Annals of Clinical Otolaryngology

Research Article
Published: 12 May, 2021

Outcomes of Microvascular Reconstruction for Head and Neck Cancer in a COVID-19 Hot Spot

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Abstract

Objectives: Since the onset of the COVID-19 pandemic, institutional guidelines have suggested postponing non-emergent surgical cases to prevent nosocomial spread of the SARS-CoV-2 virus. However, it is well established that delays in Head and Neck Cancer (HNC) treatment are associated with increased morbidity and mortality. Current data on outcomes of major surgeries for HNC during the pandemic is limited. To address this, we compared the clinical and surgical outcomes of these surgeries performed during the pandemic to those prior to the pandemic.

Materials and Methods: This is a retrospective cohort study, with the post-COVID cohort consisting of all HNC patients who underwent major surgeries including free flap reconstruction from March 11th, 2020 to December 21st, 2020, and the pre-COVID cohort including HNC patients who had similar surgeries from March 11th, 2019 to December 21st, 2019. A chart review was conducted for data regarding patient demographics, comorbidities, and clinical and surgical outcomes. Statistical analysis was done using Welch's t-test of unequal variance and Fisher's exact test.

Result: There were no significant differences in treatment delays, hospital stays, surgery duration, Estimated Blood Loss (EBL), postoperative complications, and 30-day mortality between the two cohorts. However, readmission rates were significantly reduced and ICU stays were longer for post-COVID patients.

Conclusion: Surgical treatment for HNC patients requiring free flap reconstruction can continue during the pandemic. With necessary precautions in place, surgeons may operate on HNC patients in a timely manner while maintaining clinical and surgical outcomes comparable to those prior to the pandemic.

Keywords: COVID-19; Head and neck cancer; Free flap reconstruction; Pandemic; outcomes; Level of Evidence: III

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Received Date: *14 Apr 2021*
Accepted Date: *08 May 2021*
Published Date: *12 May 2021*

Citation:
Paik CB, Kim C, Nurimba M, Castellanos CX, Martinez E, Kokot N, et al. Outcomes of Microvascular Reconstruction for Head and Neck Cancer in a COVID-19 Hot Spot. Ann Clin Otolaryngol. 2021; 6(1): 1050.

Introduction

Since the World Health Organization (WHO) declared COVID-19 a global pandemic on March 11th, 2020, various precautionary measures have been implemented in order to help mitigate the spread of the virus, including limiting the number of non-urgent patient interactions with medical care staff in order to prevent nosocomial spread. The American Academy of Otolaryngology - Head and Neck Surgery recommended prioritizing "emergent" and "urgent" cases, while considering postponing "time-sensitive" and "routine" cases, though it is up to the individual surgeon to determine which patients fall under these descriptors on a case by case basis [1].

Patients diagnosed with Head And Neck Cancer (HNC) are at increased risk of adverse outcomes from COVID-related complications, given the patients' immune suppression and likelihood of Major Comorbid Conditions (MCCs) [2,3]. Early studies have reported higher mortality and complication rates associated with COVID-19 in both surgical patients and cancer patients [4-6]. Additionally, head and neck surgeries present a high risk of nosocomial spread, as the virus primarily replicates in the nasopharynx, oropharynx, and nasal cavity [7]. However, it is well established that delays in HNC treatment are associated with worsened morbidity and mortality [8-10]. A recent survey-based study of head and neck surgeons in the United States and Canada revealed that no participants were willing to delay cancer treatment by greater than 6 weeks [3]. The current circumstances present head and neck surgeons with the difficult task of weighing the risks of delayed cancer treatment against the risk of nosocomial COVID-19 infection and subsequent

complications.

Because delaying HNC treatment may have deleterious effects, it is imperative to characterize what can and cannot be accomplished safely, in terms of prompt treatment and minimizing COVID-19 exposure risk. In the current study, we investigate the impact of COVID-19 on the outcomes of major head and neck cancer surgeries requiring reconstruction using a microvascular free flap. This study was conducted at a tertiary care center in a COVID-19 hotspot, Los Angeles. Outcomes of the surgeries performed during the COVID pandemic were compared to a historical cohort. In addition, we aim to evaluate the safety and efficacy of our institutional COVID-19 protocols with regards to HNC assessment and treatment.

