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The treatment of node negative squamous cell carcinoma of the postcricoid region

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Abstract

This study includes 155 patients with T_{1-4} N_0 carcinoma of the postcricoid region seen between 1963 and 1993. Sixty-seven were treated by primary surgery, 50 by primary irradiation therapy, 36 were unsuitable for curative treatment and two patients were lost to follow-up. Reasons for deciding against curative therapy were: advanced age, poor general condition and advanced disease at the primary site. This study included only those patients who had no neck node metastases at presentation.

Patients receiving surgery tended to be in better general physical condition and tended to have more advanced disease than those treated by irradiation in this series. The tumour-specific five-year survival rate for those treated by surgery was 43 per cent (95 per cent confidence interval (CI) 23–60 per cent). For those patients treated by irradiation the five-year survival rate was 48 per cent (95 per cent CI 27–66 per cent) and for those receiving no treatment the median survival rate was three months (95 per cent CI two–six months). The observed survival for the surgery group was only 18 per cent and for the radiotherapy group 25 per cent at five years.

Multiple logistic regression showed no significant difference in proportions of host and tumour factors between the group receiving radiotherapy and the group receiving surgery. Recurrence at the primary site and the appearance of neck node metastases were not predicted by any host or tumour factor.

Twenty-one patients out of 67 receiving primary surgery had recurrence at the primary site compared with 26 patients out of 50 receiving primary irradiation. Neck node metastases occurred in 16 out of 67 patients receiving surgery and in eight out of 50 receiving radiotherapy. The difference was statistically significant for recurrence at the primary site ($\chi^2_1 = 4.261$; $p = 0.039$) but not significant for neck node metastases ($\chi^2_1 = 0.661$; $p = 0.416$). The data were further analysed using Cox's proportional hazards model for survival and no host or tumour factors were found to be predictive of eventual outcome apart from poorly differentiated histology. This adversely affected survival ($\chi^2 = 6.4444$; $p = 0.011$). If patients not treated were included in the model, treatment became a significant factor in improving the survival ($\chi^2 = 4.4197$; $p = 0.034$).

Radiotherapy appears to be at least as good as surgery for treating patients with an early carcinoma of the postcricoid region. We would recommend radiotherapy is used in patients with no detectable neck node metastases and in tumours <5 cm long. The complication rate from radiotherapy was reduced when compared with that of surgery.

Key words: Head and neck neoplasms; Carcinoma, squamous cell; Radiotherapy; Pharyngolaryngectomy; Jejunum, surgery; Stomach, surgery

Introduction

Carcinoma of the hypopharynx is an uncommon disease with an incidence of approximately 1:100 000. Postcricoid carcinoma occurs in Northern Europe, North America, India and Japan but is very rare elsewhere (Harrison, 1970; Ramanjaneyulu, 1974; Pandhi *et al.*, 1975; Kleinsasser, 1988; Hatta *et al.*, 1991). Unlike most cancers of the head and neck with a high male predominance that of the postcricoid is more common in women; a fact partly explained by the occurrence of the Paterson Brown–Kelly syndrome (Richards *et al.*, 1971). In Sweden the latter condition has become less common since iron has been added to flour used in the baking of bread.

The UICC (1992) define the postcricoid region as the pharyngo-oesophageal junction, extending from the level of the arytenoid cartilages and connecting folds to the inferior border of the cricoid cartilage. The previous definition appeared to split the postcricoid region into an anterior and a posterior wall, the lateral walls being formed by the apex of the pyriform sinuses which were defined as extending from the pharyngo-epiglottic fold to the upper end of the oesophagus.

The postcricoid region may be defined anatomically

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TABLE I
POSTCRICOID CARCINOMA: TREATMENT GROUPS

Factor	Palliation	Surgery	Radiotherapy	χ^2 Surgery/Radiotherapy	χ_2 all three groups
Number of patients	36	67	50		
Host factors					
Age (mean)	70	58	59		
Age (number below 60 years)	6	31	27	$\chi^2_1 = 0.410$ $p = 0.52$	$\chi^2 = 14.84$ $p = 0.0006$*
Male:female	1:1.3	1:1.4	1:3.2	$\chi^2 = 3.27$ $p = 0.07$	$\chi^2_1 = 5.02$ $p = 0.08$
General condition					
ECOG 0	19	53	36	$\chi^2_1 = 0.45$	$\chi^2_1 = 10.95$
>1	20	14	14	$p = 0.50$	$p = 0.004$*
Tumour factors					
T-stage					
T_{1-2}	18	52	45	$\chi^2_1 = 2.29$	$\chi^2 = 22.66$
T_{3-4}	21	15	5	$p = 0.13$	$p < 0.0001$*
Histological grade					
Well/moderately differentiated	20	43	35	$\chi^2_1 = 0.72$	$\chi^2_1 = 4.12$
Poorly differentiated	12	15	7	$p = 0.39$	$p = 0.13$
Not graded	7	9	8		

