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Original Article

COVID-19 vaccination patterns among oral cancer patients: A comprehensive analysis in a medical center in Taiwan

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Abstract *Background/purpose:* COVID-19 vaccines are supplied at no-cost to residents as a measure to prevent comorbidities, fatalities, and the increased risk of community transmission, thus protecting public health systems. However, vaccine acceptance among cancer patients remained uncertain. This study aimed to elucidate the vaccination rates among oral cancer patients at a medical center in Taiwan.
Materials and methods: We included Individuals who attended for routine follow-ups from January 2021 to December 2022, with a total of 1448 patients subjected to comprehensive analysis. Medical records were reviewed to identify factors influencing vaccine acceptance.
Results: Our findings indicate that 1,264 patients received vaccinations, while 184 remained unvaccinated. The vaccination rates among patients in advanced disease stages and those with neck lymph node metastasis (N+) were significantly lower (both $P < 0.001$). Furthermore, a notable lower vaccination rate was evident among patients receiving active treatment modalities ($P < 0.01$). Conversely, age, and comorbidities (evaluated using the New Charlson Comorbidity Index), didn't show a significant correlation with vaccination rates. The risk of death caused by oral cancer among vaccinated patients was significantly lower compared to non-vaccinated group ($P < 0.001$). Logistic regression showed the risk of COVID infection was significant lower in vaccinated group than non-vaccinated group (OR = 0.31, P = 0.034).
Conclusion: The risk of COVID-19 infection in oral cancer patients was lower among vaccinated group, and the vaccination was not associated with more mortality. Identifying the

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characteristics of non-vaccinated individuals and understanding factors influencing vaccine hesitancy in oral cancer patients is vital for developing targeted strategies to improve vaccine uptake.

Introduction

The global landscape has witnessed unprecedented transformation since the onset of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic in 2020, profoundly impacting public health worldwide. Beyond the immediate threat to human life, the pandemic has disrupted societal and economic activities, leaving an indelible mark on the well-being of populations globally. Despite the World Health Organization (WHO) suggesting a potential end to the pandemic by 2023,[1] recent evidence indicates an alarming surge in COVID-19 cases across various regions, accompanied by the identification and monitoring of over 30 mutations in the virus's spike protein.[2] In response to this evolving crisis, pharmaceutical companies have been working tirelessly since 2020 to develop effective vaccines, such as the Pfizer-BioNTech and Moderna mRNA vaccines, and the Novavax protein subunit vaccine.[3]

Public policies worldwide advocate for vaccination to reduce morbidity and mortality from COVID-19, especially among populations vulnerable to the virus, such as oral cancer patients. These patients may be immunocompromised, have comorbidities or functional disabilities, or be undergoing active treatments.[4–6] However, achieving "herd immunity" has been met with persistent challenges, notably within cancer patient subgroups.[7] Concerns regarding the adverse effects of vaccines,[8] their impact on disease progression,[9] and the influence of immune response during active treatment contribute to hesitancy and refusal among cancer patients.[10] A lack of confidence in available information and clinical guidelines further compounds the skepticism surrounding vaccination.[11,12]

Despite the crucial role of vaccines in enhancing immunity and curbing the spread of COVID-19, the issue of vaccine uptake rates presents a substantial challenge to achieving widespread immunity. Vaccine hesitancy and refusal remain significant obstacles to reaching "herd immunity" in future pandemics.[13,14] There have been reports of high levels of vaccine hesitancy among cancer patients in several countries.[11,12,15] Prior studies indicate diverse rates of non-acceptance of the COVID-19 vaccine among cancer patients.[16] However, to our knowledge, specific statistical analyses regarding acceptance and non-acceptance rates for the COVID-19 vaccine among oral cancer patients are lacking. Understanding their vaccination rates is critical for shaping future strategies to protect communities against pandemics.

This study addressed this knowledge gap by enlisting oral cancer patients for regular follow-ups in our outpatient department from January 2021 to December 2022. By highlighting the characteristics of non-immunized patients and uncovering the factors that influence their willingness to vaccinate, this investigation aimed to provide valuable insights that could inform targeted interventions to improve vaccination uptake within the oral cancer patient population.

Methods and materials

Study design

This cross-sectional study is designed to assess the prevalence of COVID-19 vaccination among patients with oral cavity cancer who have undergone surgical treatment between April 1994 and December 2021 and are under regular follow-up at the Department of Oral and Maxillofacial Surgery, Taichung Veterans General Hospital. Excluded from the study are patients who were lost to follow-up or deceased before 2021.

