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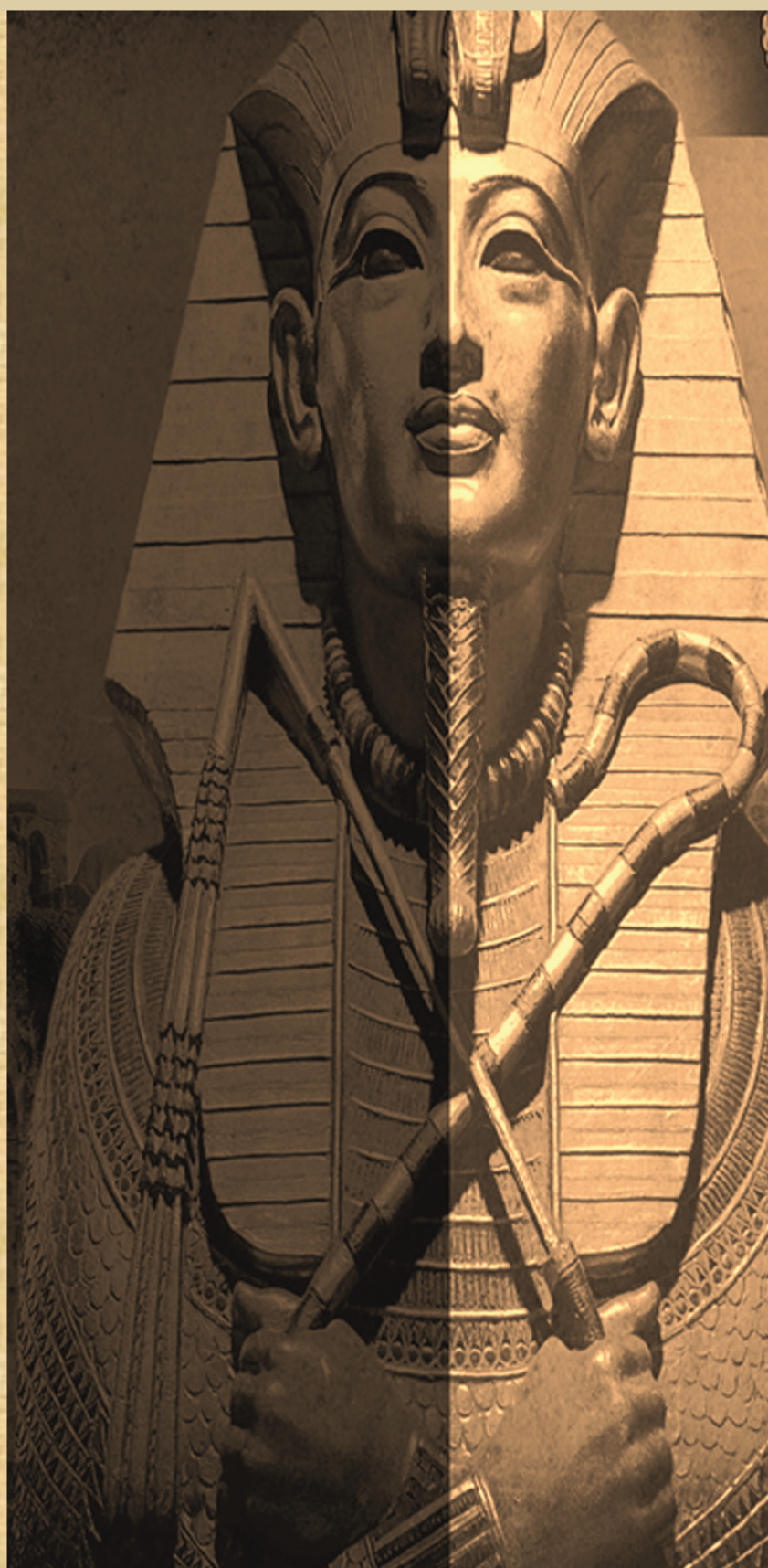
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# Study of the epidemiology and management of laryngeal cancer in Kasr Al-Aini Hospital

