### Coversheet for Network Site Specific Group Agreed Documentation

This sheet is to accompany all documentation agreed by Pan Birmingham Cancer Network Site Specific Groups. This will assist the Network Governance Committee to endorse the documentation and request implementation.

<table>
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<tr>
<th>Document Title</th>
<th>Upper GI Pathology Reporting Guidelines Including:</th>
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<td>• Dataset for the histopathological reporting of oesophageal carcinoma (2\textsuperscript{nd} edition)</td>
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<td>• Dataset for the histopathological reporting of gastric carcinoma (2\textsuperscript{nd} edition)</td>
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<td>• Amended Dataset for Oesophageal Carcinoma Histopathology Reports</td>
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| Document Date | Approved by NSSG on May 2009 |

| Document Purpose | These guidelines and datasets are intended to inform health professionals with regards to Upper GI pathology reporting. |

| Authors | Members of the Royal College of Pathologists |

| References | [www.rcpath.org](http://www.rcpath.org) |

| Consultation Process | Consultation was with the Cellular Pathology and the Upper GI Network Site Specific Group. |

| Review Date | June 2012 (must be within three years) |

| Approval Signatures: |  |
| Network Site Specific Group Clinical Chair |  |

| Date Approved by Network Governance Committee | 10/06/09 |
Upper GI Pathology Reporting Guidelines

Version History

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<td>0.1</td>
<td>Jan 09</td>
<td>The Upper GI Network Site Specific Group agreed to adopt the</td>
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<td>national guidance.</td>
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<td>10/06/09</td>
<td>Approved by the Network Governance Committee Guidelines Sub Group</td>
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1. Scope of the Guideline

   This guidance has been produced to support the following:
   • The reporting of Upper GI pathology

2. Guideline Background

   At NSSG meetings the group acknowledged the need for pathology guidance. The NSSG recommended the guidance produced by the Royal College of Pathologists and the Upper GI and Cellular Pathology NSSG have agreed to adopt these guidelines and datasets.

Monitoring of the Guideline

   Implementation of the guidance will be considered as a topic for audit by the NSSG in 2012 (unless reviewed earlier by the Royal College of Pathologists).

Authors

Royal College of Pathologists

References

Dataset for the histopathological reporting of Oesophageal Carcinoma -

Dataset for the histopathological reporting of gastric carcinoma -
http://www.rcpath.org/resources/pdf/G013GastricDatasetFINALJan07.pdf

Approval Date of Network Site Specific Group Date: January 2009
Approval Date of the Governance Committee Date: 10 June 2009

Approval Signatures

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Standards and Datasets for Reporting Cancers

Dataset for the histopathological reporting of oesophageal carcinoma (2nd edition)

February 2007

Coordinator: Dr Nicholas P Mapstone, Royal Lancaster Infirmary

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<td>Version number</td>
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<td>Produced by</td>
<td>Dr Nicolas P Mapstone on behalf of the RCPat Cancer Services Working Group</td>
</tr>
<tr>
<td>Date active</td>
<td>February 2007</td>
</tr>
<tr>
<td>Date for review</td>
<td>February 2010</td>
</tr>
<tr>
<td>Comments</td>
<td>In accordance with the College’s pre-publications policy, this document was put on The Royal College of Pathologists’ website for consultation from 18 May – 19 June 2006. Twenty-four pieces of feedback were received and the author considered them and amended the document accordingly. Please email <a href="mailto:publications@rcpath.org">publications@rcpath.org</a> if you wish to see the responses and comments made.</td>
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Professor Carrock Sewell – Director of Publications
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1 INTRODUCTION TO OESOPHAGEAL CANCER DATASET

These proposals for reporting of oesophageal cancers should be implemented for the following reasons:

- prognostic information for the patient
- prognostic information for clinicians
- feedback to the surgeon on the quality of resection and the effects of neoadjuvant therapy
- for efficient audit for individual surgeons and between surgeons and between surgical techniques
- feedback for other specialties, e.g. radiology.

As a guiding principle, the TNM staging system is used. This has the advantage of being widely accepted and familiar, and is adhered to (except for the assessment of lymph node metastases – see below) throughout this document.

The first edition of this document (1998) included little detail regarding dissection techniques, histological interpretation, etc. It was felt that there were a number of equally valid ways in which the same, minimum, data could be extracted. There have since been requests for guidance on such matters and some have been included below. It is stressed that these are for guidance and are not prescriptive. The Association of Clinical Pathologists has produced guidelines for the handling of oesophageal specimens; these address many of the above issues.

This document has been devised to include the data required for adequate reporting of oesophageal specimens containing cancer. Where possible, core data that represent a minimum standard for patient management have been distinguished from non-core data that form part of a complete report but which do not have a sufficient basis in published evidence. The dataset has been approved by the UK Association of Cancer Registries and panels of specialised and general histopathologists acting on behalf of the College.

2 SPECIMEN RECEIPT AND PREPARATION

Oesophagectomy specimens contract immediately they are removed from the patient. They lose a quarter of their natural length initially and can be as little as a third of that length if fixed without being pinned. Ideally the specimen should be delivered rapidly, to the laboratory. It is recommended that specimens are pinned out, fresh, on cork boards before being fixed. When the specimen is measured, note should be made of whether or not the specimen was pinned.

The stomach should be opened along the gastric resection margin. The oesophagus itself may be pinned out intact. This allows optimum assessment of the whole of the circumferential resection margin by serial horizontal slicing of the oesophagus and does not significantly impair fixation in most tumours. Alternatively, the oesophagus may be opened along its length. This allows detailed assessment of background abnormalities in the rest of the oesophagus. Some pathologists feel that this does not impair assessment of the circumferential resection margin. If this method is used, the outer surface of the oesophagus should be painted before opening.
3 TISSUE SAMPLING

The following blocks of tissue are recommended as a minimum sampling:

- proximal resection margin – block(s) parallel to margin
- distal resection margin – block(s) parallel to margin
- three blocks of tumour to show closest approximation of tumour to circumferential margin and relationship to adjacent mucosa
- sampling of lymph nodes.

There are two approaches to sampling the tumour:

- Blocking out the tumour with horizontal and longitudinal slices is recommended by some.4 This probably best demonstrates the relationship of the tumour to the surrounding mucosa.
- Others recommend serial horizontal slices of the tumour. This allows more readily understandable photography of specimen slices and correlation with radiological images.