Study population

Our analysis included a cohort of 1,448 patients who met the inclusion criteria. We systematically collected comprehensive demographic data, including age, gender, and tumor-related details such as stage, location, comorbidities, treatment status, and outcomes like recurrence and survival. Notably, the age of the patients was recalculated based on their age at the time of vaccination, as opposed to the year of initial diagnosis. Any COVID-19 infection incidents and complications following vaccination were meticulously recorded, with an emphasis on patient reports up until December 2022. For classification purposes, individuals attending outpatient services for routine follow-up without active treatment were categorized as non-active treatment patients, whereas those receiving adjuvant therapy for primary or recurrent tumors were considered active treatment patients.

Vaccination Information: vaccination records, including immunization dates and vaccine types, were retrieved from digitized medical documentation provided by the national healthcare system, a highly reliable source offering web-based, real-time, and synchronized records. Since April 2021, the national healthcare system has randomly scheduled vaccination appointments and determined vaccine types for each patient. Various COVID-19 vaccines, such as Oxford-AstraZeneca, Pfizer—BioNTech, Moderna, Johnson & Johnson, and Medigen COVID-19 vaccines, have been administered in Taiwan.

Time points for evaluation

The study assessed the percentages of vaccinated/unvaccinated oral cancer patients at two time points: December 31, 2021, and December 31, 2022. Based on these cutoffs, patients were categorized into three subgroups: those vaccinated on time (before December 31, 2021), those with delayed vaccination (before December 31, 2022), and those not vaccinated by the end of 2022.

Statistical analysis

Demographic data between vaccinated and non-vaccinated patients were compared by using Fisher's exact test and the Chi-squared test, with logistic regression performed for multivariate analysis. Statistical analyses were conducted using IBM SPSS Statistics for Windows, version 25 (SPSS Inc., Chicago, IL, USA).

Results

Demographics and characteristics of oral cancer patients

Table 1 presents a detailed summary of the demographic and clinical characteristics of oral cancer patients in relation to their COVID-19 vaccination status. Within the scrutinized cohort of 1,448 patients, the mean age during the observation period was 63.6-year-old. Notably, the 60–69 age group constituted 34.0% of the cohort. According to the New Charlson Comorbidity Index, the most common comorbidities had an index of 3 or below, indicating a relative state of health in these patients.

An analysis of tumor sites revealed that the buccal mucosa (39.3%) and tongue (31.0%) were the most common locations, highlighting the anatomical patterns of oral cancers. Staging data indicated that a substantial proportion of patients were at stage I (46.8%), while 25.2% were at stage IV, demonstrating diverse disease severities within the study population. Additionally, 13.5% of patients presented with neck lymph node metastasis (pN+), adding complexity to their clinical profiles. About 19.8% of patients were receiving active anticancer therapies, and 4.9% were undergoing postoperative adjuvant treatment. Locoregional recurrence or distant metastases occurred in 13.6% of the cases. The occurrence of second primary cancers or significant comorbidities was relatively low at 1.7%. These findings provide a comprehensive baseline understanding of the oral cancer patient population, critical for subsequent analysis and interpretation.

Vaccination rate and types for oral cancer patients

Figures 1 and 2 illustrate the vaccination rates and types among the 1,448 oral cancer patients at specific time points. Vaccination efforts began on May 1, 2021. By December 31, 2021, in the on-time vaccination group, 79.21% of patients (n = 1,147/1,448) were vaccinated, with the peak occurring in July 2021 (41.0%). In the delayed vaccination group, as of December 31, 2022, an additional 8.08% of patients (n = 117/1,448) were vaccinated. Overall, 87.29% of patients (n = 1,264/1,448) had been vaccinated over the span of two years, leaving 12.70% (n = 184/1,448) unvaccinated. Of the vaccinated patients, 98.89% (n = 1,264) had received two or more doses. The most frequently administered vaccine was Moderna at 35.84%, followed by Oxford-AstraZeneca at 30.73% (see Fig. 3).

Independent variables associated with non-vaccination in oral cancer patients

Table 1 examines factors associated with non-vaccination among oral cancer patients, focusing on demographic and clinical determinants. Among 123 female patients, 23 patients were not vaccinated, and the vaccination rate was significantly lower than male patients statistically. Patients aged 60–69 had the highest percentage of non-vaccination (39.1%). The patients in advanced stages (stage III&IV) or with neck lymph node metastasis (pN+) both had significantly lower vaccination rates with P value < 0.001. Additionally, patients receiving active treatments, including local radiotherapy or systemic anticancer therapies, were less likely to be vaccinated ($P < 0.001$). It is worth noting, age, comorbidities utilizing New Charlson Comorbidity Index (0–3 vs. 4–10), did not show significant associations with non-vaccination status in oral cancer patients.

