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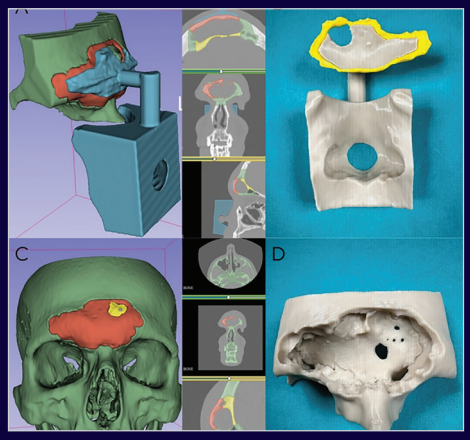

Patient-Specific 3D Models for Open Frontal Sinus Surgery: Enhancing Precision with Facial Mask-Guidance

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Why Diamond Open Access Matters: A Call to ENT Researchers

Editorial

Taner Kemal Erdağ

Otorhinolaryngology, Private Practice, İzmir, Türkiye

Keywords: Open access, academic publishing, article processing charges, research funding, otorhinolaryngology, indexing

Over the past twenty years, open access publishing has been enthusiastically embraced as a means of making scientific knowledge accessible to a wider audience. Initially, it was seen as a significant opportunity by the academic world (1). However, over time, while this model provided free access to readers, it also created significant financial burdens for authors due to the publication fees they incurred. Today, the vast majority of open access journals require authors to pay article processing charges (APCs), which typically range from $250 to $3,500 per accepted article (2,3).

This situation has created a major challenge, particularly for researchers in low- and middle-income countries where physician salaries are low and funding systems supporting scientific research are underdeveloped. In many countries, APCs can exceed physician salaries, making it very difficult for scientists to submit their work to high-quality journals. As a result, the ideal of "equality of access to information" at the heart of the "open access" concept is not being fully realized (2,4).

At this point, "diamond open access," also referred to as "platinum open access," a lesser-known but more inclusive model of open access publishing, has come to the fore. In this model, there are no fees for either readers or authors. However, the most significant challenge for this model is sustainability: very few journals worldwide have adopted it, and many of those that have are supported by universities, civil society organizations, and research institutions (5-7).

The Turkish Archives of Otorhinolaryngology, the official scientific publication of the Turkish Society of Otorhinolaryngology-Head and Neck Surgery, has been a diamond open access journal since 2013, charging no fees to readers or authors. Our association has borne this financial burden for years, dedicating itself to promoting scientific publishing and providing an equal publishing environment for both national and international researchers.

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Currently, 73 journals in otorhinolaryngology are indexed in the Web of Science (Science Citation Index Expanded and Emerging Sources Citation Index), 27 of which are open access. Among these 27 open access journals, only a few operate under the Diamond Open Access model, which does not charge authors. The Turkish Archives of Otorhinolaryngology is one of these few journals (8).

Moreover, our journal offers significant advantages not only through its free publication policy but also through the short publication timeline and increased visibility. Accepted articles added to the journal's ahead of print section become available on PubMed on the same day or the following day, which greatly enhances their international visibility in a very short time. The relatively short time between submission and the initial decision, and the publication of accepted research articles within 12-15 weeks, are other important advantages for authors.

In conclusion, the Turkish Archives of Otorhinolaryngology offers authors significant advantages by providing free publication in a reputable, indexed journal, international visibility upon acceptance, and a short, predictable publication process. The diamond open access model, which is uncommon today, strongly supports the equitable sharing of scientific knowledge. Greater recognition of this model's value will significantly help reduce geographical and economic barriers to scientific production. Given the advantages outlined above, we invite all local and international scientists to submit to our journal, which operates under the diamond open access model.

Footnotes

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Union for International Cancer Control 9th Edition TNM Classification for Head and Neck Malignancies: What is New?

Commentary

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Keywords: Head and neck neoplasms, neoplasm staging, TNM classification, squamous cell carcinoma, prognosis

The 9th edition of the Union for International Cancer Control (UICC) tumor-node-metastasis (TNM) classification of malignant tumors implements substantial, evidence-based revisions to the staging protocols for head and neck malignancies. Driven by the expanding evidence base and the imperative for refined prognostic stratification, these modifications ultimately aim to enhance the accuracy and clinical utility of the staging system within this complex anatomical region.

Building on the major innovations introduced in the 8th edition—notably, the incorporation of depth of invasion for oral cavity cancers, extranodal extension (ENE) in nodal staging, and the establishment of distinct staging for human papillomavirus (HPV)-associated oropharyngeal carcinoma (OPC), the 9th edition further advances disease stratification across multiple key subsites (1,2). Collectively, these updates represent a deliberate and strategic evolution from a purely anatomical descriptive framework toward a hybrid prognostic model that integrates robust biological and morphological variables while rigorously maintaining global applicability.

Despite anticipated implementation challenges, including variability in imaging quality, molecular testing availability, and interobserver reliability—the 9th edition provides a meaningful advancement in head and neck cancer staging. Its widespread adoption is expected to strengthen prognostic precision, improve treatment alignment, and enhance the comparability of clinical research across institutions. This commentary summarizes the notable modifications introduced in the 9th edition of the TNM classification for head and neck malignancies.

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Nasopharyngeal Carcinoma

A multicenter study of 4,900 patients by Pan et al. (3) demonstrated that advanced image-identified ENE (iENE) is a critical prognostic determinant in nasopharyngeal carcinoma (NPC). Accordingly, the 9th edition designates advanced iENE, defined as tumor invasion into adjacent structures such as the skin, the muscle, the salivary glands, and/or neurovascular bundles-as a criterion for N3 classification, reflecting its association with markedly poorer survival.

Additionally, patients presenting with distant metastasis (M1) are now stratified into M1a (≤3 lesions) and M1b (>3 lesions). This subdivision directly addresses the considerable heterogeneity within the M1 category, significantly improving prognostic discrimination among metastatic cases (3,4). Stage grouping has also undergone major restructuring for NPC. While the T1-T2 N0-N1 subgroups demonstrated comparable five-year overall survival, they were consolidated into stage I but further subdivided into IA (T1-T2N0) and IB (T1-T2N1) to retain distinction based on adjusted hazard ratios, particularly following adjustment for chemotherapy use. To optimize hazard differentiation, former stages III and IVA are down-classified to II and III, respectively. Critically, M1 disease is now exclusively assigned to stage IV, eliminating the former conflation of advanced locoregional disease with distant metastatic disease. Prognostication within this final category is further refined by its subdivision into IVA (M1a, ≤3 lesions) and IVB (M1b, >3 lesions).

HPV-Associated OPC

A separate staging system for HPV-associated OPC was first introduced in the 8th edition due to its distinct biological behavior and significantly more favorable prognosis compared to HPV-negative OPC. However, a subset of patients previously classified as stage I or II experienced poorer outcomes than expected. The 9th edition addresses this gap by refining stage groups to improve prognostic performance and better align with contemporary treatment strategies.

One of the most significant updates for HPV-positive OPC is the incorporation of iENE into the clinical regional lymph node involvement (N category). Image-iENE has been demonstrated to be an independent, adverse prognostic factor for HPV-positive OPC (5). In the 9th edition, the presence of iENE on pretreatment imaging results is an upstaging of the N category, even if lymph node sizes or laterality criteria are unchanged. Lymph nodes demonstrating clinical or imaging-defined ENE are assigned a minimum nodal category of clinical N2, irrespective of nodal size or number. In the pathological classification, while the 8th edition relied solely on the number of metastatic lymph nodes, the 9th edition recognizes pathological ENE (pENE), defined as tumor unequivocally extending through the lymph node capsule into the surrounding connective tissue, as a critical prognostic determinant. The revised pathological N categories therefore incorporate both the number of metastatic lymph nodes and the presence of pENE, yielding improved stratification and more prognostically informative stage groups for surgically treated HPV-associated OPC.

Salivary Glands

In the 9th edition, carcinomas originating from the minor salivary glands of the upper aerodigestive tract are classified according to the rules for the tumors of the salivary glands. The principal updates focus on refining the N category to improve prognostic discrimination through the formalized incorporation of both metastatic lymph node count and ENE status into both clinical and pathological staging. Patients with one to three metastatic nodes and no ENE are classified as clinical N1, whereas those with more than three nodes or any node demonstrating ENE are categorized as clinical N2.

The primary tumor (T category) remains largely consistent with the 8th edition, maintaining size-based criteria. Importantly, extraparenchymal extension, which elevates the T stage to T3, is strictly defined as clinical or macroscopic evidence of soft tissue or nerve invasion, excluding structures specified under T4a and T4b. This distinction underscores the requirement for gross or imaging-defined invasion, not merely microscopic extension.

Future Directions and Practical Limitations

The revisions in the 9th edition represent a cautious but deliberate transition toward integrating critical prognostic determinants, such as viral status [HPV, Epstein-Barr virus (EBV)], iENE, and metastatic burden into the final stage grouping. For salivary gland and nasopharyngeal cancers, the new system is predicated on revised criteria leveraging updated imaging and anatomical characteristics; similarly, for HPV-associated oropharyngeal cancers, the staging has been specifically developed to better reflect their distinct biological behavior and prognosis. This unified approach judiciously balances contemporary evidence with the necessary constraint of global applicability, consciously avoiding reliance on molecular markers not yet feasible in all resource settings.

Notwithstanding these advancements, several practical challenges remain inherent to the implementation of the 9th edition:

• **Imaging Standardization:** Global variability in the availability and quality of high-resolution imaging modalities may compromise the reliability of staging, particularly the assessment of iENE.

• **Testing Heterogeneity:** Differences in HPV/EBV testing methods and availability may reduce inter-institutional comparability and accuracy of stage assignment.

• **Resource Intensity:** Retrospective re-staging for clinical audits or research purposes will likely require substantial resource allocation and effort.

• **System Complexity:** The increased incorporation of sophisticated prognostic variables risks heightening system complexity and, consequently, increasing interobserver variability in staging decisions.

These limitations collectively underscore the critical importance of continued professional education and the urgent need for standardization of imaging protocols and pathological assessment to ensure the system's intended benefits are fully realized.

Conclusion

The 9th edition of the UICC TNM classification for malignant tumors signifies a pivotal and necessary shift in the staging philosophy for head and neck malignancies by moving decisively toward a hybrid prognostic model. By successfully integrating contemporary evidence, specifically viral status (HPV/EBV), iENE, and metastatic burden-into the final stage groupings for key subsites (NPC, HPV-OPC, and salivary glands), the system achieves superior prognostic stratification. While the new system introduces complexity and highlights ongoing challenges related to global standardization of high-resolution imaging and testing methods, these limitations do not diminish the value of the revisions. The UICC TNM 9th edition represents a significant and pragmatic leap forward, reinforcing its status as the global standard for cancer classification. Ultimately, its successful implementation hinges on continued professional education and the sustained drive toward standardized pathological and radiological assessment worldwide.

Acknowledgement: The author utilized ChatGPT (version 5.1; OpenAI Inc., San Francisco, CA, USA) exclusively for grammar and language editing to improve clarity and readability. The tool was employed solely for linguistic refinement and did not contribute to the generation or interpretation of scientific content.

Footnotes

Authorship Contributions

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Vestibulo-ocular Reflex Gain Asymmetry in Unilateral Ménière's Disease: Insights from HIMP and SHIMP Tests and Correlations with Audio-vestibular Findings

Original Investigation

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Abstract

Objective: The purpose of this study was to calculate the vestibulo-ocular reflex (VOR) gain asymmetry ratios obtained from head impulse paradigm (HIMP) and suppression HIMP (SHIMP) tests in patients with unilateral definite Ménière's disease (MD) and to investigate their relationships with clinical, audiologic and vestibular parameters.

Methods: The study included 35 (18 female, 17 male) unilateral MD patients with a median age of 50 (24-65). All patients underwent pure-tone audiometry, video-nystagmography, including caloric test, and video head impulse test. The VOR gain asymmetry indices were computed and the demographic, clinical and audio-vestibular variables were analyzed.

Results: Mean HIMP lateral canal VOR gain asymmetry ratio was -11.27±25.276 and mean SHIMP lateral canal VOR gain asymmetry was -15.63±23.993. While differences in caloric response asymmetry ratios were observed among hearing loss severity groups (p=0.05), HIMP and SHIMP asymmetry ratios did not differ. VOR gain asymmetry ratios showed significant differences among dizziness handicap inventory groups, SHIMP saccade group and visually enhanced VOR saccade group (p<0.05). Significant correlations were found between SHIMP and caloric asymmetry ratios with air-conduction pure-tone averages (r=-0.337, p=0.047 and r=-0.358, p=0.035), and between HIMP lateral canal asymmetry and hearing at 500 Hz (r=-0.362, p=0.032).

Conclusion: Our study confirmed that VOR gain asymmetry assessed by SHIMP and HIMP differs across hearing levels; and further that caloric response asymmetry is also correlated with audio-vestibular parameters in patients with unilateral MD.

Keywords: Ménière's disease, vertigo, caloric test, head impulse, vestibulo-ocular reflex

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Introduction

Ménière's disease (MD) is an idiopathic inner ear disorder characterized by episodic vertigo, fluctuating sensorineural hearing loss, tinnitus, and aural fullness. The underlying pathophysiology is commonly attributed to endolymphatic hydrops. Most patients are initially

unilateral, but bilaterality can increase to 50% with disease progression (1). A careful history taken during and between attacks, clinical evaluation, and vestibular testing are crucial for diagnosis. The diagnostic criteria for the disease were defined by the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) in 1995 and revised in 2015 (2).

Vestibular system functions are generally evaluated by testing the two most basic reflexes, the vestibulo-ocular reflex (VOR) and the vestibulo-spinal reflex (VSR). The major tests for VOR are the video head impulse test (vHIT), the video-nystagmography (VNG) and the caloric test, and for VSR the vestibular-evoked myogenic potentials and the postugrography. Vestibular testing in MD often shows discrepancies between low-frequency and high-frequency results due to the differential sensitivities of the tests. The most significant finding in vestibular testing for MD is unilateral vestibular hypofunction detected on bi-thermal caloric testing (3). However, normal caloric test results can be obtained even during attacks in nearly half of the patients. There are two paradigms: the conventional head impulse paradigm (HIMP) and the suppression HIMP (SHIMP). vHIT quantifies high-frequency angular VOR and yields canal-specific gain and gain asymmetry with characterization of overt/covert catch-up saccades. The SHIMP test has emerged in recent years as an alternative to HIMP to overcome the difficulties in calculating VOR gain due to covert saccades (4).

During VNG, a low-frequency test, suppression VOR is used to evaluate how well the cerebellum can suppress VOR when visual fixation is present. Impaired VOR suppression points to cerebellar dysfunction; recovery of suppression over time reflects central compensation after peripheral loss (5). Visually enhanced VOR (vVOR) probes visuo-vestibular integration, with a moving visual target during head motion, normal subjects show near-unity vVOR gain. Deviations inform the balance between visual and vestibular drive and may flag specific disorders (6).

However, data on VOR gain asymmetry in all semicircular canal planes in MD and how it correlates with demographic, clinical and audio-vestibular findings remain limited. The aim of this study was to investigate the HIMP and SHIMP VOR gain asymmetry and to evaluate correlations with clinical parameters in unilateral MD patients with canal paresis.

Methods

The study was approved by the Clinical Research Ethics Committee of the University of Health Sciences Türkiye, Bursa Yüksek İhtisas Training and Research Hospital (approval no: 2011-KAEK-25 2023/04-10, date: 19.04.2023). Informed consent was obtained from all the patients and subjects. The patients included in the nested cohort prospectively were those diagnosed with definite MD according to the guidelines of the Equilibrium Committee of the AAO-HNS (2).

The study was conducted with a nested cohort of a certain disease and without a control group as the study investigated the asymmetry between the affected ear and the self-control ear individually in each patient. Power analysis for two-tailed nonparametric testing with Cohen's d=0.50 (medium effect), α=0.05, power=0.80 features, the minimum sample size was calculated as 32 patients.

Patients

Individuals diagnosed with MD who presented to the ear, nose and throat outpatient clinics of a tertiary teaching hospital for routine follow-up between May 2023 and November 2023 were included in the study. Previous files of the patients were reviewed retrospectively, and demographics, disease-related clinical data, and audio-vestibular test results were noted. Pure-tone audiometry, VNG (including caloric testing), and vHIT (HIMP and SHIMP) results and tinnitus handicap inventory (THI) and dizziness handicap inventory (DHI) scores obtained at their visits in the inter-attack period were also recorded.

The inclusion criteria were:

1. age between 18 and 65 years

2. previous diagnosis of unilateral MD

3. had visited the clinic at earliest 1-month since the last attack

4. MD with unilateral canal paresis and normal ear examination

The exclusion criteria were:

1. external ear or middle ear pathology detected in otoscopy

2. type B and C tympanogram

3. conductive or mixed type hearing loss in pure-tone audiometry

4. pathological findings other than endolymphatic hydrops in magnetic resonance imaging

5. disconjugate eye movements

6. history of ototoxic or vestibulo-otoxic medication

7. central pathology

8. overlap syndrome, associating other vestibular disorders

Demographic characteristics such as age, sex, employment status, smoking, alcohol use, and comorbidity of the patients

were recorded. Anamnesis was obtained by questioning the onset time, course, and accompanying symptoms of hearing loss. In the physical examination, middle ear effusion, infection, and some neoplasms were evaluated, and a comprehensive evaluation of cranial nerves and cerebellar functions was done.

Audio-vestibular Tests

All audiometric evaluations were conducted in single-walled silent booths. Tests in the booth were performed using a clinical audiometer (Interacoustics AC40, Denmark). Pure-tone air-conduction thresholds (ACT) in the range of 250-8000 Hz were obtained with supra-aural headphones (Telephonics TDH-50), while bone-conduction thresholds at 500-8000 Hz range were obtained with a bone vibrator (Radioear B71). The pure-tone average (PTA) was calculated as the mean threshold of 500, 1000, 2000, and 4000 Hz. Tympanometry was performed with a 226 Hz probe tone at 80 dB intensity. Acoustic reflexes were assessed at 500, 1000, 2000, and 4000 Hz using a 100 dB stimulus.

All participants underwent the VNG battery including bithermal caloric test and the vHIT at lateral, right anterior-left posterior and left anterior-right posterior canal planes. Vestibular tests were recorded with the impulse control system (ICS)-impulse version 4.0 (Otometrics A/S, Taastrup, Denmark) VNG and vHIT device and ICS AirCal (GN Otometrics, Taastrup, Denmark). Caloric tests were carried out with air stimulation at 50 °C and 24 °C for 60 seconds. Canal paresis and directional superiority were calculated using Jongkees' formula [(total right ear response - total left ear response/total right + left ear response) x 100] for canal paresis. For canal paresis, the difference in nystagmographic response between both sides was determined as at least 20%.

Calculation of VOR Gain and Caloric Response Asymmetry

The asymmetry ratios for VOR gains of lateral, posterior and anterior semi-circular canals were calculated with the formula below:

Asymmetry ratio (%) =2x (ipsilateral canal VOR gain - contralateral canal VOR gain)/(ipsilateral canal VOR gain + contralateral canal VOR gain) x 100.

The asymmetry ratios for caloric responses were calculated with the formula below:

Asymmetry ratio (%) =2x (ipsilateral total caloric response - contralateral total caloric response)/(ipsilateral total caloric response + total contralateral caloric response) x 100.

In this formula and in all audio-vestibular test results, ipsilateral refers to the affected ear (diseased ear).

Quality of Life Assessment

The Turkish version of the THI assesses the emotional, catastrophic, and functional effects of tinnitus (7). The survey consists of 25 questions: a "yes" answer scores 4 points, "sometimes," scores 2 points, "no," scores 0 points (8). The classification according to total scores are: "no or slight handicap (0-16)," "mild handicap (18-36)," "moderate handicap (38-56)," "severe handicap (58-76)," and "catastrophic handicap (78-100)."

The DHI defined by Jacobson and Newman (9) and whose reliability and validity have been studied in Turkish was applied (10). The DHI consists of 25 questions regarding the presence of dizziness to determine the physical, emotional, and functional effects of vestibular disorders during the performance of certain movements. Dizziness is scored as 4 if always present, 2 if sometimes present and 0 if never present. The total score varies between 0 (no disability) and 100 (maximum disability) and three classes are defined indicating mild (0-30), moderate (31-60) and severe (61-100) degrees (10).

Statistical Analysis

The distribution of continuous variables was assessed using the Shapiro-Wilk test. Depending on the results of the normality analysis, continuous variables were summarized as mean±standard deviation (SD) for normally distributed data, or as median with minimum-maximum values for non-normally distributed data. Categorical variables were presented as absolute numbers (n) and percentages (%). In the comparisons of continuous variables between the groups, the Mann-Whitney U test or the Kruskal-Wallis test was used as the variables did not show normal distribution. When statistically significant differences were found in more than two group analyses, subgroup analyses were performed using the Dunn-Bonferroni post-hoc tests. For comparisons between groups for categorical variables, Pearson's chi-square test or the Fisher-Freeman-Halton test was used. For relationships between continuous variables, Spearman's correlation test was applied as normal distribution was not provided regarding asymmetry ratios. The SPSS (IBM SPSS Statistics for Windows, version 28.0. Armonk, NY: IBM Corp.) program was used for statistical analyses and type I error rate was taken as 5% and a p-value <0.05 was considered statistically significant.

Results

The demographic and clinical data are summarized in Table 1. The definitive analysis of audio-vestibular findings are given in Table 2.

There were significant differences in SD (p<0.001), DHI (p=0.006), lateral canal VOR gains (p=0.036) and caloric responses (p=0.036) between the hearing loss severity groups (Table 3). There were no significant differences with respect to VOR gain asymmetry ratios in lateral, posterior and anterior canals in HIMP, and lateral canal VOR gain asymmetry ratio in SHIMP (p>0.05). The caloric response asymmetry ratio difference was at significance level between the hearing groups (p=0.05).

