

A comparison of radiotherapy and surgery as primary treatment in the management of T₃ N₀ M₀ glottic tumours

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Abstract

Seventy-four patients with Stage T₃ N₀ M₀ squamous carcinoma of the glottis were treated initially by either surgery or radiotherapy between 1980 and 1985. The treatment adopted was determined by consultant preference. The long-term survival in both groups was approximately the same. Of 38 patients treated initially by radiotherapy, 25 had local recurrence. Fifteen of these underwent salvage surgery and 10 died of disease. Thirteen patients (33 per cent) retained their larynx. One of the major advantages of treating patients with stage T₃ N₀ M₀ carcinoma of larynx by radiotherapy initially is that approximately one-third will retain their larynx. Local recurrences can usually be treated readily by salvage surgery.

Key words: Laryngeal neoplasms; Surgery; Radiotherapy

Introduction

The management of T₃ N₀ M₀ glottic carcinoma is still a subject of great controversy. Some centres prefer primary surgery with or without pre- or post-operative radiotherapy and others prefer radiotherapy reserving surgery for salvage. The main advantage of radiotherapy is the retention of the larynx. The principal question is whether this is achieved at the cost of a reduced survival time.

There are many reasons for this controversy persisting, but one of the most significant is that most studies have tended to report the results of either radiotherapy or surgery, but seldom both together. The difficulty of comparing studies from different centres, is that they often use different classifications and staging criteria making evaluation difficult. Bryce (1972) has compared surgery with radiotherapy and found the results to be similar, but patients receiving primary radical surgery comprised only 13 per cent of his total group. In addition he does not record the incidence of nodal metastasis nor the extent of the tumour in either of the groups. Neither does he list the criteria used for choosing surgery. Stell *et al.* (1982) have also compared surgery with radiotherapy and found radiotherapy to be superior. However, the criteria for treatment choice were such that those patients with bulky tumours were treated by surgery and those with small lesions by radiotherapy. Stell *et al.* (1982) also included patients with nodal disease, all of whom were treated by surgery, further biasing the results. Other large studies have looked at surgery (De Santo, 1984) or radiotherapy (Harwood *et al.*, 1980; Lundgren *et al.*, 1988). Le Roux-Roberts (1975) compared surgery with radiotherapy and found surgery superior, but again did not state the criteria used for choos-

ing the treatment modality. Ideally, a randomized prospective trial is required, but this would present considerable ethical difficulty. This report examines retrospectively 74 patients treated in Glasgow for T₃ N₀ M₀ squamous carcinoma of the glottis between 1980 and 1985. During this period the criteria for choosing treatment modality was consultant preference, some choosing radiotherapy with salvage surgery and others primary surgery. By chance this resulted in a fairly even distribution of disease both in terms of numbers and tumour extent between the two treatment groups.

Patients and methods

From a review of the Glasgow Institute of Radiotherapy and Beatson Oncology Centre records, 243 patients with laryngeal tumours were traced, of whom 38 had had primary radiotherapy for T₃ N₀ M₀ lesions of the glottis. One hundred and twenty-two patients who had had laryngectomies were traced from theatre records at the Gartnavel General Hospital and the Victoria Infirmary, Glasgow, of whom 36 had primary surgery for a T₃ N₀ M₀ lesion. The tumours of the 74 patients eligible for study were staged clinically according to UICC criteria (1978). In all cases tumours were assessed by indirect and direct laryngoscopy. Tomography was also available for 33 of the radiotherapy group and 26 of the laryngectomy group. In those patients who had surgery but no tomography, the pathology was reviewed to assess site involvement though not to change staging. This allowed patients to be separated into those who had glottic-only involvement, those with glottic and either supra- or subglottic involvement,

