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The impact of COVID-19 pandemic on head and neck cancer diagnosis and treatment

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Abstract *Background/purpose:* Following the COVID-19 pandemic, there were reports of diagnostic delays and a surge in the prevalence of advanced head and neck cancer (HNC). We conducted a retrospective study on the impact of COVID-19 on the number of newly diagnosed HNC among patients who underwent screening at our center to understand the temporal changes.
Materials and methods: We investigated the Union for International Cancer Control guidelines-TNM classification, presence of subjective symptoms at the time of consultation, and initial treatment from the medical records of first-time patients with HNC who visited our head and neck surgery department during 2019–2021 and compared them with those before (2019) and after (2020–2021) the pandemic.
Results: A total of 1245 patients were included in the study. The number of patients were 437, 417, and 391 in 2019, 2020, and 2021, respectively, indicating a downward trend following the pandemic. When the incidence of early (stage 0–II) and advanced (stage III–IV) HNC cancers was compared, the proportion of patients with early-stage cancer declined. Among them, significant primary tumor progression was observed in T classification. The number of patients with no subjective symptoms at initial diagnosis was decreasing significantly.
Conclusion: A decrease in the proportion of HNC patients with early-stage cancer and primary tumor progression was observed after the pandemic in 2020 and 2021. The number

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of early-stage malignancies may have dropped due to patients' unwillingness to visit a doctor.

Introduction

The COVID-19 pandemic placed increased stress on health care systems. The imposed radical governmental restrictions such as lockdowns, declarations of states of emergency, and medical restrictions in various countries to prevent the spread of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection affected healthcare facilities worldwide including those for cancer. This resulted in decline in the number of new cancer diagnoses as the management of cancer patients suffered critical resource shortages and delays in care.[1] The impact of these changes has been reported as an increase in the number of cancer deaths in the future.[2,3] Following the first state of emergency declared by the Japanese government on 7 April 2020, restraints were imposed on events and school closures, and each governor requested the people to avoid leaving the house unnecessarily.[4] In the same month, the Centers for Medicare & Medicaid Services (CMS) recommended that medical institutions limit some outpatient consultations and postpone non-urgent surgeries, which departments in Japan responded appropriately.[5]

According to the Japan Cancer Society, the number of people who underwent screening for the five cancers, lung, stomach, colon, breast, and cervical, conducted by group branches, decreased by 27.4 % in 2020 and 10.3 % in 2021, compared to 2019.[6] According to the National Cancer Center Japan, the number of the data in the hospital-based cancer registry recovered to the same level as the average of 2018—2019 in 2021, however the figures for the stomach and larynx were still over 5% lower than the 2018—2019 average.[7] Horita[8] reported that among the 10 cancer types with the highest number of diagnoses in the hospital-based cancer registry, a significant decrease was observed, in the number of patients diagnosed, in 8 cancer types (esophageal cancer, gastric cancer, colon cancer, rectal cancer, non-small cell lung cancer, breast cancer, prostate cancer, and cervical cancer), compared to the projected 2020 numbers estimated from the patient data between 2016 and 2019. The report also found that the number of patients diagnosed with early-stage cancers tended to decrease more than those with advanced cancers.

These reports mainly describe cancers of sites with many registrations but provides few details on head and neck cancers (HNC), which have a smaller total number of registrations and are subdivided by site. Gazzini et al.[9] compared the incidence of HNC 10 months before and after the initial lockdown in Italy, and reported that after the pandemic, there was a 43 % reduction in the number of new HNC diagnoses and a significant reduction in early-stage T patients. In a report from the United States, Solis et al.[10] reported a 22 % reduction in the number of newly diagnosed cases, a significant increase in the overall proportion of stage T3/T4 cases, and an increase in primary tumor size after the pandemic, but no differences in the duration of tumor symptoms, time from presentation to diagnosis, time to surgery, extent of surgery, or postoperative adjuvant therapy before and after pandemic. Kiong et al.[11] also compared a 6-week period during the pandemic to the previous year and reported that there was a 25 % reduction in the number of new diagnoses after the pandemic, a significant increase in the T stage of squamous cell carcinoma and primary tumor size, but no difference in the duration of symptoms before initial presentation or time required for diagnosis.

