Stomach

Protocol applies to all invasive carcinomas of the stomach.

Protocol revision date: January 2004
Based on AJCC/UICC TNM, 6th edition

Procedures

- **Cytology** (No Accompanying Checklist)
- **Incisional Biopsy (Endoscopic or Other)**
- **Excisional Biopsy/Polypectomy**
- **Local Excision**
- **Gastrectomy (Partial or Complete)**

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Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2004
Applies to invasive carcinomas only
Based on AJCC/UICC TNM, 6th edition

*STOMACH: Biopsy

(Note: Use of checklist for biopsy specimens is optional)

*Patient name:
*Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

***MACROSCOPIC**

***Specimen Type**
*___ Incisional biopsy
*___ Excisional biopsy (polypectomy)
*___ Other (specify): _____
*___ Not specified

***Tumor Site**
*Specify, if known: _____
*___ Not specified

***MICROSCOPIC**

***Histologic Type**
*___ Adenocarcinoma, intestinal type
*___ Adenocarcinoma, diffuse type
*___ Papillary adenocarcinoma
*___ Tubular adenocarcinoma
*___ Mucinous adenocarcinoma (greater than 50% mucinous)
*___ Signet-ring cell carcinoma (greater than 50% signet-ring cells)
*___ Other (specify): _____
*___ Carcinoma, type cannot be determined

* Data elements ***with asterisks*** are ***not required*** for accreditation purposes for the Commission on Cancer. These elements may be clinically important, but are not yet validated or regularly used in patient management. Alternatively, the necessary data may not be available to the pathologist at the time of pathologic assessment of this specimen.

***Histologic Grade**
*___ Not applicable
*___ GX: Cannot be assessed
*___ G1: Well differentiated
*___ G2: Moderately differentiated
*___ G3: Poorly differentiated
*___ G4: Undifferentiated
*___ Other (specify): _____

***Extent of Invasion (deepest)**
*___ Cannot be determined
*___ Lamina propria
*___ Muscularis mucosae
*___ Submucosa
*___ Muscularis propria

***Margins (polypectomy only)**

*___ Not applicable

*Mucosal Margin
*___ Cannot be assessed
*___ Uninvolved by invasive carcinoma
*___ Involved by invasive carcinoma
*___ Involved by adenoma

*Deep Margin
*___ Cannot be assessed
*___ Uninvolved by invasive carcinoma
*Distance of invasive carcinoma from margin: ___ mm
*___ Involved by invasive carcinoma

***Additional Pathologic Findings (check all that apply)**
*___ None identified
*___ Intestinal metaplasia
*___ Dysplasia
*___ Gastritis (type): _____
*___ Other (specify): _____

***Comment(s)**

Surgical Pathology Cancer Case Summary (Checklist)

Protocol revision date: January 2004
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STOMACH: Resection

Patient name:
Surgical pathology number:

Note: Check 1 response unless otherwise indicated.

MACROSCOPIC

Specimen Type
___ Partial gastrectomy
___ Partial gastrectomy, proximal
___ Partial gastrectomy, distal
___ Partial gastrectomy, other (specify): _____
___ Total gastrectomy
___ Other (specify): _____
___ Not specified

Tumor Site (check all that apply)
___ Cardia
___ Fundus
*___ Anterior wall
*___ Posterior wall
___ Body
*___ Anterior wall
*___ Posterior wall
*___ Lesser curvature
*___ Greater curvature
___ Antrum
*___ Anterior wall
*___ Posterior wall
*___ Lesser curvature
*___ Greater curvature
___ Other (specify): _____
___ Not specified

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***Tumor Configuration**
*___ Exophytic (polypoid)
*___ Infiltrative
*___ Diffusely infiltrative (linitis plastica)
*___ Expansile (noninfiltrative)
*___ Ulcerating
*___ Annular

Tumor Size
Greatest dimension: ___ cm
*Additional dimensions: ___ x ___ cm
___ Cannot be determined (see Comment)

MICROSCOPIC

Histologic Type
___ Adenocarcinoma, intestinal type
___ Adenocarcinoma, diffuse type
___ Papillary adenocarcinoma
___ Tubular adenocarcinoma
___ Mucinous adenocarcinoma (greater than 50% mucinous)
___ Signet-ring cell carcinoma (greater than 50% signet-ring cells)
___ Other (specify): _____
___ Carcinoma, type cannot be determined

