Endoscopic laser treatment in pre-malignant and malignant vocal fold epithelial lesions

E. E. G. Remijn, M.D., H. A. M. Marres, M.D., Ph.D., F. J. A. van den Hoogen, M.D., Ph.D.

Abstract

Endoscopic laser treatment was performed in 43 patients with pre-malignant or malignant vocal fold epithelial lesions, 10 were treated with endoscopic laser surgery for dysplasia, 12 for carcinoma in situ (CIS), five for verrucous carcinoma and 16 patients for squamous cell carcinoma (SCC). Thirty-two patients received laser therapy as their first therapy, whereas 11 patients had had previous radiation therapy for laryngeal carcinoma (n = 9) or CIS (n = 2).

Recurrence after initial laser therapy necessitating re-treatment (a second laser treatment or radiotherapy) occurred in nine out of 32 patients (28 per cent), thus 23 (72 per cent) were maintained free of disease during the follow-up period.

Besides the 32 patients without previous therapy, patients who had already undergone radiation therapy were also included in this study. In this group there were nine patients with SCC, one patient with CIS and one with dysplasia. They all underwent laser therapy. Four were free of disease during follow-up (36 per cent) and seven developed recurrences. Six (58 per cent of all patients with previous radiation therapy) underwent total laryngectomy.

Key words: Laser Surgery; Carcinoma in Situ; Carcinoma; Vocal Cords

Introduction

Epithelial lesions of the vocal folds result in dysphonia. In the case of an early invasive glottic carcinoma, this rapidly appearing symptom often leads to early diagnosis. Up to 24–46 per cent of patients with severe vocal fold dysplasia will develop invasive vocal fold carcinoma.[1,2] The incidence of invasive glottic carcinoma in the Netherlands is 8.12:100 000 per year for men and 0.59:100 000 per year for women.[3] Laryngeal carcinoma is strongly related to smoking habits.

Sixty-five per cent of glottic carcinomas are localized at the glottic level, 30 per cent are supraglottic and five per cent are found at subglottic level. Glottic carcinoma usually affects the anterior two thirds of the true vocal fold. Lymphatic drainage of the glottic region is marginal in contrast with the supraglottic region. Lymphatic metastasis of glottic carcinomas only occurs in the late stage of the disease. Less than one per cent of the patients with T_1 glottic carcinoma present with cervical metasta-sis.[4,5] These factors lead to a favourable prognosis of glottic laryngeal disease after treatment.

In the Netherlands initial treatment for glottic T_1 carcinomas is radiation therapy, mainly because of the good quality of post-treatment vocal function.

Micro-surgical treatment of vocal fold carcinoma is infrequently performed, however, it is the treatment of choice when a dysplastic lesion is diagnosed.

Since the introduction of the CO_2 laser by Strong and Jako (1972) for laryngeal microsurgery, it has gradually gained acceptance and has become a world wide treatment modality.[4,6,7] Nevertheless there still is an on-going controversy about the treatment of pre-malignant and malignant glottic lesions with micro-laser surgery.

During the last 25 years laser technology has been developed and refined. Coupling the laser to the operating microscope has led to many advantages, such as microprecision, good haemostasis (minimiza-tion of bleeding permits better visual control) and a no-touch method of tissue destruction.[8]

There are two ways of tumour treatment using endolaryngeal laser surgery. First, after biopsy the remaining tumour can be completely vaporized. This method is suitable for most of the pre-malignant lesions, but offers no information on the histology of the resected tissue.[9] The second technique is to use the laser as a cutting device and to excise the whole tumour, suitable for the histological examination of the margins.[10] Laser treatment of carcinoma *in situ* (CIS) and severe dysplasia typically extends to the vocal ligament of one or both true vocal folds leaving

its integrity intact. Small glottic carcinomas ($T_1N_0M_0$) can be treated likewise, although a partial cordectomy is also possible, leaving the anterior commissure intact.[10]

The CO_2 laser seems to have important advantages in comparison to radiotherapy. These advantages include a one-session (day) therapy, fewer complications, cost-effectiveness and fewer side effects. Beside these advantages laser therapy can be repeated and does not preclude further or additional therapy. This is important because a second primary tumour in the head/neck region may occur in up to 20 per cent of treated patients.