In Japan, Kishino et al.[12] reported a 30 % decrease in the number of HNC cases between 2018 and 2019 and 2020, an increase in the proportion of "neck swelling" as a reason for consultation, and a decrease in the proportion of "primary tumor symptoms" and "detected on examination". Hamaguchi et al.[13] reported a 38 % decrease in HNC patients in 2020 and 18 % in 2021, with a significant decrease in patients with stage 0 and stage 1 during the COVID-19 period compared to the pre-COVID period. In addition, the number of patients with hypopharyngeal and laryngeal cancer undergoing emergency tracheostomy increased.

In Japan, COVID-19 infection continues to be endemic, and reports of changes over time after the initial outbreak are scarce. In this study, we examined the effect of COVID-19 on the number of newly diagnosed HNC among patients who underwent HNC screening at our center to understand the temporal changes in the number of newly diagnosed HNCs and the status of their tumors at diagnosis.

Materials and methods

Study design and patients

This study is a retrospective cohort study conducted within the Department of Head and Neck surgery, Osaka International Cancer Institute. Patients with newly diagnosed HNC who presented for the first time between January 2019 and December 2021, were included. Patients with recurrent disease, head and neck localization of hematological neoplasms, and head and neck cutaneous neoplasms were excluded from the analysis.

Clinical diagnosis, subjective symptoms, and treatment

Clinical diagnosis was made comprehensively based on cytology, biopsy, esophagogastroduodenoscopy and computed tomography, magnetic resonance imaging, and,

if necessary, positron emission tomography. Tumor staging was performed based on the Union for International Cancer Control guidelines (UICC-TNM, 8th ed.).[14]

The subjective symptoms at the time of the patient's initial medical examination were investigated. Patients with symptoms were also examined for the duration of their illness, from the onset of subjective symptoms to the date of their initial visit to the medical facility.

The initial treatment details were classified as surgery, chemotherapy (systemic chemotherapy), chemo-radiotherapy, radiotherapy (including heavy particle radiotherapy), and palliative treatment (including palliative irradiation).

Statistical analyses

Statistical analysis was performed using EZR version 1.55 software (Jichi Medical University, Saitama, Japan). Univariate analysis of the data was conducted using a Mann—Whitney *U* test and Kruskal—Wallis test for continuous variables; Pearson's chi-square test was used to examine associations between groups for categorical variables. Statistical significance was set at $P < 0.05$. For statistical analysis, comparisons were made between two periods during 2019—2021, with 2019 as the pre-COVID-19, and 2020 and 2021 as the post-COVID-19 pandemic periods, respectively. In addition, the number of early-stage (stage 0-II) and advanced (stage III-IV) cases, and the number of days from subjective symptoms to consultation were compared by year.

The study was reviewed and approved by the Research Ethics Committee of the Osaka International Cancer Institute (No.21124). The requirement for informed consent was waived due to the retrospective nature of the study.

Results

Baseline characteristics

Table 1 summarizes the demographics of the 1245 consecutive patients presented at the hospital from January 2019 to December 2021, who were included in the study. The number of newly diagnosed HNC among new first-time patients decreased from 437 in 2019 to 417 in 2020 and 391 in 2021. Comparing the average number of patients per month between pre- and post-COVID-19 pandemic, there were 36.4 ± 7.6 patients in the pre-pandemic and 33.7 ± 5.6 in the post-pandemic periods, a decrease of 7.4 %, although not significantly different ($P = 0.227$). There were no significant differences by age, sex, or primary site.

Tumor characteristics

Based on the UICC-TNM classification, significant differences in frequencies were observed among the different clinical stages between pre- and post-COVID-19 pandemic periods (Table 2). In addition, when the number of patients with early-stage cancer was compared according to the year, although not significantly, the proportion of patients with early-stage cancer in post-COVID-19 showed a decreasing trend. ($P = 0.082$) (Fig. 1).

