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ORIGINAL ARTICLE

Transoral laser microsurgery in locally advanced laryngeal cancer: Prognostic impact of anterior versus posterior compartments

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Abstract

Background: To evaluate the importance of larynx compartments in the prognosis of T3-T4a laryngeal cancer treated with transoral laser microsurgery.

Methods: Two hundred and two consecutive pT3-T4a larynx carcinomas. Pre-epiglottic space involvement, anterior and posterior paraglottic space (PGS) involvement, vocal cord, and arytenoid mobility were determined. Local control with laser (LC), overall survival (OS), disease-specific survival (DSS), and laryngectomy-free survival (LFS) were evaluated.

Results: The lowest LC was found in tumors with fixed arytenoid. In the multivariate analysis, positive margins (hazard ratio [HR] = 0.289 [0.085–0.979]) and anterior (HR = 0.278 [0.128–0.605]) and posterior (HR = 0.269 [0.115–0.630]) PGS invasion were independent factors of a reduced LC. Anterior (HR = 3.613 [1.537–8.495]) and posterior (HR = 5.195 [2.167–12.455]) PGS involvement were

independent factors of total laryngectomy. Five-year OS, DSS, and LFS rates were 63.9%, 77.5%, and 77.5%, respectively. Patients with posterior PGS presented a reduced 5-year LFS.

Conclusions: Tumor classification according to laryngeal compartmentalization depicts strong correlation with LC and LFS.

KEYWORDS

laryngeal cancer, larynx compartment, locally advanced, paraglottic space, squamous cell carcinoma, TOLMS, transoral laser microsurgery

1 | INTRODUCTION

In laryngeal cancer treatment, selection of patients for transoral surgery is crucial to obtain adequate oncologic and functional outcomes. This aspect is of outmost relevance in locally advanced tumors where different larynx preservation strategies have been recommended by international guidelines.[1,2] In the absence of a randomized trial, a recent systematic review highlighted the difficulties to find a consensus for an optimal organ preserving treatment in T3 laryngeal carcinomas.[3] According to the review, 5-year disease-specific survival (DSS) is around 60% for chemoradiation protocols, 70%–85% for transoral laser microsurgery (TOLMS), and 85%–94% for open partial laryngectomies.

Recently, the classification of the larynx tumors based on compartments has been emphasized as an important point to establish the indications of partial surgery.[4] The creation of a perpendicular plane to the thyroid lamina at the level of the vocal process allows to differentiate between anterior versus posterior paraglottic spaces (PGSs).[5,6] From this perspective, the anterior compartments have demonstrated to be more suitable for the resection of advanced tumors in the case of open partial surgery, as tumors with posterior involvement have worse outcomes.[5,6] On the opposite, compartmentalization does not seem to affect the prognosis of T3-T4 laryngeal cancer treated by upfront total laryngectomy.[7]

In 2010, we evaluated the prognostic factors of local recurrence and larynx preservation in a series of T3 laryngeal tumors treated with TOLMS.[8] The variables studied were mainly related to the 2002 TNM classification (vocal cord impairment, pre-epiglottic involvement, and cartilage infiltration). The underlying cause of vocal cord impairment or the presence of a fixed arytenoid was not analyzed in detail. Moreover, the infiltration of the PGS was considered as a whole, not differentiating between anterior and posterior spaces. In that study, cartilage infiltration and vocal cord fixation were negative independent factors for larynx preservation and the best local control was achieved in T3 tumors due to pre-epiglottic space (PES) involvement, suggesting that supraglottic tumors were those that fit best in a transoral approach.[8] More recently, we performed a CHAID decision tree analysis in a series of 1119 consecutive patients (all stages) treated with TOLMS. Paraglottic and vertical involvement of the anterior commissure, as well as the margin status, were the most important factors for local control.[9]