4 CORE DATA

- Maximum tumour diameter
- Siewert tumour type (cardiac tumours only)
- Maximum depth of invasion (anatomical layer)
- Polypoid or other morphology
- Histological type
- Grade of malignancy
- Serosal involvement (gastric, pleural or pericardial)
- Resection margins (proximal, distal and circumferential)
- Vascular invasion
- Lymph node status

5 NON-CORE DATA

- Comment on specimen preparation
- Overall dimensions of specimen
- Presence of Barrett’s metaplasia
- Effects of neoadjuvant therapy (if applicable)
- Molecular data (if applicable)

6 GROSS DESCRIPTION

The overall dimensions of the specimen and the lengths of oesophagus and stomach should be recorded. The maximum length of tumour should be recorded. Tumour size influences prognosis.6, 7 To conform with other datasets, the tumour size and distance to resection margins are based on macroscopic assessment, confirmed or amended on the basis of microscopy.

The macroscopic appearance of the tumour has little contribution to the prognosis, with the exception of polypoid tumours.8
The classification of carcinomas involving the gastro-oesophageal junction is difficult. There is no separate TNM system for cardiac cancers. TNM staging systems are different for the oesophagus and stomach. The decision must be made, for each gastro-oesophageal junction cancer, which dataset and which TNM scheme to use. This decision may affect the tumour’s T or N stage.

A widely used classification of cancers at the cardia divides them into three groups: those arising 1–5 cm above the gastro-oesophageal junction (Type 1), at the junction (Type 2) or 2–5 cm below the junction (Type 3). In this system, the gastro-oesophageal junction is defined as the proximal limit of the gastric rugal folds. This classification is now recommended by the British Society of Gastroenterology. The Siewert type has been included as a core data item in this dataset.

There is some evidence that Type 1 cancers are different from Types 2 and 3 cancers in features such as the pattern of lymph node metastasis. Thus there might be an argument for using the oesophageal dataset for Type 1 tumours, and the gastric dataset for Type 2 and 3 tumours. Other authorities believe that Type 2 tumours should be included with oesophageal cancers.

Recent International Union Against Cancer (UICC) guidance on these matters is contradictory. In the ‘frequently asked questions’ segment of this publication, it states that all adenocarcinomas of the gastro-oesophageal junction (GOJ) should be classified according to the gastric TNM scheme. In the main text, however, it specifically states that ‘if more than 50% of the tumour involves the oesophagus the tumour is classified as oesophageal, if less than 50% as gastric’. It further specifies that tumours exactly at the junction should be classified according to their histology, so squamous cell, small cell and undifferentiated carcinomas would be oesophageal and adenocarcinomas would be gastric. This was effectively the advice from the first edition of this dataset. In the absence of further recommendations from the UICC or a new TNM scheme for cardiac cancers, this advice stands.

This dataset should be used when more than half of the cancer (measured on the mucosal aspect) is above the GOJ. The GOJ is often obvious on the mucosal surface. Sometimes, large tumours obliterate the junction or extensive Barrett’s oesophagus can make it difficult to identify the GOJ. In these situations, the junction is probably most easily identified by the highest extent of the peritoneal reflection on the serosal surface. If more than half of the cancer is below the GOJ the Gastric dataset should be used. Thus this dataset should be used for all oesophageal cancers, cardiac cancers of Siewert type 1, and some cardiac cancers of Siewert type 2. This may be subject to revision in the near future.

The size and position of the tumour will allow its location with respect to the GOJ to be determined.

7 MICROSCOPIC FEATURES

Histological type of tumour

The vast majority of these lesions will be adenocarcinomas and squamous carcinomas, with a few adenosquamous lesions and small cell carcinomas. Whilst the type of carcinoma may have little influence on prognosis in the majority of lesions, in very early cancers (T1) it may be better to have an adenocarcinoma – they have less local recurrence and fewer new primary lesions. Irrespective of the prognostic implications, it provides useful validation of the presurgical diagnosis, which may be important in adjuvant therapy decisions.

Tumour differentiation

Opinion is divided upon the prognostic significance of tumour differentiation. In some studies, it was prognostically significant for squamous carcinomas, adenocarcinomas or both. However, in one large study it was not significant. As it is usually easy to assess and may be important prognostically, it is therefore included in the core dataset. The World Health Organization (WHO) classification in the series, International Histological Classification of Tumours, specifies that ‘when a tumour shows different grades of differentiation the higher grade should determine the final categorisation’. The
newer classification from WHO does not specify how to classify different grades of differentiation in the same tumour. In conformity with other datasets, differentiation is assessed as being that of the highest grade in the tumour.

**Dysplasia**

Occasionally an oesophageal resection will be performed upon a patient who has had multiple biopsies showing high-grade dysplasia, usually in the context of Barrett’s oesophagus. These patients usually have invasive adenocarcinoma in the resection specimen, but occasionally a resection will show only high-grade dysplasia.

**Depth of invasion**

The depth of invasion is assessed according to the TNM staging system and is one of the most consistent predictors of prognosis. It is often the only independent prognostic indicator on multivariate analysis. Some authors have attempted to go further and distinguish mucosal and submucosal invasion. Whilst this may predict the likelihood of lymph node metastases, it is not an independent prognostic factor in patients who do not have nodal metastases. Distinguishing intramucosal carcinoma from submucosal carcinoma is thus more important in endoscopic mucosal resection specimens than in oesophagectomy specimens.

**Serosal involvement**

Some tumours may involve the pleura or pericardium. Many distal oesophageal carcinomas will involve the proximal stomach. At these sites, there is no circumferential margin but there is a serosal surface. Whilst there is no evidence to confirm or refute serosal involvement as an important prognostic indicator in oesophageal carcinoma, it is undoubtedly so in the stomach and for this reason it is included in the dataset. Indeed in one study, 25.6% of patients dying of oesophageal carcinoma had serosal carcinomatosis. The different types of serosal surface (pleura, pericardium and peritoneum) are not distinguished in this dataset.

**Proximal and distal margins**

The proximal (upper) and distal (lower) resection margins of the oesophagus require histological exclusion of involvement. There is good evidence that involved proximal margins increase the likelihood of recurrence but less evidence for distal margins. The proximal margin of the oesophagus should always be sampled, no matter what the distance from the tumour, because of the risk of discontinuous foci of carcinoma in the proximal oesophagus. There are recommendations for clearance of tumour from proximal and distal margins, but this may vary depending upon the type of tumour. In conformity with other datasets, the distances are measured macroscopically.

