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Clinical Care Pathway Time Intervals and Tumor Progression Among Head and Neck Cancer Patients at East Avenue Medical Center Before and During the COVID-19 Pandemic

Fery Mai J. Rafanan, MD
Eduard M. Alfanta, MD
Romulus Roberto Peter A. Instrella, MD

Department of Otorhinolaryngology-Head and Neck Surgery
East Avenue Medical Center

ABSTRACT

Objective: To investigate the association between the time intervals of key clinical time points and tumor progression (increase in clinical staging) in head and neck cancer patients before and during the pandemic.

Methods:

Design: Retrospective Cohort Study

Setting: Tertiary Government Training Hospital

Participants: A total of 81 head and neck cancer patients who consulted at the OPD and underwent elective surgery between January 1, 2018, and December 31, 2022, under the Department of Otorhinolaryngology – Head and Neck Surgery of East Avenue Medical Center were included in the study; 40 patients comprised the pre-pandemic group and 41 patients-the pandemic group.

Results: Majority of patients were men (61.73%), and the mean age was 54 years. The most prevalent tumor site was the oral cavity (37.04%). Most patients were Clinical Stage IV at the time of diagnosis (32.10%) and at the time of surgery (58.02%). In the pre-pandemic period, median time-to-consult was 180 days, time-to-diagnosis was 14 days, and time-to-treatment was 57 days. During the pandemic, median time-to-consult significantly increased to 365 days (Mann-Whitney test, U = 589, p = .028), but time-to-diagnosis decreased to 10 days, and time-to-treatment decreased to 43 days, although these were not significant (U = 775, p = .667; U = 809, p = .917). Among the 81 patients in the study, 14 (17.28%) showed tumor progression (pre-pandemic: 6; 15%; pandemic: 8; 19.51%), but there was no significant association between time-to-consult and increase in clinical staging for both pre-pandemic ($\chi^2(38) = 34.2$, p = .646) and pandemic groups ($\chi^2(16) = 23.1$, p = .110) or between time-to-diagnosis and increase in clinical staging for pre-pandemic ($\chi^2(56) = 36.8$, p = .978) and pandemic groups ($\chi^2(23) = 28.3$, p = .267). Overall, there was no significant association between time-to-treatment and increase in clinical staging for both pre-pandemic ($\chi^2(62) = 80.00$, p = .062) and pandemic groups ($\chi^2(32) = 30.4$, p = .548), but a subset of patients with larynx primary tumor site had a statistically significant association between time-to-treatment and tumor progression ($\chi^2(5) = 12.00$, p = .035).

Correspondence: Dr. Eduard M. Alfanta
Department of Otorhinolaryngology
Head and Neck Surgery
East Avenue Medical Center
East Avenue, Diliman, Quezon City 1100
Philippines
Phone: +63 939 933 8273
Email: doctor.alfanta@gmail.com

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Conclusion: This study revealed that there was an increase in time-to-consult for head and neck cancer patients during the pandemic. However, there was no significant difference in time-to-diagnosis and time-to-treatment. This shows that the Department of ORL-HNS, East Avenue Medical Center has provided pandemic head and neck cancer care similar to before the pandemic. No significant associations were found between tumor progression and time intervals of the key clinical time points but patients who had an increase in clinical stage were noted with longer time-to-treatment. It was also observed that more patients were in advanced clinical stages during the pandemic.

Keywords: *head and neck cancer; clinical care pathway; time to consult; time to diagnosis; time to treatment; COVID 19*

Head and neck cancer (HNC) has the 7th highest incidence and mortality rate of malignancies worldwide, accounting for approximately 600,000 cases and over 250,000 deaths annually.[1] In the Philippines, HNCs ranked 4th next to breast cancer, colorectal cancer, and cervical cancer, having 5% of the total cases from the 2021 CARE PH Database.[2] Head and neck cancers occur in various anatomical subsites including the oral cavity, major salivary glands, nasopharynx, oropharynx, hypopharynx, larynx, nasal cavity and paranasal sinuses, and the thyroid. Histologically, the most common type of HNC is squamous cell carcinoma (HNSCC).[1] Head and neck SCCs have a short tumor doubling time and are relatively fast-growing compared to other tumors. Increased intervals between onset of symptoms, diagnosis, and treatment pose a high risk of upstaging thus resulting in worse outcomes.[3] Time to treatment initiation (TTI) is defined as the number of days between histopathological diagnosis and first treatment. A delayed TTI at a threshold of 60 days is associated with decreased overall survival and increased HNSCC recurrence.[4]

The global emergence of the coronavirus disease 2019 (COVID-19) and its characterization as a pandemic by the World Health Organization on March 12, 2020 put the whole world into a standstill. In the Philippines, Enhanced Community Quarantine was imposed in the same month, limiting movement and restricting travel. In our institution, the out-patient department limited consultation days and elective surgeries gave way to prioritize emergencies and cancer patients. Due to the progressive nature of head and neck cancers, it is expected that a delay at any point between onset of symptoms and treatment affects the prognosis of patients.

