

RESEARCH NOTE

Differential olfactory outcomes in COVID-19: A large healthcare system population study

Nikita Chapurin MD, MHS¹ | Douglas J. Totten MD, MBA¹ | Basil Chaballout BA² |
Julia Brennan MD¹ | Spencer Dennis^{1,3} | Rory Lubner MD¹ |
Naweed I. Chowdhury MD^{1,3} | Justin H. Turner MD, PhD^{1,3} | Timothy Trone MD^{1,3} |
Rakesh K. Chandra MD, MMHC^{1,3}

¹ Department of Otolaryngology – Head and Neck Surgery, Division of Rhinology/Skull Base Surgery, Vanderbilt University Medical Center, Nashville, Tennessee, USA

² University of South Carolina School of Medicine, Greenville, South Carolina, USA

³ Vanderbilt University Medical Center Smell and Taste Center, Nashville, Tennessee, USA

Correspondence

Rakesh K. Chandra, MD, MMHC, Department of Otolaryngology – Head and Neck Surgery, Division of Rhinology/Skull Base Surgery, Vanderbilt University Medical Center, 1215 21st Avenue South, Suite 7209, Nashville, TN 37232-8605, USA.

Email: rakesh.chandra@vumc.org

Funding information

Justin H. Turner is supported by NIH R21 AI142321. The funding organizations did not contribute to the design or conduct of this study; collection, management, analysis, or interpretation of the data; and preparation, review, approval, or decision to submit this manuscript for publication. There are no relevant financial disclosures for any of the other authors.

This work was presented as a podium presentation at the 2021 COSM American Rhinologic Society virtual meeting.

KEYWORDS

comorbidities, COVID-19, duration, olfaction, outcomes, SARS-CoV2, severity, smell loss, SNOT22, taste loss

INTRODUCTION

From the beginning of the SARS-CoV-2 pandemic, olfactory and taste dysfunction have been identified as key and distinctive presenting symptoms,^{1,2} but the evolution of these sensory deficits over time remains unclear. Using a survey-based approach of patients with confirmed COVID-19 positivity at our institution, we sought to gain insight into the prevalence, time course, and factors associated with persistent olfactory dysfunction after COVID-19, as well as any link between smell and taste variation and SNOT-22 scores.

METHODS

We conducted a cross-sectional survey study of adult patients that tested positive for SARS-CoV-2 PCR from

a single regional healthcare system between February and November of 2020. A total of 1003 respondents were included in the analysis (21.3% response rate). We collected patient demographics, comorbidities, and subjective assessment of olfaction and taste and administered the SNOT-22 questionnaire. Multivariable stepwise logistic and linear regression analyses were performed to assess the impact of selected factors on patient-reported moderate to severe hyposmia as well as symptom duration after COVID-19 diagnosis. A censored cumulative event analysis was performed to illustrate the relationship between initial severity and duration of self-reported olfactory loss. The variation of SNOT-22 total and domain scores with respect to time from diagnosis as well as the impact of comorbidities and initial symptoms on SNOT-22 scores were assessed using multivariable stepwise linear regression.

TABLE 1 (A) Demographics and symptoms of study patients. (B) Linear regression analysis of the variation of SNOT-22 scores over the time course following diagnosis of COVID-19

Demographics and symptoms (A)			
	Median	IQR	
Age	44	30-57	
BMI	27	23-32	
Gender	N	%	
Male	366	37%	
Female	630	63%	
Medical history	N	%	
Smoking history	148	15%	
CRS	34	3%	
Prior symptoms	56	6%	
Allergic rhinitis	76	8%	
COPD	7	1%	
CAD	35	3%	
DM II	66	7%	
Hypertension	151	15%	
Asthma	98	10%	
COVID-19 symptoms			
Fever	600	60%	
Sore throat	441	44%	
Body aches	703	70%	
Cough	619	62%	
Shortness of breath	410	41%	
Gastrointestinal symptoms	389	39%	
Headache	693	69%	
No symptoms	61	6%	
Stepwise regression: variation of SNOT-22 scores over time course of COVID-19 (B)			
Predictors	Beta estimates	95% CI	p-value
Time since diagnosis (days)	-0.0518	-0.0735 – -0.0302	<.001
Age	0.1196	0.0518 – 0.1874	.001
Gender (male)	-4.8791	-7.0352 – -2.7229	<.001
Duration of symptoms (days)	0.0879	0.0465 – 0.1292	<.001
<i>Comorbidities:</i>			
History of CRS	9.5712	3.4608 – 15.6816	.002
Asthma	2.9786	-0.4720 – 6.4293	.091
Diabetes	4.8236	0.4698 – 9.1774	.030
Hypertension	4.3202	1.2560 – 7.3844	.006
BMI	0.2404	0.0973 – 0.3835	.001

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CRS, chronic rhinosinusitis; DM II, diabetes mellitus type 2; IQR, interquartile range.

