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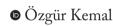
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Artificial Intelligence in Peer Review: Ethical Risks and Practical Limits

Editorial ****



Ondokuz Mayıs University Faculty of Medicine, Department of Otorhinolaryngology, Samsun, Türkiye

Keywords: Peer review, artificial intelligence, AI, publication ethics

The rapid progress of artificial intelligence (AI) has undeniably impacted academic publishing in recent years. In addition to becoming a common tool which authors use in penning scientific papers, used for various stages like data analysis, statistics, literature review, and academic writing, it is no longer rare to encounter scientific papers written entirely by AI (1). However, an even more concerning situation that has recently emerged is the use of AI tools to review manuscripts and then submit the generated reports to editors as if they were their own evaluations. This practice poses serious ethical issues that threaten the integrity and the fundamental principles of academic publishing.

The growing number of scientific journals, along with the rise in the number of manuscripts submitted to these journals, has increased the workload of scientists involved in reviewing manuscripts, forcing them to spend more time on this task, and putting peer review under strain. Clearly, manuscript evaluations using AI applications are conducted efficiently and in a short amount of time, nevertheless in good language. AI applications can

quickly determine the appropriateness of the methods, the consistency of the findings and conclusions, and whether the statistical methods are correctly selected. They can also detect plagiarism, if any, and make appropriate grammatical corrections in the text (2,3). All of these help to shorten the review time.

So, where is the problem in evaluating manuscripts using AI? Firstly, who is responsible for the evaluation report generated by the AI? Just as AI cannot be the author of a scientific article today, it cannot be accepted as the author or the party responsible for a review report. When an evaluation is made, ultimately someone must be responsible for the accuracy of its content, possible errors, or misinterpretations (4).

No matter how advanced or frequently updated AI applications are, they must work with existing data. This is one of the significant limitations of AI. In groundbreaking studies involving new concepts, AI may fail to perceive the minute details, the originality of a new perspective, or a new theory based on existing data, resulting in insufficient

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critical analysis. A reviewer with expertise in the field is more likely to be open-minded about game-changing ideas and manuscripts (4).

Moreover, for an article to be evaluated by AI, it must first be uploaded to an AI application. This constitutes significant ethical violation because it compromises the confidentiality of a manuscript submitted to a journal. The confidentiality of the text uploaded to an AI application cannot be guaranteed (4).

For these reasons, on June 23, 2023, the National Institutes of Health prohibited the use of AI tools, such as ChatGPT, in the peer review process. The Australian Research Council also banned the use of AI tools in the peer review process. Additionally, many leading academic journals do not allow the use of AI tools in peer reviews (5).

The policy of the Turkish Archives of Otorhinolaryngology on this matter is based on the current approaches of international publishing ethics organizations such as COPE, WAME, EASE, and ICMJE. AI tools may be used to a limited extent to improve the grammar and linguistic expression of the review report; however, delegating the peer review task to AI, uploading manuscripts to internet-connected AI systems, or presenting AI-generated evaluations as personal opinions is unacceptable.

In conclusion, using AI in the review process is not an appropriate approach. Nevertheless, in a world where technology and AI are advancing exponentially, it remains difficult to predict what the relationship between peer review and AI will look like in the near future.

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When Compensation Becomes Unsustainable: Rethinking Medical Liability in ENT

Commentary

Taner Kemal Erdağ

Private Practice, Otorhinolaryngology, İzmir, Türkiye

Keywords: Tonsillectomy, postoperative complications, malpractice, liability/legal, defensive medicine, otolaryngology, Türkiye

Recently, a compensation case filed on behalf of a child patient who developed cerebral palsy following a tonsillectomy operation in Gaziantep caused deep outrage and concern not only within the Turkish Otorhinolaryngology and Head and Neck Surgery [ear, nose, and throat (ENT)] community but also among other surgical branches. The court's decision to order the doctor to pay compensation exceeding 109 million TL (approximately USD 2.62 million) once again brought to the fore the risks and legal liabilities encountered in the practice of medicine. This incident not only affected the life of an ENT physician but also points to systemic problems that threaten the future of all surgical specialties. This commentary will address the concerns raised by the case, the existing legal and structural problems, and concrete proposals for resolving the situation.

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1. Compensation Limits for Medical Malpractice and the Burden of Unlimited Liability

Medicine is a science that undertakes the sacred mission of protecting and improving human health, but it is also inherently risky. It is well known that even simple medical procedures, such as intramuscular injections or urinary catheterisation, can rarely cause unexpected problems, let alone operations performed under local or general anaesthesia.

Tonsillectomy is one of the most performed commonly surgeries worldwide. While 49,500 tonsillectomies were performed in the United Kingdom between 2009 and 2010, this figure exceeds 700,000 in the United States. On the other hand, tonsillectomy is also one of the most frequently litigated surgical procedures in the ENT field, with bleeding being the most common cause of litigation (1). Bleeding is the most common complication encountered after tonsillectomy, and the incidence rate reported in the literature varies between 0.006% and 29.1%. Death is a very rare occurrence, but most of these cases develop secondary to bleeding complication, with an incidence reported between 1/7,132 and 1/170,000 (2).



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A tragic situation such as cerebral palsy following a tonsillectomy may be the result of very rare, unpredictable, or uncontrollable circumstances arising during the surgical process. Of course, the pain experienced by the patient and their family who are victims of such a situation cannot be compensated for by any amount of money. However, the court's punishing this tragedy with compensation that would ruin the doctor's life calls into question the balance of rights and justice. Material and moral compensation following medical malpractice is an important tool for redressing the victim's suffering (3). However, compensation amounts that are beyond the physician's ability to pay over their lifetime impair the sense of justice. Decisions that could provoke to the physician's financial and moral ruin and instill similar fear in all colleagues may become a deterrent to practising medicine.

In the United Kingdom, between 1995 and 2010, 34 cases involving tonsillectomy resulted in payments totalling £2.65 million (approximately 147,6 million TL), including compensation and court costs (1). The astronomical compensation of 109 million TL mentioned above far exceeds the total income a physician in Türkiye could earn throughout his/her professional career. This situation, when considered in conjunction with the fact that medical malpractice should not go unpunished, necessitates the search for a fair balance.

2. Defensive Medicine and Its Impact on Public Health

The most dangerous aspect of such decisions is the potential to set a precedent for similar cases in the future. The precedent-setting nature of court decisions may lead families facing similar situations to demand higher compensation. This will push physicians towards defensive medicine practices, discouraging them from accepting risky cases, avoiding surgical interventions even when necessary, or referring patients to other institutions. This, in turn, may result in patients not receiving timely treatment, an increase in complications, and rising costs in the healthcare system

Even in surgical procedures such as tonsillectomy, which is frequently performed in childhood and generally considered a simple operation, the existence of astronomical compensation risks may discourage physicians from practising. Young physicians' motivation to choose surgical specialties may decrease. Examples of this have been clearly observed in our country over the past 10 years (5,6).

3. Expert Witness System

In our legal system, expert witness reports play the most critical role in medical malpractice cases. Expert witnesses must be specialists with the highest level of knowledge and experience on the subject, who are objective and impartial, and who are familiar with evidence-based and current guidelines (3,4,7). There should be no suspicion among the parties to the case that the expert reports could have been prepared by individuals who are not experts in the field or who do not have sufficient knowledge on the subject.

4. Legislation and Compulsory Insurance

In Türkiye, there are annual compensation payment limits under the mandatory financial liability insurance for doctors. However, these limits are often unrealistic and are not sufficiently updated to keep pace with inflation. The fact that the insurance system provides more of a symbolic guarantee than protection against the risks doctors may encounter while practising their profession does not create a fair situation for either doctors or patients. Compensating patients and their families for damages is one of the fundamental aims of the law (3). However, placing the entire financial burden of this compensation solely on the shoulders of the physician necessitates a reassessment of the system as a whole. It is clear that the relevant legislation needs to be revised for this purpose. Solutions such as updating the mandatory financial liability insurance limits, the state assuming the burden of compensation above a certain ceiling, and the establishment of an independent "medical malpractice fund" could be considered (8,9).

5. Ethical and Social Dimension

In this case, the tragedy experienced by the victim's family should not be overlooked. Cerebral palsy is a condition that requires lifelong care and is not only emotionally devastating for families but also places a significant financial burden on them. However, the sense of justice requires that the decision be proportionate. Even if there was a mistake, the punishment should be corrective and balanced, not driving the doctor into financial and emotional ruin. Maintaining public trust in doctors is critical to ensuring that doctors can practise their profession with scientific autonomy, not fear.

Proposed Solutions

This incident reflects systemic deficiencies beyond an individual physician's error. The recommendations can be summarised as follows:

Improvement of the Expert Witness System: In medical malpractice cases, expert witnesses must be selected from among specialists who are directly familiar with the subject matter of the case and who are recommended by relevant branch associations or professional chambers.

Legal Reform: Compensation should be regulated within reasonable limits, and insurance coverage should be expanded.

Risk Sharing: Public authorities and professional organisations could establish funds to protect physicians in high-risk situations.

Education and Prevention: Standard protocols aimed at reducing complication rates should be established in medical school and postgraduate specialisation training. Educational institutions and professional organisations should take a leading role in the transparent and methodologically sound development and updating of evidence-based clinical guidelines and ensure their effective dissemination (10).

Database: Malpractice cases could be collected in a national database for analysis and studies could be conducted on the systematic reduction of risks.

Footnotes

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Investigation of the Effects of the Timing of Decompression and Topical Mitomycin-C Application on Nerve Regeneration in a Rat Model of Bell's Palsy

Original Investigation

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Abstract

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Received Date: 23.04.2025 Accepted Date: 28.07.2025 Epub: 22.08.2025 Publication Date: 26.09.2025 DOI: 10.4274/tao.2025.2025-4-7 **Objective:** The timing of facial nerve (FN) decompression (FND) for Bell's palsy is controversial. Intraneural fibrosis is one of the factors affecting post-traumatic nerve regeneration. This study aimed to investigate the effects of decompression timing and antifibrotic agent topical mitomycin-C (MMC) on nerve regeneration in rats in which a Bell's palsy model was created.

Methods: Bell's paralysis model was created by ligating the subjects' FN trunk. A total of 25 subjects were divided into five groups of five each. Group 1 was not decompressed. The FN was decompressed after one week in Groups 2,3 and after three weeks in Groups 4,5. Topical MMC was applied after decompression on the nerves of the rats in Groups 3,5. Clinical, electrophysiological and histopathological evaluations were performed at three weeks after compression in Group 1 and after decompression in the other groups.

Results: The median total clinical score in Group 1 was statistically significantly lower than the other groups (p=0.001). There were no statistically significant differences between Groups 2-5 (p>0.05). The mean left (operated)/right (undamaged) amplitude values of the subjects in Group 1 were statistically lower (p=0.006), while no statistically significant differences were found among Group 2-5 (p>0.05). It was observed that while axonal degeneration, macrovacuolization and myelin morphology disruption was more severe in subjects in Group 1 (adjusted p<0.05), there were no statistically significant differences between Group 2-5 (p>0.05).

Conclusion: FND can be effective in patients with total paralysis, even when performed in the late stages after allowing a period of recovery. Also, topical MMC applications aiming to reduce intraneural fibrosis have no effect on nerve regeneration.

Keywords: Bell palsy, facial nerve, animal experimentation, rats, surgical decompression



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Introduction

A possible treatment option for patients with Bell's palsy, facial nerve (FN) decompression (FND) intends to expand the facial canal to relieve pressure on the constricted FN. The question of when and for which patients to use this treatment option, which is highly complex and may lead to complications such as cerebrospinal fluid (CSF) leak, hearing loss and FN injury, is controversial in a condition like Bell's palsy that is associated with a high potential for recovery (1-3). The widespread opinion is that surgery is beneficial in patients with complete paralysis and poor prognosis (4-6). In terms of timing, while some authors recommend an early FND (in the first two weeks), others argue that it is possible to wait for the improvement of the paralysis and patients may benefit from surgery at later stages (7-9).

As well as factors such as age, comorbidities, duration and severity of trauma, tissue malperfusion and infection, perineural and endoneurial fibrosis can also negatively affect nerve regeneration after a peripheral nerve injury such as Bell's palsy (10). A chemotherapeutic agent, mitomycin-C (MMC) is relatively easily accessible and applied topically in ophthalmology, neurosurgery, orthopedics and otorhinolaryngology to prevent fibrosis-granulation (11).

It is quite difficult to recommend an optimal timing of FND due to reasons such as small patient sample sizes in studies, the lack of doubleblind randomized trials, and the different approaches of surgeons carrying out the surgical interventions. To develop an opinion on the matter, a rat model of Bell's palsy was created to observe the effects of decompression procedures carried out at different times on nerve repair. The effects of topical MMC application in reducing perineural and endoneurial fibrosis, which are among factors that may inhibit nerve regeneration, were also investigated.

Methods

Subjects

The study was conducted at Bezmialem Vakıf University Animal Laboratory with the approval of the same laboratory ethics committee (approval no: 2020/151, date: 26.10.2020). Twenty-five male Wistar rats weighing 300±50 g, aged 8-12 weeks, kept under standard conditions of a 12-14-hour light/dark photoperiod, 45-50% humidity and a temperature of 22+/-2 °C were included in the study. We confirmed that all subjects had normal motor function of the FN, symmetrical whisker (vibrissae) movements and a blinking reflex in response to air inflation. The subjects were provided with a standard diet with mechanisms allowing free access to water and food.

Surgical Technique and Groups

Standard Surgical Procedure Performed on All Rats

The induction of anesthesia, all surgical procedures and euthanasia at the end of the study were performed on all rats by the same surgeon. Induction of anesthesia was achieved through intraperitoneal injections of 80 mg/kg of ketamine hydrochloride and 25 mg/kg xylazine hydrochloride. 2.0x magnifying loupes were used in all surgical procedures and rats were operated on the left side. An approximately 1-cm horizontal incision was made under the auricle, parallel to the mandible. The superior parotid gland was elevated to expose the main trunk of the FN (Figure 1). The diameter of the nerve was measured using a Castroviejo caliper, and the nerve was ligated with a 5-0 nylon suture to decrease the diameter by 50%. (compression) (Figure 2). The skin was sutured with a 4-0 nylon suture. Rats were then randomized into five groups.

Mitomycin-C Application

The nerve was dried using a 1x1 cm sterile gauze swab attached to a rod and another swab with 0.4 mg/mL of MMC was used to apply MMC to this area for five minutes, after which the area was dried once again (MMC application). The dosage of 0.4 mg/mL was determined in reference to a study investigating the potential for toxicity in the local application of MMC, which found that the application of MMC at more than 0.5 mg/mL could induce neurotoxicity and that MMC should therefore be used at doses lower than 0.5 mg/mL (6).

Surgical Procedures Performed on Subgroups

Group 1 (Control Group: C, n=5): Electromyography (EMG) measurements and clinical scoring assessments were performed three weeks after compression, along with



Figure 1. Exposed facial nerve trunk

histopathological examinations of samples following the termination of subjects.

Group 2 (Early Decompression Group: ED, n=5): One week after compression the ligated FN trunk was located using the same method and the 5-0 nylon suture was removed (decompression). EMG measurements and clinical scoring assessments were performed three weeks after the decompression procedure (week 4), along with histopathological examinations of samples following the termination of subjects.

Group 3 (Early Decompression and MMC Group: ED+MMC, n=5): The decompression procedure was performed one week after compression and then MMC application was performed. EMG measurements and clinical scoring assessments were performed three weeks later (week 4), along with histopathological examinations of samples following the termination of subjects.

Group 4 (Late Decompression Group: LD, n=5): The decompression procedure was performed three weeks after compression. EMG measurements and clinical scoring assessments were performed three weeks later (week 6), along with histopathological examinations of samples following the termination of subjects.

Group 5 (Late Decompression+MMC Group: LD+MMC, n=5): The decompression procedure and MMC application were performed three weeks after compression. EMG measurements and clinical scoring assessments were performed three weeks later (week 6), along with histopathological examinations of samples following the termination of subjects.

Assessment Methods

Clinical, electrophysiological and histopathological assessments were performed in week 3 from the start of the study for Group 1 (C), week 4 for Group 2 (ED) and Group 3 (ED+MMC), and on week 6 for Group 4 (LD) and Group 5 (LD+MMC). Electrophysiological assessments were therefore conducted in the third week after compression in the control group and on the third week after decompression in the other groups.

Clinical Assessment

Clinical assessments were performed according to the scoring system defined by de Faria et al. (7), looking at vibrissa and eye movements in response to air inflation on the animal face. In this scoring system, vibrissa movements and the blinking reflex are evaluated separately and added to each other to obtain the total clinical score (minimum-maximum: 2-10) (Table 1).

Electrophysiological Assessment

We used the Natus Keypoint EMG software (Keypoint net v3.23, Denmark) for electrophysiological assessment and braided pairs of 13 mm length and 0.4 mm diameter subdermal needle electrodes for recording. The electrodes were attached to the orbicular oris muscle. A single subdermal needle electrode of 13 mm length and 0.4 mm diameter was used as a ground electrode, which was placed subcutaneously along the zygomatic bone. The FN was stimulated using braided pairs of 13 mm length and 0.4 mm diameter subdermal needle electrodes placed subcutaneously where the nerve exits the temporal bone posteroinferior to the auricle. Stimulation was achieved with square wave pulses of 60 µs duration at a strength that would maximally stimulate the FN without extending beyond it (1.5-8 mA).



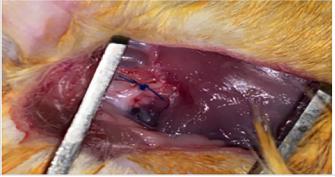


Figure 2. Ligature of the facial nerve with a 5-0 nylon suture (compression)

Table 1. Scale to evaluate facial paralysis in rats developed by de Faria et al. (7)

Score	Whisker movement	Eye movement
No movement (posterior position)		No movement (no contraction)
2	Light tremor (posterior position)	No movement (contraction present)
3	Greater tremor (posterior position)	50% (percentile) eye closure
4	Normal movement (posterior position)	75% (percentile) eye closure
5	Normal movement (anterior position)	Full eye closure

At least three pulses were delivered to each side—left (operated) and right (unaffected)—of every rat. Of motor responses recorded, those with an initial negative deflection and shortest latency were selected for consideration and the base to peak amplitude and latency of said motor response was recorded (Figure 3).

Histopathological Assessment

Following euthanasia, an incision was made to the anteroinferior region of the auricle in the rats, and the buccal branch, one of the distal branches of the FN, was exposed to its distal limits (Figure 4). A 10-mm portion of the nerve was resected and split into two parts of 5-mm each to then be fixed with an alcohol-formalin-acetic acid (AFA) fixative. Material fixed with glutaraldehyde was embedded into Epon and semithin sections of 0.5 µm were cut using an ultramicrotome (Leica Microsystems GmbH, Vienna, Austria) and then stained with thionin. Material fixed with AFA was embedded in paraffin blocks using routine paraffin tissue processing methods. Five µm paraffin sections were cut using a rotary microtome, which were then stained with hematoxylin-eosin and the Masson and Gomori trichrome. These tissues were later examined under a light microscope (4 lm; Leica RM 2145 microtome, Leica Microsystems, Wetzlar, Germany) at 100x, 200x and 400x magnifications to assess axonal degeneration, macrovacuolization and myelin morphology. Assessments were based on a grading system

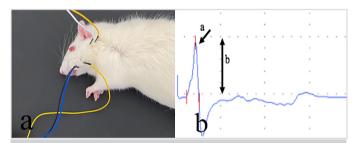


Figure 3. a) EMG performed on subjects, **b)** EMG data sample (**a:** Latency, **b:** Base to peak amplitude) EMG: Electromyography



Figure 4. Facial nerve buccal branch

modified from similar publications in the literature on this topic (8). Macrovacuolization and axonal degeneration was graded in three categories as mild (1), moderate (2) and severe (3). Myelin morphology was classified as 1 (mild morphological damage) if <25% of axons presented with myelin damage in the largest nerve fiber in the section, 2 (moderate morphological damage) if 25-50% of these axons presented with myelin damage, and 3 (severe morphological damage) if over 50% of these axons presented with myelin damage (Figure 5). The physician performing the histopathological examination was blinded to the groups.

