Greater Manchester & Cheshire Guidelines for Pathology Reporting of Oesophageal and Gastric Malignancy

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1. General Comments

1.1 Cancer Reporting

Biopsies and resection specimens are reported according to departmental protocols and may include provision for double reporting of malignant biopsies or some form of subspecialist review. Reporting protocols should comply with guidance from the Royal college of Pathologists and Cancer Peer review requirements. Guidance on referral for second opinion has been agreed through the GM&C cancer network histopathology cross cutting group.

Dissection and block selection of resection specimens should be based on good pathology practice and local operating procedures. Guidance may be obtained from RCPath cancer dataset documents and other publications.

Resection specimens for cancer should be reporting according to the Royal College of Pathologists cancer datasets for cancer reporting.

Within the network, pro forma reporting using cancer dataset items is encouraged.

All reports should carry a SNOMED code to allow data collection within the network, together with TNM7 stage.

1.2 Input to MDT Meetings

Each department will provide pathology support to local and sector MDT meetings as agreed.

1.3 Cancer Staging

All cancer reporting should be staged according to the UICC TNM staging. The current scheme is based on 7th edition which introduces significant changes to the staging of oesophageal, junctional and gastric cancers. The Royal College of pathologists recommends the use of TNM 7th edition, and this should be documented in the operational policy. The TNM stage used should be stated in the report.
An emphasis should be made at the time of tissue block taking regarding the diligence of lymph node dissection, in order to avoid understaging of the tumour; the number of lymph nodes sampled represents a combined measure of the extent and quality of surgery, together with the diligence of the pathologist. As such, low lymph node sampling could result in understaging of the tumour which may reflect on patient prognosis. It is recommended that lymph node yield is regularly audited.

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1.4 Assessment of Tumour Regression

Pathological reporting of resection specimens performed post chemotherapy should include a Mandard classification of tumour regression. This is useful, as it shows association with prognosis, with relatively low inter-observer variation. This classification has the approval of clinicians, as discussed at the Provider Board educational event – Christie Hospital September 2014.

1.5 Cancer Trials: Tissue Block Retrieval

Pathology departments are currently experiencing an increasing requirement to retrieve / send away paraffin blocks of tumour for the purpose of cancer clinical trials. At the time of initial pathology reporting, a note should be made of the appropriate tissue block number for both cancer and normal tissue. This could be incorporated into the pathology report, or alternatively, into specimen note pad, if the telepath reporting system is used.

2. Oesophageal Carcinoma

2.1 Squamous Carcinoma

2.1.1 Diagnosis

Squamous carcinoma arises in the squamous lined oesophagus and is most common in the middle and upper third. Biopsies will confirm carcinoma if invasion is identified but may be superficial and difficult to assess for invasion due to the angle of approach of the biopsy forceps.

2.1.2 Grading

Squamous carcinoma is graded as well, moderate or poorly differentiated, based on the worst grade in the tumour.

2.1.3 Precursor Lesions

Squamous epithelial dysplasia is the only recognisable precursor lesion for carcinoma. Dysplasia should be graded as high or low grade. High grade dysplasia should be reported using departmental protocols for double reporting or review and should be discussed at an appropriate MDT meeting.

2.1.4 Staging

Staging should follow standard TNM staging (7th edition)

2.2 Adenocarcinoma

2.2.1 Diagnosis

Adenocarcinoma accounts for the majority of malignant lesions of the oesophagus. Most tumours arise in the lower oesophagus, often in a background of Barrett's change/columnar lined oesophagus, but can be seen at any level, arising from submucosal glands.

2.2.2 Grading

Standard grading is used, reporting as well, moderately or poorly differentiated based on the worst grade in the tumour.

