

The survival rates of patients with head and neck carcinoma before and during the COVID-19 pandemic

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Aim To compare the survival rates of patients with head and neck cancer before and during the COVID-19 pandemic.

Methods In this retrospective study, we reviewed the medical records of 281 patients treated for squamous cell carcinoma of the larynx and oral cavity at the Clinic for Ear, Nose, and Throat Diseases and Head and Neck Surgery, University Hospital Zagreb, from 2018 to 2021. Demographic data, American Joint Committee on Cancer (AJCC) stage, the number of recurrences, and survival rates were compared between the pre-pandemic period (2018 and 2019) and pandemic period (2020 and 2021).

Results During the pandemic, survival rates for both sites were lower than in the pre-pandemic period, but the difference did not reach statistical significance. In the pandemic period, laryngeal cancer patients were significantly older. There was no significant difference between the periods in sex, age (for oral cancer patients), AJCC stage, and the number of recurrences.

Conclusion Although there was no significant difference between the periods in most of the parameters, age and the number of patients with advanced stages of the disease (especially stage-IV oral cancer) were higher during the pandemic period. Our results highlight the importance of unhindered access to healthcare and early treatment for patients with squamous cell carcinoma of the head and neck not only during pandemics but also in all circumstances.

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INTRODUCTION

The COVID-19 pandemic presented numerous challenges to healthcare systems worldwide. In Croatia, the response to the pandemic included reorganization of the healthcare system: a part of the medical staff was redirected to special COVID-19 wards, the number of beds in the wards was reduced, the number of beds for COVID-19 patients in intensive care units increased, and only emergency and oncology patients were treated surgically.

The COVID-19 lockdown in Croatia, imposed from March 16, 2020, to May 4, 2022, restricted population mobility and healthcare access. The referrals for treatment in secondary or tertiary healthcare centers decreased (1). Almost 90% of medical institutions treating patients with malignant diseases reported difficulties in providing their full range of services. Consequently, more than 50% of them reduced their capacity due to pandemic overload (2). Treatment recommendations for malignant diseases were changed. Initially, for head and neck cancer, non-surgical methods (chemoradiotherapy) were proposed when feasible. Surgery was postponed if possible, even if it was the only viable treatment (3). Simpler reconstructive options were recommended instead of complex and longer micro-surgical procedures (4).

Our previous study from 2022 (5) revealed an increase in the number of patients at our Clinic during the pandemic period. While laryngeal cancer was more prevalent in the pre-pandemic period, the number of oral cavity cancer patients increased in the pandemic period, leading to similar rates of these two types of cancer. Patients with oral cavity cancer during the pandemic period experienced significantly prolonged time from the initial presentation to the first head and neck surgeon examination. For both cancer sites, the time from the initial presentation to the beginning of treatment significantly increased. There were no differences in TNM stages between the periods. However, the previous study did not assess the survival of patients as a result of the treatment delay (5).

The current study serves as a continuation of our previous study with an aim to determine whether delaying treatment initiation during the pandemic compared with the pre-pandemic period led to different survival rates between the two periods.

PATIENTS AND METHODS

The study was conducted at the Clinic for Ear, Nose, and Throat Diseases and Head and Neck Surgery, University Hospital Zagreb. It enrolled patients who were primarily surgically treated for laryngeal and oral cavity squamous cell carcinoma (SCC) from January 1, 2018, to December 31, 2021. Exclusion criteria were distant metastatic or previous malignant disease. Tumors were classified according to the 2018 American Joint Committee on Cancer (AJCC) staging criteria.

The treatment modality for each patient was decided upon by the head and neck multidisciplinary team including otolaryngologists, oncologists, radiologists, pathologists, psychologists, speech therapists, and nurses. Given the pandemic circumstances, the multidisciplinary team met irregularly, which resulted in a lack of data for 25 patients in the digital database.

For most patients, all data were available in institutional electronic medical records (EMR). For patients with insufficient EMR, data were obtained from the electronic health records in the centralized state system. Patients' demographics data, tumor stage, survival rate, and the number of recurrences were compared between the pre-pandemic (2018, 2019) and pandemic period (2020, 2021).