This 5-year study compares the time intervals of key clinical time points in the clinical care pathway before and during the COVID-19 pandemic in HNC patients of the Department of Otorhinolaryngology – Head and Neck Surgery of the East Avenue Medical Center (EAMC ORL-HNS), and seeks to determine the association between the time intervals of key clinical time points and tumor progression (based on increase in clinical staging before treatment) among head and neck cancer patients before, and during the pandemic. The results of this study can serve as an evaluation of the efficiency of the HNC clinical care pathway of the department by comparing pre-pandemic and pandemic results. Ultimately, this study aims to advocate for the prioritization of head and neck cancer patients.

METHODS

Upon the approval by the Institutional Ethics Review Board (IERB) of the East Avenue Medical Center, data was collected by chart review of head and neck cancer patients who were admitted and operated on at the East Avenue Medical Center under the Department of ORL-HNS from January 1, 2018 to December 31, 2022.

The sample size was computed using a 95% level of confidence, guided by the most recent hospital-based cancer registry in the Philippines (the 2021 Cancer Registry and Research Philippines (CARE PH) Annual Report), showing a 5% incidence of head and neck cancers in the country.[2] A minimum of 66 participants were required for this study based on a level of significance of 5% at 95% confidence interval.

The target study population included all male and female adult patients (age >18 years) who consulted at the Out-Patient Department and were diagnosed with head and neck cancer and subsequently admitted by the Department of ORL-HNS for elective surgery as the primary and definitive treatment between January 1, 2018 and December 31, 2022.

Pediatric patients who were $\leq$ 18 years old the time of surgery were excluded. Patients who initially received chemotherapy and/or radiation therapy were excluded, as well as patients who underwent a prior surgery and were diagnosed with tumor recurrence. Patients referred to ORL-HNS OPD due to head and neck malignancy on tissue histopathology wherein biopsy was not done by the department were not included. Patients who were admitted through an initial Emergency Room consult were not considered for the study either. Patients with incomplete data upon review of records were also excluded.

The list of patients for review was based on the compiled census of operated patients of the Department of ORL-HNS. The outpatient record and admission charts were consulted. From the records, the following deidentified data were retrieved and compiled using study identification numbers instead of names: age, sex, clinical history, date of first consult at our department, date and result of biopsy, pre-operative and post-operative diagnosis and staging, and date and type of surgery performed. Head and neck cancer patients were classified into the pre-pandemic group (who underwent surgery between January 1, 2018 and March 11, 2020) and the pandemic group (who underwent surgery between March 12, 2020 and December 31, 2022).

The tumors were categorized per site (oral cavity, major salivary gland, larynx, nasal cavity and paranasal sinuses, thyroid, and cutaneous) and were staged accordingly using the 8th edition of the TNM Classification of the American Joint Committee on Cancer (AJCC). The following variables were measured: 1. Interval between patient-reported onset of symptoms and first consult at our OPD (in days); 2. Interval between the first consult and attainment of histopathologic diagnosis (in days); and 3. Interval between attainment of histopathologic diagnosis and date of definitive surgery (in days).

Operational definitions used were: 1. Time to consult: time interval in days between patient-reported onset of symptom and date of first consult at the EAMC ORL-HNS Out-Patient Department (OPD); 2. Time to diagnosis: time interval in days between date of first consult at the EAMC ORL-HNS OPD and attainment of histopathologic diagnosis; and 3. Time to treatment: time interval in days between attainment of histopathologic diagnosis and date of definitive surgery; and 4. Tumor progression: increase in clinical staging between time of diagnosis and time of surgery.

Data were encoded using Microsoft Excel version 2308, build 16731.20234 (Microsoft Corporation, Redmond, WA, USA) and IBM SPSS for Windows version 27 (IBM Corporation, Armonk NY, USA) were used for data processing and analysis. Descriptive analyses were presented as frequencies and percentages for categorical variables such as the patient demographics, tumor characteristics, and presence of tumor progression. For continuous variables such as the time intervals in the key clinical time points, mean and standard deviation were utilized for parametric distribution. Mann Whitney U test was used to compare the means of two samples with non-parametric distribution such as the time intervals in each key clinical time points in pre-pandemic and in pandemic groups. Chi-Square was utilized to assess significant association between key clinical time points among patients with tumor progression in pre-pandemic and in pandemic groups. Level of significance was set at alpha = .05.