Histologic Grade
___ Not applicable
___ GX: Cannot be assessed
___ G1: Well differentiated
___ G2: Moderately differentiated
___ G3: Poorly differentiated
___ G4: Undifferentiated
___ Other (specify): _____

Pathologic Staging (pTNM)

Primary Tumor (pT)
___ pTX: Cannot be assessed
___ pT0: No evidence of primary tumor
___ pTis: Carcinoma in situ
pT1: Tumor invades lamina propria or submucosa
___ pT1a: Tumor invades lamina propria
___ pT1b: Tumor invades submucosa
pT2: Tumor invades muscularis propria or subserosa
___ pT2a: Tumor invades muscularis propria
___ pT2b: Tumor invades subserosa

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___ pT3: Tumor penetrates serosa (visceral peritoneum) without invasion of adjacent structures
___ pT4: Tumor directly invades adjacent structures

Regional Lymph Nodes (pN)
___ pNX: Cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: Metastasis in 1 to 6 perigastric lymph nodes
___ pN2: Metastasis in 7 to 15 perigastric lymph nodes
___ pN3: Metastasis in greater than 15 perigastric lymph nodes
Specify: Number examined: ___
Number involved: ___

Distant Metastasis (pM)
___ pMX: Cannot be assessed
___ pM1: Distant metastasis
*Specify site(s), if known: _____

Margins (check all that apply)

Proximal Margin
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
___ Involved by invasive carcinoma
___ Carcinoma in situ/adenoma absent at proximal margin
___ Carcinoma in situ/adenoma present at proximal margin

Distal Margin
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
___ Involved by invasive carcinoma
___ Carcinoma in situ/adenoma absent at distal margin
___ Carcinoma in situ/adenoma present at distal margin

Omental (Radial) Margins
___ Cannot be assessed
___ Uninvolved by invasive carcinoma
___ Lesser omental margin involved by invasive carcinoma
___ Greater omental margin involved by invasive carcinoma

If margins are uninvolved:
Distance of invasive carcinoma from closest margin: ___ mm
Specify margin: _____

***Lymphatic (Small Vessel) Invasion (L)**
*___ Absent
*___ Present

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*___ Indeterminate

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***Venous (Large Vessel) Invasion (V)**
*___ Absent
*___ Present
*___ Indeterminate

***Perineural Invasion**
*___ Absent
*___ Present

***Additional Pathologic Findings (check all that apply)**
*___ None identified
*___ Intestinal metaplasia
*___ Dysplasia
*___ Gastritis (type): _____
*___ Polyp(s) (type[s]): _____
*___ Other (specify): _____

***Comment(s)**

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Background Documentation

Protocol revision date: January 2004

I. Cytologic Material

A. Clinical Information

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
   d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history
      (1) previous diagnoses and treatment for gastric cancer
      (2) previous Billroth procedure
      (3) *Helicobacter pylori* gastritis
      (4) atrophic gastritis
   b. Relevant findings (eg, endoscopic/imaging studies)
   c. Clinical diagnosis
   d. Procedure (eg, brushing, washing, other)
   e. Anatomic site(s) of specimen(s)

B. Macroscopic Examination

1. Specimen
   a. Unfixed/fixed (specify fixative)
   b. Number of slides received, if appropriate
   c. Quantity and appearance of fluid specimen, if appropriate
   d. Other (eg, cytologic preparation from tissue)
   e. Results of intraprocedural consultation
2. Material submitted for microscopic evaluation
3. Special studies (specify) (eg, cytochemistry, immunocytochemistry, DNA analysis [specify type], cytogenetic analysis)

C. Microscopic Evaluation

1. Adequacy of specimen (if unsatisfactory for evaluation, specify reason)
2. Tumor, if present
   a. Histologic type, if possible (Note **A**)
   b. Histologic grade, if possible (Note **B**)
   c. Other characteristics (eg, nuclear grade/necrosis)
3. Additional pathologic findings, if present
4. Results/status of special studies (specify)
5. Comments
   a. Correlation with intraprocedural consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

II. Incisional Biopsy
(Endoscopic or Other)

A. Clinical Information
1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
   d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history
      (1) previous diagnoses and treatment for gastric cancer
      (2) previous Billroth procedure
      (3) *Helicobacter pylori* gastritis
      (4) atrophic gastritis
   b. Relevant findings (eg, endoscopic/imaging studies)
   c. Clinical diagnosis
   d. Procedure (eg, endoscopic biopsy)
   e. Operative findings
   f. Anatomic site(s) of specimen(s)