in terms of its wall and the spread of the carcinoma can be studied with respect to the contiguous structures. The anterior wall of the postcricoid region is formed of the cricoid cartilage covered by the posterior crico-arytenoid muscle. The arytenoid cartilages form the upper part of this anterior wall. Thus carcinoma at this site spreads into the muscle and then into the cricoid and arytenoid cartilages. The tumour may paralyse the vocal fold in three ways: (a) invasion of muscles; (b) fixation of the crico-arytenoid joint; and (c) recurrent laryngeal nerve invasion.

Lymph node metastases have been said to be relatively unusual in this disease with figures as little as 20 per cent being quoted (Stell and Maran, 1978). Other authors have quoted the risk of enlarged neck nodes at presentation as being much higher at 40 per cent (Hahn *et al.*, 1987; Lefebvre *et al.*, 1987; Willatt *et al.*, 1987). The difference in the figures may partly be accounted for by paratracheal and retropharyngeal node involvement which may not be evident on clinical examination. In addition over half of patients may have occult neck node metastases (Ogura *et al.*, 1960; Byers *et al.*, 1988).

One of the problems of postcricoid carcinoma, and of course oesophageal carcinoma, is the propensity for submucosal spread. Submucosal extension of 5 mm beyond the visible disease is usual and 'skip' lesions into the cervical oesophagus are not uncommon (Willatt *et al.*, 1987).

Whilst many authors have dealt with pyriform sinus cancer, studies dealing with the postcricoid region are uncommon, perhaps reflecting the relatively low incidence of this disease (Vandenbrouck *et al.*, 1977; El Badawi *et al.*, 1982; Ahmed and Fayos, 1984; Mendenhall *et al.*, 1987; Vandenbrouck *et al.*, 1987). Most authorities recommend treatment of postcricoid cancer by surgery and this seems to be the usual practice in Head and Neck Units. One of the reasons for this policy is that the disease tends to be advanced at the time of diagnosis (Million *et al.*, 1994).

Although it is suggested that postcricoid cancer is best dealt with by surgery there seems little reason why irradiation therapy should not be a reasonable alternative for this disease.

One of the pioneers of irradiation in the treatment of carcinoma of the pharynx was Lederman (1967) who noted a 20 per cent cure rate after five years using radiotherapy in patients with no palpable disease in the neck. It has been suggested that radiotherapy should be used when no neck node metastases are present and when the carcinoma is <5 cm long (Dalby, 1964; Duncan, 1971). For more advanced primary site disease and in patients with neck node metastases Stell *et al.* (1982) quoted a survival rate of 20 per cent using surgical ablation and reconstruction. Other authors have found similar cure rates to that of Stell *et al.* (1982) for this type of disease (Ong and Lee, 1960; Ong, 1964; Balasegaram, 1968; Harrison, 1972) and other authors have confirmed results for radiotherapy similar to those of Mullard (Pearson, 1966).

Several authors are worried about the extensive nature of surgery and the relatively poor rehabilitation achieved with respect to voice, tracheal stoma and, in some cases, swallowing (Lederman, 1967; Duncan, 1971).

TABLE II
OPERATIONS EMPLOYED IN PRIMARY SURGERY GROUP (N = 67)

Ablation	Total pharyngolaryngectomy (63 patients)				Total laryngectomy with partial pharyngectomy (3 patients)		Lateral pharyngotomy (1 patient)
Reconstruction	Skin flap or musculocutaneous flap	Stomach pull-up	Jejunal loop	Other	Primary repair	Musculocutaneous flap	Skin flap
No. of patients	25	21	15	2	2	1	1

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TABLE III
PRIMARY SITE AND NECK NODE RECURRENCE

	Surgery (n = 67)	Radiotherapy (n = 50)	Chi-square and p value
T recurrence	21	26	$\chi^2_1 = 4.261$; $p = 0.039$
N recurrence	16	8	$\chi^2_1 = 0.661$; $p = 0.416$

T = recurrence at primary site; N = neck node recurrence.

