

Results of radiotherapy with, or without, salvage surgery versus combined surgery and radiotherapy in advanced carcinoma of the hypopharynx

S. BAHADUR, A. THAKAR, B. K. MOHANTI*, P. LAL*

Abstract

There is considerable controversy surrounding the optimum treatment of advanced hypopharyngeal cancers. Curative radiotherapy with surgical salvage in reserve is an accepted protocol as is also a combined treatment of surgery and radiotherapy. The present study is a retrospective analysis of the survival results of 195 cases treated in a single centre. The combined surgery and radiotherapy group comprised a greater number of pyriform fossa and post-cricoid tumours whereas, the curative radiotherapy group had a higher proportion of posterior pharyngeal wall tumours. Actuarial two-year disease-free survival rates were significantly better with combined treatment when results of stage III and IV lesions (164 patients) of all sites are taken together, as compared to those obtained with curative radiotherapy without salvage ($p = 0.000$) or radiotherapy with surgical salvage for residual/recurrent tumours ($p = 0.0021$).

Key words: Hypopharyngeal Neoplasms; Surgical Procedures, Operative; Radiotherapy, Adjuvant; Radiotherapy

Introduction

Carcinoma of the hypopharynx is one of the most aggressive neoplasms in the head and neck. The high incidence of advanced disease with nodal metastasis (often bilateral), extensive subucosal spread, and the presence of skin lesions make these tumours difficult to manage either by surgery or radiotherapy.¹ However, improved imaging techniques for hypopharyngeal cancers in recent years² and proper selection of patients, may have improved the outcome.

There is considerable dilemma in the treatment of advanced hypopharyngeal cancers. Results of radiotherapy are far from satisfactory³ and laryngeal preservation is possible in a small number of cases with many patients returning with loco-regional recurrences. Surgery often entails carrying out a total laryngectomy. However, reconstruction of the hypopharyngeal defects particularly for circumferential lesions as a single stage procedure has helped to overcome a major challenge in recent years in providing excellent palliation.

The present study attempts to assess the results of radiotherapy with regards to preservation of the larynx, and survival and to compare these with a planned protocol of surgery and radiotherapy.

Materials and methods

The present paper describes our experience with 195 cases of carcinoma of the hypopharynx who underwent curative treatment by various modalities during the period 1986–1996 in the hospital of the All India Institute of Medical Sciences, New Delhi. Staging was performed as per the American Journal of Cancer (AJC) criteria, 1978. Pre-therapy work up included detailed clinical evaluation, X-rays of the chest and neck and a direct laryngoscopy and hypopharyngoscopy under anaesthesia. Further radiological assessment by computed tomography (CT) scan was carried out in selected patients.

The age of patients ranged from 21 to 75 years with a mean age of 51.4 years. Males ($n = 160$) outnumbered females ($n = 35$). The pyriform fossa was the principal site of involvement in 137 cases (70 per cent), followed by the post-cricoid region and posterior pharyngeal wall in 30 and 28 cases respectively.

Overall, 84 per cent of patients had advanced stage III or IV disease and only 16 per cent could be categorized under stage I and II. One hundred and six of 195 cases (53 per cent) presented with neck node metastasis, whereas, the remaining 47 per cent had clinically negative necks (Table I). Further break down revealed that the incidence of nodal

TABLE I
STAGE OF DISEASE

T	N				Total
	0	1	2	3	
1	4	0	0	3	7
2	27	6	12	4	49
3	37	32	18	5	92
4	21	13	13	0	47
Total	89	51	43	12	195

metastasis for the pyriform fossa, postcricoid and posterior pharyngeal wall was 60 per cent, 40 per cent and 52 per cent respectively.

The various treatment protocols administered are summarized in Table II. One hundred and fourteen (59 per cent) were treated by radiotherapy with curative intent. Of these 86 had stage III and IV disease, whereas, 28 were classified in stage I and II. The primary disease was treated with 60–66 Gy administered via cobalt/linear accelerator over six to six and a half weeks with standard fractions. The neck received a prophylactic dose of 50 Gy. Seventy-eight patients (39.5 per cent) were treated by a planned regimen of surgery and radiotherapy and nearly all of these were advanced resectable lesions. Only eight cases who failed radiotherapy, could be salvaged with surgery subsequently.

