

COMPUTED TOMOGRAPHY CONTRIBUTION TO THE STAGING OF SUPRAGLOTTIC SQUAMOUS CELL CARCINOMA*

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Abstract **OBJECTIVE:** The present study was aimed at evaluating the role of computed tomography in the local clinical staging of supraglottic tumors according to the TNM classification, as well as the interobserver agreement on the detection of the tumor extent. **MATERIALS AND METHODS:** Thirty-nine dossiers of inpatients of Hospital Heliópolis with supraglottic squamous cell carcinoma in the period between 1988 and 1998 were retrospectively evaluated. CT studies were individually analyzed by two radiologists. The kappa test was utilized for evaluating the interobserver agreement. **RESULTS:** Computed tomography has played a decisive role in the upstaging of 38.5% of cases, as a result of a deep tumor extent undetected at clinical examination. **CONCLUSION:** Interobserver agreement was considered as excellent for vocal folds and subglottis; good for supraglottic, paraglottic and preepiglottic spaces, thyroid and cricoid cartilages and for extralaryngeal tumor extension; and regular for the base of the tongue.

Keywords: Laryngeal neoplasms; Squamous cell carcinoma; Computed tomography; Tumors staging.

Resumo *Contribuição da tomografia computadorizada no estadiamento do carcinoma de células escamosas da supraglote.*

OBJETIVO: Este trabalho tem como objetivos avaliar a influência da tomografia computadorizada no estadiamento local da classificação TNM dos tumores da supraglote e avaliar a concordância interobservadores na detecção da extensão tumoral. **MATERIAIS E MÉTODOS:** Foram avaliados, retrospectivamente, 39 pacientes com carcinoma de células escamosas da supraglote atendidos no Hospital Heliópolis entre 1988 e 1998. Os exames de tomografia computadorizada foram analisados por dois radiologistas individualmente. Para a avaliação da concordância interobservadores utilizou-se o índice kappa. **RESULTADOS:** A tomografia computadorizada foi determinante no estadiamento mais avançado em 38,5% dos casos, decorrente de extensão tumoral profunda não-identificada no exame clínico. **CONCLUSÃO:** A concordância interobservadores foi considerada ótima para as pregas vocais e subglote; boa para a supraglote, espaços paraglótico e pré-epiglótico, cartilagens cricóide e tireóide e para extensão tumoral extralaringea; e regular para a base da língua. *Unitermos:* Neoplasias laríngeas; Carcinoma de células escamosas; Tomografia computadorizada; Estadiamento de neoplasias.

INTRODUCTION

Laryngeal cancer is a potentially curable disease. About 30% of these tumors occur in the supraglottis, and 95% of them are squamous cell carcinomas, with a peak of incidence in the fifth decade of life and a 5/1 men/women ratio. Radiotherapy and conservative surgery, that can preserve functions such as deglutition and voice, have made the accurate staging and definition of the tumor extent imperative for an appropriate therapeutic planning. For this

purpose, an accurate knowledge of the real tumor extent and condition of the laryngeal cartilaginous skeleton is indispensable⁽¹⁻⁵⁾. Laryngoscopy is of help in the evaluation of the superficial tumor extent, while computed tomography (CT) plays a significant role in the evaluation of the deep tumor extension, for example, to the preepiglottic and paraglottic spaces⁽⁶⁻⁹⁾.

The present study is aimed at evaluating the interobserver agreement in the detection of neoplastic involvement in several sites and extensions of the supraglottic larynx, and the influence of CT utilization on the clinical staging as regards higher levels of the T parameter in the TNM classification of supraglottic tumors.

MATERIALS AND METHODS

The present study involved inpatients of the Department of Head & Neck at Hospi-

tal Heliópolis, with supraglottic squamous cell carcinoma, in the period between 1988 and 1998. The patients inclusion criteria adopted were the following: a) tumor clinically staged by means of direct/indirect laryngoscopy; b) squamous cell carcinoma diagnosed by biopsy; c) CT study performed before any treatment (chemotherapy, radiation therapy or surgery).

