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MAIN ARTICLE

Laryngeal cancer management in a small, rural, multidisciplinary team setting: 15-year review

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Abstract

Background: The Cumberland Infirmary, Carlisle, serves a largely remote, rural population of 330 000. The aim of this study was to report the treatment and survival figures for patients treated for laryngeal cancer at this centre.

Methods: The study included 209 consecutive patients with squamous cell carcinoma of the larynx diagnosed between 1996 and 2010 at the Cumberland Infirmary.

Results: Disease-specific survival was 100 per cent for stage one, 76 per cent for stage two, 87 per cent for stage three and 46 per cent for stage four. In total, 76 patients (36 per cent) had a laryngectomy, either as primary treatment or as a salvage procedure.

Conclusion: Our tumour-specific survival rate was very high, and this success may be due in part to high rates of surgical intervention. Survival data compared favourably with other centres, despite less radical radiotherapy regimes. Laryngeal cancer can be managed effectively in a small, relatively remote, multidisciplinary team setting.

Key words: Laryngeal Cancer; Survival; Surgery; Laryngectomy

Introduction

Laryngeal cancer is the most common head and neck cancer in the UK, with over 1500 cases per year,[1] and can present at an early or advanced stage. Surgical and non-surgical therapies affect not only survival but also communication, swallowing, aesthetics and psychosocial functioning. Although the stage of disease has a significant impact on prognosis, many other factors exert considerable influence on a patient's outcome following treatment, including co-morbidity and pre-disease functioning.[2,3]

In 2004, the National Institute of Clinical Excellence published guidelines on the improvement of head and neck cancer care in England and Wales.[4] These guidelines recommended the centralisation of cancer care services in the UK. In North Cumbria, the head and neck multidisciplinary team (MDT) is based at the Cumberland Infirmary, Carlisle, and serves a largely remote, rural population of 330 000 patients. There is a real conflict in UK National Health Service strategy between treating patients as close to home as possible and centralising specialised services. It is important that individual units collect data so outcomes can be analysed and compared with peers; this is particularly important in smaller centres.

The North Cumbria head and neck MDT had engaged with the Data for Head and Neck Oncology project since its inception, and hence had accrued an accurate and comprehensive database of patients treated since 1996. The aim of this study was to report the management regime and survival figures for patients treated for laryngeal cancer, in order to demonstrate that high quality cancer care can be delivered in smaller centres.

Materials and methods

Since 1996, the combined head and neck unit at the Cumberland Infirmary had prospectively collected and collated patient information as part of the Data for Head and Neck Oncology database. Initially, the British Association of Head and Neck Oncologists' minimum dataset was utilised; however, from 2003 data were transferred to the Data for Head and Neck Oncology project database system. Data were stored using the Infoflex Chameleon Information Management System, version 5 (Chameleon Information Management Services, Rickmansworth, UK), with data entry initialised by the MDT co-ordinator and verified by the corresponding head and neck surgeon. Access to the database was protected, and was only available on hospital premises to authorised users submitting a request to the information technology department.

Consecutive patients with biopsy-proven squamous cell carcinoma (SCC) of the larynx diagnosed

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between 1996 and 2010 at the Cumberland Infirmary, Carlisle, were included in this study. All patients treated at this centre were prospectively entered into the database, with information included on patient demographics, tumour site, tumour stage, treatment modality, follow up and survival. Where insufficient data were included, we obtained further information from patient hospital notes, radiotherapy notes and/or personal knowledge. All surgery carried out at the Cumberland Infirmary was performed or supervised by one head and neck surgeon (AKR), and all radiotherapy was overseen by one oncologist (PD). All patients were managed and rehabilitated by a specialist head and neck MDT.

Patients were excluded if they had received a diagnosis other than SCC (3 patients) or had incomplete data (11 patients).

