CARCINOMA OF THE ESOPHAGUS SEEN IN A 12-YEAR PERIOD AT QUEENS HOSPITAL CENTER

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One hundred forty patients with carcinoma of the esophagus treated over a 12-year period at Queens Hospital Center were reviewed. Comparable numbers of patients were assigned at random to radiation therapy alone, surgical treatment with radiation, or treatment with combinations of radiation and chemotherapy pre- or postoperatively. Surgical mortality (survival 1 month or less) was 9 patients of 34, or approximately 26%. Mean survival including the early deaths was 7.5 months. Deaths were primarily due to respiratory tract complications, either alone or in combination, with three cases of anastomotic leaks, sepsis, inanition, and progressing carcinoma. Fifty-two patients received radiation therapy alone. Although there were only six deaths (10%) within the first month of treatment, average survival was 8.4 months, only marginally greater than those treated by surgery. Of 13 patients treated with combined radiation and chemotherapy, no deaths occurred within the first month of treatment, but the average survival was only 6.5 months. Of nine patients treated with chemotherapy alone, no deaths occurred within the first month of treatment, but mean survival of this small group was only 4.9 months.

Efficacy of chemotherapy and radiation therapy as definitive, adjuvant, or palliative therapy, in spite of recent somewhat optimistic reports, remains to be proven. Exploratory surgery should be retained as an essential staging and therapeutic modality in those patients in whom definite evidence establishing inoperability is lacking; ie, tumor fixation to vital structures, distant metastases, and other medical contraindications to surgery. Endoscopic instrumentation with the yittrium aluminum garnet laser appears to have a future as preliminary to surgery or definitive (palliative) management of obstructing esophageal carcinoma.

Key words • esophageal carcinoma • esophageal resections • right thoracotomy • radiation therapy • supportive care

This article reviews a comparative clinical experience with 140 cases of esophageal carcinoma treated by various methods over a 12-year-period at the Queens Hospital Center and makes projections for improved future management of this devastating disease.

MATERIALS AND METHODS

Cases reported were seen at the Queens Hospital Center, one of the acute general municipal hospitals of the New York City Health and Hospitals Corporation. One-hundred forty cases of primary esophageal carcinoma were seen during the 12-year period 1974 to 1985. Only one of these cases was an adenocarcinoma, the remaining 139 were squamous cell or epidermoid carcinoma. Adenocarcinomas at or just below the esophagogastric junction, which are generally

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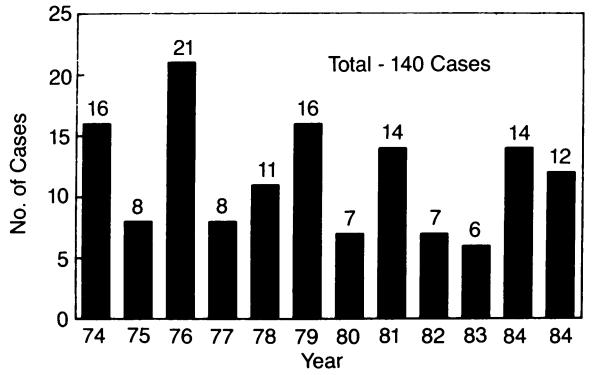

Figure 1. Esophageal cancer incidence by year. The 3 years that have elapsed since the completion of this study have shown a continual decline in incidence.

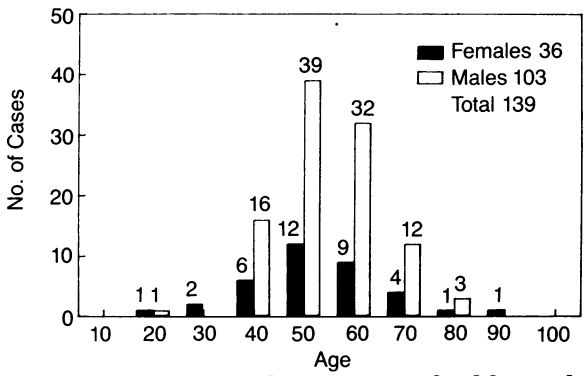

Figure 2. Esophageal cancer age incidence by gender. Twenty-five percent of females and 17% of males are in or below the fourth decade of life.

