The Laryngoscope

Prevalence of New-Onset Tinnitus after COVID-19 Vaccination with Comparison to Other Vaccinations

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Objective: To investigate how often patients are diagnosed with new-onset tinnitus within 21 days after COVID-19 vaccination in comparison to after three other common vaccinations: influenza, Tdap (tetanus, diphtheria, and acellular pertussis), and polysaccharide pneumococcus.

Methods: The TriNetX Analytics Network, a federated health research network that aggregates the de-identified electronic health record (EHR) data of over 78 million patients, was queried for patients receiving each vaccination. Instances of new-onset tinnitus within 21 days of vaccination were recorded and reported.

Results: Out of 2,575,235 patients receiving a first dose of the mRNA COVID-19 vaccine without any prior tinnitus diagnosis, 0.038% (95% CI: 0.036%–0.041%) of patients had a new diagnosis of tinnitus within 21 days. There was a higher risk of a new tinnitus diagnosis after the influenza vaccine (RR: 1.95, 95% CI: 1.72–2.21), Tdap vaccine (RR: 2.36, 95% CI: 1.93–2.89), and pneumococcal vaccine (RR: 1.97, 95% CI: 1.48–2.64) than after the first dose of the COVID-19 vaccine. There was a lower risk of a new tinnitus diagnosis after the second dose of COVID-19 than after the first dose (RR: 0.80, 95% CI: 0.71–0.91).

Conclusion: The rate of newly diagnosed tinnitus acutely after the first dose of the COVID-19 vaccine is very low. There was a higher risk of newly diagnosed tinnitus after influenza, Tdap, and pneumococcal vaccinations than after the COVID-19 vaccine. The present findings can help to address COVID-19 vaccine hesitancy during the ongoing pandemic.

Key Words: COVID-19 Vaccine, Epidemiology, Tinnitus, Vaccine Adverse Effect.

Level of Evidence: Level 3

***Laryngoscope*, 00:1–4, 2022**

INTRODUCTION

Vaccine hesitancy and fear of adverse effects from the mRNA COVID-19 vaccine are becoming more widespread and represent a significant national health concern. Consequently, the sequelae of the COVID-19 vaccine have been the topic of significant research throughout the COVID-19 pandemic. In recent months, there has been growing interest in tinnitus as a potential adverse effect of the mRNA COVID-19 vaccination. Recent case reports[1–4] describe patients experiencing life-altering tinnitus within days of the COVID-19 vaccination that may be accompanied by impaired hearing, significantly affect a patient's quality of life, and last for months. Post-vaccination otologic symptoms observed within 30 days of COVID-19 vaccination included tinnitus, hearing loss, dizziness, or vertigo.[5,6] Earlier this year, 555 cases of sudden sensorineural hearing loss after COVID-19 vaccination were reported in the North American Vaccine Related Adverse Effects System (VAERS) were investigated and no association was found between sudden sensorineural hearing loss and vaccination.[7] Symptom patterns and potential pathophysiologic mechanisms for post-vaccine tinnitus were discussed in a recent review of over 12,000 cases of tinnitus post-COVID-19 vaccination, reported by the CDC.[8] A 2021 study of national vaccine adverse event databases in Italy and the United Kingdom examining audiovestibular pathologies related to COVID-19 vaccination investigated tinnitus as a possible adverse effect but was unable to control for timing of symptomatology or provide comparisons to other vaccinations.[6] To our knowledge, there has not been a large-scale investigation into the prevalence of new tinnitus diagnoses after the COVID-19 vaccination in comparison to other common vaccinations.

Using a sample size of over 2.5 million patients who received a COVID-19 vaccine, the present study aims to investigate how often episodes of new-onset tinnitus are diagnosed within 21 days after vaccination. The purpose of this investigation is to use population-level data to examine how frequently newly diagnosed tinnitus occurs after COVID-19 vaccination in comparison to other common vaccinations for influenza, Tdap (tetanus, diphtheria, and acellular pertussis), and polysaccharide pneumococcus. The large sample size provides a unique opportunity to

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Additional supporting information may be found in the online version of this article.

Editor's Note: This Manuscript was accepted for publication on August 14, 2022.

The authors have no funding, financial relationships, or conflicts of interest to disclose.

