

ORIGINAL ARTICLE

The impact of COVID-19 on head and neck cancer diagnosis and disease extent

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Abstract

Background: Due to COVID-19, diagnostic delays and a surge of advanced head and neck cancer (HNC) is anticipated. We hereby evaluate patient and tumor characteristics before and during the early COVID-19 period.

Methods: Retrospective review of patients with HNC presented at a multi-disciplinary tumor conference from May 14, 2020 to June 18, 2020 was performed and compared to a similar 6-week period a year before. Demographics, time to diagnosis, and tumor characteristics were analyzed.

Results: There was a 25% reduction in newly diagnosed malignancies. Groups were similar in baseline characteristics, duration of symptoms, and time to diagnosis. However, median primary tumor size was significantly larger ($p = 0.042$) and T stage more advanced for mucosal subsites ($p = 0.025$) in the COVID-19 group.

Conclusion: Our findings suggest increased tumor burden in patients with HNC presenting during the pandemic, despite a similar time to diagnosis. This may become more pronounced as the pandemic duration is extended.

KEYWORDS

COVID-19, head and neck cancer, head and neck surgery, health care, SARS-COV2

1 | INTRODUCTION

In recent months, the world has been grappling with coronavirus disease 2019 (COVID-19). Individual nations have experienced differing incidences of disease and each has had to deal with challenges unique to their population and resource availability. As of July 11, the number of cases in the United States has surpassed 3.1 million and the number of deaths greater than 132 000.¹ Due to limitations in health care resources, dealing with COVID-19 has become the priority, with reduced capacity for other medical conditions including variable

restrictions on elective procedures. In the field of oncology, the need to triage cases has been recognized, with multiple oncologic societies proposing guidelines on the type of cases to prioritize for treatment.²⁻⁴ However, the potential impact of COVID-19 on the pattern of presentation of new cancer cases has not been objectively evaluated for head and neck cancer (HNC).

As COVID-19 cases start to decline in some regions and clinical services are re-opened, we anticipate an influx of cases with more advanced disease.⁵ This pattern has been observed after natural disasters such as Hurricane Katrina⁶ and the Fukushima earthquake,⁷ where delays in diagnosis persisted up to 5 years after the event. Tumors in the head and neck can potentially double in volume within 1–3 months, regardless of their size or site

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of origin.⁸ Independent of the pandemic, delays in treatment initiation, including the delay to diagnosis, are well known to impact overall survival.^{9,10}

The delayed presentation, diagnosis, and treatment of HNC during and after the COVID-19 pandemic is expected to adversely affect outcomes and survival.¹¹ It is important that we understand the early impact of the COVID-19 pandemic on the presentation of HNC so we may meet the evolving challenge. This study aims to document the impact of state-wide lockdowns and limitations on elective procedures during the early COVID-19 period on time to diagnosis and tumor burden in patients with HNC presenting to a tertiary care center as compared to a similar period before the pandemic.

2 | METHODS

A retrospective review of all cases presented at the Head and Neck multidisciplinary tumor conference (MTC) at the University of Texas M. D. Anderson Cancer Center (UTMDACC) over a 6-week period from May 14, 2020 to June 18, 2020 was performed. This was compared to a 6-week period a year before, from May 16, 2019 to June 20, 2019, before the COVID-19 pandemic. This time period during the pandemic was chosen to coincide with graduated re-opening of clinical services at UTMDACC after the initial spike in cases locally. This study was approved by the Institutional Review Board (2020-0348).

Patients presenting with newly diagnosed or recurrent HNC and reviewed at the weekly MTC were included in the study. MTC during the pandemic was conducted via teleconference but all other aspects of evaluation remained the same as the prepandemic period. Subsequent analysis was performed on the cases of newly diagnosed malignancies, excluding benign cases as well as malignant cases already on follow-up within the institution. These cases of malignancy diagnosed in patients already on follow-up within the institution (either with the head and neck department or another department for an unrelated condition) were excluded as these patients would already be within the system and are not subject to the same diagnostic or wait times as cases that arise from outside the institution. Patient demographics, country of origin, and distance from UTMDACC were collected from the electronic medical record. Distance was calculated in miles based on the zip code of the primary residential address. International addresses were excluded from this calculation.