considered to be of gastric origin, were excluded, as they are biologically and pathologically different tumors.[1,2]

Comparable numbers of patients were assigned at random to radiation therapy alone, surgical treatment with radiation, or treatment with combinations of radiation and chemotherapy pre- or postoperatively. Smaller numbers were given chemotherapy alone. Early in this series, choice of therapy was determined by the service to which the patient was referred and the patient's preference. Within the last 4 or 5 years, choice increasingly has been determined after a combined tumor conference with representatives of the various disciplines involved in management. Also included in this series is a comparable group of patients for whom no specific treatment for the tumor was given or for whom treatment was limited to hydration, attempts at alternative alimentation, pain control, and other general supportive care.

RESULTS

Annual incidence of the cases of esophageal carcinoma seen between 1974 and 1985 is shown in Figure 1. Incidence varied from a low of six to a high of 21 cases per annum. Division of incidence into 6-year intervals shows that 80 cases presented in the first 6 years and 60 cases in the second 6 years. There were 104 (74%) males and 36 (26%) females in the series. Age incidence of 103 males (age of one male patient could not be determined) and 36 females are shown in Figure 2. For females, the age range is slightly broader and the average age is slightly lower than for males; 52.9 years for females compared with 54.5 years for males. (Figure 1)

The racial/ethnic distribution of the approximately 190 000 people served by the hospital is: blacks 77.1%, Hispanic 10.4%, white 9.4%, and other (Asian, mid-Eastern, etc) 3.1%. The number of black patients in this series was 97 (67%); 75 males and 22 females. The number of white patients was 17 (12%); 12 males and 5 females. Two patients (males) were Hispanic and one (male) was Iranian. Twenty-four (17%) patients were not identified ethnically or racially. These unidentified patients undoubtedly included some additional blacks, whites, Hispanics, and others, thereby making our attempt at classification of the total group less accurate. Nevertheless, the predominating incidence of esophageal carcinoma attributed to blacks[3-7] is not borne out when the high percentage of blacks in this population is considered. Low socioeconomic status and malnutrition appear to be common denominators, along with many other possible etiologic factors that have been invoked in studies of esophageal cancer.[8-9] Our data suggest that a low socioeconomic status is strongly associated with this disease in whites as well as blacks and other racial/ethnic groups.

Percentage sites of carcinoma in our series (upper, middle, and lower thirds) were compared with a large composite series reviewed by Postlethwait[1] and were found to be roughly comparable: 16% upper, 54% middle, and 30% lower. When the types of therapy applied to these lesions were reviewed, we found the more major surgical procedures were performed in lower third lesions with gradation toward increasing use of radiation therapy in middle and upper third lesions.

The Ivor Lewis[10] procedure of right thoracotomy in combination with abdominal exploration was preferred (30 of 34 cases) for esophageal resection. Technical advantages to this procedure include easy access to the

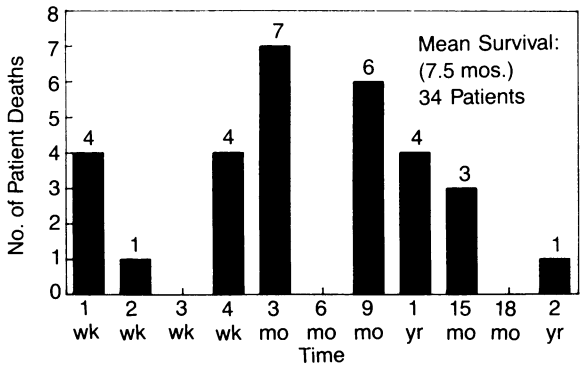

Figure 3. Resection for esophageal cancer. Of the 30 patients known dead, survival following surgery averaged 7.5 months. Of the four remaining patients, two were lost to follow-up between 3 and 6 months postsurgery, one died at 12 months, and one remains alive at 7 years.

