Profiling nasal trigeminal sensitivity to predict outcomes after nasal obstruction surgery

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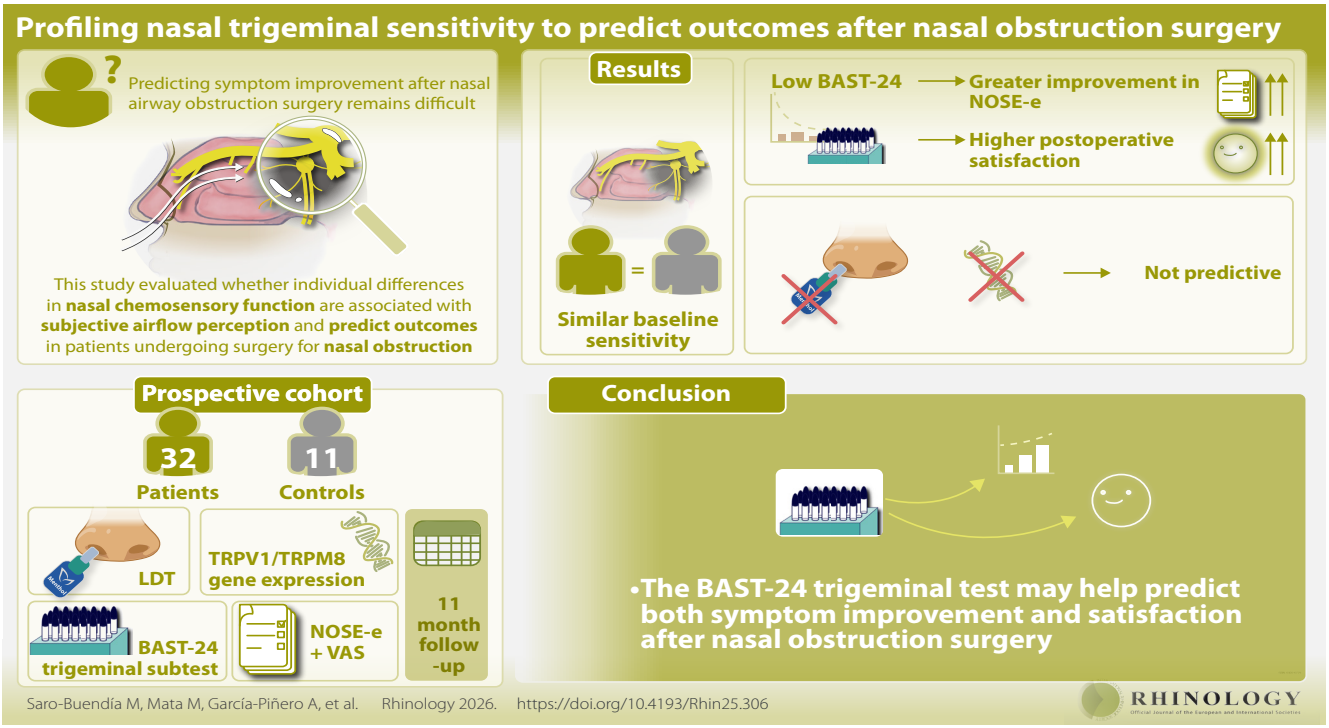

Abstract

Background: Predicting symptom improvement after nasal airway obstruction surgery remains difficult, as objective airflow metrics correlate poorly with patient-reported outcomes. Since trigeminal afferents are key in sensing nasal airflow, this study evaluated whether individual differences in nasal chemosensory function—particularly trigeminal sensitivity—are associated with subjective airflow perception and predict outcomes in patients undergoing surgery for nasal obstruction. **Methodology**: A prospective cohort study was conducted in 43 participants (32 patients with nasal airway obstruction scheduled for surgery, 11 healthy controls). Trigeminal sensitivity was assessed using measures including the menthol lateralisation detection thresholds, TRPV1/TRPM8 gene expression, and the trigeminal subtest of the Barcelona Smell Test-24. Olfactory and gustatory function were also evaluated. Nasal obstruction perception was measured pre- and postoperatively using the NOSE-e questionnaire and a visual analogue scale. Patients were followed for a mean of 10.9 months. **Results**: Trigeminal sensitivity did not differ significantly between patients and controls. However, baseline trigeminal Barcelona Smell Test-24 scores correlated with greater improvement in NOSE-e scores and satisfaction. Patients with NOSE-e improvement >6 points had lower baseline trigeminal scores than those with lesser gains. No other baseline chemosensory measures were correlated with postoperative outcomes. **Conclusions**: Trigeminal sensitivity—particularly as assessed by the Barcelona Smell Test-24 test—may serve as a predictor of both symptom improvement and overall satisfaction after surgery for nasal airway obstruction, underscoring the importance of sensory processing in shaping patient-perceived surgical outcomes.

