

## Radiotherapy and complications of laryngectomy

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### Abstract

In an effort to establish factors responsible for our post laryngectomy fistulae we reviewed 357 patients who underwent total laryngectomy between 1965 and 1990, for laryngeal carcinoma. Pharyngocutaneous fistulae occurred in 84 cases (23 per cent). There was no difference between the fistula group and the non-fistula group with regard to age, sex, general condition, or tumour differentiation. The only significant, positive association was with previous radical radiotherapy (10 fistulae out of 167 primary laryngectomies (4 per cent) versus 74 fistulae out of 190 salvage laryngectomies (39 per cent)).

The median time to occurrence of a fistula was day seven in both groups. However, in the non-radiotherapy group the median duration of the fistula was 28 days; the majority healing spontaneously, with only one patient requiring surgical closure. There were no 'hospital' deaths. In the radiotherapy group the median duration of fistulae was 112 days with 30 patients requiring a total of 66 procedures to achieve closure of the fistula. There were six 'hospital' deaths in this group.

We conclude that previous radical radiotherapy strongly predisposes towards the occurrence of a post-laryngectomy fistula. Fistulae in this group tend to be longer lasting and are more likely to require surgical repair.

**Key words:** Laryngectomy, complications; Radiotherapy.

### Introduction

A major cause of morbidity and prolongation of hospital stay following laryngectomy is the occurrence of a pharyngocutaneous fistula, due to failure of the healing process. Despite the relative frequency of this complication there is still uncertainty about predisposing factors.

A number of authors have looked at this problem in an effort to identify any significant associations. Potential factors include pre-operative radiotherapy and tracheostomy, synchronous neck dissection, low post-operative haemoglobin and residual disease. With the exception of residual disease, conflicting reports exist as to the relative importance of the rest (Hendrick, 1964; Lavelle and Maw, 1972; Bresson *et al.*, 1974; Stell and Cooney, 1974; Dedo *et al.*, 1975; Gullans *et al.*, 1979; Lundgren and Olofsson, 1979; Weingrad and Spiro, 1983; Boyce and Myers, 1989). We were particularly interested in the role of radical radiotherapy in fistula formation. There appears to be a majority consensus in the literature that fistula are more likely following radiotherapy whether this be radical or planned pre-operative radiotherapy (Stell and Cooney, 1974; Dedo *et al.*, 1975; Lundgren and Olofsson, 1979; Mantravadi *et al.*, 1981). The alternative view has been reported sufficiently frequently to force the debate to continue (Lavelle and Maw, 1972; Bresson *et al.*, 1974; Weingrad and Spiro, 1983; Boyce and Myers, 1989).

We have now performed a large series of laryngectomies over the 25 years from 1965 to 1990 and our patients have unfortunately suffered the many inevitable fistulae. We decided to review these cases to see if we could further clarify the situation.

### Patients and methods

Data on all patients presenting to our unit, since 1963, has been recorded in a prospective manner on initially punch cards, but since 1977 on a computer database. All tumours were classified according to the UICC method (1987), and patients' general physical condition by the ECOG status (AJC manual, 1990). From this group 357 patients were identified who underwent laryngectomy for laryngeal carcinoma between 1965 and 1990. One hundred and sixty seven patients had a laryngectomy as primary treatment and the remaining 190 were salvage laryngectomies for recurrent/residual disease required in a total group of 796 patients receiving primary radical radiotherapy. No patients in the primary surgery group had post-operative radiotherapy prior to the development of a fistula.

The case sheets of these 357 patients were reviewed. General condition, tumour stage and differentiation, nodal status were recorded for each patient. Primary treatment, whether radiotherapy or surgery was noted, as was any additional treatment. The time between radiotherapy and subsequent surgery was noted. The time of occurrence and duration of any fistulae and their treatment was analysed; unfortunately this information was unavailable on 15 of the fistula patients.