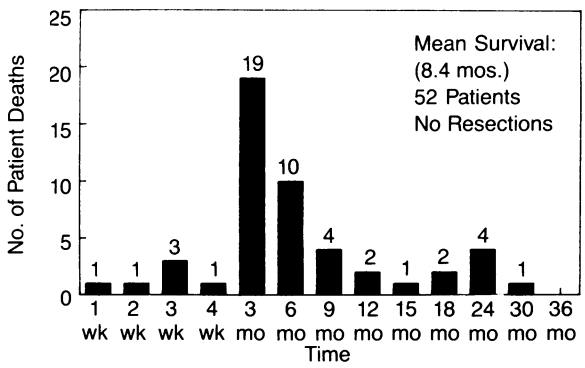

Figure 4. Radiation therapy for esophageal cancer. The 49 patients known dead survived an average of 8.4 months. Of the remaining patients, one died at 6 years and two were lost to follow-up.

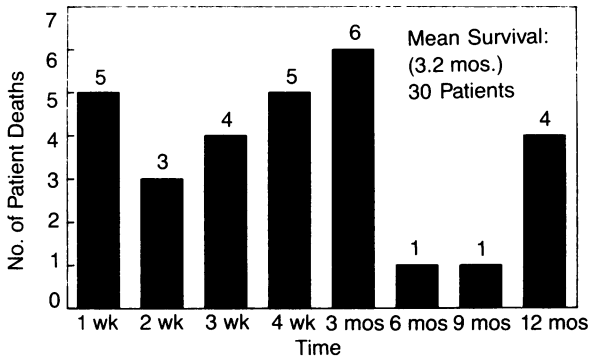

Figure 5. Supportive treatment for esophageal cancer. Of the 29 patients known dead, mean survival was 3.2 months. The remaining patient was lost to follow-up after 2 months.

entire thoracic esophagus (unlike the left-sided approaches), permitting performance of esophagogastric anastomoses without tension at any appropriate level in the right chest. Physiologic advantages for the patient include transhiatal gastric mobilization and maintenance of an anatomically and functionally intact diaphragm, important in avoiding or ameliorating pulmonary complications.

Four esophagectomies followed by esophagoenteric anastomoses were done, two of which were colon transplants and two were transhiatal gastric pull-through operations.

In comparing our postoperative complications after esophageal resections with cases reviewed by Postlethwait[1], it is notable that he cites post-anastomotic leaks as the most common single complication. In our experience, predominant complications involved the respiratory tract. These were associated frequently with preoperative radiation therapy and sometimes took the form of adult respiratory distress syndrome with high morbidity and mortality. Postlethwait's two categories, pneumonias and respiratory failure, were combined in our series as postoperative bronchopulmonary complications and accounted for approximately the same percentage of complications (22% to 28%) reported by Postlethwait. Bronchopulmonary complications were the most common in our series, with a smaller number of postanastomotic leaks, only 10% of 30 cases, as compared with approximately 25% of cases in Postlethwait's series.

The survival curve for our 34 esophageal sections for cancer is given in Figure 3. Surgical mortality (survival 1 month or less) was 9 patients of 34, or approximately 26%. Mean survival including the early deaths was 7.5 months. Deaths were primarily due to respiratory tract complications, either alone or in combination, with three cases of anastomotic leaks, sepsis, inanition, and progressing carcinoma.

Fifty-two patients receiving radiation therapy alone are represented in Figure 4. Although there were only six deaths (10%) within the first month of treatment, average survival was 8.4 months, only marginally greater than those treated by surgery.

Of 13 patients treated with combined radiation and chemotherapy, no deaths occurred within the first month of treatment, but the average survival was only 6.5 months. Of nine patients treated with chemotherapy alone, no deaths occurred within the first month of treatment, but mean survival of this small group was only 4.9 months.

Figure 5 shows the survival curve of 30 patients who

TABLE. ESOPHAGEAL CANCER: THERAPEUTIC OBJECTIVES

Cure

Palliation

- Restore Alimentation (preferably oral)
  - Resectional or bypass surgery
    - Jejunal or colonic bypass or replacement
    - Gastric tube bypass or replacement
    - Stomach bypass or replacement
  - Endoscopic instrumentation
    - Esophageal intubation
    - Total paranteral nutrition
    - Gastrostomy
    - Jejunostomy
- Specific Tumor Treatment
  - Surgery
  - Radiation therapy
  - Chemotherapy
- Therapy for Intercurrent Illness
  - Bronchopulmonary
  - Dehydration-Inanition
  - Anemia
  - Pain
  - Other