Thirty-nine dossiers meeting the pre-established criteria were evaluated. Thirty-three patients (84.6%) were men and six (15.4%) women, corresponding to a men/women ratio of 5.5/1. Patients' ages ranged between 39-74 years among men, and 40-67 years among women, with mean ages of 55 and 53 years, respectively, and 54.9 for both sexes. All of these patients were smokers, and 31 (79.5%) of them reported moderate or heavy use of alcohol.

CT studies were performed on third generation equipment, with acquisition of

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axial slices with 5 mm thickness and increment, after intravenous, iodinated contrast media injection at a dose of 1.0–2.0 ml/kg, and 60–76% concentration, with the patient in supine position with neck extension, during calm respiration and without deglutition.

The studies were individually evaluated by two radiologists with no previous knowledge of findings at physical examinations, laryngoscopic or histopathological studies. The aspects analyzed were concerned with the T parameter, according to the TNM classification defined by the International Union Against Cancer (UICC), reviewed in 1997.

The evaluation covered tumor extension towards the following supraglottic regions: epiglottis, aryepiglottic fold, ventricular folds and their eventual extensions towards the vocal folds, subglottis, base of the tongue, preepiglottic space, paraglottic space, thyroid cartilage, cricoid cartilage, and extralaryngeal soft tissues.

Deep structures were considered as affected when one or more of the following criteria were present: blurring of fatty tissues planes, local mass effect and direct involvement of the lesion, characterized by the presence of tumor with soft tissues density in the region to be evaluated. The cartilages invasion was considered in the presence of lesions internal and externally to the cartilage, or when erosion was detected (these criteria were utilized for the cartilages evaluated in the present study); sclerosis was the invasion criterion in the evaluation of the cricoid cartilage involvement. The subglottic involvement was considered in the presence of any tissue adjacent to the inner surface of the cricoid cartilage.

The staging was based on the T parameters of tumor extent defined by the UICC (reviewed in 1997). The tomographic staging was based on the analysis performed by the most experienced radiologist specialized in head and neck.

The kappa test (κ) was utilized in the evaluation of interobserver agreement in the CT studies reading (Chart 1), considering the significance level = 0.05 and a 95% confidence interval⁽¹⁰⁾. Changes in the clinical staging resulting from the CT evaluation were based on the T tumor ex-

Chart 1 Evaluation of interobserver agreement according to kappa index⁽¹⁰⁾.

κ value	Agreement
< 0.00	Bad
0.00–0.20	Feeble
0.21–0.40	Poor
0.41–0.60	Regular
0.61–0.80	Good
0.81–0.99	Very good
= 1.00	Excellent

tent criteria defined by the UICC, observing the regions involved in the upstaging.

RESULTS

1 – Interobserver agreement

Interobserver agreement was considered as good for supraglottic sites — epiglottis ($\kappa = 0.655$), aryepiglottic folds ($\kappa = 0.754$), and ventricular folds ($\kappa = 0.794$). Also, it was considered as good for evaluation of paraglottic ($\kappa = 0.693$) and preepiglottic ($\kappa = 0.744$) spaces. The evaluation of vocal folds reached a $\kappa = 0.854$, with interobserver agreement considered as very good. The agreement was good for evaluation of thyroid cartilage ($\kappa = 0.674$) and cricoid cartilage ($\kappa = 0.687$). A regular interobserver agreement ($\kappa = 0.480$) was found in the evaluation of the base of the tongue; and for the subglottis, the agreement was very good ($\kappa = 0.880$), and good in the evaluation of the extralaryngeal tumor extension ($\kappa = 0.747$).

2 – Clinical and tomographic staging

At clinical examination, the 39 patients were classified, based on the tumor extent, as follows: two patients (5.1%) T1, 13 (33.3%) T2, 18 (46.2%) T3, and six (15.4%) T4. The reclassification based on

CT studies was the following: seven patients (17.9%) T2, 21 (53.8%) T3 and 11 (28.2%) T4. A comparison between clinical and CT staging showed a coincidence in 22 cases (56.4%) — five (12.8%) T2 stage, 12 (30.8%) T3 stage, and five (12.8%) T4 stage (Tables 1 and 2). The two patients with clinical staging T1 were upstaged as T2 and T3 at CT. No patient was staged as T1 by CT (Table 1, Graphic 1).

