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CO₂ laser surgery of supraglottic carcinoma: our experience over 6 years

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KEYWORDS Laser supraglottic laryngectomy; Supraglottic carcinoma; Laryngeal cancer	 Abstract Introduction and objectives: The study goal was to analyse the oncologic and functional outcomes of transoral laser microsurgery in the treatment of carcinoma of the supraglottic larynx. Material and methods: Atotal of 53 patients were included in this retrospective review between 2000 and 2006. The follow-up period was more than 2 years and the mean follow-up for all patients was 49 months. Results: Tumour extension was as follows: T1 in 12 (22.6%), T2 in 37 (69.8%), and T3 in 4 (7.5%). Forty-seven patients (88.7%) had neck dissections. Nineteen patients (35.8%) received adjuvant radiotherapy. Kaplan-Meier estimates for disease-specific survival were 80%, 74.11%, and 65%, at 2, 3 and 5 years, respectively. The overall functional laryngeal preservation rate was 90.56% (48 of 53), and local control 81.13% During follow up, 13.2% of patients developed local recurrence, 11.3% regional recurrence, and 5.7% loco-regional recurrence. Patients started swallowing early after surgery, with a mean time of 5.83 days, and the mean hospital stay was 14.69 days. Complications included 20.75% who suffered pneumonia and 11.32% with bleeding. Only one patient (1.88%) received total laryngectomy due to the impossibility of swallowing. Conclusions: With careful selection of patients, laser supraglottic laryngectomy is a safe and
	<i>Conclusions:</i> With careful selection of patients, laser supraglottic laryngectomy is a safe and effective treatment for cancer of the supraglottic larynx. © 2009 Esevier España, S.L. All rights reserved.

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PALABRAS CLAVE Carcinoma

supraglótico; Laringectomía supraglótica láser; Cáncer de laringe

Laringectomía horizontal supraglótica láser CO2: nuestra experiencia en seis años

Resumen

Introducción y objetivos: El objetivo del estudio es analizar los resultados oncológicos y funcionales de la microcirugía láser en el tratamiento del carcinoma supraglótico de laringe.

Material y métodos: Cincuenta y tres pacientes fueron incluidos en este estudio retrospectivo entre el año 2000 y 2006. El periodo de seguimiento fue superior a 2 años y la media fue de 49 meses.

Resultados: La extensión tumoral fue T1 en 12 pacientes (22,6%), T2 en 37 (69,8%) y T3 en 4 pacientes (7,5%). En 47 pacientes (88,7%) se realizaron vaciamientos cervicales ganglionares. Diecinueve pacientes (35,8%) recibieron radioterapia (RT) postoperatoria. Las estimaciones de la supervivencia causa-específica con el método de Kaplan-Meier fueron de 80%, 74,11% y 65% a los 2, 3 y 5 años, respectivamente. La preservación de la función laríngea fue posible en el 90,56% (48 de 53) y el control local fue del 81,13% Durante el periodo de seguimiento 13,2% de los pacientes desarrollaron recidiva local, 11,3% recidiva regional y 5,7% recidiva locorregional. Los pacientes comenzaron a deglutir de forma temprana tras la cirugía con un tiempo medio de 5,83 días y la estancia media hospitalaria fue de 14,69 días. El 20,75% sufrieron neumonía y el 11,32% hemorragia. Únicamente un paciente (1,88%) precisó una laringectomía total por imposibilidad para la deglución.

Conclusiones: Con una selección cuidadosa de pacientes, la laringectomía supraglótica con láser es un tratamiento seguro y efectivo para el cáncer supraglótico de laringe.

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Introduction

Laryngeal cancer is a neoplasm that in Spain is the sixth ranking cause of cancer mortality in men and twenty-third in women. In 2000, throughout the nation there were 1768 deaths from laryngeal cancer in men and 46 in women, representing an adjusted rate per 100,000 inhabitants of 8.32 and 0.17, respectively.^{1,2}

Traditionally, it has been argued that the incidence of the supraglottic location was highest in the Latin countries, especially in Spain. In a review of 631 patients with diagnosed larynx tumours treated in the Hospital Miguel Servet in Zaragoza from 1974 to 1990, 64.05% were supraglottic tumours.³ However, the predominance of supraglottic over glottic tumours in Spain and other Mediterranean countries has changed in recent years in our environment.⁴ Around the eighties, there was a change from which, until the present, glottic malignancies have been more frequent than supraglottic.⁵

The first description of horizontal supraglottic laryngectomy (HSL) was provided by Alonso in 1947.⁶ This partial technique became very popular because it presented oncologic results similar to total laryngectomy, preserving the patient's voice and incurring in lower morbidity. The application of CO_2 laser in oropharyngeal, laryngeal and tracheobronchial lesions began in 1971 with Strong and Jako.⁷ The transoral approach for these types of tumours became a subject of controversy, since large tumours could not be removed in one piece, forcing their fragmentation prior to excision.