Hazem M. Abdel Tawab<sup>a</sup>, Mikhail W. AbdElMessih<sup>a</sup>, Nasser AA. AlNaggar<sup>b</sup>, Louay S El Sharkawy<sup>c</sup>

<sup>a</sup>Lecturer of Otorhinolaryngology, Faculty of Medicine, Cairo University, Cairo, Egypt

<sup>b</sup>Faculty of Medicine, Aden University, Aden, Yemen <sup>c</sup>Professor of Otorhinolaryngology, Faculty of Medicine, Cairo University, Cairo, Egypt

Correspondence to Hazem Mohammed Abdel Tawab, MD, Lecturer of Otorhinolaryngology, Faculty of Medicine, Cairo University, Cairo, Egypt  
Tel: +201110579379;  
E-Mail: hazemabdelatwawab77@yahoo.com

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## Objectives

Epidemiological study of laryngeal cancer and modalities of treatment according to TNM classification.

## Methods

Retrospective study was conducted on 295 patients who were admitted at the Otolaryngology-Head and Neck surgery department, Kasr-Al Aini hospital, Cairo University during the period from Jan 2009 till Dec 2011. It was done on cases of laryngeal cancers and included study of the epidemiology (age, gender, residence and smoking) and modalities of treatment according to TNM classification.

## Results

The mean age was (57.6 ± 10.5) ranging from (22 to 87) years old. Males were 93.9% while females were 6.1%, smokers were (254) 86.1% of 295 patient. In this study, the treatment modalities for primary tumor were: surgery alone, chemo-radiotherapy, surgery and postoperative radiotherapy and radiotherapy alone as well as neck dissection for lymph node control. The surgeries performed included 160 total laryngectomies, 47 partial (39 supracricoid, 4 supraglottic and 4 vertical) laryngectomies and 18 transoral endoscopic laser surgery selected according to the site and stage of the primary tumor. For lymph node control: 84 selective neck dissection, 8 radical or modified radical neck dissection and 13 combined.

## Conclusion

Total laryngectomy was the most common modality of treatment for primary tumors as the majority of cases presented at late stages. For lymph node control, the selective neck dissection was the commonest treatment as most of the patients had N0 and N1 lymph node.

## Keywords:

Epidemiology, laryngeal cancer, total laryngectomy, neck dissection, radiotherapy, chemo radiotherapy

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## Introduction

Laryngeal carcinoma is the second most common malignancy of the head and neck [1]. In the USA, the typical patient is a man in his 50s or 60s with a history of smoking and/or alcohol use. However, the male predilection for this disease has recently decreased from a male : female ratio of 15 : 1 to less than 5 : 1 currently. This change in demographics has been attributed to increased rates of smoking among women and their increasing presence in equally toxic work environments [2]. Significant variation in the distribution of carcinoma at the different laryngeal subsites exists worldwide. Supraglottic and glottic tumors are the most prominent subsites whereas subglottic carcinomas are uniformly rare. In the USA, glottic carcinomas are the most common (glottic 59%, supraglottic 40%, and subglottic 1%) [3].

Eighty-five percent of laryngeal cancers can be attributed to tobacco and alcohol use. Smoking is the predominant risk factor for laryngeal carcinoma, with alcohol use being an independent and synergistic effect [4].

Squamous cell carcinoma (SCC) represents more than 90% of laryngeal cancers. The remaining (<10%) malignant tumors include fibrosarcoma, chondrosarcoma, chemodectoma, rhabdomyosarcoma, malignant minor salivary gland tumors, adenocarcinoma, oat cell carcinoma, adenosquamous cell carcinoma, and giant cell and spindle cell carcinoma [5].