The proportion of Tis and T1 decreased in post-COVID-19 compared to pre-, while the proportion of T2 and T3 increased. The proportion of N0 in the N category

Table 1 Baseline characteristics of patients with head and neck cancer.

	Total n(%)	Pre-COVID(%) (2019; n = 437)	Post-COVID(%) (2020; n = 417, 2021; n = 391))	*P*-value
Total number	1245	437	808	
Median age, years(range)	68(17—96)	68(25—93)	68(17—96)	0.673[a]
Sex				0.503[b]
Men	899(72.2)	310(70.9)	589(72.9)	
Women	346(27.8)	127(29.1)	219(27.1)	
Tumor subsite				0.214[b]
Oral cavity	270(21.7)	91(20.8)	179(22.6)	
Maxillary sinus	39(3.1)	11(2.5)	28(3.5)	
Nasopharnx	28(2.2)	10(2.3)	18(2.2)	
Oropharynx	218(17.5)	84(19.2)	134(16.6)	
Hypopharynx	303(24.4)	96(22.0)	207(25.6)	
Larynx	172(13.8)	55(12.6)	117(14.5)	
Thyroid gland	125(10.0)	56(12.8)	69(8.5)	
Salivary gland	47(3.8)	20(4.6)	27(3.3)	
Nose and Paranasal Sinuses	24(1.9)	7(1.6)	17(2.1)	
CUP	7(0.6)	4(0.9)	3(0.3)	
Other	12(1.0)	3(0.7)	9(1.1)	

CUP, Cancer of Unknown Primary.
[a] Mann—Whitney *U* test.
[b] Pearson's Chi-square test.

Table 2 UICC classification of the 1245 head and neck cancers in this study.

	Total n(%)	Pre-COVID(%) (2019; n = 437)	Post-COVID(%) (2020; n = 417, 2021; n = 391))	*P*-value
Tumor(T)classification				0.008[a]*
Tx	11(0.9)	3(0.7)	8(0.9)	
T0	9(0.7)	3(0.7)	6(0.7)	
Tis	27(2.2)	17(3.9)	10(1.2)	
T1	318(25.5)	128(29.3)	190(23.5)	
T2	342(27.4)	108(24.7)	234(29.0)	
T3	251(20.2)	77(17.6)	174(21.5)	
T4	287(23.1)	101(23.1)	186(23.0)	
Nodal(N)classification				0.473[a]
Nx	6(0.5)	1(0.2)	5(0.6)	
N0	766(61.5)	280(64.1)	486(60.1)	
N1	218(17.5)	68(15.6)	150(18.6)	
N2	215(17.3)	76(17.4)	139(17.2)	
N3	40(3.2)	12(2.7)	28(3.5)	
Metastasis(M)classification				0.08[a]
Mx	18(1.4)	2(0.5)	16(2.0)	
M0	1170(94.0)	413(94.5)	757(93.7)	
M1	57(4.6)	22(5.0)	35(4.3)	
Clinical Stage				0.007[a]*
0	28(2.2)	18(4.1)	10(1.2)	
I	344(27.6)	126(28.8)	218(27.0)	
II	235(18.9)	84(19.2)	151(18.7)	
III	206(16.6)	60(13.8)	146(18.1)	
IV	426(34.2)	148(33.9)	278(34.4)	
Unknown	6(0.5)	1(0.2)	5(0.6)	

UICC, the Union for International Cancer Control.
*$P < 0.05$.
[a] Pearson's Chi-square test.

decreased after post-COVID-19, but the difference was not significant.