Figure 1 shows the distributions of asymmetry ratios in significant categoric variables. In DHI groups, patients with normal hearing showed less asymmetry in SHIMP and caloric tests (p=0.035 for both). Lateral canal HIMP and SHIMP asymmetry ratios and caloric response asymmetry ratios differed significantly between the SHIMP and vVOR saccade groups (p=0.025, p=0.002, and p=0.002; p=0.001, p<0.001, and p=0.002, respectively). No meaningful

Table 1. Demographic and disease characteristics of patients

Age; mean±SD	48.94±10.508
Median (min-max)	50 (24-65)
Sex; n (%)	
Female	18 (51.4%)
Male	17 (48.6%)
Employment status; n (%)	
Yes	21 (60%)
No	14 (40%)
Smoking; n (%)	
Yes	7 (20%)
No	28 (80%)
Alcohol use; n (%)	
Yes	8 (22.9%)
No	27 (77.1%)
Comorbid disease; n (%)	
Yes	8 (22.9%)
No	27 (77.1%)
Autoimmune disease; n (%)	
Yes	2 (5.7%)
No	33 (94.3%)
Ménière's disease duration; mean±SD (months)	90.66±56.338
Median (min-max)	96 (12-276)
Ménière's disease side	
Right	21 (60%)
Left	14 (40%)
Attack duration; mean±SD (minutes)	100.29±137.466
Median (min-max)	60 (15-840)
Attack severity; mean±SD (VAS)	3.49±0.612
Median (min-max)	3 (2-5)

Min: Minimum, Max: Maximum, SD: Standard deviation, VAS: Visual analogue scale

Table 2. Definitive analysis of audio-vestibular findings

		n (%)
SNHL degree		
Very mild		8 (22.9%)
Mild		9 (25.7%)
Moderate		6 (17.1%)
Moderate-severe		8 (22.9%)
Severe		2 (5.7%)
Very severe		2 (5.7%)
THI group		
Mild		16 (45.7%)
Moderate		10 (28.6%)
Severe-catastrophic		9 (25.7%)
DHI group		
Mild		7 (20%)
Moderate		16 (45.7%)
Severe		12 (34.3%)
Ipsilateral SHIMP		
Saccade, none		11 (31.4%)
Saccade, present		24 (68.6%)
Ipsilateral vVOR		
Saccade, none		25 (71.4%)
Saccade, present		10 (28.6%)
Ipsilateral SVOR		
Suppression reflex, none		1 (2.9%)
Suppression reflex, present		34 (97.1%)
	Mean±SD	**Median (min-max)**
THI	40.86±21.422	42 (10-84)
DHI	53.37±20.429	54 (16-86)
Ipsilateral PTA (dB)	47.23±26.149	41.25 (18-118)
Contralateral PTA (dB)	18.18±14.330	12.5 (5-66)
Speech discrimination (%)		
Ipsilateral	70.05±26.308	76 (0-96)
Contralateral	93.71±10.551	100 (48-100)
SHIMP VOR gains		
Ipsilateral LC	0.79±0.173	0.86 (0.30-0.98)
Contralateral LC	0.91±0.102	0.90 (0.76-1.20)
HIMP VOR gains		
Ipsilateral AC	0.93±0.190	0.90 (0.56-1.42)
Contralateral AC	0.93±0.190	0.94 (0.50-1.32)
Ipsilateral PC	0.83±0.192	0.87 (0.25-1.29)
Contralateral PC	0.90±0.167	0.88 (0.61-1.34)
Ipsilateral LC	0.84±0.192	0.89 (0.30-1.16)
Contralateral LC	0.92±0.110	0.93 (0.66-1.11)
Caloric test responses		
Ipsilateral	14.91±7.905	14 (2-34)
Contralateral	35.09±12.657	32 (15-62)
Asymmetry ratios		
HIMP LC VOR gain	-11.27±25.276	-8.38 (-87.85-23.91)
HIMP PC VOR gain	-9.67±29.030	-8.79 (-104.76-51.71)
HIMP AC VOR gain	-0.20±24.003	-2.76 (-53.85-66.67)
SHIMP LC VOR gain	-15.63±23.993	-12.76 (-86.79-12.29)
Caloric response	-83.54±38.523	-76.36 (-177.78-38.10)

AC: Anterior canal, DHI: Dizziness handicap inventory, HIMP: Head impulse paradigm, LC: Lateral canal, Min: Minimum, Max: Maximum, PC: Posterior canal, PTA: Pure-tone average, SD: Standard deviation, SHIMP: Suppression HIMP, SNHL: Sensorineural hearing loss, VOR: Vestibulo-ocular reflex, SVOR: Suppression VOR, THI: Tinnitus handicap inventory, VAS: Visual analogue scale, vVOR: Visually-enhanced VOR

significant differences were found in vertical canal gain asymmetry ratios, even diminished VOR gains were observed in the ipsilateral posterior canal in patients with severe hearing loss (Table 3, Figure 1).

The findings of the correlation analysis of asymmetry ratios with audiological and vestibular status of the cases are shown in Table 4. When the relationships between HIMP lateral canal asymmetry ratios and clinical parameters

Table 3. Comparative analysis findings of hearing groups

	Normal (n=8)	Mild HL (n=15)	Moderate HL (n=8)	Severe HL (n=4)	
	n (%)				p-value
Sex					
Female	6 (75%)	9 (60%)	3 (37.5%)	0	0.071[a]
Male	2 (25%)	6 (40%)	5 (62.5%)	4 (100%)	
DHI group					
Mild	4 (50%)	3 (20%)	0	0	
Moderate	4 (50%)	7 (46.7%)	3 (37.5%)	2 (50%)	0.083[a]
Severe	0	5 (33.3%)	5 (62.5%)	2 (50%)	
Ipsilateral SHIMP					
Saccade, none	1 (12.5%)	4 (26.7%)	4 (50%)	2 (50%)	0.304[a]
Saccade, present	7 (87.5%)	11 (73.3%)	4 (50%)	2 (50%)	
Ipsilateral vVOR					
Saccade, none	8 (100%)	12 (80%)	4 (50%)	1 (25%)	0.015[a]
Saccade, present	0	3 (20%)	4 (50%)	3 (75%)	
Median (min-max)					
Age	45.5 (32-59)	47 (24-65)	52.5 (31-62)	51.5 (48-64)	0.332[b]
Duration	72 (12-120)	96 (12-192)	108 (36-144)	66 (17-276)	0.841[b]
THI	28 (10-50)	36 (10-80)	44 (20-66)	59 (44-84)	0.118[b]
DHI	29 (16-52)	58 (22-84)	66 (34-86)	60 (58-80)	**0.006[b]**
Speech discrimination					
Ipsilateral	92 (84-96)	80 (64-92)	56 (44-68)	0 (0-48)	**<0.001[b]**
Contralateral	100 (100-100)	100 (84-100)	88 (80-96)	84 (48-100)	**<0.001[b]**
SHIMP gains					
Ipsilateral LC	0.8 (0.8-0.9)	0.8 (0.3-0.9)	0.8 (0.4-0.9)	0.6 (0.6-0.7)	0.200[b]
Contralateral LC	0.9 (0.7-1)	0.9 (0.7-1)	0.9 (0.7-1.2)	0.8 (0.7-0.9)	0.618[b]
HIMP gains					
Ipsilateral AC	0.9 (0.9-1.3)	0.9 (0.7-1.36)	0.8 (0.7-1.1)	0.7 (0.5-1.42)	0.270[b]
Contralateral AC	0.9 (0.8-1.1)	0.9 (0.5-1.3)	0.8 (0.6-1.3)	0.7 (0.5-1)	0.267[b]
Ipsilateral PC	0.9 (0.7-1)	0.8 (0.5-1)	0.8 (0.2-1.2)	0.5 (0.5-0.8)	0.051[b]
Contralateral PC	1 (0.61-1.3)	0.9 (0.7-1.2)	0.8 (0.7-1.1)	0.7 (0.7-1.1)	0.361[b]
Ipsilateral LC	0.9 (0.8-1.1)	0.8 (0.3-1)	0.8 (0.3-1)	0.6 (0.4-0.9)	0.055[b]
Contralateral LC	1 (0.8-1.1)	0.9 (0.7-1.1)	0.8 (0.8-1)	0.8 (0.6-0.9)	**0.036[b]**
Caloric test					
Ipsilateral	18.5 (11-34)	14 (2-31)	15.5 (6-32)	8 (3-14)	0.136[b]
Contralateral	29 (20-56)	37 (17-58)	30 (24-59)	20.5 (15-62)	0.241[b]
Asymmetry ratios					
HIMP LC VOR gain	-1.9 (-17.4-17.2)	-6.7 (-87.8-16)	-15.5 (-79.3-23.9)	-14.3 (-59.7-20.3)	0.546[b]
HIMP PC VOR gain	-2.5 (-35-34)	-6.5 (-47.1-27.5)	-0.1 (-104.7-51.7)	-30.4 (-47-12.1)	0.188[b]
HIMP AC VOR gain	7 (-16.9-37.9)	-7.4 (-24-66.6)	-5.9 (-53.8-31.2)	2.4 (-28.5-40)	0.885[b]
SHIMP LC VOR gain	-7.7 (-13.9-11.1)	-12 (-86.7-12.2)	-20.2 (-50.4-12.2)	-23.1 (-30.7-7.7)	0.422[b]
Caloric response	-52.6 (-80-40)	-80 (-177.7-38.6)	-77.3 (-137.5-38.1)	-99.5 (-153.8-66.6)	**0.050[b]**

[a]: Fisher-Freeman-Halton test, [b]: Kruskal-Wallis test. AC: Anterior canal, DHI: Dizziness handicap inventory, HIMP: Head impulse paradigm, LC: Lateral canal, Min: Minimum, Max: Maximum, PC: Posterior canal, SHIMP: Suppression HIMP, SNHL: Sensorineural hearing loss, VOR: Vestibulo-ocular reflex, SVOR: Suppression VOR, THI: Tinnitus handicap inventory, vVOR: Visually-enhanced VOR

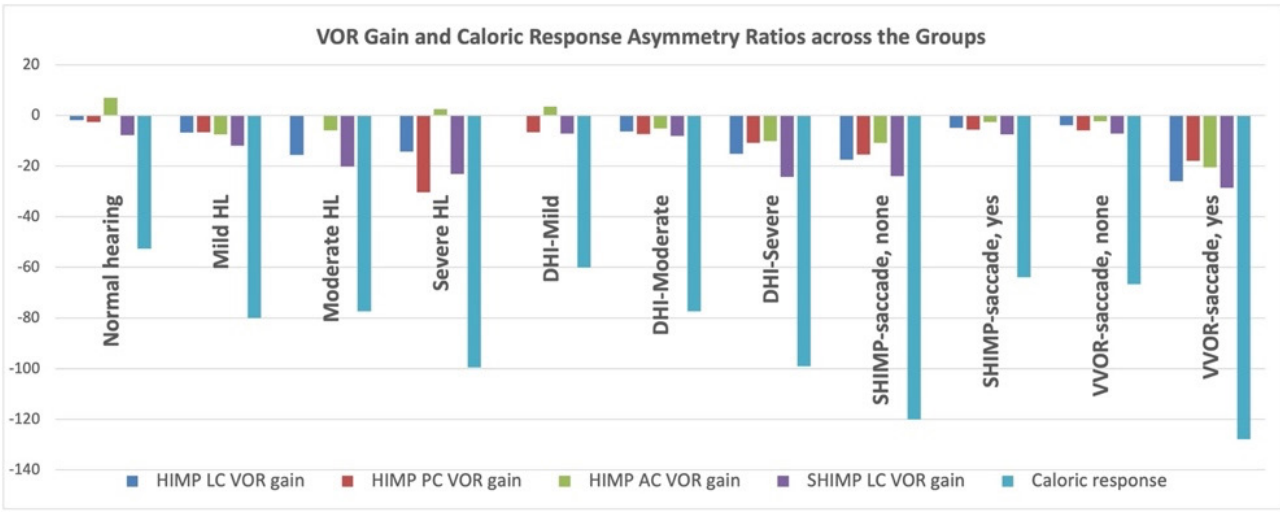

Figure 1. Summary of the comparative analysis of asymmetry ratios between the hearing, dizziness, and saccade groups
HL: Hearing loss, DHI: Dizziness handicap inventory, HIMP: Head impulse paradigm, SHIMP: Suppression HIMP, VOR: Vestibulo-ocular reflex, vVOR: Vissualy-enhanced VOR, LC: Lateral canal, PC: Posterior canal, AC: Anterior canal

were examined, there were weak negative correlations with ACT at 500 Hz (rho=-0.362, p=0.032), DHI (rho=-0.349, p=0.040) and positive correlations with HIMP ipsilateral anterior, lateral and contralateral posterior canal VOR gains (Table 4). SHIMP lateral canal VOR gain asymmetry ratios were negatively correlated with ACT at 500 Hz, 4000 Hz (rho=-0.342, p=0.044; rho=-0.322, p=0.044), ipsilateral PTA (rho=-0.337, p=0.047) and DHI (rho=-0.441, p=0.008), plus, positively correlated with HIMP ipsilateral lateral canal VOR gains (rho=0.381, p=0.024). There were negative correlations between caloric asymmetry ratio and ACT at 1000 Hz (rho=-0.411, p=0.014), DHI (rho=-0.458, p=0.006), plus, high level of positive correlations with ipsilateral and contralateral HIMP lateral canal VOR gains (rho=0.580, p≤0.001; rho=0.434, p=0.009) were observed.

Discussion

The presented study contributes to the evidence and demonstrates VOR asymmetry in unilateral MD and its associations with other clinical characteristics of the disease. Our findings support the idea that MD not only produces fluctuating vestibular hypofunction at low-frequency levels but also leads to measurable and sometimes persistent asymmetries in VOR gain. We found significant differences among the hearing groups with respect to contralateral lateral canal VOR gains and caloric response asymmetry. However, VOR gain asymmetry ratios for vertical canals and SHIMP did not differ significantly by hearing groups. Both HIMP and SHIMP lateral canal asymmetry and caloric response asymmetry also varied significantly across saccade-based (SHIMP, vVOR) subgroups. Vertical canal asymmetry was largely nonsignificant, though in those with severe hearing loss there was a trend toward reduced ipsilateral posterior canal gain. In correlation analyses, lateral HIMP asymmetry correlated negatively with ACT at 500 Hz and DHI and positively with ipsilateral anterior, lateral, and contralateral posterior canal VOR gains. Lateral SHIMP asymmetry correlated negatively with ACT 500 Hz, 4000 Hz, ipsilateral PTA, and DHI, and positively with HIMP ipsilateral lateral VOR gain. Caloric asymmetry correlated negatively with ACT at 1000 Hz and DHI, and positively with ipsilateral and contralateral HIMP lateral VOR gains.

Further, the observation of a reduced or absent lateral canal VOR gain asymmetry does not necessarily indicate recovery of the affected ear. Rather, it may reflect either early bilateral vestibular involvement or central compensatory mechanisms that normalize eye movement responses. Over time, the contralateral vestibular apparatus may also exhibit subclinical dysfunction, reducing the apparent inter-aural asymmetry. Simultaneously, central vestibular compensation can recalibrate the VOR, further masking deficits that were initially unilateral (11,12). Therefore, reliance solely on lateral canal asymmetry ratios may underestimate the true disease burden in long-standing MD, and the lack of asymmetry should prompt careful consideration of potential bilateral progression rather than assuming functional recovery.

The pathophysiological basis of VOR asymmetry in MD remains complex. It was highlighted that vHIT VOR responses could differ significantly between the affected and unaffected sides in unilateral MD patients, reflecting both peripheral vestibular damage and central compensatory mechanisms (11). We have shown that VOR asymmetry is not a static feature but could be one that evolves over time as the disease progresses (Table 4). Dynamic changes in VOR gain and asymmetry emphasize the fluctuating nature of

Table 4. Correlation analysis of variables for VOR gain and caloric response asymmetry ratios

	Correlations with VOR gain and caloric response asymmetry ratios				
	HIMP LC	HIMP PC	HIMP AC	SHIMP LC	Caloric
Variables	**rho/p**	**rho/p**	**rho/p**	**rho/p**	**rho/p**
Age	-0.302/0.078	-0.148/0.396	-0.098/0.574	-0.102/0.561	-0.246/0.154
Disease duration	-0.094/0.589	0.166/0.341	-0.147/0.398	0.064/0.713	**-0.345/0.042**
Average attack duration	-0.118/0.499	0.036/0.837	-0.131/0.453	-0.120/0.494	-0.271/0.115
Average attack severity	0.014/0.938	-0.017/0.924	0.275/0.110	-0.087/0.619	-0.101/0.563
ACT 500 Hz	**-0.362/0.032**	-0.175/0.314	-0.143/0.412	**-0.342/0.044**	-0.306/0.074
ACT 1000 Hz	-0.278/0.105	-0.147/0.400	-0.211/0.223	-0.301/0.079	**-0.411/0.014**
ACT 2000 Hz	-0.178/0.306	-0.242/0.161	-0.110/0.530	-0.287/0.095	-0.320/0.061
ACT 4000 Hz	-0.162/0.353	-0.219/0.206	-0.020/0.911	**-0.322/0.044**	-0.269/0.118
ACT 8000 Hz	-0.088/0.617	-0.212/0.221	0.068/0.696	-0.293/0.088	-0.147/0.398
Ipsilateral PTA	-0.243/0.160	-0.190/0.275	-0.138/0.430	**-0.337/0.047**	**-0.358/0.035**
Contralateral PTA	-0.102/0.561	**-0.350/0.039**	**0.370/0.029**	-0.023/0.895	-0.138/0.428
Ipsilateral SD	0.219/0.207	0.116/0.508	0.241/0.163	0.271/0.115	0.328/0.054
Contralateral SD	0.095/0.589	0.065/0.711	-0.090/0.609	-0.025/0.887	0.205/0.237
THI	-0.235/0.175	-0.151/0.386	0.021/0.906	-0.274/0.111	-0.186/0.286
DHI	**-0.349/0.040**	-0.025/0.889	-0.154/0.376	**-0.441/0.008**	**-0.458/0.006**
HIMP ipsilateral AC	**0.392/0.020**	-0.119/ 0.497	**0.519/0.001**	0.043/0.808	**0.354/0.037**
HIMP contralateral AC	0.104/0.553	**0.445/0.007**	**-0.333/0.050**	-0.089/0.612	0.156/0.371
HIMP ipsilateral PC	0.274/0.111	**0.650/<0.001**	-0.209/0.229	-0.007/0.967	**0.363/0.032**
HIMP contralateral PC	**0.480/0.003**	**-0.470/0.004**	**0.589/<0.001**	0.251/0.146	**0.367/0.030**
HIMP ipsilateral LC	**0.604/<0.001**	0.284/0.098	0.094/0.590	**0.381/0.024**	**0.580/<0.001**
HIMP contralateral LC	0.114/0.513	0.298/0.082	-0.175/0.315	0.216/0.212	**0.434/0.009**
SHIMP ipsilateral LC	**0.337/0.048**	0.097/0.581	0.112/0.520	**0.806/<0.001**	0.221/0.202
SHIMP contralateral LC	0.147/0.401	0.301/0.079	-0.215/0.214	0.026/0.884	0.080/0.647
Ipsilateral CR	0.273/0.112	0.281/0.102	0.041/0.814	0.312/0.068	**0.711/<0.001**
Contralateral CR	-0.180/0.300	0.045/0.798	-0.165/0.344	0.033/0.852	-0.192/0.270

AC: Anterior canal, ACT: Air-conduction threshold, CR: Caloric response, DHI: Dizziness handicap inventory, HIMP: Head impulse paradigm, LC: Lateral canal, PC: Posterior canal, PTA: Pure-tone average, SHIMP: Suppression HIMP, THI: Tinnitus handicap inventory, SD: Standard deviation

cochlea-vestibular dysfunction and its potential progression (12). These findings align with our observations; a decrease in both ipsilateral and contralateral lateral canal VOR gains suggests that careful monitoring of asymmetry trajectories could provide insights into disease activity and prognosis. As the disease is characterized by a fluctuating pattern of symptoms that wax and wane, vHIT gains and saccades may show the compensation state of the patient at the time of admission.

As vHIT measures the VOR gains during high-velocity rotatory head impulses, a consensus has not been reached on its role in the follow-up of MD (13). While HIMP is good for detecting VOR deficits (presence of corrective saccades), SHIMP is better for assessing how much vestibular reserve remains (presence/absence of compensatory saccades), and the caloric test shows lateral canal paresis and canal asymmetry. Together, they give a complementary picture of fluctuating and progressive dysfunction in MD (14).

Nevertheless, the dissociation between caloric deficits and relatively preserved vHIT (HIMP) is reported in many patients: caloric abnormalities are more frequent, whereas vHIT gain abnormalities (or asymmetry) are less common in the interictal period (15,16). Our data support that VOR gain asymmetry in HIMP (lateral, vertical canals) and SHIMP do not differ across hearing loss severity, indicating that gain asymmetry is not sensitive to the severity of hearing loss in MD, at least in our cohort; although the patients with normal hearing showed less asymmetry in HIMP lateral canal VOR gains and caloric responses. The correlations between the asymmetry ratios and the other variables showed that when ipsilateral weakness is more prominent DHI and hearing thresholds are increased and VOR gains, and caloric responses are diminished.

The absence of significant vertical canal asymmetry differences is also in line with many reports: in MD, the lateral canal is most often implicated, whereas vertical

canals tend to remain relatively spared in interictal testing (17). The slight gain reduction in the ipsilateral posterior canal in severe hearing loss may reflect the early spread of endolymphatic hydrops involvement beyond the lateral canal in advanced disease. Pathophysiologically, this may reflect hydrops affecting the posterior labyrinth or secondary damage to vertical canal hair cells. Along with the lateral canal, the posterior canal was the most frequently abnormal canal on vHIT, in almost 56% of peripheral vestibulopathy cases in a study (18). The distribution profiles of canal involvement from multiple reports confirm that the posterior canal is often involved (sometimes more than horizontal) in MD patients (19).

A study conducted with 36 patients with definite MD found that the most frequent gain reduction in vHIT was in the posterior canal of the affected ear and in the coupled superior canal of the "unaffected" ear (20). In another study, it was shown that over time, VOR gain in vertical canals (superior and posterior) declined, whereas the horizontal canal gain remained relatively stable in the same interval. The authors interpreted this as evidence that vertical canal deterioration could precede or outpace horizontal canal decline in early to mid-stages of MD (21).

Importantly, posterior canal hypofunction on vHIT can be asymmetric and isolated and may persist between attacks, providing an additional diagnostic marker when lateral canal asymmetry has normalized due to bilateral progression. Detecting saccades and reduction in unilateral posterior canal VOR gain offers two key advantages: sensitivity to early or subclinical involvement, and diagnostic help. Since accompanying ipsilateral posterior canal hypofunction is unusual in other peripheral disorders, its presence strongly supports MD in the context of fluctuating audio-vestibular symptoms.

Another dimension is the role of SHIMP in MD. By design, SHIMP presents a head-fixed moving target that the subject must pursue, thereby eliciting anti-compensatory saccades; SHIMP is less influenced by covert saccades that can contaminate HIMP gain measures (4). Thus, VOR gain asymmetry assessed by SHIMP and HIMP provides complementary information in unilateral MD. Asymmetry in SHIMP was also not significantly stratified by hearing groups in our cohort, but correlations suggest that even when covert saccades are suppressed, SHIMP is still sensitive to audiometric severity in MD. SHIMP asymmetry seems to be correlated better with hearing loss severity, possibly indicating higher sensitivity to residual vestibular dysfunction. In isolation, vHIT (gain) asymmetry may lack power, but when combined with saccadic behavior, it becomes more sensitive to vestibular dysfunction. For example, in the absence of saccades in SHIMP, we observed greater asymmetry in caloric responses. This observation aligns with the calls in literature to emphasize the importance of saccades rather than simple gain cut-offs (17). Our findings also depicted that asymmetry ratios are significantly increased in the presence of saccades in vVOR, which marks vestibular loss in MD (22).

With the progression of unilateral MD, the caloric-vHIT pattern tends to shift, which may reflect the deterioration of endolymphatic hydrops and vestibular hair cell impairments (12,23). In the early stages of MD, vHIT is often normal because this test assesses high-frequency vestibular fibers, and the disease initially affects primarily low-frequency systems (17,24). However, as the disease progresses, vHIT gain may decrease, and a significant gain reduction may occur in the affected ear. In some patients, changes in the VOR response may be observed in the contralateral ear due to subclinical effects or central compensation (23).

Even in cases of unilateral disease, VOR asymmetry is not pathognomonic of MD; rather, it should be interpreted in the context of the status and progress of the disease. Parameters suggesting incomplete compensation can contribute to chronic imbalance and reduced quality of life in MD patients. Our results support this idea, as persistent VOR asymmetry in unilateral MD may reflect insufficient central compensation. Periodic dysfunction of the VOR varies over time, and VOR gain may vary not only in the affected ear but also in the contralateral ear, and this can be assessed by VOR gain asymmetry. Taken together, larger study samples will highlight whether VOR asymmetry is a sensitive marker of unilateral vestibular dysfunction in MD, with diagnostic, prognostic, and rehabilitative implications. Future prospective studies should clarify how fluctuations in VOR asymmetry relate to clinical symptomatology and whether targeted interventions can mitigate long-term disability.

