

CLINICAL STUDY OF THE LOCAL AND REGIONAL SPREAD OF LARYNGEAL CANCER WITH REGARD TO THE SEX OF THE PATIENTS

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Malignant diseases of the larynx stand for multifactorial diseases. A large body of epidemiological data has shown that long-term alcohol and tobacco use, nutrition and occupation may be the causes of laryngeal cancer. It has been proved that the degree of dysplasia and carcinoma in situ is proportional to the intensity of smoking. Numerous reports have shown that the number of alcohol consumers diagnosed with laryngeal cancer is increasing. The cancerogenic potential of alcohol is enhanced by tobacco use. Laryngeal cancer is the most common head and neck malignancy.

The aim of this paper was to investigate characteristics of local and regional spread of laryngeal cancer with regard to the sex of the patients.

The subjects of this research were patients of the ENT Clinic, Clinical Center Niš. Prospective investigation included 61 patients with the local and regional spread of laryngeal cancer diagnosed and treated at Clinic during the period 2014-2016.

It was found that 61 persons were diagnosed with laryngeal cancer, of which 54 (88.5%) were male and 7 (11.6%) female. The largest number of participants were diagnosed with N₀ stage of the regional metastases. The largest number of male participants were in T₂ and T₃ stage of the local tumor spread. The largest number of women were found to be in T₁ stage of the local tumor spread. Statistically significant difference in the local spread of the tumor with regard to the sex was found ($\chi^2 = 33.07$, $p < 0.001$). Further analysis revealed that there was a statistically significant difference between stages T₁ and T_{1a} ($\chi^2 = 12.06$, $p = 0.0005$), T₁ and T_{1b} ($\chi^2 = 9.59$, $p = 0.0001$), T₁ and T₂ ($\chi^2 = 18.64$; $p < 0.0001$), T₁ and T₃ ($\chi^2 = 17.15$, $p = 0.00003$), and T₁ i T₄ stages ($\chi^2 = 9,59$ $p = 0.011$). The largest number of male participants were diagnosed with S₂ and S₃ stages, whereas the female population was mostly in S₂ stage of the disease and statistically significant difference in the stages of laryngeal cancer with regard to the sex of the patients was not found ($\chi^2 = 8.79$, $p = 0.359$).

There was predominance of the male patients with laryngeal carcinoma with significantly higher tumor grade compared to females. The significant difference in the stages of laryngeal cancer with regard to the sex of the patients was not found. *Acta Medica Mediana* 2017;56(3):12-16.

Key words: larynx, cancer, local spread, regional spread, gender

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have shown that long-term alcohol and tobacco use, nutrition and occupation may be the causes of laryngeal cancer. It has been proved that the degree of dysplasia and carcinoma in situ is proportional to the intensity of smoking. Numerous reports have shown that the number of alcohol consumers diagnosed with laryngeal cancer is increasing. The cancerogenic potential of alcohol is enhanced by tobacco use.

After setting up the histopathological diagnosis of changes in the larynx, it is necessary to perform radical surgery to remove lesions and lymphatic nodes in the neck. In circumscribed lesions with low degree of dysplasia, it is possible to achieve complete healing, with obligatory cessation of smoking and alcohol use, voice sparing, and prevention of infection. Endoscopic laser surgery should be the treatment of choice in

Introduction

Laryngeal cancer is the most common head and neck malignancy (1). Malignant tumors of the larynx stand for the disease of the modern age. A considerable number of epidemiological studies

early glottic carcinoma of the larynx (2). In T3 local spread of laryngeal cancer, sometimes, hemithyroidectomy should be performed (3). Early diagnosis is an important precondition in the treatment of precancerous conditions and early laryngeal cancer (4) In more severe cases and the occurrence of metastasis, irradiation therapy and chemotherapy should be delivered.

Aim

The aims of the research were to determine: the local spread of laryngeal cancer with regard to the sex and the regional spread of laryngeal tumor with regard to the sex of the patients.

Material and methods

The subjects of this research were patients of the ENT Clinic, Clinical Center Niš. Prospective investigation included 61 patients with the local and regional spread of laryngeal cancer.

We pay attention to the following symptoms in patients' anamensis: hoarseness, loss of voice, and difficulty breathing. Hoarseness is an indication of some laryngeal disease and it is evaluated in the way of appearance as occasional or permanent. Aphonia was registered as sudden or gradual and in these patients with hoarseness and aphonia the existence of tumor is evaluated by further physical and ENT examinations. The physical examination comprise neck palpation and determination of enlarged lymph glands presence.

