

# Malignant tumors of the larynx: Clinicopathologic profile and implication for late disease presentation

Ayotunde James Fasunla, Oluwole Agboola Ogundoyin, Paul Adekunle Onakoya, Onyekwere George Nwaorgu

Department of Otorhinolaryngology, College of Medicine, University of Ibadan, University College Hospital, Ibadan, Nigeria

## ABSTRACT

**Background:** Malignant laryngeal tumors are uncommon. Late presentation of the disease may worsen management outcomes. We described the epidemiologic, clinicopathologic profile, and management outcomes of laryngeal tumors in a tertiary health institution in Nigeria. **Materials and Methods:** An 11-year retrospective review of medical records of patients managed for malignant laryngeal tumor at the University College Hospital, Ibadan, Nigeria, was performed. **Results:** There were 97 patients comprising 74 (76.3%) males and 23 (23.7%) females with a mean age of  $60.48 \pm 12.15$  years. The mean duration of illness was  $7.3 \pm 3.8$  months. History of cigarette smoking and alcohol consumption was in 2.1% and 14.4% patients, respectively. The most common clinical presentations were hoarseness, cough, and dyspnea. Transglottis (91.8%) was the most common anatomic tumor location and 92.8% patients presented in advanced disease stage. Four histologic types were identified with squamous cell carcinoma accounting for 96.9%. About 92% patients had emergency tracheostomy and 56 (57.7%) patients had total laryngectomy. The postoperative complications were pharyngocutaneous fistula (5.2%) and peristomal recurrence (3.1%). The 5-year survival rate was 52.5%. **Conclusions:** Malignant laryngeal tumors are uncommon, but more females are getting the disease. Squamous cell carcinoma is the most common histologic variant. Late stage disease presentation and initial wrong diagnosis contributed to the poor management outcome.

**Key words:** Late disease presentation, malignant laryngeal tumor, peristomal recurrence, pharyngocutaneous fistula, tracheostomy

### Address for correspondence:

Dr. Ayotunde James Fasunla,  
Department of Otorhinolaryngology,  
College of Medicine, University of  
Ibadan, University College Hospital,  
PMB 5116, Ibadan, Nigeria.  
E-mail: ayofasunla@yahoo.com

## INTRODUCTION

Malignant tumors of the larynx are relatively uncommon in the head and neck region. It could arise from any of the epithelial and nonepithelial structures of the larynx. Squamous cell carcinoma is the most common histologic variant and accounts for 85–95% of all malignant tumors of the larynx.<sup>1</sup> According to a report from the World Health Organization, it is the second most common malignancy of the upper aerodigestive tract.<sup>2</sup> It occurs more in people above 40 years of age and more common in males. It's male preponderance has been linked to increased exposure to the risk factors of malignancies rather than an inherent gender predilection. The etiology is unknown but has been strongly associated with frequent exposure of laryngeal

mucosa to wide varieties of ingested and inhaled exogenous carcinogenic agents. Tobacco smoking and alcohol consumption are the two most important risk factors for the development of squamous cell carcinoma of the larynx.<sup>3,4</sup> Viral infections such as human papillomavirus (HPV) and human immunodeficiency virus, laryngopharyngeal reflux, exposure to industrial toxins, and some dietary deficiencies have also been associated with its development.<sup>5-13</sup>

The incidence of laryngeal tumor is high in the regions where tobacco smoking and alcohol consumption are common.<sup>14,15</sup> In the developing countries, the incidence of malignant tumor of the larynx is on the increase. The

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reason for this is unknown but may not be unconnected to frequent exposure to inhalational irritants at workplaces, homes as well as malnutrition.<sup>10-12</sup>

Malignant laryngeal tumors could involve any or all the three laryngeal subsites, namely, the supraglottis, glottis, and subglottis. The tumor in the glottis is associated with hoarseness and as a result, patients tend to present early to clinicians. In the developing countries, most patients with laryngeal cancer still present in the advanced disease stage. Other symptoms of laryngeal tumors include difficulty with breathing, noisy breathing, cough, referred otalgia, hemoptysis, neck swelling, and dysphagia.