In clinical practice, a large number of T3 laryngeal tumors are treated with organ preservation alternatives, either chemoradiation, open partial surgery, or TOLMS. Specific survival rates seem to be comparable to those achieved with a total laryngectomy, but a percentage of patients can keep the larynx.[3,10–14] Selection criteria based on classification refinements may be determinant for the treatment plan. For instance, many authors consider the cricoarytenoid joint involvement and oncologic limit for TOLMS but not a fixed vocal cord without arytenoid impairment. This is because cricoarytenoid impairment is seen as a surrogate of posterior PGS involvement in glottic tumors. Unfortunately, the AJCC 8th edition of the TNM does not distinguish between a fixed vocal cord with or without arytenoid involvement, probably because this does not translate into different prognosis when a total laryngectomy is indicated.[15] The current TNM neither differentiates between radiologic infiltration of anterior and posterior PGSs, which has been reported to be determinant when indicating partial surgery. Thus, we hypothesized that the variability of TOLMS outcomes published in the literature for locally advanced laryngeal tumors may perhaps be related to paraglottic selection bias.

The aim of our study was to analyze the importance of the anterior and posterior PGSs, regarding local control, prognostic, and larynx preservation rates of locally advanced tumors treated with TOLMS.

2 | MATERIALS AND METHODS

All consecutive patients treated for locally advanced laryngeal cancer with TOLMS during the period 1998 to 2019 were retrospectively evaluated. All data were retrieved

from a database that was prospectively updated weekly. Patients were excluded from the analysis if they had been previously treated, the histology was not a conventional squamous cell carcinoma, or when a contrast computerized tomography (CT) of the primary and the neck was not available at the time of the analysis. Data regarding vocal cord and arytenoid mobility were obtained from the clinical history or through pretreatment video recording, when available.

The classification of anterior and posterior paraglottic involvement was radiologically determined by a perpendicular plane to the thyroid lamina at the level of the vocal process as described by Succo et al.[5] and was clinically evaluated by the presence or not of impaired arytenoid mobility. Anterior PGS and PES were both considered anterior laryngeal compartments.

Transoral surgery was followed by a neck dissection in those patients with clinically or radiologically positive neck nodes. At first, radiologically negative necks systematically underwent a prophylactic neck dissection, but in the last years, glottic tumors with radiologically negative necks were no longer submitted to neck dissection and were closely followed up with either CT or ultrasound imaging during the first 2 years. Adjuvant treatment was applied to the neck in cases with >1 positive lymph node or extranodal spread, and to the T site in tumors in which the final tumor margins were reported to be affected or those presenting perineural invasion or involvement of lymphatics and vessels. In the beginning, adjuvant treatment consisted of radiotherapy alone. Since 2005, concomitant chemoradiotherapy was administered in case of extranodal extension and positive margins.

Routine follow-up after surgery was conducted every 3 months for the first 2 years and every 4–6 months for the third year and onward. A minimum follow-up of 1 year from surgery was necessary to be part of the study.

The study was approved by the local ethic committee with number HCB/2015/0733. Due to its retrospective nature, no informed consent was specifically signed by the patients.

2.1 | Statistical analysis

Data are presented as a mean (SD) or as a number and percentage. We estimated local control with laser, and larynx preservation rates according to clinical and radiological variables by the Pearson chi-square method. Variables studied included age, gender, TNM location (supraglottic, glottic), sublocation (pure supraglottic, transglottic, glottic-subglottic), involved PGS compartments in CT (anterior paraglottic, posterior paraglottic), vocal cord mobility (normal-impaired), arytenoid mobility (normal-impaired), intraoperative pre-epiglottic involvement, intraoperative cartilage infiltration, intraoperative paraglottic involvement, grade of differentiation, margins (positive-negative/close), pTN category (AJCC 8th Edition of the TNM classification), postoperative adjuvant treatment, and surgeon's experience (initial-advanced). Multivariate analysis was performed using Cox proportional hazard models and expressed as hazard ratio (HR) with 95% confidence intervals.

From the pathological point of view, the margin was classified as affected, close or free of tumor. The affected margin showed clear tumor infiltration. A close margin was considered when no final specimen could be obtained (e.g., the thyroid cartilage had been reached), when tumor nests were found at less than 2 mm from the margin, or when focal infiltration was seen histologically but additional ablation had been applied to the tumor site after presumably complete resection. All remaining situations were considered tumor-free margins. Patients treated in the first half of the period were considered in the initial experience group.

