

Times to Diagnosis, Staging, and Treatment of Head and Neck Cancer Before and During COVID-19

OTO Open
 2021, Vol. 5(4) 1–7
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 DOI: 10.1177/2473974X211059429
<http://oto-open.org>


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Abstract

Objective. The coronavirus disease 2019 (COVID-19) pandemic has reduced the demand for, and supply of, head and neck cancer services. This study compares the times to diagnosis, staging, and treatment of head and neck cancers before and during the COVID-19 pandemic.

Study Design. Retrospective cohort study.

Setting. Tertiary academic medical center in New York City (NYC).

Methods. The times to diagnosis, staging, and treatment of head and neck cancer for patients presenting to the clinics of 4 head and neck oncology surgeons with newly diagnosed head and neck cancers were compared between pre-COVID-19 and COVID-19 periods.

Results. Sixty-eight patients in the pre-COVID-19 period and 26 patients in the COVID-19 period presented with newly diagnosed head and neck cancer. Patients in the COVID-19 group had a significantly longer time to diagnosis than the pre-COVID-19 group after adjustment for age and cancer diagnosis ($P = .02$; hazard ratio [HR], 0.54; 95% CI, 0.32-0.92). Patients in the pre-COVID-19 and COVID-19 groups had no statistically significant differences in time to staging ($P > .9$; HR, 1.01; 95% CI, 0.58-1.74) or time to treatment ($P = .12$; HR, 1.55; 95% CI, 0.89-2.72).

Conclusion. This study found that time to diagnosis for head and neck cancers was delayed during a COVID-19 period compared to a pre-COVID-19 period. However, there was no evidence of delays in time to staging and time to treatment during the COVID-19 period. Our results prompt further investigations into the factors contributing to diagnostic delays but provide reassurance that despite COVID-19, patients were receiving timely staging and treatment for head and neck cancers.

Keywords

COVID-19, head and neck cancer, diagnosis delay, staging delay, treatment delay

Received October 15, 2021; accepted October 20, 2021.

The coronavirus disease 2019 (COVID-19) pandemic disrupted the diagnosis, staging, and treatment of head and neck cancers due to a complex interplay of patient, provider, and institutional factors. For patients, COVID-19 increased the risk of seeking cancer care. Patients with cancer have a higher risk of infection and serious complications from COVID-19 than patients without cancer.¹ In addition, patients with cancer risk COVID-19 exposure in the process of obtaining cancer care, for example, through transportation, exposure to other patients in a medical setting, and multiple consultations with an interdisciplinary medical team. For medical providers, the diagnosis and treatment of head and neck cancers that arise in mucosal membranes often require potential viral exposure. Furthermore, patients may remain a high aerosolization risk after treatment due to dysphagia or airway compromise. From an institutional perspective, hospitals and clinics have been overburdened with COVID-19 care and may have limited resources to care for patients with cancer. Also, many operating rooms, intensive care units (ICUs), and procedural units have either been closed or diverted to COVID-19 care, thereby limiting procedure, biopsy, and imaging availabilities for patients with cancer.

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This article was presented virtually as a poster presentation at the American Head & Neck Society 10th International Conference on Head and Neck Cancer, July 22-25, 2021.

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The confluence of these factors altered the landscape of head and neck cancer care in New York City (NYC), which emerged as an early epicenter of the COVID-19 pandemic in the United States in March 2020. On March 16, 2020, our institution suspended all elective surgeries. Subsequently, the American College of Surgeons (ACS) issued guidelines to limit “elective” surgical procedures,² and the American Academy of Otolaryngology–Head and Neck Surgery recommended only “time-sensitive” or “emergent” care.³ In response to the recommendations to reduce nonessential procedures, the ACS⁴ and Centers for Medicare & Medicaid Services⁵ published guidelines on how to triage surgical cases by priority. These general guidelines were supplemented by surgical specialty-specific guidelines from medical institutions and professional organizations. The Department of Otolaryngology at Stanford University published a framework on stratifying the urgency of head and neck cancer surgery based on risk to the oncology patient, outcomes following delay in head and neck cancer therapy, and risk of transmission during otolaryngologic surgery.⁶ A panel of 40 experts in head and neck cancer surgical, radiation, and medical oncology developed international consensus guidelines defining acceptable delay and treatment protocols for head and neck cancers.⁷