In our study, greater symmetry (less asymmetry) was associated with better hearing and less dizziness handicap. This matches clinical intuition: more preserved vestibular symmetry corresponds with milder functional impairment. However, MD is progressive and not rarely bilateral; longitudinal cohorts report contralateral ear involvement in up to 30-50% over 10-20 years (20). As the disease evolves, contralateral canal responses may deteriorate, resulting in diminished asymmetry ratios despite ongoing symptoms, as was observed in our study. Clinically, loss of asymmetry in a clinically unilateral case should raise suspicion for bilateral vestibular involvement rather than recovery. Thus, the lateral canal asymmetry ratio may underestimate disease burden in long-standing MD.

Study Limitations

Because testing was done at single timepoints with a single-center design, the influence of recent asymmetry dynamics

could not be standardized to the attack or interictal period of MD. A limitation of applying the results to clinical practice is that relying on the lateral canal asymmetry ratio alone may be misleading when contralateral involvement occurs or the disease progresses. Additionally, decreased VOR gain asymmetry over time may be an important clue in diagnosing bilateral MD.

Conclusion

VOR gain asymmetry assessed with SHIMP and HIMP offers complementary diagnostic value in unilateral MD. Both VOR gain and caloric response asymmetry rates could serve as adjunct markers for evaluating vestibular dysfunction in MD.

Ethics

Ethics Committee Approval: The study was approved by the Clinical Research Ethics Committee of the University of Health Sciences Türkiye, Bursa Yüksek İhtisas Training and Research Hospital (approval no: 2011-KAEK-25 2023/04-10, date: 19.04.2023).

Informed Consent: Informed consent was obtained from all the patients and subjects.

Footnotes

Authorship Contributions

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

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

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Main Points

- While there are relationships between head impulse paradigm (HIMP) and suppression HIMP (SHIMP) vestibulo-ocular reflex (VOR) gains and hearing thresholds at low-frequency and dizziness handicap inventory, the caloric test correlates more closely with audiological impairment and symptom burden in unilateral Ménière's disease (MD).
- SHIMP provides complementary insight, and anti-compensatory saccades might be useful for disease monitoring.
- Incorporating SHIMP and visually enhanced VOR saccade metrics and asymmetry indices into clinical reports could improve the early detection of progression.
- Given these observations, vHIT gain asymmetry alone should not be interpreted as a marker of MD severity; instead, integrated vestibular profiling is warranted.

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Investigation of Serum Calcium and Vitamin D Levels in Patients with Refractory Benign Paroxysmal Positional Vertigo

Original Investigation

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Abstract

Objective: It is not known exactly what causes recurrence in benign paroxysmal positional vertigo (BPPV) patients. We aimed to investigate the relationship between the number of maneuvers and serum vitamin D and calcium levels in BPPV cases treated with appropriate maneuvers after correct diagnosis.

Methods: A total of 86 BPPV patients, 68 (79.9%) female and 18 (20.1%) male were included in the study. Of these, 16.3% (n=14) were aged under 45 years, 29.1% (n=25) between 45-60 years, and 54.7% (n=47) over 60 years. All were evaluated with videonystagmography. Patients who underwent maneuvers for BPPV treatment were examined. Serum 25-hydroxyvitamin D and calcium levels were measured.

Results: Repeated maneuvers were performed in 43% of the patients (n=37). Serum calcium measurements did not differ significantly between the groups. Serum vitamin D levels were not significantly different between the groups in terms of sex (p=0.387) and age (p=0.323). However, vitamin D levels were significantly lower in the group that resisted the maneuvers than in the group that did not resist [resistance: 22.9, interquartile range (IQR): 12.9-27.0; non-resistance: 28.6, IQR: 18-35, p=0.009].

Conclusion: Vitamin D measurements were observed to be significantly lower in patients requiring repeat maneuvers for BPPV treatment. We recommend that vitamin D levels be evaluated in resistant cases.

Keywords: Benign paroxysmal positional vertigo, vitamin D deficiency, calcium, repositioning maneuvers, recurrence, nystagmography, therapeutic resistance

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Introduction

Benign paroxysmal positional vertigo (BPPV) is characterized by nystagmus and recurrent vertigo that occur depending on the position of the head. The periodic recurrence of symptoms significantly reduces quality of life, decreases daily activity performance, and causes loss of work productivity. BPPV results from the unintended migration of otoconia into the semicircular canals. However, the causes of otoconia degeneration and separation from the utricle, which are thought to result from macular degeneration, are not fully known (1).

Most patients with BPPV are successfully treated with canalith repositioning maneuvers (CRPs), but some patients require repeated maneuvers. Success rates with one or more CRPs vary among authors and have been reported to range from 50% to 70% (2). It has also been reported in the literature that BPPV recurs at varying rates, up to 50% (3). Therefore, it is important to clarify the factors that have been reported to predispose to the recurrence of BPPV, such as female sex, older age, hypertension, head trauma, other inner ear disorders, and vitamin D deficiency (4-8). Some studies indicate an association between vitamin D deficiency and recurrent BPPV, while others do not. Vitamin D is associated with vestibular pathology through its effects on skeletal mineral homeostasis, which in turn affects the temporal bone. The crucial calcium concentration in the vestibular endolymph required for otolithic organ function is maintained by normal serum vitamin D levels (9,10). Another hypothesis suggests that the immunomodulatory functions protect against autoimmune or inflammatory pathologies in the inner ear (11,12).

Although CRP is generally effective in improving BPPV, some patients may require more than one maneuver. In our study, we aimed to determine whether there is an association between the number of maneuvers performed and vitamin D and calcium levels in patients with BPPV treated with appropriate maneuvers after correct diagnosis.

Methods

The study was approved by the İzmir Katip Çelebi University Health Research Ethics Committee (approval no: 0297, date: 19.12.2024). All patients were informed and consent was obtained. Eighty-six BPPV patients, 68 (79.9%) women and 18 (20.1%) men, diagnosed with BPPV by videonystagmography (VNG) in the vertigo laboratory in January-December 2024 were included in the study. Those with other causes of vertigo, migraine history, and chronic ear disease were excluded. Patients with a history of head trauma or alcohol abuse that could cause refractory BPPV, and those using any calcium or vitamin D supplements were also excluded.

Demographic and clinical data such as patients' age, sex, and recurrence status were recorded. Patients were divided into three age categories: <45 years, 45-60 years, and >60 years. All patients' serum 25-hydroxyvitamin D and serum calcium levels were measured by standard biochemical analysis methods. A vitamin D level ≤20 ng/mL was considered deficiency, between 21-29 ng/mL was considered insufficiency, and ≥30 ng/mL was considered sufficiency (13,14).

In patients diagnosed with BPPV and positional nystagmus on VNG, the affected canal, type of maneuver performed, and number of maneuvers were recorded. Maneuvers were performed only by the authors participating in the study. We performed the Epley maneuver for canalithiasis and the Semont maneuver for cupulolithiasis in posterior canal involvement; the Barbecue maneuver for canalithiasis and the Appiani maneuver for cupulolithiasis in lateral canal involvement; and the Yacovino maneuver for anterior canal involvement. Patients were called for weekly follow-ups, and maneuvers were repeated if symptoms persisted and VNG findings continued. Patients who underwent at least one and at most five maneuvers were included in the study. Patients who underwent more than one maneuver were considered refractory.

Statistical Analysis

An a priori power analysis was conducted using G*Power 3.1 (t-tests, difference between two independent means, two-tailed). Assuming a standardized mean difference of d=0.61, a type I error rate of α=0.05, and a desired statistical power of 0.80 with an equal allocation ratio between groups (N_2/N_1=1), the required total sample size was estimated as 88 participants (44 per group). Under these assumptions, the non-centrality parameter (δ) was 2.86, the critical t-value was 1.99 (df=86), and the corresponding actual power was approximately 0.8. Due to practical constraints in recruitment, the final sample size slightly deviated from this target (15). Differences in calcium levels according to sex, age group, and recurrence status were analyzed using the independent samples t-test and one-way analysis of variance. For vitamin D levels, the Mann-Whitney U test and the Kruskal-Wallis test were applied. All statistical analyses were performed using IBM SPSS Statistics version 30, and a p-value <0.05 was considered statistically significant.

Results

Of the total 86 patients, 79.9% (n=68) were female; and 16.3% (n=14) were aged under 45 years, 29.1% (n=25) were between 45-60 years, and 54.7% (n=47) were over 60 years. Thirty-two underwent the Epley maneuver (posterior canalolithiasis), nine the Semont maneuver (posterior cupulolithiasis), 18 the Barbecue maneuver (lateral canalolithiasis), 16 the Appiani maneuver (lateral cupulolithiasis), and 11 underwent the Yacovino maneuver (anterior canal).

Of the 86 patients, 49 received one maneuver, 31 received two maneuvers, two received three maneuvers, two received four maneuvers, and two received five maneuvers. Patients requiring more than one maneuver (43%; n=37) were considered to have refractory BPPV. Of these 37 patients, 8 were aged <45 years, 13 between 45-60 years, and 16 >60 years. No significant differences were identified in calcium levels between the sexes (females: 9.8±0.4, males: 9.6±0.4, p=0.133), between age groups (<45 years: 9.7±0.4; 45-60 years: 9.7±0.4; >60 years: 9.8±0.5, p=0.688) and between

refractory and non-refractory groups (refractory: 9.8±0.5, non-refractory: 9.7±0.4, p=0.815) (Table 1).

Vitamin D levels were evaluated, and no significant association was observed between sexes (p=0.387) or age groups (p=0.323). However, vitamin D levels were significantly lower in the refractory group than in the non-refractory group [refractory: 22.9, interquartile range (IQR): 12.9-27.0; non-refractory: 28.6, IQR: 18-35; p=0.009] (Table 2). Vitamin D findings across sex, refractory status, and age categories are presented in Figure 1.

Discussion

It is important that serum vitamin D and calcium levels are normal for the otoconia, which are composed of calcium carbonate, to maintain their function. Imbalance in serum calcium levels, and thereby calcium levels in the vestibular endolymph, can alter the otoconia, leading to abnormal mineralization and degeneration. In the inner ear, these critical calcium levels are maintained by the transepithelial Ca_2+ channel transport system (16,17). Disturbance of the calcium metabolism in patients with osteoporosis may represent a pathogenesis resulting in BPPV because of the disruption of otoconia associated with calcium deficiency (10). Besides these classical effects of vitamin D, its immunomodulatory function, and its effect in suppressing the autoimmune and inflammatory processes have been confirmed by genome-wide analyses *in vivo* and *in vitro* studies (18).

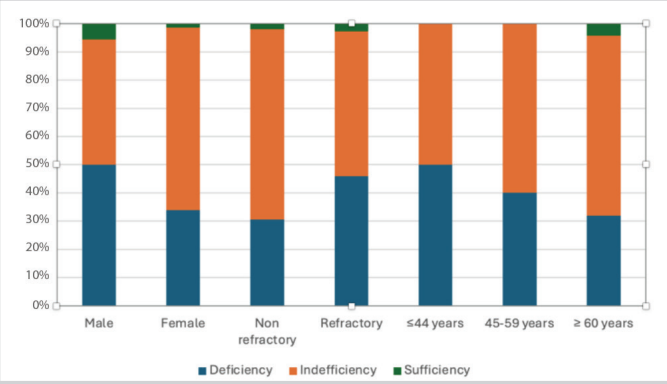

Figure 1. Vitamin D status in sex, refractory, and age categories

Table 1. Calcium levels in BPPV patients

Groups	n	Calcium levels (mg/dL)	p
Sex			0.133
Male	18	9.8±0.4	
Female	68	9.6±0.4	
Refractory categories			0.815
Non-refractory	49	9.7±0.4	
Refractory	37	9.8±0.5	
Age range			0.688
≤44 years	14	9.7±0.4	
45-59 years	25	9.7±0.4	
≥60 years	47	9.8±0.5	

BPPV: Benign paroxysmal positional vertigo

A review investigating the relationship between temporal bone diseases and vitamin D reported evidence regarding diseases such as vestibular neuritis, endolymphatic hydrops, idiopathic sudden hearing loss, idiopathic facial paralysis, and BPPV (11). Although all these diseases have various etiological factors, it has been reported that autoimmune or autoinflammatory reactions could be involved after viral infection. It has been explained that vitamin D could affect the suppression of this postviral autoimmune reaction with its immunomodulatory effect and antioxidant activity and its endothelial cell stabilizing effect. Experimental studies have shown degenerative changes in the inner ear ganglion cells, the otoconia, and hair cells in mice with vitamin D receptor deficiency (11). Gibson et al. (19) have shown that dietary vitamin D, at physiological concentrations, maintains calcium homeostasis and supports bone health, as well as having a stabilizing effect on endothelial stability and an anti-inflammatory response. While these provide a plausible link to the diseases mentioned above, further studies on the association between temporal bone diseases and vitamin D deficiency are recommended.

Vitamin D deficiency has been found to be associated with longer duration of BPPV symptoms, lower success rates of repositioning maneuvers, and higher recurrence rates (14,20-24). A study in postmenopausal women found an association between osteoporosis and idiopathic BPPV, with approximately half of these patients having vitamin D deficiency and impaired

Table 2. Vitamin D levels in BPPV patients

	Vitamin D levels (n)			
	Deficiency (≤20 ng/mL)	Insufficiency (21-29 ng/mL)	Sufficiency (≥30 ng/mL)	p
Groups (n)	32	52	2	
Sex				0.387
Male	9	8	1	
Female	23	44	1	
Refractory categories				0.009
Non-refractory	15	33	1	
Refractory	17	19	1	
Age range				0.323
≤44 years	7	7	0	
45-59 years	10	15	0	
≥60 years	15	30	2	

BPPV: Benign paroxysmal positional vertigo

local Ca_2+ homeostasis (10). Yamanaka et al. (6) stated that the recurrence of BPPV was higher in osteoporosis patients. We did not find a significant difference in serum calcium levels in the refractory BPPV group in which we performed more than one maneuver. This may be due to the fact that serum calcium levels are affected by various factors.

CRPs are mostly successful in treating BPPV, but some patients require repeated CRPs. Prolonged vertigo symptoms before application, bilateral or multiple canal involvement, and age over 50 years have been associated with the need for multiple CRP. Korkmaz and Korkmaz (25) found that hypertension was an influential factor for repetitive maneuvers in the treatment of BPPV. Response to treatment with a single maneuver varies between 37% and 87% (26). In our study, 57% of patients improved with a single maneuver, and 43% required more than one maneuver. Yoon et al. (2) found that 69.5% of their patients had improved with only one CRP and the overall success with repeat CRPs was 96.4%. In a similar study, 68% of patients improved with only one maneuver while 87.6% needed more than one maneuver for improvement (25).

Although CRPs are commonly used to reposition displaced otoconia in the inner ear, these treatments are practitioner-dependent, and it is difficult to standardize diagnostic and therapeutic tests (27). In our study, maneuvers were performed only by researchers according to nystagmus findings detected with VNG, and those requiring more than one maneuver were considered refractory. However, we did not evaluate patients with canalolithiasis or cupulolithiasis separately. Most recent meta-analyses and studies in literature have focused on recurrent BPPV. We specifically focused on refractory BPPV cases and those that required multiple maneuvers. In our study, significant decrease in serum vitamin D levels in the refractory group requiring multiple maneuvers suggests that vitamin D levels could be related to the resistance to maneuvers in disease prognosis. Therefore, measuring vitamin D levels and providing replacement to maintain adequate levels should be considered in patients with refractory BPPV. In our study, only two of the 86 patients (2.33%) had sufficient serum vitamin D levels.

In a recent study, contrary to our results, no significant association was found between persistent BPPV and vitamin D deficiency, and factors such as male sex and the presence of concomitant diseases were indicated as predictors of resistance to CRP (28).

Vitamin D deficiency has been reported to possibly be affected by seasonal conditions and that more research is needed on this subject (12,29). Our study was conducted throughout the year, and vitamin D levels, which may vary seasonally, were not considered. This is one of the limitations of our study. Another limitation is our small sample size and the non-homogeneous distribution across sex and age groups which limits the strength of subgroup analyses. Additionally, potential confounders factors such as diabetes, hypertension, and osteoporosis were not taken into consideration.

The findings of this study suggest that the evaluated predictors show a meaningful association with the clinical outcomes; however, these results should be interpreted with caution due to several methodological considerations. First, the sample size did not fully meet the a priori target determined by the power analysis, particularly in the refractory group, which remained below the anticipated 44 participants. Although the total sample was deemed acceptable based on the G*Power estimation parameters (effect size, α level, and power), this shortfall represents a limitation that may have reduced statistical precision. Additionally, the imbalance between groups (37 vs. 49 participants) may have influenced the robustness of the comparisons, potentially contributing to reduced power. Furthermore, while the observed relationships were consistent with the existing literature, the cross-sectional/observational nature of the design precludes any inference of causality; therefore, the results should be understood as demonstrating associations rather than definitive causal effects.

Study Limitations

Although our study has some limitations, such as not evaluating seasonal changes and working with a small and non-homogeneous group, our findings suggest that vitamin D levels could be predictive of resistance to maneuvers in the prognosis of the disease. We can hypothesize that extremely low vitamin D levels may impair the body's local repair capacity in the inner ear, potentially leading to permanent adhesion (cupulolithiasis) or delayed otoconia mobilization, thus contributing directly to the cases refractory to the maneuver rather than predisposing to recurrence. Nevertheless, it should be noted that many patient-related, environmental, and clinician-related factors can also have an impact on patients who show resistance to maneuvers, and the necessity of studies with larger series should be considered.

Conclusion

In our study evaluating serum vitamin D and calcium levels in patients with BPPV undergoing repositioning maneuvers, we found that vitamin D levels were significantly lower in those who were refractory to the maneuvers.

Ethics

Ethics Committee Approval: The study was approved by the İzmir Katip Çelebi University Health Research Ethics Committee (approval no: 0297, date: 19.12.2024).

Informed Consent: All patients were informed and consent was obtained.

Footnotes

Authorship Contributions

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

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

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Main Points

- Although benign paroxysmal positional vertigo (BPPV) is a disease that is treated with high efficacy using canalith repositioning maneuvers, resistant patients are encountered.
- Comorbid diseases and risk factors should be investigated in refractory patients.
- Vitamin D deficiency may be a predisposing factor for the occurrence and recurrence of BPPV.
- Vitamin D levels should be investigated in cases of BPPV resistant to maneuvers.

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Comparing Flexible Nasal Endoscopy and Lateral Neck Radiography When Diagnosing Children with Adenoid Hypertrophy: A Case-Control Study

Original Investigation

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Abstract

Objective: To compare the reliability of flexible nasal endoscopy and lateral neck radiography in grading adenoid hypertrophy preoperatively in children.

Methods: A retrospective study was performed at a single tertiary care center. Medical records of children who underwent adenoidectomy between January 2019 and December 2023 were reviewed. Preoperative adenoid size was assessed by radiography or endoscopy and compared to intraoperative grading, the reference. Adenoid hypertrophy was graded as mild (25-50%), moderate (51-75%), or severe (76-100%).

Results: A total of 360 patients, 199 males and 161 females, were included. The mean age was 4.29±2.39 years. Preoperative and intraoperative grading matched in 58% of cases using endoscopy and 44.5% using radiography (p=0.028). Accurate grading was 1.7 times more likely with nasal endoscopy than radiography [odds ratio=1.72; 95% confidence interval (1.06-2.79)].

Conclusion: Flexible nasal endoscopy is more reliable than radiography in preoperative grading of adenoid hypertrophy in children.

Keywords: Adenoid hypertrophy, nasal endoscopy, radiography, pediatric otorhinolaryngology, diagnostic accuracy, preoperative assessment

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Introduction

Adenoid hypertrophy is the most common cause of upper airway obstruction in children and adolescents with a global prevalence ranging from 34% to 49% (1). The development of adenoid hypertrophy primarily stems from infectious origins, mainly respiratory and non-respiratory viruses, as well as aerobic and anaerobic bacteria. However, various non-infectious mechanisms may also contribute as the pathogenesis is believed to entail a complex interplay among immune, hormonal, and genetic factors, and may manifest with or without concurrent acute or chronic infections (2).

Common signs and symptoms of adenoid hypertrophy include nasal obstruction, chronic mouth breathing, mucopurulent rhinorrhea, and recurrent infections such

as upper respiratory tract infections and otitis media (3). Additionally, obstructive sleep apnea and irregularities in language and speech development may be observed. Chronic mouth breathing stemming from nasal obstruction can affect facial and dental development, potentially resulting in what is commonly referred to as adenoid facies or long face syndrome (4).

Besides clinical assessment, several diagnostic modalities can be relied upon to confirm the diagnosis of adenoid hypertrophy, including lateral neck radiography and flexible nasal endoscopy. The latter represents a safe office-based procedure with minimal associated complications. By enabling direct visualization of the nasopharynx and its structures, it stands as an exceptionally precise diagnostic tool for identifying adenoid hypertrophy. Nonetheless, successful execution hinges on the child's cooperation, as some may find the procedure uncomfortable (5). In such instances, clinicians have turned to lateral neck radiography as a readily available and less invasive tool for diagnosing and grading adenoid hypertrophy. These radiographs can identify the adenoids as the underlying cause of nasal obstruction and offer valuable insights into their size, shape, and position before surgical intervention (6). While various measurements exist for grading the adenoid size, the adenoid/nasopharynx ratio (A/N ratio), is the most widely used and represents the ratio of adenoid thickness to nasopharynx thickness (7).

In the current literature, there is limited comparative research evaluating the reliability and effectiveness of these two methods in the preoperative diagnosis of adenoid hypertrophy in children, which can provide valuable insights into their respective diagnostic accuracy, potential advantages, and limitations. Therefore, the objective of this study is to compare the reliability of flexible nasal endoscopy and lateral neck radiography in the preoperative diagnosis of children with adenoid hypertrophy, thereby aiding clinicians in making informed decisions about the optimal diagnostic approach for children with such a condition.

Methods

Subjects and Study Design

After having obtained approval from the Institutional Review Board of the American University of Beirut (IRB ID: BIO-2020-0303, date: 25.11.2020), the medical records of pediatric patients (younger than 18 years of age) who presented to a tertiary care center for adenoidectomy between January 2019 and December 2023 were reviewed. Due to the retrospective nature of the study, informed consent was not obtained from the participants' parents. The study adhered to the principles outlined in the Declaration of Helsinki and was conducted according to the STROBE guidelines for observational studies.

Children exhibiting chronic obstructive symptoms such as mouth breathing, snoring, witnessed apneas, and frequent nighttime awakenings for at least three months were included in the study. Those with severe nasal septal deviation, choanal atresia, craniofacial anomaly, and neuromuscular disorder were excluded from the study. Patients with imaging performed more than one month before surgery were also excluded. Demographic and clinical data included age, gender, snoring, witnessed apneas/frequent nighttime awakenings, and recurrent ear or upper respiratory tract infections. Among the enrolled children who underwent adenoidectomy, preoperative assessment of adenoid size was conducted either by lateral neck radiography or by flexible nasal endoscopy. The preoperative adenoid grade was then compared to the intraoperative grade, which was considered the reference. In routine clinical practice, flexible nasal endoscopy is more commonly performed in older children, whereas lateral neck radiography is often preferred in younger patients due to limited cooperation. Consequently, the retrospective nature of our study resulted in an expected age imbalance between the two diagnostic groups. This potential selection bias was acknowledged, and the findings were interpreted with this consideration in mind.