Tumor characteristics, including subsite, AJCC 8th edition TNM staging,¹² primary tumor, and nodal size (largest cross-sectional diameter) were recorded for patients who had not received treatment prior to their

first visit at UTMDACC. TNM staging was only recorded for nonrecurrent disease. The duration of symptoms was defined as the number of weeks from when symptoms were first noted by the patient to the date of initial visit to UTMDACC. The number of days from when the histologic diagnosis was first made to the initial visit at UTMDACC was also recorded.

Descriptive statistics such as medians and ranges were used as appropriate. Pearson's Chi square and Fisher's exact tests were used to examine associations between groups for categorical variables and the Mann-Whitney *U* test was used for continuous variables. A *p*-value of less than 0.05 was considered significant. The analyses were performed using IBM SPSS v24 (IBM Corp, Armonk, NY).

3 | RESULTS

A total of 183 cases were presented at the MTC during the 6-week COVID-19 period, of which 117 (63.9%) cases were newly diagnosed malignancies, 25 (13.7%) cases were malignancies diagnosed on follow-up within the institution, and 41 (22.4%) cases were benign. The proportion of malignant and benign disease did not differ from the pre-COVID group ($p = 0.623$), where of a total 252 cases presented at MTC, 156 (61.9%) were newly diagnosed malignancies, 30 (11.9%) were malignancies diagnosed on follow-up, and 66 (26.2%) cases were benign. There was a 27.4% reduction in the total number of cases presented at MTC and a 25.0% reduction in newly diagnosed malignancies from the preceding year.

3.1 | Patient characteristics

Baseline characteristics did not differ between patients with newly diagnosed malignancies in the COVID-19 period group versus the pre-COVID group, with similar median age, sex, and race (Table 1). Five patients in the pre-COVID group originated from outside the United States as opposed to no international patients presenting during the COVID-19 period ($p = 0.073$). For patients residing in the United States, the median distance from their residential address to the institution did not differ between groups (157 miles in the COVID-19 period group vs. 170 miles in the pre-COVID group, $p = 0.208$). The groups did not differ in terms of presence of recurrent disease ($p = 0.257$) or having obtained treatment prior to presentation to UTMDACC ($p = 0.175$), although only 23.1% of patients in the COVID-19 period group were seeking a second opinion as opposed to 32.7% in the pre-COVID group ($p = 0.082$). Tumor subsite and MTC recommendations also did not differ between groups.

TABLE 1 Baseline characteristics

	Total n (%)	COVID period group (%)	Pre-COVID period group (%)	p-value
Total number	273	117	156	
Median age, years (range)	65 (22–95)	65 (27–89)	64 (22–95)	0.747
Sex				
Male	208 (76.2)	87 (74.4)	121 (77.6)	0.538
Female	65 (23.8)	30 (25.6)	35 (22.4)	
Race				
White	241 (88.3)	102 (88.3)	139 (89.1)	0.419 ^a
Hispanic	16 (5.9)	7 (6.0)	9 (5.8)	
Black	5 (1.8)	4 (3.4)	1 (0.6)	
Others	11 (4.0)	4 (3.4)	7 (4.5)	
Country of origin				
United States	268 (98.2)	117 (100.0)	151 (96.8)	0.073 ^a
International	5 (1.8)	0 (0.0)	5 (3.2)	
Median distance from primary address to institution, miles (range)	162 (3–4221)	157 (3–4221)	170 (4–2285)	0.208
Prior treatment for current diagnosis				
No prior treatment	231 (84.6)	103 (88.0)	128 (82.1)	0.175
Prior treatment	42 (15.4)	14 (12.0)	28 (17.9)	
Reason for first visit				
Primary evaluation	195 (71.4)	90 (76.9)	105 (67.3)	0.082
Second opinion	78 (28.6)	27 (23.1)	51 (32.7)	
Recurrent disease				
No	212 (77.7)	87 (74.4)	125 (80.1)	0.257
Yes	61 (22.3)	30 (25.6)	31 (19.9)	
Tumor subsite				
Oral cavity	51 (18.7)	21 (17.9)	30 (19.2)	0.329 ^a
Oropharynx	73 (26.7)	28 (23.9)	45 (28.8)	
Larynx/hypopharynx	26 (9.5)	13 (11.1)	13 (8.3)	
Skin	73 (26.7)	27 (23.1)	46 (29.5)	
Sinonasal	15 (5.5)	8 (6.8)	7 (4.5)	
Thyroid	12 (4.4)	7 (6.0)	5 (3.2)	
Major salivary gland	12 (4.4)	5 (4.3)	7 (4.5)	
Other	11 (4.0)	8 (6.8)	3 (1.9)	
Multidisciplinary tumor conference recommendation				
Primary surgery	129 (47.3)	50 (42.7)	75 (48.1)	0.446 ^a
Primary radiation therapy	15 (5.5)	4 (3.4)	10 (6.4)	
Primary chemoradiation	49 (17.9)	23 (19.7)	25 (16.0)	
Induction therapy	30 (11.0)	11 (9.4)	18 (11.5)	
Systemic therapy	35 (12.8)	16 (13.7)	19 (12.2)	
Further evaluation	15 (5.5)	13 (11.1)	9 (5.8)	

