

COVID-19 in patients with total laryngectomy

Total larenjektomili hastalarda COVID-19

Yetkin Zeki Yılmaz¹, Doğan Çakan¹, Begüm Bahar Yılmaz², Musa Musayev¹,
Atakan Demir¹, Ayşegül Batioğlu-Karaaltın¹

¹Department of Otolaryngology, Istanbul University-Cerrahpaşa, Cerrahpaşa Medicine Faculty, Istanbul, Türkiye

²Department of Otolaryngology, Istanbul Başakşehir Çam and Sakura City Hospital, Istanbul, Türkiye

ABSTRACT

Objectives: The aim of this study was to investigate the frequency and clinical severity of coronavirus disease 2019 (COVID-19) disease in patients with total laryngectomy.

Patients and Methods: This retrospective study was conducted with 114 participants (102 males, 12 females; mean age: 65.9±10.4 years; range, 40 to 92 years). Fifty-seven patients who underwent total laryngectomy in our clinic between June 2014 and June 2018 were included in the study group. Among the healthy individuals who applied to our clinic, 57 people were included in the control group. The frequency of COVID-19 was determined in the study groups. The severity of COVID-19 symptoms of the patients was questioned, and the obtained data were analyzed.

Results: The study group consisted of 52 (91.2%) male and five (8.8%) female patients, and the control group consisted of 50 (87.7%) male and seven (12.3%) female participants. The mean ages of the groups were 65.9±10.4 years (median age: 65 years; range, 40 to 92 years) for study group and 65.7±11.0 years (median age: 65 years; range, 40 to 94 years) for control group. The frequency of COVID-19 in study group was significantly lower compared to control group ($p=0.001$). In the evaluation of COVID-19 symptoms, cough and smell disorder symptoms were found to be significantly more severe in study group ($p=0.001$, $p=0.001$, respectively). The number of inpatients treated in study group was significantly higher than in control group ($p=0.015$).

Conclusion: The incidence of COVID-19 may be lower in patients with total laryngectomy compared to the normal population. However, the clinical course of COVID-19 may be more severe in patients with total laryngectomy compared to the normal population.

Keywords: COVID-19, diagnosis, laryngectomy, larynx cancer, symptoms.

ÖZ

Amaç: Bu çalışmada total larenjektomili hastalarda koronavirüs hastalığı 2019 (COVID-19) hastalığının sıklığı ve klinik şiddeti incelendi.

Hastalar ve Yöntemler: Bu retrospektif çalışma 114 katılımcı (102 erkek, 12 kadın; ort. yaş: 65.9±10.4 yıl; dağılım, 40-90 yıl) ile yürütüldü. Çalışma grubuna Haziran 2014 - Haziran 2018 tarihleri arasında kliniğimizde total larenjektomi ameliyatı geçiren 57 hasta dahil edildi. Kliniğimize başvuran sağlıklı bireyler arasından 57 kişi kontrol grubuna dahil edildi. Çalışma gruplarında COVID-19'un sıklığı tespit edildi. Hastaların COVID-19 semptomlarının şiddeti sorgulandı ve elde edilen veriler analiz edildi.

Bulgular: Çalışma grubu 52 (%91.2) erkek ve beş (%8.8) kadın hastadan, kontrol grubu ise 50 (%87.7) erkek ve yedi (%12.3) kadın katılımcıdan oluştu. Grupların yaş ortalamaları çalışma grubu için 65.9±10.4 yıl (medyan yaş: 65 yıl; dağılım, 40-92 yıl), kontrol grubu için 65.7±11.0 yıl (medyan yaş: 65 yıl; dağılım, 40-94 yıl) idi. Çalışma grubundaki COVID-19 görülme oranı, kontrol grubuna kıyasla anlamlı derecede düşüktü ($p=0.001$). COVID-19 semptomlarının değerlendirilmesinde, öksürük ve koku bozukluğu semptomları çalışma grubunda anlamlı olarak daha şiddetli bulundu (sırasıyla, $p=0.001$, $p=0.001$). Çalışma grubunda yatan hasta sayısı kontrol grubuna kıyasla anlamlı derecede fazlaydı ($p=0.015$).

Sonuç: COVID-19 sıklığı total larenjektomili hastalarda normal popülasyona kıyasla düşük olabilir. Bununla birlikte COVID-19 kliniği total larenjektomili hastalarda normal popülasyona göre daha ağır seyrediyor olabilir.

Anahtar sözcükler: COVID-19, tanı, larenjektomi, larenks kanseri, semptomlar.