Key words: chemosensory perception, nasal obstruction, nasal surgical procedures, patient-reported outcome measures, trigeminal physiology

Introduction

Nasal airway obstruction (NAO) is a prevalent condition that significantly affects patients' quality of life [1,2]. However, patient-reported symptoms of nasal obstruction often correlate poorly with objective airflow measurements obtained through rhinomanometry or acoustic rhinometry [3-6]. This lack of reliable markers complicates diagnosis, management, and prediction of surgical outcomes [1]. While septoplasty addresses anatomical deviations, postoperative satisfaction and symptom relief remain variable, and current objective assessments offer limited prognostic value [2,7,8].

The nasal cavity is innervated by the trigeminal nerve, which mediates mechanosensory, thermal, and chemical sensations collectively referred to as chemesthesis [9]. This somatosensory input is essential for detecting inspired air quality and initiating reflexes [9]. Unlike olfaction, trigeminal input enables localization—or lateralization—of irritants [9,10], making lateralization tasks valuable for quantifying nasal irritation without olfactory interference [9,11,12]. Psychophysical testing, including detection and lateralization thresholds, is a robust method to assess trigeminal sensitivity [3,9-11].

At the molecular level, nasal sensation, including airflow perception, is significantly mediated by transient receptor potential (TRP) channels on trigeminal nerve endings [9]. TRPM8 is a cold-sensitive receptor that can be activated both physically (by low temperatures) and chemically (by menthol and other agents), playing a central role in the perception of cooling [9,13], which is strongly linked to the subjective sensation of nasal patency or airflow [2,3,6,14-16]. TRPV1 responds to heat and capsaicin, typically causing sensations of warmth, irritation, or pain [9,13]. While TRPM8 is key for cooling-mediated patency [3,6,9], TRPV1, along with TRPA1 (which detects noxious cold and irritants) [13], contributes to the overall quality of inspired air by detecting thermal extremes and irritants, thereby impacting the complex subjective experience related to breathing sensation [9].

Computational Fluid Dynamics (CFD) modelling is a valuable tool for characterizing the physical behaviour of airflow within the intricate geometry of the nasal cavity [1-3,6]. CFD enables the quantification of critical airflow parameters, including velocity, pressure distribution, wall shear stress, and, notably, heat flux, which represents the rate of heat exchange between the nasal mucosa and inspired air [6]. Heat flux is particularly relevant as it reflects trigeminally mediated mucosal cooling, strongly linked to airflow perception [3,6,17].

Several CFD studies show that peak mucosal heat loss, especially behind the nasal vestibule, correlates with subjective nasal patency [3,6]. These results emphasize CFD´s value not only in describing airflow mechanics but also in linking them to sensory correlates of obstruction, particularly those mediated by the trigeminal system [6].

Given the known limitations of traditional objective assessments—such as rhinomanometry and acoustic rhinometry—in predicting subjective symptom severity and surgical outcomes in NAO [1-5], it is necessary to explore individual differences in nasal sensory processing.

This study investigates whether individual variability in nasal trigeminal sensitivity—assessed via menthol lateralisation thresholds, TRPV1/TRPM8 gene expression, and the BAST-24 trigeminal subtest—is associated with subjective airflow perception and surgical outcomes in patients with NAO. We hypothesize that trigeminal sensitivity profiles may help predict postoperative symptom improvement, supporting their potential role as clinical markers of surgical response.