^aFisher's exact test.

3.2 | Tumor characteristics

Comparing patients without prior treatment, the groups did not differ in terms of median duration of symptoms (12 weeks for both groups, $p = 0.391$) or median duration from date of histologic diagnosis to first visit at UTMDACC (COVID-19 period: 20 days vs. pre-COVID period: 25 days, $p = 0.133$) (Table 2). The groups also did not differ in terms of individual or group TNM staging. However, there was a statistically significant difference in

the mean size of the primary tumor (COVID-19 period: 2.9 cm vs. pre-COVID period: 2.2 cm, $p = 0.042$).

3.3 | Subgroup analysis

The mucosal subsite tumors were analyzed separately, showing a significant difference in T stage ($p = 0.025$; Table 3). The COVID-19 period had 52.0% of tumors classified T3/4, versus 39.4% classified T3/4 in the pre-COVID

TABLE 2 Tumor characteristics of patients without prior treatment

	Total <i>n</i> (%)	COVID period group (%)	Pre-COVID period group (%)	<i>p</i> -value
Total number	231	103	128	
Median duration of symptoms prior to first visit, weeks (range)	12 (1–104)	12 (1–104)	12 (4–52)	0.391
Median duration from diagnosis to first visit, days (range)	23 (0–135)	20 (0–133)	25 (0–135)	0.133
Median duration from first visit to presentation at multidisciplinary tumor conference, days (range)	2 (0–28)	2 (0–13)	2 (0–28)	0.507
Tumor (T) classification (<i>n</i> = 185)				
Tx	5 (2.7)	4 (5.1)	1 (0.9)	0.111 ^a
T0	1 (0.5)	1 (1.3)	0 (0.0)	
T1	55 (29.7)	16 (20.5)	39 (36.4)	
T2	58 (31.4)	26 (33.3)	32 (29.9)	
T3	38 (20.5)	18 (23.1)	20 (18.7)	
T4	28 (15.1)	13 (16.7)	15 (14.0)	
Nodal (N) classification (<i>n</i> = 185)				
N0	99 (53.5)	42 (53.8)	57 (53.3)	0.656 ^a
N1	32 (27.6)	23 (29.5)	28 (26.2)	
N2	32 (17.3)	11 (14.1)	21 (19.6)	
N3	3 (1.6)	2 (2.6)	1 (0.9)	
Metastasis (M) classification (<i>n</i> = 185)				
Mx	10 (5.4)	6 (7.7)	4 (3.7)	0.360 ^a
M0	168 (90.8)	68 (87.2)	100 (93.5)	
M1	7 (3.8)	4 (5.1)	3 (2.8)	
AJCC 8th edition group stage (<i>n</i> = 179)				
1	66 (36.9)	25 (33.8)	41 (39.0)	0.782
2	43 (24.0)	20 (27.0)	23 (21.9)	
3	34 (19.0)	13 (17.6)	21 (20.0)	
4	36 (10.1)	16 (21.6)	20 (19.0)	
Median size of primary tumor, longest dimension, cm (range)	2.5 (0.3–10.2)	2.9 (0.5–10.2)	2.2 (0.3–8.2)	0.042
Median size of largest nodal metastasis, longest dimension, cm (range)	2.4 (0.8–7.0)	2.6 (0.8–7.0)	2.0 (0.8–4.8)	0.145

Note: The italic *n* indicates number.

^aFisher's exact test.

