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Treatment outcomes of laryngectomy compared to non-surgical management of T_3 laryngeal carcinomas: a 10-year multicentre audit of 179 patients in the northeast of England

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Main Article

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Abstract

Objective. Wide-ranging outcomes have been reported for surgical and non-surgical management of T_3 laryngeal carcinomas. This study compared the outcomes of T_3 tumours treated with laryngectomy or (chemo)radiotherapy in the northeast of England.

Methods. The outcomes of T_3 laryngeal carcinoma treatment at three centres (2007–2016) were retrospectively analysed using descriptive statistics and survival curves.

Results. Of 179 T_3 laryngeal carcinomas, 68 were treated with laryngectomies, 57 with chemoradiotherapy and 32 with radiotherapy. There was no significant five-year survival difference between treatment with laryngectomy (34.1 per cent) and chemoradiotherapy (48.6 per cent) ($p = 0.184$). The five-year overall survival rate for radiotherapy (12.5 per cent) was significantly inferior compared to laryngectomy and chemoradiotherapy ($p = 0.003$ and $p < 0.001$, respectively). The recurrence rates were 22.1 per cent for laryngectomy, 17.5 per cent for chemoradiotherapy and 50 per cent for radiotherapy. There were significant differences in recurrence rates when laryngectomy ($p = 0.005$) and chemoradiotherapy ($p = 0.001$) were compared to radiotherapy.

Conclusion. Laryngectomy and chemoradiotherapy had significantly higher five-year overall survival and lower recurrence rates compared with radiotherapy alone. Laryngectomy should be considered in patients unsuitable for chemotherapy, as it may convey a significant survival advantage over radiotherapy alone.

Introduction

Head and neck squamous cell carcinoma is the sixth leading form of cancer worldwide. In the UK, there are 1600 new diagnoses of laryngeal cancer annually, of which 200 cases are tumour (T) stage T_3.[1] Historically, T_3 laryngeal carcinomas were managed surgically. However, this changed following a landmark study published in 1991 by the Department of Veterans Affairs,[2] which showed no differences in survival between surgically and non-surgically managed patients with advanced (T_3 or T_4) laryngeal carcinoma. Furthermore, 64 per cent of patients managed non-surgically were able to retain their larynx.

Following this, numerous case series have studied the survival outcomes of patients with T_3 laryngeal carcinoma.[3–7] It has been suggested that chemoradiotherapy offers a significant increase in five-year overall survival when compared to total laryngectomy with post-operative adjuvant radiotherapy (RT).[3] Others were not able to identify any significant difference in survival between surgical and non-surgical treatment,[4] and some have even shown that surgical treatment offers significantly higher rates of survival.[5] Within the northern region of England, patients with T_3 laryngeal carcinomas treated at the Cumberland Infirmary were found to have a five-year overall survival rate of over 57 per cent.[8]

We must bear in mind that survival alone is not the sole measure of treatment success; patients make choices about their treatment based on a wide range of factors. When provided with a hypothetical treatment choice for laryngeal cancer, participants held strong to their initial treatment choice.[9] In that study, even when significant survival advantages were given to participants' non-preferred treatment option, a third of patients still opted for their original treatment choice.[9] The study highlights that survival, along with other measures such as quality of life, affects patients' decision-making regarding treatment choice in managing laryngeal cancer.

The UK national multidisciplinary guidelines suggest that most patients with T_3 supraglottic cancers are suitable for non-surgical larynx preservation therapies. The standard of care for non-surgical management is concurrent chemoradiotherapy.[10]

Table 1. Patient characteristics

Characteristic	Number (% of total T_3)	Mean (range)	N_0 (*n*)	N_1 (*n*)	N_2 (*n*)	N_3 (*n*)
Cases						
– Total T_3	179 (100)	–				
– Deceased	84 (47)	–				
– Total N_0	118 (66)	–				
– Total N_1	23 (13)	–				
– Total N_2	36 (20)	–				
– Total N_3	2 (1)	–				
Age (years)						
– At diagnosis	–	65.65 (15–90)				
– All laryngectomy	–	66.71 (43–85)				
– Chemoradiotherapy	–	59.35 (15–84)				
– RT	–	68.03 (48–90)				
– Palliative	–	75.21 (54–85)				
– At death	–	70.49 (48–90)				
Gender						
– Male	133 (74)	–				
– Female	46 (26)	–				
Treatment						
– All laryngectomy	68 (38)	–	37	13	17	1
– Total laryngectomy	60 (34)	–	30	13	16	1
– Partial laryngectomy	8 (4)	–	7	0	1	0
– Chemoradiotherapy	57 (32)	–	38	7	12	0
– RT	32 (18)	–	27	2	3	0
– All palliative	22 (12)	–	16	1	4	1
– Palliative RT	10 (6)	–	8	1	1	0
– Palliative chemotherapy	2 (1)	–	0	0	1	1

T = tumour stage; N = nodal stage; RT = radiotherapy

Given the range of survival outcomes described for the surgical and non-surgical management of T_3 laryngeal carcinomas, we thought it prudent to evaluate these data within our own region. We therefore undertook a 10-year multicentre audit. This paper presents our treatment outcomes relating to the management of T_3 laryngeal carcinomas in the northeast of England, focusing on survival, recurrence and salvage surgery rates.