Materials and methods

Study setting

This prospective cohort study was carried out between 2022 and 2025, through a collaboration between the rhinology unit of a tertiary hospital and an academic pathology department.

Ethical considerations

The project was approved by the Institutional Review Board (Register Code: 2022-755-1) and adhered to the Declaration of Helsinki. All participants provided written informed consent.

Participant recruitment

Patients and controls

Patients with NAO and eligible for surgery (endonasal septoplasty and/or inferior turbinate reduction by radiofrequency (ITRF)) based on standard criteria were consecutively recruited from 2022 to 2025. Healthy volunteers served as controls.

Exclusion criteria

Participants were excluded if they were under 18 or had relevant neuropsychiatric, oncological, systemic, hematological disorders, active upper airway infections, prior sinonasal surgery, drug-induced rhinitis, or substance abuse history.

Study assessments

Baseline characteristics of the study population

Data collected included sex, age, and smoking status, categorized as smoker or non-smoker (including former smokers).

Baseline patient-reported outcome measures (PROMs) on NAO and olfaction

In both groups, the perception of NAO and olfaction was evaluated using PROMs. NAO was assessed with the Spanish-language version of the Nasal Obstruction Symptom Evaluation questionnaire (NOSEe) [18] and a Visual Analogue Scale (VAS) ranging from 0 (no NAO symptoms) to 10 (severe NAO symptoms). Olfactory perception was measured using a VAS ranging from 0 (normal olfaction) to 10 (anosmia). This VAS captured the patient's

subjective perception of olfactory loss, complementing the objective psychophysical testing described below.

Baseline chemosensory assessment

All sensory evaluations took place in a quiet, well-ventilated room with humidity below 30% and temperature between 21–23ºC. Participants avoided applying scented products on testing days.

Nasal trigeminal sensitivity

Menthol lateralisation detection threshold (LDT)

To assess Menthol LDT, we adapted the methodology described by Li et al. [19,20]. Clear, odourless polypropylene bottles (Merz Medizintechnik GmbH) with disposable nasal adapters (sizes 1, 2, or 3) were used. The adapter fit was adjusted to minimise dead space while avoiding nasal valve interference.

A set of 21 bottles was prepared: one blank containing 40 ml of mineral oil (Sigma-Aldrich®) and 20 test bottles with a 20-step binary dilution series of menthol (99%) in mineral oil. The highest concentration (bottle 1) was 0.125 g/ml (5 g/40 ml), with each subsequent bottle halving the previous concentration, down to 2.38×10^{-7} g/ml (bottle 20).

During each trial, two bottles—one with menthol and one blank—were hand-squeezed simultaneously toward each nostril. Participants indicated which side received the menthol stimulus. The sequence was randomized to avoid pattern recognition. A 45-second interstimulus interval minimized adaptation; bottles were shaken before each use. Testing followed a forced-choice ascending method, starting below threshold (bottle 20) and continuing until four consecutive correct responses were obtained with a confidence rating ≥7/10. The menthol LDT was recorded as the dilution step (bottle 1–20) at which threshold criteria were met and confirmed by correct lateralization at the next higher concentration.

TRPV1 and TRPM8 gene expression levels

Epithelial samples were collected by curettage of the nasal mucosa over the middle turbinate under anterior rhinoscopy or endoscopic guidance, without local anaesthesia to avoid confounding effects. Samples were preserved at –80°C in TRIzol reagent (Thermo Scientific, Madrid, Spain) until processing. Total RNA was extracted per the manufacturer's protocol and quantified using a Nanodrop 2000 spectrophotometer (Mettler Toledo, Madrid, Spain). RNA integrity was assessed by high-resolution automated electrophoresis on a Bioanalyzer (Agilent Technologies, Madrid, Spain). Only samples with a 260/280 nm absorbance ratio >1.4 and RIN >10 were included.