Laryngectomy was performed as described by Stell and Maran (1978) with a two layer vertical pharyngeal repair. Radical neck dissection also was performed as described by Stell and Maran (1978). Nineteen neck dissections were performed prophylactically, all the rest were performed for clinically positive nodal disease. Fistulae were

TABLE I  
HOST AND TUMOUR FACTORS

	Fistula (n = 84)		Non fistula (n = 273)	
Age (years)	61		61	
Sex	69M	15F	223M	50F
ECOG 0	64	(76%)	210	(77%)
1-4	20	(24%)	63	(23%)
	NS			
T Stage				
0	9	(11%)	11	(4%)
1	9	(11%)	25	(9%)
2	2	(2%)	35	(13%)
3	11	(13%)	60	(22%)
4	27	(32%)	71	(26%)
Unknown	26	(31%)	71	(26%)
	$\chi^2 = 16.05; P = 0.007$			
Tumour differentiation				
Well	20	(24%)	74	(27%)
Moderate	22	(26%)	71	(26%)
Poor	19	(23%)	63	(23%)
Unspecified	23	(27%)	65	(24%)
	NS			
Nodal status				
Negative	73	(87%)	198	(73%)
Positive	11	(13%)	75	(27%)
	$\chi^2 = 6.5; P = 0.01$			

repaired using local mucosal flaps if small, and if large the deltopectoral axial pattern flap was used prior to 1972 and the pectoralis major myocutaneous flap after 1972.

The radiotherapy technique used was megavoltage X-ray therapy using a 4MV linear accelerator until 1968 and a 6MV linear accelerator after 1968. Accurate direction of the beam was ensured by individually made plastic shells. The dose for the course was of the order of 60 Grays.

The results are presented as contingency tables and statistical analysis has been performed using the chi-squared and Mann-Whitney tests. Further analysis was carried out using multiple logistic regression to investigate the relationship of host and tumour factors on the fistula rate. Interaction between variables were included in the model. The analysis was performed using the SAS programme (SAS Institute Inc., 1985).

**Results**

Pharyngo-cutaneous fistulae occurred in a total of 84 patients (23 per cent). There were no differences between the fistula group and the non-fistula group with regard to

TABLE II  
INFLUENCE OF SYNCHRONOUS NECK DISSECTION AND RADICAL RADIOTHERAPY ON FISTULA FORMATION

	Total	Fistula
Neck dissection	105	13 (12%)
No neck dissection	252	71 (28%)
	$\chi^2 = 6.0; P < 0.05$ Odds ratio = 2.2 95% CI = 1.2-4.5	
Radiotherapy	190	74 (39%)
No radiotherapy	167	10 (4%)
	$\chi^2 = 33.0; P < 0.0001$ Odds ratio = 6.2 95% CI = 3.1-13.9	

TABLE III  
MULTIPLE LOGISTIC REGRESSION ANALYSIS OF EFFECT OF HOST AND TUMOUR FACTORS ON FISTULA RATE

Variable	$\chi^2$	P Value
Age	0.09	0.760
Sex	0.16	0.690
ECOG	0.04	0.850
T stage	0.07	0.790
N stage	0.00	0.960
Histology	0.06	0.810
Pathological T stage	1.00	0.320
Neck dissection	0.33	0.570
Treatment modality	18.53	0.000

age, sex distribution, general physical condition and tumour differentiation. There was however a negative association with advancing tumour stage and positive nodal status. These results are shown in Table I.

There was also a negative association with synchronous neck dissection but a strong positive association with previous radical radiotherapy (Table II). The odds ratio for neck dissection is 2.2 (that is patients are 2.2 times more likely to develop a fistula if they are not subjected to neck dissection than if they are. The confidence interval (CI) indicates that we are 95 per cent sure that the time increased risk due to no dissection is between 1.2 and 4.5 times that of dissection. Similarly the odds ratio for radiotherapy is 6.2 and the 95 per cent CI is between 3.1 and 13.9.

