The Role of Radiation Therapy in the Management of Esophageal Cancer

N. V. Raman, MD, and William Small, Jr, MD

Background: Esophageal cancer is a challenging clinical problem with an estimated 12,300 new cases diagnosed in 1998.

Methods: A detailed review of pertinent literature is used to describe the epidemiology and management of this disease.

Results: Radiation therapy remains an important cornerstone of therapy. In combination with chemotherapy and/or surgery, radiation therapy may offer an improved therapeutic outcome.

Conclusions: Radiation therapy remains an important therapy in the treatment of esophageal cancer.

Introduction

It is estimated that in 1998, 12,300 new cases of esophageal cancer will be diagnosed and nearly 11,900 deaths will occur. Despite these alarming numbers, treatment of esophageal cancer has been the focus of several studies in the last decade as new treatment strategies evolve. Radiation therapy plays an important role in the combined modality treatment of esophageal cancer. The following highlights the various clinical studies that have led to this current thinking.

Natural History of Esophageal Cancer

Esophageal cancers have extensive local growth and lymph node involvement before widespread dissemination. Small lymphatic channels arise within the mucosa and external muscular coat of the esophagus and drain into larger lymphatic channels located in the submucosa and muscular layers of the esophagus. The dual longitudinal interconnecting lymphatic supply of the esophagus provides a submucous pathway for the lymphatic dissemination of cancer into a large number of widely separate collections of lymph nodes. Viable tumor emboli may block a lymphatic branch and give rise to a secondary deposit that presents as a submucosal outcropping, sometimes as much as 8 cm distant from the primary cancer. The lack of a serosal lining often leads to transesophageal spread of disease into the adjacent viscera and blood vessels. The disease causes death by both local growth and distant metastases. Distant metastases have been noted in virtually every tissue, including lymph nodes (73%), lung (52%), liver (47%), adrenals (20%), stomach (15%), bones (14%), and kidneys (13%) (Table 1).

Epidemiology

Between 1973 and 1982, the overall incidence rate per 100,000 population was 2.6 for squamous-cell carcinoma (SCC) and 0.4 for adenocarcinoma. The incidence of SCC in black men and women increased by 30% between 1973 and 1982, and the rate of adenocarcinoma among white men increased by 74%. By 1990, adenocarcinomas were the predominant esophageal cancers among white men. The risk factors associated with SCC include tobacco use, alcohol use, presence of food preservatives such as nitrosamines, and caustic strictures. Dietary factors, viral agents, genetic predisposition, and exposure to ionizing radiation have also been implicated. Barrett’s esophagus is a risk factor for adenocarcinoma. Clinical reports suggest that patients with esophageal adenocarcinoma have a higher incidence of hiatal hernia and duodenal ulcer compared to patients with gastric cancer. A more detailed review is beyond the scope of this article.

Patterns of Failure

The autopsy series by Appelqvist noted the cause of death in esophageal cancer to be a local cause 2.28 times as often as a metastatic cause. Mandard et al reported that in 60% of the previously treated patients in their autopsy series, the neoplasm had spread beyond the esophageal wall and involved neighboring structures, thus supporting the importance of locoregional control. Distant nonnodal metastases are documented in approximately 17% to 69% of patients in other series.
Table 2 displays the results of patterns of failure after radiation therapy and surgery as quoted by Aisner et al.4