Laryngeal cancers differ in their propensity to spread on the basis of the site of the larynx where the tumor is located [6]. The incidence of occult metastasis in cancer larynx is generally relatively low, about 13%, and most of these cases are advanced cases and supraglottic in origin [7].

Generally, in head and neck SCC, when the primary locoregional control is achieved, this decreases the rate of distant metastases to 5% instead of 18% if the locoregional control failed [8].

The 6th ed. (2002) of the International Union against Cancer TNM classification is identical to that of the American Joint Cancer Committee (6th ed., 2002), which is the used most commonly [9].

The treatment of laryngeal carcinoma is usually planned to provide optimal survival free of disease, with maximum functional results. There are many treatment modalities and they differ from each other in the outcome of voice, swallowing, and quality of life. The decision is influenced by different variations in the size and location of the tumor [10].

Glottic laryngeal squamous carcinoma has an excellent prognosis in its early stages. The disease can be treated effectively by external beam radiotherapy, conservative open laryngeal surgery, or endoscopic excision using cold techniques or a CO<sub>2</sub> laser [11].

Advanced glottic carcinoma should be curable in most cases and treatment should include both the larynx and the neck. Classically, the treatment plan is total laryngectomy with or without neck dissection, followed by postoperative radiotherapy in many cases, but recently, it became possible to preserve the larynx without an impairment in the survival rate in many cases. Two main interventions are identified by many authors to allow this change in the treatment strategy: the supracricoid partial laryngectomy (SCPL) and the chemoradiation organ preservation protocols [12].

Early supraglottic carcinoma should also be treated by a unimodality treatment, with the conservation of the laryngeal functions like the early glottic carcinoma [13]. The elective neck management is recommended widely in T2 lesions and bilateral treatment for the neck is preferred when the carcinoma originates from or near the midline [14]. In advanced supraglottic carcinoma, the neck should be addressed in all cases: by an elective neck treatment for all the N0 lesions and combining neck dissection with postoperative chemoradiation in most of the N2–3 cases [15]. In the mean time, the larynx should be treated on a conservation basis to prevent unnecessary total laryngectomy in most advanced supraglottic lesions [16].

Modalities of treatment of nodal metastasis include radiation therapy in the N0 neck as it reduces the recurrence rate to ~5%. The node-positive neck is treated more effectively by a combination of surgery such as radical neck dissection (RND), modified or selective neck dissection (SND), and radiation. In patients with bulky nodal disease, a complete response in the neck to sequential chemotherapy and radiotherapy or radiotherapy alone may indicate that neck surgery is not necessary for good locoregional control and improved disease-free survival rates [17].

The aim of this work is to study epidemiological aspects of laryngeal cancer and its modalities of treatment according to the TNM classification.

## Patients and methods

This retrospective study was carried out on 295 patients who were admitted at the Otolaryngology-Head and Neck Surgery Department, Kasr Al-Aini Hospital, Cairo University, during the period from January 2009 till December 2011.

This study was carried out on patients with laryngeal carcinoma and included the study of epidemiology (age, sex, residence, and smoking), different presentations, stages, different modes of management, and follow-up of patients if available. Any patient with suspected laryngeal cancer proved negative by pathology was excluded from the study.

Regular follow-up of patients to detect recurrence of the tumor or complete cure was performed only for 54 patients because of missed follow-up charts. At the time of their admission, all the patients were subjected to assessment of history, which included age, sex, residence, special habits of medical importance, and all the symptoms of laryngeal carcinoma as hoarseness of voice and stridor. General medical and oncological history of the patient was also assessed to decide whether patients could tolerate surgery and postoperative rehabilitation. Physical examination of patients at the time of their admission was performed and included the search for any neck swelling such as the thyroid gland or lymph node for correct staging of the disease. An indirect laryngoscope and a flexible fiberoptic laryngoscope were used in combination to detect the site, extension of the lesion, adequacy of the airway, and the mobility of the vocal folds that directly affect the staging of the tumor. CT scan was performed routinely for all patients to detect the actual size of the tumor, its extension, cartilage invasion, the possibility of extralaryngeal spread, nonpalpable nodal metastasis, and invasion of the paraglottic and pre-epiglottic spaces. CT scan was performed for all the patients before the biopsies were taken to avoid the false results caused by edema with the biopsy procedure by direct laryngoscopy. MRI was performed in the patients with a recurrent mass after radiotherapy to exclude recurrence of the tumor from postradiation edema. Routine preoperative laboratory tests were performed for all patients whereas metastatic work-up was performed only for suspected cases on the basis of assessment of clinical history and examination. Pulmonary function tests were performed for all patients planned for partial laryngectomy.