However, microscopic vision and the effect of laser on different tissues enabled surgeons to distinguish healthy tissue from tumour tissue and, if surgical margins free of disease can be obtained, oncologic results from transoral laser surgery appear to be comparable to those obtained with conventional supraglottic laryngectomy.⁸ Among the advantages described for laser surgery versus supraglottic laryngectomy via transcervical approach are fewer days admitted, fewer temporary tracheotomies, fewer aspiration pneumonias, less frequent pharyngostomies and faster oral swallowing.⁹

In 2000 we began using CO_2 laser in larynx surgery at our service. We carried out a review of patients undergoing HSL with CO_2 laser between 2000 and 2006, with the objective of analysing both our oncologic and functional results and discussing the advantages and disadvantages of the technique.

Material and methods

This was a retrospective study of patients undergoing CO_2 laser HSL at the Service of Otorhinolaryngology at the Hospital Miguel Servet in Zaragoza between February 2000 and December 2006. To this end, we reviewed all patients present in the registry of CO_2 laser surgery at our service who were operated on during these 6 years.

Our hospital's Committee for Head and Neck Tumours, consisting of all the specialists involved in the management of patients with tumours in this location, elaborated action protocols for patients with supraglottic carcinomas. According to the protocol, laser HSL would be indicated in all supraglottic tumours classified as T1. In T2 tumours, HSL would be conducted in all cases except when there was tumour extension to the glottis; this was also true in T3 tumours, except in cases of vocal cord fixation.

The emptying performed in tumours classified in Stage N0 are functional and can be bilateral or unilateral if

the lesion is mostly localised on one side. In N1 or N2 cases, the emptying is always bilateral; in N3 cases, the treatment is generally radical cervical emptying. With regard to postoperative radiotherapy (RT), it is indicated in cases with more than 2 metastatic lymph nodes, lymph node capsule overflows or N3 tumours, in which treatment with concomitant chemotherapy would also be considered. Criteria for inoperability are poor general condition (especially taking into account lung function and age), non-treatable distant metastases and coincidence of second tumours without the possibility of curative treatment. If partial surgery were rejected, the correct treatment would be total laryngectomy, although an alternative could be treatment with chemotherapy and RT according to the "organ preservation protocol". Most patients with extensive tumours fall under this protocol, leaving total laryngectomy as a reserve for cases that do not respond well to this treatment or for tumour relapses. Despite the protocols, each case is discussed individually in an attempt to provide personalised treatment tailored to the characteristics of each patient and their lesions.

In terms of technique, the extent of supraglottic resection depends on tumour size and should be one that allows the surgeon to be sure that a complete tumour excision with negative margins has been performed. The limits are the problems for the rehabilitation of swallowing that may occur in postoperative patients. In early tumours (suprahyoid epiglottis or ventricular band), a single block resection of the tumour is attempted. For more extensive carcinomas, affecting virtually the entire epiglottis, they are divided into 2 or more fragments, crossing the midline to ensure improved safety and visibility during resection. What we consider as laser HSL is the complete or partial resection of epiglottis, bands or aryepiglottic fold. If necessary, the resection can be extended to include the extirpation, preepiglottic fat, part of the pyriform sinus, vallecula or an arytenoid (extended HSL).

Fifty-three patients were included in the study. The minimum follow-up time was 24 months and the average was 49 months (range 24-96). Disease staging was obtained through the tumour-node-metastasis (TNM) classification of the 2002 American Joint Committee on Cancer. The surgical laser equipment used was Sharplan 20 C.

All patients received a protocol of preoperative antibiotic prophylaxis with gentamicin 80 mg (this has recently been replaced by tobramycin) and clindamycin 600 mg intravenously, 30 min before surgery. This pattern was continued every 8 h until 4 doses were completed.

The parameters studied were age, gender, tumour location, extension, TNM stage, type of surgery performed, performance of lymph node emptying, intraoperative and postoperative complications, pathological anatomy, administration of postoperative RT, existence of recurrences and/ or metastases, treatment of recurrence(s), current patient condition and survival. Also, to obtain the functional results, we considered the following parameters: days of hospitalization of the patient, need for nasogastric tube (NGT), performance of tracheotomy and time of start of swallowing after the surgery.