Complementary DNA (cDNA) synthesis used random hexamer primers and the TaqMan RT Reagents Kit (Applied Biosystems, Foster City, CA, USA), per the manufacturer's instructions. Reverse transcription PCR (RT-PCR) was conducted with the High-Capacity cDNA Reverse Transcription Kit (Applied Biosystems, Madrid, Spain) and specific probes: Hs01066596_m1 (TRPM8) and Hg05063581_g1 (TRPV1) (Thermo Fisher Scientific Inc., Waltham, MA, USA). Amplification was performed on a 7900HT Real-Time PCR System (Applied Biosystems, Madrid, Spain). Gene expression was calculated using the comparative ΔΔCt method, with GAPDH (Applied Biosystems, Madrid, Spain) as the endogenous control [21]. All reactions were performed in triplicate.

BAST-24 trigeminal stimuli

Nasal trigeminal sensitivity was further evaluated using the Barcelona Smell Test-24 (BAST-24), which includes four volatile compounds specifically selected to assess nasal trigeminal function: formaldehyde, acetic acid (vinegar), ammonia (NH_4), and Dijon mustard [22]. The test was administered following the olfactory evaluation. Participants were required to identify each substance from a list of four options in a forced-choice format, with the total score expressed as a percentage of correct answers (0–100%). Participants were instructed to keep their eyes and mouth closed while sampling the odours to minimize potential confounding from ocular and oral trigeminal stimulation.

Olfaction

Olfactory function was assessed using the BAST-24, a validated test for the Spanish population. The test consists of 20 odourants stored in hermetically sealed glass containers. Each odour was presented one by one (1 cm away from the nostrils, avoiding contact) for 5 seconds. Participants identified each odour in a forced-choice manner among four options. The total score was expressed as a percentage of correct answers (0–100%).

Gustatory sensitivity (gustometry)

Taste assessment used the BAST-24 gustometry test with four basic tastes (sweet, salty, sour, bitter) [22]. Although five were tested initially, umami was excluded from the final analysis due to inconsistent participant familiarity. The total score was expressed as a percentage of correct answers (0–100%).

In addition, correlations between baseline characteristics of the study population, baseline PROMs on NAO and olfaction, and baseline chemosensory assessment were analysed.

Surgical intervention

The surgical indication required a clear concordance between the patient's clinical symptoms and the anatomical obstruction identified during rhinoscopy and endoscopy. The specific procedure was then tailored to these findings: ITRF was performed for predominant turbinate hypertrophy, whereas endonasal septoplasty (classic Cottle technique) was combined with ITRF for a clinically significant septal deviation. Different members of

Table 1. Patient demographics, baseline patient-reported outcome measures, and baseline chemosensory assessment.

		Patients with NAO (n=32)	Healthy Controls (n=11)	p-value
Patient Demographics	Age (years, mean ± SD)	35,94 ± 10,58	29,91 ± 8,1	0,09
	Sex (Female, %)	40,62%	81,82%	0,03
	Smoking habits (%)	46,87%	9,09%	0,05
Baseline PROMs on NAO and Olfaction	NOSE-e questionnaire (mean ± SD)	14,03 ± 4	1,55 ± 2,11	0
	VAS on NAO (mean ± SD)	6,53 ± 1,7	1,64 ± 1,25	0
	VAS on Olfactory loss (mean ± SD)	2,94 ± 2,23	1,68 ± 1,62	0,09
Baseline Chemosensory Assessment	Menthol LDT (dilution step number, mean ± SD)	9,97 ± 2,23	9,64 ± 1,8	0,66
	Trigeminal Sensitivity: BAST-24 (correct forced-choice answers, %)	58,06 ± 25,32	72,73 ± 26,11	0,11
	TRPV1 Gene Expression Levels (comparative ΔΔCt method ± SD)	8,99 ± 2,26	9,56 ± 2,54	0,49
	TRPM8 Gene Expression Levels (comparative ΔΔCt method ± SD)	Non detectable	Non detectable	
	Olfaction: BAST-24 (correct forced-choice answers, %)	73,87 ± 14,3	85 ± 9,49	0,02
	Gustometry: BAST-24 (correct forced-choice answers, %)	89,52 ± 23,07	97,73 ± 7,54	0,26

Abbreviations: PROMs, Patient-Reported Outcome Measures; NAO, Nasal Airway Obstruction; NOSE-e, Nasal Obstruction Symptom Evaluation (Spanish version); VAS, Visual Analog Scale; LDT, Lateralization Detection Threshold; BAST-24, Barcelona Smell Test, 24-item version; PCR, Polymerase Chain Reaction; TRPM8, Transient Receptor Potential Melastatin 8; TRPV1: Transient Receptor Potential Vanilloid 1.

the rhinology unit conducted the surgeries, all on an outpatient basis.

