

RADIOTHERAPY
FOR

**CARCINOMA
OESOPHAGUS**

GENERAL MANAGEMENT

- Treatment for esophageal carcinoma is characterized as curative or palliative.
- Only 20% patients present with cancer of the esophagus that is truly localized to the esophagus
- At the time of diagnosis, approximately 80% patients have either locally advanced or distant disease.
- Less than 15% of patients are cured

new TNM rule

GE JUNCTION

- a tumor in which the epicenter is within 5 cm of the GE junction and also extends into the esophagus is classified and staged using the esophageal carcinoma scheme
- tumors with an epicenter in the stomach that are >5 cm from the GE junction or those within 5 cm of the GE junction without extension into the esophagus are classified and staged using the gastric carcinoma scheme.

Siewert tumor type

- Assessed in all patients with adenocarcinomas involving the esophagogastric junction.
- **Siewert Type I:** adenocarcinoma of the lower esophagus with the center located within 1 cm to 5 cm above the anatomic EGJ.
- **Siewert Type II:** true carcinoma of the cardia with the tumor center within 1 cm above and 2 cm below the EGJ.
- **Siewert Type III:** sub-cardial carcinoma with the tumor center between 2 and 5 cm below EGJ, which infiltrates the EGJ and lower esophagus from below. These are considered gastric cancers

Radiation Therapy Alone

- There are no randomized studies comparing surgery alone with radiation alone
- Radiation therapy alone has been usually delivered when :
 - Lesions inoperable because of tumor extent
 - medical contraindications
 - and/or palliative treatment is indicated.

Radiation Therapy Alone

TABLE 53.11 SUGGESTED SCHEMA FOR DEFINITIVE EXTERNAL BEAM RADIATION AND ESOPHAGEAL BRACHYTHERAPY

External-Beam Radiation

From 45 to 50 Gy in 1.8- to 2.0-Gy fractions, 5 fractions/wk, wk 1 to 5

Brachytherapy

High dose rate: total dose of 10 Gy, 5 Gy/fraction, 1 fraction/wk, starting 2 to 3 wk after completion of external beam

Low dose rate: total dose of 20 Gy, single course, 0.4 to 1.0 Gy/hr, starting 2 to 3 wk from completion of external beam

All doses are specified 1 cm from the midsource or mid-dwell position.

Intra Luminal Brachytherapy

- Brachytherapy alone is a palliative modality and used for local control.
- no significant difference in local control or survival with high-dose brachytherapy compared with external beam RT.
- High rates of Fistula, Stricture, Perforations.
- Faster and simpler way of quick therapy in select cases.

Primary RADIOTHERAPY

- A large review analyzing 49 series involving >8,400 patients treated primarily with radiation therapy alone found overall survival rates:
 - 1 year : 18%
 - 2 years : 8%
 - 5 years : 6%

Earlam R, Cunha-Melo JR. Oesophageal squamous cell carcinoma: I. A critical review of surgery. *Br J Surg* 1980;67:381–390.

- In the RTOG 85-01 trial, all patients in the RT alone arm who received 64 Gy at 2 Gy per day with conventional techniques died of cancer by 3 years.

Primary RADIOTHERAPY

- Hancock and Glatstein reviewed 9,511 patients and found only 5.8% were alive at 5 years.
- Okawa et al. reported 5-year survival rates by stage.
5-year survival rate
 - Stage I : 20%
 - Stage II: 10%
 - Stage III: 3%
 - Stage IV: 0%.
- Overall, the 5-year survival rate was 9%.

- Hancock SL, Glatstein E. Radiation therapy of esophageal cancer. *Semin Oncol* 1984;11:144–158.
- Okawa T, Kita M, Tanaka M, et al. Results of radiotherapy for inoperable locally advanced esophageal cancer. *Int J Radiat Oncol Biol Phys* 1989;17:49–54.