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DOI: 10.1002/lary.30395

acquire meaningful data for this likely rare adverse effect. To give a frame of reference for the number of diagnosed tinnitus cases observed after COVID-19 vaccination, large populations of patients receiving other common vaccinations were compared to the mRNA COVID-19 group. These three other vaccination groups were analyzed as secondary outcomes and served as a reference group for the first dose COVID-19 vaccinated group.

MATERIALS AND METHODS

A retrospective cohort design was implemented using the TriNetX Analytics Network, a federated health research network that aggregates the de-identified electronic health record (EHR) data of over 78 million patients across 45 health care organizations (HCOs) within the US. There were 78,058,186 patients with any EHR contained in the US Collaborative Network of the TriNetX platform that was queried for vaccination events. Five patient groups were identified (Supplementary Cohort Criteria):

1. Received First mRNA COVID-19 Vaccine from December 15, 2020 to March 1, 2022
2. Received Second mRNA COVID-19 Vaccine from December 15, 2020 to March 1, 2022
3. Received Influenza Vaccine from January 1, 2019 to December 1, 2019
4. Received Tdap Vaccine from January 1, 2019 to December 1, 2019
5. Received Pneumococcal Vaccine from January 1, 2019 to December 1, 2019

The dates for the COVID-19 vaccinated group span from the first day of vaccine administration in the US to an arbitrary date that gave over a three-week window before the data was collected. The three other common vaccination groups were examined throughout the 2019 year to eliminate the possibility of COVID-19 vaccination within these three groups. Patients with any history of tinnitus before each respective vaccination event were excluded from all groups to more precisely focus on vaccine-related tinnitus and have findings applicable to the vast majority of the population without a history of tinnitus. Notably, the vaccination event was defined as the first time that the patients met the criteria within the time window, meaning that the first dose of the COVID-19 vaccination series was analyzed in the first dose group. The second dose COVID-19 group underwent exactly two recorded vaccination procedures. Because patients in the second dose group were excluded if they had a previous history of tinnitus, patients experiencing diagnosed tinnitus after the first dose were excluded from this population. New-onset tinnitus was defined as an encounter with a diagnosis of tinnitus in patients with no prior history of tinnitus.

Each patient group was indexed to the event of receiving the respective vaccination, and any occurrence of an encounter diagnosis of tinnitus within 21 days of vaccination was recorded. The timeline of 21 days was arbitrarily decided based on the symptomatology described in existing case reports and reviews that suggested acute to subacute onset within hours to days of vaccination.[1–5,8] Because 21 days is the earliest recommended time frame to receive a second dose of the COVID-19 vaccine after receiving the first dose, this timeline also served to exclude tinnitus caused by the second dose while examining the first dose group. The three common vaccinations were selected arbitrarily based on the most common vaccinations administered in the US in an effort to provide applicable comparison groups to the COVID-19 vaccine.

After the total number of diagnosed tinnitus cases were recorded for each of the five vaccination groups, four separate 1:1 propensity score matching procedures were performed using TriNetX's built-in logistic regression model. Full data sets and results of each propensity score matching procedure are provided in the Data S1, including standardized mean differences for each ICD-10 variable before and after matching. Matching was performed between the following groups: second dose COVID-19 vaccine to first dose COVID-19 vaccine (Table S1); influenza vaccine to first dose COVID-19 vaccine (Table S2), Tdap vaccine to first dose COVID-19 vaccine (Table S3); and polysaccharide pneumococcal vaccine to first dose COVID-19 vaccine (Table S4). Matching was performed for each group relative to the first dose COVID-19 vaccine group because our primary outcome was exploring the risk of new-onset tinnitus after the first dose of the COVID-19 vaccination as compared to other common vaccinations. Patients were matched between these groups based on age at vaccination, sex, race, and ethnicity (Supplementary Matching Criteria).

RESULTS

Out of 2,575,235 patients receiving a first dose of the mRNA COVID-19 vaccine without any prior tinnitus diagnosis, 0.038% (95% CI: 0.036%–0.041%) of patients had a new diagnosis of tinnitus within 21 days. Out of 1,477,890 patients receiving a second dose of the mRNA COVID-19 vaccine without any prior tinnitus diagnosis, 0.031% (95% CI: 0.029%–0.034%) of patients had a new diagnosis of tinnitus within 21 days of the second dose. The numbers and percentages of patients in each vaccination group with a new diagnosis of tinnitus are shown in Table I.