Squamous cell carcinoma of the larynx may spread regionally to the neck nodes and/or distantly to lungs, liver, and backbones. Isolated glottis tumor rarely spread to the regional lymph nodes because of its poor lymphatic drainage. The propensity for regional lymph nodes and distant metastatic spread depends on the involved subsite (s) and the T-stage of the tumor.<sup>16,17</sup> Early tumors (Stages I and II) are usually treated with single modality therapy, whereas advanced tumors (Stages III and IV) are treated with combined modality therapy. Treatment modalities for laryngeal carcinoma include surgery, chemotherapy, and radiotherapy. The successful management of malignant laryngeal tumors requires accurate diagnosis, tumor stage, and selection of appropriate treatment modality with close postoperative surveillance. In the developing countries, the major challenges of management are late disease presentation and acceptance of surgical treatment by patients and their families. This study, therefore, presented the epidemiology, clinical presentation, and pathologic profile of laryngeal tumors in a tertiary health institution in Southwestern Nigeria.

## MATERIALS AND METHODS

This is an 11-year retrospective study involving the review of clinical and histologic data of all patients with the diagnosis of laryngeal cancer at the Department of Otorhinolaryngology, University College Hospital, Ibadan, Nigeria, from 2005 to 2015. The study center is a tertiary health institution that manages patients referred from primary, secondary, and other tertiary health institutions in Nigerian and West African countries because of her facilities for head and neck oncologic therapy. Relevant data collected from medical records of the patients and Ibadan cancer registry were demographic data (age and gender), occupation, religion, presenting complaints, duration of illness, history of tobacco or cigarette smoking, alcohol consumption, tumor characteristics (subsites, stage, and histologic subtypes), presence of neck nodes, duration of waiting before commencement of treatment, use of tracheostomy, and type of treatment received, outcomes, and complications. Those with incomplete clinical or histologic data were excluded from the study.

## Statistical analysis

The data were computed into Statistical Package for the Social Sciences version 22 manufactured by International Business Machine cooperation, Armonk, New-York, USA. The data were analyzed using simple descriptive statistical methods and expressed as a mean  $\pm$  standard deviation. The results were presented in texts, tables, and figures. The 5-year survival rate was calculated using direct methods.

## RESULTS

There were 97 patients comprising 74 (76.3%) males and 23 (23.7%) females with a male:female gender ratio of 3. 2:1. The age of the patients ranged from 21 to 85 years with a mean age of  $60.48 \pm 12.15$  years, median of 59 years, and mode of 52 years. Malignant tumor of the larynx constituted 37.3% of all head and neck malignancies managed during the study period. The sociodemographic characteristics of the patients are shown in Table 1.

The duration of illness at presentation ranged from 2 to 15 months, with a mean of  $7.3 \pm 3.8$  months. Hoarseness and difficulty with breathing were the most common symptoms, and 89 (91.8%) patients presented in acute upper airway obstruction necessitating emergency tracheostomy. The symptomatology of the patients is shown in Table 2. Fifty-seven (58.8%) patients had clinically palpable enlarged neck nodes. The cases of laryngeal malignant tumor per year are shown in Figure 1. All the patients had radiological examination of the neck and larynx as well as direct laryngoscopy and biopsy. The tumor involved the three subsites (transglottis) in 89 (91.8%), glottis alone in 6 (6.2%), subglottis only in 1 (1.0%), and supraglottis only in 1 (1.0%) patient.

More than 90% of the patients have advanced disease stage (Stages III and IV). The distribution of the clinical staging at diagnosis of the patients is shown in Table 3. Histologic analysis revealed that 94 (96.9%) patients had squamous cell carcinoma of the larynx. Other histologic types were synovial sarcoma, chondrosarcoma, and adenoid cystic carcinoma in each of the remaining three patients.