Primary RADIOTHERAPY

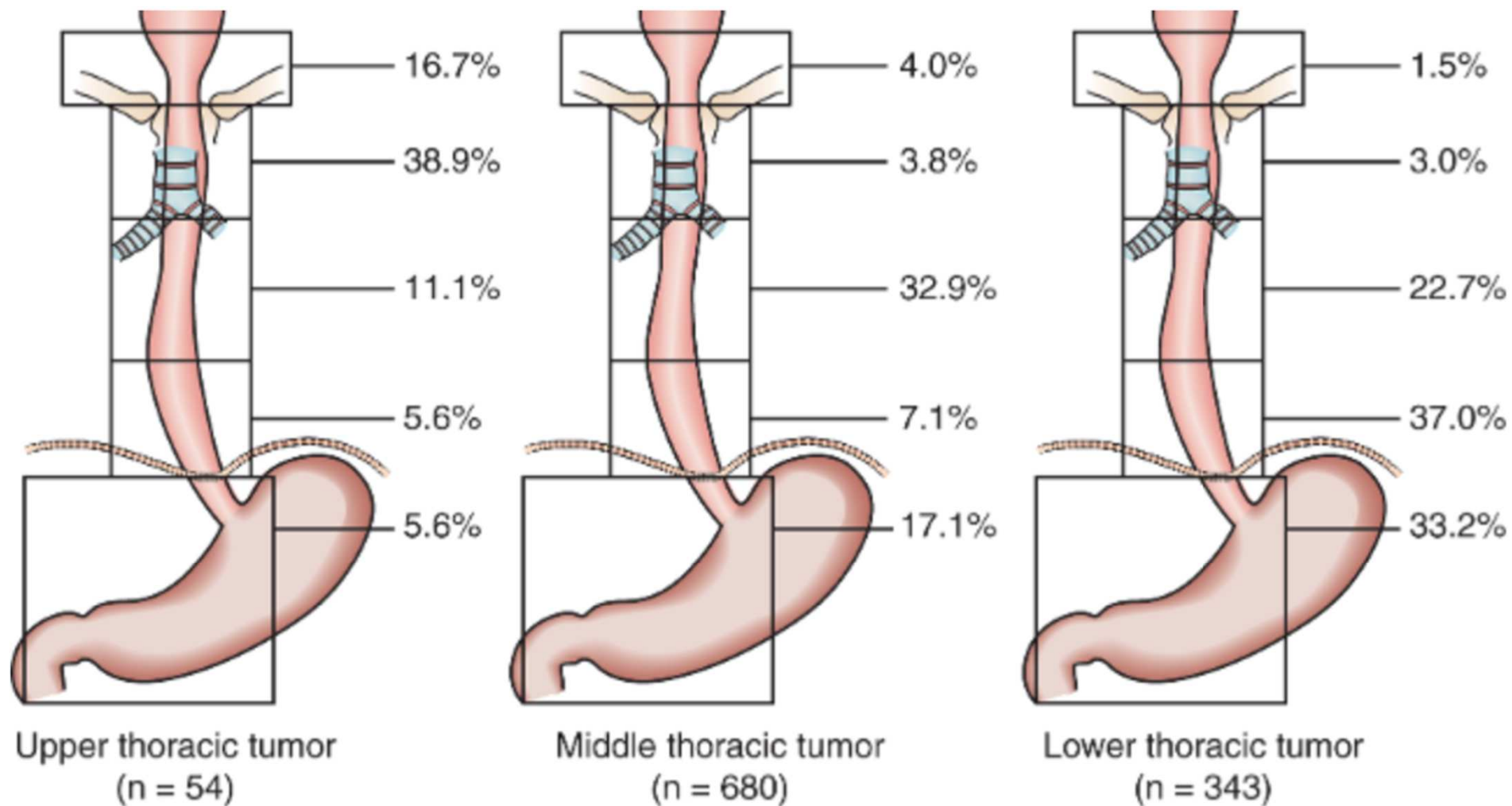
- These and other data suggest that treatment with radiation therapy alone for esophageal cancer patients is palliative in the vast majority of patients.
- The NCCN panel recommends that RT alone should generally be reserved for palliation or for patients who are medically unable to receive chemotherapy.

Alternative RT techniques

- hypoxic cell sensitizers
- hyperfractionation
- have not resulted in a clear survival advantage.
- Experience with intraoperative RT as an alternative to external beam RT is limited.
- IMRT is currently being investigated.
- Retrospective studies comparing 3DCRT vs. IMRT generally shown superior dose conformity and homogeneity with IMRT and reduction of RT dose to the lungs and heart.