Preoperative Grading of Adenoid Hypertrophy

Lateral neck radiographs were retrieved from electronic medical records and reviewed independently by a pediatric radiologist and pediatric otolaryngologist. The percentage of airway obstruction by adenoid hypertrophy was calculated as the ratio between adenoid size and nasopharyngeal size (A/N ratio). "A" refers to the distance measured perpendicular from the straight portion of the anterior border of the basioccipital bone to the point of greatest convexity in the pharyngeal tonsil. "N" refers to the distance between the posterosuperior part of the hard palate and the anterior border of the basioccipital bone (Figure 1). The authors then categorized adenoid hypertrophy as "mild," "moderate," or "severe" if the ratio was between 26-50%, 51-75%, and 76-100%, respectively.

In children undergoing nasal endoscopy, a zero-degree flexible endoscope (KARL STORZ Endovision, Inc. Charlton: USA) was inserted into the nose after nasal decongestion with lidocaine and xylometazoline nasal drops. All flexible endoscopes had the same diameter of 2.8 mm. The endoscope was navigated along the nasal floor until only the posterior end of the inferior turbinate was visible. Video recordings of this procedure were captured using a distal-chip camera and stored digitally. These videos were subsequently reviewed by two otolaryngologists with over five years of experience for assessment. The adenoids were then graded based on the percentage of nasopharyngeal (choanal) obstruction as mild (26-50% obstruction), moderate (51-75% obstruction), and severe (76-100% obstruction). None of the patients had both radiographic and endoscopic evaluations.

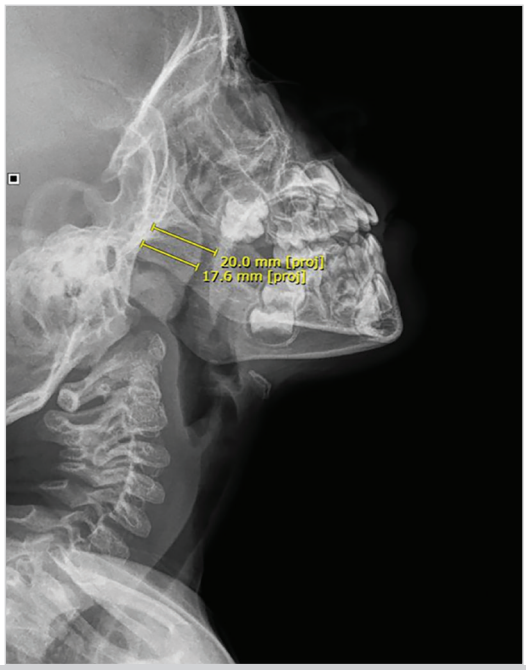

Figure 1. Lateral neck radiograph illustrating the measurement of adenoid and nasopharyngeal dimensions used to calculate the adenoid-to-nasopharynx ratio. The upper yellow line represents the depth of the nasopharyngeal airway (20.0 mm), while the lower line denotes the maximal thickness of the adenoid tissue (17.6 mm)

Intraoperative Grading of Adenoid Hypertrophy

Standard adenoidectomy was performed on each patient. Under general anesthesia, the patient was put in the rose position, and the mouth was opened with McIvor mouth gag (Aesculap AG, Tuttlingen, Germany). Two nasogastric tube catheters were introduced through the nasal cavity to retract the soft palate.

A senior pediatric otolaryngologist assessed the adenoids using a laryngeal mirror and determined their size based on the degree of nasopharyngeal obstruction. Adenoid hypertrophy was graded as mild or grade 2 if the obstruction was between 26 and 50%, moderate or grade 3 if the obstruction ranged from 51% to 75%, and severe or grade 4 if the obstruction was 76% and beyond. The results recorded intraoperatively were considered as the reference adenoid size in this study.

Statistical Analysis

The SPSS (IBM SPSS Statistics for Windows, Version 29.0. Armonk, NY: IBM Corp.) was used for data analysis. Descriptive statistics were used to analyze continuous variables (means and standard deviations) and categorical variables (numbers and percentages). The chi-square test was used to determine the association between categorical variables. To measure the strength of association between categorical variables, the odds ratio (OR) and Spearman's correlation coefficient were calculated along with their 95% confidence interval (CI). The Mann-Whitney U test was used to determine the association between independent continuous variables. A one-way analysis of covariance (ANCOVA) was conducted to compare the effectiveness of the two methods whilst controlling for age. Statistical significance was set at a p-value less than 0.05.

Results

Demographic Data

A total of 360 patients, 199 males and 161 females, were included in this study. The mean age of the study group was 4.29±2.39 years. In patients who were diagnosed with lateral neck radiography (n=272), the male-to-female ratio was 1.28 compared to 1.09 in patients who were diagnosed with endoscopy (p=0.514). Patients in the endoscopy group (n=88) were significantly older than patients in the radiography group (6.62±3.08 vs. 3.53±1.49; p<0.001). Caregivers reported that more than two-thirds of patients were snorers and had at least one episode of witnessed apnea per night. Around 34% of the patients complained of associated recurrent infections such as pharyngitis and otitis media. None of the patients had severe structural deformities of the nasal septum and inferior turbinates (Table 1).

Reliability of the Two Methods

There was a statistically significant difference in the diagnostic accuracy of the two methods. The preoperative grading of adenoid hypertrophy was identical to the intraoperative grading in 58% of the cases using the flexible endoscopy compared to 44.5% of the cases using the lateral neck radiography (p=0.028). Moreover, the odds of having an accurate preoperative grading of adenoid hypertrophy were 1.7 times greater with nasal endoscopy than with lateral neck radiography [OR=1.72; 95% CI (1.06-2.79)].

Furthermore, lateral neck radiography was reported to overestimate the diagnosis in 47.1% compared to 35.2% in the endoscopy group (p=0.088). The percentage of the cases in which the preoperative adenoid hypertrophy grading was underestimated was lower in both groups (8.5% in the radiography group vs. 6.8% in the endoscopy group) (Table 2).

A one-way ANCOVA was conducted to investigate the effect of different diagnostic methods on the accuracy of preoperative adenoid grading, while accounting for age. Levene's test and normality checks were carried out, and the assumptions were met. There was a significant difference in the accuracy of preoperative grading [$F(1,357)=4.315$, $p=0.038$] between the endoscopy and radiography groups.

Discussion

This study demonstrated that flexible nasal endoscopy provides a more reliable preoperative assessment of adenoid hypertrophy compared to lateral neck radiography.

Table 1. Demographic data of the study population

Demographic data (n=360)	X-ray (n=272)	Endoscopy (n=88)	p-value
Gender (male:female ratio)	1.28	1.09	0.514
Age in years (mean±SD)	3.53±1.49	6.62±3.08	<0.001
Snoring, n (%)	188 (69.1)	60 (68.2)	0.715
Witnessed apnea, n (%)	172 (63.2)	58 (65.9)	0.464
Recurrent infections, n (%)	92 (33.8)	30 (34.1)	0.589

SD: Standard deviation

Table 2. Reliability of diagnostic methods in assessing adenoid size

Reliability, n (%)	X-ray (n=272)	Endoscopy (n=88)	p-value
Accurate	121 (44.5)	51 (58)	0.028*
Overestimate	128 (47.1)	31 (35.2)	0.088
Underestimate	23 (8.5)	6 (6.8)	

*: Statistically significant (p<0.05)

Endoscopic grading matched intraoperative findings in 58% of the cases, whereas radiography achieved 44.5% concordance (p=0.028). The odds of accurate preoperative grading were 1.7 times higher with endoscopy [OR=1.72; 95% CI (1.06-2.79)], and this difference remained significant after adjusting for age [F(1,357)=4.315, p=0.038]. These results highlight the superiority of flexible endoscopy as a diagnostic tool that allows direct visualization of the nasopharyngeal airway and more accurate assessment of adenoid size prior to surgery.

Our findings are consistent with several previous studies comparing these two modalities. Mlynarek et al. (8) and Pisutsiri et al. (9) reported stronger correlations between endoscopic and intraoperative measurements than between radiographic and intraoperative findings, emphasizing the advantage of dynamic visualization over static imaging. Similarly, Peedikakkal et al. (10) demonstrated that endoscopic grading not only aligns more closely with intraoperative assessment but also correlates better with clinical symptoms, underscoring its clinical relevance in the evaluation of adenoid hypertrophy.

Conversely, other studies, such as those by Caylakli et al. (11) and Lertsburapa et al. (12), have shown that lateral neck radiography remains useful in selected clinical settings, particularly when endoscopic evaluation is not feasible such as in very young or uncooperative children. The A/N ratio derived from radiographs can offer a reliable estimate of adenoid size in such cases, although radiography tends to overestimate smaller adenoids and underestimate larger ones.

Our findings support previous reports highlighting the limitations of lateral neck radiography in accurately assessing adenoid size. Several factors contribute to its tendency to overestimate adenoid hypertrophy. As a two-dimensional representation of a three-dimensional structure, radiographs can distort adenoid volume due to the irregular, lobulated ("cauliflower-like") shape of the tissue (13). Moreover, patient positioning and cooperation, particularly in younger children, may affect measurement accuracy and increase variability in the A/N ratio. Interpretation is also subjective, with interobserver differences among radiologists and potential artifacts from dental fillings or metallic objects that obscure the nasopharyngeal airway (10). Transient upper respiratory infections or delays between clinical assessment and imaging can further alter adenoid size and explain inconsistent results (14).

In contrast, our study showed that flexible nasopharyngoscopy provides a more direct and accurate assessment of adenoid size. This technique allows real-time visualization of the nasopharynx, dynamic evaluation of choanal obstruction, and detection of concurrent infections that may influence adenoid hypertrophy. It also permits assessment of adjacent nasal structures, such as the septum and turbinates, ensuring a more comprehensive airway evaluation. However, nasal endoscopy remains an invasive procedure that requires patient cooperation, which may be challenging in very young children (15).

Study Limitations

Several limitations were encountered when conducting this study. One is the retrospective design, where data collection was reliant on existing medical records. This study is also a single-center study, which may limit the generalizability of the findings. Moreover, both methods are operator-dependent techniques, which could affect the accuracy and reliability of the results. Variations in the nasopharyngeal space, in addition to soft palate elevation with catheters intraoperatively, may alter nasopharyngeal dimensions, potentially affecting measurement accuracy. Additionally, both endoscopic and X-ray evaluations are done with the patient upright compared to supine in the operating room. Flexible nasal endoscopy requires patient cooperation, which may be challenging in younger children. Finally, smaller nasal cavities with the presence of mucous may make endoscopic adenoid evaluation more difficult.

Conclusion

Flexible nasal endoscopy is more reliable than lateral neck radiography for the preoperative grading of adenoid hypertrophy in children. The accuracy of flexible nasal endoscopy, as evidenced by its higher concordance with intraoperative findings, suggests it should be preferred for assessing adenoid size preoperatively. Lateral neck radiography remains a valid alternative in patients who cannot tolerate the nasal endoscope.

Ethics

Ethics Committee Approval: This study was approved by the Institutional Review Board of the American University of Beirut (IRB ID: BIO-2020-0303, date: 25.11.2020) and adhered to the principles outlined in the Declaration of Helsinki.

Informed Consent: Due to the retrospective nature of the study, informed consent was not obtained from the participants' parents.

Footnotes

Authorship Contributions

Surgical and Medical Practices: R.B., Concept: A.G., R.B., Design: A.G., R.B., Data Collection and/or Processing: J.H., O.A.H., A.G., Analysis or Interpretation: J.H., Literature Search: J.H., O.A.H., A.M.D., J.G., N.Z., Writing: J.H., O.A.H., A.M.D., J.G., N.Z.

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

Financial Disclosure: The authors declare that this study has received no financial support.

Main Points

- Flexible nasal endoscopy is more reliable than lateral neck radiography in the preoperative grading of adenoid hypertrophy in children.
- Lateral neck radiography is more likely to overestimate adenoid size compared to flexible nasal endoscopy.
- The odds of having an accurate preoperative grading of adenoid hypertrophy were 1.7 times greater with nasal endoscopy than with lateral neck radiography.

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Postoperative Otorrhea as a Predictor of Early Ventilation Tube Extrusion in Children

Original Investigation

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Abstract

Objective: To evaluate the clinical and surgical factors influencing ventilation tube (VT) extrusion time in pediatric patients, using both univariate and multivariate analyses.

Methods: This retrospective study included 227 pediatric patients (128 males, 99 females; mean age 6.46±2.27 years) who underwent VT insertion, with or without adenoidectomy and/or tonsillectomy, between January 2021 and January 2024. Demographic data, surgical indication, middle ear effusion type, and presence of postoperative otorrhea were recorded. Extrusion time for each ear was compared using the Mann-Whitney U and Kruskal-Wallis tests. Variables with $p<0.20$ were included in multiple linear regression analyses to identify independent predictors of extrusion time.

Results: The mean extrusion time was 8.41±3.01 months for the right ear and 8.28±2.81 months for the left ear. Age, sex, surgery type, and effusion type were not significantly associated with extrusion time. Postoperative otorrhea was significantly related to shorter extrusion in both ears (right: -4.77 months, $p<0.001$; left: -4.08 months, $p=0.001$).

Conclusion: Postoperative otorrhea and recurrent otitis media were associated with shorter VT retention, whereas demographic factors and concurrent adenoidectomy/tonsillectomy had no effect. Closer follow-up could be beneficial in patients with these risk factors to detect early extrusion and potential disease recurrence.

Keywords: Otitis media with effusion, otitis media, ventilation tube, postoperative complications, otorrhea, regression analysis

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Introduction

Otitis media with effusion (OME) and recurrent otitis media (ROM) are among the most common otolaryngologic problems in childhood and represent a leading cause of hearing loss, delayed speech, and reduced quality of life in the pediatric population (1,2). When conservative management fails, ventilation tube (VT) insertion is a widely accepted surgical treatment that aims to restore middle ear aeration, improve hearing, and reduce the risk of long-term complications (3,4).

While VT insertion is beneficial, tube extrusion is usually part of the natural postoperative process. The timing of extrusion varies depending on patient characteristics, middle ear status, tube type, and surgical factors. Early extrusion may

be associated with a higher likelihood of disease recurrence, whereas prolonged retention can lead to complications such as persistent tympanic membrane perforation (5).

Previous studies have examined factors that may influence VT extrusion time, including age, sex, surgical indication, middle ear effusion type, and concomitant procedures such as adenoidectomy and/or tonsillectomy (6-8). However, the findings have been inconsistent, and many studies have not evaluated multiple potential predictors simultaneously.

The presented study aimed to investigate clinical and surgical factors influencing VT extrusion time in a pediatric population, using both univariate and multivariate analyses. Identifying independent predictors of extrusion time may help optimize patient selection, surgical planning, and follow-up strategies, ultimately improving clinical outcomes.

Methods

Study Design and Population

The study was approved by İzmir Bakırçay University Non-Interventional Clinical Research Ethics Committee (approval no: 2287, date: 04.06.2025) and was conducted in accordance with the principles of the Declaration of Helsinki. This retrospective observational study included pediatric patients who underwent VT insertion, with or without concomitant adenoidectomy and/or tonsillectomy, between January 2021 and January 2024. A total of 227 patients with complete clinical and follow-up data were included in the analysis. In all patients, a Shepard Grommet VT (Medtronic Xomed, Inc., USA) was inserted through a myringotomy performed in the anterior-inferior quadrant of the tympanic membrane. In indicated patients, when no effusion was present intraoperatively, VTs were still inserted if the tympanic membrane demonstrated significant retraction, atelectasis, or other signs of eustachian tube dysfunction.

Inclusion Criteria

- Age between 0 and 18 years at the time of surgery
- Underwent VT insertion for OME or ROM
- Complete medical records available
- Minimum follow-up period of 18 months

Exclusion Criteria

- Previous VT insertion or middle ear surgery
- Presence of craniofacial anomalies, cleft palate, or syndromic conditions
- Chronic suppurative otitis media or cholesteatoma
- Incomplete follow-up data
- VT type other than Shepard grommet

Data Collection

Demographic data (age, sex), surgical details, intraoperative effusion type for each ear, and presence of postoperative otorrhea were recorded from patient files. The indication for surgery was categorized as OME or ROM. Extrusion time was defined as the interval between tube insertion and the date of confirmed extrusion on otoscopic examination. The primary outcome was extrusion time (months) for the right and left ears. Secondary outcomes included identification of clinical and surgical factors affecting extrusion time. ROM was defined as ≥3 episodes in 6 months or ≥4 in 12 months with resolution between episodes. Postoperative otorrhea was defined as ear discharge clinically documented and/or requiring topical antibiotic therapy after tympanostomy tube insertion. Otorrhea was treated with topical quinolone ± steroid eardrops (no routine oral antibiotics).

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 22 (IBM Corp., Armonk, NY, USA). Analyses were performed at the ear-level; right and left ears were modeled in separate cohorts, ensuring one observation per patient within any given model. Continuous variables were expressed as mean±standard deviation or median, and categorical variables as counts and percentages. The Mann-Whitney U test was used for two-group comparisons and the Kruskal-Wallis test for comparisons involving more than two groups. Candidate variables (univariable $p<0.20$ and/or a priori clinical relevance) were included in a multivariable linear regression; multicollinearity was assessed using variance inflation factors, and model assumptions were checked with residual diagnostics. A p-value of <0.05 was considered statistically significant.

Artificial Intelligence Declaration

Part of the manuscript text was edited for clarity and grammar using ChatGPT (OpenAI, San Francisco, CA, USA). The authors reviewed and verified all artificial intelligence (AI)-assisted content to ensure accuracy and originality. No AI-generated content was used as a primary source.

Results

A total of 227 patients were included in the analysis. Among 227 patients, tube placement was bilateral in 187 (82.3%), right-only in 19 (8.4%), and left-only in 21 (9.3%). The mean age was 6.46±2.27 years (range, 1-12 years). Of these, 128 (56.4%) were male and 99 (43.6%) were female. Regarding surgical procedures, 43 patients (18.9%) underwent VT insertion alone, 114 (50.2%) underwent adenoidectomy with VT insertion, and 70 (30.8%) underwent adenoidectomy with tonsillectomy and VT insertion (Table 1).

Table 1. Demographic and clinical characteristics of the study population (n=227)

Characteristic	n (%) or mean±SD (range)
Age (years)	6.46±2.27 (1-12)
Sex	
Male	128 (56.4)
Female	99 (43.6)
Surgical procedure	
VT only	43 (18.9)
Adenoidectomy+VT	114 (50.2)
Adenoidectomy+tonsillectomy+VT	70 (30.8)
Intraoperative effusion-right ear	
None	16 (7.0)
Serous otitis media	42 (18.5)
Glue ear	148 (65.2)
Intraoperative effusion-left ear	
None	14 (6.2)
Serous otitis media	37 (16.3)
Glue ear	157 (69.2)
Otorrhea-right ear	
Present	6 (2.9)
Absent	200 (97.1)
Otorrhea-left ear	
Present	5 (2.4)
Absent	203 (97.6)
Extrusion time-right ear (months)	8.41±3.01 (3-17)
Extrusion time-left ear (months)	8.28±2.81 (3-17)

SD: Standard deviation, VT: Ventilation tube

Intraoperative middle ear findings revealed that, in the right ear, 16 (7.0%) ears had no effusion, 42 (18.5%) had serous effusion, and 148 (65.2%) had glue ear. In the left ear, 14 (6.2%) ears had no effusion, 37 (16.3%) had serous effusion, and 157 (69.2%) had glue ear. Otorrhea occurred in 6 (2.9%) right ears and 5 (2.4%) left ears postoperatively. The mean extrusion time was 8.41±3.01 months (range, 3-17 months) for the right ear and 8.28±2.81 months (range, 3-17 months) for the left ear. Extrusion before six months occurred in 19/206 right ears [9.2%, 95% confidence interval (CI): 6.0-14.0] and 33/208 left ears (15.9%, 95% CI: 11.5-21.4).

Comparison of extrusion times according to sex revealed no statistically significant differences for either ear (right: Mann-Whitney U=5091.0, Z=-0.276, p=0.782; left: Mann-Whitney U=4861.5, Z=-1.018, p=0.308). Similarly, extrusion times did not differ significantly according to the type of surgery performed [right: $x^2(2)=2.056$, p=0.358; left: $x^2(2)=4.225$, p=0.121].

Regarding intraoperative effusion type, no statistically significant difference in right ear extrusion time was observed [$x^2(2)=0.291$, p=0.865]. For the left ear, extrusion time tended to be longer in patients without effusion, but the difference did not reach statistical significance [$x^2(2)=5.000$, p=0.082]. The presence of postoperative otorrhea was significantly associated with shorter extrusion time in both ears: right ear: Mann-Whitney U=61.5, Z=-3.795, p<0.001; left ear: Mann-Whitney U=45.5, Z=-3.502, p<0.001. When analyzed according to surgical indication, no statistically significant difference was found for the right ear (Mann-Whitney U=363.0, Z=-1.670, p=0.095). However, left ear extrusion time was significantly shorter in patients operated for ROM compared to those with OME (Mann-Whitney U=350.0, Z=-2.276, p=0.023).

Extrusion outcomes did not differ by surgical procedure. For the right ear, one-way analysis of variance showed no between-group difference [$F(2,203)=0.724$, p=0.486, $n^2=0.007$]; for the left ear, results were likewise non-significant [$F(2,205)=1.842$, p=0.161, $n^2=0.018$]. Mean extrusion values by group were: right—VT 8.41, VT+adenoidectomy 8.19, VT+adenotonsillectomy 8.77; left—VT 7.49, VT+adenoidectomy 8.48, VT+adenotonsillectomy 8.42.

Multivariate Analyses

Right ear: the presence of right otorrhea was the only independent predictor, associated with a 4.77-month shorter extrusion time (B=-4.773, 95% CI: -7.154 to -2.391, p<0.001).

Left ear: independent predictors were ROM indication (B=-3.525, 95% CI: -5.657 to -1.393, p=0.001), left otorrhea (B=-4.076, 95% CI: -6.449 to -1.704, p=0.001), and effusion type (no effusion to glue ear) (B=-0.898, 95% CI: -1.536 to -0.259, p=0.006). Age and sex were not significant predictors in either ear (Table 2).

Discussion

In this study, we evaluated clinical and surgical factors influencing VT extrusion time in pediatric patients. Ears were analyzed as two independent cohorts (right vs. left), ensuring one observation per patient within each model and thereby preserving independence. Consequently, coefficients reflect ear-level effects and are not directly generalizable to pooled patient-level outcomes. The mean extrusion time in our cohort was approximately eight months for both ears. This retention period was shorter than the findings of Alaraifi et al. (8) which is 13.96 months and aligned with the findings of Lin et al. (7), and Song et al. (6) who also observed average extrusion times between seven and nine months. Extrusion before six months occurred in 19/206 right ears and 33/208 left ears in our study and this was similar to the findings of Alaraifi et al. (8) (12.8%).

These differences in retention time could be related to variations in tube design, insertion site, patient demographics,

Table 2. Multivariate analysis of factors affecting tube extrusion time (bold indicates statistical significance) (p<0.05)

Variable	Ear	Multivariate B (95% CI)	Multivariate p-value
Age	Right	0.116 (-0.059 to 0.291)	0.194
Sex (male compared to female)	Right	-0.017 (-0.826 to 0.791)	0.966
Effusion type (glue compared to absent)	Right	-0.198 (-0.868 to 0.472)	0.560
Otorrhea	Right	-4.773 (-7.154 to -2.391)	**<0.001**
Indication (ROM compared to OME)	Right	-2.390 (-4.879 to 0.100)	0.060
Age	Left	0.126 (-0.045 to 0.297)	0.147
Sex (male compared to female)	Left	0.569 (-0.166 to 1.303)	0.129
Effusion type (glue compared to absent)	Left	-0.898 (-1.536 to -0.259)	**0.006**
Otorrhea	Left	-4.076 (-6.449 to -1.704)	**0.001**
Indication (ROM compared to OME)	Left	-3.525 (-5.657 to -1.393)	**0.001**

OME: Otitis media with effusion, ROM: Recurrent otitis media, CI: Confidence interval

and surgical indications. The relatively short persistence time observed in our cohort could partly be attributable to the use of Shepard grommet tubes, which are known to extrude earlier than long-term designs such as Paparella tubes and T tubes.