After adequate preparation, indirect laryngoscopy was performed to gain insight into the presence of tumorous changes in the larynx, after which direct laryngoscopy and laryngomicroscopy

using surgical microscope was done. The whole procedure is performed under endotracheal anesthesia. During laryngomicroscopy, a sample of suspected malignant tissue was taken for biopsy and pathohistological examination. The definite diagnosis of malignant tumor of the larynx is established after the histopathological examination and determination of the cancer type.

Biopsy included: excision of part of the tissue, curettage, puncture, biopsy „ex tempore“ and exfoliative cytology. After biopsy, the sampled material undergoes the following procedures: fixation, cutting, staining, and microscopic examination using a light microscope with magnification from 300 to 400 times.

The study represents prospective analysis of the clinical material of the ENT Clinic in Niš and biopsy specimens from the Center for Pathology and Pathological Anatomy Niš during the period 2014-2016. All patient signed inform consent before including their data in study analysis. No study related procedures were performed beyond routine clinical practice in diagnosis and treatment of the disease.

Results

Laryngeal cancer

It was found that 61 persons were diagnosed with laryngeal cancer, of which 54 (88.5%)

Table 1. Distribution of the local spread of laryngeal tumor with regard to the sex of examiners

Sex	Local spread of the tumor						Total n(%)
	T ₁	T _{1a}	T _{1b}	T ₂	T ₃	T ₄	
Men n(%)	2(15,4)	6(100,0)	4(100,0)	21(87,5)	19(86,4)	2(100,0)	54(88,5)
Women n(%)	11(84,6)	0(0,0)	0(0,0)	3(22,5)	3(23,6)	0(0,0)	7(11,6)

Pol	Stages of regional metastases						Total (%)
	N ₀	N ₁	N ₂	N _{2b}	N _{2c}	N ₃	
Men(%)	48(90.6)	1(100.0)	1(50.0)	2(66.7)	2(100.0)	0(0.0)	54(88.5)
Women n(%)	5(9.4)	0(0.0)	1(50.0)	1(33.3)	0(0.0)	0(0.0)	7(11.6)
Total n(%)	53(100.0)	1(100.0)	2(100.0)	3(100.0)	2(100.0)	0(0.0)	61(100.0)
Total n(%)	13(100,0)	6(100,0)	4(100,0)	24(100,0)	21(100,0)	2(100,0)	61(100,0)

Table 2. Distribution of regional metastases with regard to the sex of examinees

were male and 7 (11.6%) female (Table 1).

The largest number of male examinees were in T₂ and T₃ stage of the local tumor spread. The largest number of women were found to be in T₁ stage of the local tumor spread. Statistically significant difference in the the local spread of the tumor with regard to the sex was found ($\chi^2 =$

33.07, $p < 0.001$). Further analysis revealed that there was a statistically significant difference between stages T₁ and T_{1a} ($\chi^2 = 12.06$, $p = 0.0005$), T₁ and T_{1b} ($\chi^2 = 9.59$, $p = 0.0001$), T₁ and T₂ ($\chi^2 = 18.64$, $p < 0.0001$), T₁ and T₃ ($\chi^2 = 17.15$, $p = 0.00003$), and T₁ i T₄ stages ($\chi^2 = 9.59$ $p = 0.011$). (Table 2).

The largest number of men and women were in N₀ stage of regional metastases. Statistically significant difference in the stages of regional metastases with regard to the sex of examinees was not found ($\chi^2 = 4.94, p = 0.293$). (Table 3).

The largest number of men were in S₂ and S₃ stages of cancer, whereas the largest number of women were in S₂ stage of the disease. Sta-

tistically significant difference in stages of cancer spreading with regard to the sex was not found ($\chi^2 = 2,02, p = 0.567$). (Table 4). The largest number

of men were diagnosed with T₂N₀M₀S₂ and T₃N₀M₀S₃ stages of laryngeal cancer. The largest number of women were in T₂N₀M₀S₂ stage of laryngeal cancer. Statistically significant difference in stages of laryngeal cancer with regard to the sex of examinees was not found ($\chi^2 = 8,79, p = 0.359$).

Table 3. Distribution of laryngeal cancer stages with regard to the sex of examiners

Sex	Cancer staging				Total n(%)
	S ₁	S ₂	S ₃	S _{4a}	
Men n(%)	11(92,0)	18(85,7)	18(94,7)	7(77,8)	54(88,5)
Women n(%)	1(8,0)	3(14,3)	1(5,3)	2(22,2)	7(11,6)
Total n(%)	12(100,0)	21(100,0)	19(100,0)	9(100,0)	61(100,0)

Table 4. Distribution of laryngeal cancer stages with regard to the sex of examiners