RESULTS

The median age of respondents was 43 years, and 63% of patients were female (Table 1A). Baseline pre-COVID-19 taste and smell were subjectively normal in 93.8% and 91.4% of patients respectively. Any degree of postdiagnosis taste and smell loss or dysfunction was reported

by 73% of participants. Mean duration of smell loss was 19.7 days. A cumulative censored event analysis was performed (Figure 1A) and demonstrated that initial severity of smell loss was associated with symptom duration ($p < .001$) (Table S1). A significant number of patients (13.4%) reported prolonged duration of smell loss of more than 4 weeks, with over 10.7%

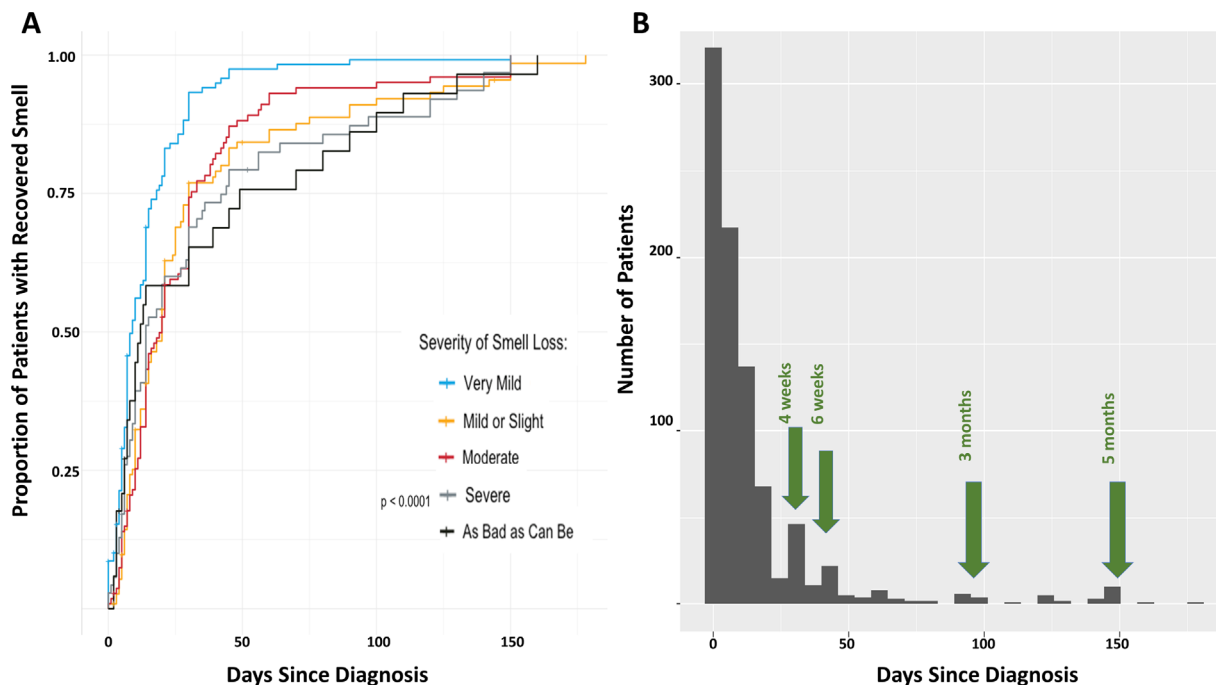


FIGURE 1 (A) Return of pre-COVID-19 olfaction on censored cumulative event analysis. The y-axis represents the proportion of patients in a cohort that returned to their pre-COVID-19 level of olfaction (1.0 = 100% return to baseline), stratified based on severity of smell loss from very mild to severe. The severity of olfactory loss appeared to correlate well with the duration of symptoms ($p < .0001$). (B) Number of patients reporting olfactory dysfunction from the time of COVID-19 diagnosis (in days). As expected, most patients reported recovery of olfaction within 4 weeks, although there are also many patients that report persistent olfactory dysfunction at 4 and 6 weeks and even as far out as 3 and 5 months post COVID-19 diagnosis

of patients reporting hyposmia longer than 6 weeks (Figure 1B).