Stage one disease was traditionally managed using primary radiotherapy. More recently, tumour excision with CO_2 laser has emerged as an alternative therapy with comparable survival and voice outcomes but a lower treatment burden for the patient.[5] Many of the earlier patients in our database therefore received radiotherapy, with a move towards surgical management in more recent years for selected cases. The established standard of care for the management of more advanced disease (i.e. tumour (T) stage T_3 and T_4) in our unit was generally surgery followed by post-operative adjuvant radiotherapy.

Statistical analysis

The Kaplan–Meier estimator was used to estimate five-year survival, by stage, for patients with diagnosed laryngeal cancer.[6] This is a method of estimating survival after cancer treatment, which is capable of taking into account censored data. In this way, five-year survival estimates can be generated from data which do not include five years of follow up for each subject.

Confidence intervals were calculated using Ramsey's method. All analyses were conducted using R software.

Results and analysis

The data set contained information on 223 individuals diagnosed with laryngeal cancer between 1996 and 2010. Fourteen patients were excluded, due to incomplete data (11 patients) or a pathological diagnosis other than SCC (3 patients), leaving 209 patients to be included in the study.

The median patient age was 70 years and 2 months (interquartile range, 62 to 78 years). Eighty-six patients were diagnosed with stage 1 disease, 43 with stage 2, 33 with stage 3 and 47 with stage 4.

Results for two-year and five-year tumour-related and overall survival, for each stage, are shown in Table I and Figures 1 and 2. Overall, 5-year survival was 80 per cent for stage 1, 48 per cent for stage 2, 58 per cent for stage 3 and 32 per cent for stage 4. Five-year disease-specific survival was much higher, at 100 per cent for stage 1, 76 per cent for stage 2, 87 per cent for stage 3 and 46 per cent for stage 4.

Details of the treatment received and laryngectomy rates are shown in Table II. The majority of disease recurrence occurred in patients who had been treated non-surgically (36 of 46, 79 per cent). Most cases of disease recurrence were therefore treated surgically, the most common procedure being total laryngectomy. Other cases of recurrence were treated with radiotherapy or laser surgery. In total, 76 (36 per cent) patients had a laryngectomy, either as primary treatment (53 of 76, 70 per cent) or as a salvage procedure (23 of 76, 30 per cent). The majority of patients in the advanced stages (i.e. stages 3 and stage 4) were treated with laryngectomy (56 of 80, 70 per cent). Only one stage three patient and three stage four patients were managed with primary palliative radiotherapy.

Discussion

Our data show that the studied laryngeal cancer patients, treated at the Cumberland Infirmary, Carlisle, had a 5-year tumour-related survival rate of 82 per cent and a 5-year overall survival rate of 59 per cent. The disease-specific survival rate was very high, especially when compared with other large cohorts. In 2005, relative survival figures for laryngeal cancer across Europe varied between 44 and 86 per cent.[7] Data from England and Wales between 1986 and 1999 showed relative survival rates of between 63 and 64 per cent.[8] Figures from the American National Cancer Database indicate relative survival

TABLE I
PATIENTS' OVERALL AND DISEASE-SPECIFIC SURVIVAL RATES

Stage	Pt age (med; years)	Overall survival (% (95% CI))		Disease-specific survival (% (95% CI))	
		2 years	5 years	2 years	5 years
1	70.2	89.3 (80.9–94.3)	79.7 (69.5–87.2)	100 (100–100)	100 (100–100)
2	66.8	79.1 (37.7–95.9)	47.6 (25.6–70.5)	85.4 (71.7–93.2)	76.1 (60.1–87.1)
3	70.4	84.8 (23.7–99.0)	57.7 (24.0–85.5)	93.6 (54.5–99.4)	86.9 (54.7–97.3)
4	70.4	52.3 (11.3–90.4)	31.8 (7.9–71.0)	61.8 (40.0–79.7)	46.3 (27.5–66.2)
Total	70.0	78.3 (72.1–83.3)	59.2 (51.9–66.0)	87.7 (82.4–91.6)	82.1 (75.7–87.1)