Materials and methods

Audit design

A retrospective multicentre audit was conducted of patients with T_3 laryngeal carcinomas diagnosed and treated in the northeast of England. The centralised cancer databases were searched to identify cases of laryngeal cancers at three university teaching hospitals in the northeast of England.

Ethical considerations

The data collected in this multicentre study were anonymous, retrospective and observational in nature, and therefore deemed not to require research registration. However, each participating centre was responsible for local registration of this study as a clinical audit, and for obtaining approval from their local Caldicott Guardian for the use of anonymised outcome data.

Patient selection

Consecutive patients were identified from local cancer service databases according to the International Classification of Diseases 10th Revision ('ICD-10') coding for a laryngeal cancer diagnosis (C32.9, malignant neoplasm of larynx), during the period from 1 January 2007 to 31 December 2016. The patients coded for laryngeal carcinoma were filtered for T_3 stage at the pre-treatment multidisciplinary team meeting.

The patients were grouped into four major treatment categories: (1) laryngectomies (encompassing total and partial laryngectomy); (2) chemoradiotherapy (encompassing all dosages of RT and forms of chemotherapy); (3) RT only; and (4) palliative care (including best supportive care, palliative RT and palliative chemotherapy). Radiotherapy treatment was delivered in the form of conformal RT pre-2009, and as intensity-modulated RT from 2009 onwards (delivered fractionated over six weeks). Once-weekly, concurrent platinum-based chemotherapy regimens were employed for those patients receiving chemoradiotherapy.

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Treatment categories for consecutive patients during the study period were available through electronic medical records; therefore, no patients were excluded. However, primary RT, adjuvant RT following surgery, and chemotherapy schedules were incomplete, and thus excluded from analysis.

Statistical analysis

Statistical analysis of the data was performed using SPSS Statistics for Windows software, version 24 (IBM, Armonk, New York, USA). Descriptive statistics for patient demographics were obtained. Overall survival data were plotted using Kaplan–Meier survival curves. The Kaplan–Meier method is able to estimate the five-year overall survival rate whilst accounting for censored data from patients who had not completed five years of follow up. Statistical differences in survival were assessed using the Mantel–Cox test, and differences in recurrence were assessed using Pearson's chi-square test.

Results

Patient characteristics

The study comprised a total of 179 patients, of which 133 (74 per cent) were male and 46 (26 per cent) were female. The mean age of patients was 65.65 years. The mean age at diagnosis for each treatment group, in descending order, was: 75 years for palliative, 68 years for RT, 67 years for laryngectomy and 59 years for chemoradiotherapy. Patients receiving RT alone had the age range encompassing the oldest patients.

The proportions of patients receiving each treatment following diagnosis were: 34 per cent ($n = 60$) for total laryngectomy, 4 per cent ($n = 8$) for partial laryngectomy, 32 per cent ($n = 57$) for chemoradiotherapy, 18 per cent ($n = 32$) for RT and 12 per cent ($n = 22$) for palliative treatment. Patient demographics are summarised in Table 1.

Overall survival

Overall survival was plotted for five years (60 months) for the four treatment groups (Figure 1a) (excluding censored cases for patients with less than five years' follow up). This revealed similar survival rates between laryngectomy (34.1 per cent) and chemoradiotherapy (48.6 per cent) groups. Treatment with RT alone showed a significant decrease in five-year overall survival (12.5 per cent), and the palliative treatment group had the worst five-year overall survival as expected (4.5 per cent).

When comparing laryngectomy with chemoradiotherapy, there was no significant difference in five-year overall survival ($p = 0.184$). However, a significant difference in five-year overall survival was observed when comparing chemoradiotherapy with RT ($p < 0.001$) and laryngectomy with RT ($p = 0.003$).