<table>
<thead>
<tr>
<th>Radiation Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiation therapy has been used definitively, both preoperatively and postoperatively. It has been delivered mainly as external-beam radiation therapy (teletherapy), with endoluminal therapy (brachytherapy) being used as a boost to initial therapy.</td>
</tr>
<tr>
<td>Radiation Therapy Alone</td>
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<tr>
<td>The British Medical Research Council Trial,15 which attempted to answer questions comparing radiation therapy alone vs surgery, was closed due to poor accrual. Definitive radiation therapy alone in doses of 50 to 70 Gy produces a median survival duration of less than 12 months and a five-year survival of less than 10% in the majority of series.16-19 Earlam and Cunha-Melo20 reviewed 49 series with 8,489 patients treated with radiation alone and found the survival rates to be 18% at 1 year, 8% at 2 years, and 6% at 5 years. Table 3 shows the results that have been obtained by various investigators. Jun et al21,22 analyzed various radiation treatment schemes and noted no survival benefit to different radiation schemes. Accelerated fractionation schemes that decrease overall treatment time may enhance local control, although esophageal stenosis, a late effect of this modality, is more commonly observed as noted by Nishimura et al.23 Recent clinical trials have shown radiotherapy as a sole modality to be inferior to chemoradiation. Patients, who are poor surgical risks and are unable to tolerate chemotherapy occasionally will need to be managed with radiation therapy alone with a small but real chance of survival.</td>
</tr>
</tbody>
</table>

| Radiation Therapy Planning Principles |
| Position: Patient positioning in the prone position is preferable in thoracic lesions and is likely to move the esophagus further from the spinal cord. Localization: The use of barium paste after ensuring that there is no aspiration helps to delineate lesions. Target volume: The tumor volume is defined by the largest volume indicated by endoscopic findings, esophageal ultrasound, barium series, computed tomography (CT) scans, or magnetic resonance imaging (MRI) scans. A margin of 5 cm or more beyond the gross primary disease superiorly and inferiorly should be used. Portals must be wide enough to include all the gross disease with 2-cm margins. Inclusion of the supraclavicular fossa should be considered, especially when the tumor extends above the carina. If the tumor is in the distal third or the celiac nodes are beyond the gross primary disease superiorly and inferiorly should be used. Portals must be wide enough to include all the gross disease with 2-cm margins. Inclusion of the supraclavicular fossa should be considered, especially when the tumor extends above the carina. If the tumor is in the distal third or the celiac nodes are beyond the gross primary disease superiorly and inferiorly should be used. Portals must be wide enough to include all the gross disease with 2-cm margins. Inclusion of the supraclavicular fossa should be considered, especially when the tumor extends above the carina. If the tumor is in the distal third or the celiac nodes are beyond the gross primary disease superiorly and inferiorly should be used. Portals must be wide enough to include all the gross disease with 2-cm margins. Inclusion of the supraclavicular fossa should be considered, especially when the tumor extends above the carina. If the tumor is in the distal third or the celiac nodes are beyond the gross primary disease superiorly and inferiorly should be used. Portals must be wide enough to include all the gross disease with 2-cm margins. Inclusion of the supraclavicular fossa should be considered, especially when the tumor extends above the carina. If the tumor is in the distal third or the celiac nodes are beyond the gross primary disease superiorly and inferiorly should be used. Portals must be wide enough to include all the gross disease with 2-cm margins. Inclusion of the supraclavicular fossa should be considered, especially when the tumor extends above the carina. If the tumor is in the distal third or the celiac nodes are beyond the gross primary disease superiorly and inferiorly should be used. Portals must be wide enough to include all the gross disease with 2-cm margins. Inclusion of the supraclavicular fossa should be considered, especially when the tumor extends above the carina. If the tumor is in the distal third or the celiac nodes are beyond the gross primary disease superiorly and inferiorly should be used. Portals must be wide enough to include all the gross disease with 2-cm margins. Inclusion of the supraclavicular fossa should be considered, especially when the tumor extends above the carina. If the tumor is in the distal third or the celiac nodes are beyond the gross primary disease superiorly and inferiorly should be used. Portals must be wide enough to include all the gross disease with 2-cm margins. Inclusion of the supraclavicular fossa should be considered, especially when the tumor extends above the carina. If the tumor is in the distal third or the celiac nodes are beyond the gross primary disease superiorly and inferiorly should be used. Portals must be wide enough to include all the gross disease with 2-cm margins. Inclusion of the supraclavicular fossa should be considered, especially when the tumor extends above the carina. If the tumor is in the distal third or the celiac nodes are beyond the gross primary disease superiorly and inferiorly should be used. Portals must be wide enough to include all the gross disease with 2-cm margins. Inclusion of the supraclavicular fossa should be considered, especially when the tumor extends above the carina. If the tumor is in the distal third or the celiac nodes are beyond the gross primary disease superiorly and inferiorly should be used. Portals must be wide enough to include all the gross disease with 2-cm margins. Inclusion of the supraclavicular fossa should be considered, especially when the tumor extends above the carina. If the tumor is in the distal third or the celiac nodes are beyond the gross primary disease superiorly and inferiorly should be used. Portals must be wide enough to include all the gross disease with 2-cm margins. Inclusion of the supraclavicular fossa should be considered, especially when the tumor extends above the carina. |
| Dosemetric evaluation: Doses to the spinal cord, heart, lungs, liver, and kidneys must be kept within the tolerance limits to reduce sequelae and morbidity. Dose: A wide range of doses has been used with radiotherapy alone and will be a function of the tumor location and the normal tissue tolerance. We usually attempt to deliver a dose of at least 65 Gy in 1.8 to 2.0 Gy fractions. |