B. Macroscopic Examination
1. Specimen
   a. Unfixed/fixed (specify fixative)
   b. Number of pieces
   c. Largest dimension of each piece
   d. Results of intraoperative consultation
2. Tissues submitted for microscopic evaluation
   a. Submit entire specimen
   b. Frozen section tissue fragment(s) (unless saved for special studies)
3. Special studies (specify) (eg, histochemistry, immunohistochemistry, morphometry, DNA analysis [specify type], cytogenetic analysis)

C. Microscopic Evaluation
1. Tumor
   a. Histologic type (Note **A**)
   b. Histologic grade (Note **B**)
   c. Extent of invasion
   d. Venous/lymphatic vessel invasion
2. Additional pathologic findings, if present
   a. Dysplasia
   b. Metaplasia
   c. Atrophy
   d. Gastritis
   e. *Helicobacter pylori*
   f. Other(s)
3. Results of special studies (specify)
4. Comments
   a. Correlation with intraoperative consultation, as appropriate
   b. Correlation with other specimens, as appropriate

c. Correlation with clinical information, as appropriate

III. Excisional Biopsy
(Local Excision or Polypectomy)

A. Clinical Information

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
   d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history
      (1) previous diagnoses and treatment for gastric cancer
      (2) previous Billroth procedure
      (3) *Helicobacter pylori* gastritis
      (4) atrophic gastritis
   b. Relevant findings (eg, endoscopic/imaging studies)
   c. Clinical diagnosis
   d. Procedure (eg, polypectomy)
   e. Operative findings
   f. Anatomic site(s) of specimen(s)

B. Macroscopic Examination

1. Specimen
   a. Unfixed/fixed (specify fixative)
   b. Number of pieces
   c. Descriptive features (eg, color, consistency)
   d. Dimensions
   e. Layers of stomach present, if grossly discernible
   f. Orientation, if indicated by surgeon
   g. Results of intraoperative consultation
2. Tumor
   a. Configuration, if appropriate (Note **C**)
   b. Dimensions (3) (Note **D**)
   c. Distance from closest margin
   d. Estimated depth of invasion (Note **E**)
3. Lesions in noncancerous stomach, if appropriate (eg, ulcers, polyps, other)
4. Tissue(s) submitted for microscopic evaluation
   a. Carcinoma, including
      (1) point of deepest penetration
      (2) interface with adjacent stomach
      (3) margin closest to tumor edge
      (4) (if a polyp) apex and stalk in same section, if possible
   b. Frozen section tissue fragment(s) (unless saved for special studies)
5. Special studies (specify) (eg, histochemistry, immunohistochemistry, morphometry, DNA analysis [specify type], cytogenetic analysis)

C. Microscopic Evaluation

1. Tumor

   a. Histologic type (Note **A**)
   b. Histologic grade (Note **B**)
   c. Extent of invasion (Note **E**)
   d. Venous/lymphatic vessel invasion (Note **F**)
   e. Perineural invasion (Note **G**)
2. Carcinoma in a polyp
   a. Specify histologic type of polyp
   b. Specify presence/absence of invasion of:
      (1) muscularis mucosae/submucosa of polyp head
      (2) submucosa at base
      (3) venous/lymphatic vessels (Note **F**)
3. Margins
   a. Distance from closest mucosal margin and deep margin
   b. Presence of metaplasia/dysplasia/adenoma
4. Additional pathologic findings, if present
   a. Dysplasia
   b. Metaplasia
   c. Atrophy
   d. Gastritis
   e. *Helicobacter pylori*
   f. Other(s)
5. Results/status of special studies (specify)
6. Comments
   a. Correlation with intraoperative consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

IV. Gastric Resection

A. Clinical Information

1. Patient identification
   a. Name
   b. Identification number
   c. Age (birth date)
   d. Sex
2. Responsible physician(s)
3. Date of procedure
4. Other clinical information
   a. Relevant history
      (1) previous diagnoses and treatment for gastric cancer
      (2) previous Billroth procedure
      (3) *Helicobacter pylori* gastritis
      (4) atrophic gastritis
   b. Relevant findings (eg, endoscopic/imaging studies)
   c. Clinical diagnosis
   d. Procedure (eg, subtotal gastrectomy, total gastrectomy, other)
   e. Operative findings
   f. Anatomic site(s) of specimen(s)

