The Journal of Laryngology & Otology (2017), ***131***, *168–172*.

doi:10.1017/S0022215116010021

MAIN ARTICLE

Transoral laser resection of glottic carcinoma: what is the significance of anterior commissure involvement?

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Abstract

Background: The optimal management of glottic carcinoma involving the anterior commissure is controversial.

Method: A retrospective analysis was conducted of 76 patients with glottic squamous cell carcinoma treated by transoral carbon dioxide laser resection by a single surgeon.

Results: Sixty-three patients (with tumour stage T_{is}–T_3) were eligible for inclusion. Thirty patients had involvement of the anterior commissure; these patients were significantly more likely to have either uncertain or positive margins (63.3 *vs* 30.3 per cent, $p = 0.012$), and were also more likely to receive adjuvant radiotherapy (40 *vs* 3.2 per cent, $p = 0.0005$). The overall laryngeal preservation rate was 96.8 per cent; there was no statistically significant difference between those with and without anterior commissure involvement (96.7 and 96.9 per cent respectively).

Conclusion: Transoral laser resection with the use of adjuvant radiotherapy in a minority of patients with adverse pathological findings can be recommended for the primary treatment of anterior commissure glottic cancer from an oncological perspective; excellent local control and laryngeal preservation rates can be achieved.

Key words: Laryngeal Cancer; Anterior Laryngeal Commissure; Larynx; Laser; Radiotherapy

Introduction

The anatomy of the anterior commissure of the larynx, and its significance in glottic squamous cell carcinoma, has been and continues to be the subject of significant clinical interest and debate. The area has been associated with an increased risk of tumour spread into the thyroid cartilage due to the attachment of the vocal fold by Broyles' ligament at a point where the laryngeal perichondrium is interrupted.[1–3] Conversely, it has been suggested that the anterior commissure tendon may act as a barrier, limiting tumour spread beyond the glottic level by preventing invasion of the thyroid cartilage.[4]

Transoral laser resection is one of the principal treatments for early glottic malignancy.[5] However, the anterior commissure may be difficult to visualise and access when using a transoral approach. Several authors evaluating this technique have reported reduced disease-free survival in cases with anterior commissure involvement when compared to early glottic cancer cases without such involvement.[6–8] Advantages of transoral laser resection for repeat resection of recurrences and high treatment success rates have also been described.[9,10]

An important factor relating to transoral laser resection for glottic cancers is the adequacy of surgical margins.[11,12] Margins may be difficult to confidently and definitively determine given heat artefacts, small specimen sizes, piecemeal resection, and inaccurate tissue orientation.[13] Laser surgeons emphasise the clear division that is typically seen between tumour and normal tissue when transecting the tumour, and the well-defined surgical plane when stripping perichondrium from the thyroid cartilage. However, it is not always possible for a pathologist to confidently state whether a margin is clear, and the surgeon then has to rely on their clinical impression of resection completeness. Decision-making about the need to take additional margins and/or to recommend adjuvant radiotherapy may therefore be both complex and subjective.

This study was conducted to evaluate the efficacy of transoral carbon dioxide (CO_2) laser resection for patients with early glottic squamous cell carcinoma

Presented at the 50th Congress of the South African Society of Otorhinolaryngology, Head and Neck Surgery, 18–21 October 2014, Cape Town, South Africa.
Accepted for publication 11 October 2016 First published online 10 January 2017

with and without involvement of the anterior commissure of the larynx, with adjuvant radiotherapy for patients with uncertain or involved margins. We aimed to test the hypotheses that anterior commissure involvement was associated with a greater likelihood of adjuvant radiotherapy and/or failure of laryngeal preservation.

Materials and methods

All patients with squamous cell carcinoma of the glottis managed by transoral laser microsurgery with curative intent between January 2003 and December 2011 were eligible for inclusion. Patients were clinically staged according to the 2010 tumour–node–metastasis staging system.[14]

The second author (JJF) was the principal surgeon for all patients included in the study. He generally treats all early glottic cancers with transoral laser resection using a Lumenis (Lumenis, Yokneam, Israel) or a C-Las (ARC Laser, Nuremberg, Germany) CO_2 laser. Computed tomography and/or magnetic resonance imaging of the neck are rarely requested for early laryngeal cancers as the laser resection simply follows the tumour margins. With tumours that only superficially involve the anterior commissure, resection of the opposing vocal fold is staged to reduce the chance of webbing and to optimise voice quality.[15] With more invasive anterior commissure tumours, the perichondrium and vocal ligament(s) are stripped off the thyroid cartilage in a subperichondrial plane and an anterior window of thyroid cartilage is resected if cartilage is found to be involved at the anterior commissure. Special care is taken to detect inferior extension of tumour below the anterior commissure so that this can be surgically resected. Intra-operative frozen section for margin analysis is very rarely employed for glottic tumours.