Male gender, sore throat, gastrointestinal (GI) symptoms, prior taste disturbances, and absence of fever were statistically significant predictors for patients reporting moderate to severe hyposmia (Table S2). Predictors for taste dysfunction were similar and tracked with predictors for hyposmia outcomes. Patient age, female gender, history of chronic rhinosinusitis (CRS), diabetes, hypertension, asthma, fewer days since diagnosis, and higher body mass index (BMI) were all statistically significant predictors of higher total SNOT-22 scores on regression analysis (Table 1B). Similar patterns were noted for rhinologic, and extranasal rhinologic symptoms; however, notably time from diagnosis and CRS were not significant predictors for the remaining SNOT-22 domains (Table S3). Total SNOT-22 scores were observed to decrease over time by 0.05 points per day following the COVID-19 diagnosis, although there was no similar association with time in the sleep, psychological, or ear/facial domains.

DISCUSSION

This large-population cross-sectional survey of 1003 confirmed COVID-19-positive patients provides insight into

the prevalence, time course, and factors associated with persistent olfactory dysfunction after COVID-19. Most patients (73%) reported some degree of olfactory and taste dysfunction at diagnosis, with mean time to improvement of 19.7 days. However, 13.4% reported prolonged duration of smell loss of more than 4 weeks, with 10.7% of patients reporting hyposmia longer than 6 weeks. These results are in line with recent findings and provide further evidence that a substantial number of COVID patients have prolonged or persistent chemosensory symptoms.⁴⁻⁶

An intuitive but important finding of our cumulative event analysis is that the initial degree of self-reported hyposmia appears to correlate with the duration of smell loss. In other words, after stratifying patients into cohorts by severity of olfactory dysfunction, patients with more severe reported hyposmia demonstrate prolonged recovery ($p < .0001$). This provides further support of recently published findings that olfactory loss severity is a predictor of long-term recovery.^{7,8} This may be important when counseling patients on expectations of long-term olfactory recovery. Additionally, on regression analysis, we discovered that lower BMI and shortness of breath on presentation were significantly associated with prolonged duration of hyposmia (Table S1), while male gender, presence of sore throat, GI symptoms, history of prior smell/taste disturbances, and absence of fever were statistically

significant predictors of reporting moderate to severe hyposmia (Table S2). These findings are all also relatively in line with recently published numbers.⁹

A unique aspect of our work is the inclusion of the SNOT-22 questionnaire, which allowed us to detect associations between the SNOT-22 scores and self-reported patient symptom scores. Our aim was to use a clinically validated tool to measure sinonasal quality-of-life scores in post-COVID19 patients because a validated COVID-specific metric is not available. Additionally, though the study design is cross-sectional, the large sample size and collection of patients at varying time points from diagnosis enabled us to approximate the evolution of symptoms over time. Our results suggest that total SNOT-22 scores correlate with many COVID-19 symptoms, including those of hyposmia and duration of olfactory dysfunction (Table 1b). Subdomain analysis of SNOT-22 scores demonstrated improvement of rhinologic-specific symptoms over time, but that did not hold true for other subdomains (Table S3). There also appears to be a statistically significant relationship between persistent smell and taste dysfunction and psychological domain scores (odds ratio [OR] 1.06, 95% confidence interval [CI] 1.04 to 1.08), suggesting an interplay between psychological symptoms and self-reported olfactory/taste symptoms from COVID, but this may be of limited clinical utility given the small effect size. A recent study also reported that COVID-19 patients had nearly double the average total SNOT-22 scores compared with the matched negative controls.¹⁰ Thus, the SNOT-22 instrument may be useful in measuring and following post-COVID-19 rhinologic symptoms and olfactory dysfunction.

There are notable limitations of our survey-based approach. We relied heavily on subjective patient-reported data, which can introduce significant response and recall bias that affects generalizations of effect estimates to the broader population. Additionally, time-based results are only descriptive of the population as a whole and may not be predictive of any individual patient's symptom trajectory. A follow-up survey of this patient group is currently planned to augment the results of the present study. However, despite these limitations, the results provide initial descriptive insights into the quality-of-life burden of COVID-19 that may be helpful while counseling patients with COVID-19-associated chemosensory dysfunction.

CONFLICT OF INTEREST

None.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Chapurin N, Totten DJ, Chaballout B, et al. Differential olfactory outcomes in COVID-19: A large healthcare system population study. *Int Forum Allergy Rhinol*. 2022;12:108–111
<https://doi.org/10.1002/alr.22870>.