Preoperative Radiotherapy Alone |
The rationale for the use of preoperative radiotherapy is to increase resectability, decrease the locoregional failure, and thus increase the long-term survival. However, the results of five randomized trials (Table 4),24-28 including the European Organization for Research on Treatment of Cancer (EORTC) trial,24 did not show any obvious increase in resectability or survival. It should be noted that because the doses used in these studies were lower than doses commonly used today and the interval from completion of radiotherapy to surgery was also shorter than currently employed, meaningful conclusions are difficult to obtain.
Postoperative Radiotherapy Alone

Adjuvant postoperative radiotherapy has been used to decrease the risk of locoregional recurrence and to attempt to improve survival. Kasai et al. reported that prophylactic postoperative radiation therapy improved survival in those patients who underwent a curative resection and those who did not have lymph nodal metastases. However, the two randomized studies by Teniere et al. and Fok et al. do not reflect any improvement in five-year survival. In the Teniere study, survival in patients was not influenced by postoperative radiation therapy. The rates of local or regional recurrence were lower in the group that received postoperative radiotherapy compared with those who received surgery alone (85% vs 70%, respectively, surviving without recurrence at five years). The difference between the rates of local or regional recurrence was statistically significant in the node-negative (N0) stratum only. The study by Fok and colleagues noted a 37% incidence of stomach (neoesophagus) complications, including gastritis and gastrointestinal hemorrhage, with 8% treatment-related fatality in the irradiated group. This may be related to the high dose per fraction (3.5 Gy) used in this trial. Table 5 briefly reviews the results of these studies.

Brachytherapy

Intraluminal brachytherapy has been used to provide a boost to the tumor with radioactive sources being introduced by a nasogastric tube introduced into the esophagus. The rapid fall of dose as the distance from the central axis of the source increases does not allow the delivery of adequate dose to the paraesophageal lymphatics. However, in lesions that are truly localized to the esophagus, this modality may be used to deliver a boost to the primary tumor of limited thickness. Various institutions have used this modality to deliver a boost using low-dose-rate (LDR) and fractionated high-dose-rate (HDR) techniques. The wide variations in the indications, prescribed doses, and dosimetry have led to the development of guidelines (Table 6) from the American Brachytherapy Society. Complications associated with this modality include perforation, aspiration pneumonitis, esophageal bleeding and mediastinitis, and development of strictures. The preliminary report of the Radiation Therapy Oncology Group (RTOG) study 92-07 observed a 34% incidence of life-threatening toxicity or treatment-related mortality when intraluminal HDR therapy was used with concurrent chemotherapy after external-beam radiotherapy. This prompted a word of caution from the investigators regarding the use of this modality in conjunction with teletherapy and concurrent chemotherapy.