The review of the treatment modalities for the tumor implemented in our department (Kasr Al-Aini Hospital) showed that they included the following: surgery alone, chemoradiotherapy, surgery, followed by

radiotherapy or radiotherapy alone, and neck dissection for lymph node control.

All collected cases were revised for completeness and consistency. Precoded data were entered on a computer using Microsoft Office Excel software program (2010) for windows.

Data were then transferred to the statistical package of Social Science Software program, version 15 (SPSS) for statistical analysis. Data were summarized using mean, SD, and frequency and percentage for qualitative variables.

*P* values more than 0.05 were considered insignificant, less than 0.05 as significant, and 0.01 as highly significant.

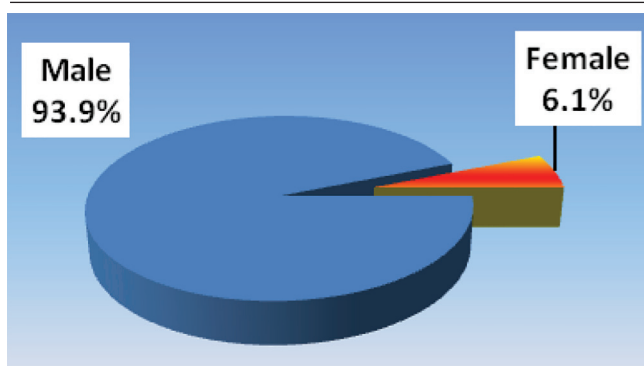
## Results

In this retrospective study, a total of 295 patients with laryngeal cancer were enrolled during the period from January 2009 to December 2011. The mean age of the patients was  $57.6 \pm 10.5$ , ranging from 22 to 87 years old. 93.9% (277) of the patients were men, whereas 6.1% (18) were women (Fig. 1).

47.1% (156) of patients admitted to our hospital were from Upper Egypt, whereas 52.9% (139) were from Lower Egypt. Two hundred and fifty-four patients (86.1%) were smokers (Fig. 2).

Our study showed that 184 patients (62.4%) were affected in the glottic and supraglottic regions, followed by transglottic regions in 61 patients (20.7%). The glottic region was affected only in 32 patients (10.8%), 5.1% had only supraglottic tumors [15], and finally, only 1.0% of patients had subglottic tumors [3], which makes it a rare subsite for laryngeal cancer.

Figure 1



Male to female ratio in the incidence of cancer larynx in the study.

In this study, 287 patients had SCC (96.6%).

Frequencies for T (Tis, T1, T2, T3, T4) and N (N0, N1, N2a, N2c) are presented in Tables 1 and 2, respectively.

Records of patients for the T staging were available for only 289. Staging of the tumor in the previous 289 patients is shown in Table 3.