Materials and Methods

This is a retrospective cohort study of patients undergoing microvascular free flap reconstruction for major HNC surgeries at the Keck Medicine of USC, a tertiary academic institution in Los Angeles, California. The post-COVID cohort consisted of surgeries performed between March 11th, 2020 and December 21st, 2020, after COVID-19 was declared a global pandemic. The pre-COVID cohort consisted of HNC patients who underwent similar surgeries from March 11th, 2019 to December 21st, 2019, and prior to the pandemic. Primary endpoints for our retrospective analysis included treatment delays, hospital and Intensive Care Unit (ICU) Length of Stay (LOS), length of surgery, Estimated Blood Loss (EBL), postoperative complications, and 30 day mortality. Additional data regarding COVID status, readmission rates, and demographics were collected. The study was approved by the University of Southern California Institutional Review Board prior collecting data.

Study data were collected and managed using RED Cap electronic data capture tools hosted at University of Southern California [11,12]. Outcomes between the post-COVID and control groups were compared for any statistically significant differences using Welch's t-test of unequal variance and Fisher's exact test on Graph Pad Prism version 9.0.0 for Windows. Averages were reported as mean ± Standard Error (S.E.). Statistical significance was defined as a p value of less than 0.05.

Results

A total of 191 patients were included in the study, with the post-COVID cohort including99patients and the pre-COVID (control) cohort including 92 patients. The average age of patients in the post-COVID group was 62.0 ± 1.5 years *vs.* 60.4 ± 1.7 years in the control group. The mean Charlson Comorbidity Index (CCI) for the post-COVID and control groups was 4.7 (± 0.2) and 4.6 (± 0.2), respectively. Squamous Cell Carcinoma (SCC) made up a majority of the HNC diagnoses at a rate of 71.7% and 65.9% in the post-COVID and control groups, respectively. For both cohorts, the most common free flap donor site was the radial forearm followed by the anterolateral thigh. Patient characteristics are further detailed in Table 1.

Table 2 summarizes the COVID status of patients in the post-COVID group. All patients in this group pre-operatively were asymptomatic and/or tested negative for COVID-19 *via* a RT-PCR nasopharyngeal or oropharyngeal swab test. Patients were only tested during their hospital stay if they exhibited any signs/symptoms of COVID-19. Only one patient in the post-COVID group postoperatively tested positive for COVID-19, though he had pre-operatively tested negative.

Table 1: Patient demographics.

	Post-COVID (n=99)	Control (n=92)
Mean Age, years (S.E.)	62.0 (1.5)	60.4 (1.7)
Gender, %	—	—
Male	55.6	70.7
Female	44.4	29.3
Ethnicity, %	—	—
Caucasian	35.4	44.6
Black	2	7.6
Hispanic/Latino	17.2	21.7
Asian	18.2	12
Multiracial	1	0
Other	26.3	14.1
Comorbidities, %	—	—
Hypertension	51.5	55.4
Hypercholesterolemia	33.3	25
COPD	9.1	8.7
Kidney Disease	7.1	12
Liver Disease	7.1	2.2
Diabetes	22.2	31.5
Anemia	6.1	12
MI/CAD/CHF	20.2	8.7
Mean CCI score (S.E.)	4.7 (0.2)	4.6 (0.2)
Histology of Cancer, %	—	—
SCC of aero digestive tract	71.7	65.9
Skin Cancer	8.1	7.7
Salivary Gland Tumor	3	4.4
Sarcoma	2	1.1
Sinonasal Undifferentiated Carcinoma	0	0
Other	15.2	20.9
Type of Free Flap, %	—	—
Radial Forearm	48.5	46.7
Anterolateral thigh	26.3	28.3
Fibula	18.2	19.6
Scapula	2	0
Latissimus	1	2.2
Other	4	3.3

Note: Table 1 lists the demographic information, cancer histology, and type of free flap reconstruction for the pre- and post-COVID cohorts

There were no significant differences in rates of surgery delays, mean hospital LOS, and the rates of patients being lost to follow up between the post COVID group and the control group. However, the mean ICU LOS, was greater in the post COVID cohort (2.84 ± 0.40 days *vs.* 1.80 ± 0.14 days, p=0.02). In addition, readmission rates were significantly lower in the post-COVID group compared to the control group (8.08% *vs.* 25.00%, p=0.01). These clinical outcomes are described in Table 3.

Surgical outcomes, including length of surgery, EBL, overall postoperative complication rates, and 30-day mortality rates, did not significantly differ between the post-COVID and control groups, as displayed in Table 4.

Table 2: COVID status of post-COVID Cohort (n=99).