Statistical Analysis

G*Power (University of Düsseldorf, Düsseldorf, Germany) was used to conduct a power analysis. Differences between groups in electrophysiological studies conducted by Wang et al. (9) was considered for the power analysis. Expected effect size was set at 1, and the required sample size was calculated as a total of 25 with 5 in each group using a one-way ANOVA test comparing the five groups with an alpha error limit of 0.05 and beta error limit of 0.95.

The Shapiro-Wilk test and a normal Q-Q plot were conducted for statistical and visual evaluation. Differences among more than two independent groups of normally distributed variables were tested using one-way ANOVA, while non-normally distributed variables were compared with the Kruskal-Wallis H test. The Bonferroni correction was applied as in post-hoc pairwise comparisons, and the adjusted p-value <0.05 was defined as statistical significance.

The chi-square test of independence was used to compare categorical variables between groups, and Fisher's exact test was used in cases where more than 25% of cells had expected counts below five.

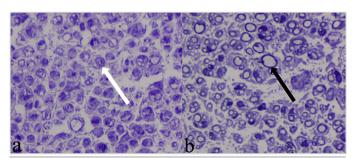


Figure 5. a) Assessment of a semithin section of the left facial nerve of subject no 4 in Group 1 (C), presenting severe macrovacuolization, moderate axonal degeneration and severely damaged myelin morphology (thionin 400x); white arrow: axon with damaged myelin sheath **b)** Assessment of a semithin section of the left facial nerve of subject no 3 in Group 3 (ED+MMC), presenting mild macrovacuolization, moderate axonal degeneration and mildly damaged myelin morphology (thionin 400x); black arrow: axon with normal myelin sheath

IBM SPSS v26.0 (IBM Corp., Armonk, NY, USA) was used for data analysis. Results were considered statistically significant at p<0.05.

Results

General Results and Observations

In controls performed in the 4th week after the start of the study (two days after decompression), one of the subjects in Group 4 (LD) presented with an open abdominal wound possibly due to cannibalism. Following debridement after anesthesia, the wound was irrigated with cefazolin diluted by half with saline, after which primary skin closure was performed. The subject was monitored in isolation from other subjects. In the absence of problems such as woundsite infection and lack of appetite in follow-ups, the subject was terminated six weeks after the start of the study as planned. No complications were observed in the other 24 subjects in the study.

Clinical assessments were performed on all subjects in the first week of the study. All subjects experiencing a surgical intervention to compress the FN presented with an absence of vibrissa movements and no blinking reflex in response to air inflation confirming the onset of total facial paralysis.

Clinical Results

Vibrissa movements, eye movements and total clinical scores were evaluated separately by groups.

A statistically significant difference was observed between the groups in terms of median eye movement, vibrissa movement and total clinical score (p-values 0.004, 0.017 and 0.001, respectively). Analyzing the median values of eye movements and total clinical scores in pairwise comparisons, scores of subjects in Group 1 (C) were found to be statistically significantly low (adjusted p<0.05), while no statistically significant differences were observed among the median values of the other groups (p>0.05) (Table 2). In terms of vibrissa movements, statistically significant differences were found between Group 1 (C) and Group 2 (ED) (adjusted p=0.036), and Group 1 (C) and Group 3 (ED+MMC) (adjusted p=0.036). No statistically significant differences were observed in comparisons of other combinations, potentially due to small sample size (p>0.05).

Electrophysiological Results

Amplitude values on the left (operated) and right (unaffected) sides of each group were averaged to perform a statistical comparison of groups based on mean values. A statistically significant difference was found between groups in terms of left/right amplitudes (p=0.006). On post-hoc analysis, left/ right amplitude values of subjects in Group 1 (C) were found to be statistically significantly lower than the other groups

(p=0.006), while no statistically significant differences were found among the other groups (p>0.05) (Table 3).

Latency values were, on the other hand, evaluated in terms of latency differences between the left and the right sides, and no statistically significant differences were found [F(4,18)=2.238,p=0.105] (Table 4). We observed that latency values presented varying results in some of the previous animal studies in the literature as well. This inconsistency in latency values is believed to be a result of the relatively short course of the FN in rats, creating a shorter interelectrode distance between the stimulating and recording electrodes in EMG testing (10).

Histopathological Results

For every group, macrovacuolization and axonal degeneration was classified as mild/moderate or severe and myelin morphology as mildly/moderately damaged or severely

Table 2.	Median values of clinical	assessment scores	
Group	Whisker movement	Eye movement	Total score
1	1 (1-1)	1 (1-1.5)	2 (2-2.5)
2	2 (2-3)	2 (2-2.5)	5 (4-5)
3	2 (2-3)	2 (2-2)	4 (4-5)
4	2 (1.5-3)	2 (2-2)	4 (3.5-5)
5	2 (2-2.75)	2 (2-2)	4 (4-4.75)
p-value	0.017*	0.004*	0.001*

Data expressed as median (1st to 3rd quartile), *Denotes statistical significance (p<0.05)

Table 3. Left/right amplitudes mean values

Group	Left/Right amplitude#	Left/Right amplitude difference from Group 1+	p-value
1	0.05+0.05		
2	0.20+0.09	0.15 (0.02-0.29)	0.019**
3	0.22+0.06	0.17 (0.03-0.31)	0.008**
4	0.20+0.10	0.15 (0.02-0.29)	0.020**
5	0.17+0.09	0.16 (0.01-0.30)	0.028**
p-value	0.006*		

#: Data are presented as mean+standard deviation, +: The differences between the means of the other groups and Group 1 are provided (with 95% confidence intervals), *: Represents statistical significance in multiple analysis, **: Represents statistical significance in pairwise comparisons (p-values have been adjusted)

Table 4. Left-right (L-R) latency differences mean values

Group	L-R latency difference
1	1.52+0.53
2	0.88+0.34
3	1.07+0.31
4	0.80+0.63
5	0.58+0.55
p-value	0.105
Data are present	red as mean+standard deviation

damaged to perform a statistical analysis. Statistically significant differences were found between groups in terms of axonal degeneration, macrovacuolization and myelin morphology (p-values: 0.001, 0.021, and 0.001, respectively). In pairwise comparisons it was observed that while axonal degeneration was more severe in subjects in Group 1 (C) (adjusted p<0.05), there were no statistically significant differences between the other groups (adjusted p>0.05). Again, while macrovacuolization and myelin morphology disruption was found to be more severe in subjects in Group 1 (C), no differences were observed between the other groups. However, in post-hoc analyses of the data on macrovacuolization, no differences were observed between any of the groups in pairwise group comparisons, most probably due to the small sample size (adjusted p>0.05). Post-hoc analyses of data on myelin morphology showed statistically significant differences only between Group 1 (C) and Group 2 (ED) (adjusted p=0.008) and between Group 1 (C) and Group 3 (ED+MMC) (adjusted p=0.004), while no significant differences were observed between the other groups, again possibly due to small sample size (adjusted p>0.05) (Table 5).

To briefly summarize the findings, no differences were found in terms of recovery between the early and late decompression groups based on clinical evaluations of eye movements and total clinical scores; electrophysiological evaluations of amplitudes; histopathological evaluations of macrovacuolization, myelin morphology disruption and axonal degeneration.

Discussion

Our study found that subjects undergoing decompression showed significantly better FN regeneration than those who did not. No differences in nerve regeneration were observed between rats decompressed in week 1 and those decompressed in week 3. These findings can be interpreted as favoring the view that FND proves beneficial even when performed at later stages. However, it should not be forgotten that in cases of FN paralysis showing no improvement for over 12 months, decompression will not be of use due to the onset of muscle atrophy and fibrosis caused by denervation (11).

Topical MMC application following decompression was, on the other hand, seen to have no impact on nerve regeneration in our study.

The question of when and for which patients the surgical procedure known as FND is indicated in the treatment of Bell's palsy is a long-standing topic of discussion and research (2). It is known that nerve ischemia is reduced, and axonal regeneration increases after surgery (3). FND is considered a relatively infrequent and complicated surgical procedure. A survey conducted in 2011 found that only 22% of the members of the American Neurotology Society performed more than five FND procedures through the middle fossa approach in a period of ten years while only 4% did more than 10. The procedure involves serious complication risks including hearing loss, CSF leak, meningitis and FN injury (2). For this reason, it is quite difficult for physicians and patients alike to decide to move forward with it in a condition such as Bell's palsy that most often resolves on its own without sequelae. Although there are publications demonstrating that FND is a useful treatment as well as those that do not, the ones evidencing its benefits are in majority. Moreover, in most studies investigating the effects of FND, it was observed that only the mastoid segment of the FN was decompressed (3,11). Since the labyrinthine segment of the nerve is the main site of pathology in Bell's palsy, surgical intervention is found to be useful when performed through the middle cranial fossa or with a transmastoid approach to include the geniculate ganglion and the area lateral to the labyrinthine segment (3). Patients with complete paralysis and a more than 90% reduction in amplitudes in comparison to the unaffected side in electroneurography are considered candidates for surgery (2,3).

Since recovery in Bell's palsy can take up to six to nine months in certain cases although it most often occurs within three weeks, the main point of dispute with regards to FND is the timing of the surgery. In the literature on the subject, surgical interventions performed within two weeks of the onset of paralysis are considered early and those performed after two weeks are considered late. While some authors argue that surgery must be performed early on, others hold that the decision to operate or not must depend on the level of spontaneous recovery after a certain period of wait (3).

Table 5. Assessment of myelin morphology and the severity of macrovacuolization and axonal degeneration

Macrovacuolization

Axonal degeneration

Myelin morphology

C	Macrovacuolization		Axonal degeneration	on	Myelin morphology		
Group	Mild/moderate	Severe	Mild/moderate	Severe	Mildly/moderately damaged	Severely damaged	
1	2 (40%)	3 (60%)	1 (20%)	4 (80%)	0 (0%)	5 (100%)	
2	5 (100%)	0 (0%)	4 (80%)	1 (20%)	5 (100%)	0 (0%)	
3	5 (100%)	0 (0%)	4 (80%)	1 (20%)	5 (100%)	0 (0%)	
4	5 (100%)	0 (0%)	4 (100%)	0 (0%)	3 (75%)	1 (25%)	
5	5 (100%)	0 (0%)	3 (75%)	1 (25%)	3 (75%)	1 (25%)	
p-value	0.021*		0.001*		0.001*		
-							

Data are presented as numbers (percentages), *: Denotes statistical significance

The hypothesis put forward by authors advocating early surgical decompression is that Wallerian degeneration occurring three to five days after nerve injury could negatively affect recovery, causing irreversible damage (3). The hypothesis put forward by authors advocating delaying surgical decompression in Bell's palsy to allow for spontaneous nerve recovery and using it only in the absence of recovery is based on the observation that recovery could be prolonged to six to nine months in certain cases. The fact that some cases where FND was performed in the early stage could potentially have healed without surgical intervention may create a serious harm-benefit conundrum. Just as there is a general bias and publications towards the greater benefits of early FND, findings are also present in studies that late FND could prove beneficial (2-4). It is quite hard to recommend an optimal timing of FND based on the existing studies and findings given their small patient sample sizes, the lack of double-blind randomized trials, and the different approaches of surgeons carrying out the surgical interventions.

To study the mechanism of this disease, it is necessary to conduct relevant animal experiments, among which the most important task is to create an animal model with the same pathogenesis as human diseases. There are prior studies where rat and mice models of Bell's palsy were developed through an ear inoculation of the herpes simplex virus into the middle ear, cold stimulation and clamp injury (12-14). Although the precise pathophysiology of Bell's palsy has not yet been elucidated, the existing understanding is that the nerve swells due to edema caused by viral infection or other reasons to then become compressed within the confines of the fallopian tube (3,15). Fisch and Esslen (16) reported that compression was most likely to occur at the junction of the meatal and labyrinthine segments, naming this area the meatal foramen. While the diameter of the fallopian tube ranges from 1.02 to 1.53 mm, it is reduced to almost half of this width—i.e., 0.68 mm—at this junction. That nerve compression with edema takes place right at this point has been verified by subsequent clinical observations and electrophysiological assessments (16). In our study, the FN trunk was explored and ligated to decrease the diameter by 50% for the purpose of creating similar compression, hence developing a Bell's palsy model. In literature, a facial paralysis model was created with clamp injury by Heckmann et al. (15), but this model was not created with suture ligation as we did. Thus, the nerve was left under pressure for a certain period and decompression surgery was imitated by opening it for different periods of time.

It is known that in Bell's palsy the FN becomes ischemic because of sustained pressure due to the swelling inside the fallopian tube (3,16). Cases that do not recover most probably involve damage to the endoneurium and epineurium as well. Intraneural fibrosis occurring after injuries of the third and fourth degrees according to the Sunderland classification,

involving damage to the endoneurium and perineurium, is believed to negatively impact axonal regeneration (17).

Chemotherapeutic MMC is normally an agent that selectively induces fibroblast apoptosis and reduces fibrosis and scar formation. Due to these effects, it is used in ophthalmology, neurosurgery, orthopedics and otorhinolaryngology to prevent fibrosis-granulation (6). The effects of topical MMC on nerve regeneration were also investigated in our study, based on the assumption that it may have positive effects by reducing intraneural fibrosis.

Our study is the first to both develop a rat model of Bell's palsy with a long period of sustained compression and investigate the effects of decompression timing and topical MMC application on nerve regeneration. In our study, no significant difference was found between the late decompression group and the early decompression group when sufficient time was allowed for recovery. From this perspective, our study supports the publications that late decompression may also be beneficial.

One of the strengths of our study is that it involves clinical, electrophysiological as well as histopathological assessments for evaluating nerve regeneration. Our study is, however, limited by the fact that we were unable to examine with an electron microscope and that compression was achieved in a small area using a suture rather than over an entire segment. Another limitation of our study is the small number of subjects, as it leads to instability in some results.

Conclusion

Our findings support the hypothesis that decompression has value in patients with total paralysis even when performed at later stages after waiting for recovery for a certain period. It is also possible to deduce that topical MMC applications aiming to reduce intraneural fibrosis have no effect on nerve regeneration. Multicenter clinical trials are necessary both to further develop our first-time rat model of Bell's palsy and to gain a better understanding of the clinical effects of decompression timing.

Ethics

Ethics Committee Approval: The study was conducted at Bezmialem Vakıf University Animal Laboratory with the approval of the same laboratory ethics committee (approval no: 2020/151, date: 26.10.2020).

Informed Consent: Animal experiment.

Footnotes

Authorship Contributions

Surgical and Medical Practices: B.Ç., H.K., S.S., C.Ş., K.S.O., B.P., Concept: B.Ç., E.K.O., N.G.Ş.İ., G.Ü.,

K.S.O., B.P., Design: B.Ç., E.K.O., N.G.Ş.İ., G.Ü., K.S.O., B.P., Data Collection and/or Processing: B.Ç., H.K., S.S., C.Ş., E.K.O., N.G.Ş.İ., G.Ü., K.S.O., B.P., Analysis and/or Interpretation: B.Ç., H.K., S.S., E.K.O., N.G.Ş.İ., G.Ü., K.S.O., B.P., Literature Search: B.Ç., H.K., S.S., K.S.O., B.P., Writing: B.Ç., H.K., S.S., K.S.O., B.P.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Main Points

- A possible treatment option for patients with Bell's palsy is facial nerve decompression.
- There is no consensus on the timing of decompression in Bell's palsy.
- A rat model of Bell's palsy was created to observe the effects of decompression procedures carried out at different times on nerve repair.
- Our findings support the hypothesis that decompression has value in patients with total paralysis even when performed at later stages after waiting for recovery for a certain period.

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Nasal Mucociliary Clearance Time in Symptomatic versus Asymptomatic Deviated Nasal Septum: A Comparative Analysis

Original Investigation



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Abstract •

Objective: Nasal mucociliary clearance is the first barrier defense mechanism that protects the respiratory system. This study aimed to assess nasal mucociliary clearance time (NMCT) using saccharine test in patients with symptomatic and asymptomatic deviated nasal septum (DNS).

Methods: This was a prospective study conducted in a tertiary center from February 2022 to July 2023. A total of 40 patients, including 20 symptomatic and 20 asymptomatic patients with DNS, were included. The Nasal Obstruction Symptom Evaluation scale was used to assess the severity of nasal obstruction in patients with symptomatic DNS. NMCT was measured by saccharine test in both the symptomatic and asymptomatic DNS patients. NMCT between these two groups was compared.

Results: There were 27 males and 13 females with a mean age of 28.53±7.86 years. Overall median NMCT was 7 minutes 30 seconds, with a similar duration (7 minutes 30 seconds) in patients with symptomatic DNS and 7 minutes and 15 seconds in asymptomatic patients. The difference in NMCT between the symptomatic and asymptomatic groups was not statistically significant. Similarly, it did not differ based on age, gender, or severity of the nasal obstruction.

Conclusion: Although NMCT was longer in patients with symptomatic DNS compared to those with asymptomatic DNS, no statistical difference was found. Additionally, NMCT remained within normal physiological limits in both. We thus conclude that NMCT remains unaffected regardless of whether the DNS patient is symptomatic or asymptomatic.

Keywords: Nose, mucociliary clearance, nasal septum, saccharine, respiratory system

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Introduction

Mucociliary clearance of the nose is the first barrier defense mechanism that protects the respiratory system, especially the upper airway and the sinuses, against inhaled agents (1). Foreign bodies are trapped on the mucus layer and transported towards the pharynx by the ciliary beat, which acts like a conveyor belt (2,3). Alteration in the nasal mucociliary clearance time (NMCT) is often associated with the inflammatory conditions of the airway, such as allergic rhinitis, atrophic rhinitis,



chronic rhinosinusitis, asthma, and secondary to chronic exposure to environmental irritants, smoking, and post-nasal packing (4-6).

Deviated nasal septum (DNS) is most often asymptomatic, however, it may present with nasal obstruction, nasal discharge, smell disturbance, facial pain, and epistaxis, with nasal obstruction being the predominant symptom (2,7,8). The type and severity of the septal deviation can affect the aerodynamics in the nasal cavity. It can also impair mucociliary clearance due to increased mucus secretion, disruption of normal ciliary activity, cilia exfoliation, and epithelial injury (8). The effect of DNS on NMCT remains controversial (7).

An altered nasal mucociliary clearance could be contributory to a septal deviation being symptomatic. While most studies have focused on comparing NMCT between the concave and convex sides of symptomatic DNS pre- and post-operatively, with noted improvement in the NMCT post-septoplasty there is a lack of literature assessing any alteration in NMCT solely due to septal deviation without it being symptomatic (8,9). This study was thus conducted to assess for any alteration in NMCT in asymptomatic DNS or whether it differed based on whether the septal deviation was symptomatic or asymptomatic. NMCT was assessed using a widely accepted saccharine test.