Pt = patient; med = median; CI = confidence interval

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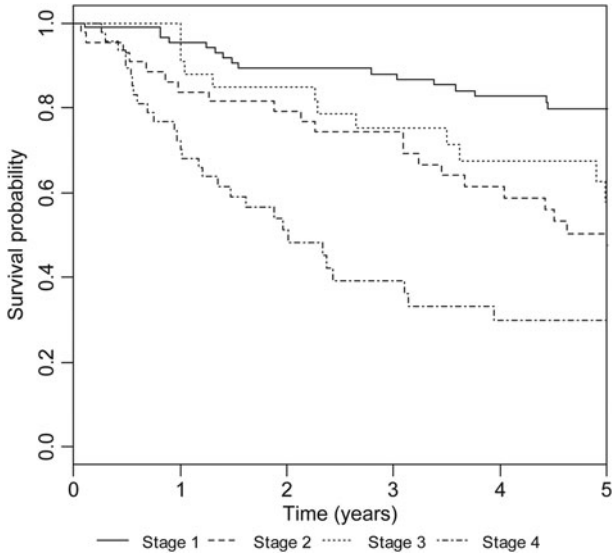

FIG. 1
Five-year Kaplan–Meier overall survival curves.

rates for laryngeal cancer ranging from 64 to 68 per cent, and an observed (or overall) survival rate of 51 to 57 per cent.[9]

Laryngeal cancer demographics, treatment and survival trends over time have been the subject of much debate in recent years. In 2006, Hoffman *et al.* argued that the survival of US laryngeal cancer patients was decreasing over time, coinciding with an increase in the use of non-surgical therapies as first-line management for advanced disease.[9] Previously, laryngectomy had been the agreed standard of care for the management of advanced laryngeal cancer.[10] More recently, large-scale randomised, controlled trials indicated that non-surgical management conferred similar survival rates, leading to organ-preserving management strategies being adopted by the majority of head and neck teams across the country.[11,12]

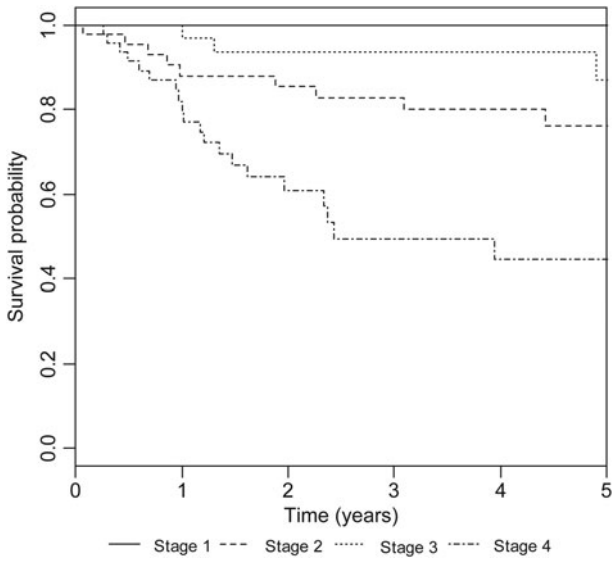

FIG. 2
Five-year Kaplan–Meier disease-specific survival curves.

The 1991 US Veterans Affairs Larynx Study reported 2-year survival figures for advanced laryngeal cancer to be the same for non-surgical and surgical management; however, there was a 5 per cent, non-significant decrease in overall survival at 5 and 10 years for the non-surgical group.[13] Similarly, a 2007 study reported that laryngectomy was associated with increased survival compared with radiotherapy and chemoradiotherapy.[14] These emerging patterns have led some commentators to exercise caution when extrapolating the results of early, closely controlled trials to the general patient population.[15,16] In the present study, the North Cumbria MDT had a high prevalence of surgical management for advanced disease. Of 33 patients who presented with stage 3 disease, 18 were managed with primary surgery with or without post-operative radiotherapy and 15 were managed with primary radiotherapy; 6 of these 15 patients required a salvage laryngectomy at a later stage. The 5-year disease-specific survival for patients with stage 3 disease at Cumberland Infirmary was 87 per cent.