RT Treatment Planning

- Use of CT simulation and 3D or IMRT treatment planning is encouraged.
- Use of IV and/or oral contrast for CT simulation to be used to aid in target localization. Use of an immobilization device is recommended for reproducibility of daily set-up.
- The GTV should include the primary tumor and involved regional lymph nodes.
- CTV is primary tumor plus a 3-4 cm expansion superiorly and inferiorly along the length of the esophagus and cardia and a 1 cm radial expansion.
- The nodal CTV should be defined by a 0.5 to 1.5 cm expansion from the nodal GTV. CTV should also include coverage of elective nodal regions
- The PTV expansion should be 0.5 to 1 cm.
- The uncertainties arising from respiratory motion should also be taken into consideration.



Lymph node treatment

- Depends upon the location of the primary.
- **Cervical esophagus:** supraclavicular nodes +/- treatment of higher echelon cervical nodes, especially if the nodal stage is N1 or greater.
- **Upper third :** Para-esophageal lymph nodes and supra clavicular lymph nodes.
- **Middle third :** Para-esophageal lymph nodes.
- **Distal third and GEJ:** para-esophageal lymph nodes, lesser curvature lymph nodes in distal lesions, and the celiac axis.

RT dosage

- The NCCN panel recommends a dose range of 41.4 to 50.4 Gy (delivered in fractions of 1.8 to 2 Gy per day) for pre-operative therapy.
- Patients who are not fit for surgery should receive doses of 50 to 50.4 Gy.
- The recommended dose for post operative 45 to 50.4 Gy
- definitive therapy : 50 to 50.4 Gy. Higher doses (60 to 66 Gy) may be appropriate for tumors of the cervical esophagus.
- However there is no evidence from randomized trials to support the additional benefit of this dose range over 50 to 50.4 Gy.

Palliative Treatment

- Palliative treatment is frequently used for the relief of symptoms of esophageal carcinoma, especially dysphagia.
- Palliative irradiation is frequently used to control the primary disease, as well as distant metastases.
- Resolution of symptoms, especially pain and dysphagia, can be accomplished in up to 80% of patients.
- Laser ablation with or without intraluminal brachytherapy can be used to improve the stenosis-free interval and prevent obstruction.

Preoperative Radiation Therapy

- The use of preoperative radiation therapy has potential biologic and physical advantages.
- Increased resectability of tumors
- Increased tumor radio-responsiveness secondary to improved tumor oxygenation
- Decreased likelihood of dissemination at the time of surgery
- Avoidance of surgery in patients with rapidly progressive disease.

Pre Op. RT

- A quantitative meta-analysis included updated individual patient data from all properly randomized trials.
- 1147 patients from five randomized trials.
- median follow-up of 9 years
- survival benefit of 3% at 2 years and 4% at 5 years
- No significant evidence that pre operative radiotherapy improves the survival of patients with potentially resectable esophageal cancer

Preoperative radiotherapy in esophageal carcinoma: a meta-analysis using individual patient data (Oesophageal Cancer Collaborative Group).

Pre OP RT

Table 1. — Randomized Trials of Preoperative Radiotherapy (RT) and Surgery vs Surgery Alone

Study	Yr	No. of Patients	Pathology	Median Survival (mos)		5-yr Survival Rate* (%)	
				+RT	–RT	+RT	–RT
Fok ⁸	1994	79	SqCC	11	22	10	16
Launois ⁹	1981	124	SqCC	4.5	8.2	10	12
Gignoux ¹⁰	1987	229	SqCC	12.3	12	10	9
Wang ¹¹	1989	206	–	–	–	35	30
Nygaard ¹²	1992	108	SqCC	10	7	–	–
Arnott ¹³	1992	196	SqCC + Adenocarcinoma	8	8	9	17

*Not statistically significant.
SqCC = squamous cell carcinoma.

Pre Op. RT

- There are multiple, largely historical randomized studies comparing preoperative irradiation followed by surgery with surgery alone.
- No differences in resectability rates or survival in almost all of the individual studies.
- These studies demonstrate no clinical benefit to the use of preoperative radiation therapy alone.
- Interpretation of these varying studies is complicated by differences in radiation techniques, suboptimal radiation doses, and inadequate radiation volumes.