Only 274 records were available of the treatment modalities as some patients refused treatment after

Table 1 Frequency of T stages in the study

T classification	Frequency (%)
Tis	1 (0.3)
T1	35 (12.1)
T2	37 (12.8)
T3	191 (66.1)
T4	25 (8.7)
Total	289 (100.0)

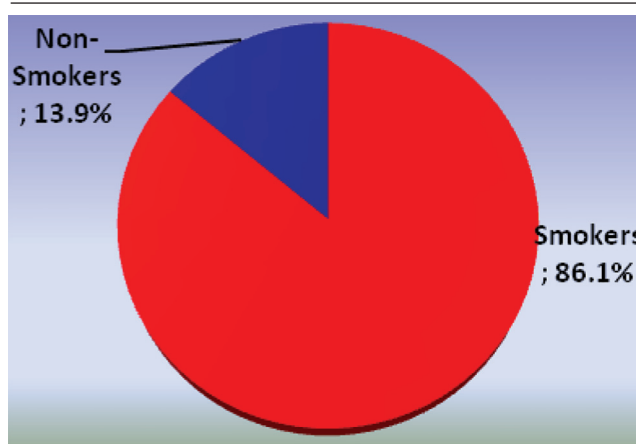
Table 2 Frequency of N in the study

N classification	Frequency (%)
N0	179 (61.9)
N1	104 (36.0)
N2a	5 (1.7)
N2c	1 (0.3)
Total	289 (100.0)

Table 3 Staging of the patients in the study

Staging	Frequency (%)
0	1 (0.3)
I	35 (12.1)
II	32 (11.1)
III	190 (68.5)
IVa	25 (5.9)
IVb	6 (2.1)

Figure 2



Incidence of smoking in cancer patients in the study.

diagnosis. The results are shown in Table 4 for the tumor itself.

One hundred and five patients were subjected to neck dissection as shown in Table 5.

Surgery for the tumor was performed for 225 patients, of which 160 total laryngectomies, 47 partial laryngectomies (39 supracricoid, four supraglottic, and four vertical), and 18 transoral endoscopic laser surgeries were performed as shown in Table 6.

The postoperative results of the treatment modalities were available for 232 patients, of whom 226 patients showed improvement whereas six patients died because of cardiac causes.

Delayed follow-up records were available only for 54 patients, of whom 48 patients did not develop recurrence of the tumor whereas six patients showed local regional recurrence.

The association between the treatment modality and T stage of the tumor and the tumor site is shown in Figs 3 and 4, respectively.

There was a highly significant association between chemoradiotherapy and T4 ( $P < 0.001$ ).

**Table 4 Available records of the treatment modalities for the tumor itself in the study**

Treatment modalities	Frequency (%)
Surgery alone	196 (71.5)
Chemoradiotherapy	33 (12.0)
Surgery+radiotherapy	29 (10.6)
Radiotherapy alone	16 (5.8)
Total	274 (100.0)

**Table 5 Types of neck dissection in the study**

Neck dissection ( $n = 105$ )	Frequency (%)
SND	84 (80.0)
MRND or RND	8 (7.6)
Combined (bilateral surgery)	13 (12.4)
MRND, modified radical neck dissection; RND, radical neck dissection; SND, selective neck dissection.	

**Table 6 Types of surgical procedures performed for patients in the study**

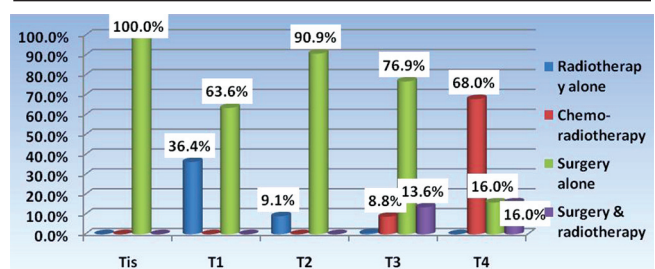
Surgery	Frequency (%)
Total laryngectomy (TL)	160 (71.1)
Transoral endoscopic laser excision (TELE)	18 (8.0)
Supracricoid laryngectomy with cricohyoidopiglottopey (SCL-CHEP)	20 (8.9)
Supracricoid laryngectomy with cricohyoidopexy (SCL-CHP)	19 (8.4)
Vertical partial laryngectomy (VPL)	4 (1.8)
Supraglottic laryngectomy (SGL)	4 (1.8)

There was a highly significant association between chemoradiotherapy, surgery+radiotherapy, and transglottic tumors ( $P < 0.001$ ).