B. Macroscopic Examination

1. Specimen

   a. Organ(s)/tissue(s) included
   b. Unfixed/fixed (specify fixative)
   c. Open/unopened
   d. Number of pieces
   e. Dimensions (Note **H**)
   f. Length of attached esophagus/duodenum
   g. Orientation, if indicated by surgeon
   h. Results of intraoperative consultation
2. Tumor
   a. Location (Note **I**)
   b. Configuration (Note **C**)
   c. Dimensions (3) (Note **D**)
   d. Descriptive features (eg, color, consistency)
   e. Ulceration/perforation
   f. Distance from margins (Note **J**)
      (1) proximal
      (2) distal
      (3) radial (soft tissue and/or mesenteric margin(s) closest to deepest tumor penetration)
   g. Estimated depth of invasion (Note **E**)
3. Lesions in noncancerous stomach
   a. Ulcers
   b. Polyps
   c. Other(s)
4. Regional lymph nodes (Notes **E** and **K**)
5. Metastasis to other organ(s) or structure(s) (Notes **E** and **K**)
6. Tissues submitted for microscopic evaluation
   a. Carcinoma, including
      (1) point of deepest penetration
      (2) interface with adjacent stomach
      (3) visceral serosa overlying tumor
   b. Margins (Note **G**)
      (1) proximal
      (2) distal
      (3) radial (soft tissue and/or mesenteric margin(s) closest to deepest tumor penetration)
   c. All lymph nodes (Notes **E** and **K**)
      (1) specify node(s) when labeled by surgeon
   d. Other lesions (eg, polyps/ulcers)
   e. Stomach uninvolved by tumor
   f. Other tissue(s)/organ(s)
   g. Frozen section tissue fragments (unless saved for special studies)
7. Special studies (specify) (eg, histochemistry, immunohistochemistry, morphometry, DNA analysis [specify type], cytogenetic analysis)

C. Microscopic Evaluation

1. Tumor
   a. Histologic type (Note **A**)
   b. Histologic grade (Note **B**)
   c. Extent of invasion (Note **E**)

   d. Extension into esophagus or duodenum
   e. Venous/lymphatic vessel invasion (Note **F**)
   f. Perineural invasion (Note **G**)
2. Additional pathologic findings, if present
   a. Chronic gastritis (type)
   b. Intestinal metaplasia
   c. Dysplasia
   d. Atrophy
   e. Adenoma
   f. Other types of polyps
   g. *Helicobacter pylori*
   h. Other
3. Margins (Note **J**)
   a. Proximal
   b. Distal
   c. Radial
4. Regional lymph nodes (Note **K**)
   a. Number
   b. Number involved by tumor
5. Distant metastasis (specify site[s]) (Note **K**)
6. Other tissue(s)/organ(s)
7. Results/status of special studies (specify)
8. Comments
   a. Correlation with intraoperative consultation, as appropriate
   b. Correlation with other specimens, as appropriate
   c. Correlation with clinical information, as appropriate

Explanatory Notes

A. Histologic Type

For consistency in reporting, the histologic classification proposed by the World Health Organization (WHO) is recommended.[1] However, this protocol does not preclude the use of other systems of classification or histologic types, such as the Laurén classification,[2] which may be used in addition to the WHO system.

With the exception of the rare small cell carcinoma of the stomach, which has an unfavorable prognosis, most multivariate analyses show no effect of tumor type, independent of stage, on prognosis.[3]

WHO Classification of Carcinoma of the Stomach

Adenocarcinoma
    Intestinal type
    Diffuse type
Papillary adenocarcinoma[#]
Tubular adenocarcinoma[#]
Mucinous adenocarcinoma (greater than 50% mucinous)
Signet-ring cell carcinoma[#] (greater than 50% signet-ring cells)
Adenosquamous carcinoma
Squamous cell carcinoma

Small cell carcinoma[#]
Undifferentiated carcinoma[#]
Other (specify)

[#] Not usually graded (see below).

The Laurén classification, namely intestinal or diffuse type, and/or the Ming classification, namely expanding or infiltrating type, may also be included. The WHO classifies in situ carcinoma as intraepithelial neoplasia. The term "carcinoma, NOS (not otherwise specified)" is not part of the WHO classification.

B. Histologic Grade
For adenocarcinomas, a histologic grade is based on the extent of glandular differentiation is suggested as shown below.