did not receive specific anticancer therapy but received supportive care. This group provides explicit and poignant examples of many patients who had advanced or end-stage disease when first seen. Early diagnosis, the sine qua non of successful treatment in most cancers, is lacking in this series. Early dysphagia, the bellwether, is subtle and ignored by many patients, including those who, because of poor dentition or alcoholic predisposition, choose semisolid or liquid alimentation, thereby delaying recognition of the cardinal symptom. Moreover, physicians frequently do not have a high enough index of suspicion when interviewing patients to identify and follow-up what may be an incipient problem with the swallowing mechanism. First-month mortality in this group was 17 of 30 patients, or 57%. Those patients surviving 3 or more months included several patients who refused specific treatment. Causes of death were inanition, sepsis, pneumonitis secondary to aspiration, and carcinomatosis. Other than those refusing treatment, specific treatment was not instituted in these patients because their clinical status was so debilitated and prognosis so poor that it was not considered appropriate to give other than supportive therapy pending reassessment as, or if, there was clinical improvement.

DISCUSSION

It is hoped that a review of these grim statistics will provide a basis for selecting modalities for treatment which will be most humane and appropriate. Our cases are like those in many municipal hospitals in central urban areas where major social and economic problems produce and perpetuate economic and medical indigents, who after periods of societal and self-neglect gravitate to this and similar institutions with advanced states of disease. Clinical cures or significant palliation have been remote by any methods of treatment. The Table outlines our clinical objectives and the modalities available to accomplish them.

Cure is listed principally for completeness. Interestingly, our most prolonged survival is a patient now approaching 7 years postoperative for transhiatal esophagectomy with cervical esophagogastrostomy after a gastric pull-through. This patient had postoperative radiation and chemotherapy, and the resected specimen showed penetration of tumor through the entire esophageal wall. He has since resumed a normal quality of life and remains well after surgery for repair of a right inguinal hernia 3 years ago. Our objective, almost always, has been palliation, to which the attempt to restore alimentation by mouth is essential. Gastrostomy, jejunostomy, and total parenteral nutrition as definitive palliative efforts have not proven generally satisfactory. Ostomies, with feeding, produce large volumes of reflex salivary secretion, thereby increasing hazards of aspiration and making patients more miserable. Total parenteral nutrition simply does not catch up with or allay the patient's catabolic processes ("tumor cachexia") due to progressing tumor.[11] Our experience has suggested that early operation, as soon as patients can tolerate a palliative resection or a bypass procedure, is probably superior to subjecting patients to longer preoperative periods, hyperalimentation, radiation therapy, or chemotherapy during which they continue to deteriorate. If the tumor is resectable, we are in a better position, with the patient's nutrition improving, to engage adjuvant therapy of choice.

Specifically, we lean toward a right thoracotomy combined with abdominal exploration in lower lesions, although considerable flexibility of approach is exercised depending on size of the lesion, proximity of carinal or major bronchial or vascular structure, or the likelihood of resectability. The cervical transhiatal approach permits avoidance of open thoracotomy and, properly chosen, permits an expeditious palliative resection and anastomosis at the safest level in the

neck. This has met with increasing approval in our experience. This procedure, performed successfully for the first time by Turner[12] in the early 1930s, has more recently been popularized by Kirk[13] and Orringer,[14] among others.

Among newer modalities that have been employed in treatment is endoscopic instrumentation, the purpose of which is to burn away portions of the obstructing tumor by laser with a minimum of challenge to the patient. This re-establishes the esophageal conduit and restores more effective swallowing almost immediately.[15-17] This is not a new principle. Endoscopic resections in the 1930s (Moersch, Seiffert) were referred to by Ivor Lewis,[10] but now they are used with greater precision, as the laser has become available as an endoscopic instrument. Use of in-lying esophageal tubes of the Celestin or similar types has been associated with generally poor results but is kept as part of our armamentarium to be used when applicable.