Methods

The study was conducted in the Department of Ear, Nose, and Throat-Head and Neck Surgery at Tribhuvan University Institute of Medicine, Teaching Hospital Kathmandu, Nepal, from February 2022 to July 2023. Ethical permission was obtained from Tribhuvan University Teaching Hospital, Institute of Medicine Institute of Medicine Institutional Review Committee [approval no: 286 (6-11) E2/078/079, date: 11.01.2022]. Written informed consent was obtained from the patients for enrollment in the study.

The sample size was calculated using the two-sample comparison of means (equal variances) formula, where n per group =[$2\times(Z_{1-\alpha/2}+Z_{1-\beta})^2\times sp^2]/\Delta^2$. With α =0.05 (two-sided; $Z_{1-\alpha/2}$ =1.96) and 95% power (β =0.05; $Z_{1-\beta}$ =1.645), pooled standard deviation (SD) sp=2.545, and target mean difference Δ =3.45 from Chandra and Bylappa (10), the required size was \approx 14 per group. With the addition of 20% potential dropout, it was \approx 17 per group. To further increase the statistical power, 20 patients per group were included, for a total of 40.

Patients aged 18 years or more, with symptomatic DNS were taken as one group, and those without symptoms as another. Nasal obstruction was taken as the predominant symptom of septal deviation. The severity of the nasal obstruction amongst the symptomatic DNS group was assessed using

the Nasal Obstruction Symptom Evaluation (NOSE) scale form (11). It was categorized as mild (range, 5-25), moderate (range, 30-50), severe (range, 55-75), or extreme (range, 80-100) nasal obstruction, based on the response score on the NOSE scale form (12). Septal deviation of any type, with or without contralateral compensatory inferior turbinate hypertrophy, was included. Diagnostic nasoendoscopy was done to rule out any other concomitant pathology.

Patients with previous nasal surgery, concomitant nasal polyposis, allergic rhinitis, chronic rhinosinusitis, acute upper respiratory tract infection, loss of taste and smell sensation, smokers, use of pharmacological agents affecting nasal mucociliary clearance within three months, namely nasal decongestants, beta-adrenergic agonist, anti-histaminic, steroids, or any systemic disease likely to impair ciliary activity were excluded.

Each patient was comfortably seated in a chair and asked to gently blow their nose and slightly extend their head (~10 degrees). The saccharine test was done on the convex side of DNS. After visualizing the anterior nasal cavity with a Killian's speculum, the saccharine crystals, sized around 0.5 mm, were placed on the inferior turbinate one cm posterior to the anterior end of inferior turbinate as described previously (2,6,13-15). This was to avoid the area on the anterior end of the inferior turbinate where cilia tend to beat in an anterior direction (14). The patients were instructed to swallow every 60 seconds (sec) to reduce the time latency of taste perception. Furthermore, they were instructed to maintain their natural breathing through the nose and avoid getting up, talking, coughing, sneezing, or manipulating their nose. The flavor and taste of the particle were not disclosed. NMCT was taken as the duration between the saccharine crystal placement on the inferior turbinate and the first perception of taste. Non-perception of taste, even after 60 minutes, or accidental expulsion of the saccharine particle, mostly due to sneezing, would terminate the test.

Statistical Analysis

Statistical tests were done using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.). All quantitative variables were estimated using measures of central tendency and measures of dispersion. Data normality was tested using the Kolmogorov-Smirnov test for continuous variables. The values of NMCT were not normally distributed (p=0.013). Comparison of mean age, gender, and side of septal deviation between the two groups was done using an independent samples t-test, a chi-squared test, and Fisher's exact test, respectively. Comparison of NMCT between the two groups was done using the Mann-Whitney U test, whilst comparison of NMCT based on gender and severity of the NOSE scale was done using the Mann-Whitney U and Kruskal-Wallis tests, respectively. A p-value <0.05 was considered statistically significant.

Results

Demographics

There were 40 patients (27 males and 13 females), 20 each in the symptomatic and asymptomatic DNS groups. Their ages ranged from 18 to 50 years (mean 28.53±7.86). There were no statistically significant differences in age and gender distribution in the symptomatic and asymptomatic groups. Out of 40 patients, 26 (65%) had left-sided while 14 (35%) had right-sided septal deviation. Seven (17.5%) had contralateral inferior turbinate hypertrophy. Among the symptomatic patients, the majority had an obstructive type

of DNS with moderate and severe nasal obstruction (80%) (Table 1).

Nasal Mucociliary Clearance Time

The overall NMCT ranged from 2 minutes (min) 30 sec to 16 min (median 7 min 30 sec). In patients with symptomatic DNS, it ranged from 4 to 16 min (median 7 min 30 sec) whilst in asymptomatic DNS, it ranged from 2 min 30 sec to 12 min (median 7 min 15 sec), with no statistically significant differences (p=0.455) (Table 2). There were no statistical differences in NMCT based on gender and severity of nasal obstruction among symptomatic patients (Table 3).

Parameters		Symptomatic DNS (n=20)	Asymptomatic DNS (n=20)	p-value
Mean age (in years)±SD		29.4±9.38	27.65±6.08	0.939a
Gender	Male	14	13	0.72 <i>(</i> h
Gender	Female	6	7	— 0.736 ^b
C·1 C . 11 · .·	Left	15 (75%)	11 (55%)	0.320°
Side of septal deviation	Right	5 (25%)	9 (45%)	
Contralateral inferior turbinate	Left	1	1	
hypertrophy	Right	2	3	
	Mild	2 (10%)		
	Moderate	9 (45%)		
Severity of nasal obstruction ^d	-	F (0 F0/)		

^{2:} Independent samples t-test, b: Chi-squared test, c: Fisher's exact test, d: Based on NOSE scale, DNS: Deviated nasal septum, SD: Standard deviation, NOSE: Nasal Obstruction Symptom Evaluation

7 (35%)

2 (10%)

Table 2. Nasal mucociliary clearance time in patients with symptomatic and asymptomatic deviated nasal septum (n=40)

	Nasal mucociliary clearance time				
Groups	Minimum	Maximum	Median	p-value	
Symptomatic DNS (n=20)	4 min	16 min	7 min 30 sec		
Asymptomatic DNS (n=20)	2 min 30 sec	12 min	7 min 15 sec	0.455*	
Overall (n=40)	2 min 30 sec	16 min	7 min 30 sec		
* Mann-Whitney II test DNS: Deviated pasal sentum					

Table 3. Nasal mucociliary clearance time based on age, gender, and severity of nasal obstruction

Severe Extreme

D		Nasal mucociliary clearance time			
Parameters		Minimum	Maximum	Median	p-value
A : (40)	≤40 (37)	2 min 30 sec	15 min	7 min	0.08 ^b
Age in years (n=40)	>40 (3)	7 min	16 min	16 min	0.08
C 1 (40)	Male (27)	2 min 30 sec	16 min	7 min	0.168 ^b
Gender (n=40)	Female (13)	5 min	16 min	8 min 30 sec	
	Mild (2)	7 min	10 min	8 min 30 sec	
S	Moderate (9)	4 min	12 min 30 sec	7 min 30 sec	0.204°
Severity of nasal obstruction ^a (n=20)	Severe (7)	5 min	16 min	6 min 30 sec	
	Extreme (2)	15 min	16 min	15 min 30 sec	

Discussion

Alterations in nasal mucociliary clearance, although not diagnostic, indicate the severity of the pathological condition in the respiratory system (4). The saccharine test, which was initially developed by Andersen et al. (16) in 1974, is invaluable as a screening test for mucociliary clearance. It is simple, economical, well-tolerated, and reproducible (13,15). Saccharine is soluble and spreads into the fluid layer of the mucus (17).

Caponnetto et al. (15) found consistent findings of NMCT when repeating the saccharine test thrice in 29 healthy individuals, demonstrating its reproducibility. The mean values (±SD) of NMCT were 7.085 (±2.19), 7.788 (±2.11), and 7.790 (±2.06) min at baseline, day 3, and day 30, respectively. The values were close to the mean pooled value of 9.42±3.04 min calculated in the systematic review by the same authors. It was well-tolerated with infrequent transient side effects like nasal itch, nasal irritation, and sneezing.

In our study, the procedure was well-tolerated. Three patients reported having a short-lived metallic taste before sensing the sweet sensation of the saccharine. Keeping in mind the notable change in the mucociliary clearance due to circadian rhythm, the procedure in our study was conducted in the morning, avoiding performing it past noon, when the mucociliary clearance is likely to alter (17).

The procedure was performed on the convex side since it was the side of nasal obstruction, avoiding concomitant inferior turbinate hypertrophy, which was noted in seven of our cases. Although Passàli et al. (17) reported normal NMCT in patients with inferior turbinate hypertrophy, skepticism remains that it may decrease mucociliary clearance (7). Performing saccharine test on either the concave or convex side has shown mixed findings. Berkiten et al. (7) found no difference in the NMCT between the convex (12.04±4.94) and the concave sides (10.30±4.99) amongst 50 patients (20 females and 30 males) with six different types of septal deviation based on the Baumann and Baumann classification. This was echoed by Polat and Dostbil (18) who also noted no difference in mucociliary clearance rate between the sides, assessed using rhinoscintigraphy, in both symptomatic and asymptomatic patients. However, Jang et al. (9) reported impaired mucociliary clearance on the concave side (16.52±8.06) as compared to the convex side (12.36±4.83), attributing this to ciliary loss, increased inflammation, and decreased density of glandular acini on the concave side of the septum noted on histological examination. Yigit et al. (19) found that mucociliary clearance was faster on the concave side, slower on the obstructed side, but comparable to that of the control, so they concluded that septal deviation did not alter mucociliary clearance (19). On the contrary, Ginzel and Illum (2) opined that the epithelium at the site of deviation becomes highly differentiated, resulting in faster mucociliary

clearance on the convex side. However, Ulusoy et al. (20) noted impaired nasal mucociliary clearance on both sides of septal deviation in both symptomatic and asymptomatic, non-smoking patients. A notable improvement was seen in symptomatic patients after septoplasty.

Normal NMCT ranges between 7 and 15 min, whilst values greater than 20 min are considered pathological (7,15). Some have reported 11 min as the lower and 17.45 min as the upper limit of the normal range (8,21). In the study by Uslu et al. (8), the NMCT amongst 15 patients with DNS was higher than the normal (21.25 to 29.45; mean 26.25±9.45) which returned to a normal range post-septoplasty. Similarly, Jang et al. (9) noted altered MCT amongst DNS patients (mean NMCT 22.50±2.70) which further worsened amongst smokers (mean 26.35±1.78). Smoking alters the NMCT by changing the viscoelasticity of the mucus layer and also by its cilia toxic effect (9).

In our study, the overall NMCT, along with the values for both symptomatic and asymptomatic DNS, was well within 20 minutes, the cut-off point that separates normal from dysfunctional MCT. None of our patients were smokers. Based on our findings, we found no abnormalities in NMCT or significant differences between symptomatic and asymptomatic DNS. The same was observed for age, gender, and the severity of nasal obstruction in symptomatic patients. Ginzel and Illum (2) reported no significant differences in NMCT between the obstructed and non-obstructed sides, indicating no difference between the symptomatic and asymptomatic sides. Ho et al. (22) found significant differences in NMCT in patients aged under 40 years and over 40 years (9.3±5.2 min versus 15.4±5.0 min, respectively), unlike Kao et al. (23) who noted no differences based on age. The latter had taken 59 years as the cut-off age to categorize the group into two. However, both studies agreed on the NMCT remaining similar based on gender (22,23). Some patients in our study had an NMCT as low as 2 min 30 sec. This could be due to ethnic variation, as NMCT has been noted to vary based on ethnicity (23). Kao et al. (23) found relatively shorter NMCT amongst healthy Chinese adults as compared to published data involving other ethnicities.

Similar to our study, the NMCT values reported by Berkiten et al. (7) and Jang et al. (9) were well under 20 min. This also corresponds to the findings of Yigit et al. (19) who indicated that septal deviation did not pathologically alter mucociliary clearance. As per Yigit et al. (19), obstructive pathologies like DNS can affect the airflow; however, if the mucosal function is maintained, inflammatory mediators that are likely to increase the viscoelasticity of the mucus are not released and thus mucociliary activity is preserved. Assessing NMCT by saccharine and charcoal powder, it remained within the physiological range for patients with septal deviations, in contrast to the increased time in patients with chronic

sinusitis in the study by Passàli et al. (17). In contrast, Dogan et al. (24) observed that severe septal deviation (types 4 and 6 according to the Baumann and Baumann classification) had impaired mucociliary clearance, which improved following septoplasty. This suggested the likeliness of specific structural features of the deviation to alter nasal mucociliary clearance. Similarly, Polat and Dostbil (18) found that the mucociliary clearance rate differed significantly between symptomatic and asymptomatic, with the former showing a notable improvement three months after surgery. Interestingly, Kamani et al. (25) observed that the NMCT values for both groups were less than 20 minutes, while finding a difference between the symptomatic and asymptomatic DNS in the saccharine-dye test. Furthermore, their study revealed that the ultrastructural ciliary structure of the nasal mucosa remained unchanged irrespective of symptoms.

The strength of this study was the assessment of the NMCT in asymptomatic DNS and its comparison with that of symptomatic DNS. Such an assessment has not been made in our context, so the findings of our study can serve as a baseline for further research. The environmental factors, such as air temperature and humidity during the procedure, which were likely to alter the result, were beyond our control when performing the saccharine test (23). Standardizing the environmental conditions where such tests are carried out is recommended to obtain reproducible results.

Considering that NMCT was within physiological limits in both groups, and there were no statistical differences between symptomatic and asymptomatic DNS in our study, septal deviation-related symptoms, mainly nasal obstruction, do not necessarily reflect impaired mucociliary transport. So, the decision for septoplasty for DNS is guided by the patient's symptoms without a need for a pre-operative NMCT assessment.

Conclusion

Although NMCT was longer in patients with symptomatic DNS compared to those with asymptomatic DNS, no statistical differences were found. Additionally, NMCT remained within normal physiological limits regardless of whether the DNS was symptomatic or not. Furthermore, it did not differ based on age, gender, or severity of nasal obstruction. Thus, NMCT remains unaffected regardless of whether a patient with a DNS is symptomatic or asymptomatic.

Ethics

Ethics Committee Approval: Ethical permission was obtained from Tribhuvan University Institute of Medicine Institutional Review Committee [approval no: 286 (6-11) E2/078/079, date: 11.01.2022].

Informed Consent: Written informed consent was obtained from the patients for enrollment in the study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: U.G., R.B., K.D., Concept: U.G., R.B., K.D., Design: U.G., R.B., K.D., Data Collection and/or Processing: U.G., R.B., K.D., Analysis and/or Interpretation: U.G., R.B., K.D., Literature Search: U.G., R.B., K.D., Writing: U.G., R.B., K.D.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Main Points

- · Patients with deviated nasal septum had nasal mucociliary clearance times that remained within the normal range, indicating preserved mucociliary function.
- · Nasal mucociliary clearance times did not differ significantly between symptomatic and asymptomatic patients, so a symptomatic deviated nasal septum may not necessarily indicate impaired mucociliary function.
- Age, gender, and severity of nasal obstruction did not alter nasal mucociliary clearance times, suggesting these variables may not affect the mucociliary clearance of the nose.

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From Thesis to Publication: Publication Rates and Determinants of Otorhinolaryngology Residency Theses in Türkiye (2016-2020)

Original Investigation



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Abstract

Objective: To identify the publication rates and determinants of otorhinolaryngology/ear, nose and throat (ENT) residency theses completed in Türkiye between 2016 and 2020.

Methods: A retrospective review was conducted on 460 ENT theses listed in the National Thesis Center database of the Council of Higher Education. Publication statuses were determined through searches in PubMed, Web of Science, TRDizin and Google Scholar on May 10, 2025, using thesis titles, author names, and keywords. Variables including subspecialty, study design, completion year, institution type, city, and journal indexation were recorded.

Results: Among 460 theses, 43.5% were published, with an average time to publication of 3.2±1.7 years. Institution type and city did not significantly affect publication rates (p=0.566, p=0.088). Pediatric ENT (63.6%) and head and neck surgery (57.7%) showed significantly higher publication rates (p=0.019). Cadaveric (66.7%), animal (50%), and prospective (43.5%) studies had higher publication rates than average, but without statistical significance (p=0.292). Most published theses (72%) appeared in international journals and 134 were indexed in the Science Citation Index Expanded.

Conclusion: This study showed that 43.5% of ENT residency theses in Türkiye were published, with an average publication time of 3.2 years. No significant institutional differences were observed. Higher publication rates were noted in pediatric and head and neck surgery theses. Supporting residents in disseminating their research remains essential for fostering academic development.

Keywords: Otorhinolaryngology, academic dissertation, scientific publication, medical education, bibliometrics

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Introduction

In Türkiye, a dissertation is required for the completion of a medical residency program. This requirement aims to teach scientific methodology and contribute to the advancement of science in the residency program. Every year, residents invest time, money and resources to prepare their theses. Although the theses are not required to be published in scientific journals, publication makes the results more accessible and shareable (1,2). The results of a thesis can only be shared with the scientific community when published in peer-reviewed journals.



Medical residency education in Türkiye is coordinated under the Council of Higher Education (YÖK) and the Ministry of Health. Residency training is conducted in university hospitals, training and research hospitals affiliated with the Ministry of Health, and foundation universities (3). Otorhinolaryngology residency is typically structured as a five-year program that combines clinical practice, surgical training and research. As part of this training, the completion of a dissertation is mandatory, providing residents with the opportunity to acquire research experience and academic writing skills.

Although theses are crucial for the scientific database, their publication rates are low (4,5). The transformation of a thesis into a scientific article is the best indicator of its scientific value. The index, quartile, and impact factor of the publishing journal are also important factors to consider. These scientific parameters indicate the quality and strength of the work.

In our study, we aimed to identify the factors that influence the conversion of [otorhinolaryngology/ear, nose and throat (ENT)] theses into scientific publications.

Methods

A retrospective analysis was performed on the theses completed in the field of ENT following a residency program in Türkiye between January 1, 2016, and December 31, 2020. Our study included the theses that were listed in the YÖK National Thesis Center's internet database (http://tez.yok.gov.tr/UlusalTezMerkezi/). To access the theses, the subject "otorhinolaryngology" was selected in the subject tab of the detailed search page in the YÖK thesis center database, and the thesis type was specified as medical residency. The listed theses were then reviewed.

The publication status of each thesis was searched on Google Scholar, PubMed, Web of Science (WoS) and TRDizin platforms using both the English and Turkish titles of the thesis, the names of the thesis author and supervisor, and the specified keywords. The search was conducted on May 10, 2025. The following information was recorded as a result of the search: the subspeciality of the thesis related to ENT [otology/neurotology, rhinology/obstructive sleep apnea syndrome (OSAS), head and neck surgery, laryngology, facial plastics, pediatric ENT and general ENT], the year the thesis was completed, the institution type (state university, training and research hospital, or foundation university), the city (İstanbul, Ankara, İzmir, other), thesis design (prospective, retrospective, animal experiment, genetic, cadaveric, in vitro), the year of publication, the journal in which the article was published, whether the journal was a national or an international one, and the index of the journal. In this study, journals indexed in TRDizin were classified as national, whereas those indexed in Science Citation Index

Expanded (SCIE), Scopus, or similar international databases were classified as international. If an article related to the thesis could not be found on Google Scholar, PubMed, WoS, or TRDizin, it was concluded that no such article existed.