In agreement with several previous reports, neither age nor sex significantly affected tube extrusion time in our analysis (6,9). This suggests that demographic variables alone are unlikely to be major determinants of retention time when other clinical factors are accounted for. Similarly, the type of primary surgery—whether VT insertion alone, adenoidectomy with VT, or adenotonsillectomy with VT—did not significantly influence extrusion duration. This is consistent with the findings of Alaraifi et al. (8) who reported no significant difference in extrusion timing between patients undergoing VT alone and those receiving concurrent adenoidectomy.

While some earlier studies claimed that effusion type did not significantly affect extrusion time, Song et al. (6) reported that serous effusions were associated with shorter extrusion times compared to mucoid effusions (8,10). In our cohort, the extrusion time decreased as the effusion type progressed from no effusion to serous effusion to glue ear, indicating that mucoid effusion was associated with the highest risk of early extrusion; however, this difference was only significant for the left ears with a relatively small effect (B=-0.898, 95% CI: -1.536 to -0.259, p=0.006). Differences in effusion classification methods and sample composition may account for these inconsistencies.

Postoperative otorrhea is one of the most frequently reported complications after VT insertion, with incidence rates in the literature ranging from 15% to over 50%, depending on study design, follow-up duration, and patient population (11,12). In our cohort, postoperative otorrhea was observed in 2.9% of the right ears and 2.4% of the left ears, which is markedly lower than most published series. This difference may be related to the uniform use of the Shepard grommet tubes, careful postoperative care protocols, and possibly underreporting of mild or transient episodes by patients or caregivers. Because our definition prioritized clinically documented and treatment-requiring episodes, mild, self-limited discharges may have gone unrecorded, potentially underestimating otorrhea incidence and yielding conservative effect estimates. One of the notable findings of our study was the significant association between postoperative otorrhea and shorter extrusion times in both ears. This is biologically plausible, as chronic inflammatory processes can accelerate epithelial migration, thereby hastening tube expulsion (13). While most studies have emphasized the role of effusion viscosity or adenoid size, fewer have focused on postoperative otorrhea as a predictor of extrusion time (6). Our results suggest that postoperative otorrhea may be an important factor in early extrusion. Valtonen et al. (14) also stated that postoperative otorrhea is related to earlier VT extrusion and recurrent OME. Postoperative otorrhea should be interpreted as a clinical marker of mucosal inflammation and impaired middleear ventilation rather than a sole causal pathway for extrusion.

In our cohort, early extrusion was more frequent among patients who were operated on for ROM compared with those with OME. This difference may reflect the higher inflammatory burden and epithelial remodeling that accompany ROM, which could facilitate faster epithelial migration and earlier tube rejection. Although ROM as the surgical indication was significantly associated with shorter retention time in the left ear, this relationship did not reach statistical significance in the right ear (p=0.060). Given the proximity of the p-value to the significance threshold, it is possible that the observed side-to-side difference reflects a limitation in statistical power rather than a true biological asymmetry. The sample size, when stratified by ear and surgical indication, may have been insufficient to detect a modest but clinically relevant effect on the right side. Future studies with larger cohorts are warranted to clarify whether this association is bilateral and to determine whether ear-

specific anatomical or physiological factors contribute to extrusion timing.

Unlike some previous studies, our cohort was homogeneous with respect to tube placement—all tubes were inserted in the anteroinferior quadrant. This eliminates one potential confounding factor. Yoo et al. (10), Alaraifi et al. (8), and Lin et al. (7) have emphasized that tube material, design, and flange diameter could significantly influence retention time, with long-term tubes such as Paparella type II persisting significantly longer than Shepard grommets. We could not assess these effects, as tube type was not varied in our series.

Patients with postoperative otorrhea or ROM may warrant closer follow-up, as they appear at increased risk for early tube loss. Future prospective studies should incorporate standardized tube types, document insertion site, and assess middle ear parameters in more detail. Including these variables could clarify their relative contributions and help tailor surgical approaches for individual patients.

Study Limitations

This study has several limitations. Firstly, its retrospective design may be subject to incomplete documentation and recall bias, particularly regarding postoperative complications such as transient otorrhea, which could lead to underreporting. Secondly, all patients had the same tube type (Shepard grommet) placed in the anteroinferior quadrant, which, while reducing variability, also limits the generalizability of findings to other tube designs or placement sites. Thirdly, extrusion time was based on the date of clinical detection rather than continuous monitoring, so the exact extrusion date may be imprecise. Some clinically important factors such as allergic rhinitis and eustachian tube disfunction were not included in the analysis due to lack of data. Moreover, detailed tympanic membrane findings such as retraction or atelectasis were not uniformly documented, and their potential relationship with extrusion time could not be evaluated. Finally, the relatively small number of patients operated on for ROM and the low incidence of postoperative otorrhea in our cohort may have reduced the statistical power to detect certain associations. As a result, some clinically relevant effects may not have reached statistical significance.

Conclusion

In our pediatric cohort, the average VT retention time was approximately eight months, which is within the lower range reported in the literature. Age, sex, surgical procedure type, and effusion type were not significant predictors of extrusion time. However, postoperative otorrhea and ROM were independently associated with earlier extrusion, highlighting the need for closer postoperative monitoring in these patients. Standardized prospective studies considering tube type, insertion site, and middle ear pathology in detail are needed to better understand modifiable factors that could optimize retention time and reduce recurrence rates.

Ethics

Ethics Committee Approval: The study was approved by İzmir Bakırçay University Non-Interventional Clinical Research Ethics Committee (approval no: 2287, date: 04.06.2025) and was conducted in accordance with the principles of the Declaration of Helsinki.

Informed Consent: Not required due to the retrospective design of the study, as approved by the Ethics Committee.

Footnotes

Authorship Contributions

Surgical and Medical Practices: T.U., T.M., Concept: E.U., T.U., M.K.G., Design: E.U., T.M., Data Collection and/or Processing: E.U., M.K.G., T.M., Analysis or Interpretation: E.U., T.U., M.K.G., Literature Search: E.U., T.U., M.K.G., Writing: E.U., T.M.

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

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Main Points

- Postoperative otorrhea is an independent predictor of early ventilation tube extrusion, reducing tube retention time by approximately four months in both ears.
- Age, sex, and additional surgeries like adenoidectomy with or without tonsillectomy do not significantly influence extrusion time.
- Close postoperative monitoring is crucial in children with postoperative otorrhea or a history of recurrent otitis media to detect early tube loss.

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A Bibliometric Review of Residency Theses on Vertigo in Türkiye

Original Investigation

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Abstract

Objective: In our study we analyzed the residency theses on vertigo in Türkiye by year, subject, and specialty with the aim of identifying academic trends.

Methods: A bibliometric review was conducted using the National Thesis Database (1972-2025). The search was performed with the keywords vertigo, vestibular, dizziness, and Ménière. Only medical specialization theses were included. Titles and abstracts were screened, and eligible theses were classified by year, specialty, and topic.

Results: A total of 180 theses were identified. The highest number of theses was produced between 2016 and 2020, followed by a decline after 2021. In the study period 103 theses were published in otorhinolaryngology, 29 in neurology, 10 in physical medicine and rehabilitation, 23 in emergency and family medicine, and 15 in other specialties. While studies showed an apparent increase in vestibular testing and rehabilitation in recent decades, these emphasized etiology and diagnostic approaches in the earlier years.

Conclusion: Most theses on vertigo were produced between 2016 and 2020, with otorhinolaryngology providing the most significant contribution. Over time, interest shifted from etiology and diagnosis towards vestibular testing and rehabilitation. The findings confirm that vertigo is a central subject in otorhinolaryngology, but also attracts growing attention in neurology, physical medicine and rehabilitation, emergency medicine, and family medicine.

Keywords: Vertigo, vestibular disease, bibliometrics, benign paroxysmal positional vertigo, vestibular migraine, otorhinolaryngology, neurology, postgraduate medical theses

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Introduction

Vertigo is a common symptom characterized by bodily or environmental rotation sensation without actual movement. As a typical manifestation of vestibular system disorders, it is a shared focus of several medical disciplines, including otorhinolaryngology, neurology, emergency medicine, and physical medicine and rehabilitation (1). This multidisciplinary nature increases the complexity of diagnosis and treatment, broadening the scope and diversity of scientific research on vertigo (2).

In clinical practice, its evaluation varies across specialties. Neurologists often emphasize imaging methods and the exclusion of central pathologies, whereas otorhinolaryngologists prioritize audiovestibular tests, positional assessments, and vestibular maneuvers (3). In

emergency departments, the Head-Impulse-Nystagmus-Test-of-Skew protocol is critical in differentiating peripheral from central causes (4). More recently, vestibular rehabilitation has gained importance, particularly in the management of chronic vestibular dysfunction. Studies have shown that vestibular exercise protocols improve balance, dizziness, postural stability, and quality of life (5).

Medical specialization theses represent a cornerstone of scientific knowledge production in Türkiye. Beyond providing original data that support clinical practice, they foster scientific reasoning, research ability, and critical analysis among physicians in training. Bibliometric analyses on medical theses have been reported in the literature (6). Vertigo is one of the core topics in otorhinolaryngology training, yet it is also relevant to other specialties. However, the historical trajectory, thematic diversity, disciplinary distribution, and evolving academic trends of theses on vertigo—a symptom of multidisciplinary significance—have not been systematically evaluated.

The presented study, therefore, conducts a systematic bibliometric analysis of vertigo-related medical specialization theses available in the National Thesis Center (7), aiming to reveal their distribution by subject, specialty, and year. In doing so, it also seeks to provide a reference to guide future clinical and academic research on vertigo.

Methods

This descriptive study was conducted to determine the temporal distribution of medical specialization theses on vertigo in Türkiye and to classify them by subject and specialty. Data were obtained from the open-access database of the Council of Higher Education Thesis Center (7). Ethical approval was obtained from Pamukkale University Non-Interventional Clinical Research Ethics Committee (approval no: E-60116787-020-734874, date: 13.08.2025).

Vertigo, vestibular, dizziness, and Ménière were used as keywords. Only medical specialization theses were included, while master's, doctoral, proficiency in art, and other thesis types were excluded. Titles and abstracts were reviewed in detail, and only theses related to vertigo were evaluated.

The included theses were manually classified by year of publication, medical specialty (e.g., otorhinolaryngology, neurology, physical medicine and rehabilitation, emergency medicine, family medicine), and main subject headings [e.g., benign paroxysmal positional vertigo (BPPV), vestibular migraine, vestibular tests, vestibular rehabilitation, central/peripheral vertigo differentiation].

Statistical Analysis

The theses were grouped into seven periods to assess temporal changes: <1995,1995-2000, 2001-2005, 2006-2010, 2011-2015, 2016-2020, and 2021-2025. Categorical data were presented as frequencies and percentages, and all analyses were conducted using Microsoft Excel (Microsoft Corp., Redmond, WA, USA).

Results

In this study, a total of 180 residency theses on vertigo prepared in Türkiye between 1972 and 2025 were analyzed. Clear trends were observed in their distribution by specialty and year. Otorhinolaryngology, neurology, physical medicine and rehabilitation, emergency medicine, and family medicine were analyzed separately, while disciplines with fewer theses were grouped under "others" (Figure 1).

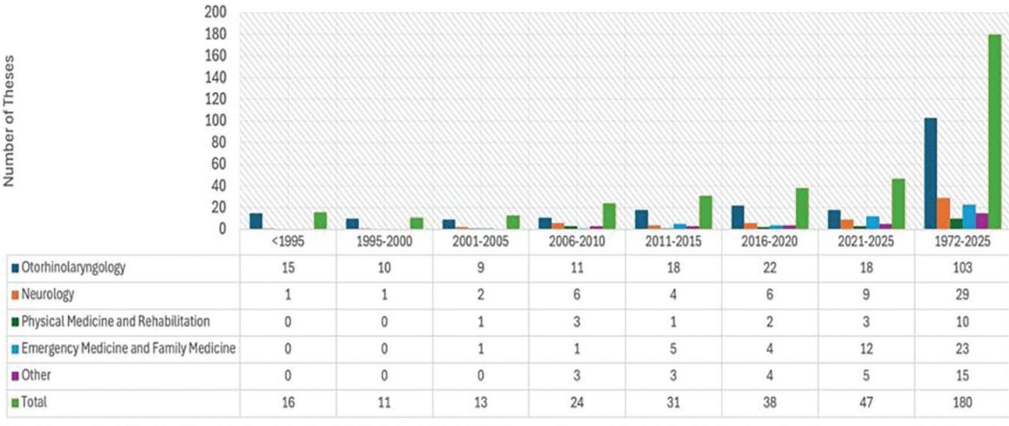
Otorhinolaryngology had the largest share, especially in the early years (1972-2000), and peaked with 22 theses between 2016 and 2020, though a relative decline was noted in 2021-2025. A marked rise was observed in this field during 2016-2020, with subtopics such as vestibular tests, BPPV, and vestibular migraine becoming prominent. Vestibular migraine first appeared between 2006 and 2010, while Ménière's disease, once a leading focus before 2001, declined steadily and ranked lowest between 2011 and 2020. Since 2006, vestibular test-related theses remained the leading subtopic (Figure 2). In otorhinolaryngology, Ménière's disease has declined as a research focus, whereas BPPV and vestibular migraine have become increasingly frequent topics.

Neurology showed a steady increase in vertigo-related theses after 2006, reaching its highest contribution in 2021-2025 with nine theses (Figure 3). Migraine and vestibular testing were the most common themes.

Although fewer, physical medicine and rehabilitation theses demonstrated a notable upward trend after 2006. The predominant topics were vestibular rehabilitation and the management of balance disorders. Between 2021 and 2024, ten theses were completed in Physical Medicine and Rehabilitation, of which nine (90%) focused on vestibular rehabilitation and one (10%) on BPPV.

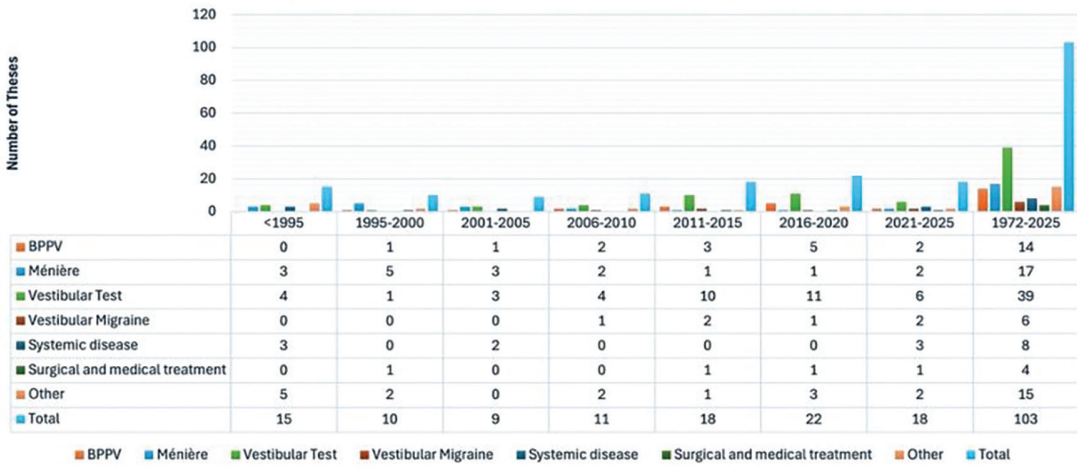
In emergency medicine and family medicine, vertigo-related theses increased markedly after 2011 (Figure 1). Most studies in these fields focused on distinguishing peripheral from central vertigo, particularly on clinical evaluation, diagnostic algorithms, and referral criteria.

Finally, other disciplines, including radiology, psychiatry, and obstetrics, produced a limited but noteworthy number of theses, underscoring the multidisciplinary nature of vertigo research.



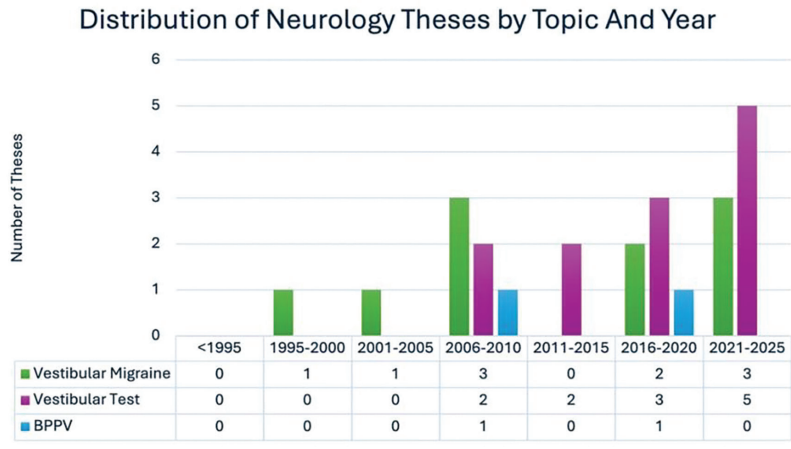
	<1995	1995-2000	2001-2005	2006-2010	2011-2015	2016-2020	2021-2025	1972-2025
Otorhinolaryngology	15	10	9	11	18	22	18	103
Neurology	1	1	2	6	4	6	9	29
Physical Medicine and Rehabilitation	0	0	1	3	1	2	3	10
Emergency Medicine and Family Medicine	0	0	1	1	5	4	12	23
Other	0	0	0	3	3	4	5	15
Total	16	11	13	24	31	38	47	180

Figure 1. Distribution of residency theses on vertigo by specialty and year



	<1995	1995-2000	2001-2005	2006-2010	2011-2015	2016-2020	2021-2025	1972-2025
BPPV	0	1	1	2	3	5	2	14
Ménière	3	5	3	2	1	1	2	17
Vestibular Test	4	1	3	4	10	11	6	39
Vestibular Migraine	0	0	0	1	2	1	2	6
Systemic disease	3	0	2	0	0	0	3	8
Surgical and medical treatment	0	1	0	0	1	1	1	4
Other	5	2	0	2	1	3	2	15
Total	15	10	9	11	18	22	18	103

Figure 2. Topic distribution of vertigo-related theses in otorhinolaryngology
BPPV: Benign paroxysmal positional vertigo, ENT: Ear-nose-throat



	<1995	1995-2000	2001-2005	2006-2010	2011-2015	2016-2020	2021-2025
Vestibular Migraine	0	1	1	3	0	2	3
Vestibular Test	0	0	0	2	2	3	5
BPPV	0	0	0	1	0	1	0

Figure 3. Topic distribution of vertigo-related theses in neurology
BPPV: Benign paroxysmal positional vertigo

Discussion

The findings of this study demonstrate that vertigo has gradually expanded beyond otorhinolaryngology to attract growing attention from other medical disciplines. In particular, the marked rise in neurology theses during 2021-2025 appears to be closely linked to the recognition of vestibular migraine as a neurological syndrome, as well as the increasing applicability of objective vestibular tests such as vestibular evoked myogenic potentials (VEMP) and video head impulse test (vHIT) in central nervous system disorders (8). Subjects previously studied in otorhinolaryngology, such as BPPV, were also revisited from a neurological perspective, indicating both qualitative and quantitative growth of scientific interest in vertigo within neurology.

In otorhinolaryngology, the decline in thesis numbers after 2021 can be attributed to the impact of the coronavirus disease 2019 (COVID-19) pandemic. Reduced patient numbers and a shift towards retrospective studies led researchers to focus on shorter and pandemic-related topics. By contrast, the sharp increase in numbers between 2016 and 2020 can be explained by the introduction and wider use of objective vestibular tests, including the vHIT, VEMP, and videonystagmography. These methods enabled broader research on vestibular migraine and vestibular rehabilitation. Unlike the limited interest reported by Kerber and Fendrick (9) in 2010 regarding dizziness, academic attention to this field has since grown steadily.

Ménière's disease presents a different trend. While international publications have shown steady growth in the past two decades, interest in Türkiye declined markedly after 2001 (10,11). This may be due to inconsistent diagnostic criteria, the absence of standardized treatment protocols, and the limitations of objective diagnostic tools. At the same time, researchers have increasingly focused on topics offering measurable outcomes and rapid data collection, such as vestibular tests, BPPV, and vestibular migraine.

BPPV has been the subject of increasing national and international academic attention. Globally, studies in otorhinolaryngology have most frequently addressed BPPV, Ménière's disease, and psychogenic vertigo (12). BPPV-related publications rose consistently each year, accelerating after 2005 and peaking in 2021 (10). Hu et al. (10) suggested that this surge was associated with increased productivity among leading researchers and a higher incidence of BPPV during the COVID-19 pandemic. Yang et al. (13) reported similar findings. Data from Türkiye reflect this global trend, with a notable rise in BPPV-related theses between 2016 and 2020. This increase is likely due to the greater availability of vestibular diagnostic tools and the fact that BPPV is both common and treatable in clinical practice.

Another significant trend is the growing interest in vestibular rehabilitation. In Türkiye, theses from otorhinolaryngology, neurology, and physical medicine and rehabilitation have increasingly addressed this area, reflecting its multidisciplinary character. These studies have emphasized vestibular retraining, improved balance control, and enhanced quality of life, thereby contributing both functional and diagnostic perspectives. International studies have highlighted similar developments. Wang et al. (5) proposed that motion sickness arises from mismatches between visual and vestibular autonomic pathways and demonstrated the effectiveness of virtual reality (VR) in rehabilitation. Since 2013, publications on VR applications in rehabilitation medicine have expanded substantially, reflecting increasing research interest. Similarly, Pan et al. (14) showed that publications on vestibular vertigo and cognition were limited before 2015. Still, a steady rise has occurred, particularly concerning vestibular disorders, vertigo, and cognitive functions in older adults, peaking in 2022 (14). These trends suggest that the vestibular system is now being evaluated not only in relation to balance but also in broader clinical contexts, including cognition, ageing, and virtual rehabilitation applications (15). Trends in Türkiye also mirror this global orientation.

Similarly, the increase in vertigo-related theses within emergency medicine and family medicine likely reflects the high frequency of vertigo presentations in emergency and primary care settings. These findings indicate that specialists in these fields are adopting more systematic and diagnosis-oriented approaches to vertigo management.

Conclusion

A peak in vertigo-related medical specialization theses was observed between 2016 and 2020, with otorhinolaryngology contributing the largest share. While early theses primarily focused on etiological and diagnostic approaches, more recent years have shown increasing interest in vestibular testing and rehabilitation. The findings confirm that vertigo remains a central subject in otorhinolaryngology, but has also attracted growing research interest in neurology, physical medicine and rehabilitation, emergency medicine, and family medicine. Over time, Ménière's disease has declined as a focus in otorhinolaryngology theses, whereas BPPV and vestibular migraine have become more prominent topics.

Ethics

Ethics Committee Approval: Ethical approval was obtained from Pamukkale University Non-Interventional Clinical Research Ethics Committee (approval no: E-60116787-020-734874, date: 13.08.2025).

Informed Consent: Bibliometric analysis.

Footnotes

Authorship Contributions

Concept: G.A., C.O.K., F.N.A., Design: G.A., C.O.K., F.N.A., Data Collection and/or Processing: G.A., Analysis or Interpretation: G.A., Literature Search: G.A., C.O.K., Writing: G.A., F.N.A.

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

Financial Disclosure: The authors declare that this study has received no financial support.

