

Laryngeal Cancer in Iranian Women

Payman Dabirmoghaddam¹, Jaleh Yousefi², Ebrahim Karimi¹, Kayvan Aghazadeh¹, Mahdi Moteshaker Arani²

¹ Department of Otorhinolaryngology, Otorhinolaryngology Research Center, Tehran University of Medical Sciences, Tehran, Iran

² Department of Otorhinolaryngology, New Hearing Technologies Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

Received: 02 Mar. 2022; Accepted: 19 Dec. 2022

Abstract- Laryngeal cancer is the most common malignant neoplasm in respiratory tract after lung cancer. The incidence is very different and male to female ratio has been decreased in previous decades. Different characteristics of laryngeal cancer in men and women have been described based on previous studies, so we decided to study its characteristics in Iranian women. This study's design is cross-sectional retrospective from 2010 to 2019 in Amir-Alam Hospital, Tehran University of Medicine. All patients with laryngeal cancer admitted to this hospital, were included. Females' records were studied exclusively. Among 1456 patients included in this study, 1391 were male and 65 were female (M/F=21.4:1). The mean age of males was 60.6 years and for females was 56.6. From 65 females, 60 were Squamous cell carcinoma and 5 were Sarcoma. Findings of 60 female SCC patients: The main risk factors were cigarette smoking and opium abuse. The subsite of tumor was supraglottic in 40%, glottis in 31% and transglottic in 29%. Treatment options were surgical (55%) and non-surgical (45%). Survival rates for one, two and five years were 84.3%, 67.4% and 44% respectively. Two-year survival of surgically treated patients is significantly better than non-surgically treated patients ($P=0.048$). The mean age of females was less than males. Two-year survival rate was better in surgically treated patients. The five-year survival of female patients was 44% and there is an emerging need for survival studies of male patients for comparison.

© 2023 Tehran University of Medical Sciences. All rights reserved.

Acta Med Iran 2023;61(1):7-11.

Keywords: Larynx; Neoplasm; Survival; Women

Introduction

Laryngeal cancer is the most common cancer in respiratory tract after lung cancer. Its incidence varies between different races and countries and sexes. For example it is more prevalent among African-Americans than Caucasians (1) and among Americans than Japanese (2) and among men than women.

The most important risk factors through the world are cigarette smoking and alcohol consumption. In Iran, opium abuse has been encountered in inducing laryngeal carcinoma. Other risk factors are genetic susceptibility, increase intake of red meat and fat and deficiency of fruit and vegetables in diet, occupational exposure to toxic agents such as mustard gas, aromatic polycyclic hydrocarbons, sulfuric acid, asbestos, wood, stone, cement and textile dust, asphalt, etc.

The role of laryngopharyngeal reflux and human

papilloma virus are still controversial and under investigation (1).

The incidence of this cancer was increasing among women in previous decades and the male to female ratio was decreasing (3).

This ratio in United States has been decreased from 15:1 in 60 years ago to 3.8:1 in recent years. The cause of this decrease has been mostly related to increase of smoking among women (3).

In Iran there is some reports about statistics of laryngeal cancer, although male to female ratio is very different among them and ratios of 5.8:1 to 20:1 has been reported.

The overall 5-year survival of laryngeal cancer in USA is 61% (4). We didn't find survival rate in men and women separately.

Hitherto characteristics of laryngeal cancer of Iranian women haven't been investigated, therefore we decided

Corresponding Author: J. Yousefi

Department of Otorhinolaryngology, New Hearing Technologies Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran
Tel: +98 9122141224, E-mail address: yousefidr.jy@gmail.com

Copyright © 2023 Tehran University of Medical Sciences. Published by Tehran University of Medical Sciences

This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International license (<https://creativecommons.org/licenses/by-nc/4.0/>). Non-commercial uses of the work are permitted, provided the original work is properly cited

to conduct this study about this issue.

Materials and Methods

This study is a cross sectional descriptive retrospective study which was carried out based on data gathering from archive of a single tertiary referral center, Amir-Alam hospital, Tehran university of medical sciences, Iran. The protocol complies with recommendations of the Declarations of Helsinki and Tokyo guidelines and are approved by the ethics committee of the University.

All documents of histologically verified patients with laryngeal cancer from April 2010 to April 2019 were contained in this study. Identification of patients was based on their first name, last name, father's name and hospital ID number. Patients suffering from tumor of hypopharynx that invaded larynx were excluded. Also, some patients were admitted for several times, in this situation the data of these documents were collected as one patient. Then documents of female patients were selected and all data (including demographic and pathologic characteristics, treatment protocols and survival) were obtained from them. If additional

information was needed, they were gathered by calling and asking from patients or their families.

Based on these documents and after excluding hypopharyngeal cancers and repeated admissions, files of 1456 cases were compiled.