RESULTS

A total of 81 head and neck cancer patients who consulted the OPD and underwent elective surgery between January 1, 2018, and December 31, 2022, were included in this study, wherein 40 comprised the pre-pandemic group and 41 the pandemic group. Of the 81 participants in our study, 50 (61.73%) were men and 31 (38.27%) were women and the mean age was 54 years old (range: 20-76).

The most prevalent tumor site was the oral cavity (30; 37.04%) both for pre-pandemic (13; 32.5%) and pandemic (17; 41.46%) groups, with the tongue as the most frequent oral cavity subsite (14; 46.67%). At the time of diagnosis, most of the participants were clinical stage IV (36; 44.44%) for both pre-pandemic (14; 35%) and pandemic (22; 53.66%) groups. Most patients were at tumor stage T3 (35; 43.21%), and nodal stage N0 (41; 50.62%). However, at the time of surgery, most patients were in clinical stage IV (47; 58.02%) in the pre-pandemic (19; 47.5%) and pandemic groups (28; 68.29%). At the time of surgery, most patients were at tumor stage T4 (36; 44.44%), and nodal stage N0 (36; 44.44%). *Table 1* summarizes the tumor characteristics.

Figure 1 shows the median time intervals between key clinical time points. The median time-to-consult in the pre-pandemic group was 180 days (mean = 637 days; range: 21-5,840 days). This was lower compared

Table 1. Tumor Characteristics

Characteristics	Overall	Pre-pandemic group	Pandemic group
	N/81 (%)	N/40 (%)	N/41 (%)
Tumor Site			
Oral cavity	**30 (37.04)**	**13 (32.50)**	**17 (41.46)**
Major Salivary Gland	6 (7.41)	2 (5)	4 (9.76)
Larynx	21 (25.93)	12 (30)	9 (21.95)
Nasal Cavity and Paranasal Sinuses	8 (9.88)	3 (7.50)	5 (12.20)
Thyroid	12 (14.81)	7 (17.50)	5 (12.20)
Cutaneous	4 (4.94)	3 (7.50)	1 (2.44)
Clinical staging at time of diagnosis			
Clinical stage (AJCC 8th Edition)			
I	16 (19.75)	10 (25)	6 (14.63)
II	4 (4.94)	4 (10)	0
III	25 (30.86)	12 (30)	13 (31.71)
IV	**36 (44.44)**	**14 (35)**	**22 (53.66)**
Tumor stage			
T1	11 (13.58)	7 (17.50)	4 (9.76)
T2	9 (11.11)	6 (15)	3 (7.32)
T3	**35 (43.21)**	**17 (42.50)**	**18 (43.90)**
T4	26 (32.10)	10 (25)	16 (39.02)
Nodal stage			
N0	**41 (50.62)**	**21 (52.50)**	**20 (48.78)**
N1	23 (28.40)	13 (32.50)	10 (24.39)
N2	17 (20.99)	6 (15)	11 (26.83)
Clinical staging at time of surgery			
Clinical stage (AJCC 8th Edition)			
I	15 (18.52)	9 (22.50)	6 (14.63)
II	4 (4.94)	4 (10)	0
III	15 (18.52)	8 (20)	7 (17.07)
IV	**47 (58.02)**	**19 (47.50)**	**28 (68.29)**
Tumor stage			
T1	9 (11.11)	6 (15)	3 (7.32)
T2	9 (11.11)	6 (15)	3 (7.32)
T3	27 (33.33)	**15 (37.50)**	12 (29.27)
T4	**36 (44.44)**	13 (32.50)	**23 (56.10)**
Nodal stage			
N0	**36 (44.44)**	**18 (45)**	**18 (43.90)**
N1	19 (23.46)	10 (25)	9 (21.95)
N2	26 (32.10)	12 (30)	14 (34.15)

to the pandemic group with a median of 365 days (mean = 609 days; range: 30-2,555 days) and using Mann-Whitney U test, results showed a significant difference between the two groups (U = 589, p = .028). The median time-to-diagnosis was 14 days (mean = 58 days; range: 1-779 days) for the pre-pandemic group, and 10 days (mean = 23 days; range: 1-260 days) for the pandemic group. Time-to-treatment for the pre-pandemic group had a median of 57 days (mean = 72 days; range: 0-285 days), and 43 days (mean = 98 days; range: 0-1,422 days) for the pandemic group. No significant difference was seen between the pre-pandemic and pandemic groups in time-to-diagnosis (U = 775, p = .667) and time-to-treatment (U = 809, p = .917) using Mann-Whitney U test.