The association between the T staging and the different surgical methods is shown in Fig. 5, whereas the association between the N staging and the different types of neck dissection is shown in Fig. 6.

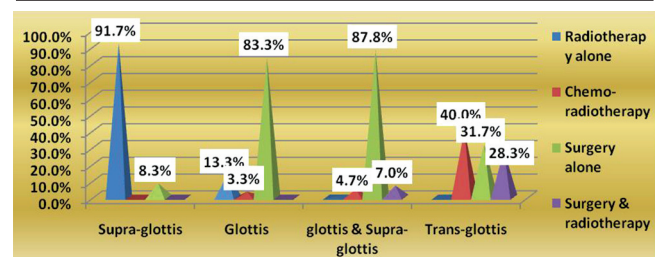
There was a highly significant association between total laryngectomy (TL) and T3, T4 ( $P < 0.001$ ).

**Figure 3**



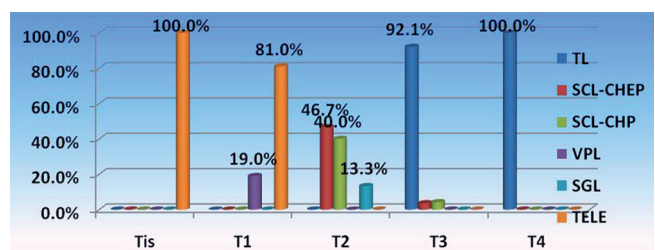
Association between the T stage of the tumor and the treatment modality in the study.

**Figure 4**



Association between the tumor site and the different treatment modalities in the study.

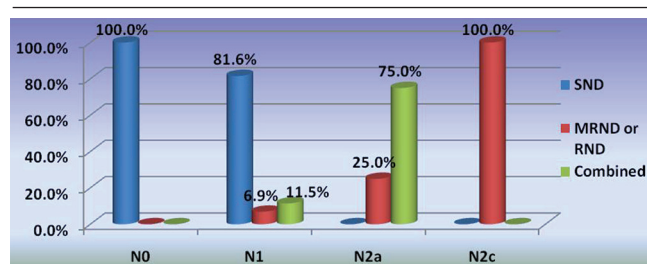
**Figure 5**



Association between the T staging and the different surgical methods in the study. SCL-CHEP, supracricoid laryngectomy with cricohyoidopiglottopey; SCL-CHP, supracricoid laryngectomy with cricohyoidopexy; SGL, supraglottic laryngectomy; TELE, transoral endoscopic laser excision; TL, total laryngectomy; VPL, vertical partial laryngectomy.



Figure 6



Association between the N staging and the different types of neck dissection in the study. MRND, modified radical neck dissection; RND, radical neck dissection; SND, selective neck dissection.

There was a highly significant association between transoral endoscopic laser excision and Tis, T1 ( $P < 0.001$ ).

There was a highly significant association between SND and N0, N1 ( $P < 0.001$ ).

There was a highly significant association between MRND, RND, and N2a, N2c ( $P = 0.001$ ).

## Discussion

Laryngeal tumors represent about 1% of all malignancies and 30% of the head and neck malignancies. About 85–95% of laryngeal malignancies are SCC [18]. In this study, SCC was found in 96.6% of patients.

In the present study, carried out on 295 patients, we found that the mean age of patients with laryngeal cancer was  $57.6 \pm 10.5$ , ranging from 22 to 87 years old. Parkin *et al.* [19] reported that laryngeal cancer is generally a disease of the elderly, with a peak incidence in the 50s and 60s.

Snyder *et al.* [20] reported that carcinomas of the larynx are four times more frequent in men than in women in the USA. Jemal *et al.* [18] reported that the male to female ratios in terms of incidence rates are greater than 5 : 1, possibly reflecting the increased number of women using tobacco products during this period.