Overall survival (OS), DSS, and laryngectomy-free survival (LFS) were estimated using the Kaplan–Meier method. OS was assessed from the date of surgery to the

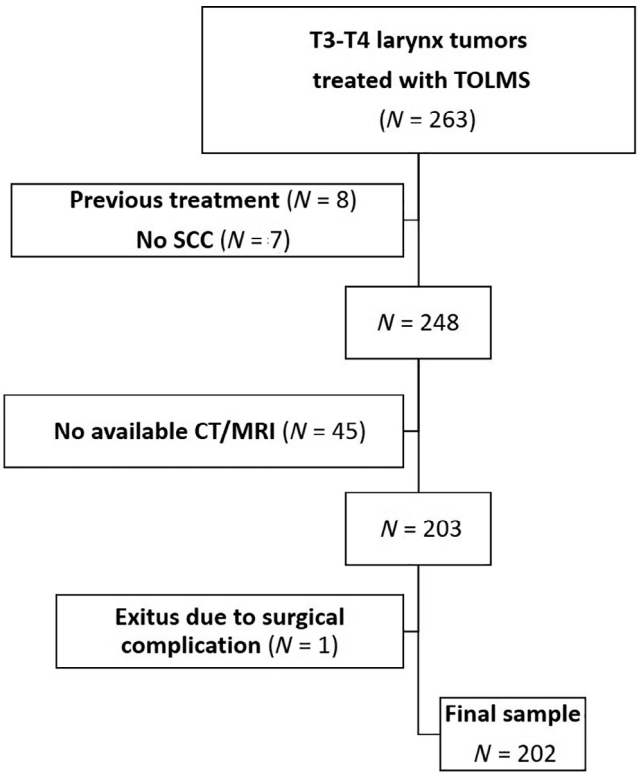

FIGURE 1 Flowchart of patients included in the study. CT, computerized tomography; MRI, magnetic resonance imaging; SCC, squamous cell carcinoma; TOLMS, transoral laser microsurgery

TABLE 1 Clinical and pathologic characteristics of the cohort ($n = 202$)

Variables	Category	*N*	Percentage
Sex	Male	182	90.1
Age (years)	≤70	149	73.8
	>70	53	26.2
Smoking habit	Yes	193	95.5
Alcohol habit	Yes	114	55.6
Diabetes mellitus	Yes	34	16.8
TNM location	Supraglottis	108	53.5
	Glottis	94	46.5
Sublocation	Pure supraglottic	64	31.7
	Transglottic anterior (AC)	28	13.9
	Transglottic lateral (ventricle)	51	25.2
	Glottic-subglottic	59	29.2
Vocal cord fixation	Yes	97	48
Arytenoid fixation	Yes	22	11.6
Radiologic anterior PGS involvement	Yes	75	37.1
Radiologic posterior PGS involvement	Yes	54	26.7
Succo's classification	Anterior pT3 with normal arytenoid mobility	153	80.5
	Posterior pT3 with impaired arytenoid mobility	22	11.6
	Anterior pT4a with normal arytenoid mobility	15	7.9
Surgical exposure	Adequate	164	81.2
	Difficult	38	18.8
Intraoperative PES infiltration	Yes	102	50.5
Intraoperative cartilage infiltration	Yes	47	23.7
Intraoperative posterior PGS infiltration	Yes	46	24.1
Grade of differentiation	G1	8	5
	G2	89	55.3
	G3	64	39.8
Surgical margins	Positive	17	8.4
pT category	pT3	176	87.1
	pT4a	26	12.9
pN category	pNx	110	54.5
	pN0	41	20.3
	pN1	13	6.4
	pN2a	1	0.5
	pN2b	15	7.4
	pN2c	20	9.9
	pN3	2	1
Positive nodes	Yes	50	24.8
Adjuvant treatment	RT or (C)RT	56	27.9
Experience period	Initial	118	58.4
	Advanced	84	41.6

Abbreviations: (C)RT, postoperative chemoradiotherapy; Advanced experience, surgery performed in the second half of period studied; Initial experience, surgery performed in the first half of period studied; PES, pre-epiglottic space; PGS, paraglottic space; RT, postoperative radiotherapy.

