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## HIGHER LARYNGEAL PRESERVATION RATE AFTER CO<sub>2</sub> LASER SURGERY COMPARED WITH RADIOTHERAPY IN T1A GLOTTIC LARYNGEAL CARCINOMA

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Accepted 10 September 2008

Published online 3 March 2009 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/hed.21027

**Abstract:** *Background.* Clinical outcome of endoscopic CO<sub>2</sub> laser surgery and radiotherapy in early-stage glottic laryngeal carcinoma is difficult to compare because of differences in treatment selection and patient groups. Therefore, we compared local control, overall survival, and laryngeal preservation in a homogenous group of patients with T1a glottic carcinoma with normal/diminished mucosal wave treated with either CO<sub>2</sub> laser surgery or radiotherapy.

*Methods.* Retrospective survival analysis was performed on 100 patients with T1a glottic carcinoma treated with CO<sub>2</sub> laser surgery ( $n = 49$ ) or radiotherapy ( $n = 51$ ), diagnosed at the University Medical Center Groningen between 1990 and 2004.

*Results.* No significant differences in local control and overall survival were found. Ultimate 5-year laryngeal preservation was significantly better in the CO<sub>2</sub> laser surgery group (95% vs 77%,  $p = .043$ ).

*Conclusion.* Patients with T1a glottic carcinoma with normal/diminished mucosal wave treated with CO<sub>2</sub> laser surgery

had a significantly better laryngeal preservation rate than patients treated with radiotherapy. © 2009 Wiley Periodicals, Inc. *Head Neck* 31: 759–764, 2009

**Keywords:** CO<sub>2</sub> laser surgery; radiotherapy; laryngeal preservation; T1a glottic laryngeal carcinoma; head and neck cancer

**H**ead and neck cancer is the sixth most common type of cancer in the world, with an annual worldwide incidence of 700,000 patients.<sup>1</sup> Twenty percent to 30% of these tumors are laryngeal tumors, with the majority arising in the glottic region.<sup>2</sup> Because of the involvement of the vocal folds, most patients with glottic carcinoma were seen with hoarseness of the voice in an early stage of the disease.

The most commonly used types of treatment for T1a glottic laryngeal carcinoma are radiotherapy and endoscopic CO<sub>2</sub> laser surgery.<sup>3</sup>

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Clinical outcome in early-stage glottic carcinoma (local control, survival, and laryngeal preservation) are reported to be similar with both treatment modalities.<sup>4-8</sup>

At the University Medical Center Groningen (UMCG), a tertiary referral hospital, CO<sub>2</sub> laser surgery has been increasingly applied as the treatment of first choice for T1a glottic laryngeal carcinoma with normal or diminished mucosal wave indicating superficial tumor growth. Radiotherapy used to be the treatment of first choice. Currently, however, radiotherapy is reserved for deeper infiltrating tumors without vocal cord mucosal wave and for recurrences after treatment with CO<sub>2</sub> laser surgery. This shift in treatment of first choice is due to the development of more advanced CO<sub>2</sub> lasers. Currently, no randomized controlled trials comparing radiotherapy and CO<sub>2</sub> laser surgery in early glottic cancer have been performed. Therefore, information regarding the comparison between these 2 treatment modalities is mainly derived from retrospective studies. In general, the interpretation of these studies is hampered by the fact that in some studies CO<sub>2</sub> laser was preserved for the more superficial tumors, while radiotherapy was applied for the larger, deeper infiltrating tumors.<sup>9</sup> Moreover, in other studies, the selection criteria for choosing between the 2 treatment options remained unclear.<sup>10-12</sup>

Therefore, the main objective of this retrospective analysis was to compare clinical outcome among a well-defined subset of patients with T1a glottic laryngeal carcinoma with normal/diminished mucosal wave treated with either CO<sub>2</sub> laser surgery or radiotherapy.