Grade X	Cannot be assessed
Grade 1	Well differentiated (greater than 95% of tumor composed of glands)
Grade 2	Moderately differentiated (50% to 95% of tumor composed of glands)
Grade 3	Poorly differentiated (49% or less of tumor composed of glands)

Tubular adenocarcinomas are not typically graded but are low-grade and would correspond to grade 1.

Signet-ring cell carcinomas are not typically graded but are high-grade and would correspond to grade 3.

Small cell carcinomas and undifferentiated carcinomas are not typically graded but are high-grade tumors and would correspond to grade 4.

For squamous cell carcinomas (rare), a suggested histologic grading system is shown below.

Grade X	Grade cannot be assessed
Grade 1	Well differentiated
Grade 2	Moderately differentiated
Grade 3	Poorly differentiated

Note: Undifferentiated tumors cannot be specifically categorized as adenocarcinoma or squamous cell carcinoma. Instead, they are classified as undifferentiated carcinoma by the WHO classification and may be assigned grade 4 (see Note **A**).

For all stage groupings, grading correlates with outcome.[4,5]

C. Configuration
Macroscopic configuration types as described by Borrmann include polypoid (Borrmann type I), ulcerating (Borrmann type II), ulcerating and infiltrating (Borrmann type III), and diffusely infiltrating (Borrmann type IV or linitis plastica). Tumor configuration has been shown to have prognostic significance in several large studies.[3] Specifically, polypoid and ulcerating cancers (Borrmann types I and II) have a better prognosis than

infiltrating cancer (Borrmann types III and IV). However, the prognostic value of tumor configuration is controversial since numerous smaller studies have failed to demonstrate independent prognostic significance for this pathologic feature.

D. Tumor Size

Although not a factor in the T classification of gastric carcinoma (see Note **E**), tumor size has been shown to be an independent adverse prognostic factor in many studies.[3] However, the prognostic value of tumor size is controversial since a large number of other studies have failed to demonstrate independent prognostic significance for this pathologic feature.

E. TNM and Stage Groupings

The TNM staging system for gastric carcinoma of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) is recommended and shown below.[6,7]

By AJCC/UICC convention, the designation "T" refers to a primary tumor that has not been previously treated. The symbol "p" refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathologic staging is usually performed after surgical resection of the primary tumor. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumor has been completely removed. If a biopsied tumor is not resected for any reason (eg, when technically unfeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

Primary Tumor (T)

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ: intraepithelial tumor without invasion of the lamina propria
T1	Tumor invades lamina propria or submucosa
T1a	Tumor invades lamina propria[#]
T1b	Tumor invades submucosa[#]
T2	Tumor invades muscularis propria or subserosa[##]
T2a	Tumor invades muscularis propria
T2b	Tumor invades subserosa
T3	Tumor penetrates serosa (visceral peritoneum) without invasion of adjacent structures[###]
T4	Tumor directly invades adjacent structures^

[#] An optional expansion of T1 is proposed by the UICC based on the observed difference in frequency of lymph node metastasis. In addition, the substratifications may be important as indicators for treatment by limited procedures.[8]

[##] Separation of T2 into T2a and T2b is justified because postsurgical survival following resection for cure has been shown to be significantly different for T2a and T2b (see below).[8]

	2-Year Survival Rate	**5-Year Survival Rate**	**Median Survival Rate (Months)**
pT2a	74%	62%	119
pT2b	57%	40%	36

[###] A tumor may penetrate the muscularis propria with extension into the gastrocolic or gastrohepatic ligaments or into the greater or lesser omentum without perforation of the visceral peritoneum covering these structures. In this case the tumor would be classified as T2. If there is perforation of the visceral peritoneum covering the gastric ligaments or omenta, the tumor is classified as T3.

^ The adjacent structures of the stomach are the spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine, and retroperitoneum. Intramural extension into the duodenum or esophagus is classified by the depth of greatest invasion in any of these sites, including the stomach.