**Circumferential resection margin (CRM)**

Before Sagar et al published their study of CRM involvement in the oesophagus, few studies even mentioned this as a possible parameter. Sagar’s retrospective study and a follow-up prospective study showed CRM involvement to be a predictor of poor prognosis, especially in patients with no or few involved lymph nodes. Longer follow up on still more patients rather confusingly found CRM status to be only significant on univariate analysis. However, as R status was included in the factors investigated and R status (presumably) included CRM status, this is perhaps not surprising. R status was an independently significant factor. (R0 resection is a fully resected tumour with no involvement of any margins; R1 resection is macroscopically a clear resection but which proves on histological examination to have positive margins; R2 resection is one in which margin involvement is obvious macroscopically, either to the surgeon or pathologist). Another study to have looked at this parameter concluded that it has no prognostic significance on multivariate or even univariate analysis.

It is perhaps not surprising that CRM involvement is not significant in patients with very early (T1 or T2) tumours or advanced (T4 or those with large numbers of nodal metastases) tumours. However, when T3 tumours with fewer than 25% of nodes involved are investigated, CRM status is again shown to be of major prognostic significance. The same authors who produced the negative study mentioned above were unable to show any significance to margin involvement in their node negative
cancers. Improved margin clearance is related to improved survival following neoadjuvant treatment.

Some authors have suggested that CRM status should not be included in the dataset. However, CRM status also provides surgical and radiological feedback and may be a useful audit tool. Whilst opinion is still mixed on the prognostic significance of this parameter, it is suggested that it remain as a core data item in the dataset. It is said to be involved if carcinoma is identified microscopically within 1 mm of the CRM.

Some surgeons prefer to remove lymph nodes from an oesophagus before sending the specimen to the laboratory. The circumferential resection margin cannot be assessed in this situation and the margin should be recorded as ‘not assessable’.

Vascular invasion
Vascular invasion is an effective prognostic indicator. Different studies have detected involvement in different ways, some using special stains, some specifying venous over lymphatic invasion and some with no details on how it was identified. Many showed a significant effect on univariate analysis and, in two studies, it was as independently prognostic as depth of invasion on multivariate analysis. Lymphatic invasion has specifically been shown to indicate a poor prognosis. There is no separate data comparing intra- and extramural vascular invasion. It is recommended that invasion of any vascular space is recorded.

Perineural invasion
There is less evidence for perineural invasion as a prognostic indicator. In one study, the only significance here was lost on multivariate analysis. However, in another study, neural invasion was an important prognostic factor.

Lymph node stage and numbers of involved nodes
All studies in which crude lymph node status is assessed show it to be a significant indicator of prognosis. In many of those papers, it was the most significant prognostic indicator.

The TNM staging system indicates only whether or not lymph nodes are involved, with no subclassification into N2 or N3, unlike the system used in the stomach. However, when assessed, a large number of involved nodes is usually, although not always, a significant factor. The ratio of involved to uninvolved nodes is also important. This reinforces the importance of documenting not only the number of involved nodes, but also the total numbers examined.

There is little information upon the significance of the location of involved lymph nodes, and few papers on features such as extracapsular invasion. In the absence of more evidence, these features are not included in the dataset.

The search for involved lymph nodes has been refined in some sites by the use of immunohistochemistry and serial sections to detect ‘micrometastases’. Some studies indicate this provides important prognostic information. Such techniques have demonstrated micrometastases in some patients identified as being node negative using conventional histology. Some authors claim this is prognostically significant, whilst other deny the significance. Immunohistochemistry is not recommended in the routine search for lymph node metastases. Other techniques, such as rtPCR are obviously beyond the scope of a dataset.

Some confusion has arisen over the classification of lymph nodes in the new (6th edition) version of TNM. In this edition, a tumour nodule in the connective tissue is classified as a regional lymph node metastasis if it has the form and smooth contour of a lymph node. A tumour nodule with an irregular contour is classified in the pT category. Prior to this change, a tumour nodule was classified as a regional lymph node metastasis if it was larger than 3 mm in diameter, irrespective of its shape.
In a further departure from previous practice, very small deposits in lymph nodes are classified as ‘isolated tumour cells’. These are defined as clusters of cells not more than 0.2 mm in greatest dimension. The classification indicates that such small deposits should be ignored for the purpose of counting lymph node metastases. The presence of isolated tumour cells as the only lymph node metastasis may be indicated as N0(i+) in TNM 6th edition.

Until these changes reach wide acceptance and are validated by some supporting evidence, it is proposed that the dataset should adhere to previous practice. Thus deposits greater than 3 mm in size and small deposits in lymph nodes identified on routine microscopy (irrespective of size) are counted as lymph node metastases. A separate area on the form is available as ‘non core’ data for those who wish to record TNM stage in the 6th edition format.

See appendix A for details of which lymph node metastases should be included in the N stage and which in the M stage.

**Barrett’s metaplasia**

Some studies indicate a positive prognostic effect of the presence of Barrett’s metaplasia in the adjacent oesophagus.\(^52\) Whilst this may identify less advanced tumours, many of these patients may have been screened for Barrett’s and documentation of its presence is useful for audit. It is included as a non-core data item.

**Other markers**

Many other markers of prognosis have been investigated, including ploidy\(^ {16, 23, 53,}\) angiogenesis,\(^ {54}\) CD44\(^ {55}\) and EGFR.\(^ {56}\) Many show some prognostic significance, but without confirmatory evidence in larger studies the use of such special techniques is not justified in a core dataset.

**Neoadjuvant treatment**

Neoadjuvant treatment is increasingly being used in oesophageal carcinoma. Consequently, oesophageal resection specimens will increasingly show the effects of such treatment. Mucin lakes or collections of keratin are often taken to identify areas where tumour has been ablated by chemotherapy or radiotherapy. These structures will often contain no identifiable tumour cells (it may be necessary to confirm this by a cytokeratin immunohistochemical stain). For the purposes of this dataset, tumour is only assumed to be present in lymph nodes and resection margins when viable (i.e. non apoptotic) tumour cells are seen.\(^ {57}\) This approach is now supported by one small study of mucin lakes in post-treatment specimens.\(^ {58}\)

A number of schemes have been suggested for the classification of response to chemotherapy,\(^ 2, 59\) but none has been universally accepted and these are most likely to be used in a research setting. A specimen in which no tumour is identified following neoadjuvant treatment is staged as ypT0N0.