	The stages of laryngeal cancer												
	T ₁ N ₀ M ₀ S ₁	T _{1a} N ₀ M ₀ S ₁	T _{1b} N ₀ M ₀ S ₁	T ₂ N ₀ M ₀ S ₂	T ₁ N ₁ M ₀ S ₃	T ₂ N ₂ M ₀ S ₄	T ₃ N ₀ M ₀ S ₃	T ₃ N _{2b} M ₀ S ₄	T ₃ N _{2c} M ₀ S ₄	T ₄ N M ₀ S ₄	T ₃ N ₂ M ₀ S ₄	T ₂ N ₂ M ₀ S ₄	T ₂ N _{2c} M ₀ S ₄
M	1 (50,0)	6 (100,0)	4 (100,0)	18 (85,7)	1 (100,0)	1 (100,0)	17 (94,4)	1 (50,0)	1 (100,0)	2 (100,0)	0 (0,0)	1 (100,0)	1 (100,0)
W	1 (50,0)	0 (0,0)	0 (0,0)	3 (14,3)	0 (0,0)	0 (0,0)	1 (5,6)	1 (50,0)	0 (0,0)	0 (0,0)	1 (100,0)	0 (0,0)	0 (0,0)
Σ	2 (100,0)	6 (100,0)	4 (100,0)	21 (100,0)	1 (100,0)	1 (100,0)	18 (100,0)	2 (100,0)	1 (100,0)	2 (100,0)	1 (100,0)	1 (100,0)	1 (100,0)

Discussion

The largest number of male examinees were diagnosed with T₂ and T₃ stage of the local spread of the tumor. The largest number of women were in T₁ stage of the disease. The existence of statistically significant difference in the local spread of the tumor with regard to the sex of examinees was not found. A further analysis determined that statistically significant difference was observed between T₁ and T_{1a} stages, T₁ and T_{1b} stages, T₁ and T₂ stages, T₁ and T₃ stages, and between T₁ and T₄ stages. This can be a consequence of different long-term alcohol and tobacco use, nutrition and occupational habits between genders, assuming that males were more frequently alcohol and tobacco users (1).

A direct laryngoscopy and tumor biopsy or excision were essential for establishing a correct diagnosis (5, 6). Histological diagnosis of precancerous conditions and laryngeal cancer is set on the basis of cytological changes in the biopsy tissue (7).

In the early laryngeal cancer, the presence of possible regional metastases, denoted as N₀, N₁, N₂ and N₃ is expected, depending on the tumor size i.e. lymphatic gland.

An early diagnosis is an important precondition for successful treatment of the early laryngeal cancer.

Palpation of the neck is very important for the determination of the regional spread of la-

ryngeal carcinoma. During palpation, various shapes and sizes of lymph nodes in physiological conditions should be considered. Enlarged lymph node does not always point to a metastatic process.

Sometimes, a reaction of lymphatic tissue to some inflammatory process occurs, or a simple immunological response. However, there is a correlation between the size of a lymph node and a possibility of tumor infiltration. Taylor proved that in 91% of cases, cervical nodes larger than 2 cm contain a tumor. The regional metastases are the consequence of the hematogenous or lymphatic spread of laryngeal cancer cells as well as the enlargement of lymphatic glands. Sometimes, in T₃ local laryngeal cancer spread, hemithyroidectomy should be performed (3). Depending on the lymph node diameter, metastases are denoted by N:

- N – regional metastases;
- N_x – regional lymph nodes;
- N₀ – no regional metastases;
- N₁ – metastases in the ipsilateral node, the diameter of which is 3 cm;
- N₂ – metastases in the ipsilateral node greater than 3 cm and lesser than 6 cm in the greatest diameter;
- N_{2b} – multiple ipsilateral lymph nodes of which none is larger than 6 cm;
- N_{2c} – bilateral or contralateral lymph nodes of which none is larger than 6 cm;
- N₃ – single lymph nodes larger than 6 cm.

In the research of the stages of the regional metastases, the largest number of both men and women were in N₀ stage. Statistically significant difference with regard to the sex of examinees was not found.

The largest number of men were in N_{2b} and N_{2c} stages (66.7% and 100%, respectively). The number of men in N₀ stage was 48 i.e. 90.6%, and the number of women was 5 i.e. 9.4%, which shows that the majority of patients visit a doctor when the tumor has spread locally. Out of the total number of examinees – 61, 53 i.e. 86.89% of patients were diagnosed with N₀ stage. Laryngeal cancer was more common in men compared to women, with the ratio 8:1.

In the table showing the distribution of cancer stages according to the sex, the male sex is prevalent in S₂ and S₃ stages, whereas the female population prevailed in S₂ stage of the disease.

