The Royal College of Pathologists

Pathology: the science behind the cure

Standards and Datasets for Reporting Cancers

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

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January 2007

Unique document number	G013
Document name	Dataset for the histopathological reporting of gastric carcinoma
Version number	2
Produced by	Professor Marco R Novelli, Working Group on Cancer Services
Date active	January 2007
Date for review	January 2009
Comments	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 publications@rcpath.org if you would like to see the feedback received. **Professor Carrock Sewell** **Director of Publications**

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CONTENTS

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[1]

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.[2] 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[3] 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 neoadjuvent 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 analysis[1] 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 prognostically 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*).[21] 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.[13,17,22] Over recent years, there has been a shift from simple lymphadenectomy to radical lymphadenectomy.[23] 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).[17,24,25]

Lymphatic, vascular and perineural invasion

In gastric carcinoma, univariant analyses have demonstrated that the presence of perineural,[26] lymphatic[13,19] and vascular invasion[12,13,19] are all associated with a poor prognosis. However, perineural invasion was not found to be an independent prognostic factor in multivariate analysis.[26] Results for lymphatic and vascular invasion are variable, with some multivariate analysis studies showing them to be independent prognostic factors,[12,19] but a recent large study failed to confirm these results.[13]

6 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[27] and possibly neoadjuvant chemoradiotherapy[1] 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.

7 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).[2] 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.

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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.

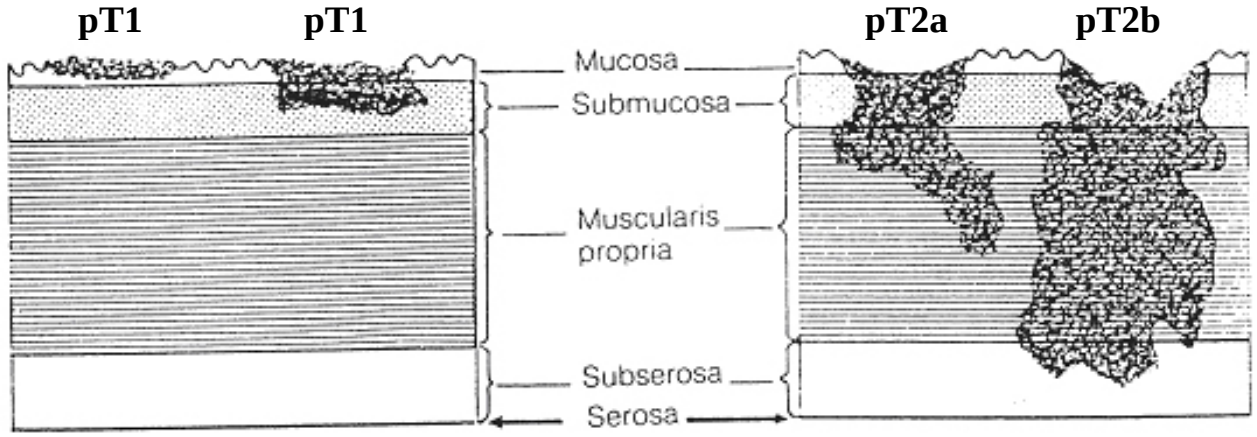
T2b Tumour invades muscularis propria and extends into subserosa.

T3 Tumour penetrates serosa (visceral peritoneum) without invasion of adjacent structures.

T4 Tumour invades adjacent structures.

'Adjacent structures' include transverse colon, spleen, liver, pancreas, adominal wall, adrenal gland, kidney, small intestine and retroperitoneum. A carcinoma that extends into the omenta or gastric ligaments without penetrating through the visceral peritineum 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.



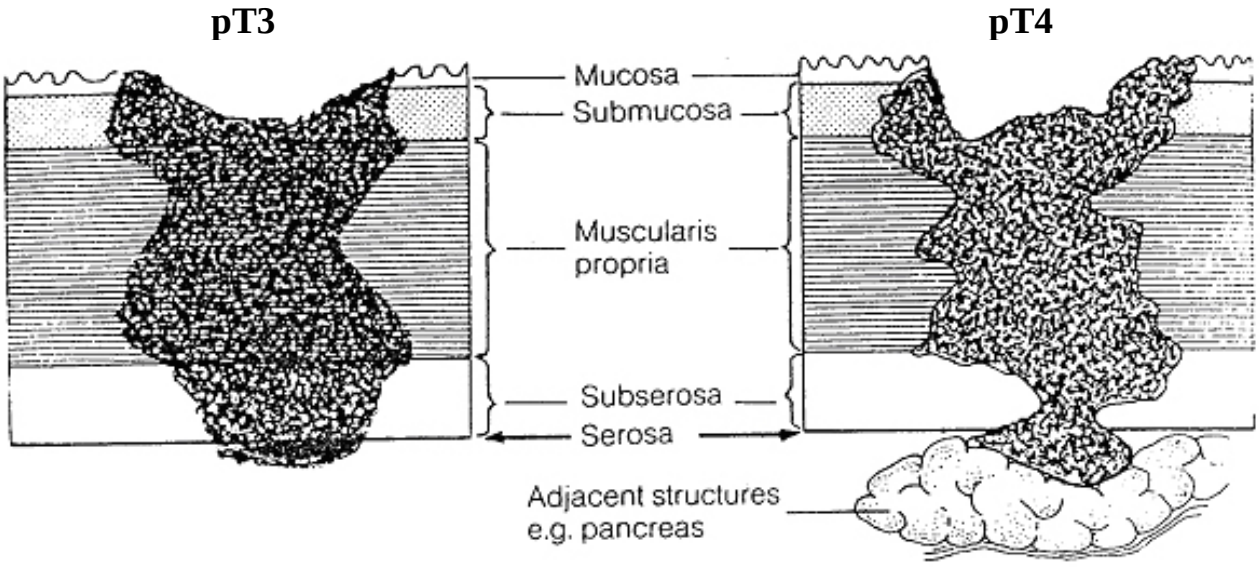


Diagram adapted from Sobin LH, Wittekind Ch (editors). *TNM Classification of Malignant Tumours (5th edition).* New York: John Wiley & Sons, Inc., 1997, pp. 84–86. Reprinted by permission of Wiley-Liss, Inc., a division of John Wiley & Sons, Inc.

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. **y**pT2bN1Mx). 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 *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 ..... mm

Length of stomach - lesser curve ..... mm

Length of oesophagus ..... mm

Length of duodenum ..... mm

Site of tumour .....

Maximum tumour diameter …….....mm

Distance of tumour to nearest margin (cut end)

……....mm

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 ☐ No ☐ N/A ☐

(If no, distance of tumour to nearest circumferential margin .....… mm)

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……..…