One of the disadvantages is the cost of laser equipment. The CO_2 laser also requires well-experienced ENT specialists to make this modality successful.

In this study we analysed the results of an early series of patients who underwent CO_2 laser therapy of glottic pre-malignant and malignant epithelial lesions treated at the ENT department of the University Medical Centre Nijmegen between 1986 and 1997. Results are compared with those in the literature.

Materials and methods

The retrospective data of 43 patients (40 men and three women) treated between 1986 and 1997 at the University Centre Nijmegen for severe dysplasia, CIS, SCC $T_1N_0M_0$ and verrucous carcinoma were included. Treatment of glottic CIS and T_1N_0 squamous cell carcinoma (SCC) was according to the protocol composed by the Nijmegen Working Group of Head and Neck Tumours (Table I). This protocol has not been changed during the evaluation period.

Surgery including laser surgery is the preferential treatment for verrucous carcinoma. Laser surgery of CIS and SCC was only incidentally performed in selected patients meeting favourable criteria since the preferential treatment was radiation therapy.

In this retrospective study special attention was given to previous therapy, the tumour stage of lesion and treatment, follow-up, development of recurrence after laser surgery and following treatment, time-lapse before the first recurrence developed, co-morbidity and mortality. Voice quality after treatment has been evaluated by means of scoring on a scale representing the patient's own judgement.

Results

Of 43 patients, 10 have been treated for dysplasia, 12 for CIS, five for verrucous carcinoma and 16 patients for SCC. Thirty-two patients received laser therapy as their first therapy, whereas 11 patients had previous radiation therapy for laryngeal carcinoma (n = 9) or CIS (n = 2).

The mean age at time of first laser treatment was 67 years (range: 39–86 years). The follow-up period varied from two to 119 months (mean 44 months), being defined as the time between first laser treatment and last follow-up appointment or date of death due to non-related causes. Recurrence after initial laser therapy necessitating re-treatment occurred in nine out of 32 patients (28 per cent), thus 23 (72 per cent) were maintained free of disease during follow-up after one laser treatment.

Of these nine patients suffering a recurrence, two were originally diagnosed as dysplasia, four as CIS, one as verrucous carcinoma and two as SCC.

Recurrence after dysplasia resulted in one patient with SCC (*Case 1*). It was successfully treated with radiation therapy. A second patient with a dysplastic lesion (*Case 2*) was successfully treated with the CO_2 laser.

Of four CIS recurrences, three (*Cases 3, 4* and *5*) were dysplastic lesions successfully treated with CO_2 laser and one (*Case 6*) CIS, treated by radiation therapy because of its extension.

A second CO_2 laser treatment was performed in a patient with a recurrence of verrucous carcinoma. Two patients initially treated for SCC had positive resection margins, which were defined as a recurrence and consequently were treated by radiation therapy (Table II). Thus of these 32 patients who underwent laser treatment as a single treatment modality, 28 were maintained free of disease during follow-up.

Besides the 32 patients without previous therapy there were 11 patients who had already undergone radiation therapy (Table III). In this group there were nine SCC, one CIS and one dysplasia. They all

TABLE I
NIJMEGEN WORKING GROUP PROTOCOL OF TREATMENT OF LARYNGEAL SQUAMOUS CELL CARCINOMA, CARCINOMA IN SITU AND DYSPLASIA UNTIL 2000 AND SINCE 2001

Carcinoma in situ and dysplasia
If there is a CIS or dysplastic lesion, an excision biopsy is suitable. If the CIS is doubtful, close follow-up is preferable to therapy. If CIS is proved twice, treatment will be the same as T_1 squamous cell carcinoma.