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Table 5: Results of Postoperative Radiotherapy or Surgery for Esophageal Cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of Patients</th>
<th>Surgery</th>
<th>RT + Surgery</th>
<th>Rate Median Survival</th>
<th>Late regional Failure %</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kasai et al.</td>
<td>112</td>
<td>52</td>
<td>60 Gy</td>
<td>25.6% 60 Gy</td>
<td>-</td>
<td>Prophylactic RT improved survival in 82 patients with 72 (67.5%) of 84 patients in the radiation arm vs 52 (37.5%) of 138 in the surgery arm.</td>
</tr>
<tr>
<td>Teniere 1998</td>
<td>219</td>
<td>102</td>
<td>63-93 Gy</td>
<td>10 mos 199</td>
<td>199</td>
<td>This difference between the rates of local or regional recurrence was statistically significant (40.9%) in node-negative (N0) stratum.</td>
</tr>
<tr>
<td>Fok 1999</td>
<td>80</td>
<td>32</td>
<td>45-47.5 Gy</td>
<td>19 mos 199</td>
<td>199</td>
<td>37% incidence of gastroesophageal complications in the radiation group with 7% lymph node metastases. No significant increased incidence of local recurrence with RT in the radiation and surgery group (P=0.46).</td>
</tr>
<tr>
<td>70</td>
<td>32.5-51.5 Gy</td>
<td>7 mos 199</td>
<td>29</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

Table 6: American Brachytherapy Society Consensus Guidelines for Brachytherapy of Esophageal Cancer

**INTENTIONAL TREATMENT**

- Good Conditions:
  - Uniform primary esophageal carcinoma of type 1 and 2
  - No advanced hilar obstruction
  - No nodal disease or metastatic disease

- Poor Conditions:
  - Type 3, 4, or 5 tumors
  - Carcinoma of the larynx or hypopharynx
  - Carcinoma of the stomach or pancreas
  - Carcinoma of the esophagus or stomach

**DOSIMETERS FOR DEFINITIVE TREATMENT**

- External Beam Radiation (EBRT):
  - 45-50 Gy in 1.8-2.0 Gy BID to a total volume of 16-18 cm²
  - 50-54 Gy in 2.0 Gy BID to a total volume of 16-18 cm²

- HDR-19: 45 Gy in 1.8 Gy BID for 5 fractions

**DOSIMETERS FOR PALLIATIVE TREATMENT**

- EBRT and/or TACE with Staged Disease Externally:
  - Brachytherapy: HDR 42.5 Gy in 1.8 Gy BID for 5 fractions
  - EBRT: 45-50 Gy in 1.8 Gy BID for 5 fractions

- EBRT with TACE and Brachytherapy:
  - Brachytherapy: HDR 42.5 Gy in 1.8 Gy BID for 5 fractions

- EBRT with TACE and Brachytherapy:
  - Brachytherapy: HDR 42.5 Gy in 1.8 Gy BID for 5 fractions

**EXTRASPECIAL TREATMENTS**

- All doses specified from tumor center to chest wall

- All fractions: 1.8 Gy boost or 1.8 Gy BID for 5 fractions

- All patients with type 3, 4, or 5 tumors

- All patients with type 3, 4, or 5 tumors

- All patients with type 3, 4, or 5 tumors

- All patients with type 3, 4, or 5 tumors
Neoadjuvant Chemotherapy

The rationale for use of preoperative chemotherapy includes an attempt to decrease the size of the primary tumor, thereby increasing the surgical resection rate and eliminating micrometastases or delaying their appearance to prolong survival. Table 7 lists the details of three preoperative chemotherapy vs surgery studies. In the Scandinavian study, a survival disadvantage was seen with chemotherapy. Roth et al. compared adjuvant chemotherapy given both preoperatively and postoperatively vs surgery alone and did not find any significant difference in the resectability rates or in the actuarial survival of their patients. The median survival for patients responding to chemotherapy was longer than 20 months, whereas patients not responding to chemotherapy had a median survival of 6.2 months, which was statistically significant (P=0.008). The survival of responders was also significantly longer than that of the patients in the surgery group (P=0.05). The closed Intergroup trial (INT-0113) compared neoadjuvant cisplatin and 5-fluorouracil (5-FU) for three cycles followed by two more cycles after resection vs surgery alone in randomized 467 patients. Preliminary analysis reports that 61% of the patients received all three cycles of planned chemotherapy, and 20% had grade 3 or 4 hematologic toxicity. Early results have failed to reveal any median survival difference.