We used SPSS for Windows (version 11.0) for the statistical analysis of data, with which a descriptive study of all

parameters collected was carried out, as well as an analysis of overall and cause- and stage-specific survival using the Kaplan-Meier method.

Results

Peviewing the Otolaryngology Service database of our hospital, we registered 243 patients operated on by CO_2 laser surgery between 2000 and 2006. Of these patients, 153 were cordectomies, 53 HSL, 3 partial pharyngectomies, and 33 benign lesions: most were glottic or supraglottic stenosis scars secondary to prior laser surgery, but there were also Zenker diverticula, one case of laryngeal amyloidosis and one hemangioma of the base of the tongue.

We included in the study the 53 patients operated on for HSL over these years. Of the 53 patients, 50 were men (94.3%), and 3 were women (5.7%). The average age at the time of surgery was 61.04 years with an age range from 43 to 79 years and a standard deviation of 9.7.

The anatomical pathology result was of squamous cell carcinoma in all parts. In terms of location, most tumours were settled in the epiglottis (73.6%, followed by the band (22.6%), the aryepiglottic fold (1.9%), and the arytenoid (1.9%).

As to the TNM classification, 12 patients were T1 (22.6%), 37 patients were T2 (69.8%), and 4 patients were T3 (7.5%); 64.2% patients were N0, 9.4% were N1, 18.9% were classified as N2, and 7.5% as N3. None of the patients presented distant metastases. As to stages, 13.2% were in tumour Stage I, 45.28% in Stage II, 15.09% in Stage III, and 26.41% in Stage IV (Table 1).

The majority of patients underwent a simple HSL. In 32.1% it was necessary to expand the exercises to other areas of the larynx, the most frequent being the arytenoid (7 cases), followed by the pre-epiglottic space (3 cases), part of the vocal cord (3 cases), vallecula (3 cases) and lastly, the pyriform sinus in only one case.

We carried out functional or radical cervical emptying in nearly all cases, except in those who had been treated for other neck injuries. In cases where there were metastatic lymph nodes in the extension study, they were usually bilateral; although in N0 patients with lateralized tumour lesions (aryepiglottic fold or unilateral band involvement), we normally carried out a unilateral emptying on the side of the lesion.^{10,11} When it was necessary to conduct a bilateral lymph node emptying, we performed the HSL plus

Table 1	Tumour staging		
Stages		No. of Patients	%
1	T1N0M0	7	13.2
II	T2N0M0	24	45.28
III	T3N0M0	3	
	T1N1M0	0	15.09
	T2N1M0	5	
	T3N1M0	0	
IV	ANY N2/ N3	14	26.41

the cervical emptying on the side of the lesion in a first surgery, and then in a second surgery (usually within a time period of less than one month), the emptying of other side. The purpose of this procedure was to decrease the risk of oedema of the airway and therefore to reduce the number of tracheotomies practiced. Cervical lymph node emptying was performed in 88.7% with 56.6% being bilateral. Most of the emptying was functional (87.23%) and only 6 patients underwent radical emptying of one side (12.76%). Additional postoperative RT was given to 35.8% (19 patients).

None of the patients presented intraoperative complications, but 11 patients suffered postoperative pneumonia (20.75%), although not all were by aspiration. The second most common complication (11.32%) was postoperative bleeding, which was attributed in the majority of cases to the cervical emptying. Two patients died postoperatively (3.77%), one of them due to massive haemorrhage and the other from pneumonia complicated by renal insufficiency and multiple organ failure. Only one patient (1.88%) required total laryngectomy due to the impossibility of swallowing. Only 13.2% were carriers of NGT postoperatively.

Regarding the length of admittance, the average number of days that the patients remained hospitalised after the first surgery was 9.89 days, with a range of 2 to 36 days and a standard deviation of 7.8. Some patients underwent cervical emptying in a second stage, so considering the total number of days of hospital stay, including HSL and emptying, the average was 14.69 days, with a range between 2 and 37 days and standard deviation of 7.84. The average number of days it took for patients to swallow was 5.83.

Scar stenosis was presented by 18.86% of patients later; it was necessary to resect this with laser over subsequent years.

Local and regional control

Tumour recurrences were local in most cases (13.2%). In 11.3% of cases, they were ganglionary and in 5.7% the recurrence was local and ganglionary. The average time in months for the occurrence of relapse after surgery was 11 months for local recurrence and 7 months in ganglionary recurrences.