$T_1N_0M_0$
Initial treatment of a small T_1 glottic laryngeal carcinoma is irradiation. Radiation therapy of primary tumour: 64 Gy

Exception until 2000
When microscopic evaluation shows tumour free margins, an excision biopsy of a squamous cell carcinoma by CO_2-laser is sufficient.

Since 2001
Treatment with CO_2 laser is the treatment of choice in dysplasia, carcinoma in situ and superficial squamous cell carcinoma of the focal folds (T_{1a}).

TABLE II
TREATMENT HISTORY OF PATIENTS AND TREATMENT OUTCOME

Number of patients and histology	Number of patients & history	No recurrences after CO_2-laser	Recurrences after CO_2-laser	Final treatment of recurrences
10 Dysplasia	9 RT –	7	2	1 RT 1 CO2
	1 RT +	1	0	
12 CIS	11 RT –	7	4	3 CO_2 1 RT
	1 RT +	1	0	
5 VC	5 RT –	4	1	1 CO_2
	0 RT +	–	–	
16 SCC ($T_1N_0M_0$)	7 RT –	5	2	2 RT
	9 RT +	2	7	6 TL 1 NT

RT – = no radiation therapy in previous history; RT + = radiation therapy in previous history; CIS = carcinoma in situ; CO_2 = laser therapy; SCC = squamous cell carcinoma; TL = total laryngectomy; VC = verrucous carcinoma; NT = no treatment

underwent laser therapy. Four (36 per cent) stayed free of disease during follow-up and seven developed recurrences. Six (58 per cent of all patients with previous radiation therapy) underwent total laryngectomy, one refused this treatment.

Post-treatment voice quality has been scored by patients as: normal, satisfactory, unsatisfactory or absolutely unsatisfactory. Patients with previous radiotherapy underwent a more extensive laser treatment, all resulting in unsatisfactory voices, otherwise most patients were satisfied by treatment outcome. However, more objective data were lacking; only the results of patients without previous radiotherapy are demonstrated in Figure 1.

Discussion

Until 1997 laser surgery has only incidentally been used as a treatment of pre-malignant and malignant epithelial lesions of the larynx in the Netherlands.[9,11] As shown in this study, laser treatment has a high success rate (curative and saving function of voice) after strict patient selection. Nowadays a 'Profes-
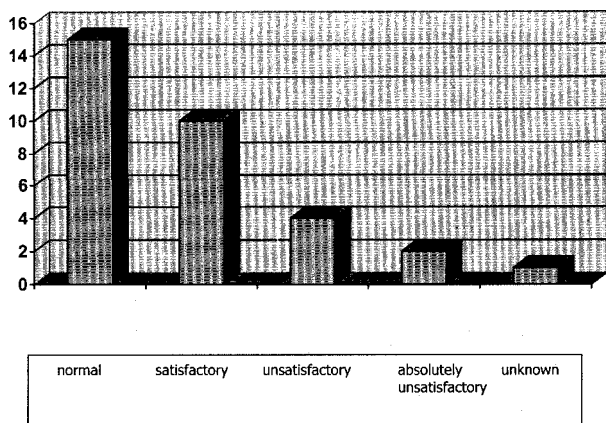

FIG. 1

Voice quality after laser treatment scored by 32 patients all with no previous radiation therapy (19 patients with dysplasia, 11 with CIS, five for verrucous carcinoma and seven with PCC).

sional guideline on larynx carcinoma' has been accepted nationally and based on the criteria formulated by Mahieu (1996) CO_2 treatment is the treatment of choice in dysplasia, carcinoma *in situ* and T_{1a} superficial squamous cell carcinoma of the vocal folds.[9,12]

In the case of dysplastic lesions of the vocal fold(-s) laser surgery is preferable to 'uncontrollable' stripping of the vocal fold (-s).[13] Laser therapy has been used successfully in this study in nine out of 10 patients (90 per cent) with dysplastic lesions. One patient developed a SCC and received subsequent radiation therapy successfully. None of these patients required external ablative surgery and all voices were apparently intact, however objective studies have not been performed in this group. Annyas *et al.* (1984) described 17 patients with dysplastic laryngeal lesions treated with CO_2 laser in whom local control was achieved in 15/17 (88 per cent) of all cases.[11] Two patients underwent radiation therapy because of developing a SCC. The final tumour control rate was 17/17 (100 per cent) and in 16 patients (94 per cent) of the vocal function was maintained.