Received: January 3, 2021 Accepted: August 12, 2021 Published online: September 13, 2022

Correspondence: Yetkin Zeki Yılmaz, MD. İstanbul Üniversitesi-Cerrahpaşa, Cerrahpaşa Tıp Fakültesi, Kulak Burun Boğaz Anabilim Dalı, 34098 Fatih, İstanbul, Türkiye.

e-mail: yetkin.yilmaz@iuc.edu.tr

Citation:

Yılmaz YZ, Çakan D, Yılmaz BB, Musayev M, Demir A, Batioğlu-Karaaltın A. COVID-19 in patients with total laryngectomy. KBB Uygulamaları 2022;10(2):51-56.

It was announced to the world on January 7, 2020, that a new type of coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was isolated by the Chinese government in the Wuhan region of China.^[1] This virus affected the entire world and the coronavirus disease 2019 (COVID-19) was declared a pandemic by the World Health Organization (WHO) on March 11, 2020.^[2] As of June 30, 2022, 551,874,526 confirmed cases and approximately 6,356,428 deaths have been reported for COVID-19 worldwide.^[3]

Severe acute respiratory syndrome coronavirus 2 is transmitted by inhalation or by contact of infected droplets with the mucosa.^[4] The primer and dominant infection site of SARS-CoV-2 in the respiratory tract is the nasal cavity.^[5] Two hypotheses have been proposed regarding the spread of COVID-19: the inhalation of infected droplets into the lung or the replication of the virus in the nasal cavity, from where it reaches the lung through the naso-oropharynx via microaspirates.^[6-8] Therefore, the WHO recommends staying away from the crowd, maintaining physical distance, providing hand hygiene, and using masks to prevent disease.^[9]

Laryngeal cancer is the second most common head and neck cancer, and a total of 177,000 estimated new cases and 94,000 deaths due to laryngeal cancer were reported in 2018.^[10,11] More than 95% of cases are in the type of squamous cell carcinoma, and the main risk factor in etiology is smoking.^[12] Although many factors, such as the location, size, and condition of the lymph nodes, are effective in the treatment selection of laryngeal cancer, total laryngectomy is a therapeutic option as a first-line treatment for patients who are not suitable for organ-preserving techniques and is the standard surgical method in salvage surgery.^[13,14]

Severe acute respiratory syndrome coronavirus 2 multiplies in the upper respiratory tract, particularly in the nasopharynx.^[5,6] After total laryngectomy, the connection between the upper and lower airways is permanently separated. Air reaches the lower respiratory tract directly through the stoma. The permanent loss of the warming, humidification, and mucociliary clearance provided by the upper airways is the cause of predisposition to severe lower respiratory tract infections for patients with a total laryngectomy.^[15] Based on this information, we hypothesized that a SARS-CoV-2 infection would be less frequent in total laryngectomy patients compared to healthy individuals; however, COVID-19 would be more severe in total laryngectomy patients. Hence, the aim of this study was to investigate the prevalence of COVID-19 and the clinical course of the disease in patients with total laryngectomy, as the first in the literature.

PATIENTS AND METHODS

This retrospective study was conducted with 114 participants (102 males, 12 females; mean age: 65.9±10.4 years; range, 40 to 92 years) at the Istanbul University-Cerrahpaşa Cerrahpaşa School of Medicine, Department of Otolaryngology. The files of 246 patients who underwent total laryngectomy for laryngeal squamous cell carcinoma between June 2014 and June 2018 in our clinic were reviewed. One hundred fifty-eight of these patients could be reached. Patients who did not wear a mask on both their face and tracheostomy, who received chemotherapy or radiotherapy, who had known chronic lung disease, who had lack mentality, and who did not want to participate in the study were excluded from the study. Among the patients with total laryngectomy included in the study, patients with suspected COVID-19 but who did not receive a tracheal swab sample for real-time polymerase chain reaction (RT-PCR) were excluded from the study. The control group consisted of individuals who did not undergo laryngectomy. According to the inclusion and exclusion criteria of the study, 57 patients were included in the study group. Among the patients who applied to our otorhinolaryngology outpatient clinic for hearing examination and did not have any diagnosis other than sensorineural hearing loss, 57 subjects were included in the control group without knowing their COVID-19 status.

The patients who underwent total laryngectomy were reached by phone, and their mask usage status was questioned. Of these patients, those who had COVID-19 were asked how their swab samples were taken. Coronavirus disease 2019 symptoms were questioned, and the severity of these symptoms was given a score between 0 and 10 by the patients. The same procedures were applied to the control group. The diagnosis of COVID-19 was confirmed by examining the medical records of the subjects who stated that they had COVID-19. SARS-CoV-2 positivity rates, presence, and severity of clinical symptoms of the groups were analyzed.

