Esophageal Cancer

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Current estimates for 1998 indicate that 12,300 new cases of carcinoma of the esophagus will occur in the United States (9,300 in men and 3,000 in women) and that 11,900 people will die of esophageal cancer this year. Esophageal cancer will account for approximately 3.2% of all cancer deaths in this country. Florida is second only to California in total annual esophageal cancer deaths. Esophageal cancer is recognized as the most difficult to treat and is second only to pancreatic cancer as the most lethal of all gastrointestinal malignancies.

Squamous carcinoma of the esophagus is exceptionally common in China, Japan, the current Russian republics, Iran, South America, South Africa, and France. It is relatively uncommon in the United States and in Europe. Adenocarcinoma of the esophagus currently is considered to be increasing at a faster rate than any other malignant lesion in white men in this country. Until the late 1970s, the most common histological type of esophageal cancer in the United States was squamous cell carcinoma, which is associated with the abuse of tobacco and alcohol. However, during the last two decades, the incidence of distal esophageal adenocarcinoma and adenocarcinoma of the gastric cardia have shown a remarkable increase. Adenocarcinoma of the esophagus is related to acid reflux and now accounts for at least 50% of esophageal malignancies in the United States and Europe.1

In the United States, black men are at highest risk of developing esophageal squamous cancer, the risk being almost four times greater than that of white men. The risk of squamous cell cancer is reported to increase by a factor of 18 in alcoholics who drink more than 80 g per day and by a factor of 44 in this group if they also have a daily consumption of 20 g of tobacco. Adenocarcinoma of the esophagus accounts for nearly 70% of esophageal malignancies in our institution, and nearly all cases are associated with a columnar-lined (Barrett) esophagus (CLE).2 Adenocarcinoma associated with CLE occurs in white men at an average age of 57 years.

CLE is an acquired condition that develops first along the normal squamocolumnar junction as a consequence of injury by reflux of gastric acid. One recent study revealed that 18% of patients with chronic acid reflux disease had histologic evidence of variable degrees of CLE.3 Approximately 58% of patients with acid reflux-related distal esophageal strictures will be found to have an associated CLE.4 Very short segments of CLE are being recognized with increasing frequency.5

The type of epithelium with the potential to develop dysplasia and ultimately carcinoma is a form of specialized intestinal goblet cell metaplasia that is not normally found in the esophagus or stomach. Confirmation is achieved by specific staining with periodic acid-Schiff/Alcian blue stain at pH 2.5. This type of epithelium has premalignant potential and consequently requires surveillance biopsies.

The risk of adenocarcinoma in CLE has been estimated at between 30 and 125 times greater than in age- and sex-matched controls. Eighty-five percent of patients with adenocarcinoma of the esophagus or cardia are white. Conversely, only 30% of the patients with carcinoma of the gastric body or antrum are white. The typical reported man:woman ratio for adenocarcinoma of the esophagus is 9.2:1.

Most cancers involve at least a 4-cm length of the esophagus before diagnosis, and the typical patient will have had three to six months of dysphagia and some weight loss before first contacting a physician.6 When the lesion exceeds 5 cm in length, over 90% will have regional lymph node metastases. The early growth pattern of the cancer favors longitudinal and extramural spread over circumferential extension. As a consequence of this growth pattern, lumen stenosis occurs relatively late, as does the resulting dysphagia. Both esophageal obstruction and anorexia leading to weight loss are common and, along with chest pain, are poor prognostic signs. Dysphagia and weight loss generally are less severe on presentation with adenocarcinoma than with the squamous type.

Staging Esophageal Cancer

A decision regarding potentially curative surgical therapy or palliation by surgery or nonsurgical means depends on proper staging. Pretreatment staging has been relatively imprecise in past years; however, our ability to more accurately stage these diseases has been improved by the development of computed tomography (CT), magnetic resonance imaging (MRI), and endoscopic ultrasonography (EUS). The stage of the disease appears directly related to survival. Nonsurgical stage-dependent therapies are being developed. Staging is of significant clinical as well as research benefit in evaluating various forms of treatment.

The recent development of endoscopic mucosal resection of lesions confined to the esophageal mucosa has been possible through the use of EUS, which has proven to be the most sensitive method for T staging. EUS has also been proven superior to radiologic imaging methods (CT and MRI) in assessing the degree of lymph node involvement (N stage). EUS is reported to have an accuracy at least 15% to 20% greater for determining N staging.7 This is particularly important since the number of lymph nodes involved in the periesophageal region has a profound effect on prognosis. If EUS reveals that the tumor does not invade through the esophageal wall (T1 or T2) and fewer than five enlarged lymph nodes are imaged, a curative resection is usually considered to be possible and appropriate.