1391 were male and 65 were female. Risk factors for laryngeal cancer were selected from textbooks and literatures about this issue. According to the aim of this study to analyze characteristics of laryngeal cancer of women, only the age of male patients was collected but documents of female patients were studied comprehensively. Statistical analysis was done using Microsoft excel and SPSS version 20.

Results

Among 1456 patients diagnosed with laryngeal cancer from April 2010 to April 2019, 1391, were male and 65 were female. The male to female ratio was 21.4:1.

The mean age of male patients was 60.6 years with SD of 10.3 and for females was 56.6 years with SD of 13.2. Difference of mean age of men and women was statistically significant with $P=0.019$ (Table 1).

Table 1. Age distribution between men and women

Gender	Men	Women
Number	1391	65
Mean age (year)	60.63	56.63
Standard Deviation	10.344	13.265
Maximum	89	87
Minimum	25	17
<i>P</i>	0.019	

Between 65 female patients, tumor of 60 patients was laryngeal squamous cell carcinoma and 5 patients involved with laryngeal sarcoma. (One patient with synovial cell sarcoma and four patients with chondrosarcoma).

Thanks to basic differences between characteristics of carcinomas and sarcomas of larynx (risk factors, treatment, survival...), we decided to do the rest of statistical analyses only on cases of laryngeal carcinoma (60 patients).

Analysis of data about risk factors (after extracting 4 missed data) revealed that the most prevalent risk factors are cigarette smoking and opium abuse. 48% of patients had been using cigarette with (16%) or without (32%) opium and 5% had been using opium solely. No report of alcohol consumption was found in our female patients (Table 2).

The subsite of laryngeal tumor after extracting 8

missed data in order of frequency was supraglottic (40%), glottis (31%) and transglottic (29%). There wasn't any case of subglottic tumor in our patients. So supraglot was the most frequent involved area in female patients of laryngeal cancer in this study (Table 3).

Stage of tumor based on analysis of existing data after extracting of three missed data showed stage 1 in 28%, stage 2 in 19%, stage 3 in 32% and stage 4 in 21%. Table 4 shows the frequency of different stages of laryngeal carcinoma in our female patients.

Lymph node involvement was diagnosed in 14 patients, after subtracting of two missed data, the incidence of lymph node involvement among 58 patients was 24%.

Distant metastasis was seen in three patients (5%) and lung was the only site for these metastases.

Treatment of patients was encountered in documents of 58 patients and there were two missed data. 32 cases

were treated surgically (16 cases of Transoral Laser Microsurgery and 16 cases of open laryngeal surgery+adjuvant chemoradiation) and 26 cases were treated non-surgically, with chemoradiation (23 cases) or radiotherapy alone (2 cases) or chemotherapy alone (1 case).

The stage of tumors in two groups of treatment were not significantly different and there were cases of all four stages in surgically and nonsurgically treated patients.

Among 16 cases who had been underwent total

laryngectomy with or without neck dissection 4 cases (25%) developed pharyngocutaneous fistula.

Results of survival analysis of female laryngeal carcinoma patients after excluding of missed data showed that one year survival was 84.3%, two-year survival was 67.4%- and five-year survival was 44%.

We also compared survival of two groups of treatments. It has been shown that survival of surgically treated patients was better than non-surgically treated patients although this difference was statistically significant only in two-year survival (Table 5).

Table 2. Prevalence of risk factors in female patients with laryngeal carcinoma

Risk factor	Frequency	Valid percent
Smoking	18	32
Passive smoking	2	3.5
Opium	3	5
Smoking and opium	9	16
Hookah	3	5
Baking Oven	1	2
Familial History	2	3.5
No Risk factor	18	32

Table 3. Subsite of laryngeal carcinoma

Subsite	Frequency	Valid percent
Glottic	16	31
Supraglottic	21	40
Transglottic	15	29

Table 4. Stage of laryngeal carcinoma

Stage	Frequency	Valid percent
1	16	28.1
2	11	19.3
3	18	31.6
4	12	21.1

Table 5. Comparison of survival between two groups of treatments

Survival	Surgical	Nonsurgical	P
One year	85.7%	82.6%	0.767
Two year	80%	52.4%	0.048
Five year	50%	33.3%	0.442

Discussion

Up to the best of our knowledge, this is the first comprehensive study about laryngeal cancers of women in Iran. As regards to some differences of laryngeal cancer in men and women that was reported in literature, we conducted this project to evaluate this issue in Iran.

Our study is a retrospective cross sectional

descriptive study which have enrolled cases of laryngeal cancer in Amir Alam hospital between April 2010 to April 2019. The ratio of men to women was 21.4:1 in our study. Several studies from Iran have reported this ratio very differently. In study of Gholizadeh *et al.*, it was 20:1 (5), in study of Mafi *et al.*, was 12:1 (6), in study of Mirzaei *et al.*, was 7.6:1 (7), in study of Rad *et al.*, was 5.9:1 (8) and in meta-analysis of Hassanipour *et*

Laryngeal cancer

al., was 5.8:1 (9).