The cancers of upper aerodigestive tract (UADT) including the sites of oral cavity, pharynx, esophagus and larynx are common cancers among males in the world (8). Data analysis did not show statistically significant differences in the stages of laryngeal cancer with regard to the sex of participants ($\chi^2 = 2.02$; $p = 0.567$). The patients were mostly diagnosed with S₂ and S₃ stages. Statistical data processing did not demonstrate statistically significant differences in the stages of laryngeal

cancer with regard to the sex of the patients ($\chi^2 = 8.79$; $p = 0.359$). The decade of life, duration of cigarette smoking, alcohol consumption, exposure to urban and industrial pollution and nutrition influenced the appearance of precancerous states and laryngeal cancer in a certain decade of life. The largest number of women diagnosed with laryngeal cancer were in T₁ stage of the tumor spread locally. Fifty-three (100%) patients, i.e. 48 (90.6%) men and 5 (9.4%) women had N₀ stage of regional metastases, and they account for the majority of patients diagnosed with laryngeal cancer.

Conclusion

In the course of research, we found that the largest number of participants of male sex diagnosed with laryngeal cancer were in T₂ and T₃ stages, whereas women were in T₁ stage of the local spread of the tumor. The largest number of participants were found to be in N₀ stage of the regional metastases. S₂ and S₃ stages of the disease prevailed among the male population, whereas S₂ stage was dominant in the female participants. Statistical data processing did not demonstrate statistically significant differences in the stages of laryngeal cancer with regard to the sex of the patients.

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Originalni rad

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doi:10.5633/amm.2017.0302**KLINIČKO ISPITIVANJE LOKALNE I REGIONALNE
PROŠIRENOSTI KARCINOMA LARINKSA U
ODNOSU NA POL***Slaviša Radosavljević¹, Miško Živić^{2,3}, Ljubiša Milošević⁴,
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Maligna oboljena larinksa predstavljaju multifaktorijalnu bolest. Znan broj epidemioloških dokaza ukazuje da su hronično konzumiranje alkohola i duvana, ishrana, zanimanje uzroci pojave karcinoma larinksa. Dokazano je da su stepen displazije i karcinoma in situ značajno češći kod pušača proporcionalno sa intenzitetom pušenja. Poslednjih godina je dokazano da veliki broj obolelih od karcinoma larinksa konzumira alkohol. Kancerogeni potencijal duvana pojačava se konzumiranjem alkohola. Karcinom larinksa je najčešći malignom glave i vrata.

Cilj rada bio je da se analizira kliničko ispitivanje u vidu lokalne i regionalne proširenosti karcinoma larinksa u odnosu na pol.

Prospektivno ostraživanje je sprovedeno kod 61 bolesnika sa laringealnim karcinomom koji su lečeni na Klinici za ORL Kliničkog centra u Nišu tokom 2014-2016. godine. Analiza je obuhvatila TNM i S klasifikaciju i statističku obradu između polova.

Utvrđeno je da je od karcinoma larinksa obolela 61 osoba, od čega je 54 (88,5%) muškarca i 7 (11,6%) žena. Kod lokalne proširenosti karcinoma larinksa očekuju se stadijumi T₁, T₂, T₃ i T₄. Najveći broj ispitanika muškog pola se nalazi u T₂ i T₃ stadijumu lokalne proširenosti tumora. Najveći broj žena je u T₁ stadijumu lokalne proširenosti tumora. Endoskopska laserska hirurgija treba da bude prioritetni tretman kod ranog glotičnog karcinoma. Utvrđeno je postojanje statistički značajne razlike u lokalnoj proširenosti tumora u odnosu na pol ($\chi^2 = 33,07$; $p < 0,001$). Daljom analizom je utvrđeno da statistički značajna razlika postoji između T₁ i T_{1a} stadijuma ($\chi^2 = 12,06$; $p = 0,0005$), T₁ i T_{1b} stadijuma ($\chi^2 = 9,59$; $p = 0,0001$), T₁ i T₂ stadijuma ($\chi^2 = 18,64$; $p < 0,0001$), T₁ i T₃ stadijuma ($\chi^2 = 17,15$; $p = 0,00003$) i T₁ i T₄ stadijuma ($\chi^2 = 9,59$; $p = 0,011$). Hemitireoidektomija se nekad treba uraditi kod T₃ lokalne proširenosti karcinoma larinksa.

Najveći broj ispitanika sa karcinomom larinksa muškog pola je u T₂ i T₃, a žena u T₁ stadijumu lokalne proširenosti tumora. Najveći broj ispitanika je sa N₀ stadijumom regionalnih metastaza. Najveći broj muškaraca je sa S₂ i S₃, a žena sa S₂ stadijumom proširenosti karcinoma. Nije utvrđena statistički značajna razlika među stadijumima karcinoma larinksa u odnosu na pol ispitanika. *Acta Medica Medianae 2017;56(3):12-16.*

Ključne reči: larinks, karcinom, lokalna proširenost, regionalna proširenost, pol