Postoperative outcome evaluation and correlation with baseline chemosensory assessment and PROMs

Final postoperative assessments took place in early 2025. NAO perception was re-evaluated using both the VAS and NOSE-e questionnaire, while olfactory perception was reassessed with a separate VAS. Surgical outcomes were measured as the improvement from baseline in NOSE-e scores and NAO VAS ratings, expressed as score reductions. Overall satisfaction was recorded on a four-point ordinal scale from 1 (best imaginable outcome) to 4 (worse than preoperative status).

Postoperative outcomes—specifically, changes in NOSE-e and VAS scores, and overall satisfaction—were analysed in relation to baseline chemosensory function and PROMs to identify potential predictors of subjective surgical benefit.

Statistical analysis

Quantitative variables were compared between groups using the Student's t-test or Mann–Whitney U test, depending on data distribution. Qualitative variables were compared with the chi-square or Fisher's exact test. Within-group comparisons, both before and after surgery, were performed using the paired t-test. Correlations were assessed using Pearson or Spearman coefficients, as appropriate. Multiple linear regression analysed variables significantly correlated with NAO improvement and relevant confounders. Ordinal logistic regression assessed associations between baseline variables and satisfaction (rated 1–4), adjusting for confounders. Analyses were performed in R (v4.3.4), with $p < 0.05$ considered significant.

Results

Baseline characteristics of the study population

A total of 43 participants were included: 32 patients with NAO and 11 healthy controls. The mean age was 34.4 ± 10.26 years, with no statistically significant difference between groups ($p = 0.09$). As shown in Table 1, the groups differed significantly in their distribution by sex ($p=0.03$), with a higher proportion of females in the control group. Furthermore, the proportion of smokers was significantly higher in the patient group (46.87%) compared to controls (9.09%) ($p = 0.05$). Detailed demographic data are presented in Table 1.

Baseline PROMs on NAO and olfaction

Patients exhibited significantly greater nasal obstruction than controls, as indicated by higher VAS NAO scores (6.53 ± 1.7 vs. 1.64 ± 1.25; $p < 0.001$) and NOSE-e scores (14.03 ± 4 vs. 1.55 ± 2.11; $p < 0.001$). No significant difference was observed in self-reported olfactory dysfunction (VAS; $p = 0.09$). Results are

Table 2. Correlations among different nasal trigeminal sensitivity assessments.