The cause of this diversity in reports is not completely understood. It may be due to difference of risk factors distribution and social habits between men and women and between various regions of the country. It was known that this ratio has been decreasing along last decades in the world. For example, this ratio in the United States has been decreased from 15:1 in 70 years ago to 3.8:1 in 2019. This decrease has also been encountered in other reports such as study of Van Dijk *et al.*, in Netherland (10) and Marcou *et al.*, in Greece (11).

These decreasing ratios have been attributed to increase of risk factors such as tobacco consumption among women (3,11) or decrease of them in men more than women (10).

The mean age of women was lesser than men in our study (56.6 in comparison to 60.6 with $P=0.019$). this finding is in agree with the report of Rad *et al.*, from Kerman that the mean age for women was 55 years and for men was 61 years (8). In study of Gallus *et al.*, on 68 cases of laryngeal cancer in women from Italia and Switzerland, the mean age of cases was 60 years (12).

The first risk factor in our patients was smoking that is in accordance with other studies in the world. The second risk factor in most of studies is alcohol consumption (1,10) but in our study was opium abuse that is prevalent in Iranian patients, although up to now, it has not been known as a risk factor for laryngeal cancer in the world. Many studies in Iran have been conducted to clarify the role of opium abuse in inducing cancer of body organs such as lungs, larynx, esophagus, stomach and bladder (13-15). There is also some reports from other countries in Asia such as Hong Kong and Singapore (13,16). It is necessary to evaluate the role of this risk factor more comprehensively in the world to achieve a global consensus about it.

Subsite of tumor in larynx is important not only in expectance of lymph node involvement, but also in survival rate of patients. Comparing between supraglottic and glottic tumors, the former have more lymph node involvement and survival of patients is less than glottic tumors (3). Therefore, glottic tumors have better prognosis. Generally, in countries that smoking is more common, the glottis is predominant site of involvement, however if alcohol consumption is dominant risk factor, supraglottic involvement is more common (1,3). Thus, we expect that glottic tumors be more common in Iran and it was supported by some studies (17,18). In our study about female patients, unlike to our expectation, supraglottic tumors was more

prevalent.

We searched literature for information about this difference between men and women and found study of Van Dijk in Netherland on about 15000 cases of laryngeal cancer (10). The most common subsite of involvement in men was glottis (69%) and in women was supraglottis (55%). We need more researches about this discrepancy and its causes in our country and in the world.

We analyzed survival of women with laryngeal carcinoma and it was 44% in 5 years. We didn't have any report of survival of men simultaneously for comparison. Gholizadeh *et al.*, have also reported 5 year survival in 136 cases of laryngeal carcinoma and it was 47% in men and women altogether (5). In the report of American Society of clinical oncology, 5-year survival of supraglottic tumor was 46%, glottic tumor 76% and subglottic tumor 52%. The overall 5 year survival in USA was 61% (4). We didn't find survival of men and women separately in this report.

Survival of women was less than men in study of Van Dijk in Netherland (66% versus 71%). It was due to higher incidence of supraglottic tumors in women which have worse prognosis in comparison to glottic tumors.

We found an important conjunction between kind of treatment and survival. Survival of surgically treated patients was better than non-surgically treated group and it was statistically significant in two-year survival ($P=0.048$).

There is some reports about decrease of survival of laryngeal cancer patients in recent decades from 66% to 63% (1) and it was attributed to increase use of chemoradiation instead of total laryngectomy followed by radiotherapy in locally advanced (T3 or T4) disease (19).

According to study of Pan and associates in China, surgery is useful even in cases with metastatic disease and surgery of primary tumor and its metastasis increases the survival of patients compared with non-surgically treated patients (20).

The ratio of laryngeal cancer between men and women was 21.4:1 and the mean age of men was higher than women at presentation (60.6 versus 56.6 respectively).

The most common type of malignancy in larynx of women was squamous cell carcinoma (60 from 65 cases) and the remainder 5 cases were sarcoma.

The subsite of laryngeal involvement with carcinoma in women in order of frequency was supraglottic, glottis, transglottic (40%, 31%, 29% respectively).

Overall, 5-year survival was 44% in women and

survival of surgically treated patients was better than non-surgically treated ones that was significant in 2-year survival.

Further studies are needed to reveal the difference in survival between men and women in Iran and its causes.

Acknowledgements

The authors would like to thank registration clerks of medical records archive section of Amir-Alam hospital, Tehran, Iran, for helping in data collection.

They would also like to thank Dr. Mina Abdollahi for her good comments on study design and Mrs. Ahmadi for editing the paper.

