\(^{th}\) edition Staging Systems as follows:

- G1: Well differentiated
- G2: Moderately differentiated
- G3: Poorly differentiated, undifferentiated

The AJCC 8\(^{th}\) edition also recommends that the highest grade is recorded if there is evidence of more than one grade or level of differentiation of the tumour.\(^{13}\) The Stomach ER Dataset Authoring Committee recommended the UICC/AJCC grading system because tumour differentiation may be more relevant in the locally excised tumour specimens.

It is noted that the WHO Classification of Tumours of the Digestive System, 5\(^{th}\) edition, 2019\(^{7}\) recommends a two-tiered system: low grade (well and moderately differentiated) and high grade (poorly differentiated).\(^{7}\)

Histopathological grading does not independently affect patient survival after R0 resection; however, poor histopathological grade is associated with high rate of R1 and R2 resections.\(^{21}\)

As discussed in Endoscopic Procedure, the criteria for ER are different between well/moderately differentiated and poorly/undifferentiated tumours. Some (but not all) studies have shown that undifferentiated mucosal and submucosal gastric cancer are associated with a high risk for lymphovascular invasion/lymph node metastasis.\(^{4,22,23}\)
Note 10 – Tissue layers present (Core)

Sometimes it is not possible to accurately stage the tumour when there are limited tissue layers present in ER specimens. For example, submucosal invasion cannot be determined if an ER specimen consists only of the mucosa with presence of cancer at the deep margin. Therefore, reporting the tissue layers present in the specimen is very important.

Note 11 – Extent of invasion (Core)

The term “carcinoma in situ” is not commonly applied to glandular epithelium. However, high grade dysplasia in a gastric resection specimen is also reported as “carcinoma in situ” as recommended by the UICC\textsuperscript{12}/AJCC\textsuperscript{13} 8\textsuperscript{th} edition Staging Systems mainly for tumour registry reporting purposes.

The depth of invasion is associated with increased risk of lymph node metastasis in early gastric cancer. Tumour invasion into the submucosa >500 µm (0.5 mm) from the muscularis mucosa has been reported as an independent risk factor for lymph node metastasis after noncurative ER.\textsuperscript{4}

Note 12 – Lymphovascular invasion (Core)

Lymphovascular invasion is an independent predictor of lymph node metastasis in endoscopically resected early gastric cancers.\textsuperscript{24,25} Therefore, additional gastrectomy is recommended for patients who have ER showing lymphovascular invasion.

Note 13 – Margin status (Core)

For ER gastric carcinomas, margins include mucosal and deep margins. ER can be en bloc or piece meal resection. Mucosal margin status is impossible to assess if it is a piecemeal resection with no orientation provided. At this stage no clear consensus on the definition of margin positivity has been reached.
Note 14 – Coexistent pathology (Non-core)

Based on the updated Sydney system, chronic gastritis is classified into Helicobacter gastritis, ex-Helicobacter gastritis, chemically induced/reactive gastritis, autoimmune gastritis and other special forms of gastritis. Helicobacter gastritis and autoimmune gastritis are recognised risk factors for gastric carcinoma. Both cause atrophic gastritis with intestinal metaplasia, which may develop into dysplasia/adenoma and further progresses into intestinal-type adenocarcinoma. In addition, pyloric gland adenoma may arise in a background of autoimmune atrophic gastritis, which can also progress into gastric carcinoma.

Gastric polyps include fundic gland polyp, hyperplastic polyp and different types of adenoma. Hyperplastic polyps can be seen in the setting of long-term gastritis, and intestinal metaplasia may be seen in large hyperplastic polyps, which may progress into dysplasia and eventually into invasive carcinoma. Rarely dysplasia is seen in fundic gland polyps, but it almost never progresses to adenocarcinoma. Gastric adenomas include intestinal type, foveolar-type, pyloric gland adenoma and oxyntic gland adenoma, all of which can progress to invasive carcinoma.

Other risk factors associated with gastric carcinoma include previous gastric surgery and Epstein-Barr virus (EBV) infection. In addition, approximately 10% of gastric cancers develop in a familial/hereditary setting, including hereditary diffuse gastric cancer in patients with CDH1 mutations and patients with Lynch syndrome with microsatellite instability (MSI)-high gastric cancer. Some patients with familial adenomatous polyposis can have multiple foveolar-type adenomas, which have a potential to become invasive carcinoma but at a consistently low rate.

Note 15 – Ancillary studies (Core & Non-core)

For mixed neuroendocrine-non-neuroendocrine carcinomas (MiNEC) and NECs, “Ancillary studies” is a core element to report neuroendocrine marker expression, whereas this element is non-core for other types of gastric cancer. Gastric neuroendocrine neoplasms are classified into NETs, NECs and MiNENs.

NETs are graded 1-3 using the mitotic count and Ki-67 proliferation index but pure NETs are not considered within the scope of this dataset. Most NECs show marked cytological atypia, brisk mitotic activity, and are subclassified into small cell and large cell subtypes. NECs are considered high-grade by definition, typically with a Ki-67 proliferation index >55%. MiNENs are usually composed of a poorly differentiated NEC component and an adenocarcinoma component. If a pure or mixed neuroendocrine carcinoma is suspected on morphology, immunohistochemistry is required to confirm neuroendocrine differentiation, usually applying synaptophysin and chromogranin A as a minimum.

PD-L1 expression and HER2 amplification/overexpression are only useful for patients with advanced/metastatic gastric cancer; therefore, they are not normally performed on the ER specimens. Mismatch repair may be examined in patients where there is a suspicion for Lynch syndrome-associated gastric cancer.

Epstein-Barr virus (EBV) associated gastric cancer accounts for approximately 10% of total gastric cancers, most of which are located in the upper part of the stomach. Histologically, EBV-associated
gastric cancer is poorly differentiated, with abundant tumour-infiltrating lymphocytes. Although poorly differentiated, EBV-associated gastric cancer is a distinct subtype with a low risk of lymph node metastasis. Extension of the criteria for ESD in early EBV-associated gastric cancer is under discussion.

Lymphovascular invasion is an independent predictor of lymph node metastasis in endoscopically resected early gastric cancers. However, immunohistochemical stains for lymphovascular markers are not routinely performed, unless there is a high histological suspicion of lymphovascular invasion.

Note 16 – Pathological staging (Core)

The TNM Staging System for gastric carcinoma of the UICC12/AJCC13 8th edition Staging Manuals are recommended and shown below (Figure 4). However, staging is only applicable to specimens with sufficient tissue layers present.

According to the UICC/AJCC convention, the designation “T” refers to a primary tumour that has not been previously treated. High grade dysplasia in a gastric resection specimen is reported as “carcinoma in situ” (Tis) as recommended by the UICC12/AJCC13 8th edition Staging Systems mainly for tumour registry reporting purposes.

For endoscopic resection only T1 and T2 are used as ER specimens do not contain the subserosa but very rarely may contain superficial muscularis propria.

![Figure 4: T1a is defined as tumour that invades the lamina propria. T1b is defined as tumour that invades the submucosa. T2 is defined as tumour that invades the muscularis propria, whereas T3 is defined as tumour that extends through the muscularis propria into the subserosal tissue. Used with permission of the American College of Surgeons, Chicago, Illinois. The original source for this information is the AJCC Cancer Staging Manual, Eighth Edition (2016) published by Springer Science+Business Media.13](image-url)
References


