

# The Role of Radiotherapy in Management of Esophageal Cancer

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There are four questions in radiation treatment of esophageal cancer

1. Is preoperative radiation superior to postoperative radiation with survival as the major endpoint ?
2. Is radiotherapy superior to chemotherapy as adjuvant treatment ?
3. Is surgery plus adjuvant treatment superior to surgery alone. ?
4. What is the best treatment in inoperable esophageal cancer ?

## 1. Comparison of preoperative radiation and postoperative radiation

< JEOG trial >

randomized in patients who are curative resectable without distant metastasis

- ┌ In preoperative RT group (median survival time 394 day)  
30 Gy RT → OP was performed 7 to 14 days after RT → additional RT(50 Gy)
- └ In postoperative RT group (median survival time 648 day)  
50 Gy to bilateral SCL and mediastinum

*conclusion : radiotherapy should be given only after operation in patients whose tumors are resectable and do not have any distant organ metastasis*

## 2. Comparison of RT alone or chemotherapy alone as postoperative adjuvant treatment

< JEOG trial >

- ┌ In RT group (postoperative) : 50 Gy to both SCL and mediastinum
- └ In chemotherapy group : cisplatin by slow drip infusion + vindesin by bolus IV infusion

**Cumulative Survival Rate in the Study Comparing Radiotherapy and  
Chemotherapy as a Postoperative Treatment**

	Cumulative Survival Rate					
	No.	1Yr	2Yr	3Yr	4Yr	5Yr
Radiotherapy	128	80.3	61.4	51.1	45.6	44.0
Chemotherapy	130	98.7	60.3	52.4	46.9	42.4
$\chi^2$		p < .05	NS	NS	NS	NS

NS, not significant at level of .05

*Conclusion : the combination of cisplatin and vindesine has an effect potentially equivalent to postoperative radiotherapy on survival*

### 3. Comparison of preoperative or postoperative RT and surgery alone

**Preoperative or Postoperative Adjuvant RT Plus Esophageal  
Carcinoma Resection Phase III Trials**

Series	Treatment	No.	Relapse site		Median (mo)	Survival(%)		
			Locoregional	Distant		1-yr	2-yr	5-yr
EORTC	Surgery	106	44/70(67%) <sup>b</sup>	32/70(46%)	11	45 <sup>c</sup>	30 <sup>c</sup>	10 <sup>c</sup>
	Preoperative 33 Gy:10 fx <sup>a</sup>	102	26/56(46%) <sup>b</sup>	29/56(52%)	11	45 <sup>c</sup>	28 <sup>c</sup>	10 <sup>c</sup>
Launois	Surgery	57			12	50 <sup>c</sup>	35 <sup>c</sup>	12
	Preoperative ~40Gy:10 fx <sup>a</sup>	67			11	45 <sup>c</sup>	20 <sup>c</sup>	10
Wang	Surgery	102	25/48(52%) <sup>c</sup>	24/48(50%) <sup>c</sup>				30 <sup>e</sup>
	Preoperative 40 Gy: 8 fx <sup>d</sup>	104	25/52(48%) <sup>c</sup>	26/52(50%) <sup>c</sup>				35 <sup>e</sup>
Arnott	Surgery	86			10 <sup>c</sup>	40 <sup>c</sup>	30 <sup>c</sup>	17
	Preoperative 20 Gy: 10 Fx <sup>f</sup>	90			10 <sup>c</sup>	40 <sup>c</sup>	25 <sup>c</sup>	9
Teniere	Surgery	119	(30%) <sup>g</sup>		18	74 <sup>c</sup>	35 <sup>c</sup>	19
	Postoperative 45 to 55 Gy/25 fx	102	(15%) <sup>g</sup>		18	65 <sup>c</sup>	35 <sup>c</sup>	19

<sup>a</sup>Surgery within 8 days following RT. <sup>b</sup>p < 0.05.

<sup>c</sup>Extrapolated from survival curves. <sup>d</sup>Surgery within 2 to 4 weeks of RT.

