

Editorial

What is the treatment of choice for T1 squamous cell carcinoma of the larynx?

ALFIO FERLITO, M.D., D.L.O., D.PATH., F.R.C.S. (ED.), F.R.C.S., F.A.S.C.P., F.R.C.S. (GLASG.), M.C.A.P., F.R.C.S.I., F.A.C.S., M.R.C.PATH., F.H.K.A.M., PATRICK J. BRADLEY, M.B., B.CH., B.A.O., D.C.H., M.B.A., F.R.C.S.I., F.R.C.S. (ED.), F.R.C.S.* , ALESSANDRA RINALDO, M.D.

The management of T1 laryngeal squamous cell carcinoma has a long and interesting history characterized by various phases and developments, and it remains a topic of widespread controversy in the world, largely because of the absence of a definitive prospective comparative analysis of treatment options.

Cancer of the larynx is a relatively rare disease, but it is the commonest head and neck cancer, excluding skin cancer.¹ Traditionally, T1 squamous cell carcinoma of the larynx is treated with equal effectiveness by either conservative surgery or radiotherapy, as assessed by univariate and multivariate analysis.²

The preferred treatment modality at present is highly dependent on geography, with radiation tending to be the treatment of choice in Canada, northern Europe, Australasia and South Africa, whereas surgery is more usually used in southern Europe and in many centres of the United States. Since the 1970s, CO₂ laser has been used to treat patients with T1A glottic carcinomas.³ In the past two decades, several reports by German, Belgian, Italian, Swiss, Spanish, Dutch, Japanese, Israeli, Indian and American colleagues have presented convincing evidence that endoscopic CO₂ laser surgery can be considered a valid alternative for T1 glottic and supraglottic squamous cell carcinomas.^{4–20} The majority of patients neither require a tracheotomy nor the use of tube feeding. Conversely, as a result, open neck surgery for non-advanced laryngeal cancer has been recommended less.

Clinicians generally used the term ‘early’ cancer in an arbitrary way, and we take this opportunity to clarify the terminology in order to avoid any misinterpretation. Ferlito *et al.*²¹ considered ‘early’ laryngeal cancer to be confined to the lamina propria, but potentially to be capable of forming lymph node metastases when localized in the supraglottic area. The lesion does not invade muscle or cartilage. Therefore, ‘early’ cancer includes T1 lesions but excludes Tis, T2, T3 and T4 lesions. Microinvasive carcinoma and superficial extending

carcinoma are subtypes of ‘early’ cancer. Early stages are not synonymous of ‘early’ cancer. To avoid an inadequate or overzealous approach to treatment and prognosis, a clinical diagnosis of ‘early’ invasive laryngeal cancer should be substantiated by careful microscopic pathological evaluation, which should exclude both carcinoma in situ and, particularly, deeply infiltrating carcinoma.²¹

In recent years endoscopic surgery and radiotherapy have undergone significant technical improvements, however, complications may result if either treatment methods are used.^{2,15} Some causes of treatment failure are not related to the treatment modality used. Residual cancer should be distinguished from local recurrence.²² Recurrent cancer is more often seen in patients who continue to smoke after treatment, in association with an underestimation of the initial tumour volume and its invasion and also in non-conventional squamous cell carcinoma. The clinical staging may not correlate with pathological staging, resulting in a T4 cancer of the glottis being included as ‘early’ cancer when pathological evaluation is not available to show microscopic invasion of adjacent cartilage or extralaryngeal soft tissues.²¹ This understaging is obviously a possibility with radiotherapy when only clinical staging is available.² Most laryngologists have encountered patients in whom a carcinoma located in the vicinity of the anterior commissure was evaluated clinically and staged as a T1 lesion, but in whom subsequent pathological evaluation of a laryngectomy specimen revealed microscopic invasion of the adjacent cartilage or extralaryngeal soft tissues – a finding that forced reclassification of the carcinoma as a T4 lesion.²¹

The combination of cure with organ preservation and function is the most desirable outcome for patients with laryngeal cancer. Both radiotherapy and surgery, especially CO₂ laser surgery, are equally effective at treating T1 glottic cancer, however, radiotherapy is often preferred over surgery because of the better functional results in terms of voice quality.

In 2004, Jones *et al.*² demonstrated very clearly that speech and voice quality are significantly better in patients treated by irradiation than in those treated by surgery (endoscopic laser surgery and microscopic surgery). Several studies have been published indicating that the voice is near-normal after radiotherapy while poor voice quality is present after endoscopic laser treatment.^{23–25} In particular, Rydell *et al.*²⁶ reported that the voice quality after laser treatment for T1A glottic cancer was inferior after treatment with full dose radiotherapy, as assessed both with acoustic and perceptual variables. Voice recordings prior to treatment, and at both 3 months and 2 years after completed treatment, were analyzed. Acoustic measures of shimmer, jitter, breathiness, harmonic-to-noise ratio and fundamental frequency average were calculated with the Soundscope programme. Two plain measures were also used: time required to read a running speech voice sample, and number of breaths. Perceptual voice analysis was performed blindly by two groups of listeners (experienced and naïve).