EUS is of little value for determining distant metastases (M stage). A complete staging procedure that includes general patient physical assessment, radiologic imaging (including CT), and EUS properly used will provide correct staging of esophageal cancer that approaches an accuracy of 90%.

Diagnostic laparoscopy has been used for over 50 years as a valuable staging method for esophageal cancer. Laparoscopy has proven to be superior to other preoperative imaging methods for abdominal staging of carcinoma of the esophagus and esophagogastric junction and should be used in assessment of patients before excisional surgery.8

Surgical Therapy

Esophagectomy can cure esophageal cancer that is limited to the esophagus and nodes removed at operation.9 Approximately 90% of patients have no chance of cure by surgery. Patients with T4 cancer (metastatic to the mediastinum and paraesophageal organs) are incurable by any current method and survive as long or longer with nonsurgical palliation.

Surgery with or without preoperative radiation and/or chemotherapy is indicated in selected patients, ideally under research protocol. When accurately staged and operated on by an experienced esophageal surgeon, patients have an improved stage-dependent survival and even a five-year cure in a few. However, esophagectomy performed by an inexperienced, “occasional” esophageal surgeon has the highest operative mortality of any elective surgical procedure.

Guidelines for staging and therapy of esophageal cancer have been recommended (Figure).
Goals and Techniques of Palliation

Since less than 10% of all patients with esophageal cancer survive five years, 90% of patients will need palliative care. Physicians who are responsible for the care of these patients must accept the obligation to assure that palliation is provided early and effectively to assure the best possible quality of life for the limited lifespan.

Three major problems arise in patients with advanced inoperable esophageal cancer: dysphagia, chest pain, and malnutrition. Each of these complications requires a different primary therapy, although relief provided for one may benefit the other two. All three of these sequelae of malignant growth are present in the majority of patients before death.

A major complication of esophageal carcinoma is the development of an esophagopulmonary fistula that typically leads to pulmonary infection and death. A fistula develops in approximately 15% of cases and should be attributed to the natural history of this disease. Fistulas are the consequence of tissue destruction by the invasion of carcinoma in normal tissue. They may first become manifest after irradiation therapy has produced the desired destruction of the invading cancer. The fistula, however, is not a complication of irradiation, dilation, or other therapy for this malignancy; it is a natural event to be expected when necrotic, neoplastic tissue necroses or is removed or displaced.

With the exception of the recently introduced technique of mucosectomy for stage T1 esophageal carcinoma, all endoscopic treatments are considered palliative. Photodynamic laser therapy (PDT) currently is under evaluation for treatment of high-grade dysplasia (carcinoma in situ) in the CLE.

Pain relief, nutritional and psychological support are an essential part of any program of palliation. One of the great sins of cancer treatment is the failure of the patient’s physician to either provide or seek from other physicians the most effective palliation therapy available. Too many patients are referred too late for transendoscopic palliative methods to provide a reasonable period of dysphagia relief.

The most widely used palliative methods applied with endoscopic assistance include dilation, thermal laser (Nd:YAG), bipolar diathermy (BICAP tumor probe), thermal heater probe, plastic and metal expandable prostheses, and chemical ablation (alcohol, sclerosants, chemotherapeutic drugs). The use of photodynamic laser therapy (PDT) is now under investigation. No one palliative method is ideal, and optimum therapy often requires at least two of these procedures to provide adequate relief of dysphagia during the usual limited survival.

**Peroral Dilation**

Peroral dilation should be used initially to restore patency prior to therapy and later as needed to maintain patency after radiation, chemotherapy, and/or palliative surgery. There is no evidence that properly performed esophageal dilation of obstructing carcinoma carries an unusually high risk. Fear of dilating a malignant esophageal stricture is due more to a lack of proper training of the physician or surgeon in dilation therapy than to inherent dangers of the methods. Dilation with any of the standard instruments (Maloney, Savary, and hydrostatic balloons) is effective when carried to diameters above 45F (15 mm), but the dysphagia relief typically lasts only a few days or weeks.

**Peroral Esophageal Prosthesis**

Plastic or metal expandable peroral stents offer some distinct advantages over other forms of palliation used for dysphagia and are safe when properly inserted. Since currently available commercial prostheses are not suitable for all types of malignant strictures, the operator must be qualified to make sound judgments on which cases are suited for their use.

