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Authors

Solis, Roberto N
Mehrzaad, Mehrnaz
Faiq, Samya
et al.

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Roberto N. Solis, MD^{1*} , Mehrnaz Mehrzad^{1*}, Samya Faiq¹,
 Roberto P. Frusciante¹, Harveen K. Sekhon¹,
 Marianne Abouyared, MD¹, Arnaud F. Bewley, MD¹,
 D. Gregory Farwell, MD¹, and Andrew C. Birkeland, MD¹

Abstract

Objectives. To describe the impact that the coronavirus disease 2019 (COVID-19) pandemic had on the presentation of patients with head and neck cancer in a single tertiary care center.

Study Design. Retrospective cohort study.

Setting. Academic institution.

Methods. We performed a retrospective review of patients with newly diagnosed head and neck squamous cell carcinoma (HNSCC) who presented as new patients between September 10, 2019, and September 11, 2020. Patients presenting during the 6 months leading up to the announcement of the pandemic (pre-COVID-19 period) on March 11, 2020, were compared to those presenting during the first 6 months of the pandemic (COVID-19 period). Demographics, time to diagnosis and treatment, and tumor characteristics were analyzed.

Results. There were a total of 137 patients analyzed with newly diagnosed malignancies. There were 22% fewer patients evaluated during the COVID-19 timeframe. The groups were similar in demographics, duration of symptoms, time to diagnosis, time to surgery, extent of surgery, and adjuvant therapy. There was a larger proportion of tumors classified as T3/T4 (61.7%) in the COVID-19 period vs the pre-COVID-19 period (40.3%) ($P = .024$), as well as a larger median tumor size during the COVID-19 period ($P = .0002$). There were no differences between nodal disease burden ($P = .48$) and distant metastases ($P = .42$).

Conclusion. Despite similar characteristics, time to diagnosis, and surgery, our findings suggest that there was an increase in primary tumor burden in patients with HNSCC during the early COVID-19 pandemic.

Keywords

COVID-19, head and neck cancer, pandemic, head and neck cancer care, delays in care

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Since the World Health Organization (WHO) announced the novel coronavirus disease 2019 (COVID-19) a global pandemic on March 11, 2020,¹ health care systems across the globe have been affected in various degrees based on disease prevalence, resources, and vaccinations. As of August 24, 2021, there have been over 37 million documented infections and over 600,000 deaths recorded due to COVID-19 within the United States.² The pandemic's immediate concern forced health care systems to prioritize the prevention and management of patients with COVID-19, which has had consequences on treating other medical conditions. In a global collaborative survey study that included 356 cancer centers from 54 countries, approximately 88% of centers reported facing challenges in delivering care, demonstrating a widespread detriment that the pandemic has had on cancer care.³

Early in the pandemic, there were proponents of delaying care for patients with mild symptoms or less aggressive forms of head and neck cancers (HNCs) given the vulnerability of this patient population to pulmonary complications associated with the virus.^{4,5} Albeit this recommendation seemed prudent for the safety of patients, delays in HNC care delivery and time to surgery have been observed, negatively affecting tumor burden and overall survival.^{6–8} While the pandemic in

¹Department of Otolaryngology–Head and Neck Surgery, University of California, Davis, Sacramento, California, USA

*These authors contributed equally to this article.

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Corresponding Author:

Andrew C. Birkeland, MD, Department of Otolaryngology–Head and Neck Surgery, University of California, Davis, 2521 Stockton Blvd, Suite 7200, Sacramento, CA 95817, USA.
 Email: acbirkeland@ucdavis.edu



the United States continues to have fluctuating spikes in transmission across regions, it is anticipated there may be a surge of patients presenting with HNC with more advanced HNC.⁹

It is important to evaluate the impact that COVID-19 has had on HNC cancer care delivery to continue to evolve and provide optimal care for patients through updated cancer care policy. To our knowledge, only one study from the United States from the University of Texas M. D. Anderson Cancer Center (UTMDACC), a cancer quaternary care center, has explored the impact of COVID-19 on the disease characteristics of patients presenting with HNC during the pandemic; it demonstrated an increase in tumor burden.¹⁰ Herein, we aim to compare time to diagnosis and treatment, ability to provide curative intent surgery, and metastatic disease rates in patients newly diagnosed with mucosal head and neck squamous cell carcinoma (HNSCC) before the pandemic vs those seen during the early pandemic at a single tertiary care center.

