Glottic carcinoma with anterior commissure involvement – Is understaging a reality?

Original Article

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Abstract

Objectives: To determine if anterior commissure (AC) involvement in glottic cancer (GC) is a prognosis factor to recurrence and 5-year survival rate.
Study design: Observational retrospective.
Methods: Assessment of medical files of patients who were diagnosed with GC with T1a and T1b staging during a 12-year period (2010-2021).
Results: Twenty-three patients (67,6%) were classified with T1a stage (10 cases with AC involvement) and 11 patients (32,4%) with T1b staging (7 cases with AC involvement). AC involvement was associated with higher risk of recurrence for T1b cases ($p<0,05$), but not for T1a cases. Five-year mortality rate had no significant statistically difference.
Conclusions: AC involvement was a negative prognostic factor in local disease control during follow-up, thus raising the possibility of AC inclusion in T staging in glottic tumors.

Keywords: glottic carcinoma; anterior commissure; recurrence; survival rate

Introduction

Glottic carcinoma (GC) is the most frequent laryngeal tumor (75% of laryngeal tumors)[1].
Approximately 20% of glottic tumors involve the anterior commissure, although it is not a common site of origin for this tumor (1% of glottic tumors)[2]. The therapeutic approach for early-stage GC includes treatment modalities that preserve the larynx with the least possible morbidity. The therapeutic options include transoral microsurgery (with or without the use of LASER), radiotherapy (RT), and (rarely) cervicotomy.
Based on its embryonic origin, the anterior commissure (AC) is defined as the area of the glottis located anteriorly between the vocal folds, which extends in a vertical direction, both cranially and caudally[3]. It is widely

regarded as a point of fragility for tumor dissemination because it is more susceptible to invasion of the thyroid cartilage because, at this level, the thyroid cartilage is not covered by perichondrium. In other laryngeal locations, other structures prevent tumor spread, such as muscle tissue, the paraglottic space, and/or perichondrium in the interposition between the mucosa and the cartilage[4]. To understand the pattern of tumor dissemination, it is important to recognize the role of the Broyles' ligament. This ligament is a band of fibrous connective tissue that connects the vocal ligament, where it extends from, to the posterior surface of the thyroid cartilage. It is precisely in this region of insertion of the ligament that the thyroid cartilage is devoid of perichondrium[5]. Moreover, the short distance (2–3 mm) between the mucosa of the AC and thyroid cartilage favors tumor dissemination. Thus, even smaller tumors can invade the thyroid cartilage and change the T staging from T1 to advanced laryngeal carcinoma (T3 or T4), which requires modification of the therapeutic strategy in this subgroup of patients. Therefore, it is assumed that GCs with AC involvement are associated with a higher risk of understaging and tumor persistence than GCs without AC involvement. However, the current classification of the American Joint Committee on Cancer and Union for International Cancer Control (UICC) does not consider AC involvement as a factor for poor prognosis, with no increase in the T stage if it is affected. In the eighth edition of this classification, three distinct sites of the glottis are referenced for TNM staging: vocal cords, AC, and posterior commissure. Despite this subdivision, the AC does not influence the T1 stage. T1 corresponds to a GC limited to the vocal cords with preserved mobility and is subdivided into T1a (limited to one vocal cord) and T1b (both vocal cords are affected). Thus, this study aimed to determine whether AC involvement is a prognostic factor in GC for recurrence during the follow-up period and survival at five years.

Materials and Methods

This was a retrospective cohort study that involved a retrospective review of the clinical records of patients with a diagnosis of stage T1a and T1b GC, conducted over 12 years (2010–2021). Demographic and clinical data were retrieved (age, comorbidities, risk factors, histology, type of treatment, follow-up period, and date of death – when applicable). Involvement of the AC was defined based on an objective examination (videolaryngoscopy) and/or computed tomography (CT) of the neck or the histopathological report. The presence or absence of relapse during the follow-up period was noted, as well as survival at five years. The patients whose clinical records were deemed incomplete by the authors were excluded. Statistical analysis was performed using the SPSS26 software. Discrete variables were expressed as frequencies and percentages, while continuous variables were described as means and standard deviations. Pearson's chi-square test was used for categorical variables. Survival analysis was performed using Kaplan-Meier curves. A literature review was also conducted in PubMed using the MeSH terms "glottic carcinoma," "anterior commissure," "recurrence," and "survival rate."