The concern over delays in head and neck cancer care stem from studies demonstrating a relationship between delays, especially treatment delays, and increased patient morbidity and mortality.^{8,9} While guidelines have sought to limit delays by standardizing cancer care in the COVID-19 era and evidence has established the importance of timely treatment of head and neck cancer to survival, few studies have examined whether cancer timelines for head and neck cancer were delayed during the COVID-19 pandemic in comparison to a pre-COVID-19 period.^{10,11} This study aims to address this gap in knowledge by comparing diagnosis, staging, and treatment intervals for head and neck cancer before and during the COVID-19 pandemic in an academic department of otolaryngology–head and neck surgery in NYC.

Methods

Pre-COVID-19 and COVID-19 Periods

We defined the COVID-19 period as March 16, 2020, to the initiation of the study on July 16, 2020. We defined a pre-COVID-19 period of equivalent length from September 16, 2019, to January 16, 2020. We left a 2-month gap between the 2 periods to minimize overlap. We chose March 16, 2020, as the beginning of the pandemic period because it is when public and hospital activities became severely restricted due to isolation and lockdown measures in our region. On March 16, our institution suspended all elective surgeries, and shortly afterward, on March 22, a statewide stay-at-home order was issued for New York. While elective surgeries were suspended, a triage system was instituted to schedule emergent surgeries in the 5 operating rooms in the hospital that remained open.

Patients and Data Collection

Using billing records, we identified all patients who visited the clinics of 4 otolaryngologists subspecializing in head and neck oncology at a large tertiary academic medical center in NYC during these 2 periods with *International Classification of Diseases, 10th Revision (ICD-10)* diagnosis codes, suggesting potential for a head and neck cancer diagnosis (see Suppl. Table S1 in the online version of the article). We screened these patients and included those with a new histopathologic diagnosis of cancer in our study. Patients with missing dates of initial suspicion of cancer were excluded from the study. For each patient, demographic data, clinical characteristics, and key oncologic time points were obtained by retrospective chart review.

Key Clinical Time Points

Key time points included the dates of initial suspicion of cancer, histopathologic diagnosis, initial staging procedures and imaging, and initial treatment. The date of initial suspicion of cancer was defined as the date of first documentation of cancer suspicion by a medical provider on the electronic health record (EHR). The 3 primary outcomes of interest compared between pre-COVID-19 and COVID-19 periods were the times to diagnosis, staging, and treatment. The time to diagnosis was defined as the time in days from the date of initial suspicion of cancer to the date of histopathologic diagnosis. The time to staging was defined as the time in days from the date of initial suspicion of cancer to date of initial staging procedures and imaging. The time to treatment was defined as the time in days from the date of histopathologic diagnosis to the date of initial treatment.

Statistical Analysis

Descriptive statistics were generated to describe the study population using number (%) and median (interquartile range [IQR]). Fisher exact, χ^2 , and Wilcoxon rank sum tests were used to compare patients from the pre-COVID-19 and COVID-19 time periods on demographic and clinical characteristics. Kaplan-Meier curves were generated to visualize diagnosis-free, staging-free, and treatment-free survival, and log-rank tests were used to identify any differences in median survival time between the 2 time periods. Cox proportional hazards models were used to estimate hazard ratios (HRs) for the relationship between time period and the outcomes mentioned above, adjusted for age and cancer diagnosis. Statistical significance was evaluated at the .05 α level, and 95% CIs were generated for all predictor estimates. All analyses were performed in R (4.0.3) for Windows.

This study was approved by the institutional review board of Weill Cornell Medicine.