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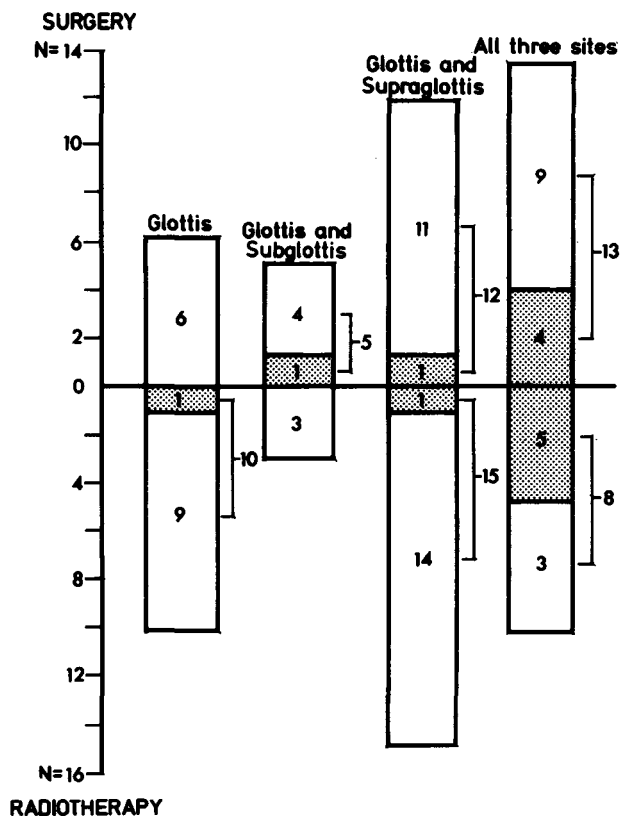


FIG. 1

Distribution of disease in patient groups. (Patients requiring tracheostomy represented by shaded area.)

and those with all three sites involved. Sixty-nine of the patients were confirmed smokers, four had no record of smoking and only one patient was a non-smoker.

Radiotherapy patients received megavoltage radiation using a linear accelerator. The dose was between 60 and 65 Gy given in 25 to 30 fractions with fields of between 6 × 6 to 6 × 9 cm. The surgical patients all received total laryngectomy and none had neck dissections. The patients' records were then examined to determine treatment outcome. The length of survival, the cause of death and the presence or absence of tumour at death was noted. Analysis of survival by age, sex, extent of disease and treatment type was carried out using the log-rank method (Peto *et al.*, 1978).

Results

The distribution of disease sites involved between the two patient groups and the numbers of patients in each group who need tracheostomy were comparable (Figure 1) as were the age and sex distributions (Table I). Crude measurements of treatment outcome are presented in Table II. Virtually identical numbers of patients died of

TABLE I

AGE AND SEX DISTRIBUTION OF PATIENTS IN EACH TREATMENT GROUP

	Surgery	Radiotherapy
Age range	45-78	45-84
Mean age	64	66
Males	29	34
Females	7	4

their disease: 37 per cent in the radiotherapy group *versus* 39 per cent in the surgery group. A large number of patients died from other causes, a reflection in part of advanced age, but also of the incidence of second primary tumours. Eleven of the 25 patients who died from other causes died of second primary tumours, seven of which were bronchial in origin. Thirty-four per cent of patients in the radiotherapy group were alive and well at end of follow-up, between 25 and 95 months after treatment. This compared with 22 per cent in the surgery group. In the surgery group four received post-operative radiotherapy and 12 had salvage radiotherapy at a later date. In the radiotherapy group, 15 patients had further surgery and 10 had recurrence of tumour but no surgery (four refused surgery, three were considered unfit and three had disease that was either too extensive or metastatic). Six radiotherapy patients had no recurrence and therefore retained their larynx. The actuarial survival of the radiotherapy group compared with the surgery group is shown in Figure 2.