Results

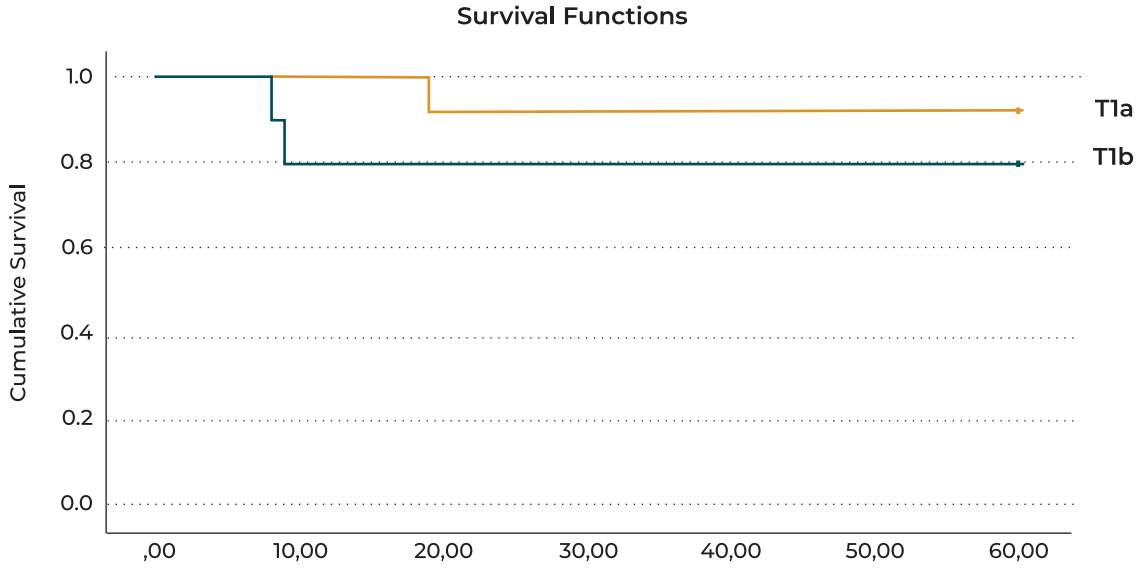
Thirty-four of the 188 patients with a diagnosis of GC met the stage I inclusion criteria. The mean age of the patients at the time of diagnosis was 64.2 years (±10.2 years). Thirty-two patients (94.1%) were men, and two (5.9%) were women. Twenty-three patients (67.6%) were classified as stage T1a (10 cases with AC involvement), and 11 patients (32.4%) were stage T1b (seven cases with AC involvement). Twenty-six patients were treated with RT, while eight patients were treated with transoral laser microsurgery (TLM), as decided in multidisciplinary meetings. The mean follow-up time was 48 months (minimum 18 months; maximum 72 months). Regarding the histopathological diagnosis, 33 patients had histological findings compatible with epidermoid carcinoma (97.1%), and one

patient had verrucous carcinoma (2.9%). Twelve patients (35.3%) experienced tumor relapse. Five of these patients were T1a cases, and seven were T1b cases. Involvement of the AC was associated with a risk of relapse in T1b cases ($p<0.05$), but the disease-free time in T1a cases was not statistically significant (Table 1). There was no statistically significant difference in mortality at five years between the two groups (Figure 1).The results are summarized in Table 1.