Patients and methods

One hundred and fifty-five patients, with no neck node disease on clinical examination, were included in the study, 67 were treated by primary surgery and 50 by primary irradiation therapy. A further 36 patients were unsuitable for curative treatment and two patients were lost to follow-up. Patients referred from elsewhere were excluded, as were those who had received irradiation or surgical therapy for other neck tumours. Patients included in the study were treated between 1963 and 1966. Details of treated and untreated patients are given in Table I.

The stage of the tumour at presentation was recorded using the UICC (1992) classification and the general physical condition of the patient was recorded using the method recommended by the Eastern Cooperative Oncology Group (ECOG) (AJC, 1983). A variety of pathologists assigned a histological grade as either well, moderately or poorly differentiated, or in some cases the tumour was classified merely as squamous cell carcinoma. All data was stored on a data base which, from 1963 to 1976 was kept on a punch card system and, from 1976 onwards a purpose programmed microcomputer database. The dates of death and follow-up times were recorded from clinic visits, from general practitioner records and the Mersey Region Cancer Registry. The median potential follow-up was 15 years.

Where surgical treatment was employed patients were either treated by partial laryngectomy with partial pharyngectomy, total laryngectomy with partial pharyngectomy, or total pharyngolaryngectomy and reconstruction using a variety of methods (Table II). The procedures were carried out according to methods described by Stell and Maran (1978). Radiotherapy was delivered by external beam irradiation using a 4, 5 or 6 MV linear accelerator. The dose of radiation ranged from 55 Gy in 15 fractions to 60–66 Gy given over 25–33 fractions. The patient was immobilized in a beam directing shell and treated using anterior oblique double-wedged fields (Garrett, 1971).

The general policy of our department over the time scale of the present study was for unimodal primary treatment with salvage surgery if necessary. Thus, most patients received either radiotherapy or surgery for their primary treatment. There were exceptions however, and in the group submitted for primary surgery four patients received radical post-operative radiotherapy and six pre-operative radiotherapy. In the latter case the dose was in the region of 40 Gy.

TABLE IV
FATE OF PRIMARY SITE RECURRENCE: SURGERY GROUP (N = 21)

Further major resection	Alive	Died of tumour	Died of ICD	Died of second tumour
4	4	14	2	1

Five also had neck node recurrence. ICD = intercurrent death.

Survival curves were constructed using the life table method (Armitage and Berry, 1987) and 95 per cent confidence intervals (CI) calculated by applying a double-log transformation. Two types of survival calculations were performed: the first was adjusted survival calculated on the basis of tumour-specific death rates and the second was observed survival where all deaths were counted as failures. Differences in adjusted survival curves were analysed using the log rank test (Peto *et al.*, 1977). Prognostic factors were further analysed using Cox's proportional hazards model (Cox, 1972) on the SAS software. Differences between the two treated groups and factors determining primary site recurrence or the development of neck node metastases were sought using multiple logistic regression by the CATMOD procedure (SAS Institute, 1985).

Results

Of 153 patients available for follow-up, 63 were treated by primary surgery, 50 by primary irradiation therapy and 36 patients were unsuitable for curative treatment. The details are shown in Table I. There were no significant differences between host and tumour factors for the surgery or radiotherapy groups (Table I). There were, however, significant differences between the group not suitable for curative treatment and those having curative treatment. Those not receiving curative treatment tended to be older ($\chi^2 = 14.84$; $p = 0.006$), to be in poor general condition ($\chi^2_1 = 10.95$; $p = 0.004$) and had more advanced disease at the primary site ($\chi^2_1 = 22.66$; $p<0.0001$) (Table I).

Primary site recurrence occurred in 21 out of 67 (31 per cent) patients receiving surgery and 26 out of 50 (52 per cent) patients receiving radiotherapy ($\chi^2_1 = 4.261$; $p = 0.039$) (Table III). There was no significant difference in the time of primary site recurrence between the two groups ($\chi^2_1 = 0.931$; $p = 0.332$). Of particular importance was that survival of primary site recurrence was unaffected by primary treatment modality ($\chi^2_1 = 1.864$; p = NS). The fate of patients developing a primary site recurrence in the surgery group and in the radiotherapy group are shown in Tables IV and V respectively.