<sup>e</sup>Numbers are of patients surviving resection. <sup>f</sup>Surgery immediately following RT.

<sup>g</sup>p < 0.05 in number of patients LRF 10% with versus 35% without postoperative RT.

*Conclusion : the routine use of adjuvant RT as a single modality therapy is presently not warranted on the basis of these randomized trials. Patients with either gross or microscopic tumor present after resection have occasionally apparently been cured with postoperative RT and such therapy is reasonable in carefully selected patients.*

#### 4. Preoperative chemoradiotherapy

Esophageal Cancer Preoperative Chemoradiotherapy Phase II-Trials

Investigator	Regimen/RT	Patient No.	Operable (%)	Resectable (%)	Operative Mortality(%)	Major Response/ Path.CR(%)	Median Survival(mo)	5-Year Survival(%)
Franklin	FU-Mito/3,000cGy	30	76	76	13	NS/20	18 *	30 * †
Leichman	FU-CDDP3,000 cGy	21	90	71	27	NS/24	18	NS
SWOG	FU-CDDP3,000 cGy	106	63	49	11	NS/17	12	16 †
RTOG	FU-CDDP3,000 cGy	41	66	66	4	NS/20	13	8 †
Forastiere	FU-VLB-CDDP/3,750 to 4,500cGy	43 †	95	91	2	42/24	29	34
Urba	FU/4,900cGy	24 ¶	79	79	4	41/8	11	33

RT, radiation therapy; FU, 5-fluorouracil; Mito, Mitomycin C; CDDP, cisplatin; VLB, vinblastine, NS, not stated. \* Completely resected patients only.

†3-year survival. † Adenocarcinoma and epidermoid carcinoma patients. ¶ Adenocarcinoma only.

#### Conclusion

\* Franklin, Leichman, SWOG, RTOG : high operative mortality and disappointing survival surgery appeared to have minimal or no ability to salvage those patients who did not achieve a histologic CR at the time of surgery

\* Forastiere(University of Michigan) study

- Chemotherapy

Vinblastin, Cisplatin, 5-FU

- Radiation Therapy

3750 cGy/ 15 fx (250cGy per day)

4500 cGy/ 30 fx (150 cgy bid)

- Op : transhiatal esophagectomy with a cervical esophagogastric anastomosis routine sampling of accessible subcarinal, periesophageal and celiac axis nodes.

pattern of failure : distant disease is the major problem

## 5. Concurrent chemoradiation without surgery

Esophageal Cancer Chemoradiotherapy Nonoperative Phase II/III Trials

Investigator	Regimen/RT	Patient No.	Major Response (%)	Treatment Mortality (%)	Median Survival (mo)	5-Year Survival (%)
<b>Phase II Trials</b>						
Leichman	FU-CDDP/3,000cGy+MITO-BL/2,000cGy	20	NS	0	22	NS
Coia	FU-MITO/6,000cGy	57	NS	4	18	18
John	FU-CDDP-MITO/4,140 to 5,040cGy/FU-LV-MTX	60	77	3	15†	29†
<b>Phase III Trial</b>						
Herskovic(97)	FU-CDDP/5,000cGy 6,400cGy	61	NS	2	14.1	27†
		62	NS	0	9.3	0†

RT, Radiation therapy; FU, 5-fluorouracil; CDDP, cisplatin; MITO, Mitomycin C;

BL, belomycin; LV, leucovorin; MTX, methotrexate.

\* Median survival in responders only. † Survival at 24 months. ‡ P < .001.

*Phase III trial conclusion : Cisplatin and 5-FU infusion given during and post-RT of 50 Gy is statistically superior to standard 64 Gy RT alone in patients with locally advanced esophageal cancer.*

## 6. Recent development in radiation field

CT-based treatment planning system : adequate coverage of the target volume and avoid potentially serious normal tissue morbidity

Endoesophageal intraluminal brachytherapy : provide palliation of dysphagia in some patients who develop either local recurrence or fail to achieve satisfactory palliation with external beam therapy

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