This retrospective study used publicly available data and did not involve human subjects directly; thus, institutional review board approval was not required. The study adhered to the guidelines of the Declaration of Helsinki.

Statistical Analysis

Data are presented as numbers, percentages, mean and standard deviation (minimum-maximum) using Microsoft Office Excel 2016 (Microsoft Corp., United States) and SPSS 21.0 (IBM Corp., Armonk, NY, USA) software. Fisher's exact test was used to compare categorical variables. Pearson's chi-square test and Fisher's exact test were used to compare categorical variables. P<0.05 was considered statistically significant.

Results

A total of 460 ENT theses were completed between 2016 and 2020. Of these, 147 (32%) were conducted in a training and research hospital affiliated with the Ministry of Health, 295 (64.1%) in a state university, and 18 (3.9%) in a foundation university. In terms of location, 102 (22.2%) of these theses were written in Ankara, 91 (19.8%) in İstanbul, 38 (8.3%) in İzmir, and 229 (49.8%) in other cities (Table 1).

When analyzed by years, 102 ENT residency theses were uploaded to the system in 2016, 108 in 2017, 83 in 2018, 88 in 2019, and 79 in 2020. The rate of conversion of these into publications was 43.5% (200/460). Among the theses uploaded, the proportion that resulted in publication was 58.8% in 2016, 44.4% in 2017, 38.5% in 2018, 40.9% in 2019, and 30.4% in 2020. The average publication time after uploading was found as 3.2±1.7 (range: 0-8) years (Table 2).

Table 1. Distribution of theses by city and institution, publication rates

	Theses		Publis theses	
	n	%	n	%
Institution type				
State University Hospital	295	64.1	126	63
Training and Research Hospital	147	32.0	64	32
Foundation University Hospital	18	3.9	10	5
City of institution				
Ankara	102	22.2	49	24.5
İstanbul	91	19.8	46	23
İzmir	38	8.3	11	5.5
Other	229	49.8	94	47

Of the institutions where the published theses were prepared, 126 were state universities, 64 were training and research hospitals, and 10 were foundation universities. There was no statistically significant difference in terms of institution types (p=0.566). The publication rates were 42.7% for state universities, 43.5% for training and research hospitals, and 55.6% for foundation universities (Table 3).

In terms of the cities where the published theses were prepared, 50.5% were prepared in İstanbul, 48% in Ankara, 41% in İzmir, and 28.9% in other provinces; no statistically significant differences were found in terms of the cities (p=0.088) (Table 3).

The ratio of the number of publications of the theses in each subspeciality to the number of theses on that subject was analyzed. Pediatric ENT theses were found to have the

highest publication rate (63.6%), followed by head and neck surgery (57.7%), facial plastic surgery (46.7%), laryngology (42.3%), rhinology/OSAS (39.4%) and otology/neurotology (38.6%). A statistically significant difference was observed

Table 2. Distribution of thesis and publication numbers by years

Years	Theses		Published theses	
	n	%	n	%
2016	102	22.2	60	30
2017	108	23.5	48	24
2018	83	18	32	16
2019	88	19.1	36	18
2020	79	17.2	24	12
Total	460	100	200	100

Table 3. Statistical	differences i	n published	theses
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Table 3. Statistical differences in published the	cscs				
	Yes, n (%)	No, n (%)	Total	p-value	
Institution type					
Training and Research Hospital	64 (43.5)	83 (56.5)	147		
State University Hospital	126 (42.7)	169 (57.3)	295	0.5661	
Foundation University Hospital	10 (55.6)	8 (8)	18		
City of institution					
İstanbul	46 (50.5)	45 (49.5)	91		
Ankara	49 (48)	53 (52)	102	0.0001	
İzmir	94 (41)	135 (59)	229	0.0881	
Other	11 (28.9)	27 (71.1)	38		
Subspeciality					
Otology/neurotology	73 (38.6)	116 (61.4)	189		
Rhinology/OSAS	50 (39.4)	77 (60.6)	127	0.0191	
Head and neck surgery	45 (57.7)	33 (42.3)	78		
Laryngology	11 (42.3)	15 (57.7)	26		
Pediatric ENT	14 (63.6)	8 (36.4)	22		
Facial plastic surgery	7 (46.7)	8 (53.3)	15		
General ENT	0 (0)	3 (100)	3		
Thesis design					
Retrospective	38 (35.8)	68 (64.2)	106		
Prospective	98 (43.6)	127 (56.4)	225		
Animal	52 (50)	52 (50)	104	0.2022	
Genetic	7 (41.2)	10 (58.8)	17	0.292^2	
In vitro	1 (50)	1 (50)	2		
Cadaver	4 (66.7)	2 (33.3)	6		
Animal type					
Rabbit	11(68.8)	5 (31.2)	16		
Rat	41 (50.6)	40 (49.4)	81	0.0072	
Guinea pig	0 (0)	5 (100)	5	0.037^2	
Mouse	0 (0)	2 (100)	2		

Data are presented as numbers (percentages). Row percentages are given.

¹Pearson's Chi-square test, ²Fisher's exact test

OSAS: Obstructive sleep apnea syndrome, ENT: Ear, nose and throat

between these subspeciality groups (p=0.019) (Table 3 and Figure 1).

Analysis of the publications to theses ratio according to study design reveals that 66.7% (4/6) of cadaveric studies, 50% (52/104) of animal experiments, 43.6% (98/225) of prospective studies and 35.8% (38/106) of retrospective studies were converted into publications. There were no statistically significant differences in the publication rates among the study design variables (p=0.292) (Table 3).

Among experimental animal studies, 50.6% (41/81) of the studies conducted with rats and 68.8% (11/16) of the studies conducted with rabbits were published, but none of the studies conducted with guinea pigs or mice were published and the difference between them was found to be statistically significant (p=0.037) (Table 3).

Of the published studies, 56 were published in national (ULAKBİM) and 144 in international journals. When evaluated according to the indexes in international journals, 134 were published in SCIE, seven in Emerging Sources Citation Index (ESCI) and three in non-SCI/SCIE/ESCI international journals (Table 4).

The journals in which the studies were published had different publication rates. The journals with the highest number of ENT theses were European Archives of Oto-Rhino-Laryngology, which published 10% of the studies (n=20), Turkish Archives of Otorhinolaryngology, which published 6% (n=12), Brazilian Journal of Otorhinolaryngology, which published 5% (n=10), ENT Journal, which published 5% (n=10), and ENT Updates, which published 3.5% (n=7). This information is shown in Table 5.

Table 4. Distribution of the indexes in which the publications are included

	n	%
National (TRDizin)	56	28
International	144	72
Index of the international journal		
SCIE	134	67
ESCI	7	3.5
non-SCI-SCIE-ESCI	3	1.5

SCI: Science Citation Index, SCIE: Science Citation Index Expanded, ESCI: Emerging Sources Citation Index

Table 5. Distribution of the journals in which the studies were published

Journal name	n	%
European Archives of Oto-rhino-laryngology	20	10
Turkish Archives of Otorhinolaryngology	12	6
Brazilian Journal of Otorhinolaryngology	10	5
Ear, Nose & Throat Journal	10	5
ENT updates	7	3.5
Acta Oto-Laryngologica	6	3
B-ENT	6	3
International Journal of Pediatric Otorhinolaryngology	6	3
Journal of Ear Nose Throat Head and Neck Surgery	5	2.5
The Journal of International Advanced Otology	5	2.5

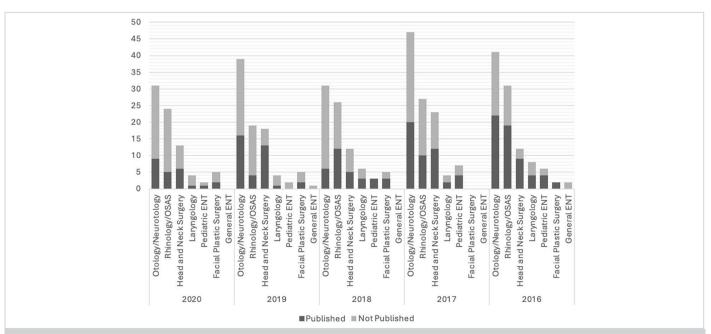


Figure 1. Subspeciality and publication rates of these by year OSAS: Obstructive sleep apnea syndrome, ENT: Ear, nose and throat

Discussion

This study investigated the publication outcomes of ENT residency theses in Türkiye from 2016 to 2020, identifying the factors that influenced their conversion into scientific publications. Our study observed an overall publication rate of 43.5%, which is relatively higher compared to several other medical specialties, such as neurosurgery and microbiology/infectious diseases (1,6).

The specialty thesis is one of the first experiences of a physician as a scientist in the scientific community. Publishing the thesis in peer-reviewed journals is crucial for converting the work performed during the thesis production process into scientific data. Throughout the process of developing a specialty thesis from hypothesis to publication, adherence to scientific methodology and research integrity should be emphasized.

The conversion of a medical residency thesis into a publication has been reported to vary considerably across institutions and periods. Previous studies indicated that theses from university or military hospitals were more often converted into publications, whereas theses from state hospitals showed lower rates (2,7,8). However, in line with more recent studies, our analysis showed no statistically significant institutional differences that could indicate a shift in research culture and an increasing homogenization of training standards across Türkiye (9). Nevertheless, variations in infrastructure, academic tradition and workload balance between service-oriented and academically focused centers likely continue to play a role.

In terms of timing, our mean time-to-publication of 3.2 years was consistent with previous reports (7-10). Methodological differences among studies, such as whether only SCI/SCIE-indexed journals were considered, may partly explain the discrepancies in the reported publication rates. Restricting analysis to higher-impact journals naturally yields lower publication proportions, reflecting the greater scientific rigor required.

When compared with other medical specialties, ENT remains distinctive for its relatively higher thesis publication rates, surpassing fields such as neurosurgery (18%), emergency medicine (27.1%), microbiology and infectious diseases (11.4%), and even general medical theses in Türkiye (6.2%) (1,2,6,11). These findings suggest that ENT residency training in Türkiye has maintained a relatively strong research output, comparable to or exceeding international benchmarks, such as the 17% rate reported in France (5).

An important contribution of our study was the identification of the thesis subject areas with higher publication potential. In line with previous studies, we observed that theses in pediatric otorhinolaryngology and head and neck surgery were statistically more likely to be published (7-10). These

subspecialties often address problems with high clinical impact and objective endpoints (e.g., airway patency, hearing thresholds, oncologic management), concentrate on cases in tertiary referral pathways with multidisciplinary follow-up, and generate projects perceived as novel or practice-changing (e.g., airway reconstruction, cochlear implantation, organ-preserving oncologic strategies), aligning with editorial priorities for originality and broader readership appeal. In addition, cadaveric, animal-based and prospective studies tended to yield higher publication rates than retrospective designs, but statistical significance was not identified. This suggests that beyond study design, novelty and clinical relevance may increasingly drive the likelihood of publication.

The statistically significant difference observed between animal types may be partly explained by the uneven distribution of the studies. Rats and rabbits are the most widely used and standardized models in otorhinolaryngology research, which likely facilitates methodological rigor and publication acceptance. By contrast, studies using guinea pigs and mice were few, and often addressed narrower research questions, which may have limited their publication potential.

Our finding that the European Archives of Oto-Rhino-Laryngology is the journal featuring the highest number of ENT theses aligns with existing literature (10). This is due to the journal's recognition and fast response time. In addition to European Archives of Oto-Rhino-Laryngology, several theses were also published in national journals indexed in TRDizin. This suggests that both international and national journals are preferred as publication platforms for ENT theses in Türkiye. However, it should be noted that the distinction between national and international journals is somewhat interpretative, given that some ENT journals based in Türkiye have been included in international indexing services in recent years. This evolving situation should be taken into account when interpreting the findings.

One potential limitation of our study is the absence of a geographic analysis of thesis origin within Türkiye. Regional variations in healthcare infrastructure and academic culture may influence research productivity. For instance, metropolitan universities with higher research budgets may provide greater opportunities for publication compared with smaller regional centers. Future studies could explore these differences to provide a more comprehensive understanding of national research output.

The strengths of our study lie in its contemporaneity, large sample size, and systematic evaluation of thesis-to-publication conversion. Nevertheless, several limitations should be acknowledged. Firstly, as a retrospective study, our findings rely on database accuracy. Secondly, by including only indexed publications, the actual publication rate may be underestimated. And thirdly, although the five-year follow-up period was based on the average publication interval, some theses were published

up to eight years after completion, suggesting that additional publications may appear in the future. These limitations notwithstanding, our study provides valuable insight into the academic productivity of ENT residency training in Türkiye and offers guidance for young physicians aiming to publish their theses.

Conclusion

This study shows that 43.5% of ENT residency theses in Türkiye were published, with an average publication time of 3.2 years. No significant differences in publication rates were found between institution types. Higher publication rates were observed in pediatric otorhinolaryngology and head and neck surgery theses. Supporting residents in the dissemination of research remains essential for their academic development.

Ethics

Ethics Committee Approval: Ethical approval was not required.

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.Y., Ç.B., Concept: A.Y., Ç.B., Design: A.Y., Ç.B., Data Collection and/or Processing: A.Y., Ç.B., Analysis and/or Interpretation: A.Y., Ç.B., Literature Search: A.Y., Ç.B., Writing: A.Y., Ç.B.

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Main Points

- This study analyzed 460 ear, nose and throat residency theses in Türkiye between 2016 and 2020 to evaluate their publication outcomes.
- The overall publication rate was 43.5%, which is higher than the rates reported in many other medical specialties.
- Pediatric otorhinolaryngology and head and neck surgery theses had significantly higher publication rates compared to other subspecialties.
- Institution type and city location did not significantly affect the likelihood of publication.
- The average time from thesis completion to publication was approximately 3.2 years, consistent with previous literature.

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Trends in Public Search Behavior for Otorhinolaryngology: A Two-Decade Analysis

Original Investigation



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Abstract •

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Objective: Google Trends provides data on searches made on Google from a specific region in a specific period. The aim of this study is to determine the focus of interest in otorhinolaryngology in Türkiye between 2004-2024 using this method.

Methods: Otorhinolaryngology was studied in five subbranches; namely, otology, rhinology, laryngology, head and neck surgery, and facial plastics. The 70 most searched terms in the last 20 years related to these subbranches were determined. The change in the search rates of the terms belonging to each subbranch and the change in the search percentages of the subbranches compared to the total number were determined and evaluated over the years.

Results: In all terms examined, significant increases were observed in general since 2004. However, decrease was observed in all terms, except a few, in 2020-2021, i.e., during the pandemic. In the comparison between subbranches, in the last few years, the lowest search rate was seen in laryngology with 16.86%, and the highest search rate was seen in otology with 24.06%.

Conclusion: Knowing the topics where interest is clustered can be used to guide future medical practices and scientific research.

Keywords: Google Trends, otorhinolaryngology, rhinology, otology, laryngology, head and neck surgery, facial plastic surgery

Introduction

The rapid expansion of Internet usage coupled with the diversification of information sources has positioned Internet-based data as a primary resource for health-related inquiries within society. Notably, approximately 5% of all Internet searches executed through Google, a leading global search engine, have been identified as pertaining to health-related content (1).

Among these search engines, Google Trends (Google LCC, Alphabet Inc., Mountain View, California, USA), with its open data access, enables the tracking of changes in public interest in various keywords and topics over time.



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Infodemiological studies in the literature have examined the tendency of societies to obtain information about various diseases (2-4).

Our study was designed to examine the perception of the otorhinolaryngology field by the society in our country between the years 2004 and 2024. In addition to determining the status of the interest in the subbranches of our field, this study also attempted to understand which topics tended to increase/decrease through the words examined. In light of the data obtained in this study, we otolaryngologists can draw more attention to topics where there is little interest in the society or prevent information pollution by providing correct guidance on topics where interest is concentrated. At the same time, the topics in which interest in the society has increased can be determined and be given more space when planning specialization or in-service training meetings.

Methods

The data obtained through Google Trends (https://trends.google.com/trends/) is proportional, calculated by dividing the number of searches for a given term in a specific region by the total number of searches made in that region in a given month. Since the total search information will reach very high numbers, Google simplifies this data proportionally. With this data, Google Trends creates relative search volume (RSV). RSV is presented on a scale of 0-100 according to the ratio of a term to all other searches.

In our study, the field of otorhinolaryngology was studied in five subbranches; namely, otology, rhinology, laryngology, head and neck surgery, and facial plastic surgery. For each subbranch, at least five terms from the subjects of anatomical structure, symptom, diagnosis, diagnostic examination, and treatment (an attempt was made to include the highest number of terms here without any limitation) were included and a total of 70 terms were used. These terms are shown in Table 1. Changes in the search rates of the terms used over the years and total search rates were recorded. Afterwards, each term, then each subbranch within itself and finally subbranches with each other were compared.

As the data were obtained from the public domain and did not involve human participants, the study did not require local ethics approval or informed consent. The collection and evaluation of the data, followed by re-verification and processing, took approximately 12 days.

Statistical Analysis

In statistical analysis, firstly, Shapiro-Wilk analysis was performed to evaluate the normality of distribution of the search rates. The data was found to be distributed nonparametrically. The Friedman test was applied to study the change within each subbranch (p<0.05 was considered significant). Then, total search rates were calculated for each year. The percentage value of each subbranch was calculated from this total. The Wilcoxon signed-rank method was used to evaluate the changes within the subbranches over the years (p<0.05 value was considered as statistically significant). Statistical analyses were made using IBM SPSS Statistics version 20.0 (IBM Corp., Armonk, NY, USA).

Results

The search rates of the terms were studied separately for each subbranch and term. The search rates and changes for rhinology terms are shown in Figure 1. The most searched terms in 2024 were "nasal septum," "sleep test" and "allergy

Rhinology	Otology	Laryngology	Head and neck surgery	Facial plastic surgery
Nose	Ear	Larynx	Neck	Nasal tip
Nasal polyp	Eardrum	Vocal cord	Thyroid	Auricle
Nasal septum	Inner ear	Throat	Tongue	Facial aesthetics
Snoring	Tinnitus	Hoarseness	Neck pain	Big nose
Nosebleed	Cerumen	Speech disorder	Wound of the tongue	Wide nose
Postnasal drip	Ear itching	Throat pain	Mouth ulcers	Bags under the eyes
Nose curvature	Ear infection	Larynx cancer	Thyroid cancer	Protruding ear
Nasal deviation	Vertigo	Laryngomalacia	Thyroid nodule	Retrognathia
Sinusitis	Middle ear infection	Vocal cord paralysis	Throat culture	Droppy nose
Polysomnography	Balance test	Laryngoscopy	Thyoid scintigraphy	Rhinoplasty
Sleep test	Hearing test	Vocal cord surgery	Neck MRI	Nose aesthetics
Allergy test	Hearing screening	Voice thinning	Tonsillectomy	Prominent ear surgery
Septoplasty	Eardrum surgery	Voice theraphy	Adenoidectomy	
Nazal strip	Hearing aid		Thyroidectomy	
Nasal aspirator	Cochlear implant			

test." Analysis of the change in the average search rates of the terms over the years revealed that the terms "nose," "sinusitis," "nosebleed" and "snoring" were searched since 2004. In general, an increase was observed in the search rates of the terms. However, there was a general decrease in search rates in 2020, when the coronavirus disease 2019 (COVID-19) pandemic emerged. During this period, the terms "nosebleed," "postnasal drip" and "nasal strip" increased. A decrease was observed in other terms. The terms with the most significant decrease during this period were "nasal deviation," "nasal curvature," "septoplasty," and "polysomnography," respectively. The decreased search rates in this period started to increase starting from 2021 and 2022.