Outcomes measured included the need for repeat resection, use of adjuvant radiotherapy, locoregional control and laryngectomy-free survival, and incidence of second primaries. Demographic and outcome data were evaluated using Microsoft Excel software (Microsoft, Redmond, Washington, USA). Stata 11 software (StataCorp, College Station, Texas, USA) was used to carry out all analyses. Fisher's exact test (two-sided) was applied to evaluate the possible difference between the two groups, with and without anterior commissure involvement. A p value of less than 0.05 was deemed to be statistically significant.

The Human Research Ethics Committee of the University of Cape Town, South Africa, granted approval for this study.

Results

A total of 76 patients with early squamous cell carcinoma of the glottis were treated with transoral laser resection between 2003 and 2011 by a single surgeon (JJF). Thirteen patients were excluded, as the follow-up period was less than two years. Data relating to a total of 63 patients were therefore evaluated. The patients ranged in age at presentation from 29 to 90 years (median, 66 years), and included 4 females and 59 males, giving a male-to-female ratio of approximately 15:1. The mean follow-up period was 51 months (range, 24–129 months).

Table I demonstrates the distribution of the clinical tumour (T) stages of the 63 cases. All patients were nodal stage N_0.

Transoral laser resection procedures performed in stages, in cases of bilateral glottic involvement and crossing of the anterior commissure, were recorded for the purpose of the study as a single cancer procedure. A total of 87 transoral laser resection procedures were performed. The majority of patients (66.7 per cent) underwent a single procedure. A further 19 patients underwent 2 procedures, whilst 2 further patients received either 3 or 4 procedures respectively. Radiotherapy was contraindicated in the latter patient because of severe claustrophobia. Only 5 of the 25 repeat transoral laser resections were linked to recurrences of the original cancers; this represents 7.9 per cent of all patients. Of 16 patients who underwent prompt repeat transoral laser resection for suspected residual disease, there was no pathological evidence of residual malignancy in 9 of the 16 (56.3 per cent).

The anterior commissure was involved in 30 of 63 cases (47.6 per cent). A comparison of results according to anterior commissure status is displayed in Table II. Patients with anterior commissure involvement were more likely to have either uncertain or involved margins ($p = 0.012$). The differences in local control and laryngeal preservation rates between tumours involving the anterior commissure and those without anterior commissure involvement were not statistically significant ($p = 1.0$). A comparative analysis of laryngeal preservation is displayed in Figure 1.

Adjuvant radiotherapy was recommended for involved or uncertain margins in 13 of 61 cases (21.3 per cent); the remaining 2 patients had previously received radiotherapy. In one case, post-operative radiotherapy was recommended on the basis that the patient could not be closely monitored post-operatively. Patients with anterior commissure involvement were significantly more likely to receive adjuvant radiotherapy ($p = 0.0005$).

The laryngeal preservation rate was 96.8 per cent, with the exclusion of a single patient who required a

TABLE I
CLINICAL TUMOUR STAGE AT PRESENTATION

Initial tumour (T) stage	Patients (n (%))
T_{is}	8 (12.7)
T_{1a}	22 (34.9)
T_{1b}	8 (12.7)
T_2	21 (33.3)
T_3	4 (6.3)

https://doi.org/10.1017/S0022215116010021 Published online by Cambridge University Press

