Saudi Oncology Society clinical management guideline series

Gastric cancer 2014

Magdy S. Kandil, *MD, PhD,* ***Shouki N. Bazarbashi,*** *MBBS,* ***Mohammed M. Rahal,*** *MD, PhD,* ***Ahmed S. Al-Shehri,*** *MBChB, FRCPC,* ***Ali M. Alzahrani,*** *MBChB, FRCR,* ***Ali H. Aljubran,*** *MD,* ***Jamal E. Zekri,*** *MBBCh, FRCP (UK),* ***Ashwaq A. Al Olayan,*** *MBBS,* ***Abdullah A. Alsharm,*** *MD,* ***Nizar M. Yamani,*** *MBBS, ABS,* ***Ibrahim S. Alomary,*** *MD,* ***Mosa A. Fagih,*** *MBBS, FRCPC.*

A total 291 cases of stomach cancer were diagnosed in 2010 in the Kingdom of Saudi Arabia according to the Saudi Cancer Registry data.[1] Stomach cancer ranked eleventh among the male and female population. It account for 2.9% of all diagnosed cancers. The overall age standardized rate was 2.7/100,000, with a rate of 3.1/100,000 for males and 2.3/100,000 for females. The median age at diagnosis was 65 years for males (range 4-94 years), and 60 years for females (range 23-100 years).

A committee of experts in the medical and surgical treatment of colorectal cancer was established under the supervision of the Saudi Oncology Society (SOS). The evidence adopted in these guidelines is rated at 3 levels: 1) Evidence level (EL)-1 (highest level) evidence from phase III randomized trials or meta-analyses, 2) EL-2 (intermediate-level) evidence from good phase II trials or phase III trials with limitations, and 3) EL-3 (low-level) from retrospective or observational data and/or expert opinion. This easy-to-follow grading system is convenient for the reader and allows accurate assessment of the applicability of the guidelines in individual patients.[2]

All gastric cancer cases are preferably seen or discussed in a multidisciplinary form.

Definitions

The term "esophagogastric junction tumor" covers lower esophageal adenocarcinoma, junctional tumors, and cancer of the cardia. The Siewert classification is used to subdivide esophagogastric junction tumors into type I, II, and III.[3] The classification covers the area 5 cm either side of the gastro-esophageal junction.

1.1 Type I - the center of the cancer or more than two-thirds of identifiable tumor mass is located >1 cm proximal to the anatomical gastro-esophageal junction

1.2 Type II - the center of the cancer or the tumor mass is located in an area extending one cm proximal to the gastro-esophageal junction to 2 cm distal to it

1.3 Type III - the center of the tumor or more than two-thirds of identifiable tumor mass is located >2 cm below the gastro-esophageal junction

1.4 Barrett's esophagus is identified as an esophagus in which the normal squamous lower esophageal epithelium has been replaced by intestinal type mucosa, which is visible macroscopically.

Type I will be treated as esophageal cancer and types II and III will be treated as gastric cancer.

From the Oncology Department (Alzahrani, Kandil) Prince Sultan Military Medical City, Section of Medical Oncology (Bazarbashi, Aljubran), Department of Oncology (Zekri), Oncology Center, King Faisal Specialist Hospital and Research Center, Department of Oncology (Al Olayan), Department of Surgey (Yamani), King Abdulaziz Medical City, Medical Oncology Department (Alsharm), Anatomic Pathology Department (Fagih), King Fahad Medical City, Riyadh, Department of Oncology (Rahal), Oncology Center, King Fahad Specialist Hospital, Dammam, and the Department of Oncology (Al-Shehri, Alomary), Princess Nora Oncology Center, King Abdulaziz Medical City, Jeddah, Kingdom of Saudi Arabia.

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Address correspondence and reprint request to: Dr. Shouki N. Bazarbashi, Oncology Center, King Faisal Specialist Hospital and Research Center, PO Box 3354 (MBC 64), Riyadh 11211, Kingdom of Saudi Arabia. Tel. +966 (11) 4423935. E-mail: Bazarbashi@gmail.com

1. Pre-treatment evaluation

1.1 Clinical and physical examination
1.2 Blood count, renal, and hepatic function tests
1.3 Tumor markers (optional: carcinoembryonic antigen, CA-19-9)
1.4 Flexible upper gastrointestinal endoscopy is recommended as the diagnostic procedure of choice in patients with suspected esophageal or gastric cancer[4]
1.5 Biopsy: all biopsy pathologic reports should include the following checklist:[5]
1.5.1 Histologic type
1.5.2 Histologic grade
1.5.3 Ancillary studies: HER-2 immunoperoxidase studies (in accredited labs or with external quality control) and HER-2 florescent *in-situ* hybridization (FISH) - for patients with immuno score 2+ (in accredited labs or with external quality control)
1.6 Computed tomography (CT) scan of the chest, abdomen, and pelvis to assess the local, nodal, and distant spread. Limitations include low sensitivity to detect peritoneal metastasis <5 mm and underestimation of depth of wall invasion[6-9] (EL-2)
1.7 Barium studies (optional to define extent of surgery)[10]
1.8 Endoscopic ultrasonography (optional)[11-15] (EL-2)
1.9 Staging laparoscopy: recommended for gastric tumors being considered for surgery where full thickness gastric wall involvement is suspected, T3-4 or N positive (EL-2)[16-20]