Statistical analysis

Categorical data are presented as counts and percentages, while continuous data are presented as means and standard deviations, or medians and ranges. The normality of distribution was tested using the Shapiro-Wilks test, while homogeneity of variance was tested using the Levene test. Differences between the groups of independent continuous variables were assessed using the t-test and the Mann-Whitney test. Differences between categorical variables were assessed using the chi-square test. Survival was evaluated by Kaplan-Meier curves and compared using the log-rank test. Statistical significance was set at $p < 0.05$. Statistical analysis was performed using SPSS v.29 (IBM Corp., Armonk, NY, USA).

RESULTS

Of the 281 patients included in the study, 118 patients were enrolled in the pre-pandemic (87 with laryngeal and 31 with oral cancer) and 163 in the pandemic period (81 with laryngeal and 82 with oral cancer).

TABLE 4. Age and sex distribution of patients with laryngeal and oral cancer in both periods

		Laryngeal cancer			Oral cavity cancer		
		2018-2019	2020-2021	p	2018-2019	2020-2021	p
Sex, n (%)	male	78 (89.7)	70 (86.4)	0.518	19 (61.3)	57 (69.5)	0.406
	female	9 (10.3)	11 (13.6)		12 (38.7)	25 (30.5)	
Age (years), mean±standard deviation		63.5±9.5	66.3±9.7	0.025	60.03±10.9	63.4±11.7	0.154

Survivors' follow-up was at least 45 months. Thirty-six patients were lost to follow-up. There were no differences in TNM and AJCC stage distributions between the observed periods.

Demographic characteristics are shown in Table 1. Most of our patients were men (79.7%) in the seventh decade of life (mean age 63.9 years). There was no significant difference in sex between the two periods for both localizations. Laryngeal cancer patients were significantly older in the COVID-19 than in the pre-COVID-19 period, but for oral cancer patients there was no difference in age.

Due to cases of disease progression and published data on treatment delays, together with the loss of a significant number of patients from follow-up, we retested the stage distribution before survival analysis. For further analysis, due to the small sample size, we merged patients into early (AJCC stage I and II) and advanced (AJCC stage III and IV) disease groups.

The distribution of laryngeal cancer patients across AJCC stages in both periods is shown in Table 2. There

TABLE 5. The American Joint Committee on Cancer (AJCC) stage of patients with laryngeal cancer

AJCC stage	2018-19		2020-21		$\chi^2=3.523$ p=0.060
	No.	%	No.	%	
I-II	55	63.2	62	76.5	
III-IV	32	36.8	19	23.5	
Total	87	100	81	100	

was no significant difference in the distribution of patients with early and advanced disease between the two periods ($\chi^2=3.523$, p=0.060). Survival analysis showed that patients in early disease groups had significantly longer survival in both periods (Figure 1).

In the follow-up period, 14 (16.1%) patients with laryngeal cancer in the pre-COVID-19 group and 8 (9.9%) patients in the COVID-19 group developed recurrence ($\chi^2=1.424$, p=0.233) (Table 3). Three patients in the pre-COVID-19 group had two recurrence sites and one had all three recurrence sites. One patient in the COVID-19 group had two recurrence sites.