Of 13 patients (33.3%) with clinical staging T2, only five (38%) were coincidental at CT. The remaining eight patients (61%) were upstaged at CT as follows: seven T3 and one T4. Of 18 patients with clinical staging T3, 12 (67%) were coincidental at CT. The remaining six patients (33%) were not coincidental; five were upstaged as T4. One patient was substaged as T2 at CT (Table 1, Graphic 1).

Five of the six (83%) patients clinically staged as T4 had the same result at CT; in only one patient (17%) the CT staging (T3) was different from the clinical staging. This may be explained since there was a clinical suspicion of invasion of the cartilage by the tumor that had not been observed at CT (Table 1).

There was a coincidence between clinical and tomographic staging in 38.5%, 66.7%, and 83.3% of cases respectively classified as T2, T3 and T4.

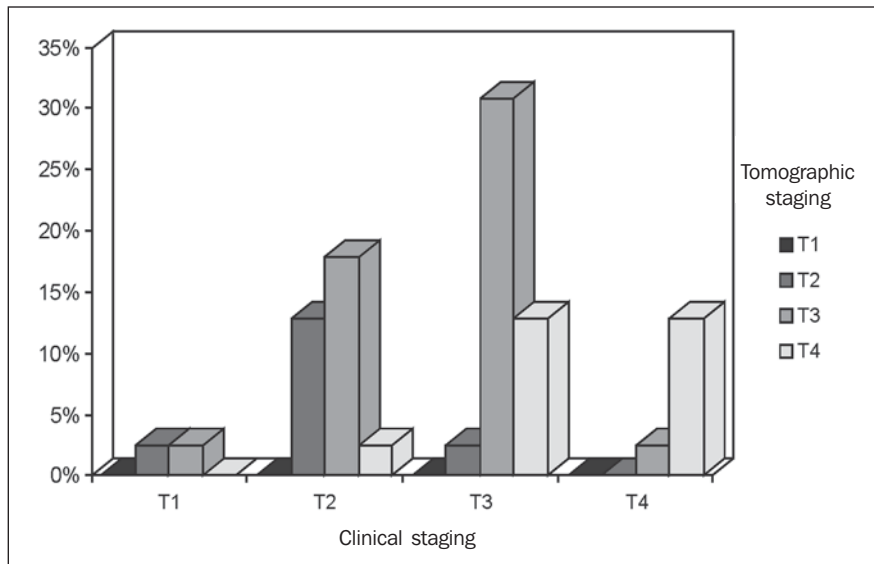
The tomographic staging increased the clinical staging in 61.5% of T2-staged cases, and in 27.8% of T3-staged cases. As previously mentioned, two T1-staged cases were upstaged at CT. Two cases were substaged at CT; the first one because the TC failed to detect vocal fold fixation, decreasing the clinical staging from T3 to T2; in the other case, the staging decreased from T3 to T2 as a result of the clinical suspicion of invasion of the cartilage by the tumor that had not been confirmed at CT.

Table 1 Distribution of patients according clinical and tomographic stagings.

Tomographic staging	Clinical staging				Total
	T1	T2	T3	T4	
T1	0	0	0	0	0
T2	1	5	1	0	7 (17.9%)
T3	1	7	12	1	21 (53.8%)
T4	0	1	5	5	11 (28.2%)
Total	2 (5.1%)	13 (33.3%)	18 (46.2%)	6 (15.4%)	39 (100.0%)

Table 2 Sites of neoplastic invasion determining upstaging at computed tomography.

Determining factors	T1→T2	T1→T3	T2→T3	T2→T4	T3→T4
Involvement of two supraglottic subsites	1				
Preepiglottic space invasion		1	1		
Paraglottic space invasion			1		
Preepiglottic and paraglottic spaces invasion			4		
Invasion of the preepiglottic space and base of the tongue			1		
Cartilages invasion				1	1
Invasion of cartilages and extralaryngeal soft tissues					4
Total	1	1	7	1	5