Results

Demographic and Clinical Characteristics

We identified 68 patients in the pre-COVID-19 period and 26 patients in the COVID-19 period with newly diagnosed head

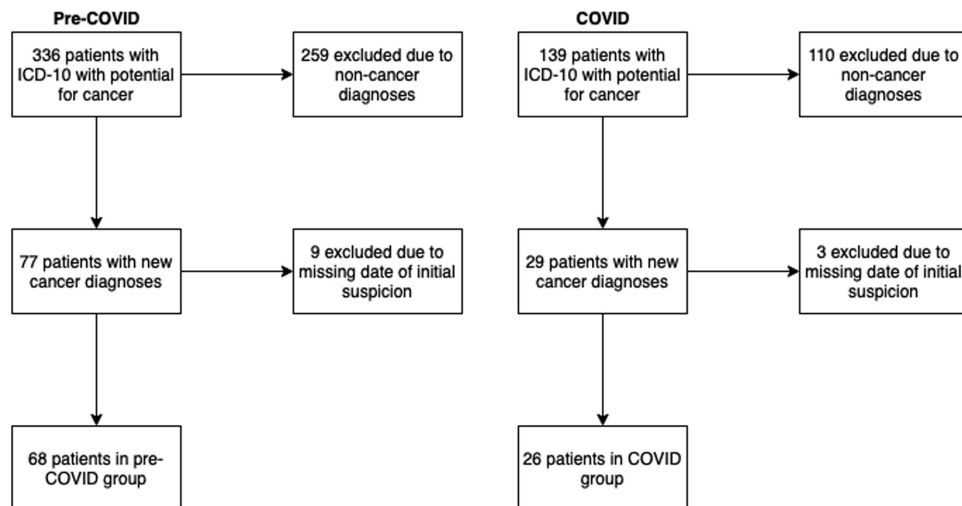


Figure 1. Flow diagram demonstrating selection of patients for the pre-COVID-19 and COVID-19 groups. COVID, coronavirus disease 2019; ICD-10, International Classification of Diseases, 10th Revision.

and neck cancer (**Figure 1**). All patients were seen in person at a head and neck oncology clinic. Overall, the median patient age was 64 years, 46% were female, 46% had a history of tobacco use, and 7% had a history of high-risk alcohol use. The most common cancer diagnoses were head and neck squamous cell carcinoma (33%), thyroid cancer (27%), and lymphoma (24%). The most common staging group was stage I (56%), and the most common initial treatment was surgery (62%). **Table 1** summarizes the demographic and clinical characteristics for the entire cohort and identifies any key significant differences between the pre-COVID-19 and COVID-19 groups.

Patient age ($P = .004$) and cancer diagnosis ($P = .007$) varied significantly between the pre-COVID-19 and COVID-19 groups. The median age in the pre-COVID-19 group was 55 years vs 77 years in the COVID-19 group. The most common cancer diagnoses were head and neck squamous cell carcinoma (34%), thyroid cancer (34%), and lymphoma (21%) in the pre-COVID-19 group vs lymphoma (35%), head and neck squamous cell carcinoma (31%), and skin cancer (23%) in the COVID-19 group. Sex, tobacco use, alcohol use, race, performance status, and staging group did not vary significantly between the 2 periods.

Time From Suspicion of Cancer to Diagnosis

A Kaplan-Meier curve was used to visualize the time from suspicion of cancer to diagnosis in the pre-COVID-19 and COVID-19 groups (**Figure 2A**). A comparison of survival curves using the log-rank test showed no difference in diagnosis-free survival between the pre-COVID-19 and COVID-19 groups ($P = .17$). The estimated median time from suspicion of cancer to diagnosis was 12.5 days (95% CI, 9-21) in the pre-COVID-19 group vs 12.5 days (95% CI, 8-34) in the COVID-19 group. A Cox proportional hazards model was used to test for difference between time to diagnosis in the 2 groups after adjustment for age and cancer diagnosis. In the unadjusted model, there was no statistically significant

difference between the time to diagnosis in the pre-COVID-19 and COVID-19 groups ($P = .2$; HR, 0.72; 95% CI, 0.45-1.16). However, after adjustment for age and cancer diagnosis, the COVID-19 group had a significantly longer time to diagnosis than the pre-COVID-19 group, or those in the COVID-19 group were less likely to be diagnosed in comparison to the pre-COVID-19 group ($P = .02$; HR, 0.54; 95% CI, 0.32-0.92; **Table 2**).

