Correlation between preoperative endoscopic findings and computed tomography with postoperative histopathology in the staging of laryngeal carcinoma

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Background
Laryngeal cancers represent 4.5% of all malignancies and 28% of malignancies of the upper aerodigestive tract. Different modalities for pretherapeutic assessment have been advocated including endoscopy and radiology.
Aim
The objective of the current study is to assess the accuracy of preoperative CT and clinical/endoscopic staging of laryngeal tumors by comparing clinical and imaging findings of each modality with histologic cross-sections of surgical specimens.
Methods
This prospective study included thirty patients with cancer larynx who underwent surgical treatment. All patients underwent transnasal fiberoptic laryngoscopy with photographic documentation. CT scan axial slices of 2-mm thickness with contrast were obtained. The surgical specimens were cut in whole-organ slices parallel to the plane of the axial CT.
Results
The T stage was correctly determined by both endoscope and CT scan in 23 cases. The agreement between perceived T stage by endoscope and CT with histopathological analysis was 100% for T1, 66.7% for T2, 80% for T3 and 66.6% for T4.
Conclusion
Multi Slice CT scan is superior to laryngoscopy in the evaluation of T3 and T4 tumors. However, laryngoscopy is better than MSCT in the evaluation of T1 and T2 lesions.

Keywords:
laryngeal carcinoma, laryngoscopy, multislice computed tomography

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Introduction

Laryngeal cancers represent 4.5% of all malignancies and 28% of malignancies of the upper aerodigestive tract. Squamous cell carcinoma constitutes 90% of the malignant laryngeal tumors with different incidences of prevalence according to the subsite affected (glottic, supraglottic, and subglottic regions) [1].

The management of laryngeal carcinoma depends on accurate preoperative TNM staging of the tumor. Such preoperative TNM staging relies on the combination of information from cross-sectional imaging and endoscopic examination [2].

There is currently no recommendation from the UICC (The Union for International Cancer Control) for pretherapeutic assessment [endoscopy, computed tomography (CT), and MRI] specifying in particular the indication of each modality of them [3].

The aim of this work was to assess the accuracy of preoperative CT and clinical/endoscopic staging of laryngeal tumors by comparing clinical and imaging findings of each modality with histologic cross-sections of surgical specimens and to clarify the impact of these diagnostic modalities on the pretherapeutic staging of laryngeal carcinoma.

Patients and methods

Patients

This prospective study was conducted on 30 randomly selected patients with cancer larynx who underwent surgical treatment (total or partial laryngectomy) at the Otorhinolaryngology Department, Faculty of Medicine.

All procedures performed in this study were in accordance with the ethical standards of the Institutional and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Inclusion criteria

(1) Willing patients and those able to sign a written informed consent for the surgery.
(2) Generally fit for surgery with 'adequate cardiological and hematological functions'.
(3) Adult male or female.
(4) No prior treatment modality.
(5) Histologically confirmed diagnosis of laryngeal squamous cell carcinoma (SCC).

Exclusion criteria

(1) Patient is refusing surgery.
(2) Patients who are unfit for surgery or patients with distant metastasis.
(3) Any prior or current treatment modality other than surgery.
(4) Carcinomas other than SCC.
(5) History of another malignancy within the last 5 years.

Methodology

Clinical and radiological staging 'TNM' of the primary tumor as well as neck nodes were based on physical examination, endoscopic assessment, and radiological findings according to TNM staging of the American Joint Committee on Cancer (AJCC) Staging classification of 2010.

All the patients in the study were subjected to the following.

History

Full history taking including full demographic data and otorhinolaryngological history with special concern about the type and duration of laryngeal symptoms, previous operations, or radiotherapy.

Examination

Full otorhinolaryngological examination with fiberoptic laryngoscopic assessment was done to assess subglottic as well as anterior commissure extension and vocal cord mobility.

Imaging

Machines used

All patients underwent CT scanning performed using a 64 detector, multislice CT device (Aquillion 64; Toshiba, Tokyo, Japan). Iohexal 75% was used as the contrast material (Omnipaque 300, GE Healthcare Ireland Limited, Cork, Ireland).