Considering the treatment costs, radiotherapy is marginally more expensive or similar to transoral endoscopic laser treatment but considerably cheaper than partial laryngeal surgery.^{2,27,28} The use of laser therapy does not preclude further treatments, if indicated, for cancer treatment (surgery or radiotherapy). Irradiation treatment failures can be salvaged by open partial laryngectomy.²⁹

Although intensively debated, definitive radiotherapy remains a primary option for management of T1 glottis, considering long-term survival, local tumour control, quality of life, direct medical and nonmedical costs, indirect costs, and intangible costs.²⁷ Endoscopic surgery with the CO₂ laser can be considered a valid alternative but with a probably poorer voice quality.

Patients presenting with a T1 supraglottic cancer are relatively uncommon and have been encountered by accident during routine visits of patients being followed up for a different, treated primary head and neck cancer. The neck must be carefully examined because ‘early’ supraglottic cancers can be associated with metastases. ‘Early’ glottic cancer is synonymous with localized cancer; ‘early’ cancer of the supraglottis may invade lymphatic channels and metastasize to the neck and is considered a potentially disseminated type of disease. In fact, lymph node metastases have been reported in approximately 20 per cent of T1 supraglottic cancer.³⁰ Considering that the risk of occult node disease is relatively high, even in the presence of a T1 supraglottic cancer, the nodes at risk (levels 2, 3 and 4) must be treated bilaterally with irradiation in conjunction with the primary malignancy.

Patients with T1 subglottic squamous cell carcinoma, although very rare in occurrence, have a high probability of cure with definitive radiation therapy alone and with preservation of normal voice,³¹ however, data supporting this approach are limited.

The recent published literature intimates that

patients and physicians prefer to select a nonsurgical treatment for ‘early’ laryngeal cancer especially in the United States.^{32,33}

References

- 1 Ferlito A. The natural history of early vocal cord cancer. *Acta Otolaryngol* 1995;**115**:345–7
- 2 Jones AS, Fish B, Fenton JE, Husband DJ. The treatment of early laryngeal cancers (T1-T2 N0): surgery or irradiation? *Head Neck* 2004;**26**:127–35
- 3 Strong MS, Jako GJ. Laser surgery in the larynx. Early clinical experience with continuous CO₂ laser. *Ann Otol* 1972;**81**:791–8
- 4 Steiner W. Results of curative laser microsurgery of laryngeal carcinomas. *Am J Otolaryngol* 1993;**14**:116–21
- 5 Rudert HH, Werner JA. Endoscopic resections of glottic and supraglottic carcinomas with the CO₂ laser. *Eur Arch Otorhinolaryngol* 1995;**252**:146–8
- 6 Shapshay SM, Hybels RL, Bohigian RK. Laser excision of early vocal cord carcinoma: indications, limitations, and precautions. *Ann Otol Rhinol Laryngol* 1990;**99**:46–50
- 7 Eckel HE, Thumfart W, Jungehulsing M, Sittel C, Stennert E. Transoral laser surgery for early glottic carcinoma. *Eur Arch Otorhinolaryngol* 2000;**257**:221–6
- 8 Peretti G, Piazza C, Balzanelli C, Mensi MC, Rossini M, Antonelli AR. Preoperative and postoperative voice in Tis-T1 glottic cancer treated by endoscopic cordectomy: an additional issue for patient counseling. *Ann Otol Rhinol Laryngol* 2003;**112**:759–63
- 9 Hirano M, Hirade Y. CO₂ laser for treating glottic carcinoma. *Acta Otolaryngol Suppl* 1988;**458**:154–7
- 10 Zeitels SM. Laser versus cold instruments for microlaryngoscopic surgery. *Laryngoscope* 1996;**106**:545–52
- 11 Remacle M, Lawson G. Transoral laser microsurgery is the recommended treatment for early glottic cancers. *Acta Otorhinolaryngol Belg* 1999;**53**:175–8
- 12 Gallo A, de Vincentiis M, Manciooco V, Simonelli M, Fiorella ML, Shah JP. CO₂ laser cordectomy for early-stage glottic carcinoma: a long-term follow-up of 156 cases. *Laryngoscope* 2002;**112**:370–4
- 13 Moreau PR. Treatment of laryngeal carcinomas by laser endoscopic microsurgery. *Laryngoscope* 2000;**110**:1000–6
- 14 Tamura E, Kitahara S, Ogura M, Kohno N. Voice quality after laser surgery or radiotherapy for T1a glottic carcinoma. *Laryngoscope* 2003;**113**:910–4
- 15 Vilaseca-González I, Bernal-Sprekelsen M, Blauch-Alejandro J-L, Moragas-Lluis M. Complications in transoral CO₂ laser surgery for carcinoma of the larynx and hypopharynx. *Head Neck* 2003;**25**:382–8
- 16 Motta G, Esposito E, Cassiano B, Motta S. T1-T2-T3 glottic tumors: fifteen years experience with CO₂ laser. *Acta Otolaryngol Suppl* 1997;**527**:155–9
- 17 Shvero J, Koren R, Zohar L, Hadar T, Marshak G, Gal R, *et al.* Laser surgery for the treatment of glottic carcinomas. *Am J Otolaryngol* 2003;**24**:28–33
- 18 Goor KM, Mahieu HF, Leemans CR, Peeters AJ, Langendijk JA, van Aghoven M. CO₂ laser decortication: an efficient alternative to radiotherapy in the treatment of T1a carcinomas of the glottis. *Ned Tijdschr Geneesk* 2003;**147**:1177–81 [in Dutch]
- 19 Stoeckli SJ, Schnieper I, Huguenin P, Schmid S. Early glottic carcinoma: treatment according patient’s preference? *Head Neck* 2003;**25**:1051–6
- 20 Pradhan SA, Pai PS, Neeli SI, D’Cruz AK. Transoral laser surgery for early glottic cancers. *Arch Otolaryngol Head Neck Surg* 2003;**129**:623–5
- 21 Ferlito A, Carbone A, Rinaldo A, DeSanto LW, D’Angelo L, Barnes L, *et al.* ‘Early’ cancer of the larynx: the concept as defined by clinicians, pathologists, and biologists. *Ann Otol Rhinol Laryngol* 1996;**105**:245–50
- 22 Goerres GW. Imaging literature and terminology: when is it residual cancer and when recurrence? *Arch Otolaryngol Head Neck Surg* 2004;**130**:120–1
- 23 McGuirt WF, Blalock D, Koufman JA, Feehs RS, Hilliard AJ, Greven K, *et al.* Comparative voice results after laser resection or irradiation of T1 vocal cord carcinoma. *Arch Otolaryngol Head Neck Surg* 1994;**120**:951–5