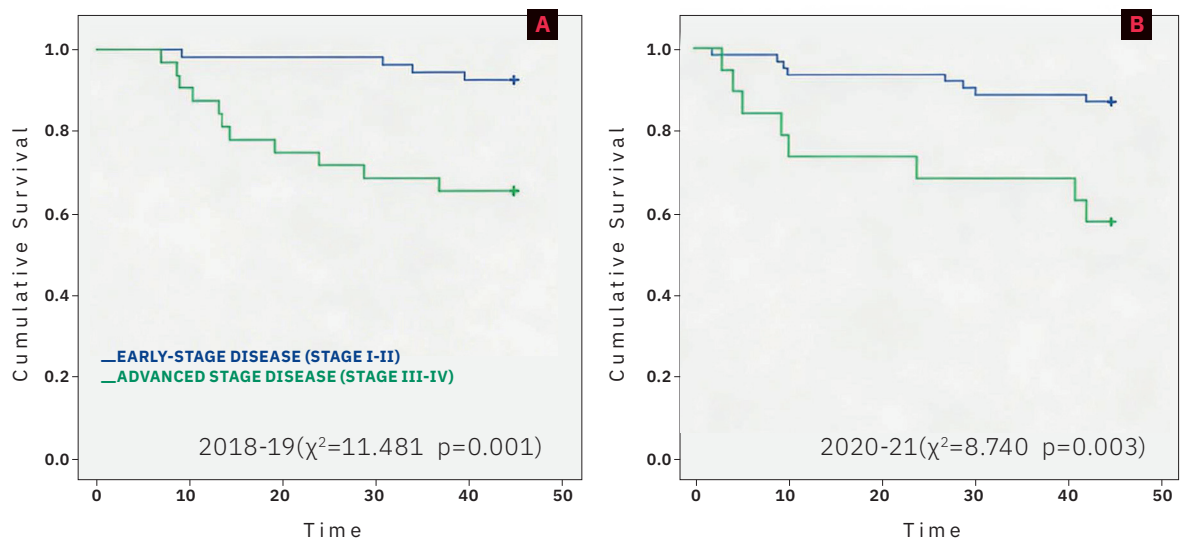
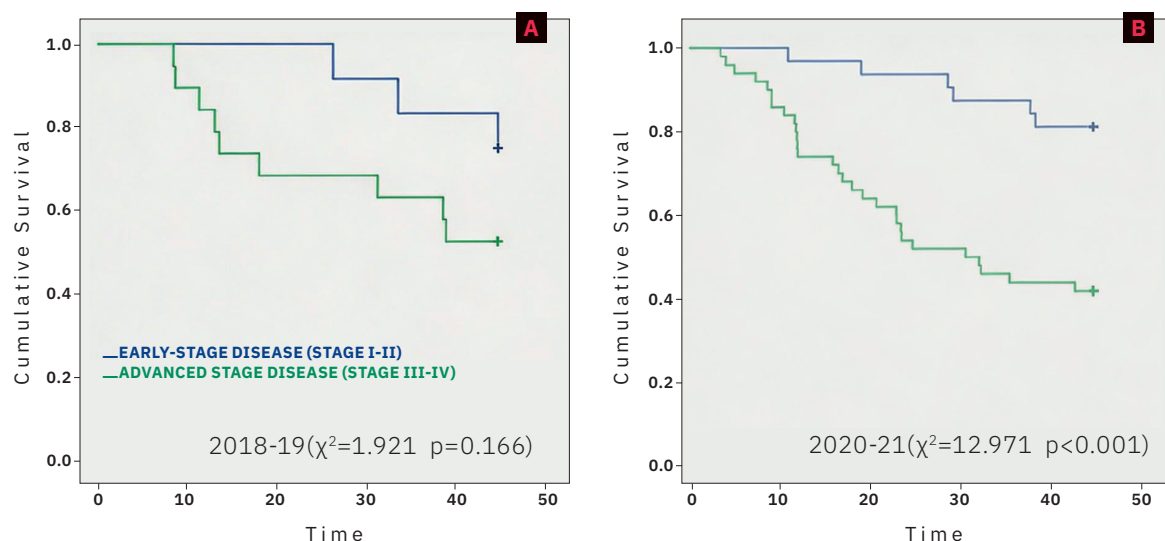
**FIGURE 1.** The survival of laryngeal cancer patients. (A) Pre-pandemic period. (B) Pandemic period.

