Gastric Breast Cancer 2002; 1(1): 7-10

MINI-REVIEW

Gastric Cancer: Diagnosis, Staging, Prognosis

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Gastric carcinoma at early tumor stage typically produces mild or no symptoms. This explains why at the time of disease detection in the West the tumor is often locally advanced or metastatic. As the tumor becomes more extensive, an insidious upper abdominal discomfort may develop, ranging in intensity from a vague sense of postprandial fullness to a severe, steady pain. Anorexia, nausea, vomiting and weight loss are also frequently reported at the time of presentation, whereas dysphagia may be the main symptom associated with a lesion of the cardia. Hematemesis or melena is reported by 20 percent of patients but it is more likely to be associated with leiomyoma and leiomyosarcoma. There are no physical findings associated with early gastric cancer, and the presence of a palpable abdominal mass generally indicates long-standing growth and regional extension.[1,2] Laboratory tests may demonstrate anemia, hypoproteinemia, abnormal liver function, and fecal occult blood. [3]

Patients with gastric carcinoma infrequently present with various paraneoplastic conditions such as microangiopathic hemolytic anemia,[4] membranous nephropathy,[5] the sudden appearance of seborrhcic Keratoses (the Leser-Trelat sign),[6] filiform and popular pigmented lesions in skin folds and mucous membranes (acanthosis nigricans),[7] chronic intravascular coagulation leading to arterial and venous thrombi (Trousseau's syndrome),[8] and in rare cases, dermatomyositis.[9]

Diagnostic Studies

An upper gastrointestinal series and double-contrast techniques are performed to evaluate symptoms related to the upper gastrointestinal tract but their diagnostic accuracy to differentiate a benign tumor from a malignant ulcer is not high.[10] Fiberoptic endoscopy and biopsy had a diagnostic accuracy of 95 percent in previous studies.[11,12]

Since the accuracy increases with the number of biopsies, multiple biopsies are recommended.[13] Gastric carcinomas may be difficult to distinguish from gastric lymphomas, and because of the submucosal location of lymphoid neoplasms, it is important to obtain biopsy specimens at an adequate depth.

Computed tomography (CT) scans of the abdomen can delineate the extent of the primary tumor, as well as the presence of nodal or distant metastases.[14,15] Endoscopic ultrasound (EUS) significantly increases the preoperative accuracy particularly of tumor depth (T-category) and nodal status (N-category)[16] and despite some previous debate for routine use[17] is currently considered essential in the preoperative staging for an appropriate treatment option.

Tumor Markers

Despite the initial enthusiasm about serologic tumor markers, they have not been useful in diagnosing gastric carcinoma in an early stage. Carcinoembryonic (CEA), alpha-fetoprotein and CA 19-9 levels,[18] as well as recently CA 72-4 levels have no clinical value for early detection and even in the follow-up period after a curative surgery their contribution to the improvement of outcome is of little efficacy.

STAGING AND PROGNOSIS

The pathological tumor stage (pTNM) and the completeness of surgical resection (R-classification) remain the most important determinant of the prognosis of gastric cancer. Both have been identified as independent predictor of survival in multiple reports with multivariate analyses. The tumor depth into the stomach wall (T-category) and the presence or absence of metastases to regional lymph nodes (pN-category) or distant organs (M-category) are important predictors of disease-free and overall survival.[1,19]

In the past there were major differences between Japan and Western world regarding the classification of the local spread of gastric cancer. Currently, classification

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according to tumor depth (T-stage) and distant metastasis (M-stage) is identical in Western countries (International Union Against Cancer/American Joint Committee on Cancer (UICC/AJCC)[20,21] and in Japan (Japanese Research Society for Gastric Cancer [JRSGC). [22] However, the nodal staging system remains different. The Japanese nodal system is based on the anatomical location of lymph nodes. According to the guidelines of the JRSGC, the upper abdominal lymph nodes are grouped into 16 stations, which are subsequently divided into four levels (N1-N4) according to the location of the primary tumour.