Sixteen out of 67 (24 per cent) patients treated by surgery developed a neck node metastasis compared with eight out of 50 (16 per cent) treated by irradiation. Whilst irradiation appears more successful at reducing the risk of developing a neck node metastasis, this difference was not statistically significant ($\chi^2_1 = 0.661$; $p = 0.416$) (Table III). The time to neck node metastasis was unaffected by primary treatment modality ($\chi^2_1 = 3.338$; $p = 0.066$). In the primary surgery group 16 patients developed a neck node metastasis and three survived, whereas of the patients treated by primary irradiation eight developed a nodal metastasis and one survived. The difference was not

TABLE V
FATE OF PRIMARY SITE RECURRENCE: RADIOTHERAPY GROUP (N = 26)

Major resection	Alive with larynx	Alive without larynx	Died of tumour	Died of ICD	Died of second tumour
8	2	1	16	7	0

Five also had neck node recurrence. ICD = intercurrent death.

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TABLE VI
FATE OF NECK NODE RECURRENCE IN PATIENTS TREATED BY PRIMARY SURGERY (N = 16)

Radical neck dissection	Alive	Died of tumour	Died of ICD
13	3	12	1

Five also had primary site recurrence. ICD = intercurrent death.

statistically significant ($\chi^2_1 = 1.952$; $p = 0.323$). The fate of those patients developing a neck node recurrence who were treated by primary surgery and by primary irradiation are shown in Table VI and VII respectively.

The tumour-specific survival is shown in Figure 1. For irradiation the five-year cure rate was 48 per cent (95 per cent CI 27–66 per cent) and for surgery the five-year cure rate was 43 per cent (95 per cent CI 23–60 per cent). The median survival of those having palliative treatment was three months (95 per cent CI two–six months). The five-year cure rate for the whole group of 153 patients was 32 per cent (95 per cent CI 21–44 per cent). There was no difference in survival between the patients treated by irradiation therapy or by surgery ($\chi^2_1 = 3.672$; $p = 0.061$). Observed survival for the patients receiving irradiation after five years was 25 per cent (95 per cent CI 13–39 per cent) and for those receiving primary surgery was 18 per cent (95 per cent CI 9–28 per cent).

The survival data for those patients suffering from T_1 and T_2 tumours were analysed separately. The five-year survival of all such patients was 38 per cent (95 per cent CI 25–50 per cent), for the radiotherapy group it was 49 per cent (95 per cent CI 26–67 per cent) and for the surgery group 44 per cent (95 per cent CI 24–61 per cent). It should be noted that only a minority of treated patients had advanced (T_{3-4}) tumours.

Multiple logistic regression confirmed that there was no significant difference in host or tumour factors between those patients treated by irradiation therapy or by surgery. In addition no factor appeared to predict either a primary site recurrence or a future neck node metastasis.

Tumour specific survival was further analysed using Cox's proportional hazards model. Poorly differentiated histology tended to have the worst prognosis ($\chi^2 = 6.444$; $p = 0.011$). For treated groups there was no difference in survival whether the patient received irradiation or surgery.

Complications of surgical treatment and radiotherapy are shown in Table VIII.

Discussion

There was no significant difference between the survival of patients treated by primary surgery or by primary radiotherapy with the salvage surgery option. It has been the policy of this department for many years to treat relatively small tumours, i.e. <5 cm long with irradiation and reserving surgery for larger tumours. Whilst χ^2 analysis for T-stage did not produce any significant value only five cases in the radiotherapy group were of T_3 or T_4 tumours. Thus, almost all the cancers in this group were early, being either T_1 or T_2.

Ninety-seven patients in the treated group generally were early (T_1 or T_2) and only 20 were advanced (T_3 or T_4). The relatively early stage of the disease is reflected in the five-year survival figures of 48 per cent for the irradiation group and 43 per cent for those treated by primary surgery. The slight difference in the figures is probably explained by the increased number of patients with T_3 and T_4 disease in the surgery group. The results of the present study compare favourably with Mullard's five-year survival figure of 38 per cent (Mullard, 1968) but his series included more advanced tumours. Stell *et al.* (1982) noted a five-year survival for patients that included advanced disease and neck node metastases in the order of 20 per cent. In a series of 22 patients with hypopharyngeal cancer treated by total pharyngolaryngectomy and stomach transposition Moores *et al.* (1983) quoted a 30 per cent five-year survival. Harrison and Thompson (1986) noted a 37 per cent three-year survival rate for patients with postcricoid cancers treated by pharyngolaryngectomy and stomach transposition. In a recent study from Japan Hatta *et al.* (1991) reported a 47 per cent five-year survival rate for patients undergoing radical surgery. Lederman (1967) noted a 20 per cent cure rate for patients with well differentiated carcinoma of the hypopharynx but his series included many advanced cases and also included many patients treated in the relatively early years of radiotherapy. Griffiths and Shaw (1973) quoted 34 per cent of patients who had had resection of the cervical oesophagus and colon interposition who were alive when last contacted. The duration of follow-up was however short. The few publications on this subject quote survival rates in the region of 20–30 per cent (Ong and Lee, 1960; Ong, 1964; Pearson, 1966; Balasegaram, 1968; Mullard, 1968; Harri-