Statistical analysis

Data were analyzed using IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean±standard deviation (SD), and categorical variables were expressed as numbers (%). Normal distribution and homogeneity of data were analyzed with the Kolmogorov-Smirnov test and Levene's tests, respectively. The Mann-Whitney U test and the Pearson chi-square test were used in the statistical analysis. A *p* value <0.05 was considered statistically significant.

Table 1
Demographic data of the patients

Parameters	Study group (n=57)			Control group (n=57)			p		
	n	Mean±SD	Median	Min-Max	n	Mean±SD		Median	Min-Max
Age (year)		65.9±10.4	65	40-92		65.7±11.0	65	40-94	0.677
Sex									0.542*
Male	52				50				
Female	5				7				
Symptoms	Patients in Study group (n=10)			Patients in Control group (n=27)			p		
	Median	Min-Max		Median	Min-Max				
Fatigue	3	0-8		3	0-6		0.743		
Fever	0	0-9		0	0-8		0.621		
Cough	4	2-7		1	0-5		0.001**		
Sputum	0	0-2		0	0-2		0.311		
Dyspnea	0	0-5		0	0-3		0.744		
Headache	0	0-1		0	0-1		0.379		
Sore throat	0	0-5		0	0-5		0.916		
Runny nose	0	0-6		0	0-4		0.959		
Nasal congestion	0	0-4		0	0-3		0.360		
Taste disorder	0	0-2		0	0-3		0.213		
Smell disorder	6	0-9		0	0-5		0.001**		

* Pearson chi-square test, value= 0.373; df=1, p>0.05; ** Mann-Whitney U test, p<0.05

RESULTS

The study group consisted of 52 (91.2%) male and five (8.8%) female patients, and the control group consisted of 50 (87.7%) male and seven (12.3%) female participants. There was no difference between the groups in terms of sex ($p=0.542$). The mean ages of the groups were 65.9 ± 10.4 years (median age: 65 years; range, 40 to 92 years) for study group and 65.7 ± 11.0 years (median age: 65 years; range, 40 to 94 years) for control group. No significant difference was found between the groups in terms of age ($p=0.677$, Table 1).

The number of patients with a history of COVID-19 is given in Table 2. When the groups were examined in

terms of SARS-CoV-2 positivity, it was found that the frequency of COVID-19 in study group was significantly lower compared to control group ($p=0.001$, Table 2).

Information about the COVID-19 symptoms of the patients is given in Table 1. In the evaluation of COVID-19 symptoms, cough and smell disorder symptoms were found to be significantly more severe in study group ($p=0.001$, $p=0.001$, respectively). There was no significant difference between the groups in terms of other symptoms ($p>0.05$, Table 1).

While three (42.86%) patients in study group were hospitalized and treated, all patients ($n=27$, 100%) in the control group were treated as outpatients. The number

Table 2
SARS-CoV-2 RT-PCR positivity in groups

Groups	SARS-CoV-2 +		SARS-CoV-2 -		p
	n	%	n	%	
Study group	10	17.54	47	82.46	0.001*
Control group	27	47.37	30	52.63	

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; RT-PCR: Real-time polymerase chain reaction; * Pearson chi-square test, value= 11.564; df=1, p<0.05.

of inpatients treated in study group was significantly higher than in control group (Fisher's exact test, value=8,815; df=1; p=0.015, p<0.05).

DISCUSSION

Coronavirus disease 2019, which is the first pandemic after the Spanish flu epidemic between 1918 and 1920, affected all of humanity.^[16] Patients with chronic diseases are at the forefront of those who are affected by this acute condition. In this study, we examined the frequency and severity of the clinical state of COVID-19 in total laryngectomy patients, one of the patient groups frequently followed up in otorhinolaryngology. As a result of our study, we found that the frequency of COVID-19 was significantly lower in patients with total laryngectomy compared to healthy individuals (p=0.001). When the clinics of the patients were examined, we found that cough and smell disorder symptoms were significantly more severe in patients with total laryngectomy, and we found that the number of hospitalized patients was significantly higher in the total laryngectomy patient group (p<0.05).