Regarding otology, the terms "ear," "ear infection," "middle ear infection," "vertigo," and "hearing aid" were searched since 2004. In 2020, when the COVID-19 pandemic started, the search rates of the terms "ear itch," "cerumen," "balance test," "vertigo" and "tinnitus" increased, while the others decreased. This decrease was most clearly observed in the terms "eardrum" and "eardrum surgery." In 2024, the terms searched for at the highest rate were "cerumen," "tinnitus,"

and "cochlear implant," respectively. The search rates and change graph of otology terms are given in Figure 2.

Regarding the terms related to laryngology, "larynx" and "larynx cancer," were searched since 2004. Even among the terms that we have identified as being the most searched for this subbranch, we can see that the years in which searches first began are later than in other subbranches and that the curve showing the rate of searches is flatter (Figure 3). In addition, it is seen that the terms that decreased due to the COVID-19 effect in 2020, especially those related to treatment (vocal cord surgery, voice thinning, and voice therapy), still did not reach their pre-COVID rates in 2024. The term "throat pain" showed a significant increase in 2020, however, the search rates of "larynx" and "voice thinning" are terms that increased slightly. The term with the highest rate of decrease during this period was "voice therapy."

In the head and neck area, the most searched term in 2024 was "thyroid." The most significant decrease in search rates in this subbranch in 2020 was observed in the terms "tonsillectomy," adenoidectomy," and "throat culture." It was also observed that the terms "oral wound," "wound of the

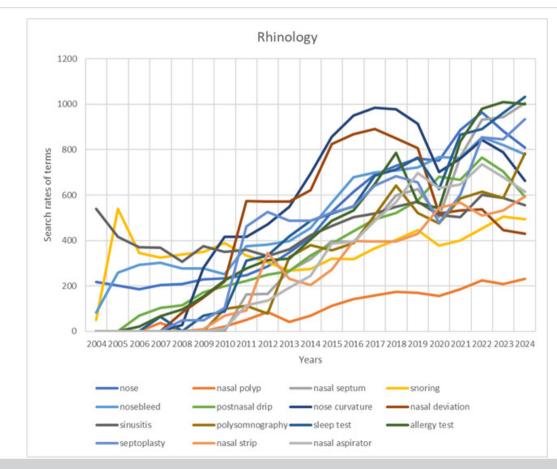


Figure 1. Search rates for the most searched terms related to rhinology by year. As seen, in recent years, the terms "polysomnography," "sleep test," "nasal strip," "nasal septum" and "septoplasty" increased in popularity

tongue," and "neck pain" increased during this period. In this subbranch, the search started in 2010, and its rate increased, then decreased during the pandemic, but continued with a rapid increase in the following years. In 2024, "neck magnetic

resonance imaging" comes forth as the second most searched term in this subbranch. The search rates of the terms and their changes over the years are given in Figure 4.

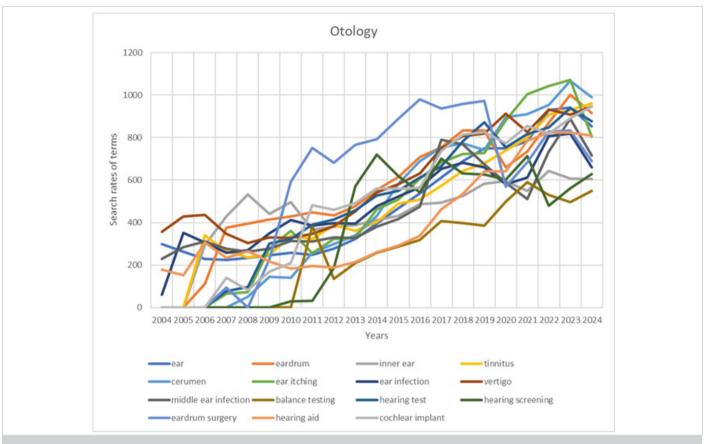


Figure 2. Search rates of otology-related terms and their changes over the years. The graph shows that the terms "cochlear implant," "hearing screening," "balance test" and "middle ear infection" have increased in popularity over the last few years

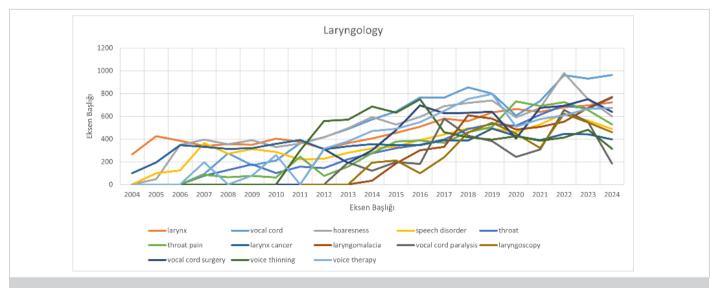


Figure 3. Search rates for the terms related to laryngology. As seen, the terms "vocal cord," "vocal cord surgery," "laryngomalacia," "larynx" have increased in popularity in recent years

While only the terms "nose aesthetics" and "rhinoplasty" were searched for facial plastic surgery in 2004-2005, interest in the terms "protruding ear" and "bags under eyes" increased in the following three years. All terms decreased or slightly increased during the pandemic period. The terms that showed the most significant decrease were "bags under eyes" and "facial aesthetics," respectively. The terms with the highest interest after 2020 were "nasal tip," "nose aesthetic," "protruding ear," and "wide nose." The term "prominent ear surgery," which had the highest search rate between 2011-2015, has decreased in recent years. The search rates of the

term "otoplasty," which is synonymous with this term, were low in total and were not included in our study. However, we can see in the search graph that the search rate of this term has increased in recent years (Figure 5). A similar situation was seen in the rise of the term "belpharoplasty" against the term "bags under eyes," which has fallen from interest in recent years (Figure 6). The term "retrognathia" started to gain attention in 2011, but it rose rapidly and became one of the top five most searched terms in 2024. The graph showing the search rates of terms related to facial plastic surgery is shown in Figure 7.

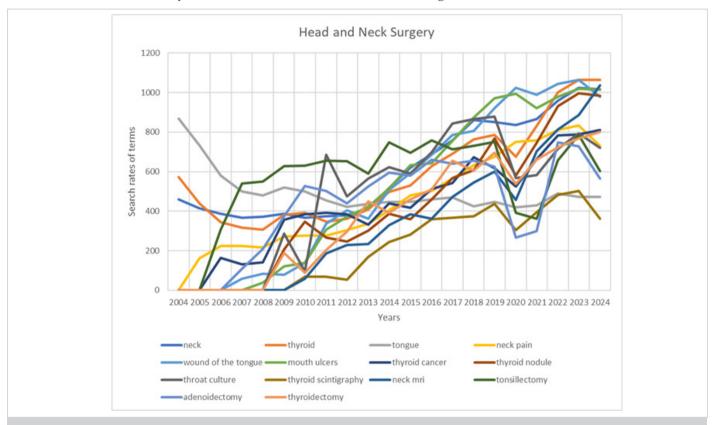


Figure 4. Search rates for terms related to head and neck surgery. As seen, the terms "neck magnetic resonance imaging," "thyroid cancer" and "thyroidectomy" have increased in popularity in recent years

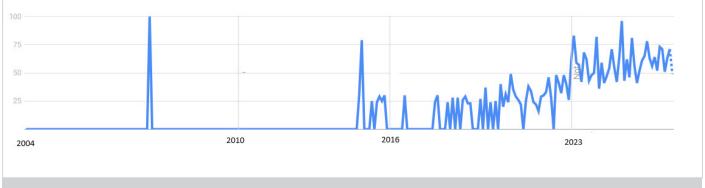
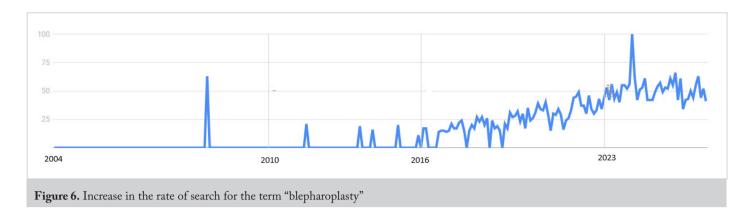


Figure 5. Increase in the rate of search for the term "otoplasty"



Facial Plastic Surgery 1200 1000 800 Search rates of terms 600 400 200 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021 2022 2023 2024 Years nasal tip -facial aesthetics auricle big nose wide nose bags under the eyes protruding ear retrognathia

Figure 7. Change in search rates for terms related to facial plastic over the years. Here, while it increased after the beginning of the pandemic, the popularity of all other terms except "retrognathia" decreased as of 2022

nose aesthetics

rhinoplasty

Finally, the total search rates of the subbranches were compared. The graph showing the changes in all years is given in Figure 8. To make the comparison more understandable, the years were examined in four periods. The distribution of the percentages in the total search rate according to these periods and the changes over the years are shown in Table 2. According to the table, a significant increase was observed in rhinology in the 3rd and 4th periods compared to the 2nd period. In otology, a significant decrease was observed in the 2nd and 3rd periods after the 1st period, and an increase occurred again in the 4th period, but this was not significant.

droppy nose

A significant decrease was observed in laryngology in the 2nd, 3rd, and 4th periods compared to the 1st period. In head and neck surgery, an increase was observed in the 2nd period compared to the 1st period, but this was not significant. A significant decrease was observed in the 3rd period compared to the 2nd period. Although there was an increase in the 4th period, it was not significant. The last period was found to be significantly lower compared to the 1st period. In facial plastic surgery, although the 3rd period showed a significant increase compared to the 2nd period, a significant decrease was observed in the last period.

prominent ear surgery

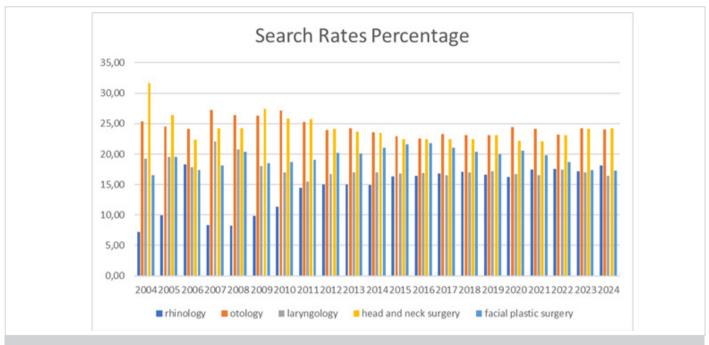


Figure 8. Graph created by calculating the percentage values of the total search rate of each subbranch compared to the total of all otorhinolaryngology

Table 2. Search rates (as percent	entages) of terms by su	ıb-branch and year			
	2004-2008 (1st period)	2009-2013 (2 nd period)	2014-2018 (3 th period)	2019-2024 (4 th period)	p value*
D1.11	8.37	14.42	17.41	17.25	0.043 (2 nd -3 rd periods)
Rhinology	8.37	14.43	16.41	17.35	0.043 (2 nd -4 th periods)
					0.042 (1st-2nd periods)
Otology	25.37	25.23	23.13	24.06	0.043 (1st-3rd periods)
					0.043 (2 nd -3 rd periods)
					0.043 (1st-2nd periods)
Laryngology	19.51	16.97	16.86	16.86	0.043 (1st-3rd periods)
					0.043 (1st-4th periods)
Head and neck surgery	2.4.2.4	25.74	22.47	23.12	0.043 (1st-4th periods)
	24.21				0.043 (2 nd -3 rd periods)
Facial plastic surgery	10.00	10.00	21.02	19.24	0.043 (2 nd -3 rd periods)
	18.08	19.09	21.03		0.043 (3 rd -4 th periods)

The table presents the percentage search rate values for each subbranch relative to the total search rate, categorized by year. Statistically significant differences across these periods are also indicated in the table (the Wilcoxon signed-rank method was used for statistical evaluation). *: p<0.05 value was considered as statistically significant

Discussion

The Internet is increasingly being used in the society to obtain information about health-related issues. A 2010 study conducted in the United States of America, involving interviews with 3,001 adults, demonstrated that individuals perceived the Internet as a very valuable source of information for reasons such as obtaining quick information about health, evaluating other treatment options, or learning more about prescriptions (2).

Health information seeking behavior can be useful in tracking people's trends, disease epidemiology, etiology, and management of certain health conditions (3). Google Trends data has previously been used to track infectious diseases and epidemics and is also known to provide useful information about consumer behavior. Using Google Trends to analyze health-related topics can provide big data, but it is still not widespread (4). By analyzing recorded search terms, public interests can be effectively determined, thereby enabling healthcare providers to leverage this data for

both disseminating accurate information and enhancing healthcare policies.

However, after many problems were experienced because of information pollution, especially during the pandemic, the science of infodemiology, which examines the ways of obtaining information over the Internet and aims to provide accurate information presentation, emerged. Searches made on Internet search engines and social media are recorded in real time, enabling infodemiological research (5). This big data analysis derived from Internet searches holds significant promise for utilization in health research.

Google Trends, which extracts data from a portion of approximately three billion daily searches, is an important data source for assessing public behavioral trends. In addition, Google Trends has been proven to be effective in many studies in the literature (6). It has been suggested that Google can be used to predict disease occurrence and epidemics by examining this search traffic (7). On the other hand, the reliability of Google Trends data has also been evaluated in the literature. In the methodology of our study, the results of a reliability study on Google Trends, which was previously included in the literature, were taken into account. Accordingly, the method we used to evaluate the change in interest in a term over time, social trends and correlations was found to be reliable (8).

Determining public interest using Internet search engines can be leveraged to shape preventive medicine activities by revealing the need for information on topics such as head and neck malignancies. For example, the search rate for the term "nasopharynx cancer" has been 221 in total since 2004. This rate is below the annual search rate for many other terms, as seen in the figures in our study. In addition, the increase in public interest in some scientifically unproven treatments can also be determined through Google Trends data. In this context, an orthopedic study reviewed the search rates for platelet-rich plasma (PRP) treatment for hip and knee osteoarthritis. The authors suggested that, in instances where public interest increases for treatments like PRP whose efficacy remains unproven—academic governing bodies ought to initiate informational campaigns targeting both surgeons and the general public (9). Similar studies can be conducted in otorhinolaryngology.

Some studies using Google Trends to obtain information about otorhinolaryngology have been published in the literature in recent years. One study concluded that throat cancer screening rates could vary across the years and communities (3). In another similar study, research conducted in Spain to obtain information about oropharyngeal cancer was examined (10). A study aimed at measuring public awareness of nasal polyposis reported an increase in related searches (4). A study on sinusitis reported a positive correlation between the search rates for sinusitis symptoms

and the search rate for the term "sinusitis." The same study reported that the seasonal variation in the search terms was consistent with real life (11). Another study found that Google Trends searches related to bruxism increased during the winter months (12). A study examining searches on the term "laryngectomy" on Google reported that search rates remained stable between 2017 and 2022, and the most searches were on the topics of post-laryngectomy speech, laryngectomy comparison to tracheostomy, stoma and stoma care, survival/recurrence, and post-laryngectomy eating (13).

In a publication similar to ours, the change in awareness and interest in chronic liver diseases between 2004-2017 years was examined. This publication reported that people avoided complex medical terms in their searches. It was also reported that current scientific data did not rapidly affect the searches (14). We, too, did not identify such rapid changes in our study. There were seasonal changes in the terms we examined regarding symptoms, diseases, and surgical interventions (for example, an increase in terms related to allergic rhinitis in the spring months), but there were no rapid increases in interest in new medical methods.

In our study, we found changes in the search rates of Google Trends search terms during the COVID-19 pandemic. A comparable situation was observed for the terms related to other branches. For example, one study reported that the diagnosis of acute coronary syndrome decreased in the field of emergency, but the search rate for the term chest pain, which is known to be highly searched for with this diagnosis, increased. This was associated with patients' search for information on the Internet because of their tendency to avoid emergency room visits (15).

A study in literature has shown that although the search rate for terms related to aesthetics and cosmetic procedures decreased in the months when the COVID-19 pandemic began, it increased significantly in the following months (16). Consistent with this, our study found that the field of facial plastic surgery continued to increase during the pandemic.

Another recently published study found that all surgical procedures examined (including non-aesthetic procedures such as cataract surgery) decreased at the beginning of the pandemic. However, a statistically significant increase was observed later in the terms blepharoplasty, facelift, neck lift, and Botox compared to the pre-pandemic period. This study reported that interest in the term "rhinoplasty" initially increased and then returned to pre-pandemic levels by the end of 2022 (17). In our study, we found that search rates for the terms "blepharoplasty" and "otoplasty," which were not among the most searched terms overall, remained stable during the pandemic and then increased compared to the pre-pandemic period (Figures 5 and 6). Similarly, the terms "nose aesthetics," "facial aesthetics," and "protruding ear surgery" decreased during the pandemic, increased again

the following year, and decreased after 2023, showing lower search rates compared to the pre-pandemic period.

Since no similar studies were found in the literature, we have no way of comparing the search rates of otorhinolaryngology-related terms from Türkiye with searches from other countries. However, our study provides important information about the perception of otorhinolaryngology by the public in Türkiye.

The limitations of our study are that data was obtained from a single search engine, and there is no data that could allow for analyzing detailed search behavior (such as demographic data, search location, and possible interactions with media or social media that were not scanned back), and terms may have meanings other than their medical meanings. The reason why Google was chosen as the search engine in our study is that Google offers the most preferred search engine in the world, with more than 89% of the market share (18). Data collection from Google Trends required twelve days. Although Google Trends generally provides stable normalized values, minor variations may occur due to the platform's sampling and updating algorithms. This time span is therefore acknowledged as a potential limitation. To enhance the contribution of our study to the literature, the number of terms searched should be increased and the locations searched should be examined in more detail.

Conclusion

The change in the terms searched for regarding subbranches of otorhinolaryngology on Internet search engines is important in terms of reflecting the interests of society today. Keeping this data up to date will make it possible to shape preventive medicine practices, identify disease clusters and apply them to future clinical research.

Ethics

Ethics Approval: The study did not require local ethics approval.

Informed Consent: Patient consent were not required.

Footnotes

Authorship Contributions

Concept: S.S.G., H.A., Design: S.S.G., Data Collection and/or Processing: L.A., F.B., Literature Search: L.A., F.B., Writing: S.S.G., F.B.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Main Points

- In our country, Internet searches for terms related to all topics of ear, nose and throat have increased significantly between 2004 and 2023 compared to the previous year.
- The sub-branch with the highest interest was head and neck surgery.
- The sub-branch with the lowest interest was laryngology.
- In our country, during the coronavirus disease pandemic in 2020-2021, it was determined that interest in rhinology and facial plastics continued to increase, but interest in other topics decreased.

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Are ChatGPT's Answers to Questions About Salivary Gland Diseases Accurate and Reliable?

Original Investigation



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Abstract

Objective: Chat Generative Pre-Trained Transformer (ChatGPT) is an artificial intelligence model that can generate human-like text dialogs to inputs. There are no ChatGPT studies in the literature only on salivary gland diseases. This study evaluates the accuracy and reliability of ChatGPT's answers to questions in salivary gland diseases, focusing on its potential use in training otolaryngology professionals.

Methods: Sixty-one questions, categorized as "basic knowledge," and "salivary gland tumors" were posed twice using ChatGPT-4. Answers were categorized as 1 (completely correct and comprehensive), 2 (partially correct), 3 (misleading information containing correct and incorrect statements), or 4 (completely incorrect). The accuracy of the answers was evaluated by two ear, nose and throat specialists. Inconsistencies in the rating were resolved by a third reviewer. Reproducibility was assessed by the agreement between the first and second answers.