## PATIENTS AND METHODS

**Patients.** In the period from 1990 to 2004, 242 patients with T1a glottic laryngeal carcinoma were diagnosed at the UMCG. Of these patients, all medical charts were retrospectively revised for clinical data. T1a glottic carcinoma was defined as tumor limited to 1 vocal cord with normal vocal cord mobility (American Joint Committee on Cancer [AJCC] Cancer Staging Manual, 6th edition). Videolaryngostroboscopy (VLS) data of 135 patients were available. In 35 patients (26%), mucosal wave of the affected vocal cord was absent, in 85 patients (63%) VLS showed diminished mucosal wave, and in 15 patients (11%) normal symmetrical vibration patterns of the vocal cords

during VLS were reported. All VLSs were judged by an otorhinolaryngologist in the UMCG at the time of diagnosis. For the purpose of this study, we only included patients with diminished or normal mucosal wave as assessed with VLS. To avoid selection bias, patients with deeper infiltrating tumors were excluded because in these patients radiotherapy was considered as the standard treatment. Therefore, the final study population was composed of 100 patients. All patients had biopsy-proven T1aN0M0 glottic laryngeal carcinoma. Of these 100 patients, 51 were treated with radiotherapy and 49 with CO<sub>2</sub> laser surgery. The choice of treatment was mainly time dependent. Most patients diagnosed before 1997 were treated with radiotherapy, while most patients diagnosed from 1997 were treated with CO<sub>2</sub> laser surgery. Eighty-eight patients were men, their median age was 65.5 years, and most patients (93%) were seen with hoarseness of the voice as primary symptom. Seventy-three patients had a smoking history, 10 patients did not smoke, and for 17 patients this information was not available. Clinical data of patients in both groups are presented in Table 1.

This study was approved by the UMCG and written informed consent was obtained from all patients included in this study.

## Treatment

**Radiotherapy.** Radiotherapy was delivered using megavoltage equipment, using a 6-MV linear accelerator. All patients were treated either in the UMCG, in the Isala Clinics Zwolle, or in the Radiotherapeutic Institute Friesland. The target volume included only the vocal cords and thyroid cartilage. The tumors were irradiated with 2 opposing lateral fields. All patients were treated with conventional fractionation (2 Gy per fraction, 5 times per week), using a median dose per fraction of 2 Gy (range, 2.0–2.4 Gy) to a median total dose of 66 Gy (range, 60–70 Gy).

**CO<sub>2</sub> Laser Surgery.** Forty-nine patients were treated with CO<sub>2</sub> laser surgery, all in the UMCG. Tumor vaporization was performed endoscopically using a Lumenis laser (model 30 C; Lumenis, Santa Clara, CA), using the continuous pulse mode. All patients were treated with a type I or II cordectomy according to the European Laryngological Society (ELS) criteria.<sup>13</sup>

**Statistical Analysis.** Kaplan–Meier analysis was performed to measure differences in local

**Table 1.** Patient characteristics: T1a glottic carcinoma diagnosed at the UMCG between 1990 and 2004.

	Radiotherapy (n = 51)	CO <sub>2</sub> laser surgery (n = 49)
Sex		
Male	45 (88%)	43 (88%)
Female	6 (12%)	6 (12%)
Age, y		
Median (range)	67 (41–83)	64 (38–83)
Primary symptom		
Hoarse voice	45 (88%)	48 (98%)
Swallowing disorder	0 (0%)	1 (2%)
Other	6 (12%)	0 (0%)
Duration of primary symptom, wk		
Median (range)	20 (0–104)	20 (0–98)
Vocal cord mobility		
Normal	4 (8%)	11 (22%)
Diminished	47 (92%)	38 (78%)
Tobacco use past (per day)		
0	7 (14%)	3 (6%)
1–20	25 (49%)	27 (55%)
>20	10 (20%)	11 (22%)
Unknown	9 (18%)	8 (16%)
Tobacco use present (per day)		
0	32 (63%)	31 (6%)
1–20	11 (22%)	10 (20%)
>20	3 (6%)	3 (6%)
Unknown	5 (10%)	5 (10%)
Alcohol use past (per day)		
0	12 (24%)	13 (27%)
1–6	27 (53%)	31 (63%)
>6	1 (2%)	1 (2%)
Unknown	11 (22%)	4 (8%)

Abbreviation: UMCG, University Medical Center Groningen.

control, overall survival, and laryngeal preservation between the radiotherapy and CO<sub>2</sub> laser group. Differences were considered to be significant with a *p* value of <.05 measured by log-rank test. To measure differences in clinical patient features, a chi-square test was performed for nominal variables and the Student's *t* test was used for the continuous variables. Local recurrence was defined as tumor recurrence at the primary tumor site and was calculated from the date of diagnosis until the day of local recurrence or last follow-up. Overall survival was defined as the day of diagnosis until the day of death or last follow-up. All statistical analysis was performed using the statistical package SPSS 14.0.0 (SPSS, Chicago, IL).