TABLE 2 Local control and larynx preservation rates according to clinical and pathologic variables

Variable	Local control with laser (%)	*p* value	Total laryngectomy (%)	*p* value
Sex (M, F)	67, 80	0.237	28.6, 15	0.196
Age (years) (≤71, >70)	70.5, 62.7	0.270	24.2, 35.8	0.101
DM (no, yes)	68.1, 67.6	0.961	26.5, 32.4	0.487
TNM location (supraglottic, glottic)	75.9, 59.6	0.013	19.4, 36.2	0.008
Sublocation (supraglottic, transglottic, glottic)	82.8, 63.7, 59.3	0.009	12.5, 30.4, 39	0.003
Vertical involvement AC (no, yes)	69.4, 62.1	0.435	27.2, 27.6	0.963
Anterior PGS involvement (CT) (no, yes)	85.3, 58.3	<0.001	10.7, 37	<0.001
Posterior PGS involvement (CT) (no, yes)	75, 50	0.001	19.6, 48.1	<0.001
Vocal cord mobility (normal, impaired)	78.1, 57.7	0.002	14.3, 41.2	<0.001
Arytenoid mobility (normal, impaired)	73.8, 36.4	<0.001	21.4, 63.6	<0.001
Posterior involvement (CT/arytenoid) (no, yes)	75, 40	<0.001	20, 60	<0.001
Surgical exposure (adequate, difficult)	67.7, 71.1	0.687	26.8, 28.9	0.792
Intraoperative PES infiltration (no, yes)	58, 78.4	0.002	39, 15.7	<0.001
Intraoperative cartilage infiltration (no, yes)	72.3, 55.3	0.029	23.9, 38.3	0.052
Intraoperative paraglottic infiltration (no, yes)	79.5, 60.2	0.004	14.5, 36.4	0.001
Grade of differentiation (I, II, III)	75, 69.7, 73.4	0.855	25, 23, 27.4	0.885
Surgical margins (negative, positive)	70.3, 47.1	0.049	25.9, 41.2	0.177
pT (pT3, pT4a)	68.3, 68.8	0.969	26.9, 31.3	0.706
Nodal status (negative, positive)	66.4, 74	0.319	30.3, 18	0.091
Stage (III, IV)	68, 69.4	0.853	28.1, 24.5	0.621
Succo's classification (applied) (anterior T3 mobile arytenoid, posterior T3 impaired arytenoid, anterior T4 mobile arytenoid)	74.5, 36.4, 66.7	0.001	20.3, 63.6, 33.3	<0.001
Larynx compartments (anterior, posterior)	74.7, 51.8	0.002	19.9, 46.4	<0.001
Adjuvant treatment (no, yes)	66.4, 73.2	0.354	29.5, 21.4	0.251
Experience (years) (<10, ≥10)	66.1, 71.4	0.423	31.5, 22.6	0.214

Abbreviations: AC, anterior commissure; PES, pre-epiglottic space; PGS, paraglottic space; Succo's classification, classification that combines anterior/posterior larynx compartments with T3-T4 tumor extension and arytenoidPlease spell out "CT and DM" in Table 2. mobility.

date of death (regardless of the cause) or the date of the last consultation for censored observations. To calculate DSS, only deaths related to tumor or complication of the treatment were considered. The endpoint for larynx preservation was the date of total laryngectomy. Comparisons in survival rates between groups were assessed with the Log-rank test.

Data were analyzed using IBM SPSS for windows version 24.0. A p value of 0.05 was defined as statistically significant.

3 | RESULTS

From 1998 to 2019, 262 patients with locally advanced laryngeal cancer were treated with TOLMS in our center. Of them, 202 fulfilled the inclusion criteria and were considered for the analysis (Figure 1). The mean age of the patients was 63.5 ± 11.5 years (range, 20–95) and the mean follow-up was 67.2 ± 49 months (range, 1–230). Clinical and pathological characteristics together with the adjuvant treatment of the cohort are described in Table 1.

