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Is Extended Volume of External Beam Irradiation Beneficial in Post-esophagectomy High Risk Patients Receiving Combined Chemoradiation Therapy?

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Title:

Is extended volume of external beam irradiation beneficial in post-esophagectomy high risk patients receiving combined chemoradiation therapy?

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ABSTRACT

OBJECTIVE: To assess the value of extended volume irradiation with anastomotic coverage in high risk resected esophageal cancer patients.

METHOD: A retrospective study was undertaken at LRCC from 1989-1999 for high risk resected esophageal cancer patients. Adjuvant treatments consisted of 4 cycles of chemotherapy (epirubicin/fluorouracil/cisplatin or cisplatin/fluorouracil), and local regional irradiation with or without coverage of the anastomotic site. Radiation dose ranged from 45-60Gy at 1.8-2.0 Gy/fraction given with initial anterior-posterior/posterior-anterior arrangement with either extended (with anastomotic coverage) or small (without anastomotic coverage) field followed by oblique fields for boost.

RESULT: One hundred eighty-eight charts were reviewed. Seventy-two patients were eligible for post-resection chemoradiation therapy. Three patients had disease progression prior to therapy, and 69 patients were analyzed. There were 81% T₃N₁ and 13% T₂N₁. Thirty-four patients had margin involvements (radial 53%; proximal/distal 32%), 65% were adenocarcinoma and 33% were squamous carcinoma. Median followup was 23.6 months (3.4 - 78.4 months). Two year survival was 50%; 5yr 24%. Relapse rate was 62.3% and median time to relapse was 20 months. Recurrence locally to anastomosis or adjacent to anastomosis was 9/43(20.9%) with small field and 2/26(7.7%) with extended field. Of 31 patients with relapse outside anastomosis, 14/20(70%) relapsed locoregional/distal when treated with small field and 3/11(27%) relapsed locoregional/distal when treated with extended field (p=0.02). There was no excess treatment interruption or chronic gastrointestinal toxicity with extended field irradiation.

CONCLUSION: There is significant decrease in locoregional/distal relapse with use of extended field in high risk resected esophageal cancer patients.

Introduction

- surgery has been the standard treatment for localized esophageal cancer (1)
- anastomotic recurrence of disease after transthoracic esophagectomy can occur, particularly with histologically involved surgical margins (2)
- frequency of locoregional recurrence is related to the length of resection margin (3), lymph node involvement (4), invasion of neighbouring organs (5) and circumferential resection margin involvement (6)
- radiation treatment planning and target volume for esophageal cancer patients is controversial (7). There is no clear consensus as to what constitutes the optimal treatment volume and the balance between tumor control and normal tissue toxicity for high risk patients (close or positive microscopic margins and lymph node involvement) after esophagectomy
- at LRCC thoracic radiation oncologists have different practice preferences on the inclusion of the post-surgical anastomotic site within the irradiation volume even if the pathological margins (proximal and distal) are not involved
- the present study is to review the results of those high risk patients after esophagectomy treated with either small (without anastomotic coverage) or extended (with anastomotic coverage) field of radiation at LRCC during the period of 1989-1999

Patient & Methods

- a retrospective chart review was undertaken at London Regional Cancer Centre (LRCC) from 1989-1999, for high risk resected esophageal cancer patients (T₃ disease with nodal involvement, positive margin and/or with residual disease)
- adjuvant treatments consisted of 4 cycles of chemotherapy i.e. ECF (epirubicin 50 mg/m², 5 FU 200 mg/m² and cisplatin 60 mg/m²) with epirubicin omitted during the concurrent phase with radiation therapy or 4 cycles of cisplatin (100 mg/m²) and 5 FU (1000 mg/m²)
- irradiation was given during the 3rd cycle of chemotherapy. Irradiation dose ranged from 45-60 Gy at 1.8 - 2.0 Gy/fx given with initial anterior-posterior/posterior-anterior arrangement with either extended (with anastomotic coverage - field size range 22 x 12 cm - 28 cm x 12 - median 24 x 12 cm) or small (without anastomotic coverage - field size range 12 x 10 cm - 22 x 12 cm - median 19 x 12 cm) field followed by oblique fields for boost
- resection margins were covered within the radiation portal if it was close or involved regardless of whether small or extended field was used
- megavoltage machine with energy \geq 6 MV were used
- statistic was analyzed with chi-square and Log Rank
- treatment toxicity including chemo/radiation delay, chemotherapy dose reduction GI symptoms such as esophagitis, diarrhea, bowel obstruction, tracheo esophageal fistula etc. were analyzed

Results

Total: 188 patient charts reviewed
72 patients referred to LRCC with high risk features for adjuvant chemoradiation therapy
3 patients with disease progression while on treatment
69 patients analyzed

Results

Patient Characteristics:

Age	<	65 yo	41	(59%)	range	35-82 yo.	median 60 yo
	≥	65 yo.	28	(41%)			
Sex		male	62	(90%)			
		Female	7	(10%)			
Pathological							
Stage		T ₂ N ¹	9	(13%)			
		T ₃ N ¹	55	(81%)			
		T ₄ N ⁰	2	(3%)			
		T ₄ N ¹	2	(3%)			
Surgery		Transhiatal	59	(86%)			
		Transthoracic	10	(14%)			
Pathology							
		Squamous	23	(33%)			
		Adenocarcinoma	45	(65%)			
		Other	1	(1%)			

Results

Margin features

34 patients with margin involvement

proximal/distal margins	11/69	(15%)
close/involvement		
radial margins	18/69	(26%)
close/involvement		
both	5/69	(7%)