TABLE 6. Recurrence sites in patients with laryngeal cancer

No. (%) of recurrences	2018-19	2020-21
Local	10 (11.5)	4 (4.9)
Regional	4 (4.6)	3 (3.7)
Distant	5 (5.7)	2 (2.5)
Total	14 patients 19 recurrence sites	8 patients 9 recurrence sites

TABLE 7. The American Joint Committee on Cancer (AJCC) stage of oral cancer patients

AJCC stage	2018-19		2020-21		$\chi^2=0.0009$ $p=0.976$
	No.	%	No.	%	
I-II	12	38.7	32	39.0	
III-IV	19	61.3	50	61.0	
Total	31	100	81	100	

**FIGURE 2.** The survival of oral cancer patients. (A) Pre-pandemic period. (B) Pandemic period.

The distribution of oral cancer patients across the AJCC stages for both periods is shown in Table 4. There was no significant difference ($\chi^2=0.0009$, $p=0.976$) in the distribution of patients with early and advanced disease between the periods (Table 4). In survival analysis, patients with early disease showed longer survival (Figure 2), but the difference did not reach significance in the pre-pandemic period.

In the follow-up period, 11 (35.4%) patients in the pre-COVID-19 group and 30 (36.6%) patients in the COVID-19 group developed recurrence ($\chi^2=0.012$, $p=0.913$) (Table 5). Three patients in the pre-COVID-19 group had two recurrence sites and two had all three recurrence sites. Five patients in the COVID-19 group had two recurrence sites and four patients had all three recurrence sites.

Although survival rates for both sites were lower in the COVID-19 period, the difference did not reach statistical significance (Figure 3).

TABLE 8. Recurrence site distribution in oral cancer patients

No. (%) of recurrences	2018-19	2020-21
Local	7 (22.6)	16 (19.8)
Regional	6 (19.4)	17 (21)
Distant	5 (16.1)	10 (12.3)
Total	11 patients 18 recurrence sites	30 patients 43 recurrence sites

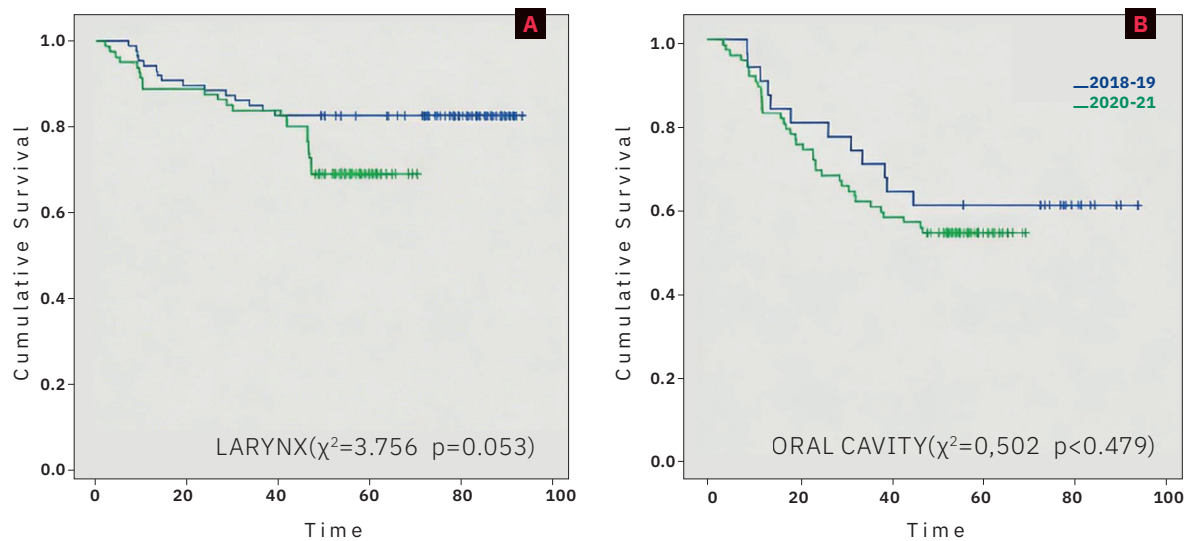


FIGURE 3. Survival rates for both sites and both periods.

DISCUSSION

In this study, the total number of patients in the pandemic period was higher due to a greater number of patients with oral cavity cancer. The prolonged time to first examination and time to treatment did not affect the stage distribution or survival rates.

In the COVID-19 pandemic, our institution for the first time treated more patients with oral cavity cancer than patients with laryngeal cancer. Our results are contrary to the results of other authors (6,7), who, in the first six-week or first six-month period of the pandemic, registered a 25% drop in the number of patients compared with the same period in 2019, and a 22% decrease compared with the six months before the pandemic (6,7).