Regional Lymph Nodes (N) (also see Note **K**)
NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis[#]
N1 Metastasis in 1 to 6 perigastric lymph nodes
N2 Metastasis in 7 to 15 perigastric lymph nodes
N3 Metastasis in more than 15 lymph nodes

[#] A designation of N0 should be used if all examined lymph nodes are negative, regardless of the total number removed and examined.[6]

Regional Lymph Nodes (pN0): Isolated Tumor Cells
Isolated tumor cells (ITCs) are single cells or small clusters of cells not more than 0.2 mm in greatest dimension. Lymph nodes or distant sites with ITCs found by either histologic examination, immunohistochemistry, or nonmorphologic techniques (eg, flow cytometry, DNA analysis, polymerase chain reaction [PCR] amplification of a specific tumor marker) should be classified as N0 or M0, respectively. Specific denotation of the assigned N category is suggested as follows for cases in which ITCs are the only evidence of possible metastatic disease.[8,9]

pN0 No regional lymph node metastasis histologically, no examination for isolated tumor cells (ITCs)
pN0(i-) No regional lymph node metastasis histologically, negative morphologic (any morphologic technique, including hematoxylin-eosin and immunohistochemistry) findings for ITCs

pN0(i+)	No regional lymph node metastasis histologically, positive morphologic (any morphologic technique, including hematoxylin-eosin and immunohistochemistry) findings for ITCs
pN0(mol-)	No regional lymph node metastasis histologically, negative nonmorphologic (molecular) findings for ITCs
pN0(mol+)	No regional lymph node metastasis histologically, positive nonmorphologic (molecular) findings for ITCs

Distant Metastasis (M)

MX	Presence of distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Stage Groupings

Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage 1B	T1	N1	M0
	T2a/b	N0	M0
Stage II	T1	N2	M0
	T2a/b	N1	M0
	T3	N0	M0
Stage IIIA	T2a/b	N2	M0
	T3	N1	M0
	T4	N0	M0
Stage IIIB	T3	N2	M0
Stage IV	T4	N1-3	M0
	T1-3	N3	M0
	Any T	Any N	M1

TNM Descriptors

For identification of special cases of TNM or pTNM classifications, the "m" suffix and "y," "r," and "a" prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The "m" suffix indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

The "y" prefix indicates those cases in which classification is performed during or following initial multimodality therapy (ie, neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a "y" prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The "y" categorization is not an estimate of tumor prior to multimodality therapy (ie, before initiation of neoadjuvant therapy).

The "r" prefix indicates a recurrent tumor when staged after a documented disease-free interval, and is identified by the "r" prefix: rTNM.

The "a" prefix designates the stage determined at autopsy: aTNM.

Additional Descriptors

Residual Tumor (R)

Tumor remaining in a patient after therapy with curative intent (eg, surgical resection for cure) is categorized by a system known as R classification, shown below.[10]

RX Presence of residual tumor cannot be assessed
R0 No residual tumor
R1 Microscopic residual tumor
R2 Macroscopic residual tumor

For the surgeon, the R classification may be useful to indicate the known or assumed status of the completeness of a surgical excision. For the pathologist, the R

classification is relevant to the status of the margins of a surgical resection specimen. That is, tumor involving the resection margin on pathologic examination may be assumed to correspond to residual tumor in the patient and may be classified as macroscopic or microscopic according to the findings at the specimen margin(s).

Vessel Invasion
By AJCC/UICC convention, vessel invasion (lymphatic or venous) does not affect the T category indicating local extent of tumor unless specifically included in the definition of a T category. In all other cases, lymphatic and venous invasion by tumor are coded separately as follows.

Lymphatic Vessel Invasion (L)
LX Lymphatic vessel invasion cannot be assessed
L0 No lymphatic vessel invasion
L1 Lymphatic vessel invasion

Venous Invasion (V)
VX Venous invasion cannot be assessed
V0 No venous invasion
V1 Microscopic venous invasion
V2 Macroscopic venous invasion

F. Venous/Lymphatic Vessel Invasion
Both venous and lymphatic vessel invasion have been shown to be adverse prognostic factors.[3,11] However, the microscopic presence of tumor in lymphatic vessels or veins does not qualify as local extension of tumor as defined by the T classification. It is codified by L1 or V1, respectively.[6]

G. Perineural Invasion
Perineural invasion has been shown to be an adverse prognostic factor.[3]

H. Specimen Dimensions
Open specimen along greater curvature, avoiding tumor if located in this position. Measure length of stomach along lesser curvature and circumference of distal margin. Measure length and width of tubular esophagus.