Results: Fifteen (24.6%) of the questions were about basic knowledge, while 46 (75.4%) were about salivary gland tumors. ChatGPT gave "completely correct and comprehensive" answers to 54 (88.5%) questions and "partially correct" answers to seven (11.5%) questions. "Misleading information containing correct and incorrect statements" and "completely incorrect" answers were not received. The reproducibility rate of first and second answers was 97%.

Conclusion: ChatGPT provided highly accurate and reproducible answers to questions about salivary gland diseases. ChatGPT is thought to be an important source of information for otolaryngology professionals. Although the results of our study show that ChatGPT is highly successful, more studies are needed in this field.

Keywords: Salivary gland, salivary gland tumor, sialadenitis, generative artificial intelligence, medical education, professional practice

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Introduction

In recent years, developments in artificial intelligence (AI) models have started to have an impact on many areas of life. The integration of AI into medical fields affects human health. One of these AI applications is the Chat Generative Pre-Trained Transformer (ChatGPT), which is an interactive chat engine, and a large language model trained with internet text data.

ChatGPT is an AI model capable of generating human-like conversational dialogue by generating answers to questions from a large knowledge database (1-4). ChatGPT, a large language model developed by Open AI and trained on internet-based data, is one of the important developments in AI (5). ChatGPT, which has a wide range of information sources, can generate human-like responses to text and sentence inputs (1-3). It is also capable of providing information on various topics, answering questions, and chatting. It can do so in both medical and non-medical fields (6). Since applications and information in the medical field require high responsibility and transparency, it is of great importance to develop an AI system with accurate and reliable medical knowledge (7). The need for both healthcare professionals, and medical students, as well as patients, to obtain information from ChatGPT makes the reliability of this application even more important. Its performance improves with continuous and repetitive inputs, in other words, with user interaction (6).

The use of ChatGPT, especially in the medical field, has brought some controversies. While some researchers consider the medical information provided by ChatGPT as valuable, others have distanced themselves from this issue due to misuse during medical writing, security issues, accuracy of information, and legal concerns (8,9).

ChatGPT serves as an additional source of information that otolaryngology professionals can use for their academic training and exam preparation. In the field of otolaryngology, AI studies have been reported on clinical staging methods, analyzing cochlear implant performance, detection of parathyroid gland, prediction of prognosis in otolaryngology and head and neck surgery patients, determination of accuracy and reliability of information about head and neck cancers (4,10-13). Our study is unique in that it only included questions about salivary gland diseases. The aim of this study is to determine the accuracy and reliability of ChatGPT's answers to questions about salivary gland diseases, and thereby to determine whether the AI application can be used as a resource in the training of otolaryngology professionals on this subject.

Methods

Study Design

The GPT-4 version of ChatGPT (OpenAI, San Francisco, CA) was used for the study. ChatGPT was asked a total of 61 questions about salivary glands. The questions were developed based on standard otolaryngology textbooks, clinical guidelines, and the authors' clinical experience. They were not formatted as examination questions but were designed to reflect clinically relevant scenarios that can be encountered in practice. All questions were prepared by an ear, nose and throat (ENT) specialist with over ten years of clinical experience. To prevent bias, the evaluation of ChatGPT's answers was conducted by different ENT specialists who were not involved in the question preparation process.

The questions were systematically divided into two different groups: basic knowledge and salivary gland tumors. To evaluate the consistency and reproducibility of ChatGPT's answers and to reduce memory bias, each question was asked twice on the same day, one after the other, from the same computer using the "new input" function. Thus, each answer for the same question was reproduced twice and scored independently. All questions asked to ChatGPT were asked in English and the questions and answers received were archived (Supplementary File). Since our study was not a study involving humans and animals, ethics committee approval and patient consent were not required.

Grading System

Two ENT specialists who were actively working, experienced in their field (more than 10 years of experience), and who did not communicate with each other about the questions independently reviewed and graded the ChatGPT answers (first and second) for accuracy and reproducibility. The accuracy of the answers was determined by the scoring method of Kuşcu et al. (4):

- 1. Comprehensive/correct: Completely correct and comprehensive data
- 2. Incomplete/partially correct: Partially correct data
- 3. Mixed: Misleading information containing correct and incorrect statements
- 4. Completely inaccurate/irrelevant: Completely incorrect data

Reproducibility was assessed and scored independently by two ENT specialists according to the consistency of the two answers from ChatGPT to each question. If the two answers were similar, only the first answer given by ChatGPT was recorded and scored. If the answers were different, both answers were scored and recorded by the ENT specialists. Both ENT specialists had more than 10 years of experience and were actively involved in both clinical and academic studies. No residents or junior doctors participated in the evaluation process.

When the scores of the first and second answers given by ChatGPT were different, the answers were considered not reproducible, i.e., incongruent. All discrepancies in the accuracy and reproducibility of answers between the two reviewers were reviewed and resolved by a third experienced ENT specialist (with more than 10 years of experience) who was blinded to the initial reviews.

Statistical Analysis

Statistical analysis of the data was performed with IBM SPSS Statistics for Windows, version 27 (IBM Corp., Armonk, NY, USA). Descriptive statistics were calculated as number, percentage, mean, standard deviation, median and min-max. Inter-measurement consistencies were evaluated by intraclass correlation coefficient (ICC). In the evaluation of ICC coefficients below 0.4 was considered poor, between 0.4-0.59 moderate, between 0.60-0.74 good and above 0.75 excellent relationship. P-values less than 0.05 were considered statistically significant (Mann-Whitney U test). The Wilcoxon sign test was performed to study whether there was a statistically significant difference between the answers obtained from the questions asked to ChatGPT two times.

Results

A total of 61 questions were asked to ChatGPT about salivary gland diseases. Fifteen (24.6%) of the questions were

about basic knowledge and non-tumor diseases of the salivary glands, while 46 (75.4%) were about salivary gland tumors. The distribution of ChatGPT answers to both question groups is shown in Table 1. ChatGPT gave "completely correct and comprehensive" answers to 54 (88.5%) questions and "partially correct" answers to seven (11.5%) questions. None of the questions were scored as "misleading information containing correct and incorrect statements" or "completely incorrect." These results are shown graphically in Figure 1.

The agreement of ChatGPT's answers to questions first and second, in other words reproducibility, was 96.7% (59 out of 61 questions). This rate was 100% for basic knowledge questions and 95.6% for salivary gland tumors questions. These results are shown graphically in Figure 2. There was no statistically significant difference between the first and second answers given by ChatGPT (p=0.157) (Table 2). In general, the first answers of ChatGPT were more accurate than the second answers. A total of 91.8% of the first answers and 88.5% of the second answers were evaluated as completely accurate and comprehensive.

ICC was used to examine the consistency of the decisions made by the reviewers who evaluated the answers given by ChatGPT. Accordingly, there was no statistically significant difference between the scores given by the reviewers to the questions in both groups (p=0.779). For the basic knowledge questions, the ICC rate was 1.00, indicating high consistency. When the answers related to salivary gland tumors were evaluated by two reviewers, ICC was found to be 0.899 for ChatGPT's first answers and 0.959 for second answers, indicating a high degree of consistency between the two reviewers (Table 3).

Table 1. Distribution of answers received from ChatGPT according to question grou	ups
	Number of questions (%)
Basic knowledge (n=15)	
Completely correct and comprehensive	15 (100)
Partially correct	-
Misleading information containing correct and incorrect statements	-
Completely incorrect	-
Salivary gland tumors (n=46)	
Completely correct and comprehensive	39 (84.8)
Partially correct	7 (15.2)
Misleading information containing correct and incorrect statements	-
Completely incorrect	-

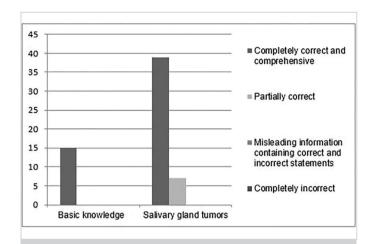


Figure 1. Graphical representation of the answers provided by ChatGPT according to the question categories

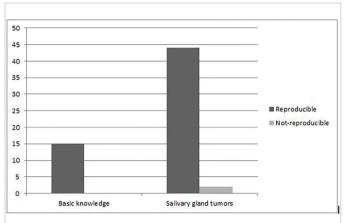


Figure 2. Reproducibility of answers according to the question categories

Table 2. Concordance analysis of 1st and 2nd answers from ChatGPT

Λ.	Reproducibility	Reviewers compliance		
Answers	n (%)	1st answers, n (%)	2 nd answers, n (%)	
Basic knowledge	15 (100)	15 (100)	15 (100)	
p-value	1.00	1.00	1.00	
Salivary gland tumors	44 (95.6)	45 (97.8)	45 (97.8)	
p-value	0.157	0.779	0.779	
Total	59 (96.7)	60 (98.3)	60 (98.3)	
p-value	0.157	0.779	0.779	
*p<0.05				

Table 3. Accuracy rate of answers from ChatGPT according to reviewers

			Completely correct and comprehensive n (%)	Partially correct n (%)	Misleading information containing correct and incorrect statements n (%)	Completely incorrect n (%)	p-value	ICC
	1st answers	1	15 (100)				1.00	1.00
Basic knowledge	1 allswers	2	15 (100)				1.00	
Dasic knowledge	1st answers	1	15 (100)				1.00	1.00
	1 allswers	2	15 (100)				1.00	1.00
		1	41 (89.1)	5 (10.9)			0.538	0.899
	1st answers	2	39 (84.8)	7 (15.2)			0.556	
Salivary gland		3	41 (89.1)	5 (10.9)				
tumors		1	39 (84.8)	7 (15.2)			0.779	0.959
	2^{nd} answers	2	38 (82.6)	8 (17.4)			0.779	0.959
		3	39 (84.8)	7 (15.2)				
		1	56 (91.8)	5 (8.2)				
	1st answers	2	54 (88.5)	7 (11.5)			0.545	0.902
T 1		3	56 (91.8)	5 (8.2)				
Total		1	54 (88.5)	7 (11.5)				
	$2^{\rm nd}$ answers	2	53 (86.9)	8 (13.1)			0.784	0.961
			54 (88.5)	7 (11.5)				

ICC: Intraclass correlation coefficient, p: Mann-Whitney U test p-value

(1: First reviewer / 2: Second reviewer / 3: Third reviewer)

Discussion

In this study, the accuracy and reproducibility of ChatGPT's answers to questions about salivary gland diseases were found to be acceptably high. However, the study was aimed solely at ENT healthcare professionals. There were no questions intended to inform patients or their relatives.

The use of AI models in various fields, especially in healthcare, is increasing. Since ChatGPT was introduced to the market in November 2022, it has become an important source of information, especially for healthcare professionals, to access medical information related to their field. It is important for both clinicians and patients to note that not every response received from ChatGPT should be taken as medical advice (4). Medical information obtained from AI models should not be considered as direct information, but as a reference that directs us to primary information (4). Park et al. (14) stated that ChatGPT helped clinicians in their decision-making processes; however, since the model has the potential to give erroneous information and is mostly based on previously taught data, its limitations should be well known and used carefully in view of patient safety. In a study supporting this statement, ChatGPT gave completely correct answers to eight out of 20 questions about allergic rhinitis for patient education, five partially correct answers and the remaining questions with varying degrees of misinformation. In this study, it was pointed out that it may be risky to rely completely on chatbots such as ChatGPT for medical advice. It was reported that patients should always seek the opinions of health professionals and online resources should only be used as a complementary information tool. ChatGPT and similar chatbots may be useful for patient education, but they can never replace healthcare professionals (15).

Since it is a new application, there are limited number of studies on the use of ChatGPT in otolaryngology. A literature review reveals two studies involving ChatGPT on salivary glands. However, in one of these studies, the effectiveness of ChatGPT in sialendoscopy decision-making was evaluated, not its ability to provide information about salivary gland diseases. For this, ChatGPT answers were compared with the decisions of 10 expert sialendoscopists. A statistically significant agreement was found between ChatGPT and sialendoscopists and it was concluded that ChatGPT was a promising model for clinical decision making, especially for patients suitable for sialendoscopy treatment (16). Another study was conducted by Hoch et al. (6) with questions about 15 sub-branches of otolaryngology, including 138 questions about salivary glands. Our study was a ChatGPT study that included only questions about salivary glands. The questions consisted of two separate question groups: questions about basic knowledge about salivary gland diseases and questions about clinical approach including diagnosis, treatment and management of salivary gland tumors. The purpose of preparing the questions in two different categories was to compare ChatGPT's answers to the more easily accessible basic knowledge and clinical-based questions that are considered to be relatively more difficult and comprehensive. In fact, it is thought that ChatGPT's success in basic medical sciences questions is higher than in clinical-based questions that require making a diagnosis by interpreting the symptoms. This is because information on basic medical sciences can be accessed directly in the literature. In our study, in support of this information, the accuracy rate of ChatGPT on basic knowledge about salivary gland diseases was higher than that of questions about tumors. The findings of the study by Seifen et al. (17) also support this statement. Seifen et al. (17) compared the answers of ChatGPT and a certified specialist in sleep disorders on the interpretation of polysomnography results and treatment recommendations for sleep apnea. There was 97% agreement between ChatGPT and the sleep specialist in the diagnosis of simple cases and 100% agreement in treatment recommendations. In patients with positive airway pressure intolerance, there was 70% agreement between ChatGPT and the sleep specialist in diagnosis and 44% agreement in treatment recommendations. Consistent with our findings, ChatGPT performs better on basic questions, whereas its success rate decreases for more complex topics such as treatment management.

One of the remarkable results of our study is that "misleading information containing correct and incorrect statements" and "completely incorrect" answers were not received to any of the questions. Kuşcu et al. (4) investigated the accuracy and reliability of ChatGPT answers to 154 questions about head and neck cancers. ChatGPT answered "completely correct and comprehensive" to 86.4% (133/154) of the questions. The rates for "partially correct" and "misleading information containing correct and incorrect statements" were 11% and 2.6%, respectively, and no "completely incorrect" answers were received. To evaluate the performance and reproducibility of ChatGPT, Tessler et al. (18) repeatedly asked ChatGPT 24 clinical otolaryngology questions based on the American Academy of Otolaryngology guidelines. While 59.7% (43/72) of the answers were completely correct, only 2.8% (2/72) were incorrect.

The ChatGPT study with the largest question archive in the field of otolaryngology is the study conducted by Hoch et al. (6) with 2,576 questions (479 multiple-choice and 2,097 single-choice questions) on 15 different subbranches of otolaryngology. When ChatGPT's answers to these questions were evaluated, 57% of the questions were answered correctly. ChatGPT had the highest number of correct answers to allergy questions (72%), and the lowest number of correct answers to questions related to legal otolaryngology (29%). In this study, there were 138 singleanswer multiple-choice questions related to salivary glands, and ChatGPT answered 60.9% of these 138 questions correctly and 39.1% incorrectly. Compared to these studies, the accuracy rate of ChatGPT answers was found to be quite high in our study.

Open-ended questions aim to simulate real-life clinical scenarios that clinicians often encounter and assess clinicians' judgement and ability to draw conclusions (19). Some of our questions included real case scenarios. "What should be the surgical approach when intraoperative facial nerve invasion is encountered in a patient with a malignant parotid tumor who had no preoperative signs of facial paralysis?" or "What does it mean if a pathology report for malignant salivary glands includes the term lymphovascular and/or perineural invasion?" are examples to such questions. ChatGPT was observed to be very successful in these questions. The questions in our study and in the study of Kuşcu et al. (4) were open-ended questions. When the results of these two studies were compared with those of Hoch et al. (6) it was observed that ChatGPT was more successful with openended questions rather than single-answer multiple-choice questions. The results of the study by Zalzal et al. (20) also support this statement. In the study by Zalzal et al. (20), ChatGPT was first asked 30 open-ended questions and then 30 single-answer multiple-choice questions about otolaryngology and the answers were checked by two experienced ENT specialists. In the open-ended questions, the ChatGPT model initially gave 56.7% completely correct and 86.7% partially correct answers. When the questions were repeated, the model increased to 73.3% completely correct and 96.7% partially correct. However, ChatGPT performed significantly worse on single-answer multiplechoice questions, with only 43.3% correct answers. When answering open-ended questions, it may be sufficient to give general information about the subject. However, single-answer multiple-choice questions are not based on interpretation and may require knowledge of the finest detail about the subject.

Kuşcu et al. (4) included questions in their study on head and neck cancers that were designed to inform both healthcare professionals and patients/patient relatives. In contrast, the questions in our study were exclusively aimed at healthcare professionals and did not include questions intended to inform patients or their relatives. It is thought that more accurate and adequate results can be obtained by conducting more studies on salivary gland diseases, improving the areas of use of ChatGPT, adding up-to-date information, and improving the database. In addition, studies investigating the accuracy and reliability of the information that patients and their relatives will obtain from ChatGPT on this subject should also be conducted.

In our study, the fact that three different experienced ENT specialists evaluated independently of each other enabled us

to avoid examiner-induced errors and biases. In addition, the fact that there was no statistically significant difference between the scores given by the examiners and that the ICC rate was high for the answers received increased the reliability of the results. It is thought that asking each question to ChatGPT separately, rather than asking two questions in one sentence, will increase reliability and accuracy.

In the study of Kuşcu et al. (4) the reproducibility rate between the answers of ChatGPT was found 94.1%. In another study, the agreement between the answers of the model was found 70.8% and it was stated that there was a reasonable consistency between the answers (18). Lechien and Rameau (21) reported that ChatGPT was a helpful model for editing scientific manuscripts, preparing study protocols, preparing student and assistant exams, and that the consistency of the answers given to repetitive questions in these subjects was high.

Despite its positive aspects, there are also studies showing that ChatGPT has significant shortcomings and needs to be improved over time. The best examples are the studies by Karimov et al. (22) and Hoch et al. (6). In the study by Karimov et al. (22) in which ChatGPT was compared with the UpToDate search engine, it was shown that UpToDate provided more accurate and reliable answers to the findings of 25 different clinical scenarios in the field of otorhinolaryngology than ChatGPT, and that UpToDate, unlike ChatGPT, supported the information it provided with tables, figures and algorithms. Hoch et al. (6) stated that ChatGPT can be a supplementary resource in otolaryngology examinations, but it needs to be further improved due to its error tendency and lack of knowledge in some areas of otolaryngology. Another study in which concerns were expressed about the use of ChatGPT in otolaryngology education was conducted by Long et al. (19). Twenty-one open-ended questions were taken from the sample exam of the Royal College of Physicians and Surgeons of Canada and asked to ChatGPT-4. ChatGPT-4 was successful in this exam with a passing grade. However, the success rate of the answers increased when clues were given. In addition, the fact that some of the answers given were incorrect and contradictory was considered a worrying situation. As a result, it was suggested that additional adjustments should be made to obtain more reliable and accurate answers for clinical practice, as they may provide erroneous information that may threaten patient safety. It is deemed important to integrate ChatGPT into a broader learning strategy. Information from AI models should be supported by textbooks, lectures, and training with subject experts. This combination provides a better learning experience and alleviates potential credibility and ethical concerns regarding the use of AI models alone for educational purposes (6). The fact that ChatGPT compiles information from other sources may cause the information accessed about different sub-branches of medicine to have

different limits. The best example of this is expressed in the article by Hoch et al. (6) who stated that the category of legal issues with the lowest accuracy rate referred to German medical laws and the database used in this field could be more limited, which posed a challenge for ChatGPT. On the other hand, the higher correct response rates in some subbranches of otolaryngology were attributed to the wider data sources and comprehensive pools of accessible information. In addition, topics with a high rate of correct answers, such as allergy, may be topics that ChatGPT users frequently search for medical advice. This is interpreted as regular user interaction improving the performance and the accuracy of the model (6).