### 8 DATASET FOR AN INITIAL BIOPSY DIAGNOSIS OF OESOPHAGEAL CARCINOMA

An initial biopsy report should identify the type of carcinoma: squamous cell or adenocarcinoma. The presence of overlying squamous cell dysplasia, glandular dysplasia or Barrett’s metaplasia will also provide support for a primary oesophageal origin and so should also be included if present. The depth of invasion may also be useful information. Submucosal invasion (as opposed to intra-mucosal invasion only) is a prognostic indicator of nodal metastases.\(^ {17}\) This would be of little use in a resection specimen where the nodes are available for dissection and thus the TNM classification of depth of invasion (which does not differentiate between mucosal and submucosal invasion) is used for resection specimens. However, it may be helpful for the clinicians to know if submucosal invasion is identifiable in a biopsy specimen and thus the presence or absence of submucosal tissue, and its involvement should be included in biopsy reports.
There is evidence that some types of adenocarcinoma, such as mucinous or signet ring cell types (assessed in post-therapy and pre-treatment specimens), may respond better to chemotherapy, but there is insufficient evidence to require subclassification of adenocarcinomas as a core data item.

9 REFERENCES


APPENDIX A  TNM CLASSIFICATION OF MALIGNANT TUMOURS

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
pT2  Tumour invades muscularis propria
pT3  Tumour invades adventitia
pT4  Tumour invades adjacent structures

pN Regional lymph nodes

pNX  Regional lymph nodes cannot be assessed.
pN0  No regional lymph node metastasis
pN1  Regional lymph node metastasis

M Distant metastasis

MX  Distant metastasis cannot be assessed.
M0  No distant metastasis.
M1  Distant metastasis

For tumours of lower thoracic oesophagus:
M1a  Metastasis in coeliac lymph nodes
M1b  Other distant metastasis

For tumours of upper thoracic oesophagus:
M1a  Metastasis in cervical lymph nodes
M1b  Other distant metastasis

For tumours of mid-thoracic oesophagus:
M1a  Not applicable
M1b  Non-regional lymph node or other distant metastasis
APPENDIX B  SITES AND SUBSITES FOR DESCRIPTION AND THEIR ASSOCIATED SNOMED ‘T’ CODES

T-56000  Oesophagus
T-56010  Oesophageal mucosa

APPENDIX C  COMMON SNOMED ‘M’ CODES USED IN OESOPHAGEAL NEOPLASIA

Note: This is not a comprehensive list of all malignancies and other codes should be used as necessary.

M-73000  Metaplasia
M-80413  Small cell carcinoma
M-80772  Squamous intraepithelial neoplasia grade 3
M-80703  Squamous carcinoma
M-80833  Basaloid squamous cell carcinoma
M-80743  Spindle cell squamous carcinoma
M-81482  Glandular intraepithelial neoplasia grade 3
M-81403  Adenocarcinoma
M-85603  Adenosquamous carcinoma
M-80203  Undifferentiated carcinoma
M-89361  Gastrointestinal stromal tumour
M-87203  Malignant melanoma
APPENDIX D

NATIONAL DATASET FOR
OESOPHAGEAL CARCINOMA HISTOPATHOLOGY REPORTS

Surname .........................................................  Forenames ................................................  Date of birth ............... 

Hospital ..........................................................  Hospital no ...............................................  NHS no .............................. 

Date of receipt ...............................................  Date of reporting ......................................  Report no ........................... 

Pathologist ........................................................  Surgeon ....................................................  Sex ..................................... 

______________________________________________________________________________________________

Shaded data items = ‘non core’ data

GROSS DESCRIPTION

Maximum length of specimen: ......................... mm
Length of oesophagus: ......................... mm
Length of stomach: ......................... mm
Length of tumour: ......................... mm
Width of tumour: ......................... mm
Tumour edge to nearest distal margin: ................ mm
Tumour edge to nearest proximal margin: ................ mm

Type of tumour
[ ] Polypoid  [ ] Other
[ ] Pinned  [ ] Not pinned

Siewert tumour type (cardiac cancers only)  [ ] 1  [ ] 2

HISTOLOGY

Type of tumour
[ ] Squamous  [ ] Adenocarcinoma
[ ] Other (specify) ........................................................

Differentiation by worst area:
[ ] Well  [ ] Moderately  [ ] Poorly differentiated

Depth of invasion
[ ] Tis high-grade dysplasia
[ ] T1 invasion of lamina propria/submucosa
[ ] T2 invasion of muscularis propria
[ ] T3 invasion beyond muscularis propria
[ ] T4 invasion of adjacent structures

Proximal margin
[ ] Normal  [ ] Dysplasia  [ ] Carcinoma  [ ] Barrett’s
Distal margin
[ ] Normal  [ ] Dysplasia  [ ] Carcinoma

Involvement (<1 mm):  [ ] Yes  [ ] No  [ ] N/A
(If no: distance of carcinoma to nearest circumferential margin  ................ mm)

Other features
Vascular invasion  [ ] Yes  [ ] No
Barrett’s metaplasia  [ ] Yes  [ ] No
adjacent to tumour

Lymph nodes
Number examined……………… Number positive………………
(N0 if no nodes positive, otherwise N1)

Distant metastases
Coeliac axis node positive  [ ] Yes  [ ] No
(M1a if lower thoracic carcinoma, otherwise M1b)
Cervical node positive  [ ] Yes  [ ] No
(M1a if upper thoracic carcinoma, otherwise M1b)
Other distant metastasis (M1b)  [ ] Yes  [ ] No

COMMENTS

______________________________________________________________________________________________

PATHOLOGICAL STAGING

Complete resection  [ ] Yes(R0)  [ ] No(R1 or R2)  (y) pT…… pN…… pM……. TNM 5th edition

(y) pT…… pN……(i +/-) pM……. TNM 6th edition

Signature ………………………………………...    Date …../……/…..     SNOMED codes T ……….. / M …………

15
Standards and Datasets for Reporting Cancers

Dataset for the histopathological reporting of gastric carcinoma (2nd edition)

Coordinator: Professor Marco R Novelli, University College London

January 2007

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<td>2</td>
</tr>
<tr>
<td>Produced by</td>
<td>Professor Marco R Novelli, Working Group on Cancer Services</td>
</tr>
<tr>
<td>Date active</td>
<td>January 2007</td>
</tr>
<tr>
<td>Date for review</td>
<td>January 2009</td>
</tr>
<tr>
<td>Comments</td>
<td>Supersedes 1st edition, published 2000. This document was placed for comment on the College website from 26 June to 24 July 2006 and received 15 comments. The authors have considered the comments and amended the document accordingly. Please email <a href="mailto:publications@rcpath.org">publications@rcpath.org</a> if you would like to see the feedback received.</td>
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Registered charity in England and Wales, no. 261035
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1 INTRODUCTION

This dataset has been revised according to College’s February 2006 guidelines. It is suggested that this dataset be used in the reporting of gastric cancer resection specimens to:

i) provide both the patient and clinician with prognostic information

ii) to allow the clinician to determine the most appropriate clinical management for the patient

iii) to facilitate audit of surgical and medical therapies and diagnostic modalities.