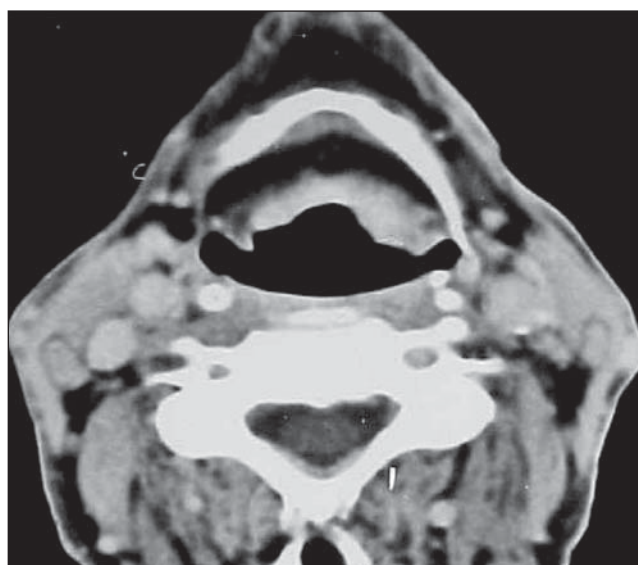
Graphic 1. Tomographic staging as compared to clinical staging.

Computed tomography has played a decisive role in the upstaging in 15 (38.5%) cases of the whole casuistic according to the factors listed on Table 2.

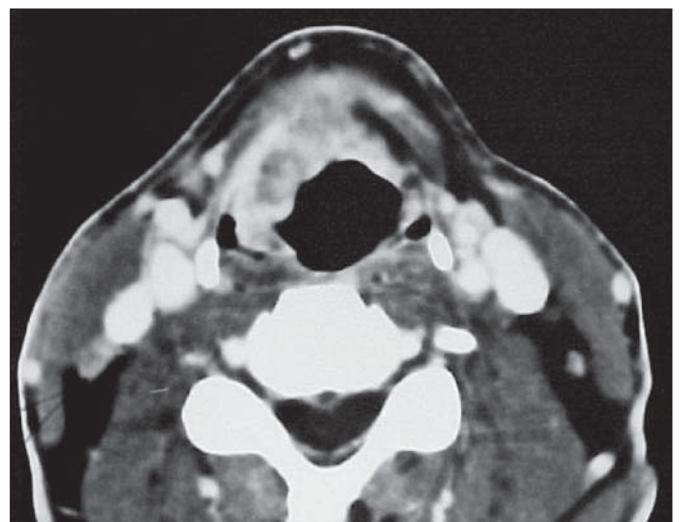
DISCUSSION

According to the literature, CT presents a higher staging accuracy (between 68% and 82.7%) than the clinical examination (between 52% and 74.3%) for supraglottic tumors. This staging accuracy potentialized with the association between CT and clinical evaluations, reaching 91.4% of effectiveness^(4,7,11-17).

Also, according to data in the literature, CT determines an increase in clinical staging ranging between 19.4% and 30.7%^(3, 12,15,18). In the present study, this upstaging



A



B

Figure 1. Supraglottic squamous cell carcinoma with extension into the pre-epiglottic space. Clinical staging T1; tomographic staging T3. **B:** Aryepiglottic fold squamous cell carcinoma. Clinical staging T2; tomographic staging T3.

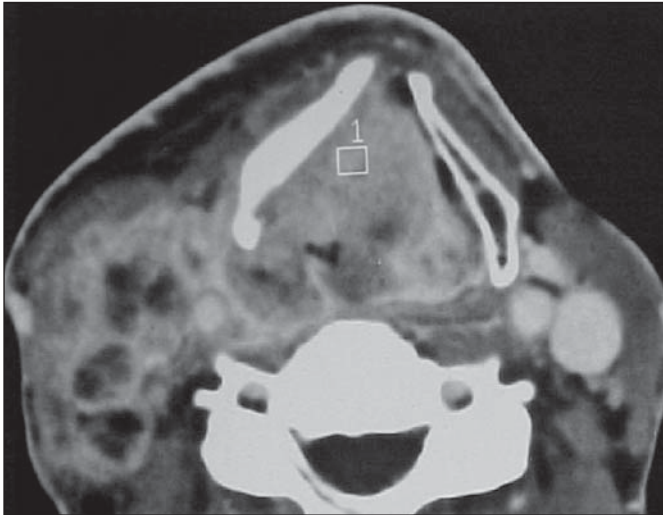


Figure 2. Axial tomographic view at the level of ventricular folds, where a voluminous tumor-like lesion is observed, causing constriction of the larynx lumen. There is a tumor-like component invading the right paraglottic space. Sclerosis is observed on the right wing of the thyroid cartilage, as well as lymphadenomegalies with hypodense nucleus at right.