The surgery consisted of total laryngectomy with partial pharyngectomy or total laryngopharyngo-oesophagectomy depending upon whether the lesion was circumferential or not (Table III). A gastric pull-up procedure was employed to reconstruct the hypopharyngeal defect in circumferential lesions. Radical neck dissection was carried out concurrently in patients with palpable neck node metastasis. In 46 of 78 cases undergoing the combined regimen of treatment, surgery was followed by post-operative radiotherapy, whereas in 32 radiotherapy preceded surgery. The patients received pre-operative or post-operative radiotherapy consisting of 50–55 Gy administered over five to five and a half weeks, by standard fractions to both the primary and the neck within four to six weeks of surgery. In three cases (1.5 per cent) surgery was the only mode of treatment used.

Results

Tables IV and Figure 1 illustrate the Kaplan-Meier actuarial survival. Mean follow-up was 18 months.

Of 75 patients with stage III, 40 were treated by radiotherapy with curative intent. Thirty-three per cent of cases without salvage and 47 per cent with salvage surgery were disease-free at 24 months.

TABLE II
TREATMENT

Stage	Radiotherapy	Comb	Surg	Total
1	3	0	1	4
2	25	2	0	27
3	40	33	2	75
4	46	43	0	89
Total	114	78	3	195

TABLE III
SURGICAL PROCEDURES (N = 83)

Total laryngectomy and partial pharyngectomy (without or without PMMF)	56
Total laryngopharyngo-oesophagectomy with gastric pull-up	27
Concurrent/secondary RND	44

There were a further 33 cases who underwent a planned combined regimen of surgery and radiotherapy and 80 per cent of these were disease-free. Results of the combined regimen are statistically superior to those obtained with radiotherapy without salvage. ($p = 0.003$ and $p = 0.0102$ respectively).

Eighty-nine patients had stage IV lesions. Forty-six were treated by radiotherapy with curative intent. However, only 36 per cent of cases were disease free at 24 months without salvage surgery, in contrast to 52 per cent of patients who later underwent salvage surgery for radiation failures. On the other hand, 65 per cent of 43 patients treated with a planned combined regimen of surgery and radiotherapy were disease-free at 24 months. These figures of combined treatment when compared to those of radiotherapy without salvage were highly significant ($p = 0.0011$). However, they are not significant when compared with results of radiotherapy and salvage surgery ($p = 0.1007$).

When the results of stage III and IV lesions (164 patients) of all sites were taken together, again combined therapy of surgery and radiotherapy provided significantly superior results to those obtained by radiotherapy without salvage ($p = 0.000$), or radiotherapy with salvage surgery ($p = 0.0021$).

Discussion

Hypopharyngeal cancers often present late and a high index of suspicion is required for an early diagnosis. The proportion of advanced lesions (stage III and IV) has been reported to vary from 50 to 97 per cent.³ In the present series, 84 per cent of patients presented with advanced lesions, whereas, only 16 per cent had stage I and II disease. The frequency of nodal metastasis in carcinoma of the hypopharynx has been reported to vary from 65 to 75 per cent.⁴ The corresponding figure in this series