Concurrent Chemoradiation

The studies of Byfield et al. and Kolaric et al. reported the use of definitive concurrent chemoradiation. A larger Eastern Cooperative Oncology Groups (ECOG) phase III trial failed to demonstrate the advantage of concurrent bleomycin given with radiation vs radiation alone. Fox Chase Cancer Center reported on 90 patients treated with concurrent chemoradiation. Radiation therapy (60 Gy/6-7 wks) was delivered with two 96-hour infusions of 5-FU and bolus mitomycin C. A total of 57 patients with stage I/II disease received a curative dose of 60 Gy with chemotherapy, while 33 patients with stage III/IV disease received a palliative dose of 50 Gy with the same chemotherapy. The overall median survival of stage I/II patients was 18 months, with three- and five-year actuarial survival of 29% and 18%, respectively. The actuarial–determined relapse-free rate for stage I and II at both 3 and 5 years was 70%. The median survival of patients with stage III and IV disease was 9 months and 7 months, respectively. Significantly, palliation was rendered to patients with advanced disease with relief of dysphagia in 77%, with 60% being free of dysphagia at the time of death. Severe acute reactions were noted in 11 (12.2%) patients. Three (3.3%) patients developed significant late toxicity requiring hospitalization with 2 (2.2%) treatment-related fatalities.

Four randomized studies evaluating definitive chemoradiation vs radiation alone have been completed recently (Table 8). The recently published ECOG EST-1282 trial reports improved overall survival of patients with SCC of the esophagus compared to those treated with radiation alone. The median two- and five-year survival for the combined modality treatment was 14.8 months (27% and 9%, respectively) compared to 9.2 months (33% and 7%, respectively) for the radiation arm. Interestingly, the study also reports that surgery that was optional on the treatment protocol had a marginally significant impact on survival. An update of the RTOG study compared neoadjuvant cisplatin and 5-FU infusion given preoperatively and followed by two more cycles of chemotherapy vs surgery alone in 90 patients treated with advanced disease of dysphagia in 77%, with 60% being free of dysphagia at the time of death. Severe acute reactions were noted in 11 (12.2%) patients. Three (3.3%) patients developed significant late toxicity requiring hospitalization with 2 (2.2%) treatment-related fatalities.

The studies of Byfield et al. and Kolaric et al. compared chemotherapy and radiotherapy vs radiotherapy alone in patients with locally advanced esophageal cancer. The main objective of the study was to compare overall survival between the two randomized treatment groups. Sixty-two patients were randomized to receive RT alone and 61 were randomized to the combined arm. The median relapse-free survival was 14.1 months and the five-year survival rate was 27%, while in the RT-alone group, the median survival duration was 9.3 months with no patients alive at 5 years (P<.0001).

Fever local failures and distant recurrences were also noted in the combined-modality group in this study. The study concluded that cisplatin and 5-FU infusion given during and following RT of 50 Gy is statistically superior to standard 64-Gy RT alone in patients with locally advanced esophageal cancer. In the EORTC study, addition to the above, the progression-free survival advantage was statistically significant. All four studies report a superior median survival in the chemoradiation arm vs radiation alone. Thus, definitive chemoradiation vs radiation alone appears to provide an improved therapeutic outcome.
Neoadjuvant Chemoradiation Followed by Surgery

Locoregional disease limited to the esophageal and its draining lymphatics continues to remain the major cause of mortality and morbidity in esophageal cancer. Triple modality therapy has emerged in an effort to maximize the effectiveness of current treatment strategies. The earliest trials of preoperative chemoradiation were based on the success of treating anal carcinoma. Franklin et al treated 30 patients with 30 Gy/3 wks concurrent with 5-FU (days 1-4 and 29-32) and mitomycin C (day 1) followed by surgery (day 49-64). Postoperatively, 20 Gy was delivered to patients with residual disease. Follow-up revealed that four of the six histologically negative disease-free patients were alive for 95 to 190 weeks. One of the patients who refused surgery after radiation and chemotherapy was alive at 4 years.

