

EDITORIAL

## 7th Edition of the AJCC Cancer Staging Manual: Stomach

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### GOALS OF THE REVISED GASTRIC CANCER STAGING SYSTEM

Despite declining incidence in the United States and many other western countries, gastric cancer continues to be a worldwide health problem, with more than 600,000 cases reported annually, far higher than pancreatic cancer with 125,000 cases. The highest rates occur in Japan, China, Eastern Europe, and South America, with 42% of worldwide cases occurring in China.<sup>1</sup>

Development of an evidence-based universally applicable staging system for gastric carcinoma is challenging for a number of reasons. For instance, evidence is accumulating that the anatomic location of the primary tumor in the stomach influences survival, with tumor location in the antrum or distal stomach associated with better prognosis.<sup>2</sup> This influence of tumor location means that any system best suited for TNM staging of distal gastric tumors may not be ideal for staging more proximal tumors, which are more commonly seen in western countries. Thus, any data set used for development or refinement of a gastric cancer staging system should incorporate cases from both Asian and western countries, or should be tested on such a set for validation purposes, if the goal is development of a TNM system applicable worldwide. In addition, two-thirds of gastric cancers occur in developing countries,<sup>1</sup> and to be widely applicable a staging system must be based on data elements easily obtained in the setting in which the tumors most commonly occur. This limitation means that elements based on molecular or immunohistochemical features of the tumor—if such were available—are not practical for the majority of gastric cancers, and staging must continue to rely on the TNM classification for the near future.

There is a critical need for the staging system for tumors arising in the gastric cardia or esophagogastric junction to be harmonized with that for tumors of the distal esophagus. Many tumors in this region are bulky at the time of diagnosis, and ascertainment of the anatomic site of origin of the tumor in the esophagus or stomach may be problematic. With the 6th edition of the *AJCC Tumor Staging Manual*, a tumor predominantly located at the esophagogastric junction could be staged as esophageal or gastric carcinoma, depending on the judgment or bias of the physicians involved, resulting in different stage groupings depending on the designation. Eliminating this potential source of ambiguity was one of the overriding goals of the revision of gastric cancer staging for the *AJCC* 7th edition.<sup>3</sup> A secondary goal was harmonization of tumor (T) categories across the tubular gastrointestinal tract, from esophagus to colorectum, to simplify the conceptualization of this important staging element.

With these goals in mind, the AJCC Foregut Task Force worked with the Esophageal Staging Group of the Thoracic Task Force to examine ways to harmonize the gastric cancer and esophageal cancer staging systems. The revised esophageal cancer staging system is based on a data set of 4,627 treatment naïve surgically resected cases assembled by the Worldwide Esophageal Cancer Collaboration and analyzed using Random Forest Analysis.<sup>4</sup> However, the staging system and stage groupings as optimized for esophageal cancer did not perform sufficiently well for distal gastric cancers. Based on further analysis using data sets from Japan and Korea contributed by Dr. Takeshi Sano from National Cancer Center Hospital in Tokyo and Dr. Han-Kwang Yang from Seoul National University, and with consideration of requests from UICC and the international community, the anatomic stage/prognostic grouping as outlined below was developed. A consensus was reached to use the esophageal cancer staging system for esophagogastric junction cancers, and any cancer arising in the proximal 5 cm of the stomach and crossing the esophagogastric junction.

## HIGHLIGHTS OF THE 7TH EDITION OF THE AJCC GASTRIC CANCER STAGING SYSTEM

Key features and changes to the recommendations to the TNM gastric cancer staging system for the 7th edition include the following:

- Tumors arising at the esophagogastric junction, or arising in the stomach 5 cm or less from the esophagogastric junction and crossing the esophagogastric junction, are staged using the TNM system for esophageal carcinoma. The revised gastric cancer staging system applies to tumors arising in the more distal stomach and to tumors arising in the proximal 5 cm but not crossing the esophagogastric junction.
- T categories (Table 1) have been harmonized with T categories of the esophagus and small and large intestine, with T2 defined as a tumor that invades the muscularis propria, and T3 defined as a tumor that invades the subserosal connective tissue. T4 is now defined as a tumor that invades the serosal (visceral peritoneum) or adjacent structures.