Correlations (rho value, p-value)		Menthol LDT	Trigeminal Sensibility: BAST-24	TRPV1 gene expression	Olfaction: BAST-24	Taste: BAST-24
Menthol LDT	HC	1	0,25 (p 0,47)	- 0,1 (p 0,77)	0,12 (p 0,73)	0,48 (p 0,13)
	NAO	1	0,39 (p 0,037)	-0,29 (p 0,13)	0,34 (p 0,07)	0,2 (p 0,31)
	Total	1	0,32 (p 0,047)	-0,25 (p 0,12)	0,25 (p 0,12)	0,19 (p 0,24)
Trigeminal Sensibility: BAST-24	HC	0,25 (p 0,47)	1	-0,06 (p 0,86)	-4,59e-17 (p 1)	-0,03 (p 0,93)
	NAO	0,39 (p 0,037)	1	-0,1 (p 0,59)	0,01 (p 0,96)	0.04 (p 0,83)
	Total	0,32 (p 0,047)	1	-0,05 (p 0,74)	0,09 (p 0,58)	0,07 (p 0,65)
TRPV1 (Gene Expression)	HC	- 0,1 (p 0,77)	-0,06 (p 0,86)	1	-0,13 (p`0,7)	-0,23 (p 0,5)
	NAO	-0,29 (p 0,13)	-0,1 (p 0,59)	1	-0,07 (p 0,73)	-0,08 (p 0,7)
	Total	-0,25 (p 0,12)	-0,05 (p 0,74)	1	-0,03 (p 0,87)	-0,06 (p 0,72)
Olfaction: BAST-24	HC	0,12 (p 0,73)	-4,59e-17 (p 1)	-0,13 (p 0,7)	1	-0,17 (p0,61)
	NAO	0,34 (p 0,07)	0,01 (p 0,96)	-0,07 (p 0,73)	1	-0,04 (p 0,85)
	Total	0,25 (p 0,12)	0,09 (p 0,58)	-0,03 (p 0,87)	1	0,02 (p 0,92)
Taste: BAST-24	HC	0,48 (p 0,13)	-0,03 (p 0,93)	-0,23 (p 0,5)	-0,17 (p0,61)	1
	NAO	0,2 (p 0,31)	0.04 (p 0,83)	-0,08 (p 0,7)	-0,04 (p 0,85)	1
	Total	0,19 (p 0,24)	0,07 (p 0,65)	-0,06 (p 0,72)	0,02 (p 0,92)	1

Abbreviations: PROMs, Patient-Reported Outcome Measures; NAO, Nasal Airway Obstruction; HC, Healthy controls; NOSE-e, Nasal Obstruction Symptom Evaluation (Spanish version); VAS, Visual Analog Scale; LDT, Lateralization Detection Threshold; BAST-24, Barcelona Smell Test, 24-item version; PCR, Polymerase Chain Reaction; TRPM8, Transient Receptor Potential Melastatin 8; TRPV1: Transient Receptor Potential Vanilloid 1.

summarised in Table 1.

Baseline chemosensory assessment

No significant group differences were observed in trigeminal sensitivity, assessed via menthol lateralisation detection threshold (9.97 ± 2.23 vs. 9.64 ± 1.80; p = 0.66), TRPV1 gene expression (8.99 ± 2.26 vs. 9.56 ± 2.54; p = 0.49), or BAST-24 trigeminal odour identification (58.06 ± 25.32 vs. 72.73 ± 26.11; p = 0.11). TRPM8 expression was undetectable in most samples and was therefore excluded from analysis.

Conversely, olfactory performance (BAST-24) was significantly lower in the patient group (73.87 ± 14.30%) compared to controls (85.00 ± 9.49%; p = 0.02). No significant difference was found in gustatory function (89.52 ± 23.07 vs. 97.73 ± 7.54; p = 0.26). Table 1 summarizes the results.

Correlations between baseline characteristics of the study population, baseline PROMs on NAO and olfaction, and baseline chemosensory assessment

Age showed a significant negative correlation with Gustometry using BAST-24 (r = –0.48, p = 0.002), while no significant associations were observed between age and trigeminal sensitivity (BAST-24), menthol LDT, TRPV1 gene expression, or olfactory performance (BAST-24). Supplementary data are presented in Table S1.

Non-smokers exhibited significantly higher BAST-24 trigeminal sensitivity scores compared to smokers (68.27 ± 27.89 vs. 51.56 ± 19.30; p = 0.042). No smoking-related differences were found for menthol LDT, TRPV1 gene expression, olfaction (BAST-24), or gustometry. Supplementary data are shown in Table S2.

In the full cohort, menthol LDT correlated positively with Trigeminal Sensitivity using BAST-24 (r = 0.32, p = 0.047), a relationship that remained significant within the NAO group (r = 0.39, p = 0.037). NOSE-e scores strongly correlated with VAS ratings for NAO (r = 0.76, p < 0.001), and VAS on NAO scores showed a moderate negative correlation with Olfaction using BAST-24 (r = –0.32, p = 0.04). Table 2 summarises correlations between trigeminal sensitivity measures.