N1 level includes the perigastric lymph nodes directly attached to the stomach (stations 1 to 6), N2 level the extraperigastric lymph nodes along the left gastric artery (no. 7), common hepatic artery (no. 8), coeliac artery (no. 9), and splenic artery (no. 11) and at the splenic hilus (no. 10) [N2 level], and N3, N4 levels include hepatoduodenal, retro-pancreatic, mesenteric and para-aortic lymph nodes (stations 12 to 16). Although the prognostic significance of this, based on the anatomical location of lymph nodes nodal system, may be clear, it is very complicated for routine practice. A number of observational studies have shown the prognostic significance of the number of positive nodes and thus a classification based on the number of positive nodes has been proposed with a variety of cut-off points ranging from 2 to 16 involved lymph nodes.[23-26] The new UICC/AJCC classification is based on the number of positive nodes; pN1: metastasis in 1 to 6 lymph nodes, pN2: 7 to 15 nodes, pN3: 16 or more nodes.[27] Several studies have confirmed the superiority of this new nodal system in estimation of the prognosis.[28-31] In addition, these studies have shown that the new pN classification can be applied without methodological problems and appears more reproducible than the old pN system or the Japanese nodal system. However, the value of the D classification for the description of the extent of a surgical procedure and the analysis of the treatment results remains unchanged. Nevertheless, for clinical trials that evaluate the therapeutic benefit of extended node dissection the classification of nodal status should include both anatomical location and number of positive nodes per N level .

Table 2 demonstrates the grouping of TNM-system according to the latest 5th-edition of UICC/AJCC (1997).

STAGE GROUPING (UICC/AJCC 1997)

Stage0

Tis N0 M0

Stage IA

T1 N0 M0

Stage IB

T1 N1 M0

T2 N0 M0

Stage II

T1 N2 M0

T2 N1 M0

T3 N0 M0

Stage IIIA

T2 N2 M0

T3 N1 M0

T4 N0 M0

Stage IIIB

T3 N2 M0

Stage IV

T4 N1,N2,N3 M0

T1,T2,T3 N3 M0

Any T Any N M1

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 Lamina propria, submucosa

T2 Muscularitis propria, submucosa

T3 Penetrates serosa (visceral peritoneum) without invasion of adjacent structures

T4 Invades adjacent structures

Notes:

1. A tumor may penetrate muscularitis propria with extension into the gastrocolic or gastrohepatic ligaments or the greater lesser omentum without perforation of the visceral peritoneum covering these structures. In this case, the tumor is classified as T2. If there is perforation of the visceral peritoneum covering the gastric ligaments or omenta, the tumor is classified as T3.
2. The adjacent structures of the stomach are the spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine, and retroperitoneum.
3. Intramural extension to the duodenum or esophagus is classified by the depth of greatest invasion in any of these sites including stomach.

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Metastasis in 1 to 6 regional lymph nodes

N2 Metastasis in 7 to 15 regional lymph nodes

N3 Metastasis in more than 15 regional lymph nodes

MX Distant metastasis cannot be assessed

M0 No distant metastasis

M1 Distant metastasis

R Classification

The absence or presence of residual tumor after treatment may be described by the symbol R. The definitions of the R classification apply to all digestive system tumors.

These are:

RX Presence of residual tumor cannot be assessed

R0 No residual tumor

R1 Microscopic residual tumor

R2 Macroscopic residual tumor

Several other factors have been reported to predict survival but their importance remains controversial. It has been reported that the intestinal type cancer is associated with a higher rate of five-year survival than diffuse cancer.[2]

Similarly, the poorly differentiated tumors, tumors with abnormal DNA content (i.e., aneuploidy),[32] and tumors with genetic alterations in proto-oncogenes[33] or tumorsuppressor genes[34] have been associated with a diminished survival rate. The location of the primary tumor also appears to predict the outcome.[2,32]

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