Main Points

- This is the first bibliometric analysis of vertigo-related medical specialization theses conducted in Türkiye.
- The highest number of theses was produced between 2016 and 2020, with otorhinolaryngology providing the largest contribution.
- Research trends shifted from etiological and diagnostic approaches in earlier years to vestibular testing and rehabilitation in recent decades.
- Vertigo, while remaining a central theme in otorhinolaryngology, has also attracted increasing academic interest from neurology, physical medicine and rehabilitation, emergency medicine, and family medicine.
- Our findings highlight the multidisciplinary nature of vertigo research and provide a reference for future clinical and academic studies.

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Evaluation of Clinical and Laboratory Findings at Admission in Diabetic Patients with Acute Invasive Fungal Rhinosinusitis

Original Investigation

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Abstract

Objective: Acute invasive fungal rhinosinusitis (AIFR) is a disease with rapid progression, and high mortality and morbidity rates. The objective of this study was to retrospectively study the clinical and surgical findings of diabetic AIFR patients who were recently followed up in our clinic, with a view to determining whether these findings are in accordance with the current literature on the subject.

Methods: The study cohort comprised 30 patients with a pathological diagnosis of invasive fungal sinusitis who were evaluated at Hatay Mustafa Kemal University Hospital, Department of Otorhinolaryngology, between 2017 and 2022 and subsequently underwent surgical intervention.

Results: A total of 30 patients were included in the study. Of these, 16 were male and 14 were female. All patients were diagnosed with diabetes mellitus. The patients were divided into two groups: those who did not survive (n=12) and those who survived (n=18). Significant differences were observed between the groups in age, presence of diabetic ketoacidosis at presentation, skull base involvement, C-reactive protein (CRP), leukocyte, and neutrophil counts at presentation ($p=0.013$, $p<0.001$, $p=0.024$, $p=0.013$, $p<0.001$, $p<0.001$, $p<0.001$, respectively).

Conclusion: In our study, age, the presence of diabetic ketoacidosis at presentation and CRP values were significantly higher in the non-surviving patient group, and this was consistent with the findings of previous studies. The presence of skull base involvement and significantly higher leukocyte and neutrophil values at presentation in the non-surviving patient group could be a new finding to focus on.

Keywords: Rhinosinusitis, mucormycosis, fungal infections, diabetes mellitus, diabetic ketoacidosis, prognosis

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Introduction

Acute invasive fungal rhinosinusitis (AIFR) is a disease characterized by invasive infiltration of the paranasal sinuses and nasal cavity mucosa with mycotic agents, and high mortality and morbidity rates (1,2). Fungal rhinosinusitis is histopathologically classified as invasive or non-invasive, depending on the extent of tissue invasion (2). Non-invasive fungal rhinosinusitis has two subtypes: allergic fungal rhinosinusitis and mycetoma (3). Invasive fungal rhinosinusitis, on the other hand, is classified into three subgroups: acute, chronic, and granulomatous invasive fungal rhinosinusitis. The occurrence of these subgroups is contingent upon the state of the patient's immune system. It is possible for chronic invasive and non-invasive forms to occur in individuals with normal immune systems; however, AIFR is observed in patients with severe immune system disorders (2,3). It is for these reasons that AIFR is defined as the most aggressive type of fungal rhinosinusitis, with high morbidity and mortality. The cause of immune system impairment in AIFR patients may be uncontrolled diabetes, malignancy, immunosuppressive and chemotherapeutic drugs, acquired immunodeficiency syndrome, solid organ transplantation, severe malnutrition, trauma, severe burns, and the recently described infection caused by the coronavirus disease 2019 (COVID-19) virus (4). In the existing literature, the reported mortality rates vary considerably, from 20% to 80%. However, majority of the studies reported mortality rates above 40% (5-8).

The objective of this study was to retrospectively study, and review in reference to the current literature, the clinical and surgical findings of diabetic AIFR patients who presented to the emergency department and were treated and followed up in our clinic. We hypothesized that there would be significant differences between the clinical and laboratory data of the surviving and non-surviving groups.

Methods

The study was planned to include all patients who were diagnosed with histopathologically invasive fungal sinusitis and underwent surgical intervention at the Otolaryngology Department of Hatay Mustafa Kemal University Hospital from 2017 to 2022. Thirty patients with a histopathological diagnosis who underwent surgical intervention were retrospectively identified and included in the study. Patients who did not have a histopathological diagnosis of invasive fungal sinusitis, did not undergo surgery, and did not have diabetes were excluded. All patients were provided with strict glycemic control in collaboration with the endocrinology department. The diagnosis of invasive fungal sinusitis was determined by the presence of the appropriate clinical findings, endoscopic and radiological evidence of necrotic tissue, and histopathological confirmation of fungal invasion. Given the exigencies of the disease, culture confirmation was deemed unnecessary; instead, histopathological detection of invasion was considered sufficient for intervention. Medical treatment was started in a timely manner for all patients with clinical suspicion. Liposomal amphotericin B was administered as a medical agent, intravenously and locally using cotton pads, at a dose of 5-10 mg/kg/day, over a period of 30-60 minutes, for 6-8 weeks. The surgical approach employed for these patients was determined by the extent of the pathology. In cases where the involvement was confined to the paranasal sinuses, endoscopic surgery was employed. Conversely, in cases with palatal, dermal, or orbital involvement, a combined approach was the preferred surgical modality. The objective of the surgical intervention, whether endoscopic or combined, was to thoroughly excise the necrotic tissue up to vital structures, such as the skull base and major vascular structures. The debridement procedure was continued until the perfused tissue became visible, and residual tissue was left only if within vital boundaries. In cases of orbital spread, the procedure was carried out together with the ophthalmology department. Orbital spread was assessed clinically and using magnetic resonance imaging, and the decision to perform exenteration was made together with the ophthalmology department based on parameters such as vision, pupil reflexes, ocular motility, advanced fundus changes, orbital apex involvement, and proptosis associated with orbital involvement. Demographic data, laboratory data, and clinical findings at the time of admission, underlying diseases, pathology results, and outcomes of patients were reviewed. The study was approved by the Hatay Mustafa Kemal University Non-Interventional Clinical Research Ethics Committee (approval no: 21, date: 01.09.2022).

Statistical Analysis

Statistical analysis was conducted using the IBM SPSS Statistics version 23 package program (IBM Corporation, Armonk, NY, USA). The data were calculated as mean±standard deviation or percentage. In the statistical analysis, the distribution of the groups was studied using the Kolmogorov-Smirnov test. The independent samples t-test was employed for comparisons between two groups for continuous variables that exhibited a normal distribution, whereas the Mann-Whitney U test was utilized for comparisons between two groups for continuous variables that did not conform to a normal distribution. Comparisons between categorical variables were conducted using Pearson's chi-squared test and Fisher's exact test. The level of statistical significance was set at $p<0.05$.

Results

The study cohort comprised 30 patients of whom 16 were male and 14 were female. The age of the patients ranged from 28 to 79 years, with a mean of 59.46±12.54 years. The

demographic data, clinical information and comorbidities of the patients are presented in Table 1. All patients were diagnosed with diabetes mellitus. The second most prevalent comorbidity was hypertension, occurring in 30% of the cases. No patients presented with a hematological or other systemic malignancy. A history of steroid treatment for a previous infection with the COVID-19 virus was present in seven patients (23.3%) within the last six months. A single patient (3.3%) was identified as having an active case of COVID-19 at admission from the emergency department. Following the examination of the biopsy materials, it was determined that mucor from the mucoraceae family was the responsible pathogen in 28 cases (93.3%), while aspergillus was identified in two cases (6.7%). In 10 patients, a purely endoscopic approach was deemed sufficient (33.3%), while in the remaining 20 patients, an endoscopic and open surgical approach was necessary (66.6%).

The clinical findings at the time of initial presentation are given in Table 2. The most prevalent clinical manifestation observed in all patients (100%) was facial pain. The second most prevalent clinical finding was facial fullness, occurring in 86.7% of cases. Other common clinical findings included ophthalmoplegia (66.7%), diplopia (63.3%), visual loss (60%) (Figure 1) and proptosis (56.7%). Ketoacidosis was observed in 13 patients at the time of presentation (43.3%). Thirteen patients exhibited facial paralysis (43.3%), and 12 demonstrated palatal necrosis (40%) (Figures 1 and 2). Four patients exhibited fever at the time of initial presentation, while no fever was observed in the remaining patients.

Table 1. Demographic data, associated comorbidities, causative organisms, surgical approach, and outcomes of patients

Variable	Number	Frequency (%)
Total cases	30	100
Age (years) (mean±SD)	59.46±12.54	
Sex		
Male	16	53.3
Female	14	46.7
Comorbidities		
DM	30	100
HT	9	30
CAD	5	16.7
Asthma	2	6.7
COVID-19 (active)	1	3.3
Post-COVID-19	7	23.3
Organism		
Mucor	28	93.3
Aspergillus	2	6.7
Surgical approach		
Endoscopic	10	33.3
Open+endoscopic	20	66.7
Orbital exenteration	14	46.7
Outcomes		
Did not survive	12	40
Survived	18	60

DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, COVID-19: Coronavirus disease 2019, SD: Standard deviation

Table 2. Clinical and examination findings at the time of admission

Variable	Number	Frequency (%)
Fever	4	13.3
Facial pain	30	100
Nasal discharge	9	30
Ophthalmoplegia	20	66.7
Proptosis	17	56.7
Diplopia	19	63.3
Visual loss	18	60
Altered mental state	10	33.3
Palatal necrosis	12	40
Facial paralysis	13	43.3
Septal perforation	9	30
Diabetic ketoacidosis	13	43.3

Review of the laboratory findings of the patients at the time of admission, revealed that all patients exhibited hemoglobin A1c values above the normal range, with a mean of 10.26±2.2%. In addition, the laboratory findings of the patients at the time of admission included evaluations of other parameters, including C-reactive protein (CRP), haemoglobin, platelet, lymphocyte, leukocyte, and neutrophil counts. The data related to these parameters are presented in Table 3.

The degree of involvement of the nasal and paranasal sinuses was evaluated both radiologically and intraoperatively. The radiological data demonstrated a range of findings, from mucosal thickening to the presence of osteomyelitis in the affected area. In intraoperative debridement, the most crucial factor was the presence or absence of a blood supply in the affected region. The data indicated that the most frequently affected sites were the lateral nasal wall (100%), the maxillary sinus (100%), and the ethmoid sinus (96.7%). Twenty patients exhibited orbital involvement, representing a prevalence of 66.7%. A detailed account of the clinical dissemination of the patients is provided in Table 4.

Review of the patient outcomes in terms of mortality showed that 60% (18 patients) had recovered, whereas 40% (12 patients) succumbed to their conditions. The patients were divided into two groups, namely, those who did not survive (n=12) and those who survived (n=18), and a statistical comparison was conducted. Further details of this evaluation can be found in Table 5. Statistically significant differences were observed between the two groups in terms of age, the

Figure 1. a) Postoperative follow-up image of a patient with facial paralysis among the admission findings, **b)** preoperative examination image of a patient with eye involvement

Figure 2. a) Preoperative view of a patient with palate involvement, **b)** postoperative view of another patient with palate involvement

presence of diabetic ketoacidosis (DKA) at presentation, skull base involvement, CRP levels, white blood cell (leucocyte) counts, and neutrophil counts at presentation (p=0.013, p<0.001, p=0.024, p=0.013, p<0.001, p<0.001, p<0.001, respectively).

The results of the receiver operating characteristic (ROC) analysis indicated that the optimal cut-off value for CRP in predicting invasive fungal sinusitis was 93.45 mg/L, with sensitivity and specificity of 75% and 72.2%, respectively [area under the curve (AUC): 0.782; 95% confidence interval (CI): 0.61-0.96]. The optimal cut-off value was determined to be 93.45×10^3/μL for neutrophil count and 15.55×10^3/μL for leukocyte count, with sensitivity and specificity values of 100%-92% and 100%-94%, respectively (AUC: 1; 95% CI: 1-1, AUC: 0.995; 95% CI: 0.98-1, respectively) (Table 6).

Discussion

Initial symptoms in patients with AIFR are not distinctive. Patients frequently present with non-specific initial symptoms of acute-chronic rhinosinusitis. In literature, the most commonly reported presenting symptoms are fever, facial swelling, nasal congestion, and facial pain, with varying rates of occurrence (1-3,5). In a systematic review of 52 studies and 807 patients conducted by Turner et al.

Table 3. Laboratory findings at the time of admission

Variable	Number (mean±SD)
HbA1c	10.26±2.2 %
CRP	111.75±70.34 mg/L
Hb	11.38±1.93 g/dL
Platelet	332.17±126.65 10^3/µL
Lymphocyte	1.82±0.87 10^3/µL
Leukocyte	14.48±6.16 10^3/µL
Neutrophil	11.43±5.75 10^3/µL

CRP: C-reactive protein, HbA1c: Hemoglobin A1c, Hb: Hemoglobin, SD: Standard deviation

Table 4. Clinical extension of patients

Variable	Number	Frequency (%)
Nasal		
Maxillary	30	100
Ethmoid	29	96.7
Sphenoid	23	76.7
Frontal	21	70
Lateral nasal wall	30	100
Septum	9	30
Orbital involvement	20	66.7
Intracranial involvement	5	16.7
Skull base involvement	12	40
Palate	12	40
Skin	5	16.6

(6), the most common presenting symptoms were identified as facial swelling, fever, and nasal congestion, respectively. Depending on the progression of the disease at the time of presentation, early symptoms may include facial pain, nasal congestion, and nasal discharge. Symptoms such as visual loss, proptosis, diplopia, blurred vision, facial swelling, and facial paralysis may also be observed in patients presenting in the advanced stage. When the patients in our study were examined clinically, radiologically, and surgically, it was found that most of them presented in the advanced stage. The most commonly observed symptom in our patient cohort was facial pain, which was present in 100% of the cases. Other common symptoms included facial fullness, ophthalmoplegia, diplopia, visual loss, and proptosis. In contrast to the findings of previous studies, the prevalence of the first five most common symptoms was higher in our sample. It is postulated that this may be attributable to the fact that majority of the patients admitted to the facility exhibited advanced dissemination.

As the symptoms of AIFR disease are non-specific, the examination findings are of greater significance. In literature, the earliest examination finding is reported to be a change in the appearance of the nasal mucosa (1,3,5,9,10). In the initial stages, the presence of white discoloration is indicative of ischemia, whereas in the later stages, black discoloration suggests the onset of necrosis. Mucosal discoloration may be observed in the entirety of the nasal mucosa. In numerous references in literature, the most prevalent site of this alteration is the middle turbinate (1,3,5,8-10). Subsequently,

Table 5. Comparison of the surviving and non-surviving groups in terms of demographic, clinical and laboratory data

Variable	Survived (n=18)	Not-survived (n=12)	p-value	95% CI
Age (years) (mean±SD)*	54.94±10.74	66.25±12.36	0.013	2.6-20
Sex				
M	44.4%	66.7%	0.232	
F	56.6%	33.3%		
Fever	1	3	0.274	
Diabetic ketoacidosis*	1	12	<0.001	
Orbital involvement	11	9	0.694	
Intracranial involvement	1	4	0.128	
Skull base involvement*	4	8	0.024	
Facial paralysis	9	5	0.654	
COVID-19	5	3	1.000	
HbA1c (mean±SD)	10.41±2.29%	10.03±2.12%	0.652	-2.08-1.32
CRP*	86.43±63.82 mg/L	149.74±64.24 mg/L	0.013	14.47-112.16
Hb	11.48±2.09 g/dL	11.23±1.74 g/dL	0.744	-1.74-1.25
Platelet	370.33±131.18 10^3/µL	299.92±80.80 10^3/µL	0.109	-157.5-16.7
Lymphocyte	2.09±0.96 10^3/µL	1.60±0.37 10^3/µL	0.060	-1.01-0.02
Leukocyte*	10.11±2.89 10^3/µL	21.02±3.03 10^3/µL	<0.001	8.66-13.16
Neutrophil*	7.28±2.54 10^3/µL	17.66±2.62 10^3/µL	<0.001	8.41-12.34

*: Statistically significant parameters, M: Male, F: Female, CRP: C-reactive protein, Hb: Hemoglobin, COVID-19: Coronavirus disease 2019, HbA1c: Hemoglobin A1c, SD: Standard deviation, CI: Confidence interval

the nasal septum, nasal floor and inferior turbinate are examined. Furthermore, the absence of pain during endoscopic examination suggests mucosal anesthesia and is indicative of fungal invasion. Table 4 shows the clinical manifestations observed in the patients included in this study. Accordingly, the most common site of involvement in our patients was the maxillary sinus and the lateral nasal wall, affecting 100% of the cases. The second most common site of involvement was the ethmoid sinuses, with a prevalence of 96.7%. In accordance with the findings in the existing literature, we proceeded to obtain full-thickness biopsies from the nasal cavity areas exhibiting suspicious characteristics, with a particular focus on the middle turbinate.

In literature, the most common computed tomography finding in cases of AIFR is reported to be intranasal or sinus mucosal thickening (3,5,9,11). In their study, Silverman and Mancuso (12) proposed that periantral adipose tissue infiltration could be the earliest radiological finding, and that bone erosion and destruction are indicative of the disease's advanced stages. Magnetic resonance imaging is a more effective method for demonstrating the extent of disease spread to the surrounding soft tissues, differentiating mucus edema, and identifying instances of extra-sinus involvement (3,5). In our study, radiological imaging proved an effective tool in the process of clinical suspicion, determination of the margins of invasion and prediction of the surgical margins to be applied (Figures 3 and 4).

Even when the patient's clinic, endoscopic examination, laboratory data, and imaging findings are consistent with AIFR, a definitive diagnosis can only be reached through a histopathological examination of the biopsy tissue. During endoscopic examination, both suspicious foci should be identified, and biopsies should be taken from these suspicious areas. Given that the middle turbinate is the most commonly reported site of fungal invasion in literature, it would be an appropriate decision to select this site for biopsy (1,3,5,8-10). The presence of fungal elements in the mucosal biopsy may be considered indicative of invasive fungal rhinosinusitis until proven otherwise (13). Süslü et al. (1) argued that mucosal biopsies had limited utility due to the potential for false-positive and false-negative results, bleeding complications, and the risk of creating mucosal damage susceptible to subsequent aspergillus invasion. In contrast, the authors propose that a deep biopsy, encompassing the mucosa, submucosa, and potentially even the cartilage tissue, should be conducted under operating theater conditions with the use of electrocautery. It is of the utmost importance to perform early debridement to effectively manage the disease. In the early stages of the disease, an endoscopic approach may be sufficient; however, in advanced disease, additional procedures such as orbital exenteration, fascial resection, or maxillectomy may be necessary. In the presented study, endoscopic approach was sufficient in 10 patients, while endoscopic and open approaches were required in 20 patients.

Table 6. ROC analysis of patients' admission values

Variable	AUC (95% CI)	Cut-off	p-value	Sensitivity (%)	Specificity (%)
CRP	0.782 (0.61-0.96)	93.45	0.01	75	72.2
Neutrophil	1 (1-1)	12.93	<0.001	100	100
Leukocyte	0.995 (0.98-1)	15.55	<0.001	92	94

AUC: Area under curve, CI: Confidence interval, ROC: Receiver operating characteristic, CRP: C-reactive protein

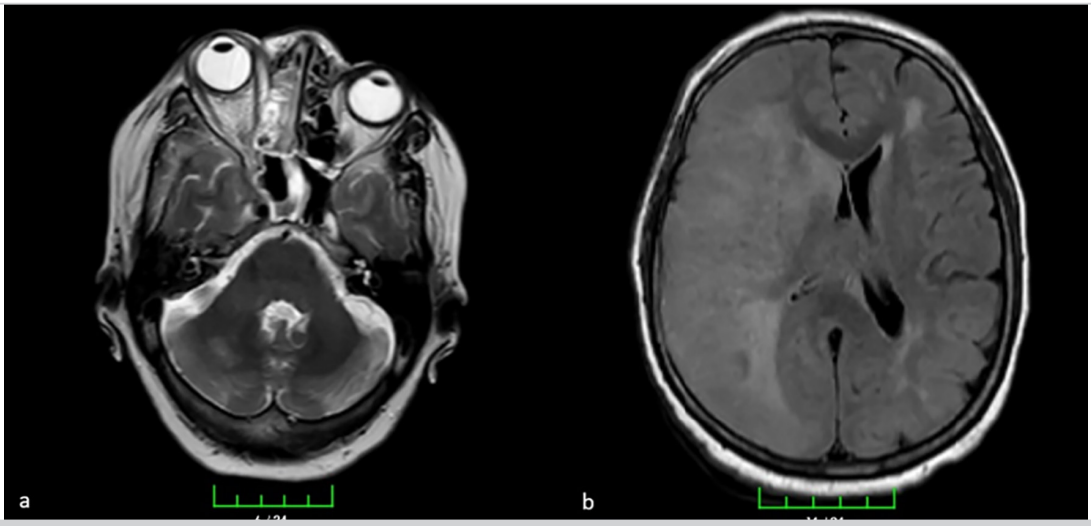

Figure 3. Patient with intracranial involvement **a)** eye extension and conspicuous proptosis, **b)** intracranial involvement

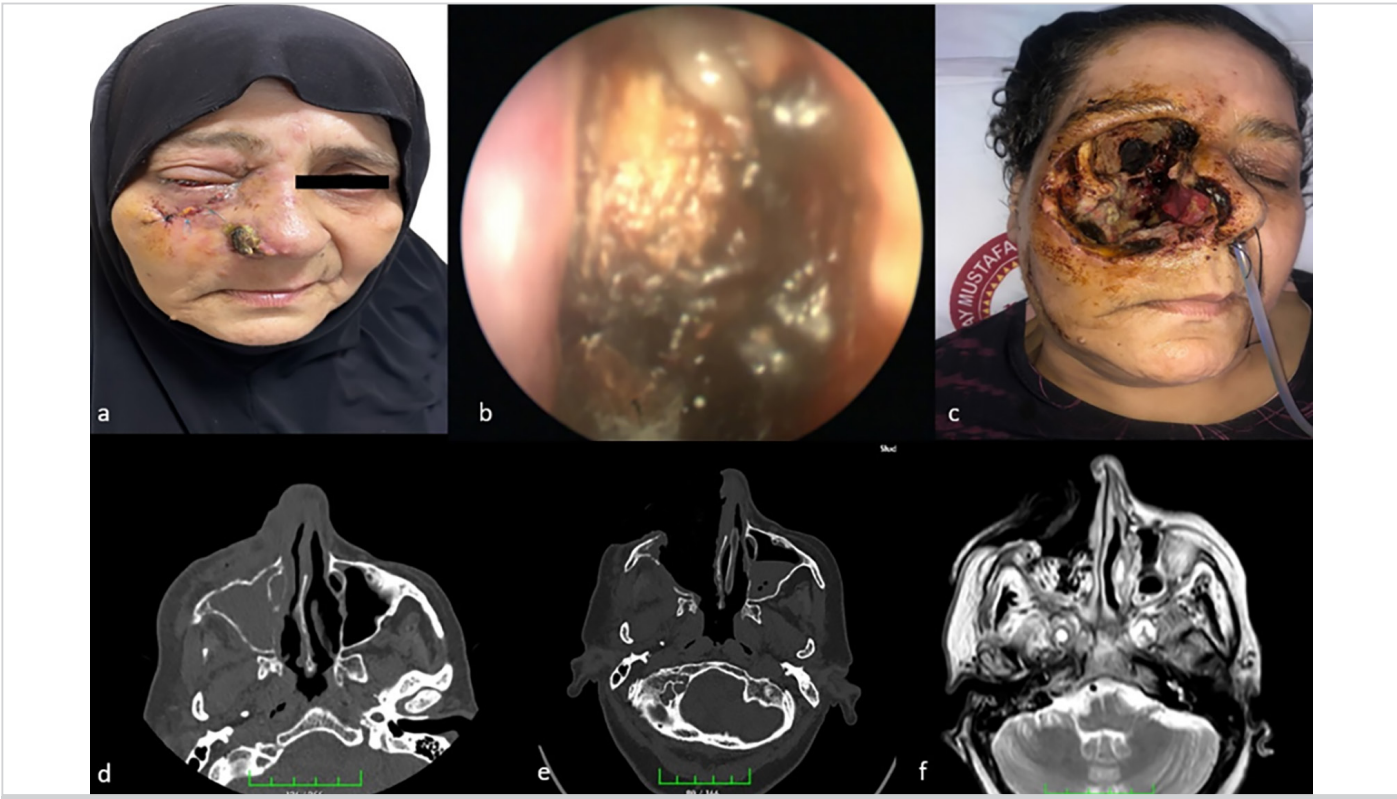

Figure 4. a) Image of an AIFR patient with skin involvement at presentation, **b)** endoscopic view of the same patient at admission, **c)** view of the operation site after surgical debridement, **d)** preoperative CT image of the patient. Periantral and premaxillary adipose tissue involvement and bone erosion and decalcification are worth noting, **e)** postoperative CT imaging **f)** postoperative MR imaging
MR: Magnetic resonance, CT: Computed tomography, AIFR: Acute invasive fungal rhinosinusitis

A total of 14 patients underwent orbital exenteration. In cases where the pathology to be debrided was limited to areas accessible via endoscopy, an endoscopic approach was the preferred method.