I. Tumor Location
Tumor location should be described in relation to the following landmarks:
- gastric region: cardia (including gastroesophageal junction), fundus, corpus, antrum, pylorus
- greater curvature, lesser curvature
- anterior wall, posterior wall

For tumors involving the gastroesophageal junction, specific observations should be recorded in an attempt to establish the exact site of origin of the tumor. The gastroesophageal junction is defined as the junction of the tubular esophagus and the stomach irrespective of the type of epithelial lining of the esophagus. The pathologist should record the:
(1) proportion of tumor mass located in the esophagus and stomach

(2) greatest dimensions of esophageal and gastric portions of the tumor
(3) anatomic location of the center of the tumor

If more than 50% of the tumor involves the esophagus, the tumor is classified as esophageal. If more than 50% of the tumor involves the stomach, the tumor is classified as gastric.[10] If the tumor is equally located above and below the gastroesophageal junction and/or is designated as being at the junction (anatomic center of the tumor), carcinomas of the squamous, small cell, and undifferentiated types are classified as esophageal, whereas adenocarcinomas and signet-ring cell carcinomas are classified as gastric.[8]

Tumor site has been shown to be an independent prognostic factor in gastric carcinoma. The long-term prognosis for patients with proximal carcinomas (ie, tumors of the upper third of the stomach, including the gastric cardia and gastroesophageal junction) is poorer than for those with distal cancers.[3]

J. Margins
Margins include the proximal, distal, and radial margins. The radial margins represent the non-peritonealized soft tissue margins closest to the deepest penetration of tumor. In the stomach, the lesser omental (hepatoduodenal and hepatogastric ligaments) and greater omental resection margins are the only radial margins. It may be helpful to mark the margin(s) closest to the tumor with ink. Margins marked by ink should be designated in the macroscopic description.

K. Regional Lymph Nodes
The specific nodal areas of the stomach are listed below.[6]

Greater Curvature of Stomach
Greater curvature, greater omental, gastroduodenal, gastroepiploic, pyloric, and pancreaticoduodenal

Pancreatic and Splenic Area
Pancreaticolienal, peripancreatic, splenic

Lesser Curvature of Stomach
Lesser curvature, lesser omental, left gastric, cardioesophageal, common hepatic, celiac, and hepatoduodenal

Involvement of other intra-abdominal lymph nodes, such as hepatoduodenal, retropancreatic, mesenteric, and para-aortic, is classified as distant metastasis.[6]

References

1. Tumours of the stomach. In: Hamilton SR, Aaltonen LA, eds. *World Health Organization Classification of Tumours. Pathology and Genetics. Tumours of the Digestive System.* Lyon, France: IARC Press; 2000:37-68.
2. Lauren P. The two histological main types of gastric carcinoma. *Acta Pathol Microbiol Scand*. 1965;64:31-49.

3. Van Krieken JHJM, Sasako M, Van de Vele CJH. Gastric cancer. In: Gospodarowicz MK, Henson DE, Hutter RVP, O'Sullivan B, Sobin LH, Wittekind C, eds. *Prognostic Factors in Cancer.* New York: Wiley-Liss; 2001:251-265.
4. Rohde H, Gebbensleben P, Bauer P, Stützer H, Zieschang J. Has there been any improvement in the staging of stomach cancer?: findings from the German Gastric Cancer TNM Study Group. *Cancer*. 1989;64:2465-2481.
5. Carriaga MT, Henson DE. The histologic grading of cancer: histology of cancer, incidence, and prognosis, SEER population-based data, 1973-1987. *Cancer*. 1995;75:406-421.
6. Greene FL, Balch CM, Fleming ID, et al, eds. *AJCC Cancer Staging Manual.* 6th ed, New York: Springer; 2002.
7. Sobin LH, Wittekind C, eds. *UICC TNM Classification of Malignant Tumours.* 6th ed. New York: Wiley-Liss; 2002.
8. Wittekind C, Henson DE, Hutter RVP, Sobin LH, eds. *TNM Supplement. A Commentary on Uniform Use.* 2nd ed. New York: Wiley-Liss; 2001.
9. Singletary SE, Greene FL, Sobin LH. Classification of isolated tumor cells: clarification of the 6th edition of the American Joint Committee on Cancer Staging Manual. *Cancer*. 2003;90(12):2740-2741.
10. Wittekind C, Compton CC, Greene FL, Sobin LH. Residual tumor classification revisited. *Cancer*. 2002;94:2511-2516.
11. Bunt AM, Hogendoorn PC, van de Velde CJ, Bruijn JA, Hermans J. Lymph-node staging standards in gastric cancer. *J Clin Oncol*. 1995;13:2309-2316.