In the univariate analysis, pure supraglottic tumors with PES invasion achieved the highest local control with laser and a reduced total laryngectomy rate compared to transglottic and glotto-subglottic locations (82.8%–63.7%–59.3% and 12.5%–30.4%–39%, respectively) (Table 2). Regarding the PGS, both anterior and posterior subunits significantly correlated with a decreased local control compared to PES involvement, being the lower rate of local control with TOLMS in those tumors with clinically

TABLE 3 Factors of local control with laser and total salvage laryngectomy in the multivariate analysis

	HR	95% CI	*p* value
Local control with laser			
Anterior PGS involvement (CT)	0.278	0.128–0.605	0.001
Posterior PGS involvement (CT/arytenoid)	0.269	0.115–0.630	0.003
Positive surgical margins	0.289	0.085–0.979	0.046
Total laryngectomy			
Anterior PGS involvement (CT)	3.613	1.537–8.495	0.003
Posterior PGS involvement (CT/arytenoid)	5.195	2.167–12.455	<0.001
Age	1.932	0.892–4.181	0.095

Abbreviations: CI, confidence interval; CT, computerized tomography; HR, hazard ratio; PGS, paraglottic space.

TABLE 4 Five-year overall, disease-specific, and laryngectomy-free survival according to different categories

	Five-year OS (%)	Five-year DSS (%)	Five-year LFS (%)
TNM location			
Supraglottic	61.1	72.9	85.4
Glottic	67	83.6	71
All	63.9	77.5	78.5
T subclassification			
Pure supraglottic	56.2	71.9	88.7
Anterior transglottic	64.2	87.1	82.3
Lateral transglottic	66.3	74.9	77.5
Pure glotto-subglottic	70.2	82.3	67.9
T topography			
Anterior compartments	61.1	77.3	81.1
Posterior compartments	71.1	78.1	72.9
T classification			
T3	63.2	77	78
T4a	68.1	80.9	81
Nodal burden			
N−	69.2	82.1	76.2
N+	48.7	63.7	87.4
Margins			
Negative	64.3	78.1	79.6
Positive	57.4	69.6	65.7
Stage			
Stage III	69.5	83	78.5
Stage IVa	48	61.9	78.7
Stage IVb	0	0	—
Adjuvant treatment			
No	66.6	80.2	78.1
Yes	57.2	70.6	80.1

Abbreviations: DSS, disease-specific survival; LFS, laryngectomy-free survival; OS, overall survival.

