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Impact of the COVID-19 pandemic on the stage and the type of surgical treatment of laryngeal cancer

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ABSTRACT

Purpose: Changes in the entire health care system during COVID-19 epidemic have affected the management of patients with head and neck cancer and posed several clinical challenges for ENT surgeons. Therefore, the present study aimed to investigate the effect of COVID-19 on the stage and the type of surgical treatments used in laryngeal cancer (including total laryngectomy, supracricoid partial laryngectomy (SCPL) and transoral laser microsurgery (TLM)) and also to compare the results of April 2020 to April 2021 with the previous year.

Materials and Methods: This cross-sectional study was performed on all patients with a diagnosis of laryngeal cancer who underwent surgery in the tertiary care center from April 2020 to April 2021 and the year before the pandemic in the same time. Demographic, cancer stage, and treatment data of all patients were recorded and analysis in two groups.

Results: Patients referred at the time of the virus outbreak; 111 were male and 5 were female, and in the group of patients referred before COVID-19, 90 were male and 12 were female. The type of surgical treatment of laryngeal cancer, mean time elapsed from sampling to surgery, stage of disease and mean tumor volume was statistically significant differences in patients before and during the outbreak.

Conclusion: Patients who referred for diagnosis and treatment at the time of COVID-19 outbreak had more advanced stages of the disease and also the tumor volume was higher in them than patients who had referred before the outbreak. It is necessary to provide new solutions, education and treatment management for patients with laryngeal cancer in such pandemics.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) the recently identified cause of coronavirus diseases (COVID-19) belongs to the genus Beta-coronavirus [1]. The global number of newly reported cases of the disease (July 12–18, 2021) was more than 3.4 million. Globally, the weekly incidence of COVID-19 is reported at an average of about 490,000. Approximately 57,000 deaths have been reported [2]. Millions of people around the world are infected with COVID-19, although most recover, but cancer patients are at higher risk for SARS-CoV-2 infection and its severe consequences. The inability of the immune system to distinguish between self and non-self leads to a link

between cancer pathogenesis and viral infections. Both virus and cancer express proteins that can be detected by host T cells and both stimulate T cell-mediated inflammation [3]. According to the World Health Organization (WHO), the mortality rate of COVID-19 patients with cancer as a comorbid disease is 7.6% versus the 3.8% mortality rate in the total COVID-19 population. One type of cancer that affects COVID-19 is laryngeal cancer. Two types of treatment for this type of cancer include; surgery and radiotherapy [3–6]. A study conducted in the UK in 2020 showed that; reduction of immediate referrals decreased by –70.4% and attendance for chemotherapy decreased by –4.5% during COVID-19. In 40% of cancer patients, overall mortality was directly and indirectly affected by COVID-19 [7]. The total number of these surgeries in April

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and May 2019 for the same period in 2020 decreased to 79% due to the indirect effect of COVID-19. In ears, nose and throat (ENT) - oropharyngeal cancer, which was the main site of surgery, in February 2020, 4993 cases were reported, which decreased to 33% in March. Although the banned measures did not include patients with emergencies or neoplasms, in April the rate dropped to 83% to 556 cases [6]. The mortality rate from COVID-19 is reported to be 0.66–7.8%, while the mortality rate from a head and neck cancer is 1.5% of all cancer deaths. Thus, the COVID-19 mortality rate may be indirectly increased by patients who did not seek medical advice during this period [8,9].

Given the above, and the weak immune system of cancer patients, changes in the overall health care system during COVID-19 epidemic have affected the management of patients with head and neck cancer and posed several clinical challenges for ENT surgeons. Therefore, it seems that the pre-epidemic teachings of COVID-19 about neck cancer need to be re-evaluated and updated, given the extremely specific risks of COVID-19 for surgery. The aim of this study was to investigate the effect COVID-19 infection on the disease stage and types of surgical treatments used in laryngeal cancer including open surgery (total laryngectomy and supracricoid partial laryngectomy (SCPL)) and transoral laser microsurgery (TLM) and compare the results of April 2020 to April 2021 with a recent year before the epidemic of COVID-19.

2. Material and method

This cross-sectional study was performed on all patients with a diagnosis of laryngeal cancer who underwent open surgery (total laryngectomy and SCPL or TLM) in the tertiary care from April 2020 to April 2021. Also, all patients diagnosed with laryngeal cancer that underwent surgery the year before the pandemic were included in study as a benchmark. Patients were selected by convenience sampling and entered into the study. The diagnostic method of laryngeal cancer is based on the pathology response from biopsy and tissue sampling available in patients' clinical records.