In the present study, 277 patients were men whereas 18 patients were women; the male to female ratio was 15 : 1.

Smoking is responsible for up to 95% of causes of laryngeal cancer [21]. In the current study, 86.1% of patients with laryngeal cancer were smokers.

Our study was carried out on 295 patients admitted to our hospital with SCC of larynx and showed that the most common tumors were glottic–supraglottic (62.4%), transglottis (20.7%), glottic (10.8%), supraglottic

(5.1%), and finally subglottic (1.0%), which is a rare subsite for laryngeal cancer. Luna-Ortiz *et al.* [22] carried out a study on 48 patients with laryngeal cancer and the results according to location were as follows: supraglottic localization in 14 patients, glottic in 30 patients, and only subglottic cancer in one patient.

In the present study, T classification was found to be as follows: T3 (66.1%), T2 (12.8%), T1 (12.1%), (8.7%) T4, and Tis (0.3%). Staging was as follows: 68.5% were stage III, 12.1% were stage I, 11.1% were stage II, 5.9% were stage IVa, 2.1% were stage IVb, and 0.3% were stage 0. The reason for this distribution is that the majority of patients presented in late stages, possibly because of their low socioeconomic status. In contrast to our study, Scola *et al.* [23] reported that 71.0% of patients were stage I, 17.2% were stage II, 9.4% were stage III, and 2.4% were stage IV, which indicates that patients presented in the early stage of disease.

According to the study by Deganello *et al.* [24] on 96 patients with cancer larynx, 57 of them presented supraglottic localization of laryngeal SCC, staged as follows: 11 patients were T1, 24 patients were T2, 10 patients were T3, and 12 patients were T4a. Thirty-nine patients presented glottic localization staged as follows: 20 patients were T2, 17 patients were T3, and two patients were T4a [24].

In the current study, the treatment modalities for the primary tumor were as follows: surgery alone for 196 patients (71.5%), chemoradiotherapy for 33 patients (12.0%), surgery and postoperative radiotherapy for 29 patients (10.6%), and radiotherapy alone for 16 patients (5.8%). Luna-Ortiz *et al.* [22], in their study on 48 patients with laryngeal cancer, found that the treatment modalities were as follows: surgery alone in 30 patients (75%), radiotherapy in 16 patients (33%), and chemoradiotherapy in two patients (4.1%).

In the current study, we treated T1 glottic cancer either by transoral laser excision (17 patients) (highly significant), vertical partial laryngectomy (four patients), or radiotherapy (12 patients). Also, we found that radiotherapy is the choice modality of treatment for supraglottic T1, T2 (11 patients) laryngeal cancer. Ambrosch [25] reported that patients with early glottic carcinomas (T1 or T2 tumors without nodal or distant metastases) may be treated with transoral laser excision, open partial laryngectomy, or radiotherapy. Mandenhall *et al.* [26] reported that radiotherapy alone is an alternative to surgery for stage T1, early-stage T2 supraglottic cancer; ultimate local control with voice preservation has been reported to be 100% for T1 and 87% for T2. However, Hinerman *et al.* [27]

documented that primary radiotherapy was the treatment for early-stage supraglottic cancer and led to local control rates of 77–100% for T1 and 62–83% for T2 cancers.

In our study, advanced laryngeal cancer (stages III and IV) was treated by chemoradiotherapy (33 patients) (highly significant), total laryngectomy (131 patients), or total laryngectomy and postoperative radiotherapy (29 patients) (highly significant). Hanna *et al.* [28] reported that their study included 42 patients with advanced stage III or IV cancer of the larynx who were treated with either concurrent chemo radiotherapy [15] or total laryngectomy [27]; patients had to show no evidence of recurrence and to have completed therapy at least 3 months before inclusion in the study [28].