Interpretation

Radiological assessments were performed by two experienced radiologists who were blinded to the endoscopic and laryngoscopic findings, evaluations on axial slices of 2–3 mm thickness obtained from the base of the tongue to the trachea and a consensus decision was reached for each case. Images were assessed at the soft tissue and the bone windows. All subsites of the larynx as well as the paraglottic space, preepiglottic space, cartilages (thyroid, cricoid, and arytenoid cartilages), and extralaryngeal tissues were inspected for tumor invasion.

Direct laryngoscopy and biopsy

For histopathologic examination and mapping of tumor extension. Hopkins endoscopes could be combined with the laryngoscope to assess and measure subglottic extension.

Surgery

The patients underwent surgery within 2 weeks. Surgery was tailored according to TNM staging. Techniques used were: total laryngectomy, supracricoid partial laryngectomy, and vertical hemilaryngectomy.

The final T assignments were based on histopathological interpretations of surgical specimens.

Postoperative histologic preparation of specimens

All surgical specimens underwent fixation in 4% formaldehyde for 72 h followed by decalcification in De-Cal-Histol decalcifying Agent for 2 weeks. Axial whole-organ slices were cut at a thickness of 1–3 mm parallel to the plane of the axial CT images. At each level at least one slice was processed for microscopic examination and stained with hematoxylin and eosin.

Collection of data and statistical analysis

All collected data were recorded completely on clinical sheets for all patients. Data were then entered on the computer using the program Microsoft Excel 2010. Statistical package for the social sciences (SPSS; SPSS Inc., Chicago, Illinois, USA) software program version 20 was used for statistical analysis.

Data were summarized using mean and SD for quantitative variables. Frequency percentage was used for the qualitative ones.

Equations used in data analysis:

TP=true positive.

TN=true negative.

FP=false positive.

FN=false negative.

$$\text{Accuracy} = \frac{\text{TP} + \text{TN}}{(\text{TP} + \text{FP} + \text{TN} + \text{FN})}.$$

$$\text{Sensitivity} = \frac{\text{TP}}{\text{TP} + \text{FN}}.$$

$$\text{Specificity} = \frac{\text{TN}}{\text{TN} + \text{FP}}.$$

$$\text{Positivepredictivevalue(PPV)} = \frac{\text{TP}}{\text{TP} + \text{FP}}.$$

$$\text{Negativepredictivevalue(NPV)} = \frac{\text{TN}}{\text{TN} + \text{FN}}.$$

The results were then tabulated and statistically analyzed.

Results

This study included 30 men with proven diagnosis of cancer larynx. Their age ranged from 45 to 75 years with a mean of 61 years

Site of origin was detected in 10 patients at the supraglottic region, 14 patients at the glottic region, five patients had transglottic tumors, and a single patient had subglottic tumor. Of the 30 patients affected, 11 cases had the tumor epicenter on the left side, 13 had the epicenter on the right side, and six cases had the epicenter of the tumor in the midline.

Twenty patients underwent total laryngectomy, eight patients underwent supracricoid partial laryngectomy, and two patients underwent frontolateral laryngectomy.

Assessment of subglottic involvement

Subglottic area was involved in 10 patients. Endoscopy showed the presence of subglottic mucosal invasion with a sensitivity of 40%, a specificity of 100%, a positive predictive value (PPV) of 100%, an negative predictive value (NPV) of 76.9%, and anccuracy of 80% (Table 1).

Table 1 Endoscopic findings (*n*=number of patients)

	True positive (*n*)	True negative (*n*)	False positive (*n*)	False negative (*n*)
Subglottic area	4	20	0	6
Aryepiglottic fold	6	24	0	0
Vocal cord	16	4	1	9
Anterior commissure	3	16	1	10

Table 2 Computed tomography findings (*n*=number of patients)

	True positive (*n*)	True negative (*n*)	False positive (*n*)	False negative (*n*)
Subglottic area	8	19	1	2
Paraglottic space	16	8	3	3
Preepiglottic space	6	22	1	1
Aryepiglottic fold	5	23	1	1
Vocal cord	23	3	2	2
Anterior commissure	9	15	2	4
Cartilage invasion	10	10	2	8
Extralaryngeal spread	4	23	1	2

CT scan showed the presence of subglottic mucosal invasion with a sensitivity of 80%, specificity of 95%, a PPV of 88.8%, an NPV of 90.4%, and an accuracy of 90% (Table 2).