2.1. Inclusion and exclusion criteria

All patients with all age groups referred to our hospital have been diagnosed with laryngeal cancer and had undergone total laryngectomy and SCPL or TLM were included in the study. All patients who were candidates for surgery were discussed in the presence of the head and neck professors and the treatment plan was determined. Patients who had not undergone total or SCPL or TLM treatment were excluded from the study [6,10]. Patients with history of previous cancer or chemoradiotherapy were also included in study.

2.2. Data collection

The data collection tool was a checklist prepared by the researcher and using the patients' medical records. This checklist was included demographic information, patient treatment (type of treatment performed including total laryngectomy or SCPL or TLM), tumor volume, and disease stage based on the TNM staging system (by analysis permanent pathology after surgery). The time interval between the biopsy and the patient's surgery is also was recorded. In case of lack of information, patients' files were contacted by phone and the information was completed.

2.3. Ethical approval

This study was approved by the ethics committees of the collaborating hospitals. Informed consent was obtained from all participants.

The study protocol was approved by the local Ethics Review Committee of our institution (Tehran University of medical sciences). The approval ID is: IR.TUMS.AMIRALAM.REC.1400.019.

2.4. Data analysis

Statistical analysis of data was performed using SPSS software 21. Independent *t*-test or Mann-Whitney test were used to examine the differences in quantitative variables between the two groups. Chi-square test or Fisher's exact test were used to compare qualitative variables. A significant level of less than 0.05 was considered.

3. Result

In this study, there were two groups, group of A included patients who underwent laryngeal cancer surgery during the outbreak of Covid-19 infection and group of B included patients who referred for surgery in the same period a year earlier. In the group A, there were 5 females and 111 males with an average age of 59.59 years (range 59.59 ± 9.27 years) and in the group B, there were 12 females and 90 males with an average age of 59 years (range 59 ± 9.51 years). There was not significantly different between two groups (*P*-Value = 0.64 in mean age and *p*-value = 0.41 in sex distribution of patients in the two groups). Table 1 depicted the demographic characteristics of the two groups.

In the group A, the procedures performed included total laryngectomy (*n* = 90), SCPL (*n* = 9), TLM (*n* = 17), and in the group B, there were included total laryngectomy (*n* = 63), SCPL (*n* = 15), TLM (*n* = 24). The distribution of squamous cell carcinoma (SCC) patients according to the surgical method used during the outbreak of COVID-19 was significantly different from the same period before the outbreak of the virus (*p*-value = 0.02) (Table 1).

In the group A, 91 patients were in stages 3 and 4 at the time of surgery and 25 patients were in stages 1 and 2. In the group B, 66 were stages 3 and 4 and 36 were stages 1 and 2. Statistically, the ratio of patients with stage 3 and 4 in patients referred at the time of COVID-19 outbreak had significantly increased compared to the same period before the outbreak of COVID-19 (*p*-value = 0.02) (Table 1).

In patients with a history of CRT or organ preservation surgery (94 patients) there was no significant difference in staging between the two groups (*p*-value = 0.79), whereas in patients who for the first time they had referred at the time of COVID-19 and had no previous history of laryngeal cancer (84 patients) compared to those who had referred for the first time at the same time before the outbreak of COVID-19, disease stage was in advanced stages (*p*-value = 0.02).

The mean duration from the time of sampling to the time of surgery was 41 days in the group A and 45.5 days in the group B. This time interval, especially in patients with SCPL, was significantly reduced during the outbreak of COVID-19 compared to the same period before (*p*-value = 0.00). In patients who underwent total laryngeal surgery, the median waiting time from biopsy or biopsy to surgery was reduced from 51 days in the group B to 43 days in the group A. However, this difference was not statistically significant (*p*-value = 0.85). Also, in the patients that underwent TLM surgery, the waiting time interval in the group A increased compared to the same period of the previous year but was not statistically significant (*p*-value = 0.79) (Table 2).

Table 1

Demographic characteristics, type of treatment and stage of laryngeal cancer in the two groups of study. (TL; total laryngectomy, SCPL; supracricoid partial laryngectomy, TLM; transoral laser microsurgery).