Recurrence and salvage rates

Combined local and distant recurrence following primary treatment was highest in proportion (50 per cent) for patients receiving RT alone. The recurrence rates following laryngectomy and chemoradiotherapy were similar, at 22.1 per cent and 17.5 per cent, respectively. This trend remained consistent even when local and distant recurrences were assessed separately. The recurrence rates for laryngectomy, chemoradiotherapy and RT are summarised in Table 2. There was no

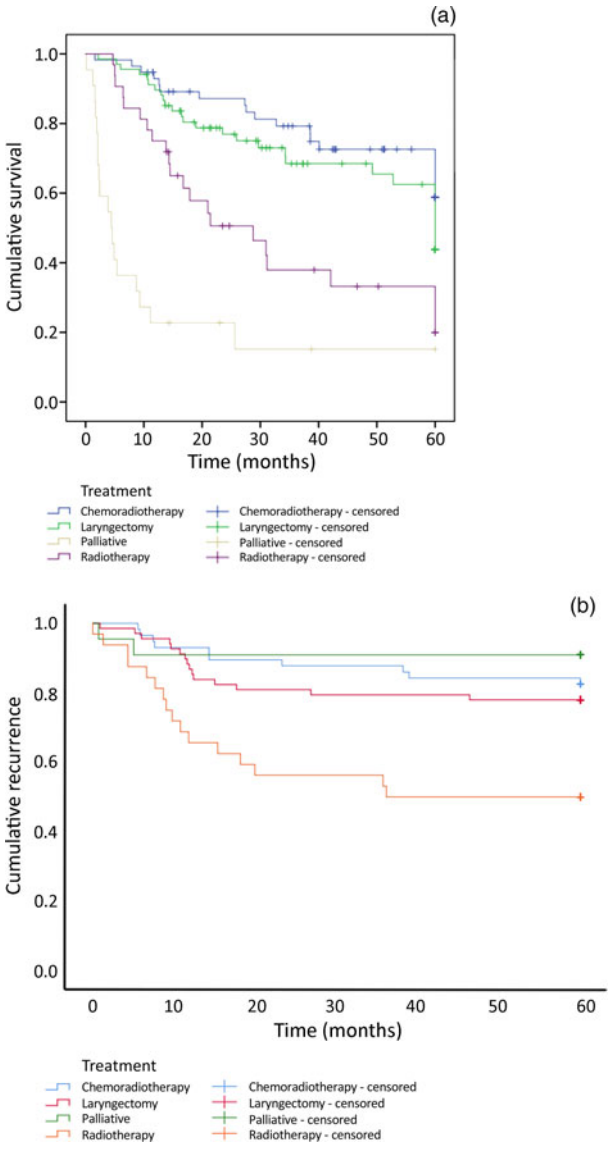

Fig. 1. Kaplan–Meier survival curves for five-year overall survival (a) and recurrence (b), for all treatment groups: chemoradiotherapy, laryngectomy, radiotherapy and palliative. Censored survival and recurrence data shown for patients with follow up of less than five years.

significant difference in recurrence rate between laryngectomy and chemoradiotherapy ($p = 0.530$); however, the difference was significant when laryngectomy ($p = 0.005$) and chemoradiotherapy ($p = 0.001$) were compared to RT.

A total of 15 salvage laryngectomies were performed: 5 for a non-functional larynx and 10 for recurrent disease. Of the patients with a non-functioning larynx requiring salvage treatment, two cases occurred after partial laryngectomy, whilst the remaining cases occurred after chemoradiotherapy ($n = 2$) and RT ($n = 1$). Only one case of local recurrence after partial laryngectomy required salvage laryngectomy, whilst five and four cases of recurrence following chemoradiotherapy and RT required salvage, respectively. The salvage rates after primary treatment for a non-functioning larynx or local recurrence are summarised in Table 3.

Discussion

This retrospective study showed that patients receiving RT alone had significantly worse five-year overall survival when

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Table 2. Recurrence rates for each treatment group at five years

Treatment group	Patients (*n*)	Combined recurrences (*n* (%))	Local recurrence (*n* (%))	Distant recurrence (*n* (%))
Laryngectomy	68	15 (22.1)	9 (13.2)	6 (8.8)
Chemoradiotherapy	57	10 (17.5)	7 (12.3)	3 (5.3)
RT	32	16 (50)	11 (34.4)	5 (15.6)

RT = radiotherapy

Table 3. Salvage rates for each treatment group at five years

Primary treatment	Non-functional larynx (*n* (%))	Recurrence (*n* (%))	Total (*n* (%))
Partial laryngectomy*	2 (25)	1 (12.5)	3 (37.5)
Chemoradiotherapy†	2 (3.5)	5 (8.8)	7 (12.3)
RT‡	1 (31.3)	4 (12.5)	5 (15.6)

*$n = 8$; †$n = 57$; ‡$n = 32$. RT = radiotherapy

compared with laryngectomy or chemoradiotherapy. When comparing overall survival, there was no significant difference between laryngectomy and chemoradiotherapy. Following primary treatment, there was significantly higher recurrence in patients receiving RT alone, but no significant difference between laryngectomy and chemoradiotherapy.