Methods

This study is a retrospective cohort study conducted within the department of Otolaryngology–Head and Neck Surgery at the University of California, Davis (UCD). Approval was obtained by the UCD Institutional Review Board prior to data extraction from patient charts. Patients with newly diagnosed mucosal HNSCC who presented between September 10, 2019, and September 11, 2020, were included. Patients who presented 6 months prior to the announcement of the pandemic by the WHO¹ (pre–COVID-19 period; September 10, 2019, to March 10, 2020) were compared to patients who presented during the first 6 months of the pandemic (COVID-19 period; March 11, 2020, to September 11, 2020). Patients who had recurrent disease, were previously treated, had incomplete records, and had nonmucosal HNSCC were excluded from analysis.

Patient demographics and distance from UCD was calculated in miles based on the ZIP code of primary residence. Symptom onset was defined as the number of weeks from when symptoms were first noticed by the patient to the initial visit with our department. Time from biopsy to the operating room (OR), time from first diagnostic scan to the OR, and time from first clinic visit with our department to the OR were compared between periods. Tumor characteristics, including tumor subsite, primary tumor, and largest nodal metastasis size on imaging (largest cross-sectional measurement), and American Joint Committee on Cancer (AJCC) eighth edition staging were also compared.

Descriptive statistics such as medians and ranges were used as appropriate. Pearson χ^2 and Fisher 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 .05 was considered significant. The analyses were performed on Microsoft Excel.

Results

A total of 137 patients were identified as having newly diagnosed mucosal HNSCC within the 1-year period, with 77 presenting 6 months prior to the onset of the pandemic

(pre–COVID-19 period) and 60 presenting during the first 6 months of the pandemic (COVID-19 period). This represents a 22% reduction in the number of patients with newly diagnosed mucosal HNSCC who presented to our clinic during the early pandemic.

Patient Demographics

Table 1 summarizes demographics of patients who presented before the pandemic and during the early pandemic. The pre–COVID-19 period and the COVID-19 period had no significant differences between demographics, with median age being 65 vs 67 years, respectively (*P* = .960), and sex (67.9% male in pre–COVID-19 vs 76.7% male in COVID-19 period, *P* = .257). There were no differences between race and smoking or drinking status. The median distance traveled from the residential address to our institution between the pre–COVID-19 period and COVID-19 period did not differ (35.5 miles in pre–COVID-19 vs 38 miles in COVID-19 period, *P* = .660).

Patient Presentation and Workup

Table 2 summarizes the tumor characteristics and timing of initial workup for patients who presented in the pre–COVID-19 and COVID-19 period. Tumor subsites were similar between both pre–COVID-19 and COVID-19 period, with the most common subsites being oral cavity (41.6%) and oropharynx (37.2%). In comparing different time intervals related to their care, the periods did not differ in median duration of symptoms (19 weeks in pre–COVID-19 vs 16 weeks in COVID-19 period, *P* = .483) and time from diagnosis to first visit with us (25 days in pre–COVID-19 vs 27 days in COVID-19 period, *P* = .938). There was a larger proportion of tumors classified as T3/T4 (61.7%) in the COVID-19 period vs the pre–COVID-19 period (40.3%) compared to T1/T2 classifications (35.0% in COVID-19 period vs 54.5% in pre–COVID-19 period, *P* = .0244). There was no significant difference between periods when comparing N staging (*P* = .483) and M staging (*P* = .419). In comparing primary tumor size on imaging, the COVID-19 period had a larger primary tumor size, with a median of 4.5 cm compared to 3.0 cm in the pre–COVID-19 period (*P* = .0002). The largest nodal metastasis measured for patients with clinically suspicious nodal disease was similar at 2.1 cm between periods.