Pre-operative COVID Status, no. (%)	—
Positive	0(0.0)
Negative	97 (98.0)
Not tested and asymptomatic	2 (2.0)
Peri-operative COVID status, no. (%)	—
Positive	1 (1.0)
Negative and/or asymptomatic	98 (99.0)

Note: Table 2 details the COVID status of the post-COVID cohort in the pre-operative and perioperative periods. COVID status was determined by RT-PCR nasopharyngeal or oropharyngeal swab tests

Discussion

Since the onset of the COVID-19 pandemic, many institutions, including our own, have made the decision to delay certain elective and non-urgent procedures in order to limit the spread of the virus, to effectively prioritize limited resources, and to protect patients, families and healthcare providers [1,13]. Head and neck surgeries have an especially high risk of COVID-19 transmission because of the involvement of the upper aero digestive tract, from which aerosolized particles can be produced [14,15]. HNC patients also have a higher risk of adverse respiratory outcomes compared to the general population, with some studies reporting up to 45% of HNC patients experiencing COVID-related severe pulmonary complications postoperatively [16,17]. Additionally, microvascular free flap reconstruction for advanced HNC is more challenging and may prolong recovery period since many of these patients have MCCs. These concerns were further magnified amongst the head and neck surgeons at our institution due to the surge of COVID cases in Los Angeles, designating it a COVID-19 hotspot.

Despite these challenges, delaying treatment for HNCs requiring major surgery can greatly affect patient prognosis. Thus, our institution aimed to maintain standard of practice by proceeding with major HNC surgeries to maximize patients' survival and quality of care. Our study focused on the outcomes of these patients in order to assess the safety and efficacy of our surgical approach during the COVID-19 pandemic.

Treatment delays and post-discharge follow up

Surgical resection remains a first-line treatment option for many locally advanced HNCs. Treatment delay can lead to progression into advanced and/or unrespectable disease, greatly impacting patient prognosis [10]. Various studies have reported an association between treatment delays and decreased patient survival [8,9]. Murphy et al. studied a total of 51,655 HNSCC patients and found that a Time to Treatment Initiation (TTI) of greater than 60 days was associated with decreased survival, compared to a TTI of 30 days or less 9. Another study reported delays in treatment of greater than 40 days being detrimental to survival, when compared to those treated within 30 days [8].

Given this risk, our study investigated any delays in surgical treatment and whether these delays could be attributed to the pandemic. All cases were discussed at our multidisciplinary Virtual Tumor Board and surgical intervention as an initial treatment modality was recommended for all patients. Treatment delays were defined as scheduled appointments for surgery that were canceled and/or rescheduled to a later date for any reason. Surgery delay rates between the post-COVID group (5.05%) and the control group (3.26%) were not significantly different, although rates in the post-COVID group were slightly higher. The mean delay time in each group was approximately 26 days, lower than the number of days cited in literature as adversely affecting survival. Furthermore, none of the delays in either group led to unresectable disease. These findings suggest that patients who required resection and free flap reconstruction for HNC during the COVID pandemic received timely surgical treatment that did not compromise survival.

An additional concern that the COVID-19 pandemic raised was the potential for greater loss to follow up postoperatively. However, our study did not show statistically significant differences in these rates between the post-COVID (7.07%) and pre-COVID (3.26%) cohorts.

Hospital and ICU LOS

HNC resections requiring microvascular free flap reconstruction involve a higher level of complexity than resection alone, often requiring longer hospital and ICU LOS [18]. Our study focused on this particular group of patients to evaluate the safety and efficacy of operating on complex HNC cases during the COVID-19 pandemic. Compared to the control group, we found no significant change in mean hospital stay during the COVID-19 pandemic, suggesting that the pandemic has not negatively impacted our department's ability to efficiently coordinate the hospital course of our HNC patients. Additionally, the average hospital LOS for the post-COVID group was comparable to prior studies citing an average and/or median postoperative LOS of 11 days after HNC free flap reconstruction [19,20].

However, the post-COVID group had a significantly longer ICU LOS than the pre-COVID group by approximately 1 day. The reason for this discrepancy in ICU LOS is unclear. Possible explanations include increased caution prior to step down within the context of a pandemic, or the slightly higher percentage of postoperative respiratory complications in post-COVID patients compared to

Table 3: Clinical outcomes of HNC free flap cases.

	Post-COVID (n=99)	Control (n=92)	P-Value
Surgery Delayed, no. (%)	5 (5.05)	3 (3.26)	0.72
Mean Surgery Delay Time, days (S.E.)[1]	26.20 (11.76)	26.67 (18.44)	0.98
Mean Hospital LOS, days (S.E.)	10.00 (0.74)	9.01 (0.56)	0.29
Mean ICU LOS, days(S.E.)	2.84 (0.40)	1.80 (0.14)	0.02*
Lost to Follow Up, no. (%)	7 (7.07)	3 (3.26)	0.33
Readmissions, no. (%)	8 (8.08)	23 (25.00)	<0.01**

[1] Only including patients that had surgery delayed
*p<0.05; **p<0.01
Note: Table 3 compares the clinical outcomes of the pre- and post-COVID cohorts after undergoing resection and microvascular reconstruction for HNC

Table 4: Surgical outcomes of HNC free flap cases.