Assessment of vocal cord invasion

Sixteen patients with glottic invasion were diagnosed endoscopically. The diagnostic accuracy of endoscopy for detecting glottic mucosal invasion was as follows: sensitivity, 64%; specificity, 80%; PPV value, 94.1%; NPV, 30.7%; accuracy 66.6% (Table 1).

Twenty-three patients with glottic invasion were diagnosed radiologically. The diagnostic accuracy of CT for detecting glottic mucosal invasion was as follows: sensitivity, 92%; specificity, 60%; PPV value, 92%; NPV, 60%; accuracy 86.6% (Table 2).

Assessment of aryepiglottic fold invasion

Aryepiglottic fold was involved in six patients. Endoscope showed the presence of aryepiglottic fold invasion with a sensitivity of 100%, a specificity of 100%, a PPV of 100%, an NPV of 100%, and accuracy of 100% (Table 1).

Table 3 T stages by endoscope, computed tomography, and pathological examinations

	Stage	Pathology (number of patients)			
		T1	T2	T3	T4
Endoscope	T1	**3**	0	2	0
	T2	0	**3**	5	2
	T3	0	0	**8**	7
CT	T0	2	0	0	0
	T1	**1**	0	3	0
	T2	0	**2**	0	1
	T3	0	1	**11**	2
	T4	0	0	1	**6**
Combined (endoscope and CT)	T1	**3**	0	2	0
	T2	0	**2**	0	0
	T3	0	1	**12**	3
	T4	0	0	1	**6**

CT, computed tomography.

Table 4 Preoperative staging in percent in consistency with pathologic staging (*n*=number of patients)

Pathology		Endoscope (%)	CT (%)	Combined (%)
Stage	*n*			
T1	3	100	33.3	100
T2	5	100	66.7	66.7
T3	13	53.3	73.3	80
T4	9	–	66.6	66.6

CT, computed tomography.

CT scan showed the presence of invasion with a sensitivity of 83.3%, specificity of 95.8%, PPV of 83.3%, NPV of 95.8%, and an accuracy of 93.3% (Table 2).

Assessment of the paraglottic space

Radiological evaluation of the paraglottic space invasion showed a sensitivity of 84.2%, specificity of 72.7%, PPV of 84.2%, NPV of 72.7%, and an accuracy of 80% (Table 2).

Assessment of the preepiglottic space

CT scan showed the presence of preepiglottic space invasion with a sensitivity of 85.7%, specificity of 95.6, PPV of 85.7%, NPV of 95.6%, and an accuracy of 93.3% (Table 2).

Assessment of laryngeal cartilage invasion

Thyroid and cricoid cartilages were assessed, CT scan showed the presence of cartilage invasion with a sensitivity of 55.5%, specificity of 83.3%, PPV of 83.3%, NPV of 55.5%, and an accuracy of 66.6% (Table 2).

Assessment of Extralaryngeal soft tissue invasion

CT scan showed the presence of extralaryngeal invasion with a sensitivity of 66.6%, specificity of 95.8%, PPV of 80%, NPV of 92%, and an accuracy of 90% (Table 2).

Assessment of staging of tumor infiltration

Histopathological examination of the surgical specimens showed three patients with T1, five with T2, 13 with T3, and nine with T4. When compared with the pathologic stage, endoscopic classification was correct in 14 cases. The endoscopic staging was consistent with histopathological staging in 100% for T1 and T2 tumors and 53.3 for T3 tumors.

The T stage was correctly determined by CT scan in 20 cases. The consistency between perceived T stage by CT and histopathological analysis was 33.3% for T1, 66.7% for T2, 73.3% for T3, and 66.6% for T4 tumors.

The T stage was correctly determined by both endoscope and CT scan in 23 cases. The consistency between perceived T stage by endoscopy coincided with CT and histopathological analysis was 100% for T1, 66.7% for T2, 80% for T3, and 66.6% for T4 (Tables 3 and 4).

Discussion

Subglottic area

Malignant infiltration of the subglottic region impacts the surgical plan markedly. There is no role for conservative laryngeal surgeries in patients with subglottic invasion.

Bulky tumor and even normal cords could hide the subglottic area. This can explain the six false negative cases by endoscopy in this thesis. CT assessment for the subglottic involvement is more accurate than endoscopy which is similar to the results of multiple researches [2,4–6].