Multiple logistic regression (Table III) confirmed the strong association between previous radiotherapy and post laryngectomy fistula formation ( $\chi^2 = 18.53, P = 0.0000$ ). The negative association for synchronous neck dissection was not confirmed ( $\chi^2 = 0.33, P = 0.5663$ ). There were no significant interactions.

In the radiotherapy group, the median time between primary radiotherapy and salvage surgery was 10.5 months (range 4-108 months) in those that developed a fistula and 13 months (range 4-200 months) in those that did not. (Mann Whitney,  $U = 3456, U^1 = 5054, N_1N_2 = 8510, P = 0.028$ ).

The median time to occurrence of fistula was seven days in both groups but the fistulae were more persistent and were more likely to require surgery in the radiotherapy group (Table IV).

There were no 'hospital' deaths in the non-radiotherapy fistula group but six deaths in the radiotherapy fistula group. One patient died of broncho-pneumonia, the remaining five died of residual disease. All six patients had persisting fistulae at the time of death.

TABLE IV

	Fistula Non radiotherapy (n = 60)	Characteristics Radiotherapy (n = 9)
Time of occurrence (days and range)	7 (0-42)	7 (5-12)
Duration (days and range)	112 (28-462)	28 (21-84)
	Mann Whitney: $P = 0.0008$	
Number requiring surgery	30 (50%)	1 (11%)
	$\chi^2 = 3.34; P = 0.064$	
No. of operations required	66	1

## Discussion

Our study, the largest to date, has analyzed only those patients undergoing laryngectomy for laryngeal carcinoma either primarily or following failure of a radical course of radiotherapy in an effort to reduce confounding variables. Our overall fistula rate of 23 per cent appears similar to most other reported series. However we have emphatically shown that the single most important factor in predicting the occurrence of a post laryngectomy fistula is the pre-operative administration of a radical course of radiotherapy. Radiotherapy is well known to compromise wound healing (Walter and Israel, 1987) and there can be little doubt that this has been the case in our series, leading to a fistula rate in this group of 39 per cent. Although our high fistula rate is associated with previous radical radiotherapy, the risk may well apply to planned pre-operative radiotherapy. Only one paper (Lundgren and Olofsson, 1979) has shown a lower fistula rate with planned radiotherapy. In most other reports where a distinction is made there appears to be no difference in the fistula rate with differing radiotherapy doses (Lavelle and Maw, 1972; Bresson *et al.*, 1974).

Our finding of a statistically significant difference between fistula and non-fistula groups for median time from radiotherapy to surgery is interesting but a 2.5 month difference is unlikely to be of any clinical importance.

Simple analysis demonstrated a negative association with advancing tumour stage and positive nodal status in contrast to a number of North American reports (Dedo *et al.*, 1975; Boyce and Myers, 1989). However, multivariate analysis did not confirm this finding. This apparently spurious result merely demonstrates the influence of these factors on choice of treatment; in the United Kingdom, patients with large tumours and positive nodes are more likely to receive surgery as primary treatment, and thus avoid radical radiotherapy. These results also imply that simple comparisons of fistula rates are inappropriate and account must be taken of any radiotherapy or surgical bias in a centre's treatment policies.

Although the fistulae occurred at the same time in the two groups, they lasted significantly longer in the radiotherapy group with a median duration of just under four months (112 days). Whilst the fistula persists the patient cannot feed properly and requires a naso-gastric tube; most patients are inpatients until their fistula has healed. In addition the radiotherapy group were more likely to require multiple operations in an effort to close their fistulae whereas the majority of fistulae in the non-radiotherapy group healed spontaneously. This finding has been previously observed by Maw and Lavelle (1972).

Post-laryngectomy fistulae obviously represent a major post-operative morbidity for these patients and a significant consumption of resources for any unit. However there can be no doubt that the more persistent and invariable morbidity of laryngectomy is the loss of voice,

which can be preserved if radical radiotherapy is successful. As the 74 fistulae in the radiotherapy group represent only 9.3 per cent of the 796 patients submitted for primary radiotherapy, we feel that this is an acceptable price to pay for the potential preservation of voice.

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