An increased number of patients in the pandemic period can be partially explained by changes in healthcare organization in Croatia. In the pre-pandemic period, many patients with oral cancer were treated at the Department of Maxillofacial and Oral Surgery at Dubrava University Hospital. However, from the beginning of March 2020 to the end of July 2021, the whole hospital was appointed a special COVID-19 hospital. Consequently, more patients sought treatment at our institution.

The number of patients with laryngeal cancer did not increase between the two periods. Moreover, the number of patients slightly decreased during the pandemic,

probably due to limited availability of healthcare and fear of infection in the general population, which delayed the first ENT exam.

Patients in the pre-COVID-19 period were approximately three years younger than patients in the COVID-19 period. The difference was significant for laryngeal, but not for oral cancer. Solis et al (7) reported similar results.

Tevetoglu et al (8) also found a significantly prolonged period from symptom onset to first ENT outpatient visit in patients with oral cancer during the COVID-19 pandemic. In patients with laryngeal cancer the delay was slightly longer, which is consistent with our results. They also noted a significant increase in the number of T3 and T4 laryngeal cancers and the number of patients with regional metastases (N+ neck) in patients with oral cancer (8). Our study found no difference in the TNM distribution between the periods. A prolonged time from symptom onset to first referral during the pandemic was also previously reported (6).

In both periods in our study, laryngeal cancer was more often diagnosed in the early stages. Patients diagnosed in early stages had significantly better survival than those diagnosed in advanced stages. This expected result classifies our series as representative, allowing the overall survival comparison between the two periods. Oral cancer was more often diagnosed in

advanced stages. In the pre-pandemic period, survival rates did not significantly differ between patients with localized and advanced disease, which could possibly be attributed to a smaller sample size. In the pandemic period, survival was significantly longer in patients with early disease stages.

This study compared cumulative survival rates for both sites between the pre-pandemic and pandemic periods. Although the survival rates were lower in the pandemic period for both localizations, the difference did not reach statistical significance. Our results are consistent with those of other studies, which reported a non-significant decrease in cumulative survival rates during the pandemic period (9-11). Only Peacock et al found a significant decrease (12).

Recurrence rates for laryngeal cancer in our study are comparable and even slightly better than reported elsewhere (13,14). The expected recurrence rate in laryngeal cancer patients was 20-30%, with local recurrences being most frequent. Previously reported recurrence rates for oral cancer patients were around 20% (15), which is slightly better than our results. This indicates the high availability of tertiary care in our department even during the COVID-19 pandemic.

As part of the reorganization of the healthcare system during the pandemic, our department faced a reduction in the number of operating rooms, anesthesiology staff, and beds in intensive care units, all of which delayed the start of treatment. As similar problems have been reported worldwide, guidelines developed in the early months of the pandemic suggested chemoradiotherapy and treatment priority for cancer patients in advanced stages (16). Oral cancer patients were particularly affected as they frequently required more complex treatment involving microvascular reconstruction.

Despite all this, we did not record significant differences in cumulative survival rates for either site between the two periods. Such a result could be attributed to the quality work of our institution's staff, including the head and neck multidisciplinary team, and timely and quality cooperation with primary and secondary health care.

The main limitations of this study are the retrospective design, the small number of patients, and the loss of a considerable number of patients to follow-up.

In conclusion, although there was no significant difference in most of the compared parameters, we observed an increase in age and the number of patients with advanced disease stages (especially stage IV of

oral cancer) during the pandemic. Our results highlight the importance of unhindered access to healthcare and early treatment for patients with SCC of the head and neck not only during a pandemic but in all circumstances.

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Ethical approval

granted by the Ethics Committee of University Hospital Center Zagreb.

Declaration of authorship

All authors conceived and designed the study; all authors acquired the data; ML, MPG analyzed and interpreted the data; ML, MPG drafted the manuscript; DL critically reviewed the manuscript for important intellectual content; all authors gave approval of the version to be submitted; all authors agree to be accountable for all aspects of the work.

Competing interests

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

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