Subjective symptoms at the time of initial examination

Table 3 shows the results by the presence or absence of subjective symptoms during the initial examination. Excluding patients who were referred to other hospitals after follow-up or unknown patients, the proportion of those with no subjective symptoms at the time of initial examination decreased significantly from 23.1 % of all patients in pre-COVID-19 to 17.3 % in post-COVID-19. Among those with subjective symptoms, the time from the onset of symptoms to medical consultation ranged from less than 1 week to a maximum of 240 months. The median time between the onset of subjective symptoms and the visit to a

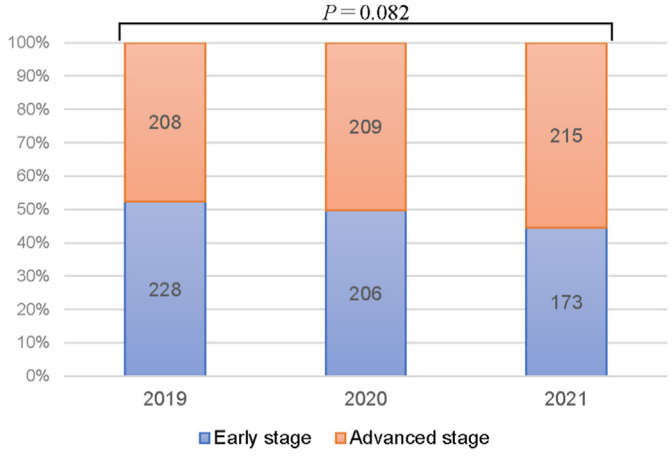

Figure 1 **Incidence of early and advanced head and neck cancers treated each year from 2019 to 2021** *P* value were calculated using Pearson's Chi-square test.

Table 3 Presence of subjective symptoms at the time of initial examination of 1131 patients with head and neck cancer (Excluding patients who were referred to other hospitals after follow-up (n = 54) or unknown (n = 60) patients).

	Total n(%)	Pre-COVID(%) (2019; n = 396)	Post-COVID(%) (2020; n = 372, 2021; n = 363))	*P*-value
Subjective symptoms				0.014[a]*
Yes	890(71.5)	295(67.5)	595(73.6)	
No	241(19.4)	101(23.1)	140(17.3)	

*$P < 0.05$.
[a] Pearson's Chi-square test.

healthcare provider was 1.5 months, and there was no significant difference (Fig. 2).

Initial treatment strategy of HNC

Regarding the initial treatment details, compared to pre-COVID-19, the proportion of surgery decreased after pandemic, while the proportion of chemoradiotherapy showed an increasing trend (Table 4). In cases of cancers of the oropharynx, hypopharynx, and larynx, where the treatment strategy is varied according to stage, the treatment approach was stratified according to early-stage and advanced stage. It was observed that in the post-pandemic period, there was an increase in the proportion of CRT for the early-stage cases; whereas, a decrease in the proportion of surgery and an increase in the proportion of chemotherapy and palliative treatment although not significantly was observed in advanced stage cases (Fig. 3).

Discussion

This study compared the pre-COVID-19 (2019) and post-pandemic (2020—2021) periods, in which a decrease in the number of HNC patients was observed in the post-pandemic period especially in the proportion of early-stage cancers. A decrease in the proportion of patients with no subjective symptoms at the time of initial diagnosis was also observed.

The study showed a 5—10 % decrease in the number of new patients diagnosed with HNC after the COVID-19 pandemic. Several international reports have documented a 22—43 % decrease in the number of new HNC diagnoses during the COVID-19 pandemic.[8—10] Globally, during the peak of the pandemic, important adjustments were introduced in the healthcare settings to avoid hospital outbreaks and ensure necessary resources for COVID-19 patients, which included partial or complete interruption of diagnostic workflows, elective treatments, and management of routine follow-ups in respective areas.[15] In addition to re-adjusted clinic