Time From Suspicion of Cancer to Staging

A Kaplan-Meier curve was used to visualize the time from suspicion of cancer to staging in the pre-COVID-19 and COVID-19 groups (**Figure 2B**). A comparison of survival curves using the log-rank test showed no difference in staging-free survival between the pre-COVID-19 and COVID-19 groups ($P = .95$). The estimated median time from suspicion of cancer to staging was 24 days (95% CI, 17-36) in the pre-COVID-19 group vs 22.5 days (95% CI, 14-32) in the COVID-19 group. A Cox proportional hazards model was used to test for difference between time to staging in the 2 groups after adjustment for age and cancer diagnosis. There was no statistically significant difference between the time to staging in the pre-COVID-19 and COVID-19 groups before ($P > .9$; HR, 0.99; 95% CI, 0.60-1.65) or after adjustment for age and cancer diagnosis ($P > .9$; HR, 1.01; 95% CI, 0.58-1.74).

Time From Diagnosis to Treatment

A Kaplan-Meier curve was used to visualize the time from cancer diagnosis to treatment in the pre-COVID-19 and COVID-19 groups (**Figure 2C**). A comparison of survival curves using the log-rank test showed no difference in treatment-free survival between the pre-COVID-19 and COVID-19 groups ($P = .57$). The estimated median time from cancer diagnosis to treatment was 24 days (95% CI, 21-30) in the pre-COVID-19 group vs 20 days (95% CI, 15-35) in the COVID-19 group. A Cox proportional hazards model was

Table 1. Comparison of Demographic and Clinical Characteristics Between the pre-COVID-19 and COVID-19 Groups.^a

Characteristic	Overall (N = 94)	Pre-COVID-19 (n = 68)	COVID-19 (n = 26)	P value ^b
Age, mean (IQR), y	64 (50, 73)	55 (47, 72)	70 (65, 82)	.004
Patient sex				.2
Female	43 (46.0)	34 (50.0)	9 (35.0)	
Male	51 (54.0)	34 (50.0)	17 (65.0)	
History of tobacco use	43 (46.0)	31 (46.0)	12 (46.0)	>.9
History of alcohol use	7 (7.4)	5 (7.4)	2 (7.7)	>.9
Patient race				.6
Ashkenazi Jewish	1 (1.1)	0 (0)	1 (3.8)	
Asian	6 (6.4)	4 (5.9)	2 (7.7)	
Black	2 (2.1)	1 (1.5)	1 (3.8)	
Declined	38 (40.0)	29 (43.0)	9 (35.0)	
Other	8 (8.5)	6 (8.8)	2 (7.7)	
White	39 (41.0)	28 (41.0)	11 (42.0)	
Cancer diagnosis				.007
HNSCC	31 (33.0)	23 (34.0)	8 (31.0)	
Lymphoma	23 (24.0)	14 (21.0)	9 (35.0)	
Other ^c	6 (6.4)	5 (7.4)	1 (3.8)	
Skin cancer	9 (9.6)	3 (4.4)	6 (23.0)	
Thyroid cancer	25 (27.0)	23 (34.0)	2 (7.7)	
Recurrent cancer	7 (7.4)	3 (4.4)	4 (15.0)	.089
ECOG performance status				.7
0	6 (17.0)	4 (17.0)	2 (17.0)	
1	22 (63.0)	14 (61.0)	8 (67.0)	
2	4 (11.0)	2 (8.7)	2 (17.0)	
3	3 (8.6)	3 (13.0)	0 (0)	
Unknown	59	45	14	
Karnofsky performance status				.3
40	2 (5.6)	2 (8.3)	0 (0)	
50	1 (2.8)	1 (4.2)	0 (0)	
60	1 (2.8)	1 (4.2)	0 (0)	
70	2 (5.6)	0 (0)	2 (17.0)	
80	13 (36.0)	10 (42.0)	3 (25.0)	
90	14 (39.0)	8 (33.0)	6 (50.0)	
100	3 (8.3)	2 (8.3)	1 (8.3)	
Unknown	58	44	14	
Staging group, lymphoma				>.9
2	2 (33.0)	2 (40.0)	0 (0)	
3	2 (33.0)	1 (20.0)	1 (100)	
4	2 (33.0)	2 (40.0)	0 (0)	
Unknown	17	9	8	
Staging group, nonlymphoma				.12
0	1 (1.9)	1 (2.4)	0 (0)	
1	33 (62.0)	28 (67.0)	5 (45.0)	
2	5 (9.4)	3 (7.1)	2 (18.0)	
3	5 (9.4)	2 (4.8)	3 (27.0)	
4	9 (17.0)	8 (19.0)	1 (9.1)	
Unknown	18	12	6	

Statistically significant values ($P < 0.05$) are bolded. Abbreviations: COVID-19, coronavirus disease 2019; ECOG, Eastern cooperative oncology group; HNSCC, head and neck squamous cell carcinoma.