References

- Steuer CE, El-Deiry M, Parks JR, Higgins KA, Saba NF. An update on larynx cancer. *CA Cancer J Clin* 2017;67:31-50.
- Machii R, Saika K. Incidence rate for larynx cancer in Japanese in Japan and in the United States from the Cancer Incidence in Five Continents. *Jpn J Clin Oncol* 2017;47:471-2.
- Armstrong WB, Vokes DE, Verma SP. Malignant Tumors of the Larynx. In: Flint PW, Haughey BH, Lund VJ, Niparko JK, Robbins KT, Thomas JR, et al, eds. *Cummings Otolaryngology Head and Neck Surgery*. 6th ed. Canada: Saunders, ELSEVIER; 2015:1601-33.
- American Society of Clinical Oncology (ASCO). Laryngeal and Hypopharyngeal Cancer: Statistics. (Accessed at January, 2022, <https://www.cancer.net/cancer-types/laryngeal-and-hypopharyngeal-cancer/statistics>.)
- Gholizadeh N, Najafi S, Zadeh MK, Afzali S, Sheykhbahaei N. Trend in laryngeal cancer, mortality and survival rate in Iran. *J Contemp Med Sci* 2018;4:7-11.
- Mafi N, Kadivar M, Hosseini N, Ahmadi S, Zare-Mirzaie A. Head and neck squamous cell carcinoma in Iranian patients and risk factors in young adults: a fifteen-year study. *Asian Pac J Cancer Prev* 2012;13:3373-8.
- Mirzaei M, Hosseini SA, Ghoncheh M, Soheilipour F, Soltani S, Soheilipour F, et al. Epidemiology and trend of head and neck cancers in Iran. *Glob J Health Sci* 2016;8:189-93.
- Rad M, Chamani G, Zarei M, Hashemipour M. Epidemiological aspects of head and neck cancers in a group of Iranian population. *Eur J Dent* 2019;10:50-6.
- Hassanipour S, Delam H, Nikbakht HA, Abdzadeh E, Salehiniya H, Arab-Zozani M, et al. The incidence of laryngeal cancer in Iran: A systematic review and meta-analysis. *Clin Epidemiol Glob Health* 2019;7:457-63.
- van Dijk BA, Karim-Kos HE, Coebergh JW, Marres HA, de Vries E. Progress against laryngeal cancer in The Netherlands between 1989 and 2010. *Int J Cancer* 2014;134:674-81.
- Markou K, Christoforidou A, Karasmanis I, Tsiropoulos G, Triaridis S, Constantinidis I, et al. Laryngeal cancer: epidemiological data from Northern Greece and review of the literature. *Hippokratia* 2013;17:313-8.
- Gallus S, Bosetti C, Franceschi S, Levi F, Negri E, La Vecchia C. Laryngeal cancer in women: tobacco, alcohol, nutritional, and hormonal factors. *Cancer Epidemiol Biomarkers Prev* 2003;12:514-7.
- Kamangar F, Shakeri R, Malekzadeh R, Islami F. Opium use: an emerging risk factor for cancer? *Lancet Oncol* 2014;15:e69-77.
- Mousavi MR, Damghani MA, Haghdoost AA, Khamesipour A. Opium and risk of laryngeal cancer. *Laryngoscope* 2003;113:1939-43.
- Bakhshaei M, Raziie HR, Afshari R, Amali A, Roopoosh M, Lotfizadeh A. Opium addiction and risk of laryngeal and esophageal carcinoma. *Iran J Otorhinolaryngol* 2017;29:19-22.
- MacLennan R, Da Costa J, Day NE, Law CH, Ng YK, Shanmugaratnam K. Risk factors for lung cancer in Singapore Chinese, a population with high female incidence rates. *Int J Cancer* 1977;20:854-60.
- Dabirmoghaddam P, Taheri AK, Ghazavi H, Ebrahimnejad S, Karimian Z. Does opium dependency affect the pattern of involvement in laryngeal cancer? *Iran J Otorhinolaryngol* 2016;28:425-9.
- Latifi H, Mikaili P, Latifi K, Torbati H. Squamous cell carcinoma of larynx in northwestern Iran. *European J Exp Biol* 2012;2:242-6.
- Grover S, Swisher-McClure S, Mitra N, Li J, Cohen RB, Ahn PH, Lukens JN, et al. Total laryngectomy versus larynx preservation for T4a larynx cancer: patterns of care and survival outcomes. *Int J Radiat Oncol Biol Phys* 2015;92:594-601.
- Pan Y, Hong Y, Liang Z, Zhuang W. Survival analysis of distant metastasis of laryngeal carcinoma: analysis based on SEER database. *Eur Arch Otorhinolaryngol* 2019;276:193-201.