The rate of patients undergoing organ-preserving treatment for laryngeal carcinoma, the most common cancer in the head and neck region, is increasing.^[17] Although the rate of total laryngectomy is gradually decreasing, these patients are still one of the largest patient groups that are followed up most frequently in otorhinolaryngology practice. The total laryngectomy procedure permanently changes the respiratory system anatomy. The primary location of entry and replication of SARS-CoV-2 is the nasal cavity and nasopharynx.^[5] Replicated viral particles are transported into the lungs by microaspirates, then causing systemic disease.^[4] The upper respiratory tract is disrupted in total laryngectomy patients, and their trachea and lower respiratory tract are directly connected to the environment.^[18] Based on this, we hypothesized that patients with total laryngectomy less frequently have SARS-CoV-2 disease; in addition, COVID-19 has a more severe clinical picture in the total laryngectomy patients since the lower respiratory tract and lungs are directly exposed to the virus. In the COVID-19 guideline of the Ministry of Health of the Republic of Türkiye, RT-PCR, which is primarily studied with a naso/oropharyngeal swab sample, is recommended for the diagnosis of SARS-CoV-2.^[19] There is no recommendation in this guideline on how to take swab samples from total laryngectomy patients.^[19] In our study, we included total laryngectomy patients whose samples were taken from the nasopharynx, oropharynx, and trachea with the same swab stick,

with the thought that SARS-CoV-2 can directly and only affect the trachea in total laryngectomy patients. While evaluating the symptoms of COVID-19 in patients, we questioned the severity of the symptoms instead of questioning the presence of symptoms to make a stronger statistical analysis.

Coronavirus disease 2019 can present with a different spectrum of clinical manifestations, from asymptomatic to death.^[20] Symptoms of COVID-19 include common upper respiratory tract infection symptoms, such as dyspnea, cough, fever, and more specific symptoms, such as smell and taste disorders.^[21] Previous studies have shown that dyspnea and cough are associated with a poor prognosis.^[22,23] The relationship between COVID-19 and total laryngectomy patients was mentioned in two studies.^[24-26] One of these studies reported that COVID-19 may show a more severe clinical course.^[24]

In our study, we found that COVID-19 was less frequent in total laryngectomy patients compared to the control (p=0.001). In addition, in our study, we found that smell disorder and cough symptoms were more severe in COVID-19 patients who underwent total laryngectomy (p<0.05). It is an expected result that among these symptoms, olfactory disorder is more severe in total laryngectomy patients, depending on the total laryngectomy surgery itself.^[27] Furthermore, in this patient group, the cough was more severe, and the hospitalization rate was higher, which may indicate that prognosis of COVID-19 is more severe.

There are some limitations to the present study. The first of these limitations is that the swab samples were taken by different personnel in different centers, and RT-PCR tests were performed with different kits in different centers. Due to the retrospective character of our study, it was not possible to standardize these conditions that are known to affect the SARS-CoV-2 test results. As a second limitation, we could not determine the mask types and brands used by the patients, although we achieved the standardization of masks used in our study. The fact that different mask types have different protection rates may have affected the results of our study. The last and most important limitation of our study is that a patient-based questionnaire was utilized. The compliance of the patients with the inclusion and exclusion criteria of our study, particularly the way the swab samples were taken, was determined according to the answers given by the patients to the questionnaire.

In conclusion, we found that COVID-19 might be less frequent in patients with total laryngectomy than in the normal population, but COVID-19 clinic might

be more severe in this patient group. The results of our study should be repeated with more comprehensive, prospective studies of higher methodological standardization qualifications.

Ethics Committee Approval: The study protocol was approved by the İstanbul University-Cerrahpaşa Ethics Committee (date/no: 106275). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Surgical and medical practices: Y.Z.Y., D.Ç., A.D., M.M.; Concept: Y.Z.Y., A.D., D.Ç., A.B.K.; Design: Y.Z.Y.; Data collection or processing: B.B.Y., A.B.K.; Analysis or interpretation: D.Ç., B.B.Y., A.B.K.; Literature search: D.Ç., B.B.Y., A.B.K.; Writing: Y.Z.Y., B.B.Y. M.M., A.D., B.B.Y.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

- Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020;382:727-33.
- WHO,WHO Virtual press conference on COVID-19 (2020). Available at: <https://www.who.int/emergencies/diseases/novel-coronavirus2019/media-resources/press-briefings>. [Accessed: March 11, 2020]
- Available at: <https://www.worldometers.info/coronavirus/> [Accessed: 18 June 2022]
- Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med* 2020;382:1199-207.
- Hou YJ, Okuda K, Edwards CE, Martinez DR, Asakura T, Dinnon KH 3rd, et al. SARS-CoV-2 reverse genetics reveals a variable infection gradient in the respiratory tract. *Cell* 2020;182:429-46.e14.
- Morawska L, Cao J. Airborne transmission of SARS-CoV-2: The world should face the reality. *Environ Int* 2020;139:105730.
- Wilson NM, Norton A, Young FP, Collins DW. Airborne transmission of severe acute respiratory syndrome coronavirus-2 to healthcare workers: A narrative review. *Anaesthesia* 2020;75:1086-95.
- Dickson RP, Erb-Downward JR, Martinez FJ, Huffnagle GB. The microbiome and the respiratory tract. *Annu Rev Physiol* 2016;78:481-504.
- World Health Organization. Advice on the use of masks in the context of COVID-19: Interim guidance, 6 April 2020. World Health Organization 2020.
- Cramer JD, Burtneß B, Le QT, Ferris RL. The changing therapeutic landscape of head and neck cancer. *Nat Rev Clin Oncol* 2019;16:669-83.
- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68:394-424.
- Gamez ME, Blakaj A, Zoller W, Bonomi M, Blakaj DM. Emerging concepts and novel strategies in radiation therapy for laryngeal cancer management. *Cancers (Basel)* 2020;12:1651.
- Obid R, Redlich M, Tomeh C. The treatment of laryngeal cancer. *Oral Maxillofac Surg Clin North Am* 2019;31:1-11.
- Forastiere AA, Ismaila N, Lewin JS, Nathan CA, Adelstein DJ, Eisbruch A, et al. Use of larynx-preservation strategies in the treatment of laryngeal cancer: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol* 2018;36:1143-69.
- van den Boer C, van Harten MC, Hilgers FJ, van den Brekel MW, Retèl VP. Incidence of severe tracheobronchitis and pneumonia in laryngectomized patients: A retrospective clinical study and a European-wide survey among head and neck surgeons. *Eur Arch Otorhinolaryngol* 2014;271:3297-303.
- Kumar P, Singh RK, Shahgholian A. Learnings from COVID-19 for managing humanitarian supply chains: Systematic literature review and future research directions. *Ann Oper Res* 2022:1-37.
- Maddox PT, Davies L. Trends in total laryngectomy in the era of organ preservation: A population-based study. *Otolaryngol Head Neck Surg* 2012;147:85-90.
- Chotipanich A. Total laryngectomy: A review of surgical techniques. *Cureus* 2021;13:e18181.
- T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü COVID-19 Rehberi. Available at: <https://covid19.saglik.gov.tr/TR-66301/covid-19-rehberi.html> [Accessed: June 30, 2022]
- Neumann-Podczaska A, Al-Saad SR, Karbowski LM, Chojnicki M, Tobis S, Wieczorowska-Tobis K. COVID 19 - clinical picture in the elderly population: A qualitative systematic review. *Aging Dis* 2020;11:988-1008.
- Ahn DG, Shin HJ, Kim MH, Lee S, Kim HS, Myoung J, et al. Current status of epidemiology, diagnosis, therapeutics, and vaccines for novel coronavirus disease 2019 (COVID-19). *J Microbiol Biotechnol* 2020;30:313-24.
- Roig-Marín N, Roig-Rico P. In elderly patients with COVID-19 early onset of cough indicates a more severe disease development. *Infect Dis (Lond)* 2022;54:159-61.
- Diep AN, Gilbert A, Saegerman C, Gangolf M, D'Orio V, Ghuysen A, et al. Development and validation of a predictive model to determine the level of care in patients confirmed with COVID-19. *Infect Dis (Lond)* 2021;53:590-9.

24. Paderno A, Fior M, Berretti G, Del Bon F, Schreiber A, Grammatica A, et al. COVID-19 and total laryngectomy-A report of two cases. *Ann Otol Rhinol Laryngol* 2021;130:104-7.
25. Fabbris C, Boaria F, Boscolo-Rizzo P, Emanuelli E, Spinato G. Discrepancies of SARS-CoV-2 testing results among patients with total laryngectomy. *Eur Arch Otorhinolaryngol* 2022;279:2193-6.
26. Fernandez IJ, Spagnolo F, Valerini S, Mattioli F, Molteni G, Marchioni A, et al. SARS-CoV-2 tracheitis in laryngectomised patients: A consecutive case-series study. *Clin Otolaryngol* 2022;47:203-6.
27. Caldas AS, Facundes VL, Melo TM, Dourado Filho MG, Pinheiro Júnior PF, Silva HJ. Modifications and evaluation of smell and taste functions in total laryngectomy: Systematic review. *J Soc Bras Fonoaudiol* 2011;23:82-8.