Potentially Curable Cancers of the Esophagus and Stomach

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Abstract

Gastric and gastroesophageal adenocarcinomas continue to be a major health burden globally and collectively represent the third leading cause of cancer death. Among patients with metastatic disease, most die of their cancer because of the limited number of modestly effective treatment regimens available today. The progress against these cancers has been slow compared with many other solid tumors despite many attempts. In-depth molecular profiling has also not been completed. Even when these cancers are localized, they impose considerable challenges for the patient, relatives, and treatment team alike. Localized gastric or gastroesophageal cancer is best managed with a multidisciplinary approach. This review focuses on the management of localized cancers by reviewing the current literature and explaining certain principles that help guide therapy for these patients. The future, however, will afford numerous opportunities, including exploitation of initial data from The Cancer Genome Atlas, to identify novel targets and drugs, harness the prowess of the immune system, and customize therapy for each patient.

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Gastric and gastroesophageal adenocarcinomas (GEACs) continue to be a major health burden globally and represent the third leading cause of cancer death.[1] Among patients with metastatic disease, most die of their cancer because the currently available armamentarium is limited. The progress against GEACs has been slow

compared with many other solid tumors despite many attempts. Even when GEAC is localized, it imposes considerable challenges for the patient, relatives, and treatment team alike. Localized GEAC is best managed by a multidisciplinary approach incorporating a team of surgeons, radiation oncologists, pathologists, gastroenterologists, radiologists, medical oncologists, nutritionists, social workers, geneticists, and midlevel providers (eg, physicians assistants). Orchestrating and administering multidisciplinary care adds a level of complexity that can be partially overcome by managing a large number of patients to improve efficiency of treatment, preemptive management of complications, and enhanced communication among teams. Treatment decisions for patients with localized GEAC are based on the information discussed in a multidisciplinary conference after an appropriate and thorough clinical staging process is completed, patients/relatives are well informed of the consensus achieved, and their choices are discussed. For all potentially curable GEACs, treatment preferably should be performed at a high-volume center of excellence. This review focuses on the management of localized GEAC. The management of metastatic disease has been recently reviewed by Murphy et al.[2]

GASTRIC ADENOCARCINOMA

Gastric adenocarcinoma (GAC) is estimated to be the 15th most common cause of cancer death among men in the United States and the third most common cause of cancer death worldwide.[1] In 2016, the estimated number of new cases and deaths from gastric cancer (GC) in the United States were 26,370 and 10,730, respectively.[3] The incidence of GC in the United States has been steadily declining.

Gastric adenocarcinoma is treated according to the clinical stage established before initiation of therapy.[4] Patients with cT1 (a or b) cancer could be treated endoscopically or by limited surgery (including a laparoscopic approach), but higher stages require more involved therapies. Clinical categories greater than T1 could designate a patient's GAC as potentially curable (technically resectable GAC in a patient who can withstand surgery) or unresectable (incurable in most cases). In such circumstance, surgery, when feasible, is one of the most effective treatments. However, surgery alone appears inadequate, resulting in a limited number of cures (often <50%). A surgical oncologist with expertise in D2 dissection should be engaged to perform GAC surgery.[5-7] Adjunctive therapy (either before or after surgery) has improved the cure rate by at least 10% above what can be achieved by surgery alone.[8-11] The type of adjunctive approach has varied by region.[12] In North America and Europe, the postoperative chemoradiation adjuvant[10] or preoperative chemotherapy approach[9] are popular, but in Asia, postoperative adjuvant chemotherapy is utilized most frequently.[13,14]

The main therapeutic goal for patients with unresectable GAC is symptom palliation using approaches similar to those used to treat advanced GAC. Treatment options for resectable GAC are discussed in the following sections.

Surgery

In the United States, 67% of patients present with stage III or IV disease and only 10% with stage I disease.[15] A detailed description of surgical techniques is beyond the scope of this review. However, a well-trained surgical oncologist should be engaged to perform formal D2 gastrectomy that can produce the best results for the patient.[16-18] Achievement of negative margins is crucial for cure because the cure rates are extremely low when margins are not clear of cancer.[19] Data from the Surveillance, Epidemiology, and End Results Program for 1973-2000[20] that analyzed 1377 patients with GAC (stages IIIA, IIIB, and IV, M0) revealed that the total lymph node (LN) count (or number of disease-negative LNs examined; $P<.0001$) and number of disease-positive LNs ($P<.0001$) were independent prognosticators for overall survival (OS). The stage-based OS also correlated with total LN count and number of nonmalignant LNs. In a previous analysis, for every 10 extra LNs dissected, OS improved by 7.6% (T1/2N0), 5.7% (T1/2N1), 11% (T3N0), or 7% (T3N1).[21] Prospective studies in non-Asian countries have not confirmed these findings.[5,22-24] Additionally, there appears to be no benefit from performing lymphadenectomy beyond a D2 dissection.[25,26] Despite the lack of unequivocal data to support the routine use of D2 dissection, current sentiments

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