The mean duration between diagnosis and definitive surgical intervention in the patients was  $4.2 \pm 2.7$  months. Fifty-three (54.6%) patients had total laryngectomy, neck dissection with adjuvant chemoradiation. Three of these total laryngectomy patients had had failed chemoradiation. Three (3.1%) patients had pharyngolaryngectomy, primary pharyngeal reconstruction with pectoralis major myocutaneous pedicle flap, neck dissection, and adjuvant chemoradiation. Thirty-one (32%) patients were treated with chemoradiation only either because they opted for it or the tumor was inoperable. The remaining 10 (10.3%) patients refused further treatment. Five (5.2%) patients developed postoperative pharyngocutaneous fistula and were managed conservatively. Three (3.1%) patients had

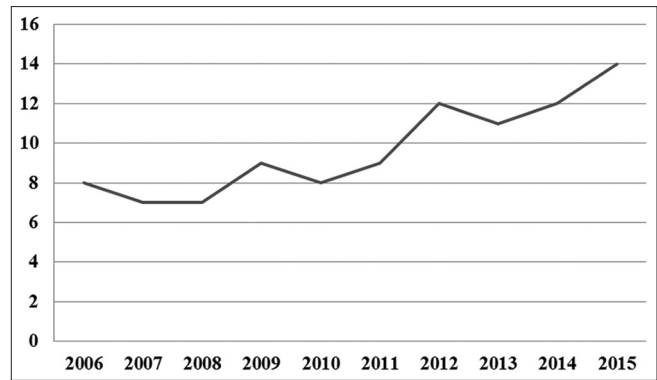
**Table 1: Sociodemographic and clinical characteristics of the patients**

Variable	Frequency (%)
Sex	
Male	74 (76.3)
Female	23 (23.7)
Age (years)	
18-35 (young adults)	1 (1.0)
36-55 (middle aged)	35 (31.1)
≥56 (older adults)	61 (62.9)
Religion	
Christianity	51 (52.6)
Islam	46 (47.4)
Tribe	
Yoruba	68 (70.1)
Ibo	29 (29.9)
Residence	
Urban	33 (34.0)
Rural	64 (66.0)
Socioeconomic class	
Low	49 (50.5)
Middle	40 (41.2)
High	8 (8.3)
Family history of cancer	
Yes	14 (14.4)
No	83 (85.6)
Tobacco/cigarette smoking	
Yes	2 (2.1)
No	95 (97.9)
Alcohol consumption	
Yes	14 (14.4)
No	83 (85.6)
Occupation	
Artisan	23 (23.7)
Trader	17 (17.5)
Retiree	15 (15.5)
Civil servants	12 (12.4)
Driver	11 (11.3)
Teacher	9 (9.3)
Trader	5 (5.2)
Clergy	2 (2.1)
Farmer	2 (2.1)
Police	1 (1.0)

**Table 2: Symptomatology of the patients**

Symptoms	Frequency (%)
Hoarseness	97 (100)
Cough	92 (94.8)
Difficulty with breathing	91 (93.8)
Referred otalgia	18 (18.6)
Dysphagia	13 (13.4)
Feeling of lump in the throat	11 (11.3)
Throat pain	7 (7.2)
Neck swelling	6 (6.2)

developed peristomal recurrence. At the time of this report, 45 (46.4%) patients had died, whereas the remaining 52 (53.6%) patients are still alive. Among the 45 dead

**Figure 1: Cases of laryngeal malignant tumor per year**

patients, only 17 (37.8%) of them lived beyond 5 years after treatment. Among the 52 patients who are still alive, only 14 (26.9%) of them were 5 years postmanagement. The 5-year survival rate was 52.5%. Postlaryngectomy speech rehabilitation was by esophageal speech in 96.9% patients. Two of the laryngectomies are using electrolarynx, whereas one is on tracheoesophageal prosthesis.