## RESULTS

**Study Cohort.** No significant differences between the 2 treatment groups were observed regarding

sex, age, primary symptoms, duration of primary symptoms, tobacco use, and use of alcohol. However, in the radiotherapy group, the proportion of patients with diminished mucosal wave pattern was significantly higher (chi-square test, *p* = .038). However, there were no associations between mucosal wave and the clinical outcome parameters, namely local recurrence, overall survival, and laryngeal preservation (data not shown).

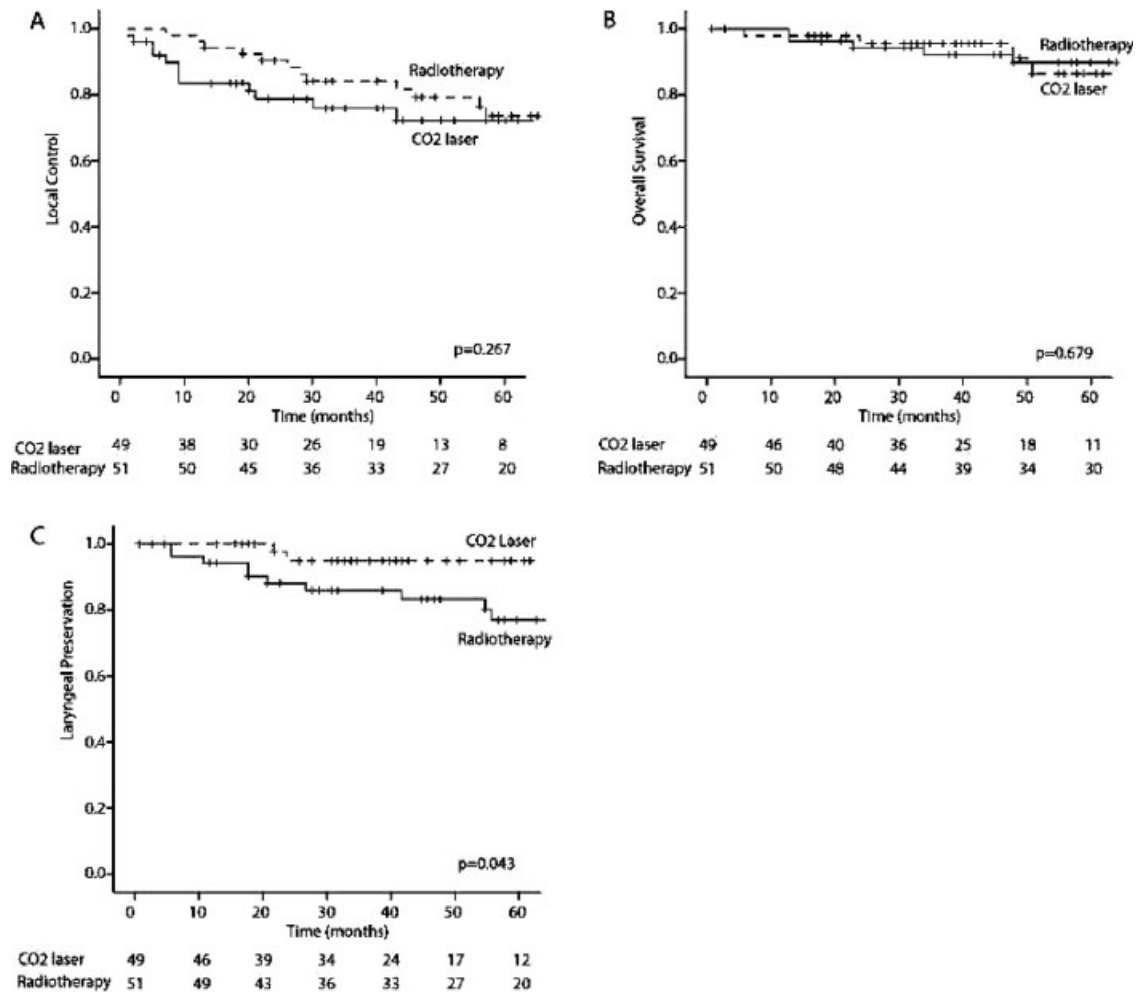
**No Difference in Local Control and Overall Survival between the Radiotherapy and CO<sub>2</sub> Laser Group.** Of all patients, 25 developed a local recurrence, 12 (24%) in the radiotherapy group and 13 (27%) in the CO<sub>2</sub> laser group. The 5-year local control rate was 73% in the radiotherapy group and 71% in the CO<sub>2</sub> laser group. The difference was not statistically significant (*p* = .267, Figure 1A).