Five-year survival was 57 per cent for those treated initially by radiotherapy and 52 per cent for those treated by surgery. There is little difference between the two groups (Chi-square test = 0.203; *p* > 0.05) although due to the small number of deaths in each group the power of this and subsequent analysis to detect a statistically significant difference is low. The survival by age (over or under 65 years) for the patients as a whole is shown in Figure 3. There is very little difference between the groups (Chi-square = 0.444; *p* > 0.50). Figure 4 shows survival by sex. Although women would appear to have an early advantage, by five years there is again no difference (Chi-square = 0.197; *p* > 0.50). Figure 5 illustrates the survival of those patients with fold-only involvement compared with those with multiple sites involved, regardless of treatment type. The former have an 80 per cent survival up to four years as against 53 per cent for the latter. However, between four and five years the survival of the fold-only group drops to 60 per cent due to the death of one of the

TABLE II
TREATMENT OUTCOME

Surgery - 36 patients	14 Dead of disease 14 Dead of other causes 8 Alive and well
Consisting of:	
Surgery alone - 20 patients	1 Dead of disease 12 Dead of other causes 7 Alive and well
Surgery and post-operative radiotherapy - 4 patients	1 Dead of disease 2 Dead of other causes 1 Alive and well
Surgery and late salvage radiotherapy - 12 patients	12 Dead of disease 0 Dead of other causes 0 Alive and well
Radiotherapy - 38 patients	14 Dead of disease 11 Dead of other causes 13 Alive and well
Consisting of:	
Radiotherapy alone - 23 patients	10 Dead of disease 7 Dead of other causes 6 Alive and well
Radiotherapy with salvage surgery - 15 patients	4 Dead of disease 4 Dead of other causes 7 Alive and well