	Post-COVID (n=99)	Control (n=92)	P-Value
Mean surgery duration, hours (S.E.)	7.23 (0.16)	7.77 (0.24)	0.07
Mean estimated blood loss, ml (S.E.)	740.7 (44.93)	839.0 (77.96)	0.27
Infectious Complications, no. (%)	26 (26.26)	15 (16.30)	0.11
Pneumonia	11 (11.11)	7 (7.61)	0.46
UTI	6 (6.06)	2 (2.17)	0.28
Head and neck wound infection	11 (11.11)	6 (6.52)	0.32
Flap Donor site infection	2 (2.02)	1 (1.09)	>0.99
Positive blood cultures	0 (0.00)	3 (3.26)	0.11
Flap Complications, no. (%)	7(7.07)	3 (3.26)	0.33
Flap compromise salvaged in OR	0	1	0.48
Partial flap loss	0	1	0.48
Total flap loss	7 (7.07)	1 (1.09)	0.06
Postoperative complications, no. (%)[1]	24 (24.24)	23 (25.00)	>0.99
Neck Hematoma	5 (5.05)	3 (3.26)	0.72
Donor Site Hematoma	0 (0.00)	2 (2.17)	0.23
Neck Wound Dehiscence	8 (8.08)	9 (9.78)	0.8
Donor Site Wound Dehiscence	3 (3.03)	4 (4.35)	0.71
MI	1 (1.01)	1(1.09)	>0.99
Stroke/TIA	2 (2.02)	0 (0.00)	0.5
Respiratory Failure requiring ventilation	9 (9.09)	4 (4.35)	0.25
Salivary Fistula	4 (4.04)	2 (2.17)	0.68
Pulmonary Embolism	0 (0.00)	0 (0.00)	—
Respiratory Complications, no. (%)[2]	18 (18.18)	10 (10.87)	0.22
Delayed Flap Loss, no. (%)	1 (1.08)	3 (3.33)	0.36
30 Day Mortality, no. (%)	3 (3.09)	2 (2.22)	>0.99

[1] Excludes flap and infectious complications
[2] Pneumonia and/or respiratory failure requiring ventilation
Note: Table 4 compares the surgical outcomes of the pre- and post-COVID cohorts after undergoing resection and microvascular reconstruction for HNC

pre-COVID patients, though this difference was not statistically significant (as described below).

Unplanned readmission rates

Unplanned readmission rate is a metric frequently used to gauge quality of care. Studies have found that HNC patients undergoing any sort of free flap procedure have higher odds of unplanned readmission, likely due to the complex nature of the surgery and the increased likelihood of complications [21]. In recent literature, readmission rates for HNC free flap patients prior to the pandemic range from 9.6% to 10.9% [22,23]. In our study, the readmission rate for our post-COVID cohort was 8.08%, which is comparable to the aforementioned rates. This suggests that quality of care for this particular group of patients has been maintained during the pandemic.

Of note, the readmission rate for our post-COVID group was significantly lower than for our pre-COVID group, as demonstrated in Table 4. One possible explanation for this decrease within our institution is that more patients may have been discharged to their homes rather than to rehabilitation facilities as a result of the pandemic. However, data on location of discharge was not collected in this study. Alternatively, objective and/or subjective thresholds for transferring and readmitting patients during the COVID-19 pandemic may have been raised to mitigate unnecessary exposure and viral spread. Further research is required to gain a better understanding of associated factors.

Figure 1: Intraoperative PPE: All major head and neck surgeries were performed using N95 respirators as pictured above.

PPE and intra-operative outcomes

Standard COVID Personal Protective Equipment (PPE) is a necessary precaution to be able to safely operate on surgical patients during the pandemic. An N95 respirator is recommended,

at minimum, for protection against airborne COVID particles. Additional consideration of higher levels of protection, such as Power Air-Purifying Respirators (PAPRs), have been suggested for high-risk aerosol generating procedures like prolonged head and neck surgery [24]. However, concerns have been raised about enhanced PPE potentially impairing the execution of major HNC surgeries [7]. For example, PAPRs interfere with adequate visualization of microvascular structures under the microscope during free flap reconstruction.