During the two-year observation period, non-vaccinated patients had a higher rate of contracting COVID-19 (2.7%) compared to vaccinated patients (0.5%). The mortality rate attributable to oral cancer is statistically higher in the non-vaccinated group ($P < 0.001$). Furthermore, the overall mortality rate, encompassing all causes of death (whether due to oral cancer or other diseases), remains significantly higher in the non-vaccinated group ($P < 0.001$). Logistic regression showed the vaccinated group had a significantly lower odds ratio of COVID-19 infection than their non-vaccinated counterparts (OR = 0.31, 95% CI: 0.11–0.92, $P = 0.034$) (Table 2). Meanwhile, the odds ratio of COVID-19-related mortality in vaccinated patients and was 0.14 compared to non-vaccinated group, however, without statistical significance (OR = 0.14, 95% CI: 0.01–2.23, $P = 0.173$) (Table 3).

Among vaccinated individuals, two patients reported severe adverse events post-vaccination, which included complete hearing loss and hospitalization due to myelodysplastic syndrome, potentially linked to vaccine administration. On the other hand, mortality rates resulting from oral cancer and non-oral cancer diseases for vaccinated versus unvaccinated patients were 1.8% versus 29.3% and 0.9% versus 9.2%, respectively.

Discussion

The analysis of vaccination patterns and characteristics of oral cancer patients is crucial for crafting effective public health strategies to mitigate the impact of future pandemics. Among the 1,448 oral cancer patients studied, an 87.29% vaccination rate reflects the concerted efforts to protect this vulnerable demographic, comparable to the general population in Taiwan, where 88.67% received at least two vaccine doses by December 2022.[17] Nevertheless,

Table 1 Demographic and clinical characteristics of oral cancer patients in relation to their COVID-19 vaccination status.

Variables	Total	Non-vaccinated (2021–2022)	Vaccinated (2021–2022)	*P* value
Numbers	1448	184	1264	
Gender (female)	123 (8.5%)	23 (12.5%)	100 (7.9%)	0.037*
Revised age	63.59 ± 11.27	62.80 ± 11.27	63.71 ± 11.27	0.306
Revised age group				0.282
30-39	17 (1.2%)	1 (0.5%)	16 (1.3%)	
40-49	144 (9.9%)	23 (12.5%)	121 (9.6%)	
50-59	361 (24.9%)	42 (22.8%)	319 (25.2%)	
60-69	493 (34.0%)	72 (39.1%)	421 (33.3%)	
70-79	309 (21.3%)	33 (17.9%)	276 (21.8%)	
80-89	103 (7.1%)	9 (4.9%)	94 (7.4%)	
90-101	21 (1.5%)	4 (2.2%)	17 (1.3%)	
New Charlson index				0.014*
0	130 (9.0%)	21 (11.4%)	109 (8.6%)	
1	315 (21.8%)	33 (17.9%)	282 (22.3%)	
2	398 (27.5%)	58 (31.5%)	340 (26.9%)	
3	326 (22.5%)	38 (20.7%)	288 (22.8%)	
4	177 (12.2%)	13 (7.1%)	164 (13.0%)	
5	63 (4.4%)	11 (6.0%)	52 (4.1%)	
6	19 (1.3%)	4 (2.2%)	15 (1.2%)	
7	15 (1.0%)	6 (3.3%)	9 (0.7%)	
8	3 (0.2%)	0 (0.0%)	3 (0.2%)	
9	1 (0.1%)	0 (0.0%)	1 (0.1%)	
10	1 (0.1%)	0 (0.0%)	1 (0.1%)	
0-3	1169 (80.7%)	150 (81.5%)	1019 (80.6%)	0.771
4-10	279 (19.3%)	34 (18.5%)	245 (19.4%)	
Tumor sites				0.022*
Lip	99 (6.8%)	16 (8.7%)	83 (6.6%)	
Gingiva	181 (12.5%)	33 (17.9%)	148 (11.7%)	
Tongue	449 (31.0%)	47 (25.5%)	402 (31.8%)	
Floor of mouth	44 (3.0%)	9 (4.9%)	35 (2.8%)	
Palate	55 (3.8%)	8 (4.3%)	47 (3.7%)	
Retromolar	51 (3.5%)	10 (5.4%)	41 (3.2%)	
Buccal mucosa	569 (39.3%)	61 (33.2%)	508 (40.2%)	
Staging				<0.001**
I	677 (46.8%)	52 (28.3%)	625 (49.4%)	
II	302 (20.9%)	41 (22.3%)	261 (20.6%)	
III	104 (7.2%)	20 (10.9%)	84 (6.6%)	
IV	365 (25.2%)	71 (38.6%)	294 (23.3%)	
I/II	979 (67.7%)	93 (50.6%)	886 (70.0%)	<0.001**
III/IV	469 (32.4%)	91 (49.4%)	378 (30.0%)	
Neck lymph node status				
pN+	195 (13.5%)	42 (22.8%)	153 (12.1%)	<0.001**
Active treatments				
Actively anticancer therapies	287 (19.8%)	81 (44.0%)	206 (16.3%)	<0.001**
Episodes of COVID-19				
COVID-19 infection	16 (1.1%)	5 (2.7%)	11 (0.9%)	0.042*
COVID-19 death	2 (0.1%)	1 (0.5%)	1 (0.1%)	0.238
Non COVID-19 death				
Died by oral cancer	77 (5.3%)	54 (29.3%)	23 (1.8%)	<0.001**
Died by other diseases	29 (2.0%)	17 (9.2%)	12 (0.9%)	<0.001**