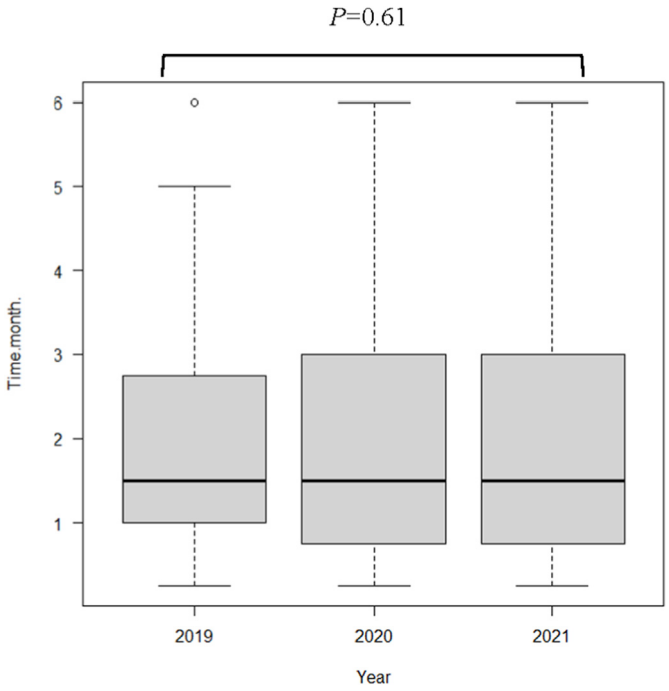

Figure 2 Time from the appearance of subjective symptoms to medical consultation Data are displayed in standard box plots with medians and interquartile ranges. *P* value were calculated using Kruskal—Wallis test.

Table 4 Initial treatment strategy for the 1245 patients with head and neck cancer.

	Total n(%)	Pre-COVID(%) (2019; n = 437)	Post-COVID(%) (2020; n = 417, 2021; n = 391))	*P*-value
Initial treatment				0.024[a]*
Surgery	574	223(51.0)	351(43.4)	
Chemotherapy	44	13(3.0)	31(3.8)	
CRT	281	83(19.0)	198(24.5)	
RT	172	56(12.8)	116(14.4)	
Palliative treatment	97	28(6.4)	69(8.5)	
Other	77	34(7.8)	43(5.3)	

CRT, Chemoradiotherapy.
RT, Radiotherapy.
*$P < 0.05$.
[a] Pearson's Chi-square test.

schedules, the need for social distance due to lockdowns and the fear of risk of contracting infection through medical visits contributed to the reluctance of patients to visit clinics.[16] In Japan, a lockdown was not implemented, and infection control measures were taken in the form of requests for self-restraint. The number of diagnoses in the national hospital cancer registry in 2020 was 94.8 % for oral and pharyngeal cancer, 89.9 % for laryngeal cancer, and 92.3 % for thyroid cancer compared to 2019.[17]

The present study showed a similar decrease in the overall number of HNCs diagnosed, although there were differences by site, with 97.2 % for oral and pharyngeal cancer, 116.4 % for laryngeal cancer, and 62.5 % for thyroid cancer. In terms of new HNC diagnosis by UICC classification, a decrease in the proportion of Tis/T1 and an increase in the proportion of T2/T3, and a decrease in the proportion of early-stage cancers and an increase in the proportion of advanced cancers in clinical stage were observed after the pandemic. The proportion of patients without symptoms at the time of initial diagnosis decreased significantly. This suggests that early detection may not have been possible due to the COVID-19 pandemic, and the frequency of detection through medical examinations decreased even when there were no restrictions on medical services in Japan.

Oral cancer is often detected during routine dental clinic visits; however, Koyama et al.[18] reported that more than 50 % of patients canceled their scheduled dental visits during the pandemic, although closure was not mandatory in Japan, and dental clinics were rarely closed. In addition, pharyngeal and laryngeal cancers are often detected by endoscopy, but the Japanese Society for Gastrointestinal Endoscopy strongly recommended, in April 2020, postponing or discontinuing gastrointestinal endoscopy during the pandemic, except in emergency cases, to protect healthcare workers and prevent the spread of infection.[19] In response to the decline in screening, in October 2020, the Ministry of Health, Labour and Welfare revised the recommendation to allow screening even during the pandemic.[20] Miyawaki et al.[21] reported that the number of esophageal cancer diagnoses decreased from April to June 2020, the first wave of the pandemic, but that there was no significant difference in the number of diagnoses throughout the year compared with the pre-pandemic period. Fujita et al.[22] reported a decrease in the number of gastric cancer diagnoses during the first wave of the pandemic, and also suggested that a decrease in the number of endoscopic examinations may have caused the decline in diagnoses after the second wave. Similarly, in HNC, pharyngeal and laryngeal cancers are often detected by endoscopy, and the pandemic may have affected the number of diagnosis.