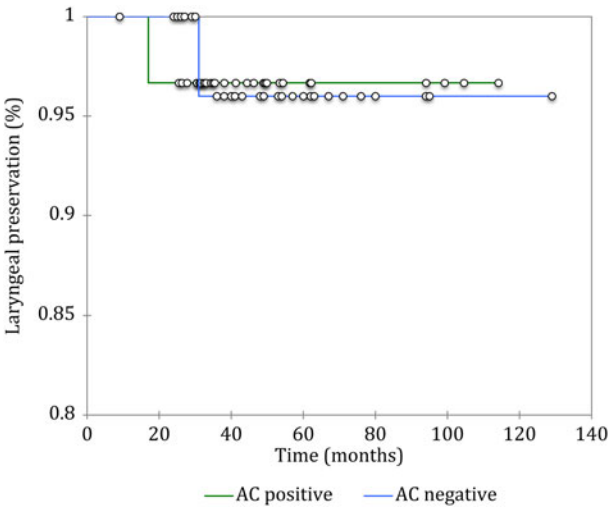

FIG. 1
Comparative analysis of laryngeal preservation. AC = anterior commissure

total laryngectomy for a metachronous tumour of the piriform fossa and the inclusion of a patient who was palliated, avoiding laryngectomy; this represents failed laryngeal preservation. Of the two cases of failed local control, the first was a T_{1a} cancer in which the initial lateral resection margin was reported to be involved. A policy of close observation was employed, given the surgeon's assessment indicating that the tumour had been completely resected, with the margin of concern being in an area where the plane of resection was the thyroid perichondrium. An ipsilateral recurrence was detected after 31 months, at which time carcinoma of the lung was also evident. A total laryngectomy was therefore not performed and the patient received palliative radiotherapy. The second case was a T_2 tumour involving the anterior commissure; initial resection margins were reported to be positive, and repeat resection showed residual malignancy with clear margins. Local recurrence was detected after 13 months; the patient remains disease-free following total laryngectomy.

No disease-specific mortality occurred within the minimum follow-up period of 24 months applied in this analysis. Overall survival was found to be 95.2 per cent; 3 of the 63 patients died at 31, 41 and 61 months post-transoral laser resection, respectively. The first patient with anterior commissure positive disease, as detailed earlier, developed ipsilateral laryngeal disease, labelled as recurrence 31 months after transoral laser resection, at which time carcinoma of the lung was also detected; this was suspected to be a metachronous tumour rather than metastasis and was treated palliatively, and was associated with rapid demise. The second patient died from unrelated medical causes. The final patient had anterior commissure negative disease and developed a metachronous piriform fossa tumour, surviving 63 months following transoral laser surgery. Of note, metachronous cancers of the upper aerodigestive tract were observed in 9 of 63 patients (14.3 per cent) during the follow-up period.

Discussion

How best to manage glottic carcinoma involving the anterior commissure remains controversial because of anatomical features and their impact on treatment. Adequate transoral visualisation and surgical access may be technically difficult (or impossible), and there are concerns regarding the use of external beam radiotherapy for anterior commissure cancers.[16,17] Anterior commissure involvement has also been interpreted as a surrogate marker for tumour volume, which has been shown to be an important prognostic factor in local control.[18]

Our highly favourable results of transoral laser resection in relation to larynx preservation for early glottic carcinoma, irrespective of anterior commissure involvement, may reflect more aggressive surgical resections, or more liberal employment of adjuvant radiotherapy in cases of uncertain or involved margins. Table III compares our results with other studies of transoral laser resection for glottic cancer with anterior commissure involvement.[8,9,19–22]

A series of 263 patients with early glottic carcinoma treated by transoral laser resection was reported by Steiner *et al.*[9] Thirteen per cent of patients underwent repeat resection because of positive or uncertain margins; residual carcinoma was found in 32 per cent. Anterior commissure involvement was found to affect local control and organ preservation, but not disease-specific survival. The authors concluded that transoral laser resection was an effective treatment for early glottic carcinoma, regardless of anterior commissure involvement. Similarly, Chone and colleagues

TABLE II
ANTERIOR COMMISSURE INVOLVEMENT

Parameter	AC not involved*	AC involved†	p‡
Mean follow-up duration (months)	53	49	
Positive or uncertain margins at index surgery (n (%))	10/33 (30.3)	19/30 (63.3)	0.012
Adjuvant radiotherapy (n (%))	1/31 (3.2)**	12/30 (40.0)	0.0005
Local control (n (%))	31/32 (96.9)§	29/30 (96.7)	1.0
Larynx preservation (n (%))	31/32 (96.9)§	29/30 (96.7)	1.0

*n = 33; †n = 30. ‡Fisher's exact test, two-sided. **Excluding two patients who had previously received radiotherapy. §Excluding one patient who required total laryngectomy for a metachronous tumour of the piriform fossa. AC = anterior commissure

https://doi.org/10.1017/S0022215116010021 Published online by Cambridge University Press