Regarding the treatment of these recurrences, 56.35% of patients with recurrence underwent surgical treatment: 3 patients underwent laser resection, which rescued all 3 patients, all of whom are currently alive and free of disease (rescue rate of 100%). Four were laryngectomized and only one of them remains free of disease (rescue rate of 25%). Others underwent surgery for lymph node metastases and the rest (43.8%) underwent cancer treatment with concomitant RT and chemotherapy or palliative chemotherapy (rescue rate of 0%).

Hence, a local control of disease of 81.13% was obtained. If we include patients with local recurrence who were rescued by laser resection in a single intervention, the local control amounts to 86.79% The regional control was 83.01%

Survival

The overall survival was 72.61% 65.02% and 37.07% at 2, 3, and 5 years, respectively. Separating the tumour stages into

initial and advanced, overall survival is 82.62% 79.54% and 58.71% at 2, 3, and 5 years in Stages I and II; it is 63.64% 56.63% and 35.17% respectively, in advanced stages (III and IV) as shown in Figures 1 and 2.

We must take into account that 10 of the 22 deaths in the study were due to causes not related to tumours of the larynx, the majority due to a second primary lung tumour.

The cause-specific survival was of 80.01%, 74.11%, and 65% at 2, 3, and 5 years, respectively (Figure 3).

With respect to secondary tumours, 9.8% had distant metastasis, with the most common location being the lung (83.33%), followed by the liver (33.33%). The incidence of second tumours was 15.09% and in all cases they were primary lung carcinomas, except one, which was a tumour at the base of the tongue.

Conservation of the larynx

It was necessary to perform a total laryngectomy in 9.43% (5/53) of the cases. In 4 patients, this was due to tumour recurrence and in one patient due to incapacity to swallow. Thus the conservation of the larynx was possible in 90.56%

In 22.64% (12 patients), it was necessary to perform tracheotomy at some point of the monitoring period. In 5 of the 12 patients, the tracheotomy was carried out due to tumour recurrence at least one year after surgery. In 4 patients, it was performed due to postoperative bleeding and 2 of them were decannulated after a few days; the other 2 died. Two patients underwent tracheotomy due to supraglottic stenosis that appeared years after the surgery and still remain so because they do not tolerate decannulation. Lastly, another patient underwent a tracheotomy at the same time as the HSL and did not tolerate decannulation. Ultimately, of the patients alive and free of disease, only 3 still remain tracheotomized (11.11%).



Figure 1 Overall survival curve in initial stages (I and II).



Figure 2 Overall survival curve in advanced stages (III and IV).



Figure 3 Kaplan-Meier curve of cause-specific survival.

Discussion

From the surgical standpoint, supraglottic tumours can be resected via the transcervical or transoral route. For the transoral approach, the carbon dioxide laser offers determinant technical characteristics such as its high precision, which reduces thermal injury, tissue necrosis and postoperative oedema, as well as the various reactions that it produces on tissues: vaporization (68°), coagulation (>100°) or carbonization (>500°). Furthermore, it enables a distinction between healthy tissue and diseased tissue, since there is no charring or lesion in the area peripheral to the target.¹² HSL via transoral route and via external route do not only differ in the surgical approach and the technical means used, the exposure is also different, as is the amount of resected tumour tissue. Therefore, the oncologic and functional outcomes of external surgery should not be extrapolated to the transoral route. However, most authors agree that this technique is associated with excellent postoperative function, with survival comparable to that of the external route surgery and a very superior quality of life.¹³⁻¹⁵

The most appropriate treatment must be individualised, taking into account the characteristics of the patient (general condition, lung function, acceptance of possible sequelae), of the tumour (volume, infiltration, regional metastases) and the experience of the surgical team.

If we review the literature, the first publications on endoscopic surgery with carbon dioxide laser for supraglottic tumours were published by Steiner¹⁶ in 1993 and subsequently by Zeitels et al.¹⁷ In 1997, Eckel et al.¹⁸ published a study of 40 patients in early stages (I and II), obtaining a 5-year overall survival of 59% and 72% (adjusted). Ambrosch et al.¹⁹ presented the results in 48 patients with T1 and T2 supraglottic tumours, obtaining overall survival at 5 years of 76%. At first, HSL by transoral route was indicated in small lesions (T1-T2) and the oncologic results obtained were comparable to those reported in external surgery, with lower morbidity and better functional quality for patients. Iro et al.⁸ subsequently presented their results of 141 supraglottic tumours in Stages I to IV, obtaining overall 5-year survival of 75.4% in Stages I and II, and 56% in Stages III and IV. The adjusted survival was 65.7%, a figure similar to the results of our study. In their study with 47 patients, Rudert et al.²⁰ concluded that the laser could be recommended as a curative method in early local tumours and also in selected cases of T3 and T4. It is currently accepted that, in supraglottic tumours in which it is possible to obtain adequate exposure through a direct laryngoscopy and surgical margins free of disease can thus be obtained, the oncologic results of laser HSL are comparable to those obtained by conventional transcervical HSL. Nevertheless, we must point out that the survival figures drop significantly in the advanced stages in our study and, therefore, we must be careful when selecting these candidates.