## DISCUSSION

Malignant laryngeal tumors could cause progressive destruction of the voice box with the loss of its functions such as voice and breathing. All but one patient are in the middle and older adult age group. This is in agreement with what other similar studies have reported.<sup>18-21</sup> The male preponderance in this study is also similar to what had been previously reported. Other earlier similar studies have reported male to female gender ratio of 9–12:1.<sup>18-21</sup> In this study, the male to female gender ratio of 3.2:1 showed that more females are getting to have the disease. This may be because women are now engaging in similar jobs such as men, which expose them to the risk factors of malignancies. Although tobacco and alcohol consumption are important risk factors for laryngeal carcinoma,<sup>3,4</sup> very few of the patients engaged in the habits. The theories for the development of nonsmoking and nondrinking laryngeal carcinoma have been described.<sup>11</sup> Majority (64%) of the patients were rural dwellers and their main source of fuel for cooking is firewood and charcoal. In our environment, the inconsistent power supply in the country makes power plants (generators) to be the main source of electricity in most homes and occupational places. These generators are usually placed very close to the residence. The prolong exposure to smoke emanating from either the firewood/charcoal or power plants (generators) might have contributed to the development of malignant laryngeal cancer. Smoke contains carcinogenic substances such as formaldehyde, benzene, and benzo(a)pyrene which, when inhaled, might irritate laryngeal mucosa and induce neoplastic changes.<sup>22,23</sup> Some occupations of these patients also exposed them to irritants which can induce chronic

**Table 3: Staging at diagnosis for the malignant laryngeal tumors**

Stage	Frequency, n (%)
I	4 (4.1)
II	3 (3.1)
III	74 (76.3)
IV	16 (16.5)

laryngeal inflammation which has been associated with laryngeal carcinoma.<sup>11</sup>

HPV is a known risk factor in head and neck cancers.<sup>5-7</sup> The infection is acquired mostly through birth canal or oral sex with someone who has the infection. In our environment, people who engage in such sexual practice are shy to volunteer the information because it is culturally and religion-wise unacceptable. However, individuals with HPV infection can be identified through laboratory testing. Nevertheless, prevention of the infection can be achieved through immunization against HPV. Laryngopharyngeal reflux and micronutrient deficiencies are other established risk factors for laryngeal carcinoma.<sup>8,9,12,13</sup> Unfortunately, such information was not collected in this study. The frequent bathing of laryngeal mucosa by gastric juice through esophageal reflux has been reported to cause repeated irritation and damage to laryngeal mucosa with resultant dysplastic, metaplastic, and neoplastic changes.<sup>8,9</sup>

Eating of diet rich in fresh fruits and vegetables can protect against aerodigestive tract cancers. More than 50% of the patients in this study belong to the low socioeconomic class and are unlikely to have healthy eating habit. Epidemiologic evidence has shown that Vitamins A and C and carotenoids (present in fruits and vegetables) are protective against epithelial cancers through control of cell differentiation and inhibition of epithelial tumors development.<sup>24,25</sup> Overcooking of food destroys these protective micronutrients hence should be discouraged. The steady increase in the number of cases of malignant laryngeal cancers [Figure 1] supports the need for health awareness program for the disease and its prevention.

Late presentation necessitated emergency tracheostomy in about 92% patients. In our environment, the delay in presentation at the hospital could be attributed, not only to the nonspecific symptoms of the lesion at an early stage but also to the religious and sociocultural beliefs and practices of the people. The reasons for this late presentation included initial self-medication, poverty, and illiteracy, which still prevail in our society.<sup>26</sup> About 66% patients are from rural communities where there is no oncologic clinic. Some patients attributed the disease to spiritual attack and thereby first sought spiritual assistance. They presented in hospitals when the disease is advanced and producing near total airway obstruction, which usually necessitated emergency tracheostomy.

The symptoms and signs of laryngeal cancer in this study are similar to what had been reported by other similar studies.<sup>18-21</sup> Six (6.2%) patients were initially wrongly treated for severe status asthmatics. Most clinicians are not well informed about laryngeal cancer because of the uncommon nature of the disease. Hence, patients presenting with noisy breathing, cough, and hoarseness are likely to be initially treated for common medical conditions such as laryngitis, chest infection, and asthma. Most of the time, the otorhinolaryngologists are only invited as the last consideration for laryngoscopy when there is no improvement in the clinical conditions of the patients. At this stage, the disease would have advanced, and tracheostomy becomes inevitable to save lives. Patients presenting with signs and symptoms of airway obstruction should be referred early for laryngeal assessment to prevent mistreatment and delay in treatment.