At our institution, N95 respirators were the standard respiratory PPE used in the operating room for HNC free flap cases (Figure 1). While we initially did consider PAPRs in the operating room, they were ultimately not used due to the aforementioned limitations. Our study found no significant difference in mean surgery duration and mean intra-operative EBL between the post-COVID and pre-COVID cohorts (Table 2). There were also no reports of any of our head and neck surgeons testing positive for COVID-19. This suggests that the standard COVID respiratory PPE used by our head and neck surgeons did not compromise intra-operative outcomes and ultimately allowed for the safe execution of major head and neck surgeries during the pandemic.

Postoperative complications

When evaluating the timeliness and safety of head and neck surgeries, it is important to assess potential postoperative complications. Our study examined the rates of postoperative infectious complications, flap complications, respiratory complications, and/or other non-infectious non-flap complications. Flap complications were defined as partial or complete flap loss that occurred during the hospital stay. Respiratory complications were defined as pneumonia and/or respiratory failure requiring ventilation and were an outcome of interest since COVID-19 significantly affects the respiratory system. We found no significant difference in overall postoperative complication rates between the pre-COVID group and the post-COVID group. While 18.18% of patients in the post-COVID group experienced postoperative respiratory complications, 7.31% higher than the pre-COVID group rate, this difference was not statistically significant. However, the rate of respiratory complications in our post-COVID group was almost double the rate reported in a similar study of HNC patients during the COVID pandemic [25]. This discrepancy could be partially due to the larger sample size in our study. Another plausible explanation is that negative COVID-19 screening tests do not definitively exclude the possibility of COVID-19 infection. While less likely, this means that it is possible that some patients in the post-COVID group had a false negative test result, thus contributing to the higher respiratory complication rate. Nevertheless, the rates of postoperative infectious complications, flap complications, respiratory complications, and other non-flap non-infectious complications were statistically comparable between our two cohorts. This suggests that operating on HNC patients who are asymptomatic and have tested negative for the SARS-CoV-2 virus during the pandemic does not appear to place these patients at a significantly increased risk for postoperative complications.

30 day mortality

Our study did not find any notable increased risk of mortality for HNC patients who underwent free flap reconstruction during the COVID-19 pandemic. It is well-established that COVID-19 is associated with increased morbidity and mortality in both surgical and cancer patients [4-6,26,27].

The mortality rates for surgical patients with COVID-19 have ranged from 16.7% to 20.5% [4,26,27]. However, for asymptomatic patients who also test negative, perioperative mortality rates have ranged from 0% to 4% in recent literature, and our study is consistent with these findings [16,25–28]. We found that HNC patients undergoing free flap reconstruction who were asymptomatic and pre-operatively tested negative for COVID-19 had a mortality rate of 3.09%, which is comparable to the 30-day mortality rate of 2.22% in our control group. Our findings suggest that in the setting of this pandemic, surgical treatment of head and neck cases may proceed without significantly compromising patients' morbidity and mortality. However, it is important to note that negative screening tests do not necessarily preclude a patient from COVID-19 infection, so all pre- and postoperative precautions should continue to be upheld [26]. In our study, only one patient who had pre-operatively tested negative for COVID-19 subsequently tested positive during their hospital stay (Table 2).

Study limitations

A major limitation of this study is its retrospective design. Firstly, retrospective studies are susceptible to confounding and selection bias and the current study must be interpreted in the context of these limitations. Secondly, the retrospective nature of this study meant that decisions about our institution's approach to HNC cases during the pandemic could not be informed by our findings in real time. In contrast, a prospective study might have offered important information that could shape ongoing decisions about surgical treatment at the peak of the pandemic. Despite these limitations, the retrospective design allowed for a larger sample size by allowing us to compare all patients who underwent major HNC surgery within a specified timeframe of interest during and prior to the pandemic.

Another limitation, not unique to our study, is that negative screening tests for COVID-19 do not definitively exclude COVID-19 infection, due to factors including variable test sensitivity, specificity, and timing of the infection [25]. Despite recent advances such as the development of vaccines against COVID-19, unknowns regarding the pathophysiology of this virus remain. This means that it is entirely possible, though less likely, that patient's within our study population may have received a false negative test result preoperatively and/or postoperatively that may explain some outcomes described in our study.

Conclusion

The COVID-19 pandemic has created a time of uncertainty and potential additional risks for surgical patients. The outcome of HNC patients is largely unknown during this time. Our findings suggest that care for complex HNC patients requiring surgery at a tertiary care institution has not been compromised during the pandemic. Overall, clinical and surgical outcomes remain comparable to patients who underwent similar operations prior to the pandemic as well as to those reported in the existing literature. With proper preoperative assessments and necessary precautions in place, head and neck surgeons may continue to operate on HNC patients in a timely manner in order to maintain standard levels of care.

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