Pecent works such as that of Oliva et al.²¹ (who studied 50 patients with tumours in Stages I to IV), obtain an overall and adjusted survival rate at 5 years of 55% and 70% respectively. Grant et al.²² obtained specific survival results at 2 years of 80% in 38 patients in Stages I-IV. In short, these figures are similar to those obtained in our patient group, in which we must also take into account the required learning period of the technique, which began in the year the study started.

Regarding the number of tumour relapses, the different authors cite figures of local or locoregional control above 90% for T1 or T2 tumours. However, in T3 tumours, the percentage drops to 70-90%¹¹ In fact, some authors do not recommend the laser technique if the tumour is in stage T3 or if it invades the pre-epiglottic space, due to the high rate of relapses.²³ Other studies cite rates of local or locoregional recurrence of 22.7%⁰ or 22%¹ in T1 to T3 tumours, which are comparable to ours of 18.9% In this aspect, HSL by transcervical route seems to have a better rate of local recurrence. In a retrospective study at our hospital, out of 83 patients undergoing transcervical HSL between 1970 and 2000,²⁴ 14.86%showed recurrence, with this being local in only 8.11% However, the laser technique has the great advantage that it can be performed as often as necessary as long as the lesion can be resected safely.

According to the literature, HSL by external route has an average hospital stay of 22.9 days,^{9,21} a figure well above the average of 14.69 days of admittance in our group of patients, including those undergoing cervical emptying. This length of admission is also lower than that of other series described that used the same technique⁹ and represents a clear advantage over HSL by external route.

In our study, only 3 patients are still tracheotomized, representing 11.11% of patients alive and free of disease. In HSL by external route, tracheotomy is systematically necessary and the described percentage of permanent tracheotomies is between 7 and 25% ^{9,25}

Regarding complications, the most common is difficulty for swallowing with aspiration problems, which has represented 20.75% of the pneumonia cases in our series. The extent of resection is a key factor, as well as overall patient condition. It has also been reported that, regardless of stage, 40-70% of patients undergoing HSL must bear, at least in the first postoperative days, a certain degree of aspiration.²⁶ This 20.75% is slightly higher than other series described using the CO₂ laser technique (18%).⁹ This may be because we do not use postoperative NGT in our patients, unless they have serious difficulty in swallowing, while patients in other studies are carriers of postoperative NGT for an average of 9 days.⁹ However, in the external HSL, the percentage of pneumonias by aspiration is also around $18\%^{24}$

Complications secondary to the treatment for primary tumour were few but some were serious, such as massive bleeding that occurred in one patient and caused his death. Smilar cases have been described in other publications, with a mortality rate of 4%^{21,27}

The lower incidence of pharyngocutaneous fistulas in the laser technique is considered an advantage over conventional surgery. In fact, none of our patients presented this complication, nor local infections such as postoperative cervical abscesses, which were the most frequent complication (15.29%) in our transcervical HSL study.²⁴ The appearance of pharyngostoma in the cases of external technique varied between 2 and 12% according to the literature. However, neither in our review of transcervical HSL nor in any other recent ones did this complication appear.^{22,25}

The emergence of second primaries increases as patients survive longer, reaching 15.09% in our series and thus becoming the leading cause of death after that caused by laryngeal tumour. In our group of patients, carcinoma of the lung appeared in 7 out of 8 cases of second primary tumour.

Conclusions

Supraglottic carcinoma, with a very high incidence in our province, can be treated with CO_2 laser surgery with

sufficient oncologic guarantees. The advantages over the transcervical surgical approach are shorter hospitalisation, fewer temporary tracheotomies and faster oral swallowing. Moreover, the possibility of pharyngostoma is nonexistent.

The most frequent complications, sometimes serious, are pneumonia and local haemorrhage. Total laryngectomy due to swallowing problems is very rare. Good candidate selection is essential to achieve satisfactory oncologic and functional results and the candidates should be evaluated based on the experience of each team.

Conflict of interests

The authors declare no conflict of interests.

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