Among the 81 patients in the study, 14 had an increase in clinical staging at the time of surgery (pre-pandemic: 6; 15%; pandemic: 8; 19.51%). *Figure 2* shows the median time intervals between key clinical time points among patients with tumor progression. However, the chi-square test revealed no significant association between time-to-consult and increase in clinical staging for both pre-pandemic ($\chi^2(38) = 34.2$, p = .646) and pandemic groups ($\chi^2(16) = 23.1$, p = .110). There was likewise no significant association between time-to-diagnosis and increase in clinical staging for pre-pandemic ($\chi^2(56) = 36.8$, p = .978) and pandemic groups ($\chi^2(23) = 28.3$, p = .267). Overall, the Chi-Square test showed no significant association between time-to-treatment and increase in clinical staging for both pre-pandemic ($\chi^2(62) = 80.00$, p = .062) and pandemic groups ($\chi^2(32) = 30.4$, p = .548), but a subset of patients with larynx primary tumor site had a statistically significant association between time-to-treatment and increase in clinical stage ($\chi^2(5) = 12.00$, p = .035) in the pre-pandemic group only.

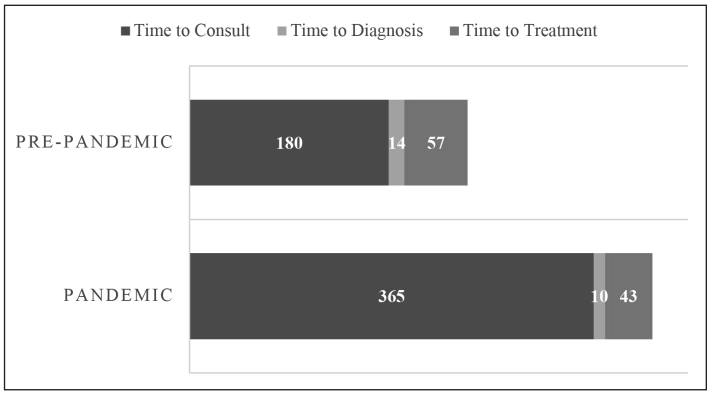

Figure 1. Median Time Intervals for Key Clinical Time Points

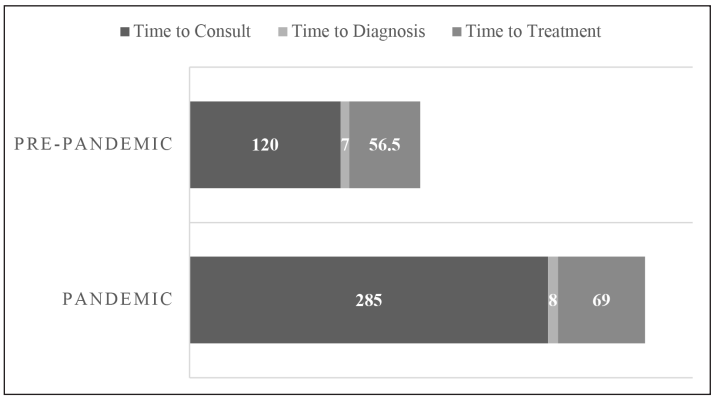

Figure 2. Median Time Intervals for Key Clinical Time Points in patients with Tumor Progression

DISCUSSION

In this study, the time intervals of the key clinical time points were measured and compared between the pre-pandemic and pandemic groups. The results showed that the time-to-consult during the pandemic significantly increased – a median of 365 days during the pandemic compared to 180 days in the pre–pandemic period. A study by Yao, *et al.* in 2021 comparing times to diagnosis, staging, and treatment of HNC before and during COVID-19 also found delays during the COVID-19 period.[5] In that study, the delays were attributed to hesitancy of patients to seek care due to risk of viral exposure and limited clinic hours during the pandemic.[5] These patient-related factors, healthcare system factors, and disease-related factors have always driven the delay in HNC diagnosis, but the crisis imposed by COVID-19 on healthcare systems and patient's heath-seeking behaviors heightened these already existing barriers to timely diagnosis.[6]

Between pre-pandemic and pandemic patients, there was no significant difference in the time to diagnosis. However, results of our current study showed slightly decreased time-to-diagnosis during the pandemic (10 days) compared to the pre-pandemic period (14 days), although this was not statistically significant. Although we did not explore this factor, an explanation may be found in the study of Psycharis, *et al.* in 2023, where the overall decreased burden on the pathology departments during the pandemic period may have contributed to a decreased wait time from biopsy to histopathological diagnosis.[7] We can also speculate that the limitations on elective surgeries in favor of emergent and cancer surgeries may have also indirectly decreased time-to-diagnosis in our institution.