The Wayne State group further modified this regimen and substituted cisplatin instead of mitomycin C. The results showed that 19 of 21 patients underwent surgery and 27% attained pathologic complete response (CR) in the resected specimen, with a median survival of 18 months overall and a disease-free survival of 24 months. Spurred by the successes, RTOG and the Southwest Oncology Group (SWOG) initiated trials (Table 9). In the RTOG 81-11 trial, 40 patients were treated with radiation (30 Gy/3 wks) and concurrent cisplatin plus short-course 5-FU infusion preoperatively. An additional 20 Gy of radiation was delivered postoperatively with 5-FU if tumor was present in the resected specimen. Eight (30%) of 27 who underwent resection had a pathologic CR. The overall two-year survival was 15% compared with 33% for those who had a pathologic CR. A 5% chemoradiation-related mortality was noted. In the SWOG 80-37 study, 33% of (18 of 55 undergoing surgery) had a pathologic CR with a 45% projected survival at 3 years. Significant postoperative mortality of 11%, possibly reflecting surgical experience in this arena, was noted. In the ECOG 72-90 neoadjuvant chemoradiation study, 33 of 46 underwent resection; 24% (8 of 33) had a pathologic CR with a median survival of 16.8 months. Table 9 briefly summarizes these trials.

Four randomized trials (Table 10) addressing the role of neoadjuvant chemoradiation vs surgery have been conducted. The Dublin study involved only patients with adenocarcinoma. Patients were to receive either surgery alone or two courses of neoadjuvant chemotheraphy (cisplatin/5-FU) with concurrent RT 40 Gy/2.67 Gy per fraction. There was a 22% pathologic CR (13 of 58 patients) from neoadjuvant chemoradiation. The survival in those who respond is significantly better than nonresponders, and the long-term survivors in these studies were those patients with a pathologic CR. Neoadjuvant chemoradiation appears to represent a step forward in achieving local control of disease. The CALGB study 9781 (RTOG 9716) is a prospective, randomized phase III trial comparing trimodality therapy to surgery alone. The protocol utilizes cisplatin 100 mg/m² BID/3wks with cisplatin + 5-FU if tumor was present in the resected specimen. Thirty (50%) of 60 who underwent resection had a pathologic CR. The overall two-year survival was 15% compared with 33% for those who had a pathologic CR. A 5% chemoradiation-related mortality was noted. In the SWOG 80-37 study, 33% of (18 of 55 undergoing surgery) had a pathologic CR with a 45% projected survival at 3 years. Significant postoperative mortality of 11%, possibly reflecting surgical experience in this arena, was noted. In the ECOG 72-90 neoadjuvant chemoradiation study, 33 of 46 underwent resection; 24% (8 of 33) had a pathologic CR with a median survival of 16.8 months. Table 9 briefly summarizes these trials.

Table 9. — Neoadjuvant Chemoradiation for Esophageal Cancer: Results of Cooperative and Individual Trials

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of Patients</th>
<th>Radiation Dose</th>
<th>Chemotherapy Regimen</th>
<th>Pathologic CR</th>
<th>Median Survival (mo)</th>
<th>Survived at 3 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Franklin a</td>
<td>20</td>
<td>30 Gy/3 wks</td>
<td>5-FU + 5-FU</td>
<td>77%</td>
<td>22%</td>
<td>11</td>
</tr>
<tr>
<td>Forster b</td>
<td>33</td>
<td>37.5 Gy/4.5 wks</td>
<td>5-FU + 5-FU</td>
<td>85%</td>
<td>70%</td>
<td>21</td>
</tr>
<tr>
<td>Franklin a</td>
<td>28</td>
<td>40 Gy/4 wks</td>
<td>5-FU + 5-FU</td>
<td>80%</td>
<td>80%</td>
<td>21</td>
</tr>
<tr>
<td>Diethelm c</td>
<td>10</td>
<td>45 Gy/3 wks</td>
<td>5-FU + 5-FU</td>
<td>73%</td>
<td>73%</td>
<td>21</td>
</tr>
</tbody>
</table>