		Before COVID-19 outbreak	During COVID-19 outbreak	<i>P</i> -value
Age		59 ± 9.51	59.59 ± 9.27	0.64
Gender	Male	90	111	0.41
	Female	12	5	
Type of treatment	TL	63	90	0.04
	SCPL	15	9	0.08
	TLM	24	17	0.35
Stage	1,2	36	25	0.24
	3,4	66	91	

Table 2

Interval time (days) between biopsy and surgery and tumor size in the two groups. (TL; total laryngectomy, SCPL; supracricoid partial laryngectomy, TLM; transoral laser microsurgery).

	Type of treatment	Before COVID-19 outbreak	During COVID-19 outbreak	P-value
Time interval between biopsy and surgery (day)	TL	43	51	0.85
	SCPL	27	46	0.00
	TLM	42	32.5	0.79
	Total	45.5	41	
Tumor size (cm ³)	TL	15	10.5	0.04
	SCPL	4.8	7.8	0.08
	TLM	1.9	1.3	0.35
	Total	5.7	12	0.04

The mean tumor volume in the group A was 12 cm³, while in the group B was 5.7 cm³, and tumor volume was increased significantly in patients referred during the outbreak of COVID-19 (p -value = 0.04). Also, in the group A of patients who chose total laryngectomy, there was a significant increase in tumor volume compared to the group B (p -value = 0.04). In the group A, patients who were candidates for TLM compared to the group B, there was an increase in tumor volume that was not statistically significant (P -Value = 0.35). Also, in the group of patients who were candidates for supracricoid partial laryngectomy during the period of COVID-19, compared to the same period before the outbreak of COVID-19, there was a decrease in tumor volume which was not statistically significant (p -value = 0.08) (Table 2).

In 9 patients in the group A, and in 8 patients in the group B, reconstruction was performed with pectoralis major flap which was not statistically significant between the two groups (p -value = 0.98).

Thyroid cartilage involvement was reported in 41 patients in the group A. In the group B, 40 cases were reported in pathology and there was no statistically significant difference (p -value = 0.55). Extralaryngeal complications frequency of laryngeal cancer patients with extra-laryngeal follow-up in the two groups of patients was not statistically significant (p -value = 0.72). Also, a total of 60 patients had perineural involvement, 32 patients in the group A and 28 patients in the group B with no significant difference in perineural involvement in the two groups (p -value = 0.98). 14 patients in the group A and 20 patients in the group B had lymphovascular invasion (p -value = 0.98).

4. Discussion

The aim of this study was to evaluate the effect of COVID-19 outbreak on the stage of the disease and surgical treatment for laryngeal cancer and to compare the results with the period before the outbreak of COVID-19. The overall results showed that the mean ages (59.59 years) of patients in the group A and B (59 years) were not significantly different and were generally equal. Also, almost the same genus distribution was observed in both groups of men and women during (111 males and 5 females) prevalence and before (90 males and 12 females) COVID-19 outbreaks.

Galli et al. in Italy in 2020 showed that, during the COVID-19 epidemic, 27 cancer patients were diagnosed and admitted in the ENT department. The mean age of patients was 67.2 years and the ratio of men to women was 3.3 to 1. In our study, the number of male patients was more than women. Also, in Galli et al. study 5 out of 27 (18.5%) patients with laryngeal cancer underwent laser cordectomy (type IV) laser type and complete laryngectomy [11], in the present study, during the outbreak of this virus, due to the increase in the stage of the disease and the progression of the disease, it was not possible to perform less invasive procedures and they had to perform a total laryngectomy. 91 and 63 patients with laryngeal SCC were treated with total laryngectomy during the outbreak period and before outbreak of COVID 19 a year earlier, respectively. The frequency of patients requiring total

laryngectomy surgery increased significantly in the group A compared to the group B. Patients who can undergo SCPL (15 patients in the group B vs. 9 in the group A) and TLM (24 patients before the COVID-19 vs 17 during the outbreak of the virus) were reduced. Gallo et al. in 2020 in Italy reported that the number of patients with laryngeal cancer with elective surgery was 2. Total laryngectomy and cT4aN0 was performed on the patients. Outpatient ENT consultations and treatments of choice decreased by 78% and 75%, respectively, while emergency surgery increased by 128% during this epidemic [12].