In another study by Ramacle *et al.* (1997) seven patients with dysplasia of the vocal fold (-s) were described, none of whom developed a recurrence following laser therapy.[14]

Four out of 12 of our patients, diagnosed as CIS, developed a local recurrence in this study. Three of these cases underwent a second laser therapy and one radiation therapy. Local tumour control in this group after microsurgical laser treatment was 11/12 (92 per cent). Final tumour control was 12/12 (100 per cent) and in all cases the voice function was preserved (Figure 1). In Table IV these results are compared with the literature. They seem to be equivalent, recalling that patient numbers in all studies are small.

Out of seven patients with squamous cell carcinoma ($T_1N_0M_0$) treated initially with laser surgery in this study, two had positive margins on histological examination. Both patients successfully underwent radiation therapy (follow up, 80 and 41 months). The other five patients were cured (mean follow up 40 months).

TABLE III
RECORDS OF PATIENTS WITH RADIOTHERAPY IN PREVIOUS HISTORY

	Period of previous RT and histology	Recurrences, histology and treatment	Period RT – first laser treatment	Period laser – final treatment	Period RT – final treatment	Final treatment
1	1982: SCC	1995: Dyspl.; CO_2	13 y.*	–	13 y.	CO_2
2	1988: CIS	1989: CIS; CO_2	1 y.	–	1 y.	CO_2
3	1986: SCC	1986: SCC; CO_2	9 m.	–	9 m.	CO_2
4	1991: SCC	1992: SCC; CO_2	8 m.	–	8 m.	CO_2
5	1989: SCC	1990: SCC; CO_2 after 6 m. dyspl.; CO_2 after 9 m. dyspl.; laser after 13 m. SCC; TL	1 y.	2 y. and 4 m.	3 y. and 7 m.	TL
6	1971: SCC	1975: SCC; microsurgery 1991: SCC; CO_2 1994: mucoderm ca.; TL	20 y.*	3 y.	23 y.	TL
7	1996; SCC	1997: SCC; $CO_2 \rightarrow$ pos. margin $\rightarrow$ **	1 y. & 10 m.	–	1 y. and 10 m.	None
8	1990: CIS	1990: SCC; CO_2 1991: SCC; TL	2 m.	1 y. & 6 m.	1 y.	TL
9	1978: SCC	1988: SCC; CO_2 1996: SCC; TL	10 y.*	7 y. & 6 m.*	18 y.	TL
10	1988: SCC	1989: SCC; CO_2 1990: SCC; TL	10 m.	10 m.	2 y.	TL
11	1990: SCC	1993: SCC; CO_2 1994: SCC; TL	3 y.	3 m.	4 y.	TL

CIS = carcinoma *in situ;* CO_2 = laser therapy; SCC = squamous cell carcinoma; TL = total laryngectomy; VC = verrucous carcinoma; m = months; y. = years.
*If recurrence > 5 year; tumour is defined as a second primary tumour
**Patient prefers no further treatment

Laser surgery was less successful in treatment of SCC recurrences after radiation therapy, or when there was a second primary tumour at glottic level after radiation therapy. In only two of these nine patients, normal voice function could be preserved. Seven of these patients developed a recurrence, six finally underwent a total laryngectomy and stayed free of disease during follow up. The average time interval between laser treatment and laryngectomy was 31 months.