Adjuvant RT

- reduce local recurrence rates.
- Several randomized trials were performed comparing surgery plus postoperative RT with surgery.
- The majority of the evidence has revealed that PORT may improve local disease recurrence but does not confer any survival benefit over surgery alone

Post operative Radiation Therapy

- The main is knowledge of the pathologic staging for appropriately selected patients for therapy.
- Postoperative therapy may allow the radiation oncologist to treat areas at risk for recurrence while sparing otherwise normal radiosensitive structures, thereby decreasing toxicity.
- pT1, N0, M0 or metastatic disease may be spared treatment.

Disadvantages of postoperative radiation :

- tolerance of normal tissues after gastric pull-up
- irradiation of a de-vascularized tumor bed
- larger fields compared to a preoperative approach
- delays in adjuvant treatment delivery.

Reevaluation of postoperative radiotherapy for thoracic esophageal carcinoma.

Yamamoto M¹, Yamashita T, Matsubara T, Kitahara T, Sekiguchi K, Furukawa M, Uki A, Kobayashi M, Tanaka E, Ueda M, Nakajima T.

Author information

Abstract

PURPOSE: To reevaluate postoperative radiotherapy for thoracic esophageal carcinoma.

METHODS AND MATERIALS: Reviewed were the outcome of 89 patients who underwent esophagectomy with systematic dissection of regional lymph nodes between 1988 and 1993. Of the 89 patients, 19 underwent no adjuvant treatment, 22 underwent adjuvant chemotherapy alone, and 48 underwent postoperative radiotherapy. Twelve of the 48 also underwent adjuvant chemotherapy.

RESULTS: All patients who experienced local-regional recurrence had lymph node metastases at the time of surgery. The actuarial local-regional control rate at 2-year of follow-up was 94% for patients with lymph node metastases at the time of surgery who underwent postoperative radiotherapy alone or plus chemotherapy, and 74% for those who underwent adjuvant chemotherapy alone. The local-regional control rate was significantly better for those who had undergone postoperative radiotherapy ($p < 0.01$).

CONCLUSIONS: Postoperative radiotherapy still plays an important role as adjuvant treatment.

Value of radiotherapy after radical surgery for esophageal carcinoma: a report of 495 patients.

Xiao ZF¹, Yang ZY, Liang J, Miao YJ, Wang M, Yin WB, Gu XZ, Zhang DC, Zhang RG, Wang LJ.

Author information

Abstract

BACKGROUND: Despite three decades of debate, no conclusion has been reached concerning the effectiveness of postoperative radiotherapy for resected esophageal carcinoma. From 1986 through 1997, a prospective randomized study was carried out with 495 patients in an attempt to define the value of this therapeutic modality.

METHODS: A total of 495 patients with esophageal cancer who had undergone radical resection were randomized by the envelope method into a surgery-alone group (S) of 275 patients and a surgery plus radiotherapy group (S + R) of 220 patients. Radiation treatment was started 3 to 4 weeks after the operation. The portals encompassed the entire mediastinum and bilateral supraclavicular areas. A midplane dose of 50 to 60 Gy in 25 to 30 fractions was delivered over 5 to 6 weeks.

RESULTS: The overall 5-year survival rate was 31.7% for the S group and 41.3% ($p = 0.4474$) for the S + R group. The 5-year survival rates of patients who were lymph node positive were 14.7% and 29.2% ($p = 0.0698$), respectively. Five-year survival rates of stage III patients were 13.1% and 35.1% ($p = 0.0027$), respectively.

CONCLUSIONS: Postoperative prophylactic radiotherapy improved the 5-year survival rate in esophageal cancer patients with positive lymph node metastases and in patients with stage III disease compared with similar patients who did not receive radiation therapy. These results were almost significant for patients with positive lymph node metastases and highly significant for patients with stage III disease.

Impact of postoperative radiation after esophagectomy for esophageal cancer.

Schreiber D¹, Rineer J, Vongtama D, Wortham A, Han P, Schwartz D, Choi K, Rotman M.

Author information

Abstract

INTRODUCTION: Though postoperative radiation for esophageal cancer is offered in selected cases, there is conflicting evidence as to whether it improves overall survival (OS). We performed a retrospective analysis using the Surveillance Epidemiology and End Results database to analyze the impact of adjuvant radiation in a large cohort of patients.

