



# Prognosis and Outcomes in Early Stage Glottic Carcinoma Involving the Anterior Commissure Treated with Laser CO<sub>2</sub> Surgery: A Retrospective Observational Analysis

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**Abstract** The anterior commissure (AC) is the area where the vocal cords attach to the thyroid cartilage through Broyles' ligament. Many authors argue that involvement of the anterior commissure in early stage glottic carcinoma (I, II) constitutes a risk factor for local recurrence. The objective of this study is to evaluate whether anterior commissure involvement in early stage glottis cancer is an independent risk factor for recurrence and mortality. The study included all those patients diagnosed with glottis carcinoma in stages I and II of the AJCC treated by transoral laser surgery at the Hospital San Pedro (Logroño, Spain) between 2005 and 2015. Patients were divided into two groups according to the presence (AC1) or absence (AC0) of involvement of the commissure. Of 29 patients treated, 44.8% were AC1. Patients with anterior commissure involvement had more local recurrence ( $p = 0.2701$ ); higher mortality rate ( $p = 0.2256$ ); lower disease-free survival ( $p = 0.0881$ ) and a lower overall survival ( $p = 0.0331$ ). The 5-year survival rate was 24.5% lower in patients with invasion of the anterior commissure. The involvement of the anterior commissure is an independent risk factor that should be considered in the prognosis of laryngeal cancer.

**Keywords** Laryngeal neoplasms · Glottis · Vocal cords · Anterior commissure · CO<sub>2</sub> laser

## Introduction

Laryngeal carcinoma accounts for 2% of all tumors diagnosed worldwide [1]. The ideal treatment for early stage glottic carcinoma would achieve the full healing of the disease with full conservation of functionality (voice, swallowing and breathing), and would keep all treatment options open in case of recurrence or second primary tumors that may appear in the upper aero-digestive tract [2, 3].

Transoral laser cordectomy is the best therapeutic option. The laser's accuracy keeps these segments of the vocal cords free of carcinoma and achieves better functional outcomes than other techniques [4, 5].

Laser cordectomy was introduced in the 1970s by Jacko and Strong. Technological advances at the turn of the century improved the technique thanks to the development of more powerful, smaller and cheaper laser generators. Laser has become an affordable tool for most centers and is accurate enough to achieve 5-year survival rates of 98% and cause-specific survival rates of 100% [6].

The European Laryngological Society classified transoral laser cordectomies into six types [7]. Types I and II do not affect vocal muscle and should be used in benign tumors, premalignant lesions as leukoplakia or carcinoma in situ. Types III and IV should be performed on small lesions (T1–T2) and type V is suitable for larger tumors. Type IV cordectomy or anterior commissurectomy should be considered if the anterior commissure is involved. Laser surgery on the anterior commissure obtains similar results

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to other treatment options such as radiotherapy or open partial surgery, but has lower associated morbidity [8].

Many authors contend that involvement of the anterior commissure in early-stage glottic carcinoma constitutes a risk factor for local recurrences [9, 10]. The anterior commissure is defined as the area where the vocal cords attach to the thyroid cartilage through the anterior commissure ligament, or Broyles' ligament. The insertion area of the ligament is believed to be a point of weakness due to the interruption of the laryngeal perichondrium at that point, increasing the risk of tumor spread through the laryngeal skeleton.

This anatomical difference of the anterior commissure is not reflected in the 8th edition of the TNM staging system by the American Joint Committee on Cancer (AJCC) [11]. Therefore, some authors have proposed the addition of a new independent classification depending on whether or not the anterior commissure is involved. Despite the fact that transoral laser microsurgery has good oncological and local control results for both malignant and premalignant lesions, treatment of early-stage glottic carcinoma involving the anterior commissure remains controversial [8].

Due to the restricted exposure of an anterior commissure lesion, extensive surgical experience is required. Alternatives to transoral laser surgery include anterior frontal partial laryngectomy, supracricoid partial laryngectomy or near-total laryngectomy [12] but the risk of complications and functional post-surgical sequelae is high. Primary radiotherapy offers good functional results although again there is a risk of recurrence, and the economic costs are higher [13]. Contradictory results have been reported in the literature regarding voice quality comparing laser surgery with radiotherapy, but conclusive studies are lacking [14].