In some studies, parameters such as diabetes, delayed diagnosis, orbital and intracranial involvement, advanced age, and neutropenia were identified as negative prognostic factors (6,14-17). In their systematic review conducted to identify the prognostic factors and survival outcomes, Turner et al. (6) identified impaired mental status, intracranial invasion, renal/liver failure, diabetes, and advanced age as the factors predictive of decreased survival, and surgical intervention, endoscopic surgical intervention, and the use of liposomal amphotericin-B in medical treatment as positive prognostic factors. Mahomva et al. (18) posited that an elevated body temperature of unknown origin, low platelet levels and low neutrophil levels would indicate increased risk. The parameters used in the comparison of surviving and non-surviving groups are provided in Table 5. The comparison of the two groups based on these parameters yielded significant results regarding age, the presence of DKA at presentation, involvement of the skull base, CRP value, and high leukocyte and neutrophil values. Advanced age and the presence of DKA at the time of presentation were identified as negative prognostic factors in numerous studies in literature. In a study of 11 patients, Butugan et al. (19) determined a mortality rate of 27.3%. The authors observed that all three patients who succumbed to their illness had DKA at the time of their initial presentation, which was identified as a negative prognostic factor. The findings of our study align with those of previous studies in that advanced age and the presence of DKA at the time of presentation yielded significant results. The relationship between CRP value and AIFR has been the subject of numerous published studies. As reported by Cho et al. (20), elevated CRP was identified as an independent prognostic factor in patients with AIFR. In our study, a significant difference was observed between the surviving and non-surviving groups in terms of high CRP value, and this is consistent with the literature (p=0.013). The results of the ROC analysis indicated that the optimal cut-off value for CRP in predicting invasive fungal sinusitis was 93.45 mg/L, with sensitivity and specificity of 75% and 72.2%, respectively (AUC: 0.782; 95% CI: 0.61-0.96).

Skull base involvement is a common occurrence in patients with AIFR. In a study conducted by Monroe et al. (15), 10 out of the 29 patients observed exhibited skull base involvement. No significant findings were noted when comparing the surviving and non-surviving patients in this regard. In our study, 12 patients had skull base involvement, which was significantly more prevalent in the non-surviving

group (p=0.024). Although skull base involvement is not typically considered a prognostic factor in the literature, and recent meta-analyses have not identified it as a significant predictor, we believe that our findings are nevertheless noteworthy. According to the available literature, orbital and intracranial involvement are generally considered as poor prognostic factors (5). In their study, Turner et al. (6) stated that patients with intracranial involvement had the lowest survival rate. Moreover, the involvement of the orbit has been identified as a risk factor for overall survival in numerous studies (6,21,22). The presented study revealed no statistically significant differences between the surviving and non-surviving groups in terms of intracranial or orbital involvement. The patients' presentation to the emergency department at a late stage, the timing of surgical treatment, non-diabetes-related comorbidities, and medical treatment may have functioned as confounders in this regard.

The results of our study showed that neutrophil and leukocyte counts at admission were significantly higher in non-surviving patients compared to survivors. In the ROC analysis, the optimal cut-off values for predicting invasive fungal sinusitis were $93.45\times10^3/\mu L$ for neutrophils and $15.55\times10^3/\mu L$ for leukocytes. These thresholds yielded sensitivities of 100% and 100% and specificities of 92% and 94%, respectively (AUC: 1.00; 95% CI: 1.00-1.00 and AUC: 0.995; 95% CI: 0.98-1.00).

In the literature, neutrophil recovery has been identified as a positive prognostic factor, particularly in patients with hematological malignancies (23). Gardner et al. (24) reported that 94% of their 21 patients had hematological malignancy and an absolute neutrophil count $\leq1\times10^3/\mu L$ at diagnosis. Similarly, Gode et al. (25) showed that leukocyte and neutrophil counts, along with CRP levels, significantly influenced survival. Navuluri et al. (26) also observed that patients with hematological malignancies typically presented with low neutrophil counts and elevated CRP values. Overall, most studies evaluating neutrophil counts have focused on patients with hematological malignancies, whereas data on diabetic patients remain scarce.

Our findings indicate a statistically significant elevation in neutrophil and leukocyte counts at admission in a patient cohort composed exclusively of diabetic individuals without underlying malignancy. This represents a novel and clinically relevant observation that diverges from prior literature and may suggest a different host response profile in this population.

Study Limitations

The limitations of our study include the retrospective design, the small number of patients and the experience of a single tertiary healthcare institution. It is our belief that future studies with larger numbers of patients, and comparative studies will prove beneficial. The homogeneity of our patient cohort, consisting exclusively of individuals with diabetes, represents a key strength of our study, in contrast to the heterogeneous patient groups observed in other studies, including those involving patients with hematological malignancies or mixed patient populations.

Conclusion

In diabetic patients with AIFR, it should be considered that the possible pathogen may be mucor from the mucoraceae family. In our study, age, presence of DKA at presentation and CRP levels were significantly higher in the non-surviving group. In the surviving group, skull base involvement, leukocyte and neutrophil levels at presentation were statistically significantly higher, which may be a new finding to focus on.

Ethics

Ethics Approval: The study was approved by the Hatay Mustafa Kemal University Non-Interventional Clinical Research Ethics Committee (approval no: 21, date: 01.09.2022).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.İ.G., E.A., M.Ç., D.G., Ş.O., Concept: M.İ.G., E.A., Ş.O., Design: M.İ.G., E.A., Ş.O., Data Collection and/or Processing: M.İ.G., F.K., Analysis or Interpretation: M.İ.G., F.K., Ş.O., Literature Search: M.İ.G., F.K., Writing: M.İ.G.

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Main Points

- Acute invasive fungal rhinosinusitis (AIFR) is a disease characterized by invasive infiltration of the paranasal sinuses and nasal cavity mucosa with mycotic agents, with high mortality and morbidity rates.
- Initial symptoms in patients with AIFR are not distinctive, patients often present with non-specific initial symptoms of acute-chronic rhinosinusitis.
- A definitive diagnosis can only be reached through a histopathological examination of the biopsy tissue.
- In our study, age, presence of diabetic ketoacidosis at presentation and C-reactive protein levels were significantly higher in the non-surviving group.
- In the non-surviving group, skull base involvement, leukocyte and neutrophil levels at presentation were statistically significantly higher, which may be a new finding to focus on.

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Prenatal Diagnosis of a Large Oropharyngeal Teratoma and Airway Management with EXIT: A Case Report

Case Report

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Abstract

We present a rare case of a large fetal oropharyngeal teratoma (epignathus) diagnosed during the third trimester and managed successfully with a planned ex utero intrapartum treatment (EXIT) procedure followed by neonatal surgical resection. A 30-year-old pregnant woman was referred to our department at 29 weeks of gestation due to polyhydramnios and the detection of an oropharyngeal mass on ultrasound. Fetal magnetic resonance imaging confirmed a 5×5 cm heterogeneous mass filling the oral cavity, raising concern for airway obstruction at birth. At 32 weeks, spontaneous pre-term labor necessitated urgent EXIT. While fetoplacental circulation was maintained, a tracheostomy was performed to secure the airway, allowing for safe delivery and ventilation of the neonate. The newborn subsequently underwent successful transoral surgical excision of the mass, which was confirmed histologically as an immature teratoma. Postoperative recovery was uneventful, and the infant remained free of recurrence during a 24-month follow-up period. This case highlights the importance of prenatal diagnosis, fetal imaging, and multidisciplinary planning in the management of airway-compromising lesions. It also introduces the EXIT procedure to otolaryngologists as a critical and effective approach for ensuring airway patency in selected high-risk cases of congenital head and neck tumors.

Keywords: Teratoma, oropharyngeal neoplasms, airway management, tracheostomy, EXIT, case report

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Introduction

Head and neck teratomas are uncommon, accounting for only about 10% of all teratomas. Among these, the nasopharynx and cervical region are the most frequently affected sites. When the lesion arises in the oropharyngeal area, it is referred to as epignathus, with a reported incidence ranging between 1 in 35,000 and 1 in 200,000 live births. These tumors are derived from all three germ layers (ectoderm, mesoderm, and endoderm) and are classified as mature (benign) or immature (malignant) (1). Although often benign, they can pose a life-threatening risk to neonates due to potential airway obstruction. Large masses in the oropharynx may interfere with fetal swallowing, leading to polyhydramnios and severe respiratory distress at birth (2).

Advances in prenatal imaging, especially ultrasound and fetal magnetic resonance imaging (MRI), allow for early detection, anatomical characterization, and evaluation of airway compromise (3,4). This enables multidisciplinary delivery planning, often involving the ex utero intrapartum treatment (EXIT) procedure. EXIT maintains fetoplacental circulation during partial delivery, providing critical time to secure the airway via intubation or tracheostomy (5). The purpose of sharing this case is to introduce the EXIT procedure to otolaryngologists and emphasize its life-saving potential in cases of anticipated neonatal airway obstruction. We present a rare case of a large fetal oropharyngeal teratoma managed successfully with EXIT and early postnatal surgical resection.

Case Presentation

A 30-year-old woman at 29 weeks of gestation presented with lower abdominal pain. Targeted ultrasound revealed a large heterogeneous mass occupying the fetal oropharynx, with accompanying polyhydramnios (Figure 1a). Fetal biometry was consistent with gestational age, and no other anomalies were identified. Maternal serum alpha-fetoprotein was markedly elevated to 48,000. Fetal echocardiography showed normal cardiac anatomy and function.

Fetal MRI demonstrated a 5×5 cm heterogeneous mass originating from the oropharynx, expanding the oral cavity and displacing airway structures, suggesting a high risk of airway obstruction at birth (Figure 1b). Although elective cesarean delivery was initially planned, spontaneous preterm labor occurred at 32 weeks, prompting urgent delivery. An EXIT procedure was performed, and a tracheostomy was established while fetoplacental circulation was maintained. The neonate was then separated from the placenta and transferred to the neonatal intensive care unit.

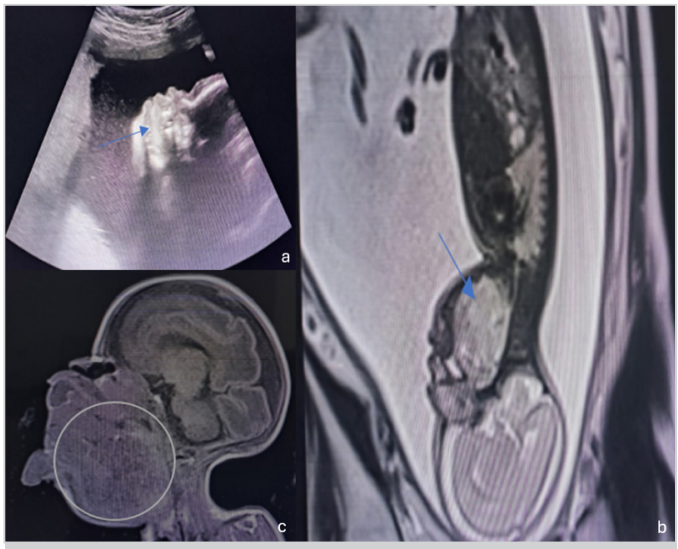

Figure 1. Prenatal and postnatal imaging showing a fetal oropharyngeal mass detected by ultrasound and magnetic resonance imaging (MRI) before birth and confirmed by computed tomography (CT) on postnatal day 2. **a)** Ultrasound image obtained 30 days prior to cesarean section showing a hyperdense mass in the fetal oropharynx. **b)** Fetal MRI obtained 25 days prior to cesarean section showing a heterogeneous mass measuring approximately 5×5 cm located in the oropharynx. **c)** Sagittal CT image of the fetus obtained on postnatal day 2 following cesarean section

Postnatal computed tomography imaging further characterized the mass, revealing extension into the prevertebral space (Figure 1c). On the second postnatal day, a transoral surgical excision was performed in collaboration with neurosurgery and the mass was completely resected (Figure 2). Histopathology confirmed an immature teratoma. Postoperative recovery was uneventful. The infant was initially fed via nasogastric tube for one week, followed by successful oral feeding. No postoperative complications occurred. Follow-up at 24 months showed no evidence of recurrence. The tracheostomy tube was successfully removed at the 5th postoperative month after confirming adequate airway patency. Written informed consent was obtained from the patient's father for publication of this case report and the accompanying images.

Discussion

This case highlights the critical importance of prenatal diagnosis and coordinated multidisciplinary planning in managing fetal oropharyngeal teratomas. Teratomas may arise in multiple anatomical locations, with the sacrococcygeal region representing the most common site,

Figure 2. Intraoperative and postoperative views showing the oropharyngeal mass before resection, the surgical field after excision, and the gross appearance of the resected specimen. **a)** Pre-resection image of the mass. **b)** The appearance of the oral cavity and laryngeal structures following mass excision. **c)** The resected mass

accounting for approximately 40% of all cases. Less than 5% are found in the head and neck. These tumors demonstrate a higher incidence in females, and when identified during early childhood, they are generally benign. Epignathus denotes a teratoma originating in the oropharynx, which, when large, can result in craniofacial distortion and severe respiratory compromise at birth. Prenatal ultrasound, particularly when complemented by fetal MRI, allows for early detection and detailed evaluation of the mass, including its size, composition, relationship to airway structures, and vascularity. In our case, the presence of polyhydramnios and a large oropharyngeal mass suggested a high likelihood of postnatal airway compromise. These findings prompted early planning and involvement of a multidisciplinary team, which contributed to the favorable outcome (4,6).

The EXIT procedure was essential in managing the airway in this case. Originally described in 1990, the EXIT-to-airway technique has become an established approach for fetuses with anticipated airway obstruction, including cervical masses, large goiters, congenital high airway obstruction syndrome, and oropharyngeal teratomas (7). The procedure involves partial cesarean delivery with ongoing placental perfusion to preserve oxygenation while securing the neonatal airway (8). This controlled setting provides a crucial window of time typically 30-60 minutes for safe intubation or tracheostomy, reducing the risk of hypoxia and emergency resuscitation (9).

In our case, we anticipated that conventional intubation would be extremely difficult due to a large mass almost completely occupying the fetal oropharynx. EXIT provided a critical window for performing a calm, controlled tracheostomy while the fetus remained oxygenated via placental support. Once the airway was secured, the neonate was fully delivered and ventilated. This approach prevented hypoxia and enabled safe transition to postnatal care. The literature strongly supports the use of EXIT in similar high-risk airway cases. King et al. (8) described twins with oropharyngeal teratomas who both underwent EXIT: one was intubated, and the other required partial tumor debulking and tracheostomy, demonstrating EXIT's flexibility. Hu et al. (2) similarly emphasized that EXIT improves survival in infants with epignathus, especially when airway obstruction is anticipated. In contrast, smaller oropharyngeal teratomas without evidence of airway compromise may be managed with routine delivery followed by prompt intubation (10). Our review showed that most large oropharyngeal teratomas in the literature were successfully managed with EXIT, which has been associated with improved outcomes compared to historical cases without it (6,9).

Definitive treatment of oropharyngeal teratomas is complete surgical excision, ideally during the neonatal period. In our case, the tumor was removed on the second postnatal day. Surgery not only resolves airway obstruction but also facilitates feeding and normal orofacial development. Resection is curative in most cases, particularly for histologically immature teratomas. For immature teratomas, which carry malignant potential, surgery remains the first-line treatment. Adjuvant chemotherapy is considered in high-grade lesions, but low-grade (grade 1,2) immature teratomas that are completely excised can often be managed conservatively with serial tumor marker surveillance (1,9). Our patient followed this conservative approach, with no recurrence observed to date.

Review of similar cases shows favorable outcomes with early diagnosis and multidisciplinary care. Zhu and Li (9) reported two postnatally diagnosed cases that were successfully resected with no recurrence. Hu et al. (2) described a case managed with EXIT and early surgery, also with good outcome. Conversely, Garg and Singh (6) presented a fatal case of undiagnosed teratoma where delayed airway management led to neonatal death. The literature emphasizes early prenatal detection, comprehensive antenatal imaging, multidisciplinary planning, and use of EXIT when airway compromise is expected. Following these principles transforms a potentially fatal condition into a survivable one (6,9).

Conclusion

We presented a rare case of a large fetal oropharyngeal teratoma diagnosed in the third trimester. Successful management included a planned EXIT procedure with tracheostomy and complete neonatal tumor resection. Histopathology confirmed an immature teratoma. The purpose of sharing this case is to introduce the EXIT procedure to otolaryngologists and emphasize its life-saving potential in anticipated neonatal airway obstruction through timely, multidisciplinary planning.

Ethics

Informed Consent: Written informed consent was obtained from the patient's father for publication of this case report and the accompanying images.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.A., F.C.E., Concept: M.A., F.C.E., Design: M.A., A.T.D., Data Collection and/or Processing: M.A., A.T.D., Analysis and/or Interpretation: F.C.E., Literature Search: M.A., Writing: M.A.

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

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Main Points

- Oropharyngeal teratomas (epignathi) are rare congenital tumors that may cause life-threatening neonatal airway obstruction.
- Prenatal imaging, especially ultrasound and fetal magnetic resonance imaging, plays a crucial role in early diagnosis and delivery planning.
- The ex utero intrapartum treatment (EXIT) procedure allows for safe airway management while maintaining placental circulation.
- In this case, a large fetal oropharyngeal teratoma was diagnosed at 29 weeks and successfully managed with EXIT and neonatal tumor resection.
- This case demonstrates the importance of a multidisciplinary approach and introduces the EXIT technique to otolaryngologists as a life-saving option in similar scenarios.

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Laryngeal Metastasis of Prostate Adenocarcinoma-A Case Report

Case Report

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Abstract

Metastases to the larynx from distant primary malignancies are quite rare, but they should be considered in the differential diagnosis of submucosal laryngeal lesions. An 80-year-old male presented to our clinic with complaints of productive cough and hoarseness. Videolaryngoscopy revealed submucosal fullness in the right hemilarynx, pushing the right band ventricle mucosa medially and causing evident narrowing of the airway. Histopathological evaluation and immunohistochemical staining of the endolaryngeal submucosal biopsy specimen, obtained from the right ventricular fold, was diagnosed as laryngeal metastasis of prostate adenocarcinoma. This case is presented due to the scarcity of laryngeal metastases from prostate adenocarcinoma and is discussed in the context of literature.

Keywords: Larynx, metastasis, prostate, head and neck, hormonotherapy, case report

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Introduction

Prostate carcinoma is known as the most prevalent malignancy affecting the male population. Metastatic lesions from prostate adenocarcinoma are reported at different rates according to their histopathological subtypes. The most common (7-40%) distant metastases are bone metastasis, while head and neck metastases of prostate cancer are uncommon (1). Metastases to the larynx from distant sites are most commonly caused by tumors such as malignant melanoma and renal adenocarcinoma while reported laryngeal metastases of prostate adenocarcinoma are uncommon (2,3). In this report, we present a case who presented to our clinic with hoarseness, productive and persistent cough complaints and was diagnosed with metastatic prostate adenocarcinoma to the larynx.

Case Presentation

An 80-year-old male patient without significant comorbidities was initially followed for benign prostatic hyperplasia

and underwent a prostate biopsy, which was reported as Gleason score 7 prostate adenocarcinoma.

During the same time interval, he was evaluated at another otolaryngology department because of hoarseness and cough starting after a recent upper respiratory tract infection. After clinical evaluation, due to the persistence of widespread edematous appearance in endolaryngeal structures, microlaryngoscopy and biopsy were performed. The histopathological evaluation of the biopsy was reported as edematous mucosa without further specific findings.

As there were no signs of improvement, the patient presented to our clinic for further evaluation. During the ear, nose, and throat examination, a 1.5 cm, hard and palpable lymphadenopathy was identified at level three of the right side of the neck; and a submucosal fullness in the right hemilarynx, pushing the right band ventricle mucosa medially; evident narrowing of the airway was also observed during videolaryngoscopy. Computed tomographic images demonstrated a locally invasive mass lesion with partial destruction of the thyroid cartilage and obliteration of the right pyriform sinus (Figures 1 and 2).

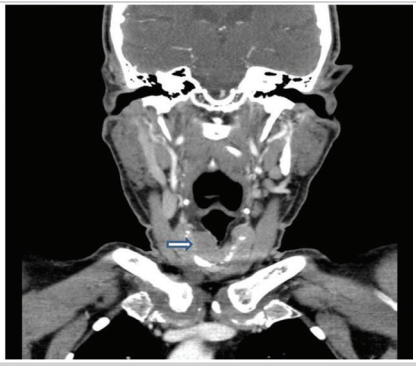

Figure 1. Computed tomography of the neck with contrast in the preoperative period (coronal image). The mass is shown by a white arrow

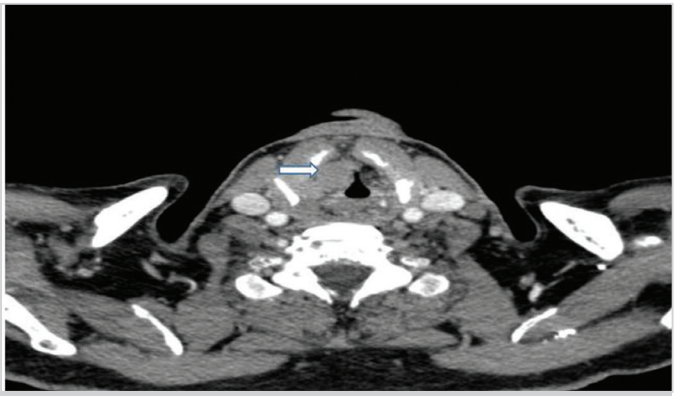

Figure 2. Computed tomography of the neck with contrast in the preoperative period (axial image). The mass is indicated by a white arrow

Microlaryngoscopy was performed under general anesthesia and numerous deep-located biopsies were taken from the indurated submucosal mass lesion after incising the right band ventricle mucosa (Figure 3). Histopathological and immunohistochemical evaluation of the biopsy samples revealed prostate-specific acid phosphatase (PSAP) and cytokeratin 5/6 negative, and prostate-specific antigen (PSA) positive high grade epithelial malignant tumor consistent with metastatic prostate adenocarcinoma (Figures 4 and 5). Gallium-68 prostate-specific membrane antigen positron emission tomography-computed tomography (PET/CT) identified the primary lesion in the prostate left lobe and widespread metastases in the right hemilarynx, right cervical level II and left cervical level VB lymph nodes and bony structures (left clavicle, vertebrae C3-T10-L4, bilateral pelvis, sacroiliac joint, anterolateral fifth and sixth costa). Lumbosacral CT findings also revealed sclerotic metastatic foci in the vertebrae, which are also consistent with the metastatic prostate carcinoma.