TABLE 3 Staging for mucosal squamous cell carcinomas (oral cavity, oropharynx, larynx, hypopharynx, sinonasal)

	Total <i>n</i> (%)	COVID period group (%)	Pre-COVID period group (%)	<i>p</i> -value
Total number	121	50	71	
Tumor (T) classification				
Tx	4 (3.3)	3 (6.0)	1 (1.4)	0.025 ^a
T1	30 (24.8)	5 (10.0)	25 (35.2)	
T2	33 (27.3)	16 (32.0)	17 (23.9)	
T3	31 (25.6)	15 (30.0)	16 (22.5)	
T4	23 (19.0)	11 (22.0)	12 (16.9)	
Nodal (N) classification				
N0	50 (41.3)	22 (44.0)	28 (39.4)	0.773 ^a
N1	40 (33.1)	15 (30.0)	25 (35.2)	
N2	28 (23.1)	11 (22.0)	17 (23.9)	
N3	3 (2.5)	2 (4.0)	1 (1.4)	
AJCC 8th edition group stage				
1	38 (31.4)	11 (22.0)	27 (38.0)	0.170
2	25 (20.7)	14 (28.0)	11 (15.5)	
3	28 (23.1)	11 (22.0)	17 (23.9)	
4	30 (24.8)	14 (28.0)	16 (22.5)	
Median size of primary tumor, longest dimension, cm (range)	2.8 (0.3–10.0)	3.0 (1.0–10.0)	2.5 (0.3–6.4)	0.092
Median size of largest nodal metastasis, longest dimension, cm (range)	2.3 (0.8–6.2)	2.6 (1.0–7.0)	2.0 (0.8–4.8)	0.351

Note: The italic *n* indicates number.

^aFisher's exact test.

group. However, there was no difference in the proportion of N stage disease. A higher proportion of tumors in the pre-COVID group (38.0%) were AJCC 8th edition group Stage 1 as compared to 22.0% in the COVID-19 period but this was not significant ($p = 0.170$). Additional analyses of skin, thyroid, and salivary gland cancers did not demonstrate such differences in the proportion of staging.

4 | DISCUSSION

Globally, many clinical services have had to limit or even cease activity during the peak of the COVID-19 pandemic in their region.^{13,14} This is especially pertinent in the field of head and neck surgery, as many aspects of clinical examination and procedures can potentially aerosolize the virus.^{15,16} Along with reductions in clinic scheduling, the lack of transportation, need for social distancing, and shelter-in-place orders have all played a role in decreasing patient attendance to clinics.¹⁷ While guidelines and multidisciplinary team care^{13,18,19} help to determine which cases are in most urgent need of attention and

treatment, we cannot account for the obstacles faced in accessing health care during the pandemic.

At our institution, there was a 25% reduction in newly diagnosed malignancies presented at the head and neck MTC from the preceding year, indicative of the reduction in clinic scheduling and referrals. One surprising finding of our study was that the median distance of patient's primary address to the institution did not differ between the COVID-19 period (157 miles) and the pre-COVID period (170 miles). This may reflect the complex baseline patient population seeking care at UTMDACC, with 19.9%–25.6% of cases presenting with recurrent disease, and 12.0%–17.6% having received treatment for their current condition prior to their first clinic visit at UTMDACC and up to one-third of patients seeking a second opinion for their HNC. Although the proportion of patients seeking a second opinion dropped from 32.7% to 23.1% during the COVID-19 period, this still indicates a willingness and ability of patients to seek out a level of care that they are comfortable with. Similarly, the proportion of tumor board recommendations for treatment did not differ between groups, which may also be due to complex and

advanced cases that present to our institution even prior to the COVID-19 pandemic. We also demonstrate that the duration of symptoms and time from histologic diagnosis to first visit has not changed significantly during the COVID-19 period; once again, supporting the concept that some patients are able to access the health care system when necessary, even amidst the pandemic. The factors leading to delays in diagnosis are complex and prevalent even in the nonpandemic era. We found that even in the pre-COVID group, the median duration of symptoms prior to presentation was 12 weeks, with a wide range of 4–52 weeks. Previously studied factors associated with delay in receiving treatment include fear of a cancer diagnosis, the asymptomatic period in a slow growing tumor, symptoms mimicking other less threatening illness, illiteracy, and lower socioeconomic class.²⁰ In the wake of natural disasters such as Hurricane Katrina, the availability of transportation significantly impacted access to cancer care in patients with early-stage cancers. However, demographic, clinical, and socioeconomic factors did not influence access to oncologic care.⁶