2.2.3 Precursor Lesions

2.2.3.1 Barrett's Change

Barrett's change is widely recognised as a metaplastic change occurring in the lower oesophagus resulting in a columnar cell lining above the gastro-oesophageal junction. Barrett's metaplasia is defined by any portion of the normal distal squamous epithelial lining being replaced by metaplastic columnar epithelium, which is clearly visible endoscopically greater or equal to 1cm above the GOJ and confirmed histologically from oesophageal biopsies. Barrett's metaplasia is characterised by three epithelial types:

- Gastric cardia type epithelium
- Gastric body type epithelium
- Specialised intestinal columnar epithelium (intestinal metaplasia)

Consideration should be given to pro forma reporting of surveillance biopsies, in accordance to revised BSG guidelines for the management of Barrett's change. This guidance also suggests that the previous nomenclature from the 2005 guidelines, involving the distinction between 'diagnostic of', 'corroborative of' and 'in keeping with' Barrett's change should be abandoned.
It should be noted that recurrently mutated genes in oesophageal adenocarcinoma are also mutated in non-dysplastic Barrett's metaplasia (mutations in driver genes occur exceptionally early in disease development with profound implications for diagnostic and therapeutic strategies). Intestinal metaplasia is the most biologically unstable type of metaplasia with the greatest neoplastic potential. However, cancer may also arise in a non-intestinalised columnar segment.

2.2.3.2 Dysplasia

Epithelial dysplasia is the only useful morphological indicator of malignant risk. Biopsies and EMR/ESD specimens should be reported according to the Vienna system:

- Negative for dysplasia
- Indefinite for dysplasia
- Low grade dysplasia
- High grade dysplasia
- Invasive malignancy

Indefinite for dysplasia includes cases of reactive atypia associated with inflammation which may regress to normal if inflammation is treated. All such cases should be reviewed by a second GI pathologist, and the reasons for use of the 'indefinite for dysplasia' category should be given in the histology report, in order to aid patient management. MDT discussion of such cases is also suggested, with consideration of high dose PPI with repeat endoscopy in 3 months.

Given the important management implications for a diagnosis of dysplasia, it is recommended that all cases of suspected dysplasia are reviewed by a second GI pathologist, with review at a cancer centre if intervention is being considered, in accordance with revised BSG guidance 2013.

The natural history of low grade dysplasia is difficult to define. There is evidence that it may regress after treatment of inflammation and acid reflux, but it may progress to high grade dysplasia and should therefore be followed up carefully. Endoscopic radiofrequency ablation is now a recognised treatment for Barrett's low grade dysplasia. Patient selection should be performed at MDT, as indicated in the BSG guidelines. Biopsy sampling is performed, with diagnosis on at least 2 occasions, with confirmation by two histopathologists with a gastrointestinal interest.

There is strong evidence that high grade dysplasia has a high malignant potential and it may progress to adenocarcinoma or it may be associated with adenocarcinoma in adjacent non-sampled tissue. Current practice is that a diagnosis of high grade dysplasia should be confirmed by a second

pathologist and should be discussed at an MDT meeting. Further biopsies should be taken, in accordance with BSG guidelines, and a confirmed second diagnosis of high grade dysplasia may be an indication for either endoscopic or surgical resection.
Close attention to, in particular, the architectural and cytological features seen on pathological examination should lead to a robust diagnosis of dysplasia, avoiding subjectivity. Intra- and inter-observer variation is recognised involving the diagnosis of low grade dysplasia, with improved agreement seen for high grade dysplasia. There should be collaboration between pathologists within the network to ensure consistency of reporting. Surface maturation does not necessarily indicate an absence of dysplasia, as the entity of crypt dysplasia is described. In such cases, review by a second specialist GI pathologist is recommended.

The use of a minimum dataset is recommended for the pathology reporting of endoscopic resections, to ensure that all prognostic information is included in reports. The presence of tumour cells at the deep margin indicates incomplete resection and warrants further treatment.

2.2.3.3 Other Markers of Malignant Risk

A number of markers have been investigated as markers of increased malignant risk, but the most accepted is the use of immunohistochemistry to assess for p53, and this may be particularly useful in distinguishing between indeterminate for dysplasia and genuine dysplasia. This should be considered as an adjunct to routine diagnosis and it may improve the diagnostic reproducibility of a diagnosis of dysplasia.