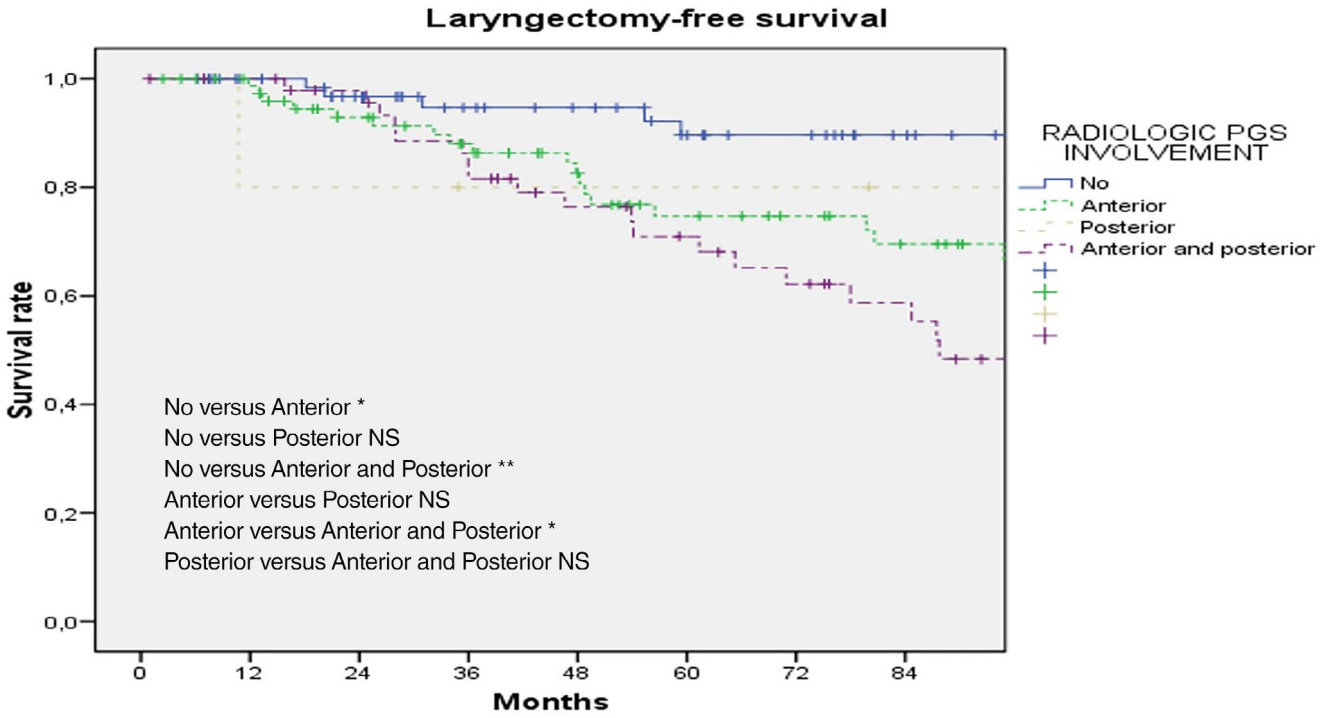

FIGURE 2 Laryngectomy-free survival according to radiologic paraglottic involvement. *$p < 0.005$. PGS, paraglottic space [Color figure can be viewed at wileyonlinelibrary.com]

fixed arytenoid. Other variables that correlated with reduced local control were positive surgical margins and cartilage infiltration (Table 2).

In the multivariate analysis, positive surgical margins (HR = 0.289, $p = 0.046$) and anterior (HR = 0.278, $p = 0.001$) and posterior (HR = 0.269, $p = 0.003$) PGS invasion were independent factors of a reduced local control (LC) with TOLMS, whereas anterior (HR = 3.613, $p = 0.003$) and posterior (HR = 5.196, $p < 0.001$) PGS involvement were independent factors of total laryngectomy (Table 3).

Five-year OS, DSS, and LFS rates were 63.9%, 77.5%, and 77.5%, respectively. Survival rates according to tumor location, tumor extension, and treatment are expressed in Table 4. Patients with posterior PGS involvement did not differ significantly in DSS with those without posterior PGS involvement, but significantly did in 5-year LFS (Figure 2).

4 | DISCUSSION

To the best of our knowledge, this is the first study that analyzes the importance of anterior and posterior PGS in advanced laryngeal tumors treated by TOLMS. The categorization of PGS into two subcompartments was performed according to radiologic landmarks obtained from contrast CT and clinically through the assessment of the arytenoid mobility by laryngeal endoscopic evaluation. These references had been previously reported in other studies, demonstrating its importance for the selection of patients amenable to be treated with an open partial surgery.[5,6]

International guidelines recommend TOLMS in selected locally advanced T3 laryngeal cancers but do not specify which are the characteristics of those cases to be treated. Peretti et al. reported some reasonable limits of transoral resection according to oncologic and functional expectatives.[16] These limits included bilateral involvement of the posterior commissure or of the cricoid cartilage, extensive subglottic growth, and wide extralaryngeal tumor growth. Other experienced surgeons agree that the best candidates are T3 laryngeal tumors located in the anterior compartments of the larynx.[8,17–19] T4a tumors are generally excluded from transoral approach except for very selected cases, and those diagnosed mainly intraoperatively. On the contrary, controversy exists in the literature regarding the indications of tumors with invasion of the vertical plane of the anterior commissure where, if feasible, supracricoid laryngectomy has demonstrated better local control than TOLMS.[20,21]

Although it was not the focus of the present study, our results clearly show that supraglottic tumors have better local control with TOLMS than glottic ones. These findings have been previously corroborated by other studies,[22,23] confirming that, in terms of local control, the best indication for TOLMS are pure supraglottic tumors.

Classification of laryngeal cancer into glottic or supraglottic is not an easy task when tumors present a

vertical extension as it might difficult to determine its origin. This is the case of those lateral tumors arising from the ventricle or anterior transcommissural tumors (in essence, both transglottic tumors). They have been considered at a higher risk than pure glottic in terms of nodal involvement and ultimately survival rates, regardless of the adopted therapeutic option. In our sample, the higher local control with TOLMS was obtained in pure supraglottic tumors, followed by transglottic and lastly by glottic ones. These results were also translated into the 5-year LFS; 88.7% in pure supraglottic, 82.3% in anterior transglottic, 77.5% lateral transglottic; and 67.9% in glottic-subglottic.