Regarding the initial treatment approach for HNC as a whole, the proportion of surgery cases declined while chemoradiotherapy cases increased. Our hospital did not restrict consultations due to COVID-19 or avoid surgical cases due to the depletion of medical supplies during the period of this study. In case of cancers of the oropharynx,

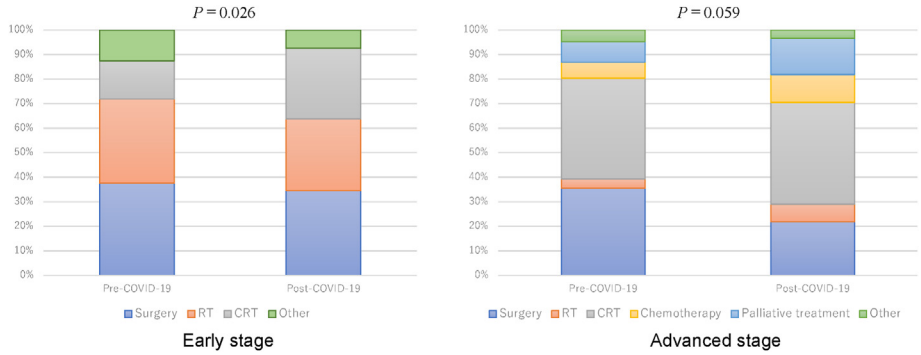

Figure 3 Initial treatment strategy for early-stage (stage 0–II) and advanced stage (stage III/IV) cancers of the oropharynx, hypopharynx, and larynx *P* value were calculated using Pearson's Chi-square test.

hypopharynx, and larynx, where the treatment strategy changes according to stage, in early-stage cancers, endoscopic surgery may have decreased and chemoradiotherapy increased due to tumor progression; while in advanced cancers, the proportion of curative treatments such as surgery and chemoradiotherapy decreased and the proportion of chemotherapy and palliative treatment increased, suggesting the possible effects of stage progression and tumor growth. Further research is needed on changes in treatment strategy, as it depends on the primary site, and the patient's age and performance status.

The impact of COVID-19 on healthcare facilities varies by country and region,[23] but facilities in Italy and the U.S. reported no impact between the time to diagnosis and time to treatment of new HNC during the pandemic.[10,11] Yao et al.[24] compared the pre-pandemic and pandemic periods in New York state, where a stay-at-home order was issued, and reported an extension in time to HNC diagnosis but no difference in staging or time to treatment. In a report on oral cancer, Koyama et al.[25] reported in the in-hospital cancer registry of 66 facilities in Osaka Prefecture that surgery for oral cancer could be performed earlier in 2020 compared to 2019 and 2020.

This study had some limitations. This was a single-center study, and the region was highly affected by the pandemic, which may have resulted in regional and inter-facility differences. However, our center had a large number of patients with HNC, and there were no restrictions on the number of first-time patients during the study period. The long-term study also allowed us to examine trends in a sufficient number of first-time patients. In addition to this, despite the pandemic's impact, we could provide HNC treatment without bed shortages or medical care or supply restrictions. This may also be due to regional and inter-institutional differences. In contrast, other facilities had difficulty maintaining sufficient conditions to provide treatment across all healthcare system levels, which may have led to significant delays in treatment. It is important to clarify and evaluate the long-term local control and disease-specific survival rates in a future study.

We conclude that a decrease in the proportion of HNC patients with early-stage cancer and primary tumor progression is observed after the pandemic in 2020 and 2021. It is possible that the number of early-stage cancers decreases due to patients' reluctance to visit a doctor.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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