Table 1
Results

Results			
			Relapse
Sex	M	32 (94,1%)	
	F	2 (5,9%)	
Age (years)		64,2 (±10,2)	
T1a		23 (67,6%)	5 (41,7%)
	With AC involvement	10 (43,5%)	p=0,169
	Without AC involvement	13 (56,5%)	
T1b		11 (32,4%)	7 (58,3%)
	With AC involvement	7 (63,6%)	p=0,045
	Without AC involvement	4 (36,4%)	
Histology			
	Epidermoid carcinoma	33 (97,1%)	
	Verrucous carcinoma	1 (2,9%)	
Type of treatment	TLM	8 (23,5%)	
	RT	26 (76,5%)	
Mean follow-up (months)		48 (minimum-18; maximum-72)	

Figure 1
Survival analysis



Discussion

Currently, the main treatment modalities for stage I GC are transoral microsurgery (with laser or cold instruments) and RT. As these modalities aim at preserving the larynx, the thyroid cartilage is not removed, which makes it impossible to detect tumor micro infiltrations in the cartilage.

In a meta-analysis, Tulli *et al.* [4] emphasized the possibility of tumor understaging and persistence. Given the unique anatomical features of this laryngeal site (located considerably close to the air-tissue interface), there is a risk of radiation underdosage at this glottic location - a lower-than-prescribed dose of radiation. Therefore, these authors proposed that AC involvement in T1 tumors should be considered a "micro-T3" stage to highlight the higher risk of disease persistence.

Although the binomial variable "yes/no" was used for AC involvement in this study, recent studies have shown that this involvement is not sufficient to determine the prognostic value in GC, which can lead to incongruous results[6]. AC involvement in GC can have a negative effect on the outcome because of the previously described reasons.

However, Hendriksma *et. al.* have stated that the inconsistencies in the literature regarding this topic are due to the poor clinical definition of the AC area. They admit that this area is too complex to be reduced to a binomial variable. Several authors have proposed a classification of this site according to the disease prognosis: Rucci *et al.*[7] proposed four subdivisions of GC involving the AC, while Piazza *et al.*[8] proposed six subdivisions to describe different patterns of growth and recurrence.

Nonetheless, in this study, AC involvement was defined by the findings in the objective examination (videolaryngoscopy) and CT. As AC is a glottic site difficult to visualize, it is often only possible to detect its cancer involvement intra-operatively by light microscopy, using 30°, 45°, or 70° endoscopes or exerting anteroposterior traction on the cricoid cartilage. However, some strategies in laryngoscopic observation facilitate the visualization of this area - with flexible laryngoscopy. Notably, the technique "dipping and rotating," described by Fleisher *et al.*[9], which combines the dipping maneuver (allows magnification of the endolaryngeal mucosa and subglottic region by approximation, using long transnasal inspiration) and rotation maneuver (the tip of the flexible endoscope is placed in the interarytenoid region and moved in the direction of the glottis), allows satisfactory magnification of the AC.

The major limitation of this study was the small sample size - 34 cases. Although GC can cause immediate symptoms such as dysphonia, the vast majority of GC patients in our institution present with a more advanced stage (>50% of cases are classified as T3 or T4). Increasing awareness of the risk factors for carcinoma of the larynx through health education is essential for ensuring early diagnosis and prevention of this disease. Despite this limitation, there was a statistically significant association between AC involvement and relapse during the follow-up period for T1b tumors. Therefore, we suggest considering AC in the T staging of glottic tumors.

Conclusion

In this study, AC involvement was a factor for poor prognosis and the rate of tumor control during the follow-up period. Therefore, it should be considered in the T staging of glottic tumors.

Thus, it is recommended that AC involvement should be actively looked for and documented. Studies with larger samples are required to confirm our results and establish whether T1a GCs are associated with higher relapse rates when there is involvement of the AC, as well as determine if mortality is higher in stage I GC when the AC is affected.

Conflicts of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

Data Confidentiality

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

Protection of humans and animals

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the 2013 Helsinki Declaration of the World Medical Association.

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Availability of scientific data

There are no datasets available, publicly related to this work.

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