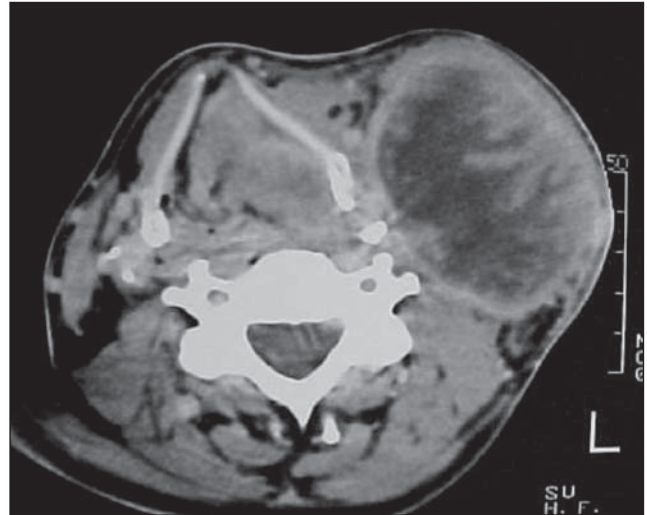


Figure 3. CT axial view at the level of supraglottis showing tumor infiltration into the left paraglottic space and tumor on both sides of the thyroid cartilage indicating invasion. Clinical staging T3, tomographic staging T4. Also, a voluminous necrotic lymph node block is observed at right.

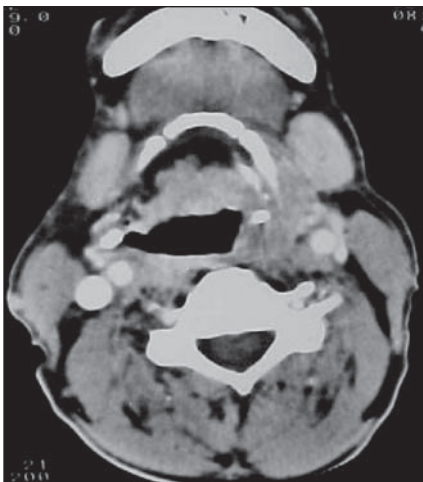


Figure 4

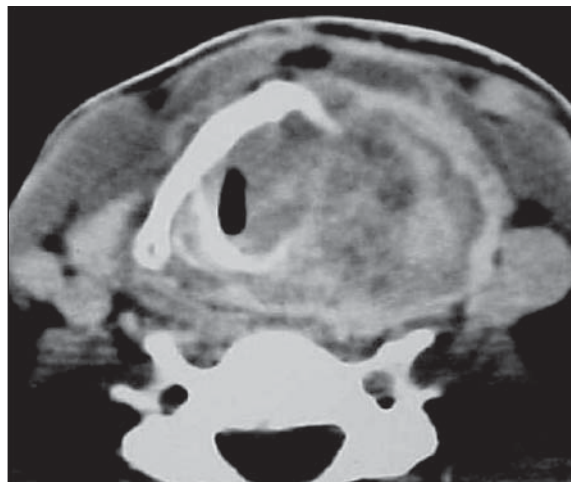


Figure 5

Figure 4. Tumor-like lesion with an infiltrative aspect in the epiglottis, invading the pre-epiglottic space, and tumor-like component infiltrating the extralaryngeal soft tissues at left. Clinical staging T2, tomographic staging T4.

Figure 5. Axial tomographic view of the thyroid cartilage region. Infiltrative process determining erosion of the left lamina of the thyroid cartilage and infiltration to extralaryngeal soft tissues. Clinical and tomographic staging T4.

was observed in 38.5% of cases, similarly to the findings of other authors; main reasons were: cartilages invasion, infiltration into the pre-epiglottic and paraglottic spaces, and extralaryngeal tumor extension that had not been detected by laryngoscopy (Table 2). Patients clinically staged as T2 were mostly upstaged at CT. Only two cases clinically staged as T1 met the initial inclusion criteria, and were upstaged. The low number of tumors initially staged as T1 may be explained by: low socio-economic level of the patients, delay in the search for medical assistance, late symptoms in supraglottic tumors, tumors clinically staged as

T1 are not routinely submitted to pretherapeutic CT.