The Scottish Intercollegiate Guidelines Network recommends that patients with early disease who are treated with radiotherapy should receive 55 Gy over 20 fractions, or 50–52 Gy over 16 fractions.[17] The radiotherapy dosage administered to the larynx for advanced disease varies: the Veterans Affairs study[13] used 66–76 Gy to the primary tumour site, while the Radiation Therapy Oncology Group study[12] used 70 Gy. In the present study, most patients treated with radiotherapy received doses of 54–60 Gy over 4–6 weeks, based on established practice over the years. However, calculations of the biologically effective dose indicate that there is no significant difference between the various dosage regimens, because the increase in tumour dose with longer fractionation regimen is often cancelled out by repopulation of tumour cells over the longer period of treatment.[18] There is thought to be a benefit from reducing the risk of late complications, but only if treatment volumes are correspondingly reduced by more conformal radiotherapy (e.g. intensity-modulated radiotherapy).

Five of the patients in the present study received chemotherapy. Radiotherapy has significant side effects which are dose-dependent and which worsen when combined with chemotherapy.[19,20] Clinicians are now required to treat many more patients suffering such ill effects, due to increased use of non-surgical therapies as first-line management of laryngeal cancer. In the Radiation Therapy Oncology Group study, 82 per cent of patients treated with radiotherapy and cisplatin-based chemotherapy experienced severe toxic effects.[12] Side effects can occur in the short term, such as skin reactions, mucositis and infection, and in the long term, with pharyngeal stenosis

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TABLE II
PATIENTS' STAGE, PRIMARY TREATMENT AND OUTCOMES

Outcome	Stage 1*		Stage 2†		Stage 3‡		Stage 4**	
	Surg	Non-surg	Surg	Non-surg	Surg	Non-surg	Surg	Non-surg
Total pts	31	55	5	38	18	15	34	13
Disease recurrence	6	10	0	15	1	10	3	1
DoD ≤5 years	0	0	2	6	2	1	14	5
Salvage laryngectomy	0	8	0	8	0	6	0	1
Total pts with laryngectomy	0	8	4	8	18	6	31	1

Data represent patient numbers. Total patient number by stage = *86, †43, ‡33 and **47. Surg = surgical primary treatment; Non-surg = non-surgical primary treatment; pts = patients; DoD = died of disease

causing dysphagia and laryngeal scarring causing dysphonia. In the most severe cases, a tracheostomy may be required. Most patients require supplementary enteral feeding, and many require nutritional assistance with permanent gastrostomy or naso-gastric tube.[21,22]

- **Five-year laryngeal cancer survival is reported for a small, remote, multidisciplinary team (MDT) setting**
- **Tumour-specific and overall survival rates were excellent**
- **This may be partly due to high rates of surgical intervention**
- **Radiotherapy regimes were less radical than elsewhere, possibly reducing side effects**
- **Non-surgical laryngeal cancer management is increasing; data monitoring is essential**
- **Laryngeal cancer can be managed effectively in a small, remote, MDT setting**

The Cumberland Infirmary, Carlisle, collected accurate and comprehensive data and was able to report excellent tumour-related survival figures. This success may have been due in part to high rates of surgical intervention, especially for patients in the advanced stages. Survival data compared favourably with other centres despite less radical radiotherapy regimes; possibly, this latter approach may also reduce the incidence of treatment-associated morbidity. Accurate data collection, in co-operation with the Data for Head and Neck Oncology project, enables accurate auditing of results at the local and national level, facilitating local commissioning of care and national research efforts. With the increasing use of concomitant chemoradiotherapy[23] for stage three and low-volume stage four disease, it is likely that the proportion of patients undergoing radical surgery for advanced laryngeal cancer in our unit will decrease. It is important that data are regularly analysed in order to assess the effect of changing disease management on long-term survival and functional outcomes.

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