Characteristics of Patients Undergoing Definitive Surgery

Of the 137 patients during the pre–COVID-19 and COVID-19 time periods, 88 (64.2%) ultimately underwent surgery for curative purposes, as illustrated in **Table 3**. Both periods had a similar percentage of patients who underwent definitive surgery (63.6% vs 65.0%, *P* = .869) compared to other modalities of treatment (ie, definitive radiotherapy, chemoradiation, palliation). There was no difference between time of initial diagnostic scan to surgery (42 days in pre–COVID-19 vs 40 days in COVID-19 period, *P* = .126) and first biopsy to surgery (53 days in pre–COVID-19 vs 52 days in COVID-19 period,

Table 1. Patient Demographics.^a

Characteristic	Total	Pre-COVID-19 period	COVID-19 period	P value
Total number	137	77	60	
Age, median (range), y	65.5 (23-93)	65 (43-92)	67 (23-87)	.960
Sex				
Male	99 (71.7)	53 (67.9)	46 (76.7)	.257
Female	39 (28.3)	25 (32.1)	14 (23.3)	
Race				
White	103 (75.2)	58 (75.3)	45 (75.0)	.968
Hispanic	10 (7.3)	5 (6.5)	5 (8.3)	
Asian	11 (8.0)	7 (9.1)	4 (6.7)	
Black	5 (3.6)	3 (3.9)	2 (3.3)	
Other	8 (5.8)	4 (5.2)	4 (6.7)	
Smoking status				
Never	50 (36.5)	30 (39.0)	20 (33.3)	.519
Former	61 (44.5)	31 (40.3)	30 (50.0)	
Current	26 (19.0)	16 (20.7)	10 (16.7)	
Alcohol status				
Never	94 (68.6)	50 (64.9)	44 (73.3)	.27
Former	13 (9.5)	10 (13.0)	3 (5.0)	
Current	30 (21.9)	17 (22.1)	13 (21.7)	
Distance traveled, median (range), miles	36 (1-281)	35.5 (2-221)	38 (1-281)	.660

Abbreviation: COVID-19, coronavirus disease 2019.

^aValues are presented as number (%) unless otherwise indicated.**Table 2.** Patient Presentation and Workup.^a

Characteristic	Total	Pre-COVID-19	COVID-19	P Value
Total number	137	77	60	
Tumor subsite				
Oral cavity	57 (41.6)	31 (40.3)	26 (43.3)	.467
Oropharynx	51 (37.2)	30 (38.9)	21 (35.0)	
Sinonasal	12 (8.8)	9 (11.7)	3 (5.0)	
Laryngeal	15 (10.9)	6 (7.8)	9 (15.0)	
Other	2 (1.5)	1 (1.3)	1 (1.7)	
Duration of symptoms prior to first visit, median (range), wk	16 (0-261)	19 (2-261)	16 (0-120)	.483
Duration from diagnosis to first visit, median (range), d	27 (0-193)	25 (0-185)	27 (0-193)	.938
Tumor (T) classification				
Tx	6 (4.4)	4 (5.2)	2 (3.3)	.154
T1	28 (20.4)	18 (23.4)	10 (16.7)	
T2	35 (25.6)	24 (31.2)	11 (18.3)	
T3	28 (20.4)	14 (18.2)	14 (23.3)	
T4	40 (29.2)	17 (22.0)	23 (38.3)	
Nodal (N) classification				
N0	54 (39.4)	30 (38.9)	24 (40.0)	.483
N1	42 (30.7)	27 (35.1)	15 (25.0)	
N2	31 (22.6)	16 (20.8)	15 (25.0)	
N3	10 (7.3)	4 (5.3)	6 (10.0)	
Metastasis (M) classification				
M0	134 (97.8)	76 (98.7)	58 (96.7)	.419
M1	3 (2.2)	1 (1.3)	2 (3.3)	
Size of primary tumor, longest dimension, median (range), cm	3.5 (0.3-9.5)	3.0 (0.3-6.9)	4.5 (0.3-9.5)	.0002
Size of largest nodal metastasis, longest dimension, median (range), cm	2.1 (0.4-9.0)	2.1 (0.6-7.0)	2.1 (0.4-9.0)	.780

Abbreviation: COVID-19, coronavirus disease 2019.

^aValues are presented as number (%) unless otherwise indicated. Bold signifies that it met our significance threshold of $P < 0.05$.