CT may determine a substaging in up to 10.6% of cases⁽³⁾; in the present study, two cases were substaged at CT in comparison with the clinical examination: one case where the clinical examination had detected fixation of vocal fold (not detected at CT), and another where the CT substaged from T4 to T3, considering the clinical suspicion of cartilage invasion not confirmed by CT.

It is important to note that false-positive cases in CT evaluation may occur as a result of inflammatory alterations or peritu-

moral edema. On the other hand, false-negative cases result from tumors restricted to the mucosal surface or presenting with microscopic tumor infiltration^(3,19-21).

The deep tumor extension into the preepiglottic and paraglottic spaces is neglected in the laryngoscopic evaluation, so CT becomes an essential method in the evaluation of these regions^(22,23). The infiltration of these spaces has been implicated in the occurrence of lymph node metastasis⁽¹⁹⁾ and tumor recurrence⁽²⁴⁾. An association between infiltration of the pre-epiglottic space and invasion of the base of the tongue has been reported⁽²⁵⁾.

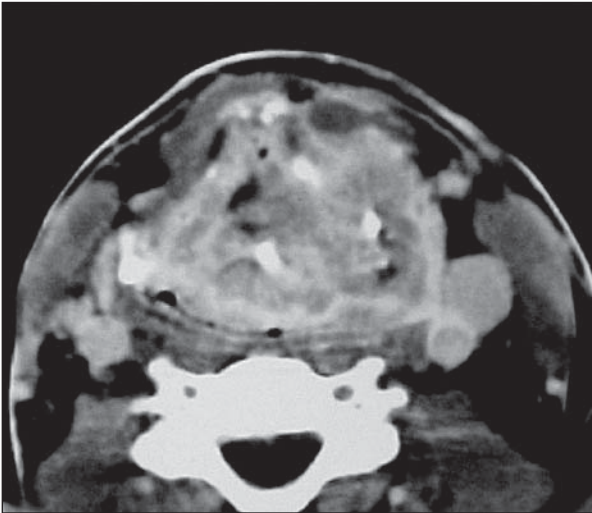


Figure 6. Extensive tumor conditioning erosion of the thyroid cartilage and extension to extralaryngeal soft tissues. Almost complete arial column obliteration is observed. Clinical and tomographic staging T4.

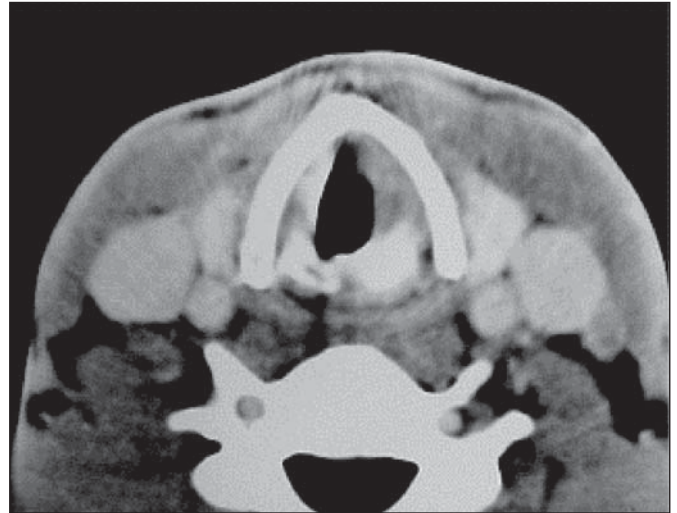


Figure 7. Asymmetrical thickening and heterogeneous attenuation of the right vocal fold. Histopathology: chronic inflammatory alterations. False-positive result.

The interobserver agreement was considered as good for all of the supraglottic sites, as well as for the pre-epiglottic and paraglottic spaces. An excellent interobserver agreement was found in the evaluation of vocal folds and subglottic space. A previous study has also demonstrated a good interobserver agreement for supraglottic and subglottic spaces, and very good for vocal folds⁽²⁶⁾.