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

^bWilcoxon rank-sum test; Pearson χ^2 , or Fisher exact test.

^cThe "other" category included salivary gland cancers, vascular tumors, and metastases to the head and neck.

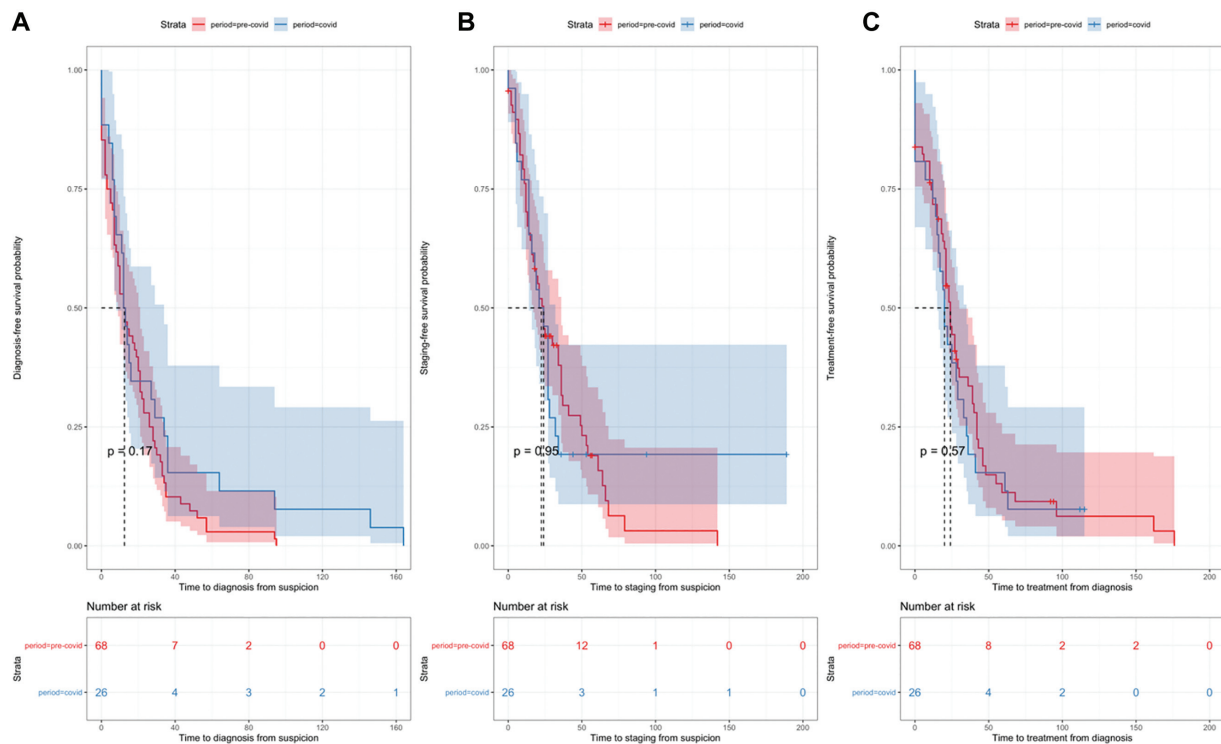


Figure 2. Kaplan-Meier curves comparing the time to diagnosis (A), time to staging (B), and time to treatment (C) between the pre-COVID-19 and COVID-19 groups.

Table 2. Cox Proportional Hazards Model Results for Time From Suspicion of Cancer to Diagnosis.