Table 3. Characteristics of Patients Who Underwent Definitive Surgery.^a

Characteristic	Total	Pre-COVID-19	COVID-19	P value
Total number	137	77	60	
Treatment				
Primary surgery	88 (64.2)	49 (63.6)	39 (65.0)	.869
Other	49 (35.8)	28 (36.4)	21 (35.0)	
Duration of scan to surgery, median (range), d	42 (2-200)	42 (3-200)	40 (2-126)	.126
Duration of biopsy to surgery, median (range), d	53 (0-245)	53 (10-147)	52 (0-245)	.737
Duration from clinic visit to surgery, median (range), d	29 (3-134)	29 (4-134)	27 (3-58)	.310
Extent of surgery				
Primary closure	45 (51.1)	28 (57.1)	17 (43.6)	.206
Free flap	40 (45.5)	20 (40.8)	20 (51.3)	
Laryngectomy	3 (3.4)	1 (2.1)	2 (5.1)	
Adjuvant therapy				
None	21 (23.9)	13 (26.5)	8 (20.5)	.560
Radiation therapy	33 (37.5)	16 (32.7)	17 (43.6)	
Chemoradiation	34 (38.6)	20 (40.8)	14 (35.9)	

Abbreviation: COVID-19, coronavirus disease 2019.

^aValues are presented as number (%) unless otherwise indicated.

$P = .938$). Both periods had similar time intervals between the first clinic visit with our team to the OR for definitive surgery (29 days in pre-COVID-19 vs 27 days in COVID-19 period, $P = .310$). The extent of surgery was similar, with 40.8% of patients undergoing free flap surgery in the pre-COVID-19 period compared to 51.3% in the COVID-19 period ($P = .206$). The pre-COVID-19 period pursued adjuvant radiotherapy (32.7%) and chemoradiation (40.8%) at similar rates compared to the COVID-19 period (adjuvant therapy, 42.6%; chemoradiation, 35.9%; $P = .560$).

Discussion

At our institution, we found there was a 22% reduction in the number of newly diagnosed mucosal HNSCC patients presenting to UCD in the COVID-19 period compared to the pre-COVID-19 period. National and statewide lockdowns may have posed a significant barrier for patients seeking medical care, and many medical services were limited as the pandemic presented with surges across the country.¹¹ In addition, dentists, who often identify early oral cavity cancers,¹² and many primary care providers shut down offices for some time. This may have further affected our referral base and contributed to the decreased proportion of T1/T2 tumors observed. Our data show the median distance traveled from patient homes to the hospital was not significantly different between the pre-COVID-19 (35.5 miles) and COVID-19 (38 miles) periods, indicating that patients were still willing to travel to receive the care they needed. Also reassuring from our findings was that despite fewer patients presenting to our clinic, our team was able to maintain the same level of urgency in providing time-sensitive care. Time from diagnosis to first visit (pre-COVID-19 being 25 days and COVID-19 period being 27 days) and time from first visit to surgery (pre-COVID-19 being 29 days and COVID-19 period being 27 days) were similar in both periods. In addition, while patient reports of

symptom onset may be unreliable and subject to recall bias, both periods had similar times of symptom onset to first clinic visit with wide ranges (19 weeks [range, 2-261] vs 16 weeks [range, 0-120]). Although patients were receiving timely care, we did note a significant increase in the proportion of T3/T4 tumors in the COVID-19 period (61.7%) compared to the pre-COVID-19 period (40.3%), which correlated with the median primary tumor size being 4.5 vs 3.0 cm, respectively. Interestingly, we had similar rates of free flap surgery and adjuvant therapy, which perhaps indicates that the primary tumor burden may not have been clinically significant in our cohort. There were no differences noted in nodal disease burden or rates of distant metastatic disease between both periods.