As a guiding principle, the TNM staging system is used. This document has been devised to include the data required for adequate reporting of gastric specimens containing carcinomas, but it is not suggested that this dataset be applied to carcinoids/well differentiated endocrine carcinomas or non-epithelial malignant gastric tumours (e.g. GISTs). The dataset has been subdivided into core and non-core data. Core data are the suggested minimum requirement for appropriate patient management, such data having been shown to be of prognostic significance. Non-core data are additional data that do not have a sufficient basis in published evidence to be a requirement, but may be of potential interest and use in patient management. Since the publication of the first Minimum Dataset for Gastric Cancer Histopathology Reports (April 2000), there have been a number of developments in the treatment of gastric carcinomas. It is now not uncommon for UK surgeons to perform radical lymph node dissections and the use of neo-adjuvant chemotherapy is becoming widespread. This revised dataset has been adjusted to take account of such changes.

The dataset has been approved by the UK Association of Cancer Registries and the following panels of specialised and general histopathologists, acting on behalf of the College:

- Association of Upper Gastrointestinal Surgeons (www.augis.org)
- British Society of Gastroenterology (www.bsg.org.uk, medics and pathologists)
- National Translational Cancer Research Network (www.ntrac.org.uk, oncologists, with David Cunningham leading the upper GI board).

2 CLINICAL INFORMATION REQUIRED ON SPECIMEN REQUEST FORM

In the UK, most gastric resections for carcinoma contain a palpable tumour, which is readily identifiable on visual inspection of the mucosal aspect of the specimen. However, in some specimens tumour may not be macroscopically obvious. This is becoming increasingly the case with the widespread use of neoadjuvant chemotherapy. In all cases, and especially those without obvious macroscopic tumour, clinical information may be useful in optimising specimen sampling. Clinical information that may be helpful includes:

- site of tumour
- type of tumour (if known)
- previous histology (where performed and case number if available)
- any history of neoadjuvant chemoradiotherapy.

3 SPECIMEN PREPARATION BEFORE DISSECTION

Ideally, specimens should be received fresh as soon as possible after resection. If this is not practicable, the specimen should be suitably incised to drain gastric contents and then placed in a large volume of a formalin-based fixative, preferably with insertion of a paper wick to allow formalin access to the mucosal aspect of the specimen. Specimens received fresh or partially fixed are usually opened along the anterior margin of the greater curve, pinned on a corkboard and floated in a formalin-based fixative. After 24–48 hours’ fixation, the pins should be removed and the specimen flipped over to allow complete fixation of the serosal aspect. Where possible, it is best to avoid cutting through the
tumour before fixation as this can make subsequent assessment of serosal invasion more difficult. In cases where an incision along the anterior aspect of the greater curve would cut across the tumour, the cut can be taken in a wide arc around the tumour or when dealing with large greater curve tumours, the anterior margin of the lesser curve can be opened. Where there is a gastro-jejunostomy, the anastomosis is avoided and the jejunal loop is opened longitudinally by a separate incision. In specimens where tumours arise at/close to the gastric cardia, the circumferential resection margin of the lower oesophagus should be inked prior to block taking.

4 SPECIMEN HANDLING AND BLOCK DISSECTION

Where the stomach is received in formalin, handling will depend on the adequacy of fixation. If the surgeon has already opened the stomach and the specimen is sufficiently fixed, blocks can be taken immediately. Many specimens will be received unopened and only partially fixed. Under these circumstances, the specimen should be opened by a pathologist, pinned out (or placed flat in a large volume of formalin) and fixed as above.

**Tissue sampling**

The following blocks of tissue are recommended as a minimum sampling.

- Proximal resection margin – block(s) parallel to margin.
- Distal resection margin – block(s) parallel to margin.
- At least three blocks of tumour to show:
  - deepest penetration into gastric wall
  - closest approximation to proximal/distal resection margins
  - presence of serosal involvement.
  - presence of possible circumferential margin involvement in cardia/oesophago-gastric junction tumours.
- Lymph nodes.

Ideally, proximal and distal resection margins are initially blocked followed by a careful search for lymph nodes in peri-gastric connective tissue. Depending upon the specimen type, the following groups of nodes may be present: gastro-oesophageal junction, proximal lesser curve (paying particular attention to nodes around the left gastric artery pedicle), distal lesser curve, proximal and mid greater curve and infra-pyloric nodes. All lymph nodes found should be sampled. If the spleen is attached, nodes should also be sought at the splenic hilum. The surgeon may also send extra-gastric lymph nodes, labelled separately from the main specimen. Further blocks are usually taken to access the background gastric, oesophageal and duodenal mucosa where present. The tumour is then serially sectioned, the slices examined and blocks taken (as described above).
5 CORE DATA ITEMS

Macroscopic
- Tumour site
- Tumour size (maximum diameter)
- Tumour morphology (polypoid, ulcerative, fungating, diffusely infiltrative).

Microscopic
- Maximum extent of invasion through wall (pT staging)
- Histological type
- Histological differentiation (worst)
- Resection margins (proximal, distal and circumferential)
- Lymph node status
- Presence of lymphatic or vascular invasion.

Macroscopic assessment

The type of resection, total or partial (proximal or distal) gastrectomy or oesophago-gastrectomy, is recorded. The maximum diameter of the tumour and the distance of the tumour from the closest surgical margin (proximal or distal) should be recorded in millimetres. In conformity with other datasets, the tumour size and distance to resection margins are based on macroscopic assessment, confirmed or amended on the basis of microscopy.

Cardia/oesophago-gastric junction tumours

The classification of carcinomas involving the gastro-oesophageal junction is not straightforward as the TNM staging systems are different for the oesophagus and stomach. The guidelines described below are identical to those produced for the College’s Dataset for the histopathological reporting of oesophageal carcinoma (see www.rcpath.org/publications) to allow continuity of reporting between these two sites.

For each gastro-oesophageal junction cancer, the decision must be made regarding which dataset and which TNM scheme to use. This decision may affect the tumour’s T or N stage.