The results of our study also showed that the interval between sampling time and surgery time during the outbreak of COVID-19 was 41 days and in the same period before the outbreak was 45.5 days, and no difference was observed between these two periods. Because at the time of corona, cancer surgery was a priority for elective surgeries and the interval between sampling and surgery was shorter than in the previous period. However, numbers of patients undergoing SCPL during the outbreak of COVID-19 was lower than in the previous period. Patil et al. in India in 2020 found that in COVID-19 epidemic, there is an urgent need for guidance in the treatment of head and neck cancers, which, if delayed, could have serious consequences total laryngeal resection and heavier surgeries. Radiation therapy and surgery are both treatment options for the larynx during this period. However, radiation therapy should be preferred because surgery may expose the virus to infectious aerosols, but in general, the preferred treatment for laryngeal cancer is surgery [13].

In the results of the present study, 91 patients were in stage 3 and 4 (as a stage of cancer progression) in the group A, but 66 in the group B. Patients who first referred for surgery at the time of the COVID-19 outbreak and had no previous history of laryngeal cancer (84 patients), in Compared to people who first presented at the same time before the outbreak of COVID-19, they were in advanced stages of the disease. In a study conducted by Brody et al. in the United States in 2020; surgeons were concerned about their health and safety and were most concerned about their resident trainees. 53.3% of respondents were willing to delay the normal treatment schedule for the early stages of the tumor by 2 or 4 weeks, while 12.5% were willing to delay the treatment for the early stages of the tumor by 6 weeks. This study shows the difference in the willingness of head and neck surgeons to delay surgery or change the schedule at the time of hospitalization during the COVID-19 epidemic in hospitals, which is the reason for the progression of the disease [14]. The results of the tumor volume study in our research showed a significant increase in the mean tumor volume in the group A compared to the group B (12 cm³ vs. 5.7 cm³); Also, in the group of patients who underwent total laryngectomy and TLM during the period of the virus outbreak, an increase in tumor volume was observed compared to the same period before the outbreak of COVID-19. A study by Kiong et al. in 2021 in the United States predicted diagnostic delays and an increased incidence of neck and head cancer due to COVID-19. Tumor characteristics before and during the initial COVID-19 period showed that there was a 25% reduction in newly diagnosed malignancies. The research findings show an increase in tumor burden in affected patients, despite the same time for diagnosis, head and neck cancer occurs during the epidemic [10]. Thyroid cartilage involvement was reported in 41 patients at the time of COVID-19 outbreak and 40 patients before it. The incidence of lymph node was not significantly different between the two groups. Perineural and lymphovascular invasion were not significantly different between the two groups, too. Studies show that it is important to re-evaluate the pattern of head and neck cancer treatment during the COVID-19 epidemic. Patients with head and neck cancer are generally at higher risk for COVID-19 infection and severe side effects. In addition, there are new and specific risks for COVID-19 at several levels for patients, surgeons, healthcare professionals, institutions and the community. Immediate guidance is needed in providing safe and quality care for head and neck cancer [15]. New barriers to safe surgery for head and neck cancers include: incomplete preoperative screening for covid-19 in patients; exposure to

SARS-cov-2 aerosols; potential and long-term production of infected aerosols in one surgery, compatibility of the use of advanced personal protective equipment during surgery with surgical equipment by the patient, physician and persons in the operating room mechanical and chemical protections against COVID-19 cannot be used at the same time and surgical equipment used at the same time deficiencies of advanced protective equipment against COVID-19 during surgery. In addition, new multifunctional risks specific to COVID-19 for patients such as the use of immunosuppressive therapies, transmission of COVID-19 from the hospital environment to the patient and lack of social resources health care are reasons for the renewal of traditional teachings before the cancer and neck epidemic. On the other hand, due to the COVID-19 epidemic, 19 patients go to medical centers later for diagnosis and treatment. Also, due to quarantine to prevent the spread of this virus, surgeries have been delayed, which has led to a worsening of the disease and The tumor has grown in size and has undergone more invasive surgeries such as total laryngectomy. It should be noted, however, that these cases cannot be conclusively attributed to COVID-19 and it is suggested that they be compared with the results of the last 5 years instead of one year. In cases where surgery is the only option, pre-surgery planning and the development of specific COVID-19 protocols are recommended to maximize the safety and quality of surgical and oncological care [16,17].

5. Conclusion

In the present study, there was a significant difference in the number of patients referred during the outbreak and before the outbreak of COVID-19. Patients who referred for diagnosis and treatment at the time of COVID-19 outbreak were in more advanced stages of the disease and also the tumor volume was higher in them than patients who had referred before the outbreak. Therefore it is necessary to provide new solutions, education and treatment management for patients with laryngeal cancer.

Ethical approval

This study was approved by the ethics committees of the collaborating hospitals.

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Declaration of competing interest

None of the authors had any conflict of interest during this research.

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