When the PGS is affected, the risk of local relapse seems to be similar between anterior and posterior PGS involvement, whereas the risk of salvage total laryngectomy is higher in the case of posterior PGS infiltration. This difference can be explained by the fact that in some patients with anterior PGS involvement, the local recurrence may still be salvaged with other alternatives to total laryngectomy, for instance, supracricoid laryngectomy or chemoradiation protocols, whereas in posterior relapses a total laryngectomy is usually recommended.

Interestingly, no differences in local control with TOLMS or differences in total laryngectomy rates were found between T3 and T4a tumors in our series. This finding most likely reflects a selection bias. In fact, only a few T4a were included in the study, most of them being low volume tumors treated in the early days of TOLMS and the majority under-staged at the time of preoperative diagnosis.

As expected, the presence of positive margins was an independent factor of reduced local control. This circumstance is well known in cancer surgery and confirms that a positive margin has to be systematically addressed.[24–26] In TOLMS, the difficulty relies upon determining what can be considered a negative margin, because monoblock resection is not usually feasible in advanced tumors and shrinkage of the mucosal specimen can exceed 3 mm.[27] In our institution, the surgical limits include the internal perichondrium of the thyroid cartilage, with partial resection or laser vaporization of the cartilage when focal infiltration is suspected by the surgeon. Frozen sections are usually performed from the margins of the tumor bed.[17] The impact of positive, close, or negative margins has been evaluated in a previous study, being the percentage of total laryngectomy of 23.4% in patients with affected margins, 15.4% in the case of close margins, and 9.2% in negative margins.[24] Positive margins were also responsible of a reduced DSS, whereas it could not be demonstrated in the case of close margins.[24]

One of the difficulties in indication and treatment planning relies on the preoperative assessment of T3 cancers, especially the accurate diagnosis of cartilage infiltration and the knowledge of the underlying causes of vocal cord fixation. Regarding the immobility of the vocal cord, the endoscopic evaluation may be somewhat subjective and the impairment be due to a mass effect, muscle infiltration, or cricoarytenoid joint involvement. These three scenarios carry a different prognosis in terms of functional and oncologic outcomes.[28]

Cricoarytenoid fixation is considered a limit for TOLMS and it could be corroborated in our series, where a lower local control was found in those patients with cricoarytenoid impairment. However, posterior radiologic PGS involvement may be present without arytenoid impairment. In fact, half of the patients with intraoperatively confirmed posterior PGS infiltration did not display arytenoid fixation in the preoperative assessment. These are usually limited cases that can be removed transorally including partial arytenoid resection, although close tumor margins may indicate additional adjuvant treatment.

In a recent study, Succo et al. evaluated the radiologic and clinical correlations of arytenoid fixation with respect to partial laryngeal surgery.[28] After histologic assessment, the authors differentiated four different patterns: (I) supraglottic tumors with superior paraglottic (PG) infiltration and involvement of the arytenoid from above, with its fixation due to weight effect but without direct involvement of the cricoarytenoid unit (CAU), (II) glottic carcinoma infiltrating the inferior PGS and extending toward the CAU, (III) glottic-subglottic carcinoma invading and enveloping the cricoarytenoid joint, and (IV) transglottic and infraglottic carcinoma with massive involvement of the CAU and of the posterior cricoarytenoid muscle, reaching the hypopharyngeal submucosa. The authors stated that in Patterns I and II, open partial horizontal laryngectomy types II + arytenoid or type III according to European Laryngological Society (ELS) classification[29] was still an option whereas a total laryngectomy should be recommended in Patterns III and IV.[28]