Anterior commissure

Anterior commissure deep extension is very hard to evaluate by endoscopy and CT scan. Routine use of CT scan slices thicker than 1.0 mm may fail to detect small tumoral deep invasions important for correct stage determination.

Anterior commissure involvement on CT had a sensitivity and specificity of 88.2% and 69.2%, respectively in this study, which are close to the results of other studies [2,4–6]. Thin slices in sagittal and coronal reconstructed CT scan could help in raising the sensitivity of CT imaging.

Aryepiglottic folds

Tumor arising at the aryepiglottic fold may spread to the adjacent sites such as the epiglottis, the preepiglottic space, and upper edge of the thyroid cartilage. Therefore, proper assessment of the aryepiglottic folds is of utmost importance. In the present study, the aryepiglottic fold was involved in six patients, endoscopy showed the presence of aryepiglottic fold invasion with a sensitivity of 100%, specificity of 100%, and an accuracy of 100%. CT had high accuracy (93.3%) and specificity (95.8%) values for the evaluation of aryepiglottic folds. These results were consistent with the literature [2,4–6].

Vocal cords and paraluminal spaces

Along with the literature, this study showed that endoscopy is superior to CT in the staging of early laryngeal carcinoma which is confined to laryngeal mucosa (T1 and T2) with 100% consistency with pathological values.

Accurate assessment of preepiglottic and paraglottic is mandatory for a correct staging of supraglottic tumors' progress into T3 tumors if the preepiglottic space and/or the paraglottic space are involved. The importance of the paraglottic space lies in the accurate staging of transglottic tumors (Fig. 1). Endoscopy could give an idea about paraglottic space invasion through assessment of mobility of the vocal cords which is difficult in bulky supraglottic tumors. It was found consistent with the histopathological findings in 53.3% of T3 tumors.

The significance of the preepiglottic space lies in detecting the extension to the base of the tongue. This is crucial for decision taking for resection or conservation of the hyoid bone which is essential for conservative laryngeal surgeries.

In the present study, sensitivity and specificity values for the radiological diagnosis of the preepiglottic invasion were 85.7 and 95.6%, respectively. Sensitivity and specificity values for the diagnosis of the paraglottic invasion were 84.2 and 72.7%, respectively. It showed 73.3% consistency with histopathology for T3 and 66.6% agreement for T4 tumors. Thinner sections (0.5 mm slice thickness) are needed to raise the sensitivity values. The low specificity values may be due to the low capability of CT to differentiate reactive and inflammatory changes from tumor invasion.

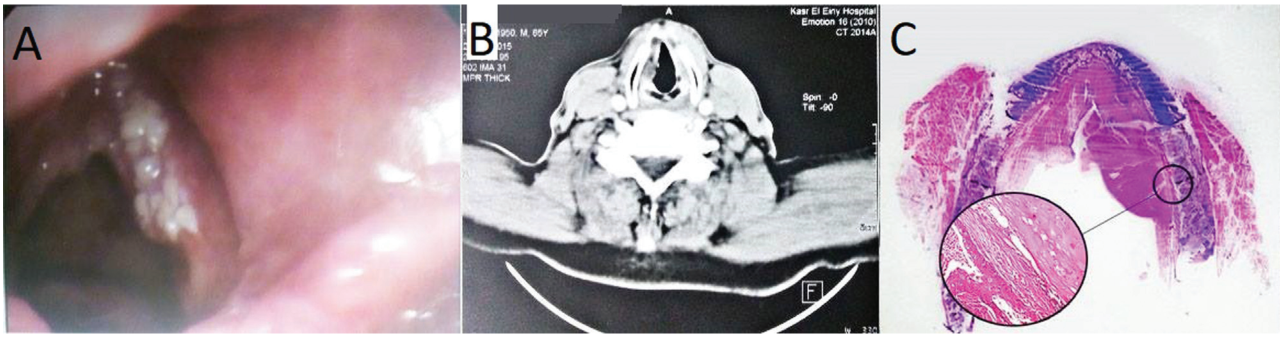
To improve CT ability in the staging of T3 tumors, scanning could be performed during phonation by patients (making the 'e' sound) to better visualize the level of the vocal cords [2].