Chemotherapy was withheld for patients receiving RT alone as the primary treatment, often because of multiple co-morbidities, poor renal function or advanced age. Retrospective studies have shown higher rates of treatment-related toxicities associated with concurrent chemotherapy for elderly patients (aged over 70 years) compared to their younger peers,[11] and a decreasing effect of chemotherapy with age.[12]

Of the patients receiving RT ($n = 32$), 16 (50 per cent) were aged over 70 years, and this group had the highest mean age (68 years) and maximum range (90 years) compared to the laryngectomy and chemoradiotherapy treatment groups. As concurrent chemoradiotherapy is the standard of care for larynx preservation treatment, adhered to by all institutions in this study, the patients receiving RT alone were deemed unsuitable for chemoradiotherapy at the multidisciplinary decision-making level, which therefore precluded treatment with chemotherapy. Individual treatment choices of RT over chemoradiotherapy could not be elucidated from the available clinical audit data, and thus it is presumed that given the higher mean age of the RT group compared to the other treatment modality groups, the decision to opt for RT treatment may be because of underlying patient-specific factors, such as multiple co-morbidities, advanced age (greater than 70 years) or frailty.

Although a difference in overall survival was shown between both laryngectomy and chemoradiotherapy over RT alone, and five-year overall survival after laryngectomy was not inferior to chemoradiotherapy, we should consider that survival alone is not the sole reason for patient choice. As demonstrated by Hamilton *et al.*,[9] patient choice and time trade-off for quality of life are important considerations when comparing non-surgical versus surgical management of laryngeal carcinoma.

Limitations

Patient assignment to treatment groups

It was not entirely possible to elucidate the reasons for patient assignment to treatment groups, because of incomplete clinical documentation. Pre-treatment laryngeal function could have influenced the decision to undergo surgical management (i.e. total laryngectomy) over non-surgical treatment (i.e. chemoradiotherapy). This potential bias towards surgical treatment may under-estimate the salvage rate in the non-surgical treatment group. The individual reasons for deciding to treat with RT over chemoradiotherapy were not available through the data collected from the clinical audit. In addition, data on adjuvant RT following surgical management, swallowing function, and quality of life measures were not all available, and thus could not be analysed to assess for differences based on these parameters.

Population and local management

The patient population selected for this study came from the northeast of England, which may have socioeconomic factors that are different from other populations with T_3 laryngeal carcinoma across the world. For example, one treating institution in this study serves a largely remote, rural population of 330 000 patients. Furthermore, the northeast of England treats a mainly Caucasian population. In addition, surgical intervention in the form of total and partial laryngectomy has a higher prevalence in the local management of advanced laryngeal cancer.

- Wide-ranging outcomes have been reported for surgical and non-surgical management of T_3 laryngeal carcinomas
- This 10-year multicentre audit of 179 patients compared outcomes of T_3 laryngeal tumours treated with laryngectomy or (chemo)radiotherapy in northeast England
- Laryngectomy and chemoradiotherapy had significantly higher five-year overall survival and lower recurrence rates compared with radiotherapy (RT) alone
- Laryngectomy should be considered in patients unsuitable for chemotherapy, as it may have a significant survival advantage over RT alone
- Patients should be informed of expected survival rates for available treatment modalities, to empower patient choice in T_3 laryngeal carcinoma management

The existing published case series literature on T_3 laryngeal cancers reports combined five-year overall survival rates ranging from 36 to 67 per cent for non-surgical treatment, and 41 to 60 per cent for surgical treatment.[3–7] Our experience of treatment outcomes for non-surgical management (five-year overall survival rate for chemoradiotherapy of 48.6 per cent) lies within this range. However, our surgical

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management outcomes (five-year overall survival rate of 34.1 per cent) falls just short of that quoted in the literature, and is short of the rate (of over 57 per cent) reported at Cumberland Infirmary.[8] This may be plausibly explained by the fact that the audited institutions which comprise our experience include a tertiary referral centre. This centre takes on complex surgical cases of T_3 laryngeal carcinoma that require specialist multidisciplinary head and neck cancer support; such cases are often referred from district general hospitals, potentially biasing the survival outcomes reported.

Conclusion

There is a significant difference in five-year overall survival for patients treated with RT alone versus those treated with laryngectomy. Patients should be informed of this difference in expected mortality if the treatment choice involves a decision between laryngectomy versus RT alone. In an ever-increasing culture of patient-centred decision-making, patients should be informed of the expected survival rates associated with the available treatment modalities, to help empower their choice in the management of T_3 laryngeal carcinomas.

Competing interests. None declared

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