The patient was discussed by the Dokuz Eylül University-Head and Neck Cancer Group and hormone therapy with androgen-deprivation therapy (ADT) was initiated. ADT

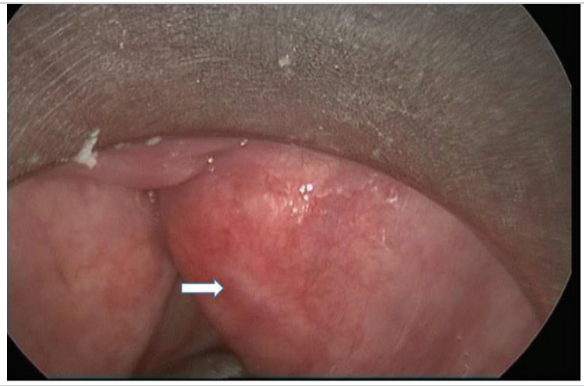

Figure 3. Direct laryngoscopic photograph illustrating submucosal mass lesion in the right band ventricle as shown by the white arrow

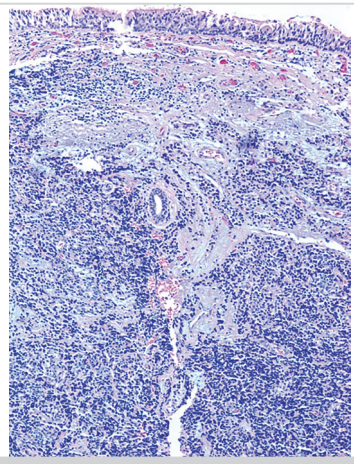

Figure 4. Submucosal malignant tumor (H&E, original magnification x10) - Reprinted with permission (4)-
H&E: Hematoxylin and eosin

had a significant impact on the patient's laryngeal findings and a near-complete response was achieved (Figures 6 and 7). The patient survived for 42 months after diagnosis and eventually died of distant metastases' progression during the follow-up period. Informed consent was obtained from the patient for publication.

Discussion

Prostate carcinoma is the most common malignancy in men and a significant cause of cancer-related mortality following lung carcinomas (1). Prostate carcinoma metastases mostly target regionally the lymph nodes and distantly the bones (7-40%), particularly the vertebrae. Head and neck metastases are relatively uncommon (1.5%). Although larynx metastases are very rare, the most common metastatic locations among head and neck sites are the brain, the dura and the supraclavicular lymph nodes (3-6).

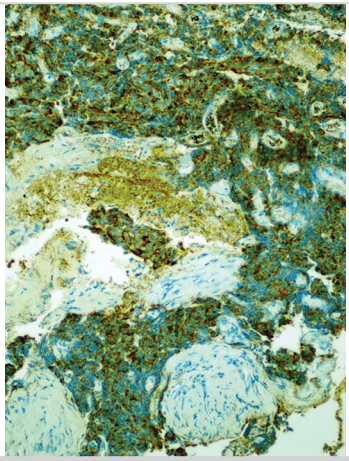

Figure 5. PSA expression in malignant cells and perineural invasion (PSA IHC, original magnification x20) - Reprinted with permission (4)-
PSA: Prostate-specific antigen, IHC: Immunohistochemistry

Figure 6. Computed tomography of the neck with contrast after ADT (coronal image) showing minor exophytic residual tumor with almost complete response to therapy
ADT: Androgen-deprivation therapy

Majority of distant laryngeal metastases arise from malignant melanoma, renal cell carcinoma, and carcinomas of the breast, lung, and colon. Only six per cent of laryngeal metastases originate from prostate carcinoma (1,2,7). Although laryngeal metastases of distant organ malignancies are uncommon due to the cartilaginous structure of the larynx skeleton, age-related ossification of the laryngeal cartilage may increase the risk of metastasis (3). Prescher et al. (2) reported that a very high incidence (97%) of bone metastases was observed in an autopsy series of patients with advanced prostate carcinoma. Theories put forth on the pathophysiology of laryngeal metastases due to prostate carcinoma in the same study were the unification of micrometastases to the hematopoietic region of the ossified cartilage and the invasion of the cartilage lamina or its spread between the perichondrium/periosteum and the laryngeal skeleton. Consequently, these tumors developing in the area far from the laryngeal lumen tend to cause late symptoms (3,8).

Although the clinical course of larynx metastasis of prostate cancer is mostly asymptomatic in the early period, in literature, voice changes at later stages are reported as the most common clinical complaint. Our case also presented with hoarseness as the initial symptom, which is consistent with the literature; however, cough which was not reported before, was also a symptom (1,8).

Cross-sectional imaging techniques like CT, magnetic resonance imaging, and PET/CT are useful for diagnosis, but the definitive diagnosis is made by histopathological and appropriate immunohistochemical evaluation with PSA and PSAP. Although NKX3.1 immunohistochemical staining is highly sensitive for detecting metastatic prostate adenocarcinoma, it hadn't been used in our patient's diagnostic work-up (9).

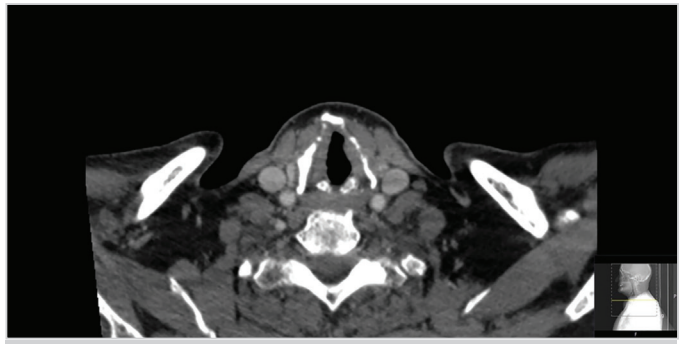

Figure 7. Computed tomography of the neck with contrast after ADT (axial image) showing almost complete response to therapy
ADT: Androgen-deprivation therapy

A review conducted by van der Toom et al. (10) stated that PSA was not expressed in 5-10% of metastatic prostatic carcinomas and PSAP was not expressed in 16-23%.

ADT has considerably extended the expected lifespan of advanced prostate carcinoma patients. In addition, palliative radiotherapy is used in patients with distant bone metastases, particularly those involving the vertebrae. Also, laryngectomy is proposed as an option in patients with solitary laryngeal metastasis (3).

In our patient, ADT caused an almost complete structural response to laryngeal metastasis, with complete resolution of the patient's laryngeal symptoms, and afterwards, it was possible to control the progression of vertebral metastases with external beam radiotherapy. Although the patient died of distant metastasis after 42 months during the follow-up period, the patient's quality of life was considerably increased due to control of laryngeal metastasis and preservation of laryngeal functions with ADT and avoidance of tracheotomy until his demise.

Conclusion

In summary, metastasis from distant sites should always be kept in mind in the differential diagnosis of laryngeal submucosal lesions presenting with voice disturbances, difficulty in breathing, stridor or cough; especially in patients with a history of malignancy. Correct sampling with incision of the mucosa and obtaining adequate submucosal tissue samples is a prerequisite for precise diagnosis. Histopathological evaluation with appropriate immunohistochemical staining is a key factor for definitive diagnosis. As represented in our case, laryngeal metastasis of prostate adenocarcinomas may yield an excellent response to ADT, and it should be the first line of treatment modality when considering more invasive options such as laryngectomy and even tracheotomy.

Ethics

Informed Consent: Informed consent was obtained from the patient for publication.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.Ö.İ., Ö.F.Z., O.Ç., Concept: A.Ö.İ., Design: A.Ö.İ., O.Ç., Data Collection and/or Processing: A.Ö.İ., N.K., Analysis and/or Interpretation: S.S., N.K., Ö.Ö., Literature Search: Ö.F.Z., Writing: A.Ö.İ., Ö.F.Z., S.S.

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Main Points

- Metastases to the larynx from distant primary malignancies are quite rare, but they should be considered in the differential diagnosis of submucosal laryngeal lesions.
- Correct sampling by incision of the mucosa and obtaining adequate submucosal tissue samples is a prerequisite for precise diagnosis of laryngeal submucosal lesions.
- Androgen-deprivation therapy has considerably increased the life expectancy of patients with advanced prostate cancer.

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Patient-Specific 3D Models for Open Frontal Sinus Surgery: Enhancing Precision with Facial Mask-Guidance

Case Report

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Abstract

In osteoplastic frontal sinus surgery, the precision of initial bony incisions is critically important. Conventional techniques such as 6-ft Caldwell radiographs, burr holes method, transillumination and navigation systems are widely used. Recently, publications on the use of three-dimensional (3D) printed models in surgical navigation have increased. We aimed to enhance the accuracy of 3D model navigation—a cost-effective and accessible method that can be used alone or alongside conventional approaches—by developing a novel facial mask component not previously described. We developed a patient-specific planning system using open-source segmentation software and a desktop 3D printer. Computed tomography scans were segmented to isolate the anterior table, the sinus walls, and the osteoma when present. A novel feature was the custom-designed facial mask, which ensured accurate alignment of the incision guide. The mask, designed from tissue landmarks, incorporated a locking cylinder mechanism. All parts were printed in polylactic-acid at a cost of approximately 1$, with production times under 8 hours. The system was tested on two patients. In case-1, a patient with an anterior table defect, the 3D-printed model provided accurate incision guidance when navigation failed intraoperatively. In case-2, a frontal sinus osteoma was visualized with 1:1 scale printed models, which facilitated surgical planning. Surgeons reported better anatomical orientation, increased confidence in performing incisions, and more effective preoperative and intraoperative planning. The application of a facial mask to the 3D model has shown promising initial results. Further refinements and comparative studies are needed to standardize production, demonstrate accuracy, and validate its broader clinical utility.

Keywords: Frontal sinus, paranasal sinus diseases, anatomy, osteoma, three-dimensional printing, surgical procedures

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Introduction

In osteoplastic frontal sinus surgery, the accuracy of the initial bony cuts is of paramount importance. Inadequate incisions may result in both increased risk of intracranial complications and incomplete disease clearance due to poor exposure of anatomical boundaries.

Among conventional techniques, 6-ft Caldwell radiographs remain a readily

accessible and cost-effective method. With the increasing availability of navigation systems, these have become the gold standard, providing high accuracy for determining incision boundaries. Burr hole and transillumination techniques are also among the methods described (1).

In rhinology, most publications related to three-dimensional (3D) printing have focused on preoperative surgical training models (2,3). However, in recent years, reports on the use of 3D models for surgical navigation have increased (4-6). Application of 3D model-based navigation has been described for various benign pathologies of the frontal sinus, including osteoma, mucocele, recurrent sinusitis, inverted papilloma, and Samter's polyps (4,6).

In this report, we present two cases in which we integrated a novel facial mask component into 3D model-based navigation. We hypothesized that this addition could improve the accuracy and usability of 3D models in frontal sinus navigation, particularly during the initial bone cuts.

Case Presentations

Device Description and Development

The device is composed of two components: a 3D-printed surgical incision guide and a patient-specific facial reference mask. Computed tomography (CT) data were segmented using 3D Slicer software to reconstruct anatomical structures. The incision guide was generated by reducing and anteriorly displacing the anterior table segment to fit above the periosteum. The mask was created by subtracting the facial soft tissue volume from a rectangular prism. Integration of a dual-cylinder alignment mechanism ensured consistent and precise reapplication of the guide to the same position (Figure 1).

All parts were printed using polylactic-acid (PLA) on a Bambu Lab P1S 3D printer (Figure 1). Total production time per case was less than 4 hours, with material costs under 2$.

Clinical Application Case-1

Case-1 involved an adult male with left forehead swelling and an anterior table defect. Models were printed in 3.2 hours. Intraoperatively, due to navigation system failure, the surgery was continued using the 3D-printed model for incision planning (Figure 2). The model provided reliable and accurate incision guidance.

Clinical Application Case-2

Case-2 involved an adult male with a right frontal sinus osteoma. Segmented models included the osteoma, sinus walls, and anterior table (Figure 3). Because of the similar radiodensity between the osteoma and sinus wall, manual segmentation was required. Print times were 10 minutes for the anterior table, 18 minutes for the osteoma, and 2.5 hours for the complete sinus model.

The 3D model allowed detailed visualization of the osteoma and the theoretical postoperative sinus cavity, assisting intraoperative orientation (Figure 3).

Discussion

Previous studies utilizing 3D-printed templates lacked reference mechanisms for accurate placement, resulting in millimetric errors (4-7). By introducing a facial reference mask, we aimed to reduce uncertainty in the model's placement on the face and standardize reproducibility. Furthermore, the use of open-source software and in-house 3D printing substantially reduced costs.

The facial mask-assisted 3D model navigation system can theoretically be applied in all osteoplastic frontal sinus cases. However, its most valuable indication may be patients with anterior table defects, as demonstrated in case-1. After elevating the periosteum, the real defect can serve as an additional anatomical landmark that can be perfectly aligned with the defect in the 3D model, thereby defining the anterior table boundaries with high accuracy. In osteoma cases, as in case 2, creating a defect-free model of the frontal sinus from CT data may facilitate intraoperative orientation and save operative time in the absence of navigation.

Although the 6-ft Caldwell radiograph is cost-effective and easily applicable, it is fundamentally a 2D projection mapped onto a 3D structure. Studies comparing 6-ft

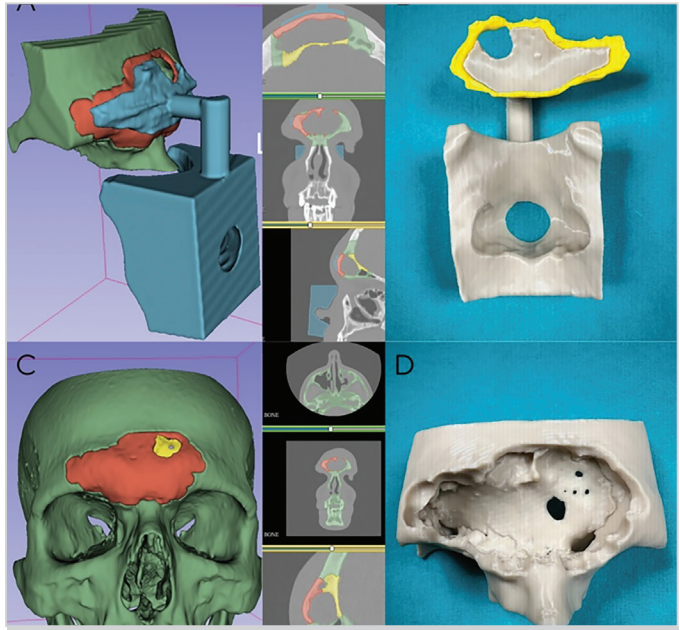

Figure 1. A) Frontal sinus (green), anterior table (red), and anterior table incision segment with facial mask (blue) segment, B) anterior table model with facial mask, C) cranium (green), anterior table (red) segments, D) 3D model of both frontal sinuses

Caldwell radiographs with CT-based 3D reconstructions and navigations have demonstrated the superiority of 3D methods in delineating anterior table boundaries (8). CT-based navigation systems are the best example of this. Our current study has introduced a low-cost, manual version of the high-cost CT-based navigation system. For centers without access to navigation systems, 3D navigation may serve as an alternative.

Navigation systems, which are CT-based, remain the gold standard when available, providing precise intraoperative orientation. However, their high cost and limited accessibility in non-tertiary centers restrict their use. In contrast, 3D-printed navigation is low-cost and accessible but depends on the operator's experience during segmentation and manual editing. In our study, we needed to repeat the segmentation process twice for the first case due to inexperience, but subsequent cases required less time and greater efficiency. This suggests a learning curve and highlights the need for further studies with larger cohorts.

PLA, although not autoclavable, was sterilized with povidone-iodine and ortho-phthalaldehyde solution. No adverse reactions were observed, but further research is needed regarding its contact with skin and subcutaneous tissues (9). A safer approach is to use sterile transparent covers to isolate the models during surgery, preventing contact with the skin and subcutaneous tissue and ensuring greater sterility.

Future work may focus on developing automated software capable of generating both surgical guides and the facial mask directly from CT images. Such software would shorten modeling time, reduce operator-dependent errors, lower costs, and improve standardization. We believe that this method may serve as a reliable incision-planning alternative in centers without navigation systems, and defect-free osteoma models may further facilitate intraoperative decision-making. However, as this was a pilot study, larger comparative studies with quantitative data are required to validate our findings.

Figure 2. Preoperative and intraoperative applications of the 3D model. Identification of the anterior table boundaries (outer margin of the yellow model) and the bone incision line (inner margin of the yellow model)

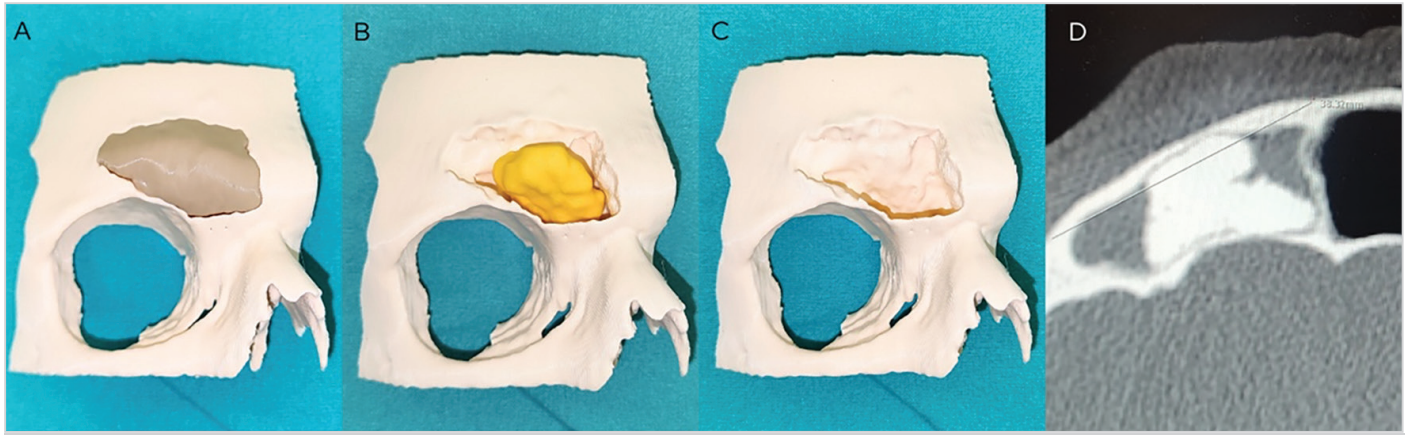

Figure 3. A) 3D model of the right frontal sinus and its anterior table, B) 3D model of the frontal sinus with the anterior table removed (the osteoma is shown in yellow), C) frontal sinus model with the osteoma removed, D) axial computed tomography image of the right frontal sinus

Conclusion

With the increasing use of 3D models in contemporary surgical planning, this study demonstrates that a patient-specific 3D model provides a practical and low-cost solution that enhances both bony incision accuracy and anatomical orientation in frontal sinus surgery. In both of our cases, the model improved anatomical guidance and increased surgical confidence. These preliminary results are promising, and further validation with standardized protocols and larger patient series will be essential to establish the method's accuracy and future clinical applicability.

Ethics

Informed Consent: Written informed consent was obtained from the patients for the use of clinical data, images, and the patient-specific 3D model for academic presentation and publication purposes.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.Ç., E.K., F.Ö., Concept: M.Ç., F.Ö., Design: M.Ç., E.K., F.Ö., Data Collection and/or Processing: M.Ç., Analysis and/or Interpretation: M.Ç., E.K., Literature Search: M.Ç., E.K., F.Ö., Writing: M.Ç.

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

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Main Points

- The use of patient-specific three-dimensional (3D) models with facial masks may provide intraoperative guidance and help to accurately locate the frontal sinus.
- This technique offers a low-cost and accessible solution for centers lacking advanced surgical navigation systems.
- Patient-specific 3D models support better planning and anatomical orientation in open frontal sinus surgery.
- When aligned using a facial mask, the model fits accurately on the patient, increasing surgical precision.
- This approach enables safer osteotomies, shortens operation time, and is especially useful in cases with complex anatomy or frontal sinus osteomas.
- The technique is easy to apply and can be integrated into routine surgical practice at low cost.

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An Insight into the Formulation of the Iraqi Version of the Pediatric Sleep Questionnaire for Children with Obstructive Sleep Apnea Syndrome

Letter to the Editor

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Keywords: Sleep apnea, obstructive, polysomnography, questionnaires, pediatric otorhinolaryngology

Dear Editor,

Pediatric obstructive sleep apnea syndrome (OSAS) is a prevalent sleep disorder featured by upper airway obstruction during sleep, leading to oxygen desaturation and sleep disruptions. It has a 1-3% global prevalence and is linked to various health issues, including cardiovascular complications, metabolic disturbances, and neurocognitive impairments. The most important causes of OSAS are adenotonsillar hypertrophy, craniofacial anomalies, and obesity (1). Polysomnography (PSG) is considered the gold standard for OSAS diagnosis. However, the cost, time, and accessibility have constrained its use in research and clinical settings, especially in underdeveloped countries. Therefore, the Pediatric Sleep Questionnaire (PSQ), which could predict OSAS and its impact on sleep and quality of life, was constructed. Various population-specific PSQs have been developed and proved to be a valid, sensitive, and reliable instrument in detecting OSAS manifestations. According to the data released by the Ministry of Health, OSAS is a noteworthy health problem in Iraq, with a prevalence of 10.5% (2). The management of numerous pediatric health disorders has been significantly impacted by the disrupted healthcare system in Iraq as a result of the antecedent armed conflicts, violence, corruption, destroyed infrastructure, and disorganized administration. Despite the crucial role of PSQ in managing OSAS, PSQ for Iraqi OSAS children has not yet been developed.

Numerous determinants have to be considered during local PSQ construction. First, the study population should mirror the entire Iraqi pediatric population from different regions, otherwise sampling bias could impact the estimated sensitivity and specificity of the PSQ as well as Cronbach's alpha for each sub-domain and whole questionnaire. Second, participants should not have co-morbidities that

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might adversely affect PSQ credibility. Third, there should be a sub-analysis of the PSQ findings based on the variables of age, gender, and body weight, as they might impact PSQ validity and reliability (3,4). Fourth, adenoidectomy/tonsillectomy is an effective modality in treating pediatric OSAS that produces significant postoperative improvements in sleep and behavioral scores and better quality of life (5). The participants must not have undergone surgery as the constructed PSQ could not be validated in this subset of OSAS patients to define the clinical change and success of surgery. Fifth, PSG is the recommended tool to diagnose OSAS. To get better insight into the diagnostic accuracy of the constructed PSQ, employing PSG for every participant and performing a statistical comparison between each patient's estimated total PSQ score and corresponding recorded PSG indices are solicited. However, we understand that filling that task is not feasible in Iraq due to many constraints such as restricted access to a sleep center, the need for professional traineeship in testing children, the strenuous kind of the PSG, and financial/social constraints. To maintain the health and well-being of OSAS children and to assist them in leading a positive quality of life, a compelling call of action is sent to the policymakers and researchers in Iraq to collaboratively work to formulate a local version of PSQ as an essential tool to back pediatricians and otolaryngologists in screening and monitoring OSAS in clinical and non-clinical setups.

Footnotes

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