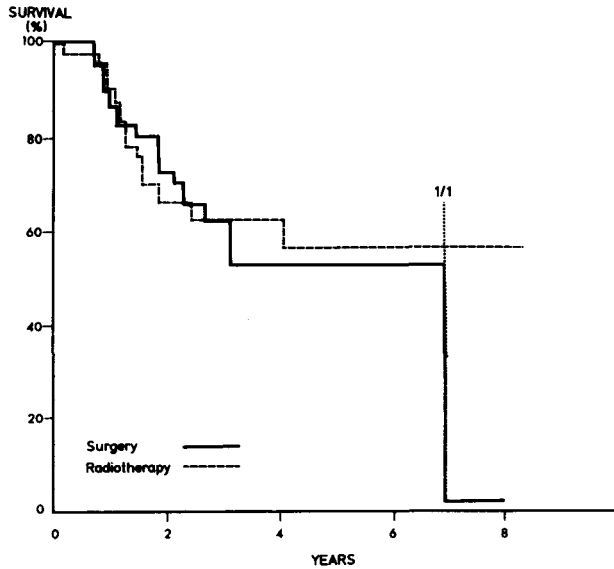


FIG. 2

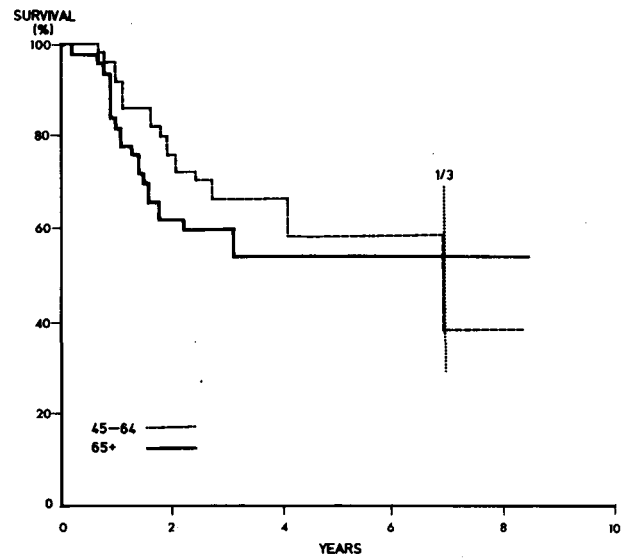


FIG. 3

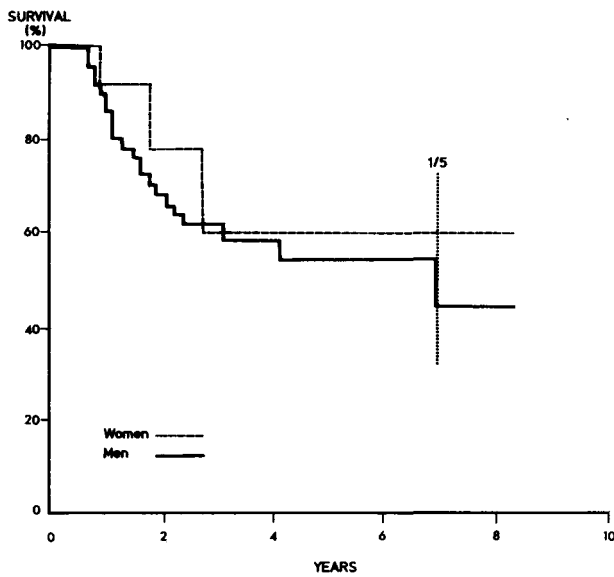


FIG. 4

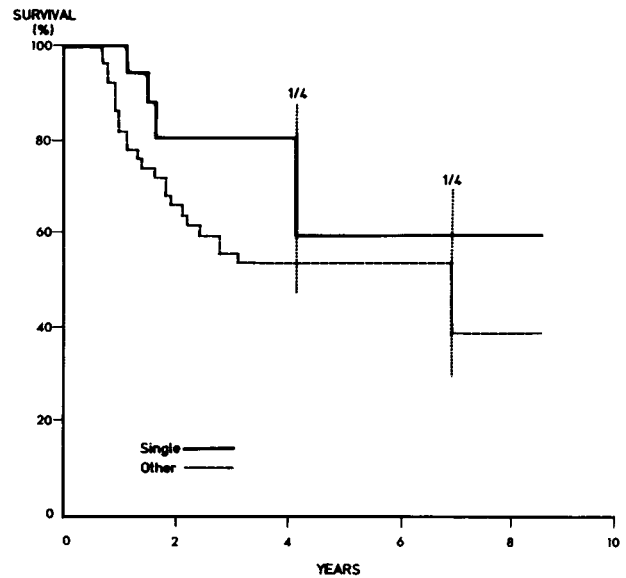


FIG. 5

Fig. 2: Survival by initial treatment; FIG. 3: Survival by age; FIG. 4: Survival by sex; FIG. 5: Survival by site in larynx. Vertical intercepts show number of deaths as a proportion of these patients remaining in each group at selected points in time.

four remaining patients. The overall survival experience of the fold-only group is not significantly different from that of those with multiple site involvement because of low numbers in the single site group (Chi-square = 1.83; $p > 0.10$), and the power of the test to detect significant differences of even this size is less than 50 per cent. Application of the Cox proportional hazard model to the analysis of the independent contribution of each variable (Table

III) confirms site as being the most promising predictor of survival, but without reaching statistical significance.

Discussion

Comparing treatment results between different centres using different treatment modalities is extremely difficult. This paper presents two groups of patients who underwent

TABLE III
COX REGRESSION ESTIMATES

Standardized normal statistics				
Independent variable risk group	Coefficient (Beta)	Significance (Z value)	Relative hazard	95 per cent confidence limits
Age (65+)	0.3137	0.800	1.368	0.634-2.952
Sex (male)	0.3353	0.542	1.398	0.416-4.701
Site (multiple)	0.8054	1.462	2.238	0.760-6.589
Treatment (surgery)	0.0609	0.155	1.063	0.493-2.290

different treatments for a similar disease spectrum. The groups were comparable with respect to age, sex and extent of disease.