2.2.4 Gastro-oesophageal Junction Lesions

Adenocarcinoma may arise around the level of the gastro-oesophageal junction in the presence or absence of Barrett's metaplasia, in gastric cardia or from the fundus / body. These tumours should be classified in accordance with the Siewert system:

Type 1 centre of tumour>1cm above GOJ
Type 2 centre of tumour between 1cm above and 2cm below GOJ
Type 3 centre of tumour between 2cm and 5cm below GOJ

The importance of this classification is in planning resections and lymphatic drainage. Siewert type is included as a data idem in the RCPath minimum data set (2nd edition).

2.2.5 Staging

All cancer reporting should be staged according to the UICC TNM staging. The current scheme is based on the 7th edition which introduces significant changes to the staging of oesophageal, junctional and gastric carcinomas. Each MDT should document which edition of TNM staging used in the operational policy and this should also be stated in individual pathology reports. In accordance with RCPath recommendations, it is suggested that TNM 7th edition should be universally used.

Difficulty arises in the staging of adenocarcinomas of the gastro-oesophageal junction. TNM 7th edition states a tumour with the epicentre of which is within 5cm of the junction and extends into the oesophagus is classified according to the oesophageal scheme. All other tumours with an epicentre in the stomach greater than 5cm from the junction or those within 5cm of the junction without extension into the oesophagus are staged using the gastric carcinoma scheme. As a practical measure the pathologist may liaise with the surgeon to agree staging appropriate to the operation performed.

Oesophageal TNM 7th Edition Staging:

pT Primary tumour
pTX Primary tumour cannot be assessed.
pT0 No evidence of primary tumour.
pTis Carcinoma in situ.
pT1 Tumour invades lamina propria or submucosa
pT1a lamina propria or muscularis mucosae
pT1b submucosa.
pT2 Tumour invades the muscularis propria.
pT3 Tumour invades adventitia.
pT4 Tumour invades adjacent structures.
pT4a pleura, pericardium, diaphragm or adjacent peritoneum.
pT4b other adjacent structures e.g. aorta, vertebral body, trachea.

pN Primary tumour
pNX Regional lymph nodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 1-2 regional lymph node metastasis
pN2 3-6 regional lymph node metastasis
pN3 >6 regional lymph node metastasis

M Distant metastasis
M0 No distant metastasis
M1 Distant metastasis

2.2.6 HER2

Currently the HER2 status is requested by an oncologist at the MDT meeting. The Greater Manchester Upper GI provider board aspires towards routine HER2 status request for all gastric and junctional adenocarcinomas – this will depend on further discussions across the region and funding agreement.

2.3 Other Malignancies

Rarely other types of malignant tumour can involve the oesophagus. These may be primary or secondary tumours. Examples of primary tumours include sarcoma, gastrointestinal stromal tumour (GIST) or melanoma. GISTs should be reported as per the RCPath dataset for GISTs (2011) and TNM7, as recommended by RCPath. Lymphomas of the oesophagus are rare, but when seen consideration should be given to referral to a Haematology Malignancy Diagnostic Service (HMDS Leeds, or other) - in accordance with NICE Guidance recommendations. Secondary tumours should always be considered, especially if a malignancy from a different site has been previously diagnosed, or if the clinical, endoscopic or imaging is unusual. Immunohistochemistry may be helpful together with discussion at the MDT.

3. Gastric Carcinoma

3.1 Adenocarcinoma

3.1.1 Diagnosis

Adenocarcinoma is the commonest form of malignant tumour in the stomach. It is usually diagnosed on endoscopic biopsy. There are four commonly used histological classifications of gastric

adenocarcinoma (Goseki, Lauren, Ming and WHO). In British practice the Lauren classification is most widely used and it is included in the RCPath cancer dataset. Tumours are classified as diffuse, intestinal or mixed types.