The latest palliative innovation for malignant strictures is the metal expanding stent. Metal stents can be inserted with a delivery apparatus of approximately 8 mm in diameter. This feature is appealing, especially to those who have not been trained in all the unpredictable variants that occur with malignant strictures and stent placement. Self-expanding metal stents offer promise for adequate lumen restoration if durable silicone coating, better design for position fixation with adequate radial force, and a dependable deployment apparatus can be developed.

Lumen obstruction and esophagopulmonary fistula can be effectively treated by a peroral stent. Used for either stenosis alone or for fistula blockage, the stent is placed following adequate dilation in several sessions under fluoroscopic control using mild sedative/analgesic medication. The actual placement usually requires less than one minute for conventional plastic/silicone stents and less than five minutes for metal stents. The complication rate is low when proper technique is used. Since these patients also suffer from severe anorexia, special efforts at nutritional support are necessary even though dysphagia is relieved.

**Laser (Nd:YAG) Photothermal Ablation**

The use of Nd:YAG laser ablation of obstructing esophageal cancer is well established. However, laser therapy is expensive and requires repeated treatment sessions for the remainder of the patient’s life. Compared to esophageal stents, laser therapy is more difficult to use, is less effective, and has a higher risk in lesions of
the cervical esophagus and cardia.11

Chemical Ablation by Injection

Absolute alcohol and other sclerosant solutions injected into exophytic tumor masses can safely provide relief from obstruction at much less expense than laser therapy. The safety and general applicability for this therapy is indefinite due to lack of proper studies, but results are promising and may prove to be a good laser substitute.

Nutrition Support

Exceptional effort must be made to restore nitrogen balance in all patients by the most appropriate route. Oral intake alone usually is inadequate for restoring the nutritional deficits. We prefer enteral feeding by percutaneous endoscopic gastrostomy as the most effective method presently available for supplementation and long-term maintenance of nutrition. A feeding gastrostomy should not be done unless the patient has some form of palliation for the dysphagia of esophageal obstruction and has a reasonable life expectancy of several months.

Surveillance to Detect Dysplasia and Curable Cancer

Although several regimens, including variations of combined modality therapy, appear promising, overall five-year survival from 1986 to 1993 was approximately 10% (12% for whites, 8% for blacks). Five-year survival for 1960 through 1963 was 4% for whites and 1% for blacks, and for 1980 to 1982, 8% and 5%, respectively. The best chance for improved survival remains with surveillance of high-risk patients and early detection of lesions confined to the esophageal wall.12

"Early" esophageal cancer was originally defined as carcinoma confined to mucosa and submucosa without lymph node metastasis. However, "early" cancer is now defined as malignancy confined to the mucosa without submucosal or detectable nodal involvement. This stage of malignancy is reported to have a survival rate of 90% at five years after surgical treatment. Only screening by endoscopy with biopsy in high-risk patients (head and neck cancer and CLE) can detect such cases for curative therapy.

Surveillance for esophageal cancer is dependent on familiarity with several essential elements of diagnosis: (1) a high index of suspicion, (2) knowledge of the precancerous conditions, (3) top-quality endoscopes and accessories, (4) expert endoscopic skills including precise observation with proper use of biopsy and cytology techniques, and (5) use of vital staining of mucosa with iodine or toluidine blue solutions (chromoendoscopy) that enhance topographic features of foci of dysplasia and early carcinoma to allow recognition and precise tissue sampling.

Cumulative results from several reports show that the annual incidence of cancer in affected patients with CLE is 0.2% to 2.4%. If only those studies that use endoscopic surveillance are considered, the annual incidence of adenocarcinoma is 1.4% (1 in 69 patient years of follow-up). The proper method of surveillance in these patients remains to be determined. Endoscopy every one to two years with three to four biopsies at 2-cm intervals throughout the columnar-lined segment seems to be the most reasonable surveillance program at this time.13

The finding of dysplasia on esophageal biopsy may indicate the potential for future development of carcinoma or the existence of a synchronous carcinoma nearby. Cancerous esophagi are commonly accompanied by dysplasia that may be located at some distance from the invasive cancer.

It seems reasonable at this time to recommend close clinical observation and histologic surveillance by endoscopic biopsy in all patients known to be at increased risk of esophageal carcinoma. Early diagnosis by screening during the preinvasive stage offers the only hope for cure of most of these malignancies.

References


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