The results of treatment in the two groups are comparable and in keeping with previous studies (Harwood *et al.*, 1980; Stell *et al.*, 1982; De Santo, 1984). There would appear to be no penalty in terms of decreased survival if a policy of radiotherapy with salvage surgery is followed, although a much larger number of patients would be required to demonstrate this statistically. This policy would allow for preservation of the larynx in 16 per cent of all cases. This is slightly lower than the 24 per cent reported by Lundgren *et al.* (1988) and much lower than those of Stell *et al.* (1982) i.e. 65 per cent for glottic lesions and 51 per cent for multiregional tumours. The difference in laryngeal preservation rate between glottic-only lesions and multiregional tumours was found by Stell *et al.* (1982) to be accompanied by a comparable difference in five-year survival rates: 80 per cent for glottic-only lesions compared to 60 per cent for the multiregional group. This finding was also reflected in our study, although because of the small size of the glottic-only group the initial 80 per cent survival figure which was maintained into the fourth year then dropped sharply due to the death of only one patient in the group. This phenomenon has also been noted in previous studies both of surgery (De Santo, 1984) and radiotherapy (Lundgren *et al.*, 1988) and presumably represents the effect of tumour bulk. In keeping with previous findings, age was not a significant factor in our study (Lundgren *et al.*, 1988). It has been noted previously (Stell *et al.*, 1982) that glottic-only lesions appear to occur predominantly in men, whereas multiregional disease tends to be more evenly split between male or female. If this were the case then one might expect males to have a better overall survival. Although Harwood *et al.* (1980) has shown a better survival for females, a later study from Toronto (Lundgren *et al.*, 1988), although showing an improved local control rate for females, also noted that the actuarial five-year survival did not differ. In our study the number of females was very low, and although they did show a better survival initially, after five years there was no difference.

Survival analysis also demonstrates the well-recognized finding that most tumour recurrence occurs within three years after treatment, although there are occasional later recurrences. This has obvious implications with regard to patient follow-up. Our results also show that sal-

vage radiotherapy is ineffective in cases recurring after laryngectomy.

Conclusion

The study concludes, subject to limitations of sample size and statistical power, that long-term survival following a policy of radiotherapy with salvage surgery is no worse than for primary surgery alone and would result in the retention of a number of intact larynges.

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References

- Bryce, D. P. (1972) The role of surgery in the management of carcinoma of the larynx. *Journal of Laryngology and Otology* **86**: 669–678.
- De Santo, L. W. (1984) T₃ glottic cancer: options and consequences of the options. *Laryngoscope* **94**: 1311–1315.
- Harwood, A. R., Bryce, D. P., Rider, W. D. (1980) Management of T₃ glottic cancer. *Clinical Otolaryngology* **106**: 697–699.
- Le Roux-Robert, J. (1975) Panel discussion on glottic tumours. IV. A statistical study of 620 laryngeal carcinomas of the glottic region personally operated upon more than 5 years ago. *Laryngoscope* **85**: 1440–1452.
- Lundgren, J. A. V., Gilbert, R. W., van Nostrand, A. W. P., Harwood, A. R., Keane, T. G., Briant, T. D. R. (1988) T₃ N₀ M₀ glottic carcinoma — a failure analysis. *Clinical Otolaryngology* **13**: 455–565.
- Peto, R., Pike, M. C., Armitage, P., Breslaw, N. E., Cox, D. R., Howard, S. V., Montel, N., McPherson, K., Peto, J., Smith, P. G. (1977) Design and analysis of randomized clinical trials requiring prolonged observation of each patient. II. Analysis and examples. *British Journal of Cancer* **35**: 1–39.
- Stell, P. M., Dally, J. E., Singh, S. D., Ramadan, M. F., Bainton, R. (1982) The management of T₃ glottic carcinoma. *Clinical Otolaryngology* **7**: 175–180.
- UICC (1978) *TNM classification of malignant tumours*, 3rd Edition.

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