The objective of our study was to determine whether anterior commissure involvement is a risk factor for recurrence and mortality in early stage glottic cancer (I or II) treated with transoral laser surgery.

## Material and Methods

The sample comprised 29 patients, 28 men (96.6%) and one woman. The mean age was 68.2 years (SD = 10.3, range 44–96). The inclusion criteria chosen were a recent diagnosis of squamous cell glottis carcinoma stages I or II, and CO<sub>2</sub> laser transoral microsurgery treatment.

We excluded patients who had any other oncological history, previous laryngeal surgery, history of radiotherapy or chemotherapy for any reason, either uncertain or involved surgical margins, and who failed to complete 5-year follow-up.

All patients who presented diagnostic suspicion of glottic carcinoma underwent a detailed medical history,

with special emphasis on risk factors for laryngeal carcinoma. A complete physical examination was also performed including direct visual examination of all structures of the upper airway with a nasofibrolaryngoscopy, and a cervical palpation. If the suspected diagnosis remained the same after these explorations, a neck CT scan was performed. The CT scan helped the multidisciplinary committee to determine the oncological stage and to decide on the best treatment options, bearing in mind the patients' preferences. Those classified as stage I or II were offered laser surgery; those who provided informed consent, were scheduled to undergo a laser cordectomy. The cordectomies were performed using a Sharplan 40C surgical laser system by Lumenis® attached to an AcuBlade™ micro-manipulator and a Carl Zeiss® Opmi 111 microscope.

After surgery, controls were held monthly during the first year, bi-monthly during the second year, quarterly during the third year, six-monthly during the fourth year, followed by a final visit at 5 years at which the patient received the oncological discharge. The aim of this follow-up period was to detect possible recurrences as soon as possible following the recommendations of the National Committee Cancer Network (NCCN) [15].

In this retrospective observational study, the data were obtained from the medical records and individually recorded for each patient in the database. The data collected were: date of diagnosis, tumor size (T1a, T1b, T2), involvement of the anterior commissure (AC0 or AC1), date of last control, local recurrence, date of recurrence, salvage treatment, disease-free survival and total survival. For the statistical analysis the RCommander® software was used. In the statistical calculations the involvement of the anterior commissure was used as a grouping factor.

## Results

Of the 29 patients treated, 44.8% were AC1. Tumor size was T1a in 19 patients (six AC1), T1b in five (all AC1) and T2 also in five (two AC1) (Table 1).

Ten of the 29 patients presented carcinoma recurrence; six of these had involvement of the anterior commissure. Local recurrence rates were 46% in patients with involvement of the anterior commissure and 25% in patients without involvement, although these differences were not statistically significant ( $p = 0.2701$ , Table 2).

Ten patients who presented local carcinoma recurrence underwent salvage treatment. Four received repeat transoral laser microsurgery again, three radiotherapy, one concomitant chemotherapy and radiotherapy, and two total laryngectomy.

Organ preservation treatment was possible in all patients without invasion of the anterior commissure, while in the

**Table 1** Tumor size

	T1a	T1b	T2	
AC0	13 (44.8%)	0 (0.0%)	3 (10.3%)	16 (55.2%)
AC1	6 (20.7%)	5 (17.2%)	2 (6.9%)	13 (44.8%)
	19 (65.5%)	5 (17.2%)	5 (17.2%)	29 (100%)

**Table 2** Local recurrence

	No local recurrence	Local recurrence	
AC0	12 (41.4%)	4 (13.8%)	16 (55.2%)
AC1	7 (24.1%)	6 (20.7%)	13 (44.8%)
	19 (65.5%)	10 (34.5%)	29 (100%)

group with commissure involvement the larynx could be preserved in 66% of cases, although the differences were not statistically significant ( $p = 0.3333$ ).

The mortality rate was 3.1% per year. Mortality was 4.62% in patients with commissure involvement and 1.88% in patients without, although the differences were not significant ( $p = 0.2256$ ).