In the total population, 13 patients died. Twelve died of disease unrelated to the tumor, and 1 patient in the radiotherapy group died of disease. Follow-up and survival data of both groups are shown in Table 2. Kaplan–Meier analysis and log-rank test showed no statistically significant difference in overall survival between the 2 groups (*p* = .679, Figure 1B).

**Laryngeal Preservation is Better in the CO<sub>2</sub> Laser Group.** In the radiotherapy group, 9 patients with a local recurrence underwent salvage treatment with a total laryngectomy, 1 with CO<sub>2</sub> laser surgery, and 2 patients were given palliative treatment. The patient who was salvaged with CO<sub>2</sub> laser treatment developed a second local recurrence after 2.5 years and ended up with a total laryngectomy as well. In the CO<sub>2</sub> laser group, 9 patients with a local recurrence were treated with radiotherapy and 4 were given salvage treatment with CO<sub>2</sub> laser surgery for a second time. In the group of 9 patients treated with salvage radiotherapy, 2 patients developed a second local recurrence and were then treated with a total laryngectomy. Overall, 12 patients were treated with a total laryngectomy, 10 in the radiotherapy group and 2 in the CO<sub>2</sub> laser group. Ultimately, after 5 years, the laryngeal preservation rate in the radiotherapy group was 77% against 95% in the CO<sub>2</sub> laser group (*p* = .045, Figure 1C).

## DISCUSSION

CO<sub>2</sub> laser surgery and radiotherapy are both considered effective treatment options in early-stage



**FIGURE 1.** Local control (A), overall survival (B), and laryngeal preservation (C) in T1a glottic laryngeal carcinoma treated with primary radiotherapy or CO<sub>2</sub> laser surgery. The 5-year laryngeal preservation rate is significantly better in the CO<sub>2</sub> laser surgery group. *p* values are calculated with the log-rank test.

glottic squamous cell carcinoma, with similar reported clinical outcome rates. However, comparison among the different studies reported is difficult because of the differences in selection criteria for either CO<sub>2</sub> laser surgery or radiotherapy as primary treatment. In general, the choice between the 2 treatment modalities is based on tumor infiltration depth or preference of the physician, but in many studies comparing these modalities is not clearly defined.<sup>9-12</sup> Regarding tumor infiltration depth, Goor et al applied CO<sub>2</sub> laser treatment for the more superficial tumors while radiotherapy was applied for larger, deeper infiltrating tumors.<sup>9</sup> Mortuaire et al showed that tumor infiltration in the vocal muscle had an adverse effect on local control rate in patients treated with CO<sub>2</sub> laser surgery.<sup>14</sup> This shows that a selection bias may occur when using different criteria to choose

between CO<sub>2</sub> laser surgery and radiotherapy. Interpretation is further hampered by differences regarding the distribution of T classification, which is also a well-known and established prognostic factor for local control. In the last decade, there was a shift from radiotherapy toward CO<sub>2</sub> laser surgery as primary treatment for T1a glottic laryngeal carcinoma. To create a homogenous study group, we included only patients with biopsy-proven T1a glottic carcinoma and a normal or diminished mucosal wave measured with VLS. The choice between CO<sub>2</sub> laser or radiotherapy in our group is mostly time dependent, with patients before 1997 treated with radiotherapy and afterward with CO<sub>2</sub> laser surgery. Those patients treated with CO<sub>2</sub> laser were all treated with a type I or II cordectomy according to the ELS criteria.<sup>13</sup>

**Table 2.** Patient characteristics: follow-up.

Characteristics	Radiotherapy (n = 51)	CO <sub>2</sub> laser surgery (n = 49)
Events in follow-up		
Local recurrence	12 (24%)	13 (27%)
Second recurrence	2 (4%)	2 (4%)
Second primary	9 (18%)	3 (6%)
Death	9 (18%)	4 (8%)
DOD	1 (11%)	0 (0%)
DNOD	8 (89%)	4 (100%)
Treatment local recurrence		
Radiotherapy	0 (0%)	9 (69%)
Total laryngectomy	9 (75%)	0 (0%)
CO <sub>2</sub> laser surgery	1 (8%)	4 (31%)
Palliation	2 (17%)	0 (0%)
Treatment second recurrence		
Total laryngectomy	1 (50%)	2 (100%)
CO <sub>2</sub> laser surgery	0 (0%)	0 (0%)
Palliation	1 (50%)	0 (0%)
Total laryngectomy (total)		
Yes	10 (20%)	2 (4%)
No	41 (80%)	47 (96%)
Median follow-up, mo	64 (12–166)	41 (1–119)
Time to local recurrence, mo		
Median (range)	26 (6–56)	8 (1–66)
Time to death, mo		
Median (range)	48 (13–88)	36 (6–51)

Abbreviations: DOD, death of disease; DNOD, death not of disease.