A widely used classification of cancers at the cardia\(^4\) divides them into three groups: those arising 1–5 cm above the gastro-oesophageal junction (Type 1), at the junction (Type 2) or 2–5 cm below the junction (Type 3). In this system, the gastro-oesophageal junction is defined as the proximal limit of the gastric rugal folds. This Siewert classification is now recommended by the British Society of Gastroenterology.\(^5\)

There is some evidence that Type 1 cancers are different from Types 2 and 3 cancers in features such as the pattern of lymph node metastasis.\(^6,7\) Thus there might be an argument for using the oesophageal dataset for Type 1 tumours, and the gastric dataset for Type 2 and 3 tumours. Other authorities believe that type II tumours should be included with oesophageal cancers.

Recent International Union Against Cancer (UICC) guidance on these matters is contradictory.\(^8\) In the ‘Frequently asked questions’ segment of this publication, it states that all adenocarcinomas of the gastro-oesophageal junction (GOJ) should be classified according to the gastric TNM scheme. In the main text, however, it specifically states that “if more than 50% of the tumour involves the oesophagus the tumour is classified as oesophageal, if less than 50% as gastric”. It further specifies that tumours exactly at the junction should be classified according to their histology, so squamous cell, small cell and undifferentiated carcinomas would be oesophageal and adenocarcinomas would be gastric. This was effectively the advice from the first edition of this dataset. In the absence of further recommendations from the UICC or a new TNM scheme for cardiac cancers, this advice stands.
For the purposes of this dataset, a lesion is said to be a gastric carcinoma when more than half of the cancer (measured on the mucosal aspect) is below the GOJ. The GOJ is usually obvious on the mucosal surface, but sometimes large tumours obliterate the junction. In these situations, the junction is probably most easily identified by the highest extent of the peritoneal reflection on the serosal surface. If more than half of the cancer is above the GOJ the Oesophageal dataset should be used. Thus this dataset should be used for all gastric cancers, cardiac cancers of Siewert type 3, and some cardiac cancers of Siewert type 2. This may be subject to revision in the near future (in conjunction with the oesophageal dataset).

The size and position of the tumour will allow its location with respect to the GOJ to be determined.

**Site of tumour**

The site of the tumour within the stomach should be recorded. Proximal (cardia) tumours have a worse prognosis than more distal tumours.9,10,11

**Maximum tumour diameter**

The maximum tumour dimension is a core data item common to all the College datasets. Some studies show that tumour size is an independent prognostic factor in gastric adenocarcinoma,10,12 but others suggest that it is not an independent factor.11

**Macroscopic type of tumour**

The gross morphology of gastric tumours has been shown to have a bearing on prognosis. If tumours are classified into Borrmann types (Type 1 – polypoid, Type 2 – fungating, Type 3 – ulcerated and Type 4 – diffusely infiltrating), the Type 4 (diffusely infiltrative) is associated with a poor prognosis.13

**Microscopic assessment**

**Depth of invasion**

The depth of invasion is assessed according to the TNM staging system (see Appendix A). Depth of invasion has been repeatedly shown to be a predictor of prognosis in multivariate analysis.11,13,14,15,16

**Serosal involvement**

Serosal involvement has been shown to be an independent prognostic marker in multivariate analysis1 and has also been shown to be predictive of the likely site of cancer recurrence (peritoneal versus haematogenous).17

**Tumour classification and grading**

At least four different histological classification systems for gastric adenocarcinoma are in common use (Goseki, Lauren, Ming and the World Health Organization [WHO]). The Lauren classification (diffuse, intestinal and mixed types) is probably the most widely used, but the Ming classification (expansive and infiltrative) is perhaps the most prognstically useful.13,18 For the dataset, it is suggested that the Lauren classification system be utilised, as British pathologists are most familiar with this system. The degree of tumour differentiation (well and moderately versus poorly differentiated) has also been shown to be an independent prognostic factor.19 In conformity with most other datasets, differentiation is assessed as being that of the highest grade in any part of the tumour.

**Resection margins**

Complete surgical removal of invasive tumour is the primary aim of curative surgery, with surgical resection still considered the only potentially curative option.20 Complete macroscopic and microscopic resection of tumour (R0 resection) has been shown to be one of the strongest significant and independent predictors of outcome.17 In all cases, the proximal and distal resection margins require histological exclusion of tumour involvement. In tumours arising at the cardia, there is also the
potential for involvement of the circumferential surgical resection margin (CRM) in the lower oesophagus. Involvement of the CRM has been shown to be a predictor of poor prognosis in oesophageal carcinoma (see also Dataset for the histopathological reporting of oesophageal carcinoma). If tumour extends into the lower oesophagus, the circumferential resection margin should be assessed and the closest distance tumour lies from this margin recorded in mm. If tumour (main tumour, soft tissue deposits or lymph node metastases) lies less than 1 mm from the circumferential margin, this margin is considered to be microscopically involved by tumour (R1).

**Lymph node status**

Lymph node involvement has been shown in several studies to be one of the strongest prognostic indicators in gastric cancer. Over recent years, there has been a shift from simple lymphadenectomy to radical lymphadenectomy. Many studies show that there is a long-term survival advantage in having a radical lymph node dissection (D2 or D3) over simple local lymphadenectomy (D1).

**Lymphatic, vascular and perineural invasion**

In gastric carcinoma, univariant analyses have demonstrated that the presence of perineural, lymphatic and vascular invasion are all associated with a poor prognosis. However, perineural invasion was not found to be an independent prognostic factor in multivariate analysis. Results for lymphatic and vascular invasion are variable, with some multivariate analysis studies showing them to be independent prognostic factors, but a recent large study failed to confirm these results.

### NON-CORE DATA ITEMS

**Macroscopic**

- **Specimen dimensions:** The overall dimensions of the specimen and the lengths of stomach (greater and lesser curve) and oesophagus/duodenum should be recorded in millimetres.

**Microscopic**

- Presence of glandular atrophy
- Presence of intestinal metaplasia
- Presence of dysplasia
- Presence of Helicobacter Pylori

**Other**

- Effects of neoadjuvant therapy (if applicable)
- Molecular data (if applicable)

**Neoadjuvant treatment**

There is growing evidence that neoadjuvant chemotherapy and possibly neoadjuvant chemoradiotherapy have a part to play in the treatment of operable gastric carcinoma. In the UK, the use of neoadjuvant chemotherapy is expanding and reliable data regarding its effects will inevitably be useful for future audits.