In conclusion, although ChatGPT has some shortcomings and despite the concerns, it will continue to be an important source of information in the field of otolaryngology. The fact that it has high accuracy and reproducibility rates in some subjects, as in our study, shows that AI models are promising.

Study Limitations

The use of open-ended questions in this study allowed for more detailed responses; however, it also led to a limitation in the total number of questions that could be included. The study could be further developed by organizing questions under specific subtopics and expanding the question pool. Additionally, the evaluation was limited to text-based responses only, without considering ChatGPT's ability to interpret visual data in medical decision-making. This represents a gap in assessing the model's potential for clinical applications. Lastly, this study focused solely on the educational use of ChatGPT and did not include questions directed at patients or their relatives. Future research that encompasses a wider range of topics and includes visual elements is expected to provide more comprehensive contributions to literature.

Conclusion

The accuracy, reliability and reproducibility of ChatGPT-4 responses related to salivary gland diseases were found to be high. It is considered a reliable resource for healthcare professionals, otolaryngology residents and students. Further studies are needed to improve its role in clinical decisionmaking.

Ethics

Ethics Committee Approval: Since our study was not a study involving humans and animals, ethics committee approval were not required.

Informed Consent: Patient consent were not required.

Footnotes

Authorship Contributions

Concept: Z.K., E.A., Design: Z.K., E.A., G.S.U., A.Ö., Data Collection and/or Processing: Z.K., E.A., G.S.U., A.Ö., Analysis and/or Interpretation: Z.K., E.A., G.S.U., A.Ö., Literature Search: Z.K., E.A., G.S.U., A.Ö., Writing: Z.K., E.A.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Main Points

- Chat Generative Pre-Trained Transformer (ChatGPT) answered 88.5% of the questions "completely correct and comprehensive." None of the answers were scored as "misleading information containing correct and incorrect statements" or "completely incorrect."
- The rate of ChatGPT's answers to repeated questions, i.e., reproducibility, was 96.7%. In other words, the answers obtained by asking the same question again were found to be compatible with each other.
- · Considering the above data, ChatGPT can be a reliable additional resource for otolaryngology professionals on salivary gland diseases.

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Supplementary File:

https://d2v96fxpocvxx.cloudfront.net/34c1fd7d-947b-4954-9ae2-39560c57d146/content-images/a2c51588-86fc-40a9-b404-8cf4022c509f.pdf





Case Report

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Abstract

Phosphaturic mesenchymal tumor (PMT) is a rare mesenchymal neoplasia usually located in the soft tissue and the bone. It is seen in older ages and is most commonly localized in the extremities. Here, we present a rare case of PMT located in the sinonasal region. A 56-year-old male patient was admitted with complaints of congestion in the right nasal cavity and limitation of upward gaze in the right eye. Computed tomography revealed a contrast-enhancing mass with heterogeneous density obliterating the bilateral frontal sinus, the frontoethmoidal recess, the right osteomeatal complex and the right sphenoid sinus, extending to the superior extraconal area in the right orbit. Since the tumor type cannot be determined precisely in the pathological evaluation of incisional biopsy, an excisional biopsy was performed with the preliminary diagnosis of malignancy. But histopathological examination revealed a PMT. PMT is a highly uncommon neoplasm that remains largely unfamiliar to clinicians, surgeons, and pathologists, particularly when arising in rare locations like the sinonasal region. Its histomorphological characteristics can overlap with various other entities, necessitating a broad differential diagnosis.

Keywords: Head and neck surgery, phosphaturic mesenchymal tumor, sinonasal neoplasms, nasal cavity, case report

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Introduction

Phosphaturic mesenchymal tumor (PMT) is a rare neoplasm that is mostly located in the soft tissue and the bone, with the clinic of hyperphosphaturia, hypophosphatemia and osteomalacia (1,2). There is no significant difference between the sexes in terms of incidence rate (3). While the most common locations are the lower and upper extremities, the head and neck region account for approximately 5% of the cases (4). It is most commonly seen in

the sinonasal tract in the head and neck region (2,3). In this report, we describe an uncommon case of PMT located in the sinonasal region.

Case Presentation

A 56-year-old male was admitted to the ear, nose and throat clinic with complaints of congestion in the right nasal cavity and limitation of upward gaze in the right eye, which had been going on for about one and a half year. On the examination of the



patient, a polypoid lesion filling the right nasal cavity and extending into the nasopharynx was observed. Computed tomography (CT) revealed a contrast-enhancing mass with heterogeneous density obliterating the bilateral frontal sinus, the frontoethmoidal recess, the right osteomeatal complex, and the right sphenoid sinus. The mass extended to the superior extraconal area in the right orbit, filled the passage up to the lower nasal turbinate on the right, and resulted in secondary exophthalmos in the right eye (Figure 1). In positron emission tomography-CT examination, heterogeneously increased activity was observed in the mass (SUV $_{\rm max}$: 5.01). Simultaneous biochemical tests revealed hypophosphatemia (1.3 mg/dL; reference range: 2.7-4.5 mg/dL).

Fragmented biopsy material was sent from the mass, and hypercellular spindle cell proliferation was observed microscopically. On immunohistochemical evaluation of the specimen, widespread cyclin D1 and B-cell lymphoma 2 (BCL-2), focal transducin-like enhancer of split 1 and p53 positivity were seen. Pancytokeratin, beta-catenin, S100, smooth muscle actin (SMA), muscle-specific actin, desmin, cluster of differentiation (CD) 68, KP1, CD117, human melanoma black-45 (HMB-45), CD34, signal transducer and activator of transcription 6 (STAT6) epithelial

membrane antigen, progesterone receptor, cytokeratin 7 and synaptophysin were negative. Ki-67 proliferation index was evaluated as 2-3%. Histopathological findings supported a spindle cell mesenchymal tumor, but the findings were not sufficient to make further comments about the tumor subtype.

The patient was planned for endoscopic sinus surgery for total excision of the lesion. The surgery was performed under general anesthesia. The right nasal cavity was completely filled by mass which had eroded the anterior wall of the sphenoid sinus. The mass was removed en-bloc with the help of an endoscope, together with the anterior wall of the sphenoid sinus to which it was attached. The minor defect was repaired with oxidized regenerated cellulose (Surgicel) and muscle tissue. The frontal recess was opened. An incision was made under the right eyebrow. The anterior wall of the frontal sinus was defective. The mucocele filling the frontal sinus was totally excised. The superior and medial walls of the orbit were defective due to the mass. Ophthalmologists attended the surgery. It was decided that the eyeball was intact. Bleeders were controlled using bipolar cautery. His postoperative course was unremarkable, and he recovered well.



Figure 1. The radiological features and extensions of the right sinonasal lesion are shown in preoperative contrast-enhanced (a and b) and non-contrast (c) CT images. The right sinonasal giant mass extends from the frontal (a, short black arrows) and ethmoid sinuses to the nasal cavity (a, black asterisks) and to the orbit through the lamina papyracea (b, white arrows). Due to the obstruction of frontal sinus drainage, a mucocele (a, white arrows) causing ocular pressure (a, long black arrow) has developed. The density of the adipose component of the mass was measured with an oval ROI (c). Approximately 10 months postoperative MRI (d, contrast-enhanced T1-weighted; e, fat-suppressed T2 weighted) shows the disappearance of sinonasal obstruction and orbital compression, while soft tissue considered radiologically as sinonasal residue is seen near the olfactory fossa (asterisk)

CT: Computed tomography, ROI: Region of interest, MRI: Magnetic resonance imaging

Microscopic examination of the excision material revealed a well circumscribed spindle cell proliferation with a hypercellular appearance, showing a patternless, diffuse architecture. The tumor consisted of oval and round cells with generally uniform nuclei, eosinophilic cytoplasm, and unclear cytoplasmic boundaries. There was an edematous zone between the neoplastic cells and the epithelium (Figure 2). Generally small-caliber vascular structures with thin- and thick-wall, edematous hypocellular areas, and occasional hemosiderin deposition were observed within the tumor (Figure 3). Adipose tissue was seen at the periphery of the tumor. In focal areas, there was a grungy calcified matrix (Figure 4). Occasional mitosis was observed, but no necrosis was seen. Special AT-rich sequence-binding protein 2 (SATB2), friend leukemia integration 1

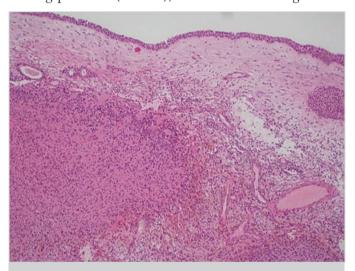


Figure 2. Patternless, hypercellular, well-circumscribed spindle cell proliferation is seen under the edematous respiratory mucosa (hematoxylin and eosin, x100)

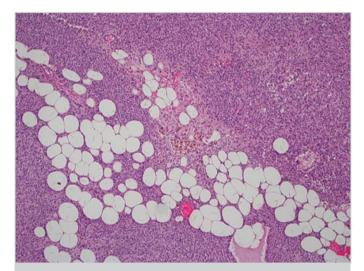


Figure 3. The tumor generally consists of oval and round cells with uniform nuclei, eosinophilic cytoplasm, and unclear cytoplasmic borders. Hemosiderin deposition and fatty tissue are also noted (hematoxylin and eosin, x200)

(FLI-1), BCL2, cyclin D1, ETS-related gene (ERG) and CD56 immunohistochemical markers were diffusely positive in neoplastic cells. D2-40 and melanoma inhibitory activity C2 protein were stained in focal areas. STAT6, S100, HMB-45, keratin, synaptophysin, beta-catenin, SMA and neuron-specific enolase were negative. Ki-67 proliferation index was 4-5%. There was faint nuclear staining with the somatostatin receptor 2A (SSTR2A) marker. fibroblast growth factor-23 (FGF-23) immunohistochemical marker was not performed at the time of diagnosis for technical reasons.

When clinical, histopathological, and immunohistochemical findings were evaluated together, the final diagnosis was compatible with PMT, and simultaneous biochemical tests revealed hypophosphatemia (1.3 mg/dL; reference range: 2.7-4.5 mg/dL). During the postoperative follow-up, the patient's complaints were resolved, and serum phosphate levels returned to normal limits (3.1 mg/dL; reference range 2.7-4.5 mg/dL). No recurrence was observed in the patient's 3-year follow-up. Informed consent was obtained from the patient for this report.

Discussion

PMT, first described in 1947, is a rare neoplasm that ectopically produces FGF-23, which is secreted by osteocytes and maintains phosphate balance of the body (1,5). FGF-23 reduces the expression of sodium/phosphate transporters and provides phosphate excretion with the urine. It prevents the reuptake of phosphate by the proximal renal tubules and reduces the reabsorption of calcium and phosphate from the intestines. Additionally, it reduces the production of 1,25-dihydroxycholecalciferol by inhibiting the 1α -hydroxylase enzyme. The resulting hyperphosphaturia

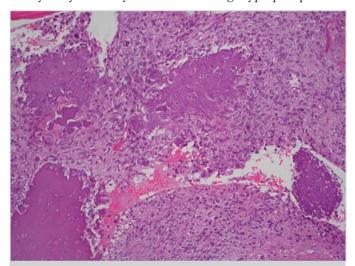


Figure 4. The distinctive and characteristic foci of "grungy" calcification in PMT appear lightly basophilic and granular or flocculent in quality (hematoxylin and eosin, x200)

PMT: Phosphaturic mesenchymal tumor

and hypophosphatemia deflect bone mineralization, and lead to osteomalacia (4,6).

Tumor-induced osteomalacia is extremely rare. Its most common cause are tumors of mesenchymal origin; it is also associated with various syndromes such as McCune Albright syndrome and neurofibromatosis-1. In the last few decades, it has been understood that almost all the cases of tumor-induced osteomalacia are caused by PMT (7).

PMT is mostly located in bone and soft tissue. However, there are few case reports of internal organs and meninges in literature (4). Tumor sizes vary between 1-15 cm but often are smaller than 5 cm. Rare multicentric tumors have been reported (1,8).

In literature, there are 153 cases of PMT described in the sinonasal region, and approximately 80% of the cases were diagnosed between the ages of 30-60 years. The male/female sex ratio is 1:1.05. The most common location is the ethmoid sinus (64.7%), followed by the nasal cavity (50.3%), the maxillary sinus (19.0%), the frontal sinus (16.4%), and the sphenoid sinus (11.8%) (9).

On CT, PMTs appear as round or oval, well-circumscribed, isodense or hypodense soft tissue masses. When the tumor is small, it shows homogenous contrast enhancement (10,11). On magnetic resonance imaging, they are isointense compared to the muscles on T1-weighted imaging, markedly hyperintense on T2-weighted imaging, and markedly enhanced after contrast administration. The increase in tumor size makes the pre- and post-contrast signal properties heterogeneous. Signal-void vascular structures can also be detected in large tumors (12).

In the case presented, the lesion was heterogeneous because of its large size. It has been reported that these lesions may contain adipose tissue pathologically (13). It is noteworthy that adipose tissue was observed in the mass on CT in the presented patient. Other CT features were not different from other sinonasal tumors.

On histopathological examination, the lesion appears hypocellular and consists of round-spindle cells with small nucleoli, indistinct nucleoli, and a calcified-collagenous matrix. Hemangiopericytoma-like vascular structures, hemosiderin pigment, multinucleated giant cells and microcystic changes can be seen in the stroma (3,8). Minimal cytological atypia, low mitotic activity, and absence of necrosis support the benign nature of this neoplasm. Histopathological findings are non-specific in cases seen in the head and neck region, especially in the sinonasal tract. Hypercellular appearance and dense hemangiopericytoma-like vascular structures may

be seen. Also, sinonasal PMTs less often contain calcified matrixes and more often mature adipose tissue. Observation of these histomorphological features in cases located in the sinonasal tract causes difficulty in diagnosis (2,7).

It has originally described four types PMT (mixed connective tissue, osteoblastoma-like, ossifying fibroma-like, non-ossifying fibroma-like types). These are now believed to represent minor morphologic variants. Histopathologic features in our case consisted of the mixed connective tissue type.

Immunohistochemically, the cells are FLI-1, *ERG*, vimentin, CD56, SATB2, SSTR2A, FGF-23, matrix extracellular phosphoglycoprotein, dentin matrix protein 1 positive; and pancytokeratin, CD34, STAT6, HMB-45, nuclear beta-catenin, synaptophysin, S100 and discovered on gastrointestinal stromal tumor 1 negative (1,2). Detection of fibroblast growth factor receptor (FGFR) mRNA by cytokine-inducible SH2-containing protein may help the diagnosis (3,5). In recent years, molecular analyses have shown that fusions of the *fibronectin 1 (FN1)-FGFR1* or *FN1-FGF1* genes play a role in the development of most PMTs (4,5).

Due to the rarity of this entity and the variability in its histomorphological and immunohistochemical features, establishing a differential diagnosis can be challenging. The differential considerations encompass a broad spectrum of neoplasms (2,3) (Table 1).

Although it is a benign lesion, distant metastasis has been reported in rare cases, and local recurrence is observed in incomplete resected tumors (7). Serum phosphate and FGF-23 levels should be monitored in the postoperative period for the possibility of distant metastasis and local recurrence (8).

Conclusion

PMTs are extremely rare neoplasms with diverse clinical manifestations and histopathological features. Due to the limited awareness among clinicians and pathologists, significant challenges and delays can occur in diagnosis. The variability in biopsy findings further complicates the diagnostic process, especially in small biopsy specimens, where a definitive diagnosis may not always be possible. This, in turn, contributes to diagnostic delays. In this case report, we aim to enhance awareness among clinicians and pathologists by presenting a comprehensive review of the clinical, radiological, and pathological characteristics of PMTs.

	Table 1.	Differential	diagnosis	of PMT
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Features	PMT	Osteoblastoma/ osteoid osteoma	Chondromyxoid sarcoma	Low-grade osteosarcoma	Hemangiopericytoma/ solitary fibrous tumor
Clinical	Hypophosphatemia, muscle weakness, associated with TIO	Painful, usually in young adults	Painful, common in pelvis and spine	Young adults, slow-growing mass	Painless mass, often asymptomatic
Paraneoplastic effect	√(TIO)	X	X	X	Χ
Histology	Irregular spindle cells, myxoid stroma, "grungy" calcification	Bone trabeculae, osteoid formation	Chondroid and myxoid areas	Atypical osteoid production	Vascular pattern, CD34 positivity
Calcification	Characteristic "grungy" calcification	Possible	Common	Often present	Generally absent
Immunohistochemistry	FGF-23 (+), SMA (+/-), CD34 (+/-)	Osteoblastic markers (+)	S100 (+)	SATB2 (+), MDM2 (+/-)	CD34 (+), STAT6 (+)
FGF-23 expression	√(high)	X	X	X	Χ

PMT: Phosphaturic mesenchymal tumor, TIO: Tumor-induced osteomalacia, FGF-23: Fibroblast growth factor-23, SMA: Smooth muscle actin, CD34: Cluster of differentiation 34, SATB2: Special AT-rich sequence-binding protein 2, MDM2: Mouse double minute 2, STAT6: Signal transducer and activator of transcription 6

Ethics

Informed Consent: Informed consent was obtained from the patient for this report.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ş.A.İ., H.Ç., Concept: H.T.E., M.F.A., Design: H.T.E., Ö.B., M.F.A., Data Collection and/or Processing: H.T.E., Ö.B., M.F.A., U.T., Analysis and/or Interpretation: H.T.E., M.F.A., Literature Search: H.T.E., U.T., Writing: H.T.E.

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Main Points

- Phosphaturic mesenchymal tumor is a rare benign neoplasm that is mostly located in the soft tissue and the bone.
- The head and neck region accounts for approximately 5% of the cases, and the most common tumor location in this region is the sinonasal tract.
- Clinicians, surgeons, and pathologists often have limited awareness of this condition, particularly when it presents in rare locations like the sinonasal tract.
- Although it is a benign lesion, distant metastasis has been reported in rare cases.
- Total excision of the lesion usually provides effective treatment.

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Post-Traumatic Pseudomeningocele Presenting as a Pulsatile Cyst of the External Auditory Canal

Case Report

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Abstract

Pseudomeningocele is a of cerebrospinal fluid filled, extracranial cystic collection resulting from a dural defect, which may occur congenitally, postoperatively, or after trauma. Post-traumatic pseudomeningocele is rare, particularly in the temporal bone region. We report a 37-year-old woman who presented with progressive hearing loss and intermittent otorrhea, two decades after head trauma. Otoscopy revealed a pulsatile cystic lesion in the right external auditory canal. Imaging showed a ~20 mm tegmen tympani defect with herniation into the tympanomastoid area. Surgical repair involved transmastoid excision of the sac and multilayer reconstruction of the tegmen defect with mastoid obliteration. This case emphasizes the need to consider skull base defects in patients with a history of head trauma and persistent otologic symptoms.