After four separate 1:1 propensity score matching procedures based on age at vaccination, sex, race, and ethnicity between patients receiving the first dose of the

TABLE I.
Numbers and Percentages of Patients with a New Encounter Diagnoses of Tinnitus within 21 days After Vaccination.

Vaccination Received	Vaccinated Patients without Any History of Encounter Diagnoses of Tinnitus	Patients with New Encounter Diagnoses of Tinnitus within 21 Days after Vaccination	Proportion with a New Encounter Diagnoses of Tinnitus (%) (95% CI)
First Dose mRNA COVID-19	2,575,235	986	0.038 (0.036–0.041)
Second Dose mRNA COVID-19	1,477,890	465	0.031 (0.029–0.034)
Influenza	1,200,749	745	0.062 (0.058–0.067)
Tetanus and diphtheria (Tdap)	456,306	314	0.069 (0.061–0.077)
Polysaccharide Pneumococcus	153,522	135	0.088 (0.074–0.100)

TABLE II.
Relative Risks for Post Vaccination New Encounter Diagnoses of Tinnitus Compared to the First Dose of COVID-19 Vaccine.

Vaccination Received	Relative Risk for New Encounter Diagnoses of Tinnitus Compared to First Dose COVID-19 Vaccination (after propensity score matching)
First Dose mRNA COVID-19	1
Second Dose mRNA COVID-19	0.80 (95% CI: 0.71–0.91)
Influenza	1.95 (95% CI: 1.72–2.21)
Tetanus and diphtheria (Tdap)	2.36 (95% CI: 1.93–2.89)
Polysaccarhide Pneumococcus	1.97 (95% CI: 1.48–2.64)

COVID-19 vaccine and the four other selected vaccinations, there was a higher risk of a new-onset diagnosed tinnitus after influenza vaccination, Tdap vaccination, and pneumococcal vaccination than after the first dose of the COVID-19 vaccine (Table II). There was a lower risk of a new diagnosis of tinnitus after the second dose of the COVID-19 vaccination series than after the first dose (RR: 0.80, 95% CI: 0.71–0.91). In the comparison for the influenza group, there were 998,991 influenza vaccine patients compared to 1,009,935 first dose COVID-19 vaccine patients, with 720 cases of a new encounter diagnosis of tinnitus in the influenza group and 374 cases of a new encounter diagnosis of tinnitus in the first dose COVID-19 group (RR: 1.95, 95% CI: 1.72–2.21). In comparison to the Tdap group, there were 444,708 Tdap vaccine patients compared to 444,721 first dose COVID-19 vaccine patients, with 314 cases of a new encounter diagnosis of tinnitus in the Tdap group and 133 cases of a new encounter diagnosis of tinnitus in the first dose COVID-19 group (RR: 2.36, 95% CI: 1.93–2.89). In the comparison for the polysaccharide pneumococcal vaccine group, there were 153,344 pneumococcal vaccine patients compared to 154,825 patients who received first dose of COVID-19 vaccine, with 132 cases of a new encounter diagnosis of tinnitus in the pneumococcal group and 79 cases of a new encounter diagnosis of tinnitus in the first dose of COVID-19 group (RR: 1.97, 95% CI: 1.48–2.64). In the comparison for the second dose of COVID-19 group, there were 1,516,282 patients who received second dose of COVID-19 vaccine compared to 1,516,282 patients who received first dose COVID-19 vaccine, with 465 cases of a new encounter diagnosis of tinnitus in the second dose COVID-19 group and 577 cases of a new encounter diagnosis of tinnitus in the first dose of COVID-19 group (RR: 0.80, 95% CI: 0.71–0.91).