TABLE III
TRANSORAL LASER RESECTION FOR GLOTTIC CARCINOMA WITH ANTERIOR COMMISSURE INVOLVEMENT

Study	Year	Patients (*n*)	Tumour (T) stage	Laryngeal preservation		
				AC not involved (%)	AC involved (%)	*p*
Steiner *et al.*[9]	2004	263	T_{1a}	99	93	0.08
			T_{1b}	100	88	0.49
			T_{2a}	97	93	0.65
Chone *et al.*[8]	2007	48	T_1–T_{2a}	100	96	0.5
Peretti *et al.*[22]	2010	475	T_{is}–T_1	98.1	98.8	0.49
Hakeem *et al.*[21]	2013	296	T_1–T_2	93.3	95.8	0.287
Lee *et al.*[20]	2013	118	T_1–T_2	95.1*	96*	0.432
Hoffmann *et al.*[19]	2016	201	T_{is}–T_2	100	91.9	0.0003
Current study	2017	67	T_{is}–T_3	96.9	96.7	1

*Local control with laser alone, not laryngeal preservation. AC = anterior commissure

studied 48 patients with early glottic cancer treated by transoral laser resection, and reported a greater likelihood of local recurrence in cases with anterior commissure involvement, although the difference was not statistically significant.[8] A significantly lower local control rate associated with anterior commissure involvement was also recently described in another large series.[19]

In contrast, Lee *et al*. did not find a significant effect of anterior commissure involvement by early glottic carcinoma on local control or survival.[20] Hakeem and colleagues also concluded that transoral laser resection is an excellent option for early glottic carcinoma patients, irrespective of anterior commissure involvement, having evaluated a total of 296 cases.[21]

Alternatives to transoral laser resection include primary radiotherapy and open surgical procedures. Open partial laryngectomies have comparable oncological outcomes, but are functionally less favourable than both transoral laser resection and primary radiotherapy.[23] Morbidity in relation to voice quality and swallowing are particular considerations.

Maheshwar and Gaffney suggested that anterior commissure involvement is a predictor of poor response to radiotherapy, as a statistically significant difference in recurrence rate was observed within a group of 53 patients with T_1 glottic tumours.[16] This is in agreement with the reports of several other groups.[24,25] Technical factors relating to radiotherapy dosing have also been emphasised as potential pitfalls when treating the anterior commissure. A theoretical risk of under-dosage of the region of the air–tissue interface at the anterior commissure exists. Tong *et al*. reported the outcomes of 400 patients with stage 1 glottic cancer treated with primary radiotherapy; anterior commissure involvement was associated with a poorer local control rate.[17]

Additional considerations in relation to the use of primary radiotherapy include: treatment time, which spans several weeks; the risk of chondroradionecrosis; oedema, making detection of residual or recurrent tumour more problematic; and secondary carcinoma. In cases of recurrence following radiotherapy as the primary treatment, salvage laryngectomy may be required; this is associated with an increased risk of post-operative complications.

Although our study includes a heterogeneous group of T_{is}–T_3 carcinomas, a great heterogeneity exists within the group of 'early' glottic tumours; a T_2 tumour may extend to either the supraglottis or subglottis (T_{2a}), or may invade the paraglottic space to impair vocal fold mobility (T_{2b}). This latter group can be likened to T_3 tumours in terms of local control and survival.[26]

- **The optimal management of glottic tumours involving the anterior commissure is controversial**
- **Patients with anterior commissure involvement were significantly more likely to have uncertain or positive margins**
- **These patients were more likely to receive adjuvant radiotherapy**
- **Transoral laser resection, with adjuvant radiotherapy for patients with adverse pathological findings, can yield excellent local control and laryngeal preservation rates**
- **Transoral laser surgical expertise is required for managing tumours involving the anterior commissure and more advanced disease**

The high proportion (approximately 15 per cent) of metachronous cancers of the upper aerodigestive tract observed in this series during the follow-up period highlights the importance of close surveillance and risk modification.

Conclusion

Although management of glottic squamous cell carcinoma with anterior commissure involvement by transoral laser resection is not associated with reduced local control or laryngeal preservation, such cases are more likely to have either positive or uncertain resection margins, and there is a greater likelihood that

https://doi.org/10.1017/S0022215116010021 Published online by Cambridge University Press

adjuvant radiotherapy will be employed. Excellent local control and laryngeal preservation rates can be achieved with the use of adjuvant radiation in a minority of select cases with positive or uncertain resection margins. Transoral laser resection can therefore be recommended as a primary treatment modality for early (T_{is}–T_2 and selected T_3) glottic cancers involving the anterior commissure.

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Dr K Stephenson takes responsibility for the integrity of the content of the paper
Competing interests: None declared