* a: Additional 25 Gy delivered for median follow-up postoperatively
* b: 24 patients treated with 37.5 Gy/4.5 wks and 20 patients treated with 40 Gy/3 wks
* c: No survival
* d: 20 Gy delivered postoperatively
* e: Mean survival
* f: 1 month survival
* CR: complete response

Table 10. — Neoadjuvant Chemoradiation for Esophageal Cancer: Results of Randomized Trials

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of Patients</th>
<th>Radiation Dose</th>
<th>Chemotherapy Regimen</th>
<th>Pathologic CR</th>
<th>Median Survival (mo)</th>
<th>Survived at 3 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vos d</td>
<td>50</td>
<td>45 Gy/3 wks</td>
<td>5-FU + 5-FU</td>
<td>32%</td>
<td>16%</td>
<td>16</td>
</tr>
<tr>
<td>Conroy e</td>
<td>90</td>
<td>45 Gy/3 wks</td>
<td>5-FU + 5-FU</td>
<td>32%</td>
<td>16%</td>
<td>16</td>
</tr>
<tr>
<td>Paccagnella f</td>
<td>149</td>
<td>37.5 Gy/4.5 wks</td>
<td>5-FU</td>
<td>26%</td>
<td>16%</td>
<td>16</td>
</tr>
<tr>
<td>Paccagnella f</td>
<td>149</td>
<td>37.5 Gy/4.5 wks</td>
<td>5-FU</td>
<td>26%</td>
<td>16%</td>
<td>16</td>
</tr>
<tr>
<td>Le Peron g</td>
<td>46</td>
<td>45 Gy/3 wks</td>
<td>5-FU + 5-FU</td>
<td>32%</td>
<td>16%</td>
<td>16</td>
</tr>
<tr>
<td>Uriami h</td>
<td>50</td>
<td>45 Gy/3 wks</td>
<td>5-FU + 5-FU</td>
<td>32%</td>
<td>16%</td>
<td>16</td>
</tr>
</tbody>
</table>

* d: Estimated from survival curves
* e: Median survival of 18.6 months in the surgery alone arm, surgery is performed within six weeks following randomization. The study seeks to compare the response, survival, and patterns of failure of trimodality therapy to surgery alone in a multi-institutional setting. Further trials in this area are needed to clarify the issue.
Discussion

Radiotherapy has a number of roles in the treatment of patients with esophageal carcinoma. A number of approaches have been attempted over the last couple of decades to treat patients with carcinoma of the esophagus in order to reduce the local tumor burden and treatment of micrometastatic disease. These include various combinations of RT, surgery, and chemotherapy. The use of RT in a preoperative setting may improve resectability. The risk of locoregional failure is likely to be decreased with preoperative and postoperative RT. Clinical trials in the areas have not translated into improvement in survival. Definitive chemoradiation has shown promising results and appears to be superior to RT as the sole modality. Recent reports on neoadjuvant chemoradiation followed by surgery may represent a step forward in the local control of this neoplasm, especially in patients with adenocarcinoma. RT offers significant palliation in patients with inoperable disease and is extremely useful in such a setting. There is a need for enrolling patients in sufficient numbers in prospective clinical trials that will allow clinicians to be able to define the optimal sequencing and actual necessity of each individual component of combined-modality therapy.

New Directions

Currently, several active protocols are studying different therapeutic regimens. The US Gastrointestinal Intergroup–0123 protocol that is accruing patients is comparing chemoradiotherapy using cisplatin/5-FU with conventional-dose vs high-dose radiotherapy. CALGB-9781 is an effort to test neoadjuvant chemoradiation vs surgery alone and started accrual in 1997. All clinicians are encouraged to enter patients in clinical trials to improve the therapy of esophageal cancer.

No significant relationship exists between the authors and the companies/organizations whose products or services may be referenced in this article.

References

8. MacDonald WC, MacDonald JB. Adenocarcinoma of the esophagus and/or gastric cardia. Cancer. 1987;60:1094-1098.


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