Bibliography

Arak A, Kull K. Factors influencing survival of patients after radical surgery for gastric cancer: a regional study of 406 patients over a 10-year period. *Acta Oncologica*. 1994;33:913-920.

Baba H, Maehara Y, Takeuchi H, et al. Effect of lymph-node dissection on the prognosis in patients with node-negation early gastric carcinoma. *Surgery*. 1995;165-169.

Cimerman M, Repse S, Jelenc F, Omejc M, Bitenc M, Lamovec J. Comparison of Lauren's, Ming's and WHO histological classifications of gastric cancer as a prognostic factor for operated patients. *Int Surg*. 1994;79:27-31.

Coller FA, Kay EB, MacIntyre RS. Regional lymphatic metastases of the stomach. *Arch Surg*. 1941;43:748-761.

Cook AO, Levine BA, Sirinek KR, Gaskill HV III. Evaluation of gastric adenocarcinoma: abdominal computed tomography does not replace celiotomy. *Arch Surg*. 1986;121:603-606.

de Almeida JCM, Bettencourt A, Costa C, de Almeida JMM. Curative surgery for gastric cancer: study of 166 consecutive patients. *World J Surg*. 1994;18:889-895.

Dulchavsky S, Dahn MS, Wilson RF. The preoperative staging of malignant tumors of the stomach by computed tomography and liver function tests. *Curr Surg*. 1989;46:26-28.

Dupont JB Jr, Lee JR, Burton GR, Cohn I. Adenocarcinoma of the stomach: review of 1,497 cases. *Cancer*. 1978;26:941-947.

Japanese Research Society for Gastric Cancer. The general rules for the gastric cancer study in surgery and pathology. *Jpn J Surg*. 1982;11:127-145.

Kennedy BJ. TNM classification of stomach cancer. *Cancer*. 1970;26:971-983.

Kennedy BJ. The unified international gastric cancer staging classification system. *Scand J Gastrenterol*. 1987;22(suppl 133):11-13.

Kim J-P, Kim Y-W, Yang H-K, Noh D-Y. Significant prognostic factors by multivariate analysis of 3926 gastric cancer patients. *World J Surg*. 1994;18:872-878.

Okada M, Kojima S, Murakami M, et al. Human gastric carcinoma: prognosis in relation to macroscopic and microscopic features of the primary tumor. *J Natl Cancer Inst*. 1983;71:275-279.

Okusa T, Nakane Y, Boku T, Takada H, Yamamura M, Hioki K, et al. Quantitative analysis of nodal involvement with respect to survival rate after curative gastrectomy for carcinoma. *Surg Gynecol Obstet*. 1990;170:488-494.

Schmitz-Moormann P, Pohl C, Himmelmann GW, Neumann K. Morphological predictors of survival in advanced gastric carcinoma: univariate and multivariate analysis. *J Cancer Res Clin Oncol*. 1986;112:156-164.

Serlin O, Keehn RJ, Higgins GA Jr, Harrower HW, Mendeloff GL. Factors related to survival following resection for gastric carcinoma: analysis of 903 cases. *Cancer*. 1977;40:1318-1329.

Shimoyama S, Kaminishi M, Joujima Y, Ohara T, Hamada C, Teshigawara W. Lymph-node involvement correlation with survival in advanced gastric carcinoma: univariate and multivariate analyzes. *J Surg Oncol*. 1994;57:164-170.

Shiu MH, Perrotti M, Brennan MF. Adenocarcinoma of the stomach: a multivariate analysis of clinical, pathologic, and treatment factors. *Hepatogastroenterology*. 1989;36:7-12.

Thomas RM, Sobin LH. Histology of gastrointestinal cancer, incidence and prognosis: SEER population-based data. *Cancer*. 1995;75:154-170.

Wagner PK, Ramaswamy A, Rüschoff J, Schmitz-Moormann P, Rathmund M. Lymph-node counts of the upper abdomen: anatomical basis for lymphadenectomy in gastric cancer. *Br J Surg*. 1991;78:825-827.

Wanebo HJ, Kennedy BJ, Chmiel J, Steele G Jr, Winchester D, Osteen R. Cancer of the stomach: a patient care study by the American College of Surgeons. *Ann Surg*. 1993;218:583-592.

Zinninger MM, Colling WT. Extension of carcinomas of the stomach into the duodenum and esophagus. *Ann Surg*. 1949;130:557-566.