In our study, 12 patients were treated for stage T1, three patients for stage T2, and one patient for stage T3 by radiotherapy alone. Hirasawa *et al.* [29] presented a study carried out between January 2001 and April 2006. All patients received radiotherapy or chemotherapy as the first-choice treatment. Patient inclusion criteria were a histological diagnosis of infiltrative SCC and no previous radiotherapy for head and neck neoplasm. Treatment with chemoradiotherapy was as follows: T1a one patient (4%), T1b four patients (30%), T2 14 patients (67%), and for radiation alone: T1a 23 patients 96%, T1b nine patients (70%), and T2 seven patients (33%) [29].

In the present study, the surgeries performed included 160 (71.1%) total laryngectomies and 47 partial [39 (17.3%) supracricoid, four (1.8%) supraglottic, four (1.8%) vertical laryngectomies], and 18 (8%) transoral endoscopic laser surgery decided on the basis of the site and stage of the primary tumor. Deganello *et al.* [24] reported that surgeries performed in their study were as follows: 14 patients underwent a total laryngectomy and 82 patients underwent a conservative and conservation surgery. According to the tumor site and stage, 31 patients underwent transoral endoscopic laser excision, 16 patients underwent supraglottic horizontal laryngectomies, 33 patients underwent SCPL [21 patients underwent cricohyoidopexy (CHP) and 12 patients underwent cricohyoidepiglottopexy (CHEP)], and two patients underwent hemilaryngectomies [24].

In our study, patients with advanced stages (T3, T4) of laryngeal cancer, either glottic, supraglottic, or transglottic, were treated by total laryngectomy (highly significant) with or without radiotherapy. Twenty nine patients with advanced laryngeal cancer (T3, T4) were treated by total laryngectomy and postoperative radiotherapy, 17 cases were transglottic and 12 cases were glottic-supraglottis. Foote *et al.* [30] reported that

primary total laryngectomy with a neck dissection, with or without postoperative irradiation, is the treatment of choice for advanced laryngeal cancer, and yielded a locoregional control rate of 69–87% and a disease-specific survival rate of 71–78%.

In our study, 36 patients with transglottic cancer were treated by total laryngectomy. Ampil *et al.* [31] reported that a review of the available records and pathology reports identified 30 patients who had transglottic cancer and managed by total laryngectomy.

In our study, patients with T2, T3 glottic-supraglottic laryngeal cancer were treated by SCPL-CHP in 19 patients and SCPL-CHEP in 20 patients, with a good functional result during follow-up. Nakayama *et al.* [32] reported that SCPL was used in the treatment of all stages of laryngeal cancer (SCL-CHP, three patients), (SCL-CHEP, 29 patients), with an overall survival rate of 86%.

In the present study, we found that 61.9% of patients were N0, (36.0%) were N1, (1.7%) were N2a, and (0.3%) were N2c; in our study, no patient had distant metastasis.

A total of 105 neck dissections were performed as follows: 84 (80.0%) were treated by SND for the N0, N1 cases (highly significant association). Zhang *et al.* [33] reported that SND of levels II–IV is an adequate treatment in patients with N0 laryngeal cancer.

Eight patients (7.6%) were treated by a radical or modified RND for palpable cervical lymph node (N2a, N2c) (highly significant) and 13 patients (12.4%) were treated by combined neck surgery. Redaelli *et al.* [34] reported that the surgical procedure of choice for N+ necks should be a comprehensive neck dissection.

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## Conclusion

Total laryngectomy was the most common modality of treatment for primary tumors as the majority of patients presented at late stages. For lymph node control, SND was the most common treatment as most of the patients had N0 and N1 lymph node.

## Recommendations

Future efforts should be multicentric and for a longer duration to yield more statistically valuable results. Special attention should be paid to complete the data on patients' files. Records should be computerized to facilitate access and analysis of data.

## Acknowledgements

### Conflicts of interest

There are no conflicts of interest.

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