The mean duration between diagnosis and definitive surgical intervention was  $4.2 \pm 2.7$  months. This is a long enough time for the tumor to have upstaged and the patients, who had emergency tracheostomy, develop increased risk for peristomal spread.<sup>27-29</sup> This might have been the reason for the 3.1% peristomal recurrence seen in this study. The observed reason for the delay in surgical treatment included a lack of funds, initial decline from treatment because of fear of losing voice box and not being able to speak, lack of theater space, and incessant strikes of personnel within the hospital.

Irradiation of the neck causes tissue fibrosis, reduces blood supply, and hinders wound healing.<sup>30</sup> Deficiencies of vitamins and micronutrients have been reported in patients with head and neck cancers.<sup>31,32</sup> These factors might have contributed to the development of pharyngocutaneous fistula, which complicated total laryngectomy seen in 5.2% patients.

The therapies received by these patients were standard for the stage of the disease and choice of the patients. The default from treatment by 10.3% patients must have been due to nonaffordability of the cost of treatment. The low percentage of patients who are still alive is not unrelated to advanced disease stage at presentation, which characterized 92.6% patients. Advanced disease stage is usually associated with high mortality and poor prognosis. It is also possible that few of the patients defaulted from follow-up because of fund. Inclusion of therapy for head and neck cancers in the existing National Health Insurance Scheme in Nigeria will reduce future default treatment rate.

The predominance of squamous cell carcinoma of the larynx in this study is similar to what had been reported in previous similar studies.<sup>1,2,14,18-21</sup> Sarcomas are generally uncommon in the larynx constituting <1% of all laryngeal malignancies.<sup>33</sup> In this study, synovial sarcoma was found in a 21-year-old male. Synovial sarcoma is very rare in the



larynx and has aggressive behavior. It is believed to arise from pluripotent mesenchymal cells and has histologically appearance that resembles a synovial membrane.<sup>34,35</sup> Chondrosarcoma, which was seen in a 56-year-old male in this study, is the most frequent nonepithelial tumor in the larynx accounting for 0.07–2% of all laryngeal tumors.<sup>36-37</sup> It is most frequently located in the posterior lamina of the cricoid cartilage (75%), followed by the thyroid cartilage (20%), the epiglottis, and the arytenoids.<sup>37,38</sup> It has been hypothesized to arise either from primary disordered ossification of the cartilage or from chronic inflammation or ischemic changes in a preexisting chondroma.<sup>37,38</sup>

One patient in this study had adenoid cystic carcinoma of the larynx. This is a very rare malignant tumor of the minor salivary gland accounting for <1% of all laryngeal tumors.<sup>39,40</sup> It is thought to arise from the submucosal glands, which make them to present late. It is commonly seen in subglottic location, followed by the supraglottic and then glottis.<sup>41,42</sup> Irrespective of the histologic type, the prognosis of treatment for early stage tumor is very good.

## CONCLUSION

Malignant laryngeal tumors are uncommon, but more females are getting the disease. Squamous cell carcinoma is the most common histologic variant. Late stage disease presentation and initial wrong diagnosis contributed to the poor management outcome as well as the high percentage of postoperative pharyngocutaneous fistula and peristomal recurrence from this study.

## Recommendation

The successful management of malignant laryngeal tumors depends on accurate diagnosis, tumor stage, and selection of appropriate treatment modality with close postoperative follow-up. Thus, targeted and well-coordinated health education on awareness of laryngeal cancers and their prevention program at the community level should be pursued through appropriate organization and relevant agencies. Furthermore, inclusion of therapy for laryngeal cancers in the existing National Health Insurance Scheme in Nigeria will likely encourage early presentation to the ORL specialist while also reducing default from treatment.

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## Conflicts of interest

There are no conflicts of interest.

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