The mean period of disease-free survival was 1033 days. Breaking these data down, this figure was 1233 days in patients without anterior commissure involvement and 787 in those with involvement. Thus, the disease-free survival rate was 36% lower in patients with anterior commissure involvement, although the differences were not statistically significant ( $p = 0.0881$ , Fig. 1).

The mean survival rate was 1266 days: 1074 days in patients with involvement of the anterior commissure and 1423 days in patients without. Thus, total survival was

24.5% lower in patients with involvement; the difference was statistically significant ( $p = 0.0331$ , Fig. 2).

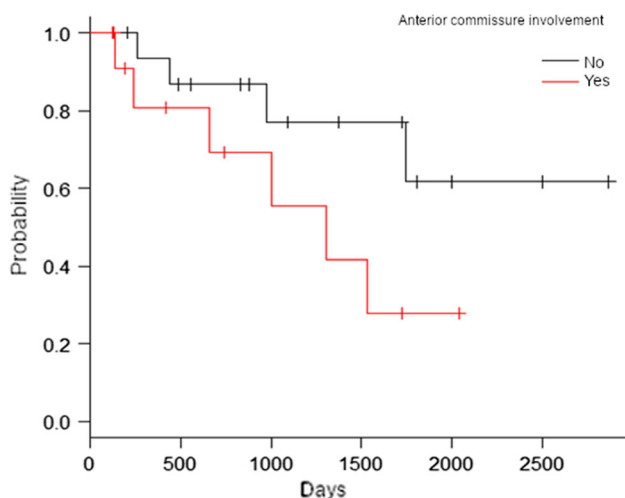
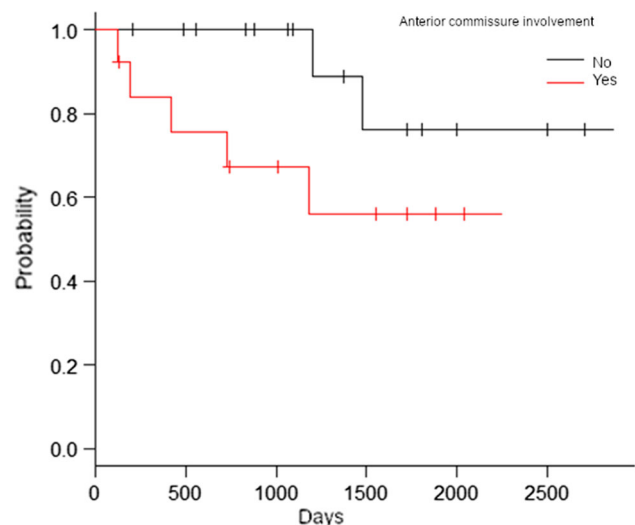
## Discussion

Twenty per cent of vocal cord carcinomas affect the anterior commissure, and 1% present as pure commissure carcinomas [16]. One of the main difficulties when studying the behavior of this carcinoma is the great difference in the results reported between different centers in terms of experience and availability of surgical material and resources at the time of diagnosis and follow-up. In fact, it is estimated that up to 40% of anterior commissure carcinomas are under-staged [17, 18].

The therapeutic management of anterior commissure carcinoma is challenging due to its anatomical characteristics, its expansion in the vertical plane and its irregular morphology. Therefore, adding the involvement of the anterior commissure to the classic TNM classification could help to establish rather more precise prognostic criteria in order to guide therapeutic decisions [19].

Treatment of the anterior commissure has always been highly controversial. Over the years, the results with different techniques have improved thanks to the advances of technology and the super-specialization of surgical teams, but since all the therapeutic options record improvements, no one technique has established itself as the gold standard.

Several studies have reported poorer disease-free survival in patients with anterior commissure involvement. In a study of 263 patients treated with CO<sub>2</sub> laser, Steiner et al. [8] reported 5-year disease-free survival to be 84% in patients with involvement vs 90% in patients without for pT1a carcinomas; 73% (with involvement) versus 92%

**Fig. 1** Disease-free survival**Fig. 2** Mean survival rate

(without) for pT1b lesions, and 79% (with involvement) versus 74% (without) for pT2 carcinomas. These differences were also shown in the lower survival rate of patients with involvement of the anterior commissure.