Cartilage invasion

Cartilage invasion impacts the staging of laryngeal cancer and consequently markedly affects the available therapeutic options for the patient in addition to the quality of life. In case of cartilage invasion, stage T4, there is no place for conservative partial laryngeal surgeries or voice preservation while the most appropriate treatment option will be total laryngectomy followed by postoperative radiotherapy for complete cure. This emphasizes the importance of proper TNM staging preoperatively to offer the best therapeutic chance for the patient [7].

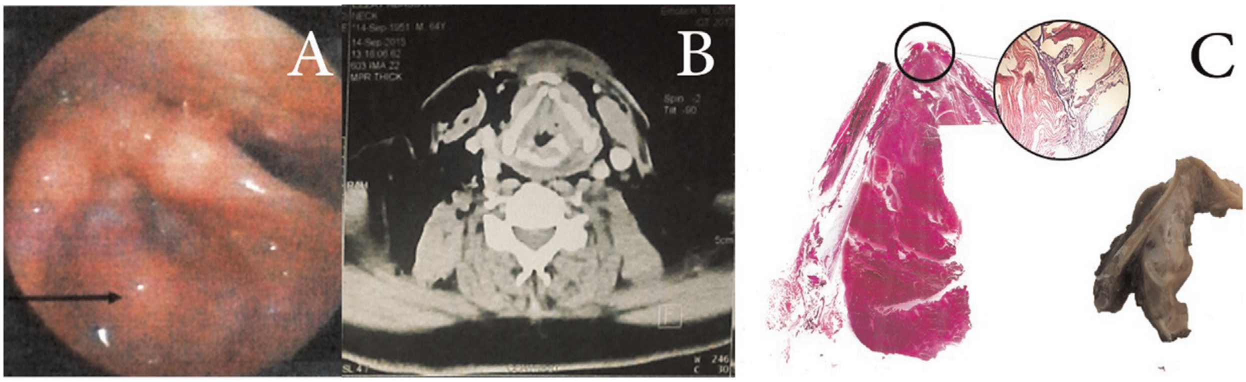
Becker described four radiological criteria with high sensitivity and specificity for the identification of cartilage invasion. The criteria were extralaryngeal spread, sclerosis, erosion, and lysis. Various studies reported sensitivity values of 46–67% and specificity values of 87–91% for CT prediction of neoplastic cartilage invasion. Despite the different criteria

Figure 1



Right glottic T1 carcinoma. (a) Endoscopic view photographed with a flexible laryngoscope. Right glottic mass with mobile cords T1; (b) computed tomography showing right cord thickening T1; (c) axial histologic slice at the glottic level with carcinoma at the right cord pT1. Right paraglottic space is tumor free (circle).

Figure 2



Left transglottic T4 carcinoma. (a) Endoscopic view photographed with a 70° Hopkins optic. Left supraglottic mass with fixed cord T3; (b) computed tomography shows left transglottic mass with intact laryngeal skeleton and infiltration of left paraglottic space T3; (c) axial histologic slice at the supraglottic level shows paraglottic space and laryngeal cartilage invasion at the anterior commissure T4 (circle).

indicating cartilage invasion, the presence of tumor on both sides of the thyroid cartilage remains the main criterion believed for the confirmation of cartilage invasion [2,4–7]. In the present study, CT showed the presence of cartilage invasion (Fig. 2) with a sensitivity of 55.5% and a specificity of 83.3%. Extralaryngeal invasion was detected with a sensitivity of 66.6% and a specificity of 95.8%.

MRI has higher sensitivity than CT at early cartilage invasion detection. However, its use is limited due to its poor sensitivity, motion artifacts as well as inability of some individuals to bare closed MRI tubes. Combination of MRI with CT may improve staging in T3 and T4 patients [8].

Conclusion

The role of multislice CT scan (MSCT) in the preoperative TNM classification of laryngeal carcinoma has been well documented. MSCT is superior to laryngoscopy in the evaluation of T3 and T4 tumors. On the contrary, laryngoscopy is better than MSCT in the evaluation of T1 and T2 lesions. Potential pitfalls of laryngoscopy and MSCT evaluation should be known and avoided by a careful analysis of data offered by both modalities.

Information gained by MSCT and laryngoscopy significantly improves preoperative staging accuracy of laryngeal carcinoma. MRI could be used in selected cases to detect early cartilage invasion.

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Conflicts of interest

There are no conflicts of interest.

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