Characteristic	Unadjusted			Adjusted		
	HR	95% CI	P value	HR	95% CI	P value
Period						
Pre-COVID-19	—	—		—	—	
COVID-19	0.72	0.45-1.16	.2	0.54	0.32-0.92	.024
Age				1.01	0.99-1.02	.4
Cancer diagnosis						
HNSCC				—	—	
Lymphoma				0.78	0.45-1.35	.4
Other				0.78	0.32-1.92	.6
Skin cancer				1.60	0.72-3.56	.3
Thyroid cancer				0.60	0.34-1.06	.081

Statistically significant values ($P < 0.05$) are bolded. Abbreviations: HNSCC, head and neck squamous cell carcinoma; HR, hazard ratio; —, The long dash indicates the reference group.

used to test for difference between time to treatment in the 2 groups after adjustment for age and cancer diagnosis. There was no statistically significant difference between the time to treatment in the pre-COVID-19 and COVID-19 groups before ($P = .6$; HR, 1.14; 95% CI, 0.71-1.84) or after adjustment for age and cancer diagnosis ($P = .12$; HR, 1.55; 95% CI, 0.89-2.72).

Discussion

COVID-19 has demanded a large proportion of health care resources, leading to concerns that the diversion of resources

may cause delays in the diagnosis, staging, and treatment of head and neck cancers. In this study of 94 patients, we compared the times to diagnosis, staging, and treatment in a tertiary academic medical center before and during the peak of the first wave of the COVID-19 pandemic in NYC. We found there were delays in diagnosis for head and neck cancers during the COVID-19 period after adjustment for age and cancer diagnosis. However, there was no evidence of delays in time to staging and time to treatment during COVID-19 before or after adjustment for clinical factors. This finding is important considering evidence that delays in treatment are

associated with increased mortality and morbidity in patients with head and neck cancer.

A typical pathway from cancer suspicion to diagnosis may involve initial suspicion by the patient's primary care provider, referral to an otolaryngologist for further evaluation, and a biopsy for pathologic diagnosis. Our finding that the time from initial suspicion of cancer to diagnosis was delayed during the COVID-19 period raises the need for further exploration of patient, provider, and institutional factors that may have contributed to the delay in diagnosis. First, patients may have been hesitant to seek care for head and neck cancer due to risk of viral exposure through contact with the health care system. Second, limited clinic hours during the peak of the pandemic may have restricted access to otolaryngologists for patients seeking specialist consultation for head and neck cancers. Third, institutional delays due to the diversion of hospital resources toward COVID-19 may have limited and delayed biopsies necessary to render a histopathologic diagnosis.

Several studies have explored the effect of diagnostic delay on the staging of the tumor and, by extension, in survival from head and neck cancer with inconsistent conclusions. Some studies have described a significant association between advanced stages and diagnostic delay.¹²⁻¹⁴ However, a systematic review of 27 studies did not find a consistent relationship between diagnostic delay and stage at diagnosis, although conclusions may have been limited by the heterogeneity of included studies.¹⁵ Another systematic review of 10 studies concluded that diagnostic delay is a moderate risk factor of mortality from head and neck cancer.¹⁶ Despite the heterogeneity of evidence, diagnostic delay remains an important predictor of survival in head and neck cancer, and our finding that COVID-19 was associated with diagnostic delays warrants further investigation into contributing causes.

We found no significant difference in times to staging or treatment between the pre-COVID-19 and COVID-19 periods, suggesting that access to imaging and procedural resources may not have been a bottleneck in head and neck cancer care at our institution during COVID-19. These findings prompt exploration into the role of operating room resource allocation and head and neck cancer triage protocols at our institution in limiting delays. At our institution, elective surgeries were suspended from March 16, 2020, to June 8, 2020. Many operating rooms were converted to rooms for patients with COVID-19, and operating room staff and resources were diverted to care for patients with COVID-19. A triage system was instituted to schedule essential surgeries in the 5 operating rooms in the hospital that remained open. In order to schedule an emergent, urgent, or semiurgent procedure, a surgeon had to submit a form describing the rationale for scheduling the surgery, the expected length of life and quality of life of the patient, and nonoperative alternatives that had been explored. The procedure required approval from the department chairperson prior to being allocated operating room resources based on urgency. Patients presenting for elective surgery were required to have a negative COVID-19 test.