Patient With Extended Field

Margin Involvement 20/26 (77%)

9/26 (35%) radical margin

7/26 (27%) proxi/distal margin

4/26 (15%) both

Patient With Small Field

Margin Involvement 14/43 (33%)

9/43 (21%) radical margin

4/43 (10%) proxi/distal margin

1/43 (2%) both

Results

Treatment

Chemotherapy

Cisp + 5 FU	=	47	(68%)
ECF	=	20	(29%)
Other	=	2	(3%)

Radiation Therapy

Extended Volume (covering anastomosis)

26/69 patients (37.6%)

Small Volume (without covering anastomosis)

43/69 patients (62.4%)

Results

Follow-up:

3.4 - 78.4 months median 23.6 months

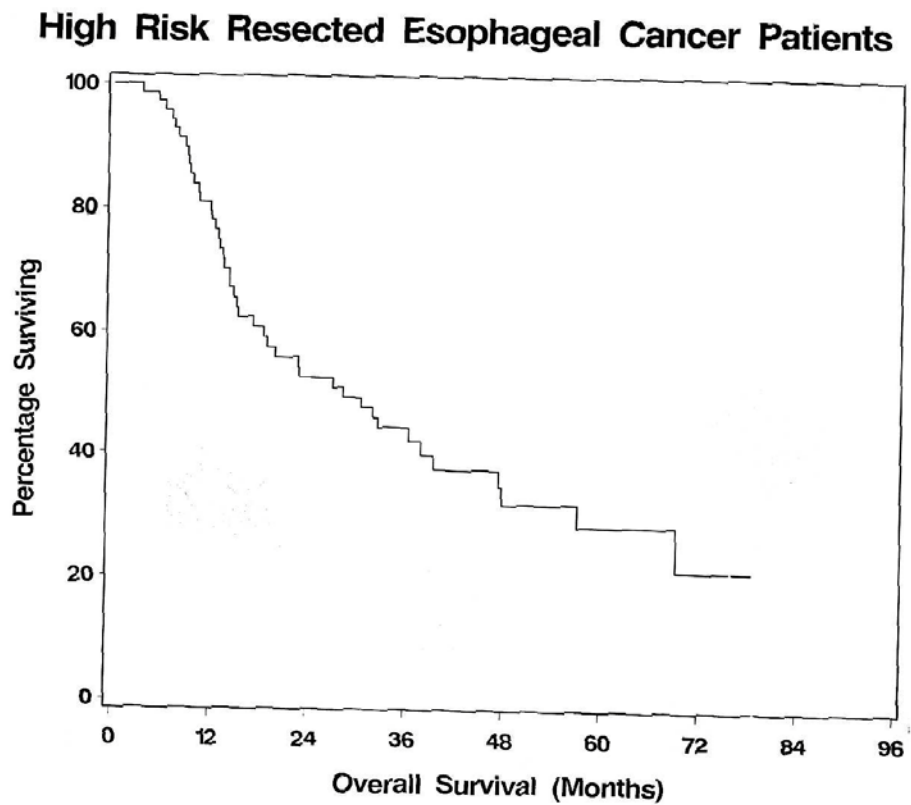
Survival:

Overall 2 years 50%

5 years 24%

Survival curve:

Overall Survival



Results

Relapse:

Rate	43/69	(62.3%)
Median time relapse	19.9 months	

Pattern:

Local Regional	9/43	(20%)
Local Regional Distal	17/43	(40%)
Distal Only	17/43	(40%)

Results

Relapse sites	Number of Relapse
neck nodes/mass	9
bone	9
abdominal mass	7
liver	6
lung	6
brain	4
skin	2
stomach	2
adrenal	2

Results

Anastomosis relapse:

of 9 patients with local regional relapse (all not covered anastomosis site)

5 recurred to anastomotic site only

4 recurred adjacent to anastomotic site

∴ anastomotic recurrence rate (without coverage by XRT) 9/43 (20.9%)

∴ anastomotic recurrence rate (with coverage by XRT) 2/26 (7.7%)

Results

Relapse outside anastomosis

31 patients

Treatment volume	Patient number	Local regional distal relapse	Distal relapse only
Small field	20	14	6
Extended field	11	3	8

p = 0.02 chi square

Results

Effects of Various Factors on Relapse-Free Interval

Factor	Log Rank P-Value
Margin-negative vs. positive	0.66
Resection margin-small field vs. extended field	0.86
Type of surgery - transhiatal vs. transthoracic	0.74
ECF Chemo regimen- yes vs. no	0.22

Results

Complications:

- | | | |
|--|--------------------------------|---------------------------|
| • XRT interruption | small field vs extended field | p = 0.26 chi ² |
| • Chemotherapy delays | small field vs. extended field | p = 0.09 chi ² |
| • Chemotherapy dose reduction | small field vs. extended field | p = 1.0 chi ² |
| • Late toxicity (L'Hermite's, trachoesophageal fistula, bowel obstruction, Liver/Kidney damage, peripheral neuropathy, weight loss, chronic diarrhea, etc) | small field vs. extended field | p = 0.70 chi ² |

Summary and Conclusion

1. In our patient population with high risk post-resection relapse rate was 62.3%.
2. Anastomosis recurrence of 20% if it is not covered with XRT portal.
3. There is significant decrease in locoregional/distal relapse with use of extended field in high risk resected esophageal cancer patients.
4. There is no increase in late toxicity, XRT interruption, and chemotherapy delay when extended irradiation field is used.
5. Ongoing phase I/II trial at LRCC to examine the feasibility of extended target volume for radiation therapy of resected high risk esophageal cancer patients.

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