- 24 Lehman JJ, Bless DM, Brandenburg JH. An objective assessment of voice production after radiation therapy for stage I squamous cell carcinoma of the glottis. *Otolaryngol Head Neck Surg* 1988;**98**:121–9
- 25 Schuller DE, Trudeau M, Bistline J, LaFace K. Evaluation of voice by patients and close relatives following different laryngeal cancer treatments. *J Surg Oncol* 1990;**44**:10–4
- 26 Rydell R, Schalen L, Fex S, Elnor A. Voice evaluation before and after laser excision vs. radiotherapy of T1A glottic carcinoma. *Acta Otolaryngol* 1995;**115**:560–5
- 27 Foote RL, Buskirk SJ, Grado GL, Bonner JA. Has radiotherapy become too expensive to be considered a treatment option for early glottic cancer? *Head Neck* 1997;**19**:692–700
- 28 Grégoire V, Hamoir M, Rosier JF, Counoy H, Eeckhoudt L, Neymark N, *et al.* Cost-minimization analysis of treatment options for T1N0 glottic squamous cell carcinoma: comparison between external radiotherapy, laser microsurgery and partial laryngectomy. *Radiother Oncol* 1999;**53**:1–13
- 29 Mendenhall WM, Werning JW, Hinerman RW, Amdur RJ, Villaret DB. Management of T1-T2 glottic carcinomas. *Cancer* 2004;**100**:1786–92
- 30 DeSanto LW. Cancer of the supraglottic larynx: a review of 260 patients. *Otolaryngol Head Neck Surg* 1985;**93**:705–11
- 31 Ferlito A, Rinaldo A. The pathology and management of subglottic cancer. *Eur Arch Otorhinolaryngol* 2000;**257**:168–73
- 32 Shah JP, Karnell LH, Hoffman HT, Ariyan S, Brown GS, Fee WE, *et al.* Patterns of care for cancer of the larynx in the United States. *Arch Otolaryngol Head Neck Surg* 1997;**123**:475–83
- 33 DiNardo LJ, Kaylie DM, Isaacson J. Current treatment practices for early laryngeal carcinoma. *Otolaryngol Head Neck Surg* 1999;**120**: 30–7

Address for correspondence:

Alfio Ferlito, M.D., D.L.O., D.Path., F.R.C.S. (Ed.), F.R.C.S., F.A.S.C.P., F.R.C.S. (Glasg.), M.C.A.P., F.R.C.S.I., F.A.C.S., M.R.C.Path., F.H.K.A.M.
Director of the Department of Surgical Sciences,
Professor and Chairman of the ENT Clinic
University of Udine,
Policlinico Universitario,
Piazzale S. Maria della Misericordia,
1-33100 Udine, Italy.

Fax: +39 0432 559339

E-mail: a.ferlito@uniud.it

Professor A. Ferlito takes responsibility for the integrity of the content of the paper.

Competing interests: None declared