TABLE VII
FATE OF NECK NODE RECURRENCE IN PATIENTS TREATED BY PRIMARY IRRADIATION (N = 8)

Radical neck dissection	Alive	Died of tumour	Died of ICD
5	1	5	2

Five also had primary site recurrence. ICD = intercurrent death.

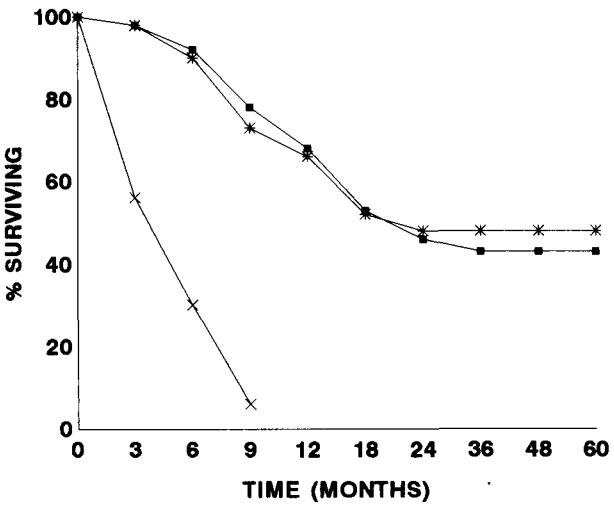

FIG. 1
Tumour-specific survival rate for patients with node negative postcricoid carcinoma comparing treatments. X, palliative; *, radiotherapy (five-year survival rate of 48 per cent); ■, surgery (five-year survival rate of 43 per cent).

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TABLE VIII
COMPLICATIONS

	Necrosis	Stenosis	Fistula	Carotid blow out	More than one complication	Medical
DXRT	0	2	1	0	1	0
Treatment DXRT recurrence	0	0	0	1	0	2
Surgery	6	3	6	1	0	0
Treatment surgery recurrence	0	0	2	0	0	0

DXRT = radical radiotherapy.

son, 1972; Stell *et al.*, 1982). These series tended to include heterogenous groups of patients, many of whom suffered lymph node metastases.

Neck node involvement has been claimed to be present in as few as 20 per cent of patients (Stell and Maran, 1978) whereas other authors have noded a 40 per cent risk of neck node involvement (Hahn *et al.*, 1987; Lefebvre *et al.*, 1987; Willatt *et al.*, 1987). Ogura and colleagues (1960), and Byers *et al.* (1988) noted that most patients were suffering from hypopharyngeal cancer had neck node disease at the time of presentation. In addition an unknown number of patients had paratracheal and retropharyngeal node involvement. It is possible that the presence of a tumour at this site is a common reason for failure. This study has included patients from as far back as 1963 and most patients, therefore, have not had modern radiological investigations such as CT or MRI scanning. The problem with paratracheal node involvement is that it is undetectable on routine clinical examination. Thus, it is likely that a proportion of patients in this study could have suffered from paratracheal node involvement although the number of patients eventually succumbing to neck node metastases in the present series is in fact quite low. Regrettably no record was kept of the level of neck node recurrence. If it had been low in the neck, this could have been taken as evidence of spread from the superior mediastinum.

Because of the risk of paratracheal node involvement it has been the policy of our department over many years to dissect out paratracheal nodes by blunt finger dissection at the time of operation or to include this area in the radiotherapy fields in those patients being treated by irradiation.

Conclusions

The primary site recurrence rate is significantly higher in the radiotherapy group (52 per cent) compared with the surgery group (31 per cent). There thus seems little doubt that surgery is superior in controlling local disease. One must remember however that the majority of patients in the radiotherapy group kept the larynx whereas all those in the surgery group lost it. Radiotherapy may be superior to surgery in reducing the subsequent risk of neck node metastases. Survival analysis demonstrates that irradiation therapy is as effective as surgery in the treatment of postcricoid carcinoma and has the huge advantage of leaving the patient with the larynx.

This study was retrospective and the patients were not randomized into treatment groups. Because of this, care should be exercised when interpreting the results.

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