In particular, our finding of no significant treatment delay during COVID-19 is important in light of substantial evidence in the literature that treatment delays in head and neck cancer are associated with worse survival. A systematic review of 51 studies found that treatment delays for head and neck cancer correlated with reduced overall survival and disease-specific survival, as well worsened functional and psychosocial outcomes.⁹ Similarly, a systematic review of 18 studies reported that treatment delays are associated with worse overall survival.⁸

Few other studies have compared key clinical time points in the head and neck cancer care pathway between COVID-19 and non-COVID-19 periods. In a study from Turkey comparing 125 patients from pre-COVID-19 and COVID-19 periods with laryngeal cancer and oral cavity cancer, Tevetoğlu et al¹⁰ found an increase in the time from first symptom to admission in the COVID-19 group. However, the authors found no difference in the time from admission to surgery. In a study from China comparing 136 patients from pre-COVID-19 and COVID-19 periods with nasopharyngeal carcinoma, Yang et al¹¹ found significant differences in the waiting times for pathological biopsy and initiation of radiotherapy. Like the 2 previous studies, we found delays in the time to diagnosis for head and neck cancers. However, in contrast to Yang et al,¹¹ we did not find delays in the time to treatment. Our study adds to the existing literature by applying time-to-event analysis using Kaplan-Meier analysis and Cox proportional hazards models to examine the difference between key oncologic intervals. Furthermore, unlike prior studies that focus on specific cancers and treatment modalities, we examine diagnosis, staging, and treatment delays for head and neck cancers broadly at our institution.

This study has several limitations. First, we compare times to diagnosis, staging, and treatment, but we were not able to compare other clinically important end points such as patient survival and recurrence due to lack of long-term follow-up data. Second, we present data from a limited sample of 94 patients from a single urban tertiary academic medical institution. Our findings may not generalize to other institutions with different geographical and patient characteristics. Multi-institutional studies with larger sample sizes are needed to investigate potential delays in diagnosis, staging, and treatment during the COVID-19 pandemic more broadly. Third, we screened patients for inclusion using *ICD-10* diagnosis codes which may have missed some patients with cancer diagnoses. However, this risk was mitigated by creating a broad list of eligible *ICD-10* codes in collaboration with an experienced head and neck oncology surgeon. Fourth, some patients had missing data, which limited our ability to fully describe the demographics and patient characteristics of our cohort. Last, our analysis used date of initial suspicion of cancer as a starting point for measuring diagnostic delay due to the reliable documentation of this information in the medical record. Our study was not able to capture other forms of delay, such as delays from patients hesitating to seek or not presenting for otolaryngologic evaluation during COVID-19. The number of patients presenting to our clinics with a new diagnosis of head

and neck cancer decreased 62% in the COVID-19 period (n = 26) compared to the pre-COVID-19 period (n = 68). Assuming the incidence of head and neck cancer was unchanged, the decrease in cancer diagnoses suggests that a large cohort of patients with undiagnosed head and neck cancer did not present for otolaryngologic evaluation during COVID-19, representing a type of diagnostic delay that was not captured by this study. Modeling studies have forecasted an increase in cancer deaths due to the reduction in demand for, and supply of, cancer services during the COVID-19 pandemic.^{17,18}

In conclusion, we compared the times to diagnosis, staging, and treatment for head and neck cancers before and during the height of the COVID-19 pandemic in NYC. We found that the COVID-19 period was associated with a longer time to diagnosis after adjusting for age and cancer diagnosis. We found no difference between the times to staging and treatment for the pre-COVID-19 and COVID-19 periods. Our results prompt further investigations into the factors contributing to diagnostic delays but provide evidence that despite COVID-19, patients were receiving timely staging and treatment for head and neck cancers.

Authorship Contributions

Peter Yao, conceptualization, study design, data collection, data analysis, data interpretation, writing, review, and editing; **Victoria Cooley**, statistical analysis, data interpretation, writing, and editing; **William Kuhel**, data collection, writing, and editing; **Andrew Tassler**, data collection, writing, and editing; **Victoria Banuchi**, data collection, writing, and editing; **Sallie Long**, data collection, writing, and editing; **Oleksandr Savenkov**, statistical analysis, data interpretation, writing, and editing; **David Ivan Kutler**, conceptualization, study design, data collection, writing, and editing.

Disclosures

Competing interests: None.

Sponsorships: None.

Funding source: None.

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Supplemental Material

Additional supporting information is available at <http://journals.sagepub.com/doi/suppl/10.1177/2473974X211059429>

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