In this study we found no statistically significant difference in the 5-year local control rate between the CO<sub>2</sub> laser (71%) and radiotherapy (73%) group. In the literature, local control rates for radiotherapy are reported between 78% and 94%<sup>10,15,16</sup> and for CO<sub>2</sub> laser surgery between 77% and 95%.<sup>4,8–10,17</sup> Our 5-year local control rates are somewhat lower than the local control rates found in the literature. A possible explanation might be that other authors reported a 3-year local control rate and included T1a carcinomas in their group.<sup>4,8,17</sup>

In the current study, we showed that patients with T1a glottic laryngeal carcinoma treated primarily with CO<sub>2</sub> laser surgery had a significantly better 5-year laryngeal preservation rate (95%) than patients treated with radiotherapy (77%), despite the lack of difference in local control. For the CO<sub>2</sub> laser group, our 5-year laryngeal preservation rate is in concordance with previously published results.<sup>10,17</sup> For radiotherapy, the 5-year laryngeal preservation rates vary between 80% and 95%.<sup>5,10</sup> A possible explanation for this variation is the difference in radiotherapy regarding fraction dose, total dose, and given schedules.

There are 2 main advantages of using CO<sub>2</sub> laser surgery as primary treatment modality for

T1a glottic laryngeal carcinoma. First, CO<sub>2</sub> laser surgery can be used multiple times in case of a local recurrence. Second, in those cases with a local recurrence in which CO<sub>2</sub> laser surgery is not possible because of tumor expansion, radiotherapy can be administered as the effective salvage treatment modality. Our present policy is to use salvage total laryngectomy only in case of tumor recurrence after initial CO<sub>2</sub> laser and salvage radiotherapy treatment.

In the majority of cases with a local recurrence after primary radiotherapy, salvage surgery by total laryngectomy is the only suitable option. Some authors reported on the use of CO<sub>2</sub> laser salvage surgery in case of local recurrence after primary radiotherapy. However, this could only be used for small tumor recurrences with limited tumor spread, as in 1 of our patients.<sup>18,19</sup> Partial laryngectomy in a previously irradiated area is not considered in most cases, because of the high probability of postoperative complications, such as wound healing problems. Therefore, the majority of patients will be salvaged by total laryngectomy.

In the current analysis, quality of voice was not taken into account. A number of other authors reported on the comparison of the voice quality between the 2 modalities which, generally, are equal.<sup>3,9,12,20</sup> Jones et al reported a better voice quality after radiotherapy.<sup>21</sup> However, this was tested on a really small study population consisting of both glottic and supraglottic carcinomas. We did not test the voice quality after treatment, but considering the fact that the ultimate laryngeal preservation rate was significantly better in the CO<sub>2</sub> laser group (95% vs 77% in the radiotherapy group), the ultimate voice quality will probably be better in the CO<sub>2</sub> laser group.

Some authors reported on the cost-effectiveness of CO<sub>2</sub> laser surgery when compared with radiotherapy. Both Goor et al and Brandenburg showed that CO<sub>2</sub> laser surgery was more cost-effective than radiotherapy.<sup>9,22</sup> However, these results could not be confirmed by others.<sup>3,9,22,23</sup> No studies were found favoring radiotherapy over CO<sub>2</sub> laser surgery when the costs are considered.

## CONCLUSION

Both CO<sub>2</sub> laser surgery and radiotherapy are good treatment options for T1a glottic laryngeal

squamous cell carcinoma, with similar local control and survival rates.

Nonetheless, we showed that in a very well-defined subset consisting only of T1a glottic laryngeal carcinoma with normal or diminished mucosal wave, CO<sub>2</sub> laser surgery is preferred over radiotherapy as the primary treatment because of the better laryngeal preservation rate. This is due to the fact that salvage radiotherapy can be used after primary CO<sub>2</sub> laser therapy for local recurrences, and the ultimate salvage total laryngectomy can be reserved for recurrences after salvage radiotherapy treatment.

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