In terms of time-to-treatment, there was also no noted significant difference between the pre-pandemic and pandemic groups. A local study of 28 patients by Lapiña, *et al*. in 2017 found that the median diagnostic-to-treatment interval in their institution was 54 days. They defined significant delay as more than 60 days from the attainment of pathological diagnosis to initiation of treatment.[8] In our study, we observed that the median time-to-treatment was 57 days in the pre-pandemic period and 43 days in the pandemic period, both showing no delay. Although it was initially thought that the pandemic would cause delay in the treatment of cancer patients, the cancellation of

non-urgent surgeries had the opposite effect and led to prioritization of cancer surgeries.[7] During the pandemic, the surgeries in our institution were limited to emergencies and cancer patients.

Among all the patients in this study, 14 (17.28%) were identified to have had tumor progression at the time of surgery; 6 (15%) from the pre-pandemic group and 8 (19.51%) from the pandemic group. Although no statistically significant association was seen between the presence of tumor progression and time intervals of the key clinical time points, it can be noted that the time-to-treatment for patients with tumor progression (59 days) was longer than that of the overall sample (52 days). It is important to note that most patients who consulted during the pandemic were in advanced clinical stages III and IV (85.37%). This is congruent with the findings in the study of Psycharis, *et al.* which showed an upward trend in cancer presentation.[7] This may possibly be attributed to the increased time-to-consult in the pandemic period, reflected in our study.

A statistically significant association between time-to-treatment and increase in clinical stage was only found among a subset of pre-pandemic patients with a larynx primary tumor site. This may possibly be explained by the more lenient treatment algorithm for patients with laryngeal masses at our OPD clinic where most patients were scheduled as elective surgery cases during the pre-pandemic period.

National statistics show that thyroid malignancies have a 4.1% incidence ranking 7th, however, this was not observed in this study (pre-pandemic: 3, 7.50%; pandemic: 1, 2.44%).[9] This discrepancy may be due to our sampling criteria: patients who consulted at the OPD with a biopsy result from other institutions, those who had their first consult at our institution through the ER, and thyroid cancer patients who did not undergo definitive surgical treatment (thyroidectomy) were excluded.

There are several limitations to our study. We compared the clinical care pathway time intervals for head and neck cancer patients in the pre-pandemic and pandemic periods. Although time to consult, time to diagnosis, and time to treatment were measured, outcomes of these time intervals such as mortality rate, success rate, and recurrence rate were not included. Patient and hospital factors during COVID-19 which could have contributed to the delays were not investigated either. As of writing, the pandemic status has been lifted and the healthcare system is adjusting to a new normal. A prospective cohort study evaluating these changes could be recommended to help improve the clinical care pathway for head and neck cancer patients.

Knowing the prognostic implications of clinical staging at presentation, efforts to decrease the barriers to accessible healthcare, increase patient awareness, and improve patient's health-seeking behaviors are some points that need attention. Moreover, elective schedule prioritization of head and neck cancer surgeries may help dampen tumor progression. Although it did not reach statistical significance, this study found that patients with tumor progression had a longer time-to-treatment during the pandemic. The limited elective surgeries and decreased hospital capacity due to the pandemic may have been factors affecting this trend. Psycharis, *et al.* investigated the effect of their guideline alterations during the COVID 19 pandemic where an OR Prioritization Committee was formed to review all surgical cases and schedule surgeries based on priority. This resulted in accelerated HNC treatment during the pandemic.[7] We recommend the adaptation of such an OR Prioritization Committee for possible future events disrupting the established healthcare delivery system.

In conclusion, our study revealed that the pandemic brought an increase in the time-to-consult in head and neck cancer patients. Despite the pandemic, there was no significant difference in time-to-diagnosis and time-to-treatment. This shows that the Department of ORL-HNS of the East Avenue Medical Center has provided pandemic head and neck cancer care similar to before the pandemic. No significant associations were found between tumor progression and time intervals of the key clinical time points but patients who had an increase in clinical stage were noted with longer time-to-treatment. It was also observed that more patients were in advanced clinical stages during the pandemic.

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