METHODS: From 1998 to 2005, patients diagnosed with stage T3-4N0M0 or T1-4N1M0 esophageal adenocarcinoma (AC) or squamous cell carcinoma (SCC) who were definitively treated with esophagectomy, with or without postoperative radiation, were selected. Kaplan-Meier and Cox regression analysis were used to compare OS and disease-specific survival (DSS).

RESULTS: A total of 1046 patients met the selection criteria: 683 (65.3%) received surgery alone and 363 (34.7%) received postoperative radiation. For American Joint Committee on Cancer stage III esophageal carcinoma (T3N1M0 or T4N0-1M0), there was significant improvement in median and 3-year OS ($p < 0.001$) and DSS ($p < 0.001$), respectively. This benefit was present for both SCC and AC. However, for American Joint Committee on Cancer stages IIA and IIB disease there was no significant differences in OS or DSS. Multivariate analysis revealed that postoperative radiation was the most significant predictor for improved OS (hazard ratio 0.70, 95% confidence interval 0.59-0.83, $p < 0.001$).

CONCLUSIONS: This large population-based review supports the use of postoperative radiation for stage III SCC and AC of the esophagus. Given the retrospective nature of this study, until appropriately powered randomized trials confirm these results, caution should be used before broadly applying these findings in clinical practice.

Limitations of these trials

- patients were not stratified by stage
- hence unlikely to detect an improvement in survival in those with high risk features (positive lymph nodes, deeply invading tumors).
- often include patients with positive celiac nodes
- include mostly squamous cell carcinomas
- no chemo were given.
- Adjuvant RT can theoretically treat microscopic disease left behind after surgery to increase local control, but cannot eradicate systemic spread of tumor cells.

NCCN Guidelines

- The management of patients with esophageal and EGJ cancers requires the expertise of several disciplines.
- Includes surgical oncology, medical oncology, gastroenterology, radiation oncology, radiology, and pathology.
- Also nutritional services, social workers, nursing, palliative care specialists, and other supporting disciplines.
- The panel believes in an infrastructure that encourages multi disciplinary treatment decision-making by members of any discipline taking care of patients.

Work up

- Newly diagnosed patients should undergo a complete history, physical examination, biopsy.
- Bronchoscopy (if the cancer is located at or above the carina).
- Double contrast barium study (for patients in whom the upper GI tract cannot be visualized).
- A complete blood cell count (CBC), multichannel serum chemistry analysis, coagulation studies, and CT scan (with oral and IV contrast) of the chest and abdomen should also be performed.

Work up

- EUS and PET/CT evaluation is recommended if metastatic cancer is not evident.
- HER2-neu testing is recommended if metastatic disease is documented or suspected.
- In all patients with EGJ adenocarcinoma assess Siewert tumor type as part of initial workup.
- Screening for family history of esophageal or EGJ cancers.
- Referral to a cancer genetics professional is recommended for an individual with a genetic predisposition to the development of esophageal or EGJ cancers.

PET/CT scans

- PET/CT scan has been shown to improve lymph node staging and the detection of stage IV esophageal cancer.
- Independent predictor of OS in patients with non-metastatic esophageal cancer.
- Useful for initial staging and evaluation of patients after chemoradiation prior to surgery for the detection of distant lymphatic and hematogenous metastases.

PET CT scans

- PET/CT scans are useful for restaging patients and monitoring response to primary therapy.
- Addition of PET/CT to standard staging led to changes in the multidisciplinary recommendations in 38.2% patients, improving the patient selection for radical treatment.
- PET/CT scans are more accurate than EUS-FNA and CT scan for predicting nodal status and complete response after neoadjuvant therapy.

Work up

- Initial workup enables patients to be classified into two groups with the following characteristics:
 - Locoregional cancer (stages I-III)
 - Metastatic cancer (stage IV)

Loco regional cancer

- Patients are further classified into the following groups after additional evaluation:
 - Medically fit patients
 - Medically unfit for surgery or surgery not elected patients medically able to tolerate chemotherapy or chemoradiation
 - Medically unfit for surgery and unable to tolerate chemotherapy or chemoradiation

NCCN Guidelines