Blakeslee *et al.* (1984) described the results of laser surgery of recurrences in 15 patients following radiotherapy for small laryngeal carcinomas ($T_1N_0M_0$).[25] Local tumour control after this inter-vention turned out to be six out of 15 (40 per cent). Final tumour control was 12/15 (80 per cent); eight patients (53 per cent) underwent total laryngectomy (one patient refused this treatment). Annyas *et al.* (1984) described seven comparable cases.[11] Three (43 per cent) developed recurrence, local tumour control after laser surgery was 57 per cent. Final tumour control of seven out of seven (100 per cent) was achieved following 'salvage surgery'. Shapshay *et al.* (1990) gave CO_2 laser therapy to five patients ($T_1N_0M_0$) with previous radiotherapy.[10] They noted a local and final tumour control of five out of five (100 per cent) and 100 per cent kept their voice functions by avoiding a laryngectomy.

TABLE IV
TREATMENT RESULTS OF ENDOSCOPIC LASER TREATMENT OF GLOTTIC CIS (NAMES REFER TO REFERENCE LIST)

Authors	Number of patients	Local tumour control (%)	Final tumour control (%)	Saved laryngeal voice function (%)
Gillis *et al.* 1983[15]	8	5/8 (63)	8/8 (100)	8/8 (100)
Annyas *et al.* 1984[11]	6	5/6 (83)	6/6 (100)	6/6 (100)
Wetmore *et al.* 1986[16]	6	4/6 (67)	6/6 (100)	6/6 (100)
McGuirt 1987[17]	9	4/9 (44)	9/9 (100)	9/9 (100)
Smith and Lockey 1989[18]	2	1/2 (50)	2/2 (100)	2/2 (100)
Wolfensberger and Dort 1990[19]	7	7/7 (100)	7/7 (100)	7/7 (100)
McGuirt and Browne 1991[20]	12	8/12 (67)	12/12 (100)	12/12 (100)
Eckel and Thumfart 1992[21]	7	7/7 (100)	7/7 (100)	7/7 (100)
Steiner 1993[22]	29	26/29 (90)	29/29 (100)	29/29 (100)
Peretti *et al.* 1994[23]	11	10/11 (91)	11/11 (100)	11/11 (100)
Rudert and Werner 1995[24]	8	8/8 (100)	8/8 (100)	8/8 (100)
Mahieu 1996[9]	17	16/17 (94)	17/17 (100)	17/17 (100)
Remijn *et al.* (present study)	12	11/12 (92)	12/12 (100)	12/12 (100)

TABLE V

TREATMENT RESULTS OF ENDOSCOPIC LASER TREATMENT OF SQUAMOUS CELL CARCINOMA ($T_1N_0M_0$ OF THE GLOTTIC LARYNX (NAMES REFER TO REFERENCE LIST)

Author	Number of patients	Local tumour control (%)	Final tumour control (%)	Saved laryngeal voice function (%)
Strong 1975[6]	11	10/11 (91%)	11/11 (100%)	11/11 (100%)
Ossoff et al. 1985[7]	25	17/25 (68%)	24/25 (96%)	23/25 (92%)
Annyas et al. 1984[11]	4	4/4 (100%)	4/4 (100%)	4/4 (100%)
Blakeslee et al. 1984[25]	35	31/35 (89%)	33/35 (94%)	33/35 (94%)
Wetmore et al. 1986[16]	15	13/15 (87%)	15/15 (100%)	15/15 (100%)
Shapshay et al. 1990[10]	20	18/20 (90%)	20/20 (100%)	20/20 (100%)
Eckel and Thumfart 1992[21]	34	32/34 (94%)	34/34 (100%)	34/34 (100%)
Steiner 1993[22]	96	93/96 (97%)	96/96 (100%)	96/96 (100%)
Perretti et al. 1994[23]	27	22/27 (81%)	27/27 (100%)	27/27 (100%)
Rudert and Werner 1995[24]	98	89/98 (91%)	98/98 (100%)	96/98 (98%)
Mahieu et al. 1996[9]	29	27/29 (93%)	29/29 (100%)	29/29 (100%)
Remijn et al. (present study)	7	5/7 (71%)	7/7 (100%)	7/7 (100%)