Contrast enhanced CT-scan is the most used imagine technique for staging and treatment planning, but has some limitations in the PGS, where the tumor can be hidden within the normal soft tissues, or in its capacity to diagnose with precision the presence of cartilage infiltration.[30,31] Pietragalla et al.[32] evaluated the current role of computed tomography imaging in the evaluation of cartilage invasion by laryngeal carcinoma. CT images were corroborated with histologic evaluation after total laryngectomy. The highest accuracy was obtained for cricoid infiltration (100%) followed by full thickness thyroid infiltration (85%), focal erosion of the inner cortex of the thyroid (75%), and arytenoid infiltration (67.5%). In the case of the inner cortex of the thyroid, the positive and

negative predictive values were 100% and 54.5%, respectively. For a T3 laryngeal cancer with radiologic PGS infiltration treated transorally, this means that the possibility of intraoperative focal infiltration of the cartilage should not be underestimated. In our series, some suspected radiological infiltration of the posterior PGS were not finally confirmed intraoperatively and the contrary occurred with the presence of focal erosion of the cartilage, confirming the difficulties to have a precise preoperative diagnosis of focal infiltration of the thyroid cartilage.

Recently, magnetic resonance imaging (MRI) acquired with optimized high-resolution protocol and surface coils has been proposed as the imaging technique of choice to assess PGS. The contrast resolution obtained with different MRI sequences accurately differentiates muscle neoplastic invasion from its inflammatory edema.[33] MRI achieves a specificity of 96.9% with a sensitivity of 78.6% for PGS evaluation, but still presents limitations in the cartilage assessment (specificity 70%).[34,35] Moreover, the limited availability of MRI in some centers and the presence of motion artifacts due to long acquisition times could make this technique not to be considered as standard everywhere.[36]

Despite being locally advanced tumors, only 28% of our patients received adjuvant treatment, the majority of them due to nodal burden. In addition, the type of adjuvant treatment differed over time in line with evidence-based medicine. The National Comprehensive Cancer Network guidelines state that surgical patients with advanced-stage head and neck cancer and risk factors other than extranodal extension or positive margins should consider postoperative adjuvant treatment. However, the advantage of its administration in T3N0-N1 remains controversial and may impair the larynx function after partial surgery. In a retrospective study of 5319 patients with Stage III-IV head and neck cancer who received primary surgical treatment with postoperative adjuvant treatment, a survival benefit was found in patients <70 years of age with T1-4N2-3 disease, but not in patients ≥70 years of age or those with T3-4N0-1 disease.[37] In our study, the administration of adjuvant treatment was not found to be an independent factor of local control or larynx preservation.

Survival rates in our series were superior to those reported in the literature for organ preservation protocols,[38,39] with the glottic tumors presenting the highest survival rates and the supraglottic ones the highest larynx preservation. As mentioned previously, only one out of four patients required adjuvant radiation, an aspect that may be considered as strategic if a salvage laryngectomy would be required or in the case of a second metachronic tumor. On the contrary, survival rates seemed to be somewhat inferior to those reported in the literature for anterior T3-T4a tumors treated with upfront supracricoid laryngectomies.[5,40] These differences were not observed for posterior compartment involvement. Finally, another important consideration is that TOLMS was not precluded by patient age, as are open partial surgery or chemoradiation protocols. Thus, for elderly patients, TOLMS may be the best alternative to total laryngectomy.

The main limitation of the study is its retrospective nature that may be responsible of some selection bias and small changes in protocols over time. PGS involvement was evaluated by CT scan, which has intrinsic limitations in determining the exact extension of the lesion, but otherwise has been the standard for preoperative staging in the past decades. Moreover, the finding of a fixed arytenoid was considered as a sign of posterior PGS involvement, although its clinical impairment was subjective, and the histologic assessment was not possible due to piecemeal resection.

Among the strengths, the large number of patients included and the long follow-up represents one of the largest series of locally advanced tumors worldwide. Moreover, being TOLMS the standard treatment for thoseT3 amenable to preserve the larynx in our center, the series represent consecutive patients who were treated according to a standardized protocol and were followed up for the same team, who prospectively completed the database over the past 20 years.

In conclusion, our study suggests that laryngeal compartmentalization has an impact on local control and larynx preservation in patients with advanced laryngeal cancer treated with TOLMS. The posterior PGS involvement is the worse location in terms of larynx preservation. Further prospective studies are necessary to validate our findings and to confirm the key relevance of laryngeal PGSs at the time of selecting the best organ preservation strategy.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data are available on request due to privacy/ethical restrictions.

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