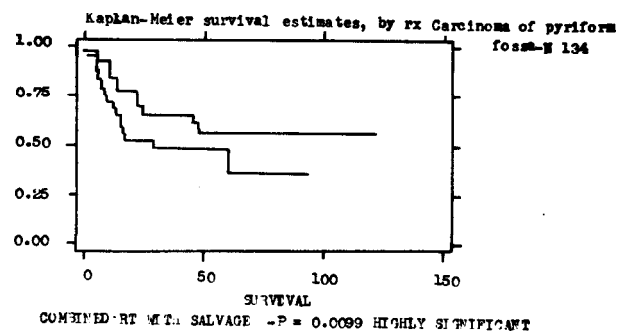


FIG. 1

TABLE IV

KAPLAN-MEIER ACTUARIAL DISEASE-FREE SURVIVAL (24 MONTHS) IN RADICAL RADIOTHERAPY GROUP AND COMBINED TREATMENT GROUP

Stage III (75 patients)	Survivor function	Standard error	95% Confidence interval
Radical radiotherapy (with laryngeal preservation)	0.3386	0.0992	0.4238–0.7650
Radiotherapy with salvage surgery	0.4793	0.1023	0.2729–0.6593
Combined treatment (33 patients)	0.8043	0.0804	0.5854–0.9152
Combined treatment vs RT without salvage $p = 0.0003$ (Highly significant)			
Stage IV (89 patients)			
Radical radiotherapy (46 patients)	0.3604	0.0841	0.2023–0.5211
Radiotherapy with salvage surgery	0.5236	0.0844	0.3484–0.6723
Combined treatment (43 patients)	0.6512	0.0884	0.4504–0.7940
Combined treatment vs RT without salvage $p = 0.0011$ (Highly significant)			
Stage III and IV (164 patients)			
Combined treatment vs RT without salvage $p = 0.0000$ (Highly significant)			
Combined treatment vs RT with salvage $p = 0.0021$ (Highly significant)			

was 53 per cent. Adverse prognostic factors have been commented upon by several authors, and these include submucosal spread of tumour,⁵ advanced local extension and positive margins,⁶ and lymph node metastasis.^{7,8}

It is well realized that in recent years CT scan and magnetic resonance imaging (MRI) have helped a great deal in assessing the extent² and resectability of the tumour and thus helping in better patient selection for therapy.

Functional study for early cancer, preserving the larynx is feasible only in early selected cases,⁹ similar to the experience in the present study. Several authors have utilized neo-adjuvant chemotherapy in conjunction with radiotherapy in advanced carcinoma of the hypopharynx in order to preserve the larynx.^{10–13} It has been reported that larynx preservation is feasible.¹¹

Results of surgery and radiotherapy in post-cricoid cancers have been compared by Axon *et al.*¹⁴ Results of surgery alone in hypopharyngeal cancers are reported to vary from 15 per cent⁵ five-year survival rates to 27 per cent.¹⁵ Radiotherapy alone provides satisfactory results particularly for early cancers and laryngeal preservation. The results have been reported to vary from 18 per cent to 52 per cent at five years.^{16,17}

In the present series, results of radiotherapy alone in terms of disease-free survival and preservation of the larynx at two years were 33 per cent for stage III and 36 per cent for stage IV disease. However, with salvage surgery for radiation failures in the neck resulted in improved figures for the same stage of disease, of 47 per cent and 52 per cent respectively. Overall, results of salvage surgery following radiation failure have been unsatisfactory.¹⁷ A significant number of radiation failures may not be salvaged with surgery either because of late diagnosis of recurrent lesions or patients' refusal to undergo subsequent surgery. Thirty-six per cent of patients' who underwent salvage surgery survived disease free at three years.³ Carpenter *et al.*¹⁶ reported 17 per cent of patients with hypopharyngeal carcinoma survived disease free at five years. They did not find any difference in results between patients treated with surgery alone or those who received

pre-operative radiotherapy. These authors also noted a poorer survival in patients treated with radiotherapy alone, as compared with those treated with either surgery alone or with surgery and post-operative radiotherapy. Many other authors have also reported superior results with a planned combined regime of surgery and post-operative irradiation.^{5,15,16}

The present study is retrospective and median follow-up is 18 months. Nevertheless, there are indications that results of a planned combined regimen of surgery and irradiation are better as compared to results of radiotherapy without salvage and even following salvage surgery ($p = 0.000$ and $p = 0.222$ respectively) for stage III and IV disease (164 patients).

It appears that radiotherapy should be reserved for stage I and II lesions and careful follow-up needed to detect local and regional recurrences which would be salvaged with surgery. However, for stage III and IV disease, a planned protocol of surgery and post-operative radiotherapy is more useful.

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Address for correspondence:

Dr Sudhir Bahadur,
Department of Otolaryngology – Head and Neck Surgery,
All India Institute of Medical Sciences,
Ansari Nagar,
New Delhi 110 029,
India.

Dr S. Bahadur takes responsibility for the integrity of the content of the paper.

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