Despite these findings, it is essential to recognize that the COVID-19 pandemic can have profound, yet-to-be-seen effects on the health care system. The number of cancer referrals by primary care physicians in the UK has dropped drastically, leading Cancer Research UK to estimate that approximately 2000 fewer cancers are being diagnosed per week.²¹ In the United States, 21% of oral cancers are diagnosed by dentists²² and the closure of many dental offices is expected to reduce the number of asymptomatic oral cancer detections, which raises concern because these early cases are of a significantly lower average clinical and pathologic stage than lesions detected during a symptom-directed examination.^{23–25} Mucosal malignancies such as those of the sinonasal cavity and larynx may be diagnosed later as these patients tend to require invasive or specialized examinations for diagnosis. We have found that in these cases, patients are presenting with higher T stage disease ($p = 0.025$), compared to a year before. A higher T stage may require more extensive surgery or a wider radiation field, with attendant morbidities. The mean primary tumor size was also significantly larger in the COVID-19 group compared to the pre-COVID group. While the absolute size difference may not appear clinically significant, these measurements do not account for invasion into structures that may make treatment more morbid and therefore should not be discounted. These findings are similarly reflected in the study by Laccourreye et al.,²⁶ who reported a higher proportion of surgeries performed on T3/4 and N2/3 tumors during the COVID-19 pandemic compared to the preceding months.

Limitations of our study include its retrospective nature, with potential recall bias in the report of variables such as duration of symptoms. This may account for the

discrepancy between lack of change in symptom duration despite the change in tumor characteristics. Also, the 6-week time period chosen for analysis is relatively short and may not reflect the seasonal variability in practice. Furthermore, the results reflect practice at a single tertiary cancer care institution and may not be applicable to every institution. Generalizability is further affected by the disparity in the regional prevalence of COVID-19 cases, differences in national level responses to the pandemic and availability of resources. As previously discussed, patients seen at our institution typically present with more complex conditions such as recurrent disease and prior treatment, often seeking a second opinion for their HNC. However, in addition to difference in case complexity, we recognize that our patient population is not fully representative of the patient population in the United States either. Comparing race and ethnicity, close to 90% of patients in this study are non-Hispanic whites, compared to 60% of white ethnicity in the entire population of the United States.²⁷ It is widely recognized that racial and ethnic differences in outcomes for HNC exist, largely attributed to the disparity in access to care and timely management of the disease.^{28–30} It is likely that patients who self-refer to our institution, especially those from other states or countries, are more proactive in seeking treatment for their symptoms or better equipped to establish care for themselves. Similarly, COVID-19 has also been shown to impact mortality in certain ethnicities in a disproportionate fashion.^{31,32} The combined impact of COVID-19 and pre-existing racial/ethnic disparities have been amplified for a range of reasons, including a shift to telehealth, loss of employment, and health insurance coverage.³³ At this point in time, the Otolaryngology-Head and Neck surgery literature is lacking objective assessments of disparate access to health care due to COVID-19.³³

In spite of this limitation, this is the first study that demonstrates an increase in T stage and tumor size in patients presenting with newly diagnosed head and neck malignancies during the COVID-19 pandemic, compared to pre-pandemic times. Given that the data are extracted relatively early in the time course of the pandemic, with a current rapid increase in new COVID-19 cases in the United States,³⁴ and that the effects of crises and natural disasters on delayed diagnoses can last for years,⁷ it is likely that our findings represent only the tip of the iceberg. We should thus anticipate that cancer-related burden will increase in the following months to years, with corresponding changes in morbidity and mortality.³⁵

5 | CONCLUSION

COVID-19 has had a profound impact on health care systems and innumerable lives. We have anticipated its

impact on oncologic care and attempted to minimize disruptions with multiple processes and guidelines. However, we are only beginning to objectively assess its effect on oncologic parameters. Preliminary results such as these are important to bring awareness to potential challenges we may face in time to come, such as more advanced disease and potential disparities in care provision. We should strive to continually track access to health care, tumor burden, and oncologic outcomes, to mitigate the negative effects of COVID-19 on cancer care where possible.

DATA AVAILABILITY STATEMENT

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

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