Our findings are largely in agreement with those of UTMDACC, which compared 6 weeks within the early pandemic (May 14, 2020, to June 18, 2020) to a similar time period from the year prior for newly diagnosed mucosal HNSCC.¹⁰ Between both time periods, they had similar demographics, time from diagnosis to first visit, and nodal disease burden but noted higher T staging and larger primary tumors (median, 2.9 vs 2.2 cm) during the COVID-19 pandemic.¹⁰ Despite proponents recommending judiciously selecting patients for oncologic surgery based on optimal oncologic control and risk to the patient and health care teams,^{4,5} our findings show that we made strong attempts to minimize disruptions in the care for our patients with HNC. The differences in T staging may be explained by patients presenting to outside providers for initial evaluation later during the pandemic, as we did not note delays in care once they were referred for definitive treatment to our institution. In addition, patients with smaller, minimally symptomatic tumors could have been waiting for evaluation and may not be captured during our study time period of the first 6 months of the pandemic; this could have led to a self-selection of

patients presenting with larger more symptomatic tumors during the early pandemic.

While our findings and those of UTMDACC tell one story, it is important to recognize that not all regions of the United States and the world were affected similarly. In the United States, physician services, hospital visits, and dental services decreased as social distancing measures were implemented. When comparing these services in April 2019 to April 2020, health spending had decreased 37%, 43%, and 61%, respectively, and from May 2019 to May 2020, spending decreased 19%, 25%, and 45%, respectively.¹³ In the United Kingdom, there has been a drastic surge in patients with HNC presenting in an emergency context after the initial UK national lockdown, indicating the significant reduction in urgent cancer referrals.¹⁴ In a multicenter prospective observation study from France, they noted a limited impact in their cancer delivery, comparing 1 month before their lockdown and 1 month into their lockdown, but did note an increase in T3/T4 ($P = .002$) and N3/N4 tumors ($P = .0004$).¹⁵ In a recent systemic review that explored global delays and disruptions in cancer care globally during the pandemic, interruptions and disruptions affected 77.5% of facilities, 79% of supply chains, and up to 60% of personnel availability in routine cancer care delivery, including surgeries.¹⁶

There are several limitations to our study. Our time interval may not capture the full effects of the COVID-19 pandemic on health care utilization and patient presentation. With the number of COVID-19 cases increasing in the following months after obtaining the initial data, the burden of COVID-19 on patients with cancer still could be undetermined. We understand that the data obtained may not represent a global picture of the effects of the pandemic in the United States, as this represents a single institution on the West Coast. It is important to highlight that our institution was in a unique position to deliver HNC care, as our system and our department did not face a temporary closure. In addition, on March 19, 2020, California's governor issued a statewide shelter-in-place order that remained in effect throughout the study's time period.¹⁷ During July to September 2020, Northern California faced a rise in COVID-19 cases, although our region's rates were not as high as other parts of the country.¹⁸ We recognize that other parts of the country and world may have faced challenges in remaining open to deliver care across all levels in the health care system, which could pose significant delays in care. Recall bias may also have been present as in any retrospective study. Future directions to be considered include an assessment on a multi-institutional level and determining the nationwide trends the pandemic had on HNC health care utilization over a longer period. If our oncologic outcomes suffer due to the pandemic, then it would support reinforcing national standards for triage and treatments of patients with HNC.

Conclusion

Despite similar characteristics, time to diagnosis, and surgery for patients presenting before and during the COVID-19 pandemic, our findings suggest that there may be an increase in

primary tumor burden in patients with HNSCC during the early pandemic.

Author Contributions

Roberto N. Solis, substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; acknowledgment of drafting the article or revising it critically for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; **Mehrnaz Mehrzad**, substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; acknowledgment of drafting the article or revising it critically for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; **Samya Faiq**, substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; acknowledgment of drafting the article or revising it critically for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; **Roberto P. Frusciante**, substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; acknowledgment of drafting the article or revising it critically for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; **Harveen K. Sekhon**, substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; acknowledgment of drafting the article or revising it critically for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; **Marianne Abouyared**, substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; acknowledgment of drafting the article or revising it critically for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; **Arnaud F. Bewley**, substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; acknowledgment of drafting the article or revising it critically for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; **D. Gregory Farwell**, substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; acknowledgment of drafting the article or revising it critically for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; **Andrew C. Birkeland**, substantial contributions to conception and

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ORCID iD

Roberto N. Solis  <https://orcid.org/0000-0003-3786-1712>

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