To estimate the amount of time that was gained in our study by deferring total laryngectomy, following initial radiation therapy, and using laser surgery instead, the time lapse between initial radiation therapy and the development of a recurrence necessitating laryngectomy was recorded (Table IV). Four (no. 5, 8, 10 and 11) patients underwent laser treatment for a recurrence following radiation therapy, rather than ablative surgery. This postponed the time to eventual total laryngectomy by a mean of 15 months (range three to 28 months). In the two patients (no. 6 and 9) who underwent laser therapy instead of ablative surgery for a second primary tumour, the time gained was even longer (three years and seven years and six months).

These data and those from the literature do support that in selected cases CO_2 laser therapy can be the treatment of choice in case of a small recurrence after radiotherapy. Not only can a laryngectomy be postponed, it sometimes can even be avoided. However, in these patients CO_2 laser treatment results in a poor unsatisfactory voice.

In the Netherlands there is a clear consensus about the way that small glottic carcinomas (T1) should be treated. Initially radiation therapy has a curative goal and has a five-year cure rate of more than 90 per cent.[12] However, comparable results appear to be achievable by laser surgery as shown in Table V and should be considered seriously in individual cases.

Other authors do advocate CO_2 laser treatment in even larger laryngeal tumours up to T_3 and claim local control rates in selected cases, that are comparable with radiotherapy.[26–28] There are only limited data available about laryngeal function (concerning voice quality and swallowing) after this more extensive local laser treatment. Because of this, but mainly because of the necessity to treat the neck by other treatment modalities, CO_2-laser treatment is not generally accepted as the treatment of choice in T_2 and T_3 laryngeal tumours.

In this retrospective study no information could be given about voice quality after treatment compared to pre-treatment other than that demonstrated in Figure 1. To our knowledge no prospective randomized study (radiotherapy versus laser) has been published which discussed treatment outcome in terms of vocal quality after treatment.

Disadvantages of radiation therapy are the longer therapy sessions required (six weeks with five sessions a week) bringing additional health care costs. If recurrences develop the only curative option is 'salvage surgery', which means a partial or total laryngectomy. Primary laser surgery is thus a good alternative, with the advantages of a one-day session and lower costs. If a recurrence does occur, laser surgery and radiotherapy are still open treatment options. In our opinion patient selection for laser treatment should be based on the criteria given by Mahieu et al. (1996):[9]

(1) Superficial extension: SCC should be limited to one true vocal fold, without involvement of the anterior commissure, or the vocal processes of arytenoid. CIS should be limited to the glottic level but extension to the anterior commissure, vocal processes of arytenoid or contralateral vocal fold is no contra-indication.

(2) Extension into depth: SCC is only treated by laser therapy if a recognizable mucosal wave pattern of the diseased vocal fold is still present on videolaryngostroboscopic examination. The laser is used in all confirmed cases of CIS.

(3) A good and clear view of the complete lesion is essential. If this is impossible, the laser therapy should be cancelled and radiation therapy becomes the choice of treatment.

These criteria are thought to be mandatory when post-treatment quality of voice is one of the aims of treatment.

Conclusion

Based on previous studies and the present study, nowadays CO_2 laser treatment is the treatment of choice in dysplasia and carcinoma in situ of the vocal folds. In patients with superficial squamous cell carcinoma (T_{1a}) of the vocal folds, laser treatment is preferred and results in high control rates.

After primary radiation therapy CO_2 laser treatment can play an important role in controlling local recurrence.

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Address for correspondence:
Dr H. Marres,
Department of Otorhinolaryngology,
University Medical Centre Nijmegen,
P.O. Box 9101,
6500 HB Nijmegen, The Netherlands.