In one case where both observers had considered that the left vocal fold was infiltrated by the tumor, the histopathological analysis demonstrated that its thickening was a result from a chronic inflammatory reaction, characterizing a false-positive case; this finding being indistinguishable from tumor infiltration. In another case of disagreement, where clinical staging was T3 — because of vocal fold fixation —, the CT substaged as T2, since this method had not detected this finding; the histopathological analysis detected the involvement of the vocal fold by the tumor. The relevance of the correlation between clinical/endoscopic and tomographic evaluations becomes clear, as the actual tumor extent is established with higher accuracy.

The CT evaluation of laryngeal cartilages is highly specific, however, its sensitivity is low, with a high rate of false-negative results, and may affect the therapeutic indication for partial laryngectomy or radical radiation therapy⁽⁷⁾. Gross carti-

lage destruction may be easily identified, while mild macroscopic or microscopic invasions are unlikely to be detected by CT^(4,27-29). The irregular calcification pattern is the factor that represents one of the major difficulties in the evaluation of cartilages, especially thyroid cartilage^(8,28-30). Good interobserver agreement was found for evaluation of tumor invasion of the thyroid cartilage and cricoid cartilage. Hermans et al.⁽³⁰⁾ have found an interobserver agreement considered as just regular. This may be explained by the fact that infiltration criteria were adopted for each of the cartilages. Sclerosis was considered as a sign of infiltration just for the cricoid cartilage, since infiltration into the thyroid cartilage frequently is just an indication of inflammatory reaction⁽⁵⁾.

The CT evaluation of the base of the tongue is not effective principally because of secretions deposition that may simulate tumor involvement, as well as the presence of redundant lymphatic tissue^(3,17). CT failed to identify one third of cases of infiltration into the base of the tongue. Interobserver agreement was considered as just regular in the evaluation of tumor infiltration into the base of the tongue. The histopathological analysis demonstrated two patients with this finding, one of them identified by both observers, and the other, by only one observer. These two cases presented invasion of the preepiglottic space

confirmed by anatomopathological analysis.

Subglottic invasion may occur both by superficial mucosal dissemination and lateral infiltration of the elastic cone⁽³⁾. On the other hand, tumor extension to other extralaryngeal soft tissues may occur through the larynx or thyrohyoid or cricoid membranes⁽¹⁷⁾. Laryngoscopy is useful in the evaluation of subglottis, but its accuracy may be impaired in case of exophytic tumors, and extralaryngeal extension may not be detected; this is one of the main reasons for clinical substaging⁽⁷⁾. CT may represent a useful tool in this evaluation, presenting a very good interobserver agreement for subglottis, and good for extralaryngeal extension.

The adequate reproducibility of the method is demonstrated by the good interobserver agreement, in spite of the lack of opportunity to compare data with histopathological results regarding each of the sites evaluated for different reasons like incomplete pathology reports or patients who had not been submitted to surgery. It should ever be held in mind that false-positive results do occur (due to reactional edema/thickening), and that they are indistinguishable from tumor infiltration findings, and so do false-negative results (due to microscopic invasion, or limited to the mucosal surface — undetectable by the current tomographs), possibly leading to

substaging. However, the good CT reproducibility becomes more significant in face of the tendency towards more conservative, and frequently non-surgical treatments for laryngeal tumors. As a result CT becomes an important tool in the pretherapeutic evaluation of these patients.

CONCLUSIONS

In the present study, computed tomography presented a very good interobserver agreement in the evaluation of tumor involvement in the vocal folds and tumor extension into the subglottis. Interobserver agreement was considered as good for analysis of epiglottis, aryepiglottic folds, ventricular folds, preepiglottic space, paraglottic space, thyroid and cricoid cartilages, and for evaluation of extralaryngeal tumor extension. For evaluation of tumor involvement in the base of the tongue, the interobserver agreement was considered as regular.

CT upstaged 38.5% of patients with supraglottic cancer. The greatest difference between clinical and tomographic stagings was found in the group of patients with clinically staged T2 tumors, and CT upstaged 61.5% of these patients.

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