### DIAGNOSTIC CODING

**TNM Classification of gastric tumours**

Between the 5th and 6th editions of the TNM Classification of Malignant Tumours, there have been some changes in the criteria for reporting lymph node metastases. Many histopathologists in the UK
are unhappy with these changes, suggesting that the new criteria are too subjective. The current recommendation for the revised colonic and oesophageal datasets is that TNM 5th edition criteria should be used in the assessment of lymph node metastases (see Appendix A). To allow continuity of reporting between gastrointestinal tumour sites, the same recommendations will be applied to the reporting of lymph nodes in gastric resection specimens.

The T staging of gastric carcinoma is out of kilter with other gastrointestinal tumour sites (pT3 being subserosal involvement in the oesophagus and colon, but serosal involvement in the stomach). In the TNM 5th edition, the pT2 stage includes a range of tumours from those just invading into the muscularis propria, to those invading right through the muscularis propria into the subserosa. The TNM 6th edition suggests a sub-division of pT2 into pT2a (invasion of muscularis propria) and pT2b (invasion of subserosa). These changes in TNM 6th edition will allow a more direct comparison of tumour stages between different gastrointestinal tumour sites and in the future may potentially be prognostically useful, so it is suggested that the TNM 6th edition pT staging is adopted for gastric tumours, but that connective tissue deposits continue to be classified using the TNM 5th edition rules (see Appendix A).

1) TNM 6th edition: pT staging (pT2a, pT2b) used for gastric tumours.
2) TNM 5th edition: pN staging used for gastric tumours.

SNOMED classification of gastric tumours

Gastric tumours should be classified using the SNOMED system (see Appendix B).

8 REPORTING OF SMALL BIOPSY SPECIMENS

In the clinical context of a gastric tumour/ulcer, the main role of the gastric biopsy is to confirm the diagnosis of adenocarcinoma and to exclude benign inflammatory causes of ulceration. Other, less common, differential diagnoses including carcinoid tumour/well differentiated endocrine carcinoma, lymphoma and gastrointestinal stromal tumour also need to be considered/excluded. Once the presence of adenocarcinoma is confirmed, an attempt to determine tumour differentiation (well/moderately versus poorly) and classify the tumour into Lauren types (intestinal, diffuse and mixed intestinal/diffuse) can be made. It should be noted that there can be marked morphological heterogeneity in gastric carcinomas so results from a small biopsy specimen cannot necessarily be extrapolated to the tumour as a whole. Clinicopathological/radiological correlation, usually in the context of a multidisciplinary team meeting, may be extremely useful here. Small biopsies can also be used to confirm the presence, and map the distribution, of dysplasia.

9 REPORTING OF FROZEN SECTIONS

There is wide variation in clinical practice in the use of frozen sections during gastric resections. Intra-operative frozen sections are not infrequently used to determine the nature of incidental small liver lesions (e.g. metastatic deposit versus bile duct hamartoma) or peritoneal/omental nodules. In some centres, frozen sections are also regularly used to examine surgical resection margins. The use of such frozen sections can be extremely helpful clinically, but it should be noted that small deposits of diffuse type gastric carcinoma may be extremely subtle and easily missed on frozen sections.

10 SPECIFIC ASPECTS OF INDIVIDUAL TUMOURS NOT COVERED ELSEWHERE

Not applicable.
REFERENCES


APPENDIX A  TNM CLASSIFICATION OF GASTRIC CANCERS

T – Primary tumour (based on TNM 6th edition)

The extent of direct spread through the stomach wall and beyond is one of the major determinants of prognosis. The levels of spread have been chosen to reflect the greatest changes in prognosis.

TX  Primary tumour cannot be assessed.
T0  No evidence of primary tumour.
Tis  Carcinoma in situ: intraepithelial tumour without invasion of lamina propria.
T1  Tumour invades lamina propria or submucosa.
T2a  Tumour invades muscularis propria.
T2b  Tumour invades muscularis propria and extends into subserosa.
T3  Tumour penetrates serosa (visceral peritoneum) without invasion of adjacent structures.
T4  Tumour invades adjacent structures.

‘Adjacent structures’ include transverse colon, spleen, liver, pancreas, abdominal wall, adrenal gland, kidney, small intestine and retroperitoneum. A carcinoma that extends into the omenta or gastric ligaments without penetrating through the visceral peritoneum covering these structures is still classified as pT2b. If there is penetration of the peritoneal aspect of the ligaments or omenta, the tumour is classified as pT3.

In the event of intramural tumour extension into the duodenum or oesophagus, the tumour is classified by the greatest depth of invasion in these sites and the stomach. In so far as the lower oesophagus lacks a peritoneal covering particular attention has to be paid to circumferential margin involvement. Involvement of the adventitia of the oesophagus is classified as pT3.
Lymph node metastases (based on TNM 5th edition)

Some confusion has arisen over the classification of lymph nodes in the new (6th edition) version of TNM.\(^3\) In this edition, a tumour nodule in the connective tissue is classified as a regional lymph node metastasis if it has the “form and smooth contour of a lymph node”. A tumour nodule with an irregular contour is classified in the pT category. Prior to this change, a tumour nodule was classified as a regional lymph node metastasis if it was larger than 3 mm in diameter, irrespective of its shape.

In conformity with the oesophageal and colorectal cancer datasets, it is suggested that TNM 5th edition criteria be applied for the assessment of lymph node metastases. These criteria are:

- A tumour nodule > 3 mm in connective tissue of a lymph drainage area without histologic evidence of a residual lymph node is classified in the pN category as a regional lymph node metastasis.
- Small tumour deposits in lymph nodes identified on routine microscopy (irrespective of size) are counted as lymph node metastases.

N – Regional lymph nodes

The regional lymph nodes are the perigastric nodes along the lesser and greater curvatures and the nodes along the left gastric, common hepatic, hepatoduodenal, splenic and coeliac arteries. Depending upon their degree of spread tumours are graded:

- **N0**  No regional node involvement
- **N1**  Involvement of 1–6 regional nodes
- **N2**  Involvement of 7–15 regional lymph nodes
- **N3**  Involvement of more than 15 regional lymph nodes

Ideally at least 15 nodes should be the recovered from a gastric cancer resection specimen, but the possible yield will depend upon the type of surgical resection performed.
M – Distant metastasis

Involvement of non-regional intra-abdominal lymph nodes such as retro-pancreatic, mesenteric and para-aortic groups is considered to be distant metastasis (M1).