Keywords: Ear surgery, hearing loss, pseudomeningocele, cerebrospinal fluid, temporal bone, otorrhea, case report

Introduction

Pseudomeningocele is a false sac that does not contain brain tissue and is formed when cerebrospinal fluid (CSF) leaks from a dural defect and accumulates in the extracranial space after congenital, surgical, or traumatic events. The sac wall consists of a fibrous structure. It does not contain meninges. There is no cranial tissue inside the sac, only CSF. Its treatment is possible through a surgical repair of the defect. The causes of pseudomeningocele can be categorized into three main groups: congenital, iatrogenic, and traumatic. Congenital cases are generally associated with genetic diseases such as Marfan syndrome and neurofibromatosis (1). Common iatrogenic conditions often result from inadvertent dural tears during spinal surgery. Finally, pseudomeningocele can also occur rarely after head and spinal traumas. Post-traumatic pseudomeningocele cases in the ear are even rarer. Upon conducting a literature review on post-traumatic pseudomeningocele cases found in the external auditory canal (EAC), only two cases were identified (1,2). In conjunction with relevant literature data, we will present the case study of this particular occurrence.

Case Presentation

A 37-year-old female patient presented with complaints of hearing loss and discharge in the right ear. Her medical

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history revealed that her symptoms began following a head trauma sustained approximately 20 years ago while living in her home country. The patient did not seek medical attention at the time, and therefore no medical reports or imaging studies from that period are available. The trauma reportedly involved a horizontal compression of the head from both sides, primarily affecting the superior region of the right temporal bone. The patient reported a gradual worsening of hearing loss over the years, along with intermittent episodes of discharge in the right ear. There is no history of meningitis during this period.

Otoscopic examination of the patient revealed that the right EAC was obliterated by a pulsatile, cystic lesion, and the tympanic membrane could not be visualized. No abnormal findings were observed during the Valsalva maneuver (VM). Pure-tone audiometry demonstrated a moderate conductive hearing loss in the right ear (Figure 1). Computed tomography (CT) and magnetic resonance imaging (MRI) revealed a minimal loss of parenchyma in the right temporal lobe, which was considered to be trauma related. Decreased aeration of the mastoid air cells in the right ear was noted, and a defect measuring up to 20 mm in the tegmen tympani was observed, particularly in sagittal sections (Figure 2). CSF was seen extending into the tympanomastoid cavity and EAC. However, no brain parenchyma was identified within the cystic formation. Based on the CT findings and the homogeneous, low T1 signal intensity and continuity of the CSF on MRI, a preliminary diagnosis of pseudomeningocele was considered (Figure 3). Additionally, evaluation of the ossicular chain revealed absence of the incus.

Based on clinical and radiological findings, the pathology was considered to be a pseudomeningocele, and surgical intervention was planned. Under general anesthesia, a mastoidectomy was initiated using a retroauricular transmastoid approach. Upon reaching the antrum, a pulsatile cystic formation extending from the antrum to the tympanic cavity was observed. The cystic structure was followed, and the mastoidectomy was continued. The lesion was found to originate from a defect of approximately 20 mm in the tegmen tympani (Figure 4). Evaluation of the ossicular chain revealed that the stapes was mobile and located beneath the

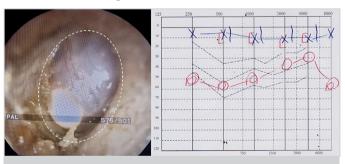


Figure 1. Preoperative endoscopic examination (left) and audiological assessment (right) of the patient

cystic lesion. The malleus was found anterior to the lesion, transposed and disconnected. The incus was not observed and was presumed to have undergone secondary erosion due to the pressure exerted by the lesion. The cystic structure was excised, and no brain parenchyma was identified within it.

To prevent CSF leakage, approximately 2×1 cm of temporalis muscle fascia and composite muscle grafts were harvested. A muscle graft was first placed to completely cover the bony defect, followed by placement of a fascia graft. Subsequently, a superiorly based palva flap was positioned over the fascia graft and reinforced with fibrin glue. Although the materials used were sufficient to repair the tegmen tympani defect, due to the size of the defect and the risk of potential CSF leakage, mastoid obliteration was performed. The mastoid cavity was obliterated using bone cement and bone pate. After removal of the pathological mucosa in the middle ear, a tragal cartilage graft was placed beneath the residual tympanic membrane, positioned over the mobile stapes. Following this, a lumbar drain was placed by the neurosurgery team. The operation was concluded, and the lumbar drain was removed on postoperative day six.



Figure 2. Sagittal section of temporal bone computed tomography showing a bony defect in the tegmen tympani measuring 19.75 mm

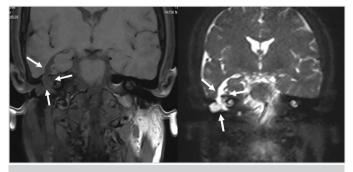


Figure 3. Coronal magnetic resonance images showing a homogeneously cystic lesion, hypointense on T1-weighted (left) and hyperintense on T2-weighted (right) sequences. The lesion extends from a tegmen defect into the middle ear and external auditory canal, suggestive of a pseudomeningocele

Histopathological examination revealed pseudocystic structures consistent with the preliminary diagnosis. No neural tissue was identified. At the patient's oneyear postoperative follow-up, the graft was found to be intact. Pure-tone audiometry demonstrated a significant improvement in the air-bone gap (Figure 5). Informed consent was obtained from the patient.

Discussion

Pseudomeningocele is a persistent condition defined by the extradurally accumulated CSF, resulting from leakage through a dural discontinuity. It can be incidentally detected. Pseudomeningocele is typically iatrogenic, but traumatic and congenital causes can also occur. Examples of iatrogenic causes include direct trauma to the dura, excessive traction, or lacerations from bone fragments during extradural surgeries such as laminectomy (3). Among the congenital causes of pseudomeningocele are diseases such as neurofibromatosis and Marfan syndrome. Individuals with neurofibromatosis and Marfan syndrome exhibit a more elastic dural layer. Consequently, they are more susceptible to pseudomeningocele formation as a result of increased vulnerability to damage in the event of any injury. Additionally, congenital pseudomeningocele is often associated with defects in vertebral bodies (3).

Taveras and Ransohoff (4) reported that the development mechanism of pseudomeningocele involves the compression of the dura mater by pulsatile cerebral pressure following a dural opening caused by head trauma, leading to the leakage

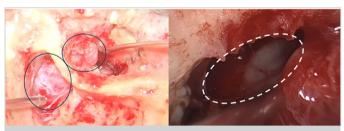


Figure 4. Intraoperative images showing a lesion extending from the mastoid cavity into the external auditory canal (left), and a tegmen defect (right)

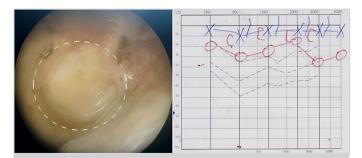


Figure 5. Postoperative one-year endoscopic examination (left) and audiological assessment (right) of the patient

of CSF into the subcutaneous space through the damaged dura mater. In cases of dura mater damage, a spherical valve-like mechanism inhibits the physiological outflow of the CSF, resulting in progressive cyst enlargement and the development of a fibrous capsule (5). Traumatic pseudomeningocele can occur in various ways. In the case presentation by Scott and Merrell (5), a pseudomeningocele developing over time in the EAC following a skull fracture was described. In this presentation, they noted that the patient's symptoms and signs of chronic otitis media began following a previous head trauma.

Diagnosis can be established through a detailed medical history, physical examination, and radiological imaging. In the medical history, suspicion for pseudomeningocele or meningocele should be raised in patients with a history of head trauma or traffic accidents, those presenting with spontaneous CSF otorrhea, individuals with conductive hearing loss confirmed by audiologic evaluation particularly when accompanied by pulsatile tinnitus as well as patients exhibiting symptoms of meningitis or presenting with a cystic lesion that changes in size with the VM (6). In the literature, two similar cases have been reported in which physical examination revealed non-pulsatile lesions and no changes with the VM. In contrast, the lesion in our case was pulsatile. One of the previously reported cases demonstrated conductive hearing loss, while the other had sensorineural hearing loss. Radiological imaging in both cases revealed a defect in the tegmen with a continuity extending into the mastoid and middle ear cavities (1,2).

Radiological diagnosis can be achieved through CT, which may reveal a defect in the tegmen, and MRI, which can demonstrate continuity of brain tissue extending into the tympanic cavity or mastoid antrum (7). Additionally, CSF typically exhibits a homogeneous, fluid-like appearance on MRI, characterized by low signal intensity on T1weighted images. Previous studies have reported that most pseudomeningocele do not exert a mass effect on the thecal (dura/dural) sac, as they are generally continuous and isobaric in nature. The combined use of CT and MRI has been shown to yield an accurate initial diagnosis in approximately 89% of the cases (8-10). In the differential diagnosis, true meningocele or meningoencephalocele should be considered. Evaluation should include determining whether the lesion is pulsatile or changes in size with the VM. Furthermore, MRI is essential for assessing the location and extent of the cystic lesion (3).

The defect responsible for pseudomeningocele can be repaired using either a transcranial or a transmastoid approach. The transcranial (craniotomy) approach offers advantages such as superior visualization of the defect and easier manipulation of the temporal lobe. However, its main drawback is its invasiveness and the associated risk of cranial

complications. As a less invasive alternative, the extracranial

transmastoid approach enables access to the defect through a retroauricular incision and mastoidectomy (4). In the first of the two previously reported cases, a similar transmastoid approach was employed; however, mastoid obliteration was not performed due to the small size of the defect and the absence of pulsation. In the second case, surgical intervention was not undertaken as the patient declined surgery (1,2). Various grafting materials may be used in both surgical approaches, including temporalis muscle, temporalis fascia, autologous cartilage, bone tissue, and fat. To date, no definitive superiority among these materials has been established in the literature. The key factor in achieving successful surgical outcomes is the implementation of a multilayer repair technique. Single-layer repairs have been associated with poor long-term outcomes. In contrast, the use of at least two graft layers whether autologous, synthetic, or a combination of both has significantly improved the success rate of primary closure. Moreover, to prevent CSF otorrhea, it is advisable to seal any exposed intracranial air cells or small bony dehiscence in the tegmen during the initial surgical procedure. In cases where CSF leakage is present, obliteration of the mastoid air cells may be beneficial to ensure closure of multiple or unidentified leak sites (11,12).

In our case, we opted for the less invasive extracranial transmastoid approach. Due to the extensive size of the defect, multilayer repair was performed using a temporalis muscle graft, temporalis fascia graft, superiorly based Palva flap, and fibrin glue, followed by mastoid obliteration.

Conclusion

The detection of a pulsatile, cystic mass in the EAC associated with hearing loss, particularly in patients with a history of previous otologic surgery or head trauma, should raise clinical suspicion of pseudomeningocele, a rare pathological condition.

Ethics

Informed Consent: Informed consent was obtained from the patient.

Footnotes

Authorship Contributions

Surgical and Medical Practices: O.Ö., A.Ç., K.H., Ö.Y., Concept: O.Ö., A.Ç., K.H., Design: O.Ö., K.H., Data Collection and/or Processing: O.Ö., A.Ç., Ö.Y., Analysis and/or Interpretation: O.Ö., K.H., Literature Search: E.C.Ö., E.D., Writing: O.Ö., A.Ç.

Conflict of Interest: The authors declare that they have no conflict of interest.

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Main Points

- Post-traumatic pseudomeningocele is an extremely rare condition.
- It is a sac deformity in which cerebrospinal fluid leaks through a dural defect and collects in the extradural space. The collection is not a true arachnoid-lined sac and does not contain brain tissue.
- The patient may present to the clinic with a pulsatile cyst in the external auditory canal and conductive hearing loss. Definitive treatment involves surgical repair of the defect.

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Tracheobronchial Aspiration of a Tracheostomy Tube Cleaning Brush in a Laryngectomized Patient

Case Report

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Abstract

Tracheobronchial foreign body aspiration is rare among patients who have undergone total laryngectomy. In this report, we describe a case involving a 75-year-old laryngectomized male patient who aspirated a tracheostomy tube cleaning brush. The brush was successfully removed without any complications in an office setting with the assistance of flexible and 70-degree rigid endoscopes, as well as forceps.

Keywords: Airway obstruction, foreign body, laryngectomy, respiratory aspiration, tracheostomy, case report

Introduction

Patients who have undergone total laryngectomy are at an increased risk for tracheobronchial foreign body aspiration (TBFBA) due to the direct accessibility of the stoma located at the front of the neck (1). However, reports of TBFBA in laryngectomized patients are relatively rare in the literature, with most documented cases involving the aspiration of voice prostheses (2). In this case report, we describe tracheobronchial aspiration and subsequent removal of a tracheostomy tube cleaning brush in a laryngectomized patient.

Case Presentation

A 75-year-old male patient who had undergone total laryngectomy and bilateral neck dissection for laryngeal squamous cell carcinoma two years earlier presented to our clinic with severe respiratory distress approximately one hour after

aspirating a brush used for cleaning a tracheostomy cannula. Examination of the trachea revealed that a tracheostomy tube cleaning brush, approximately 15 cm in length, was lodged within the trachea, nearly obstructing the left main bronchus (Figure 1). The metal part of the brush was gently grasped with forceps and carefully removed with the aid of a flexible fiberoptic endoscope and a 70-degree endoscope (Figure 2). Remarkably, the patient tolerated the procedure well and without the need for any topical anaesthesia, resulting in immediate recovery without complications. Radiological examination could not be performed due to the patient's respiratory distress, which required urgent intervention. The patient had no previous history of any medical conditions aside from laryngeal carcinoma, including mental health disorders. Although we suspected that the patient had used a brush to clean stomal and tracheal secretions and that the incident occurred during

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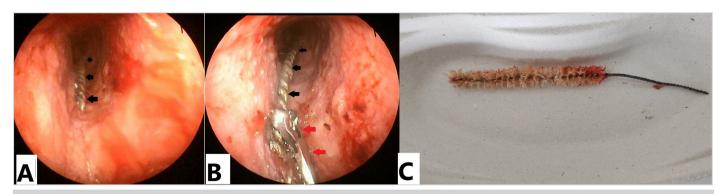


Figure 1. The aspirated foreign body. **A)** 70-degree rigid endoscope showing the metal part of the brush located in the trachea (black arrows), **B)** The metal part of the brush was gently grasped with forceps (red arrows), **C)** The aspirated tracheostomy tube cleaning brush

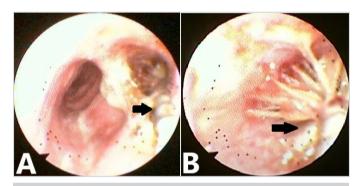


Figure 2. A-B) A flexible endoscope showing the near-total obstruction of the left main bronchus with brush (black arrows)

this process, the patient refused to provide any details about how it happened and did not wish to give an explanation. Informed consent was obtained from the patient for the writing of this case report.

Discussion

TBFBA in a laryngectomized patient can be a life-threating condition due to the occurrence of severe respiratory distress. In such a condition, a prompt intervention for the removal of the foreign body is mandatory. Although a permanent stoma theoretically increases the susceptibility of laryngectomized patients to TBFBA, fortunately, it remains a rare occurrence in their daily lives (2). In 1982 Cannon (3) documented the first case of an aspirated foreign body-a tracheostomy stomal button used to maintain stoma patency-following total laryngectomy. Since then, a variety of foreign bodies aspirated by laryngectomized or tracheostomized patients has been reported in the literature, including a voice prosthesis, a voice prosthesis cleaning brush, a Phillips-head screw, fractured metallic tracheostomy tube or fractured polyvinyl chloride tracheostomy tube, an inner cannula, and a wooden stick (1,2,4-9). In this case report, we described the tracheobronchial aspiration of a 15-cm-long tracheostomy tube cleaning brush. Gündüz et al. (10) reported a similar case, and to the best of our knowledge, we are providing

the second published case of a laryngectomized patient with tracheostomy tube cleaning brush aspiration. In the report by Gündüz et al. (10), the patient stated that the brush was aspirated during the cleaning of a tracheostomy tube. The patient presented to the hospital 15 days after aspiration with shortness of breath, fever, and cough. On the contrary, our patient was admitted to our outpatient clinic with severe respiratory distress that required an immediate intervention to remove the foreign body. However, we were unable to determine how the patient aspirated the cleaning brush. Uzaslan et al. (9) reported a case of tracheobronchial aspiration involving a wooden stick covered with cotton in a laryngectomized patient who had been using it to clean secretions. In our case, although we suspected that the patient had also aspirated the cleaning brush while cleaning the secretions around the stoma, the patient refused to explain how the aspiration had occurred. Despite further questioning, he did not provide any details about the incident. The patient came to the outpatient clinic alone, and we later learned that the patient lived alone.

The clinical symptoms of TBFBA in laryngectomized and tracheostomized patients are highly variable, ranging from asymptomatic or mild symptoms to severe cases of acute respiratory distress (1,8,11). In the four-case series reported by Mahattanasakul et al. (5), all patients experienced suddenonset dyspnea, two had severe cough, and one developed cardiac arrest. In the three cases who did not develop cardiac arrest, the average duration of symptoms ranged from two hours to two days. In such patients, the sudden onset of respiratory distress should immediately raise concern for the possibility of foreign body aspiration. A detailed clinical history as well as physical and radiological examinations are commonly done for the diagnosis (12). Rigid and flexible bronchoscopies are the preferred techniques for diagnosing and treating foreign body aspiration (6). However, particularly rigid bronchoscopy can be more challenging in laryngectomized patients because of the position of the stoma, stomal narrowing and the stiffening of neck tissues

often caused by radiotherapy (1). In cases of severe respiratory distress, particularly in outpatient settings, flexible and/or rigid endoscopy may serve as the primary diagnostic tool. In a similar scenario, in the presented case, flexible and 70-degree rigid endoscopes were employed as the first-line diagnostic approach, and simultaneous intervention to remove the foreign body was performed successfully. The procedure was surprisingly well-tolerated by the patient without utilizing any topical anaesthesia or intravenous sedation.

Conclusion

We treated a patient with tracheobronchial aspiration to remove a tracheostomy tube cleaning brush in an office setting with the assistance of flexible and 70-degree rigid endoscopes. TBFBA in laryngectomized patients can lead to severe respiratory distress, necessitating urgent hospital transport and prompt intervention, which can be lifesaving. In such cases, flexible and rigid endoscopes can serve as practical and effective tools for diagnosing and removing foreign bodies without causing any severe complications.

Ethics

Informed Consent: Informed consent was obtained from the patient for the writing of this case report.

Footnotes

Authorship Contributions

Concept: N.Ü., A.K., A.B., M.Y., İ.Ö., Design: N.Ü., A.K., A.B., M.Y., İ.Ö., Data Collection and/or Processing: N.Ü., A.B., İ.Ö., Analysis and/or Interpretation: N.Ü., A.B., İ.Ö., Literature Search: N.Ü., Writing: N.Ü., A.B.

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Main Points

- · Rare but serious condition: Tracheobronchial foreign body aspiration (TBFBA) is rare in laryngectomized patients but can lead to life-threatening respiratory distress.
- · Uncommon foreign body: This case report presents a unique instance of a tracheostomy tube cleaning brush aspiration, making it the second reported case in the literature.
- Urgent intervention required: TBFBA should be considered in any laryngectomized patient presenting with sudden respiratory distress, necessitating immediate removal of the foreign body.
- · Successful removal without anesthesia: The foreign body was successfully extracted in an office setting using flexible and 70-degree rigid endoscopes without the need for anesthesia or sedation.
- · Endoscopic approach as a primary tool: In cases of severe respiratory distress, flexible and rigid endoscopes and forceps can be valuable first-line diagnostic and therapeutic tools that help to avoid the need for more invasive procedures.

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