Chi-square test/Fisher's exact test or independent t-test. *$P < 0.05$, **$P < 0.01$.

the remaining 12.70% of unvaccinated oral cancer patients necessitate targeted interventions to improve vaccine acceptance.

Literature highlights disparate levels of COVID-19 vaccine hesitancy among cancer patient populations worldwide, often exceeding hesitancy rates in the general population. Surveys in countries like Korea, Mexico, and Australia have reported hesitancy rates ranging from 30.3% to 38.2% among cancer patients.[11,12,15] Conversely, some studies suggest higher vaccination uptake among cancer

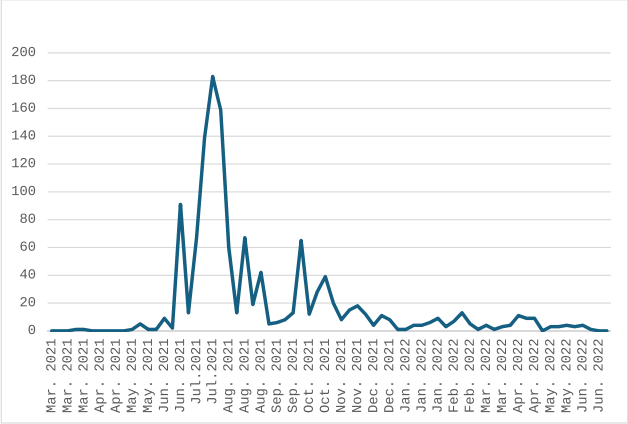

Figure 1 COVID-19 vaccination by weeks (2021–2022).

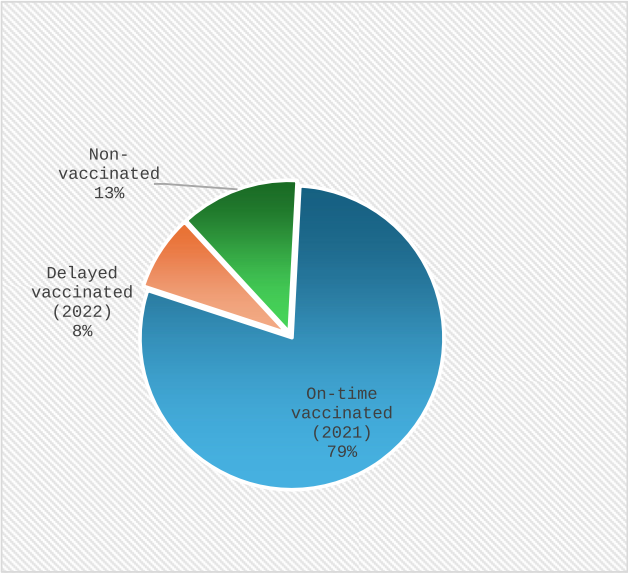

Figure 2 Status of COVID-19 vaccination in oral cancer patients.

patients compared to the non-cancer populace.[18] Despite these data, there remains an incomplete understanding of acceptance rates among specific groups such as oral cancer patients. Our research helps fill this gap by pinpointing factors that may deter oral cancer patients from COVID-19 vaccination and offering insights for healthcare providers and policymakers.[19]

The complexities of vaccine decision-making among oral cancer patients go beyond pure statistics, attributed to apprehensions and difficulties influencing their choices. Factors such as age, and comorbidities, did not significantly correlate with non-vaccination, whereas advanced disease stages (stage III&IV) and neck lymph node metastasis (pN+) were associated with a higher likelihood of being unvaccinated. Additionally, females and patients in active treatment regimens, such as those receiving local radiotherapy or systemic anticancer therapies, exhibited lower vaccination rates, corroborating findings from prior research.[20] This emphasizes the necessity for customized communication and support strategies for individuals with advanced disease and those receiving active therapies.