In a series of 126 patients, Demir et al. [20] studied factors that might worsen oncological prognosis. The only factor that showed statistically significant differences was the involvement of the anterior commissure; in patients with involvement, the risk of recurrence was 3.56 times greater than in the rest of the patients. Galli et al. [21] found a local recurrence rate that increased from 9.4 to 31.6% in the group with commissure involvement, in which disease-free survival was also worse.

In our study of 29 patients the recurrence rates were 25% in the group without involvement and 46% in the group with involvement ( $p = 0.2701$ ). The mortality rate increased from 1.88 to 4.62% ( $p = 0.2256$ ), disease-free survival decreased from 1233 to 787 days ( $p = 0.0881$ ), and finally, total survival fell significantly from 1423 to 1074 days ( $p = 0.0331$ ).

The involvement of the anterior commissure has been shown to be a negative prognostic factor for disease-free survival and local disease control [22–24]. Treatment by transoral laser surgery is effective for anterior commissure carcinoma either as primary or as salvage treatment [9, 25–30].

As a suitable margin in transoral laser surgery, the National Comprehensive Cancer Network guidelines [15] recommend a minimum distance of 1.5 mm between the lesion and the edge of the surgical specimen; margins below 1 mm are considered “narrow”. Striking a balance is important: performing a more extensive cordectomy obtains better surgical margins, but may significantly worsen the functional results of the voice [31].

Proper laryngeal exposure is one of the key factors in obtaining safe surgical margins, so the importance of a good preoperative evaluation cannot be overestimated [32, 33]. Nevertheless, as many as 50% of surgical samples have affected margins [34, 35].

Some authors argue that a resection of the anterior portion of the thyroid cartilage should be performed in all anterior commissure carcinomas because samples analysed histologically showed malignant cells invading the preepiglottic, subglottic or thyroid cartilage space. It has even been proposed that in stage II carcinomas, in which the tumor may show a slight extension to supraglottis or subglottis, transoral treatment should not be performed. In these cases, an open surgical technique with resection of the thyroid cartilage should be chosen because of the high risk of invasion [36].

However, certain authors contend that close margins (or even positive margins) do not have worse outcomes, and so it may not be necessary to administer any treatment

[34, 37, 38]. This may be because the laser photocoagulation produced during the cordectomy can lead to a false narrow or even positive margin due to the contraction of the tissues. The fact is that this photocoagulation can actually improve the results [39]. Finally, there are many who choose an intermediate option. Enlargement of the surgical margins is recommended in patients in whom the microscopic analysis indicates involvement of the deep margins; while a *wait and see* strategy should be applied for the rest [27, 40–43].

Therefore, there are doubts about the best treatment option for all patients, and in fact the NCCN guidelines are inconclusive. This is because there are no prospective randomized studies that provide enough clinical evidence to draw a clear conclusion; the studies performed to date do not present statistically significant differences in overall survival between the different treatments [44].

The choice of treatment will be made individually based on the endoscopic and imaging findings that define its length and depth, the patient’s wishes, taking into account personal expectations, age, general and functional condition, and experience of the multidisciplinary team. The patient will be informed of the different therapeutic options, including sequelae and oncological results [45].

## Conclusions

Patients diagnosed with early-stage glottic cancer treated with transoral laser surgery have a 24.5% lower 5-year survival rate when the anterior commissure is invaded ( $p = 0.0331$ ). They also present a lower organ preservation rate, lower disease-free survival, higher mortality rate and higher local recurrence rate, although these differences were not statistically significant. Therefore, the involvement of the anterior commissure is an independent risk factor that should be considered in the prognosis for laryngeal cancer.

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**Availability of Data and Materials** Data not available for data protection.

**Code Availability** RCommander<sup>®</sup> is an open source software supported by The R Foundation.

## Declarations

**Conflict of interest** All authors declare that they have no conflict of interest.

**Ethics Approval** This is an observational study. The Committee for Ethics in Clinical Research in La Rioja (CEICLAR) has confirmed that no ethical approval is required.

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