DISCUSSION

In this retrospective cohort study examining over 2.5 million patients receiving a first dose of the mRNA COVID-19 vaccine, there was a low rate (0.038%, 95% CI: 0.036%–0.041%) of a new encounter diagnosis of tinnitus within 21 days of vaccination. After matching similar patients between COVID-19 vaccination groups, the likelihood of having a new encounter diagnosis of tinnitus was lower after the second dose of the COVID-19 vaccine than after the first dose (RR = 0.80, 95% CI: 0.71–0.91). This finding may suggest that patients with a predisposition to vaccine-related tinnitus may be more vulnerable after the first dose than after the second dose, or that the first dose provokes an inflammatory response more likely to cause tinnitus. There was a higher risk of a new encounter diagnosis of tinnitus after the influenza vaccine, Tdap vaccine, and polysaccharide pneumococcal vaccine than after the first dose of COVID-19 vaccination. It is important to consider that while the risk of a new encounter diagnosis of tinnitus was higher after these three common vaccinations than after the first dose of COVID-19 vaccination, the rates of a new encounter diagnosis of tinnitus for each of these groups were extremely low (≤0.1% in each of these groups). With such low rates of a new encounter diagnosis of tinnitus after each vaccination, consideration should be given to the baseline risk of developing a new encounter diagnosis of tinnitus independent of any vaccine. However, the lower risk of a new encounter diagnosis of tinnitus after the COVID-19 vaccination than the other three common vaccinations is not obviously explained by a difference in baseline risk between patient groups. The differences in tinnitus based on vaccinations may be due to different patterns of inflammation invoked by each vaccine or may be explained by uncontrolled variables.

In the discussion of post-COVID-19 vaccination tinnitus, the risk of a new tinnitus encounter diagnosis following COVID-19 infection should be considered. COVID-19 infection, like many other viral infections, has been shown to be associated with audiological and vestibular pathologies.[9,10] A recent meta-analysis of COVID-19 infection symptomatology found tinnitus as a statistically significant side effect of infection.[11] Multiple case reports[12–14] and reviews[15,16] describe tinnitus as a direct symptom of COVID-19 infection, likely secondary to systemic inflammation. Pathophysiological explanations posit cochleovestibular inflammation, the cross-reaction of immune cells to inner ear antigens, and endothelial dysfunction leading to microvascular damage of the inner ear as explanations for the significant audiovestibular sequela of COVID-19 infection.[14] Given the current body of evidence, tinnitus is more clearly causally linked to COVID-19 infection than to COVID-19 vaccination, and the risk of developing tinnitus after the vaccine is likely lower than after the infection prevented by the vaccine.

The present findings should not be used to discourage the administration of common vaccinations but rather serve as an impetus for further exploration into mRNA vaccine side effects. When provided with evidence of low incidences of adverse effects of the vaccine, patients may be more likely to consider being vaccinated.[17] The present findings do not speak to the severity of tinnitus or the long-lasting effects of post-vaccination tinnitus, but provide important information on how often patients are diagnosed with tinnitus subacutely after vaccination on a large population level. With the advent of mRNA vaccination in humans occurring on such a widespread scale, the complications of the vaccine should be researched thoroughly and medical providers should be up to date on the prevalence of adverse events for patient

discussion and education. The rate of diagnosed new-onset tinnitus seen in this investigation provides valuable clinical information for medical providers talking to patients with fear of the vaccine or vaccine hesitancy. The present findings provide evidence for medical providers to answer patient questions about the risk of tinnitus after vaccination.

There are limitations to this population-level study with such a large EHR data set. Notably, undiagnosed or uncoded tinnitus is not included and may be better studied with a smaller cohort and direct researcher oversight. This study excluded patients with any encounter diagnosis history of tinnitus in an effort to focus on vaccine-related tinnitus, which excludes information about the reactivation of tinnitus symptoms by vaccination. Additionally, this study did not separate the specific formulations of the COVID-19 vaccine. The timeline of 21 days was arbitrarily decided based on preliminary research and case reports and could potentially miss late-onset cases of tinnitus if too short or include unrelated events if too long. The common vaccination groups were studied throughout 2019 as opposed to the COVID-19 group, which was examined from 2020 to 2022, and widespread hesitation to present to the hospital during the pandemic could have masked cases of tinnitus post-COVID-19 vaccination.[18] However, it has been posited that the emotional burden widely experienced during pandemic lockdowns increased the perceived loudness of tinnitus[19] and may have increased the perception of otherwise subclinical tinnitus symptoms. Hearing outcomes from episodes of tinnitus were not examined in this study as they are not easily quantifiable from our data set but serve as an important direction for further research.

CONCLUSION

The rate of newly diagnosed tinnitus within 3 weeks of the first dose of COVID-19 vaccination is very low. Patients are more likely to develop a new encounter diagnosis of tinnitus after the three other common vaccinations for influenza, Tdap, and pneumococcus than after the first dose of the COVID-19 vaccine. The results of this study will be valuable to medical providers providing patient education about the COVID-19 vaccine, addressing vaccine hesitancy in the ongoing pandemic, and researching the side effect profile of mRNA vaccinations.

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