Involvement of the liver or the presence of peritoneal seedlings is also staged as M1.

Residual tumour

The presence or absence of residual tumour is described using the symbol R.

R0  No residual tumour
R1  Microscopic residual tumour
R2  Macroscopic residual tumour

Neoadjuvant therapy

If there is a history of neoadjuvant chemotherapy, radiotherapy or combined chemoradiotherapy, the prefix y should be added to the TMN stage (e.g. ypT2bN1Mx). Following neoadjuvant therapy, the presence of fibrosis, haemorrhage, necrosis or acellular mucin is not considered in tumour staging. Only viable tumour/tumour cells are assessed for staging. A specimen in which no tumour is identified following neoadjuvant treatment is staged as ypT0N0Mx.
APPENDIX B  SNOMED codes

SNOMED T codes
T-63000  Stomach
T-62359  Gastro-oesophageal junction
T-63700  Pylorus

SNOMED M codes
M-73000  Metaplasia
M-74000  Dysplasia
M-81402  Adenocarcinoma \textit{in situ}
M-81403  Adenocarcinoma
M-84803  Adenocarcinoma, mucinous
M-80103  Carcinoma
M-80203  Undifferentiated carcinoma

SNOMED P codes
P-1100  Resection
P-1101  Local excision
P-1140  Biopsy
APPENDIX C  Reporting proforma

NATIONAL DATASET FOR GASTRIC CARCINOMA HISTOPATHOLOGY REPORTS

Surname .........................................................  Forenames ................................................  Date of birth .............................
Hospital ..........................................................  Hospital no ...............................................  NHS no ..............................
Date of receipt ...............................................  Date of reporting ......................................  Report no ...........................
Pathologist ........................................................  Surgeon ....................................................  Sex ....................................

GROSS DESCRIPTION

Type of specimen
- Oesophago-gastrectomy
- Distal gastrectomy
- Total gastrectomy
- Local resection

Type of tumour
- Polypoid, ulcerating or fungating
- Diffusely infiltrating

Specimen dimensions
- Length of stomach - greater curve
- Length of stomach - lesser curve
- Length of oesophagus
- Length of duodenum

Site of tumour

Maximum tumour diameter

Distance of tumour to nearest margin (cut end)

HISTOLOGY

Type of tumour
- Adenocarcinoma
- Other (specify)

Lauren classification
- Intestinal
- Diffuse/mixed

Differentiation by worst area
- Well/moderately
- Poorly

Local invasion
- T0 No tumour identified
- Tis Carcinoma in situ
- T1 Invasion of lamina propria/submucosa
- T2a Invasion of muscularis propria
- T2b Invasion into subserosa
- T3 Invasion of serosa
- T4 Invasion of adjacent structures

Proximal margin involved
- Yes
- No

Distal margin involved
- Yes
- No

Circumferential margin lower oesophagus
- Involvement (< 1 mm): Yes
- N/A

Lymphatic/vascular invasion
- Yes
- No

Lymph nodes
- Number examined
- Number positive
- N0 (0 nodes)
- N2 (7–15 nodes)
- N1 (1–6 nodes)
- N3 (>15 nodes)

Distant metastases
- Unknown (MX)
- Yes (M1)

PATHOLOGICAL STAGING

Complete resection
- Yes (R0)
- No (R1 or R2)

History of neoadjuvant therapy (y)
- Yes
- No

TNM (y)….. pT N M

Signature……………………………… Date……/……/……… SNOMED codes T…………/M………..
DATASET FOR
OESOPHAGEAL CARCINOMA HISTOPATHOLOGY REPORTS
AMENDED VERSION FOR PAN BIRMINGHAM CANCER NETWORK

Surname .........................................................  Forenames ................................................  Date of birth ......................
Hospital ..........................................................  Hospital no ...............................................  NHS no ..............................
Date of receipt ...............................................  Date of reporting .................................  Report no ...........................
Pathologist .....................................................  Surgeon ....................................................  Sex ....................................
______________________________________________________________________________________________

Shaded data items = ‘non core’ data

GROSS DESCRIPTION

<table>
<thead>
<tr>
<th>Maximum length of specimen:</th>
<th>mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of oesophagus:</td>
<td>mm</td>
</tr>
<tr>
<td>Length of stomach:</td>
<td>mm</td>
</tr>
<tr>
<td>Length of tumour:</td>
<td>mm</td>
</tr>
<tr>
<td>Width of tumour:</td>
<td>mm</td>
</tr>
</tbody>
</table>

Tumour edge to nearest distal margin: ............. mm
Tumour edge to nearest proximal margin: ........... mm

Type of tumour
- Polypoid
- Other
- Pinned
- Not pinned

Siewert tumour type (cardiac cancers only)
- 1
- 2

HISTOLOGY

Type of tumour
- Squamous
- Adenocarcinoma
- Other (specify) ..........................................................

Differentiation by worst area:
- Well
- Moderately
- Poorly differentiated

Depth of invasion
- Tis high-grade dysplasia
- T1 invasion of lamina propria/submucosa
  - A lamina propria
  - B sub-mucosa
- T2 invasion of muscularis propria
- T3 invasion beyond muscularis propria
- T4 invasion of adjacent structures
- Yes
- No – serosal involvement:

Proximal margin
- Normal
- Dysplasia
- Carcinoma
- Barrett’s

Distal margin
- Normal
- Dysplasia
- Carcinoma

Circumferential margin
- Distance of carcinoma to nearest circumferential margin
  - A/ More than 1 mm
  - B/ Less than 1 mm
  - C/ 0 mm

Other features
- Vascular invasion
- Yes
- No
- Barrett’s metaplasia
- Yes
- No

Adjacent to tumour

Lymph nodes
- Number examined…………..  Number positive…………
  (N0 if no nodes positive, otherwise N1)

Distant metastases
- Coeliac axis node positive
- Yes
- No
- (M1a if lower thoracic carcinoma, otherwise M1b)
- Cervical node positive
- Yes
- No
- (M1a if upper thoracic carcinoma, otherwise M1b)
- Other distant metastasis (M1b)
- Yes
- No

COMMENTS

______________________________________________________________________________________________

PATHOLOGICAL STAGING

Complete resection
- Yes(R0)
- No(R1B or R2)

(y) $pT$…… $pN$…… $pM$……  TNM 5th edition

(y) $pT$…… $pN$……(i +/-) $pM$……  TNM 6th edition

Signature ..........................................................  Date ................/...../.....

SNOMED codes $T$ ........... / $M$ ...........