2. Surgical pathology report requirements:[5,21]

2.1 Specimen
2.2 Procedure
2.3 Tumor site (select all that apply)
2.4 Tumor size
2.5 Histologic type
2.6 Histologic grade
2.7 Microscopic extent of tumor
2.8 Margins (select all that apply)
2.9 Treatment effect (applicable to carcinomas treated with neoadjuvant therapy)
2.10 Lymph-vascular invasion
2.11 Perineural invasion
2.12 Pathologic staging (pTNM)
2.13 TNM descriptors (required only if applicable)
2.13.1 M (multiple primary tumors)
2.13.2 R (recurrent)
2.13.3 Y (post-treatment)
2.14 Additional pathologic findings-ancillary studies:
2.14.1 HER2 immunoperoxidase studies (accredited laboratory or external quality control)
2.14.2 HER2 in situ hybridization studies / florescent in-situ hybridization (immuno score 2+) (accredited laboratory or external quality control)

3. Staging

The American Joint Commission on Cancer (AJCC)- 2007 pathological staging system will be used[21]

4. Treatment

4.1 Indicators of unresectability: presence of distant metastases, invasion of a major vascular structure, such as the aorta, or disease encasement or occlusion of the hepatic artery or celiac axis/proximal splenic artery

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4.2 Treatment of stage T_{IS} (in-situ), T1a N0M0: Endoscopic mucosal resection of early gastric cancer meeting all of the following (EL2):[22]
- 4.2.1 Well or moderately differentiated type adenocarcinoma
- 4.2.2 Superficial, elevated, or depressed (<1cm) macroscopic appearance (types I, IIa, IIc)
- 4.2.3 No ulceration
- 4.2.4 Diameter of the lesion <30 mm
- 4.2.5 No apparent invasive findings

4.3 Treatment of stage T1b-T4, N0-1, M0: Medically fit and potentially resectable patient should be given either of the following options
- 4.3.1 Gastrectomy followed by adjuvant concurrent chemoradiotherapy using 5-fluorouracil and leucovorin as per inter group 0116 protocol[23] (EL-1 or modifications[23-26] [EL-2]). Radiotherapy dose is 45 Gy in 25 daily fractions of 1.8 Gy on 5 days a week to stomach bed and draining high-risk nodal regions[23-26]
- 4.3.2 Perioperative neoadjuvant/adjuvant chemotherapy using epirubicin/cisplatin/5-FU (ECF) chemotherapy regimen, (EL-1) or its modifications (EL-2), based on the Cunningham/Medical Research Council Adjuvant Gastric (MAGIC) trial[27] (EL-1), or Cisplatin /5-Fluorouracil as per the Federation Nationale des Centres de Lutte contre le Cancer/Federation Francophone de Cancerologie Digestive (FNLCC/FFCD) trial[28] (EL-1)
- 4.3.3 Gastrectomy to be followed by post-operative adjuvant XELOX for 8 cycles[29] (EL-1)

4.4 Surgical management:
- 4.4.1 Gastrectomy.[30-35] Total gastrectomy was carried out for proximal and mid body gastric tumors with a Roux-en-Y reconstruction to avoid alkaline reflux esophagitis. Distal subtotal gastrectomy for distal gastric tumors (EL-2) with a wide macroscopically negative margin of 5 cm, along with the en bloc resection of lymph nodes (D2 lymphadenectomy, EL-1),[36-38] and adherent surrounding organs. Spleen and pancreas are spared (EL-2). If a splenectomy is anticipated preoperatively because of tumor adherence shown by CT, we administer pneumococcal polysaccharide, meningococcal, and Haemophilus influenzae vaccines before surgery.
- 4.4.2 Lymphadenectomy.[36-38] Resection of lymph nodes in gastric cancer surgery can be carried out at 3 levels: 1) D1, involves removal of all nodal tissue within 3 cm of the primary tumor (perigastric nodes); 2) D2, involves D1 plus clearance of hepatic, splenic, celiac, and left gastric lymph nodes; and 3) D3, involves D2 plus omentectomy, splenectomy, distal pancreatecomy, and clearance of porta hepatis lymph nodes and para-aortic lymph nodes.

4.5 Follow up. There is no consensus regarding follow-up after gastrectomy. There is no evidence that regular intensive follow-up improves patient outcomes. Symptom-driven visits are recommended for most cases (EL-3)

4.6 Post-operative management of residual disease. This will depend on the degree of residual disease as follows:
- 4.6.1. R1 (microscopic residual disease): treat with post-operative chemo radiation or chemotherapy
- 4.6.2. R2 (macroscopic residual disease): treat as metastatic disease

4.7 Treatment of stage T4M0 medically fit and unresectable. Treat as metastatic disease (M1) and reassess for resectability

4.8 Treatment of stage M1 disease. This will depend on patient performance status:
- 4.8.1 Patients with performance status (PS) 0-2: palliative chemotherapy with any of the following options: ECF modifications[39] (EL-1), docetaxel, cisplatin, and 5-FU (DCF) (EL1) / DCF modifications[40,41] (EL-2), 5-FU, leucovorin, and oxaliplatin 6 (FOLFOX 6),[42] (EL-2) or capecitabine and oxaliplatin (XELOX)X[43] (EL-2). Add trastuzumab to Cisplatin/Fluoropyrimidine if Her-2/neu +3 on immunohistochemistry or FISH positive[44] (EL-1)

4.8.2 Patients with PS of 3: give single agent chemotherapy or best supportive care

4.8.3 If disease progression after first line chemotherapy, consider, when appropriate in good performance status patients, a second line combination paclitaxel-ramucirumab[45] or single agent irinotecan, taxane or ramucirumab[46,47] (EL-1)

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