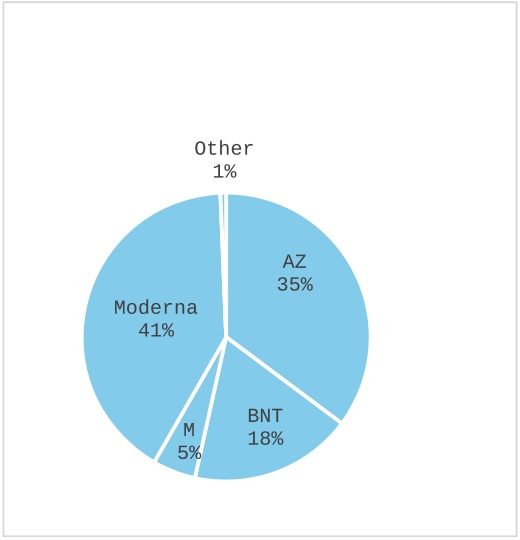

Figure 3 Types and percentages of COVID-19 vaccination in oral cancer patients. AZ, Oxford-AstraZeneca; BNT, Pfizer–BioNTech; M, Medigen.

Evidence indicates that COVID-19 vaccination is beneficial for oral cancer patients, even those on systemic anticancer treatments.[21] Our results ensured the risk of COVID-19 infection was not associated to gender, age, staging, N status, nor undergoing anticancer treatment. However, it highlighted the importance of vaccination as an only defense against COVID-19, with vaccinated patients demonstrating significantly lower rates of infection ($P = 0.034$) and relatively lower mortality rate ($P = 0.173$) compared to their unvaccinated counterparts among oral cancer individuals. Though the statistics in our study didn't demonstrate the significance, the risk of death caused by COVID-19 is lower among vaccinated patients (OR = 0.14), suggested the life-saving potential of vaccines in mitigating severe illness and death in oral cancer patients who contract COVID-19. Consequently, tailored approaches are essential to maximize vaccination benefits while considering its influence on cancer therapy outcomes.[22] Concerns about vaccine-related adverse effects and potential interactions with cancer treatments are the main factors contribute to hesitancy in this population.[8–10] However, our study demonstrated that the mortality rate due to oral cancer or other diseases was significantly lower in the vaccinated group, indicating that patients should not be concerned that vaccination would negatively impact their condition.

While this study cannot evaluate personal willingness or hesitancy to vaccinate, future research utilizing questionnaire to investigate reasons for hesitation or refusal of vaccination is worth performing.

In conclusion, this study reinforces the vital function that COVID-19 vaccination plays in diminishing infection and mortality among oral cancer patients. In the broader context of public health, our findings underscore the urgency of developing comprehensive vaccination promotion campaigns tailored to the unique circumstances of oral cancer patients, particularly those with advanced oral cancer undergoing systemic anticancer therapy.

Table 2 Risk of COVID-19 infection of oral cancer patients.

	Univariate		
	OR	95%CI	*P* value
Gender (female)	0.72	(0.09—5.47)	0.747
Revised age	0.99	(0.95—1.03)	0.585
Staging			
I	Reference		
II	1.80	(0.48—6.77)	0.382
III	1.30	(0.15—11.28)	0.809
IV	2.25	(0.68—7.41)	0.184
Neck lymph node status			
pN+	1.49	(0.42—5.28)	0.536
Active treatments			
Actively anticancer therapies	1.85	(0.64—5.38)	0.256
COVID-19 vaccination			
Non-vaccinated	Reference		
Vaccinated	0.31	(0.11—0.92)	0.034*

Logistic regression. *$P < 0.05$, **$P < 0.01$.

Table 3 Risk of COVID-19 death.

	Univariate		
	OR	95%CI	*P* value
Revised age	1.05	(0.94—1.19)	0.387
Group			
Non-vaccinated	Reference		
Vaccinated	0.14	(0.01—2.33)	0.173

Logistic regression. *$P < 0.05$, **$P < 0.01$.

Additionally, patients' concerns about vaccination can be alleviated, as our study indicates that the vaccinated group did not exhibit a higher mortality rate due to oral cancer or other diseases. As the world continues to navigate the COVID-19 pandemic, the implementation of informed and bespoke strategies becomes even more crucial to protect susceptible individuals and lessen the burden of infectious diseases on public health systems.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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