Concomitant with any treatment is management of intercurrent medical illness and complications. Bronchopulmonary complications are frequently associated with aspiration due to esophageal obstruction or complications of fistulization through the esophageal tumor into the bronchial tree. Early in management, these conditions must be recognized, and bronchoscopic examination in addition to esophagoscopic examination is routine. With fistula, it may be necessary to do cervical esophagostomy to divert the stream of saliva and other oral contents. Sometimes, an in-lying esophageal tube may be used to tamponade the fistula and, thereby, protect against further tracheobronchial soiling from the esophagus. These modalities have been used with only partial or indifferent success in these desperately ill patients. Dehydration, inanition, and anemia are managed by intravenous replacement of fluid and blood, and can be done with reasonable promptness, in spite of frequently coexisting pulmonary, cardiac, hepatic, or renal diseases. Pain control is achieved by use of careful doses of morphine or meperidine, but the pain is ominous and demoralizing.

Preoperative radiation therapy in our experience has appeared to incite additional pulmonary complications,[18,19] but newer state of the art equipment apparently can avoid some scatter to the adjacent lungs and concentrated tumoricidal doses can be delivered at precisely selected targets.[20,21] At present, however, if surgery is indicated and can be applied early, we prefer radiation therapy postoperatively.

Chemotherapy has been recently touted by a number of authors[22-27] as being a promising definitive modality or an avenue by which some patients can be better prepared for surgical resection. In our experience with small numbers of patients, chemotherapy does not appear to offer significant advantages. Carefully documented efforts are continuing, however.

Recent thoughtful editorials by Hellman[28] and Mountain[29] mirror much of our thinking regarding the current status of clinical management of this disease. Patients at Queens Hospital Center are practically all beyond clinical cure when first seen. Our policy has been to treat these patients palliatively, but we are always alert for the occasional patient that may be salvaged over a longer term. Recent developments will permit more successful palliation by endoscopic techniques, chemotherapy, and radiation in combination with properly chosen surgical procedures. In absence of gross evidence of tumor extension or distant metastases, it is difficult to stage the disease in these patients accurately by endoscopy or computerized tomography. Other, more invasive techniques (laparoscopy, mediastinoscopy) may extend this capability somewhat. Within this group lie the potentially curable and long-term salvageable patients. Therefore, we believe that selective surgical exploration for definitive staging and curative or palliative resection must be retained as an integral part of the overall therapeutic effort.

Initial treatment should be brief and include tissue diagnosis, intensive re–animation of the patient with fluids, blood, tracheobronchial toilet, antibiotics as necessary, and thorough assessment and tuning of the patient's cardiorespiratory, renal, liver, and other systemic and metabolic functions. The surgical option is then critically considered.

Of the specific tumor adjuvants preoperatively, we favor chemotherapy because of our poor experience with preoperative radiation therapy and because of favorable reports in the recent literature of the effective use, however limited, of chemotherapy. Use of chemotherapeutic agents must be brief and expeditious because the disease pursues an inexorable course. We must seize the opportunity to consolidate the patient's stamina and reserves, and exercise the surgical option at the optimal time. We have witnessed loss of patients that could not be sustained or were negatively affected by the preparatory regimen.

When resectional therapy cannot be applied, medical and surgical judgment must dictate the use of endoscopic or bypassing techniques, along with adjuvants in trying to improve the quality of life.

CONCLUSION

Carcinoma of the esophagus is primarily a disease of the poor, malnourished, and socioeconomically deprived. This demographic distribution is well demonstrated in cases of carcinoma of the esophagus seen at Queens Hospital Center and includes blacks and whites in proportionate numbers. Females, white and black, constitute approximately one fourth of the cases. Efficacy of chemotherapy and radiation therapy as definitive, adjuvant, or palliative therapy, in spite of recent somewhat optimistic reports, remains to be proven. Exploratory surgery should be retained as an essential staging and therapeutic modality in those patients in whom definite evidence establishing inoperability is lacking; ie, tumor fixation to vital structures, distant metastases, and other medical contraindications to surgery. Endoscopic instrumentation with the yittrium aluminum garnet laser (YAG) appears to have a future as preliminary to surgery or definitive (palliative) management of obstructing esophageal carcinoma.

In the United States, esophageal carcinoma remains a disease with a poor prognosis, and one for which we have not yet developed consistent or effective programs of early identification, cure, or extended palliation. After critical evaluation of our case material and results as well as recently reported results of other authors, we conclude that newer technology in radiation and chemotherapy, and endoscopic instrumentation with the YAG laser may provide, in combination with carefully chosen surgical procedures, improved palliation and occasional cures in the late-diagnosed carcinomas most often seen.

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