3.1.2 Grading

Tumours are graded by differentiation (well, moderate and poor) based on the most poorly differentiated grade identified. Significant variation in grade within a tumour may be indicated in the text of the report.

3.1.3 Precursor Lesions

Epithelial dysplasia is currently the only useful morphological indicator of malignant risk and it may be identified in biopsies from apparently normal, inflamed or ulcerated mucosa or it may be seen in the context of adenomatous polyps. Biopsies should be reported in accordance with the Vienna system:

Negative for dysplasia
Indefinite for dysplasia
Low grade dysplasia
High grade dysplasia
Invasive malignancy

The group comprising low grade dysplasia and indefinite for dysplasia includes cases of reactive atypia associated with inflammation, which may revert to normal when inflammation is treated, and there is recognised intra- and inter-observer variation in reporting. The natural history of low grade dysplasia is difficult to define, but it may progress to high grade dysplasia and should therefore be followed up carefully. All cases of indefinite for dysplasia should be reviewed by a second GI pathologist, and the reasons for use of the 'indefinite for dysplasia' category should be given in the histology report, in order to aid patient management. MDT discussion of such cases is also suggested.

Given the important management implications for a diagnosis of dysplasia, it is recommended that all cases of suspected dysplasia are reviewed by a second GI pathologist, with review at a cancer centre if intervention is being considered

High grade dysplasia is recognised more reproducibly and it has a high malignant potential and it may progress to adenocarcinoma within a period of a few years. Current practice is that a diagnosis of high grade dysplasia should be confirmed by a second pathologist and should be discussed at the MDT meeting. Further biopsies should be taken, in accordance with BSG guidance, and results discussed at the MDT meeting.

Close attention to, in particular, the architectural and cytological features seen on pathological examination should lead to a robust diagnosis of dysplasia, avoiding subjectivity. Intra- and inter-observer variation is recognised in low grade dysplasia with improved agreement for high grade dysplasia. There should be collaboration between pathologists within the network to ensure consistency of reporting.

3.1.4 Staging

The RCPath recommends the 7th edition of TNM for the staging of gastric carcinomas. This should be documented in the operational policy of each MDT and this should also be stated in individual pathology reports.

Gastric TNM 7th Edition Staging:

pT Primary tumour
pTX Primary tumour cannot be assessed.
pT0 No evidence of primary tumour.
pTis Carcinoma in situ.
pT1 Tumour invades lamina propria or submucosa
pT1a lamina propria
pT1b submucosa.
pT2 Tumour invades the muscularis propria.
pT3 Tumour invades subserosa.
pT4 Tumour invades adjacent structures.
pT4a Tumour penetrates serosa (visceral peritoneum) without invasion of adjacent structures.
pT4b Tumour invades adjacent structures.

pN Primary tumour
pNX lymph nodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 1-2 regional lymph node metastasis
pN2 3-6 regional lymph node metastasis
pN3a involvement of 7-15 regional lymph nodes.
pN3b involvement of 16 or more regional lymph nodes.

M Distant metastasis
M0 No distant metastasis
M1 Distant metastasis

3.2 Other Malignancies

Rarely other types of malignant tumour can involve the stomach. These may be primary or secondary tumours. Examples of primary tumours include sarcoma, gastrointestinal stromal tumour (GIST) or melanoma. GISTs should be reported as per the RCPath dataset for GISTs (2011) and TNM7, as recommended by RCPath. Lymphomas may occur in the stomach (MALT lymphoma), but when seen consideration should be given to referral to a Haematology Malignancy Diagnostic Service (HMDS Leeds, or other) - in accordance with NICE Guidance recommendations. Secondary tumours should always be considered, especially if a malignancy from a different site has been previously diagnosed, or if the clinical, endoscopic or imaging is unusual. A classical example is metastatic lobular carcinoma of the breast which may present in a manner resembling linitis plastica. Immunohistochemistry may be helpful together with discussion at the MDT

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