The T1 category has been subdivided into T1a (invasion of lamina propria or muscularis mucosae) and T1b (invasion of submucosa) to facilitate data collection efforts. Because gastric carcinoma, unlike colorectal carcinoma, may have associated lymph node metastases when tumor is still confined to the lamina propria, invasion of the lamina propria or muscularis mucosae is classified as T1a instead

**TABLE 1** T category definitions, gastric cancer

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, muscularis mucosae, or submucosa
T1a	Tumor invades lamina propria or muscularis mucosae
T1b	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor penetrates subserosal connective tissue without invasion of visceral peritoneum or adjacent structures. T3 tumors also include those extending into the gastrocolic or gastrohepatic ligaments, or into the greater or lesser omentum, without perforation of the visceral peritoneum covering these structures
T4	Tumor invades serosa (visceral peritoneum) or adjacent structures
T4a	Tumor invades serosa (visceral peritoneum)
T4b	Tumor invades adjacent structures such as spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine, and retroperitoneum

**TABLE 2** N category definitions, gastric cancer

NX	Regional lymph node(s) cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1 to 2 regional lymph nodes
N2	Metastasis in 3 to 6 regional lymph nodes
N3	Metastasis in 7 or more regional lymph nodes

**TABLE 3** Anatomic stage/prognostic groups, gastric cancer

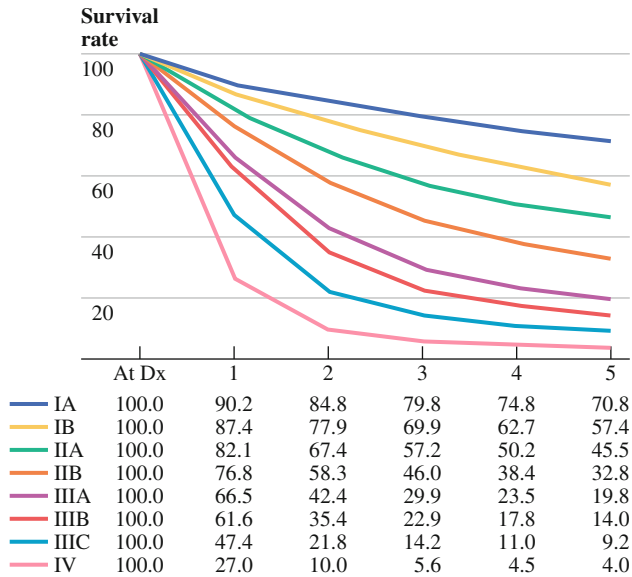
Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
	T1	N1	M0
Stage IIA	T3	N0	M0
	T2	N1	M0
	T1	N2	M0
Stage IIB	T4a	N0	M0
	T3	N1	M0
	T2	N2	M0
	T1	N3	M0
Stage IIIA	T4a	N1	M0
	T3	N2	M0
	T2	N3	M0
Stage IIIB	T4b	N0 or N1	M0
	T4a	N2	M0
	T3	N3	M0
Stage IIIC	T4b	N2 or N3	M0
	T4a	N3	M0
Stage IV	Any T	Any N	M1

of carcinoma in situ (Tis). This difference in tumor biology is attributed to the abundance of lymphatic channels in the gastric mucosa, in contrast to the colonic mucosa, in which lymphatic vessels are few and primarily located at the base of the mucosa.

- N categories (Table 2) have been modified, with N1 = 1 or 2 positive lymph nodes, N2 = 3 to 6 positive lymph nodes, and N3 = 7 or more positive lymph nodes.
- Positive peritoneal cytology is classified as metastatic disease (M1).
- Anatomic stage/prognostic groupings have been changed (Table 3; Fig. 1).

## CONCLUSIONS

To be clinically useful, a gastric cancer staging system must meet needs of diverse user groups and accommodate staging of both proximal and distal cancers, which may be biologically different entities. Providing clear rules for



**FIG. 1** Observed survival rates for 10,601 surgically resected gastric adenocarcinomas. Data from the SEER 1973–2005 Public Use file diagnosed in years 1991–2000. Stage IA includes 1,194; Stage IB, 655; Stage IIA, 1,161; Stage IIB, 1,195; Stage IIIa, 1031; Stage IIIB, 1,660; Stage IIIC, 1,053; and Stage IV, 6,148 (Fig. 11.1 from *AJCC Cancer Staging Manual, 7th edition, 2009*)

staging proximal gastric cancers that cross the esophago-gastric junction with the esophageal carcinoma staging system has eliminated the potential for assigning different

stages to tumors based on location. Implementation of these new staging rules also will improve data collection, which will provide the basis for further refinements in TNM staging for these sites. Future prognostic systems, such as the nomogram systems described by Kattan and colleagues, may allow further refinements in prediction tools, but will not obviate the need for careful assessment of anatomic extent of disease.<sup>5,6</sup>

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