Surgical intervention and postoperative outcome evaluation

During the study period, 32 patients underwent surgery: 19 received ITRF alone, and 13 underwent septoplasty with additional ITRF. The mean follow-up duration was 10.94 months, and postoperative outcomes were assessed using PROMs.

Postoperative NAO perception, measured by VAS, was 3.86 ± 2.53, while mean NOSE-e scores were 7.84 ± 5.5. Symptom improvement, reflected by reductions in VAS and NOSE-e scores, was –2.67 ± 2.09 and –6.19 ± 4.6, respectively.

Postoperative olfactory perception (VAS) averaged 2.7 ± 2.7.

Regarding overall satisfaction, 31.25% of patients reported marked improvement, 46.88% moderate improvement, and

Table 3. Surgical procedure and postoperative outcomes.

Surgical procedure, n (%)	
RFTR	19 (59,4%)
Septoplasty + RFTR	13 (40,6%)
Time of postoperative follow-up (months, mean ± SD)	10,94 ± 4,86)
Postoperative Outcome Evaluation via PROMs	
VAS on NAO (mean ± SD)	3,86 ± 2,53 Improvement after surgery: 2,67 ± 2,09
NOSE-e questionnaire (mean ± SD)	7,84 ± 5,5 Improvement after surgery: 6,19 ± 4,6
Overall satisfaction with the procedure	- Marked improvement (31,25%) - Moderate improvement (46,88%) - No perceived change (21,88%) - Worsening (0%)

Abbreviations: PROMs, Patient-Reported Outcome Measures; NAO, Nasal Airway Obstruction; NOSE-e, Nasal Obstruction Symptom Evaluation (Spanish version); VAS, Visual Analog Scale; RFTR, Inferior Turbinate Reduction using Radiofrequency.

21.88% no perceived change. No participants reported worsening symptoms.

No significant differences in postoperative outcomes were observed between patients undergoing ITRF alone and those who also underwent septoplasty. Table 3 provides a summary of surgical procedures and postoperative outcomes.

Correlations between postoperative outcome evaluation and baseline chemosensory assessment and PROMs

A statistically significant negative correlation was observed between baseline trigeminal sensitivity (BAST-24) and improvement in NOSE-e scores ($r = –0.38$, $p = 0.04$). In multiple linear regression analysis, lower baseline BAST-24 scores were independently associated with greater postoperative NOSE-e improvement ($\beta = –0.073$; $SE = 0.032$; $p = 0.032$), after adjusting for age, baseline NOSE-e score, and smoking status. These findings suggest that reduced baseline trigeminal sensitivity is linked to greater symptom improvement after surgery.

Patients with a NOSE-e improvement >6 points had significantly lower baseline BAST-24 trigeminal scores (mean = 51.25, SD = 24.97) compared to those with ≤6-point improvement (mean = 70.45, SD = 21.85; $p = 0.04$). Supplementary data are provided in Table S3.

No other baseline chemosensory measures or PROMs correlated significantly with NOSE-e improvement. Additionally, no baseline variables were significantly associated with change in VAS on NAO (Table 4 for full results).

A significant correlation was also found between baseline BAST-24 trigeminal scores and overall satisfaction ($r = 0.40$, $p = 0.03$). In multivariate ordinal logistic regression, the BAST-24 trigeminal score remained a significant predictor of satisfaction ($\beta = –0.037$; $SE = 0.017$; $p = 0.031$), adjusting for age, smoking status, and baseline NOSE-e score. Lower baseline trigeminal sensitivity was therefore associated with higher postoperative satisfaction. No other significant associations were observed. Correlations are summarised in Table 4.

Discussion

This prospective cohort study investigated baseline trigeminal, olfactory, and gustatory function in patients with NAO scheduled for surgery, compared to healthy controls, and assessed postoperative outcomes. Importantly, only patients with a clear anatomical basis for obstruction—demonstrated by concordance between reported nasal symptoms and exploratory findings on anterior rhinoscopy and nasal endoscopy—were included, ensuring that all surgical candidates had objective evidence of structural nasal pathology. This selection strategy minimized heterogeneity by excluding individuals with isolated subjective nasal obstruction or functional disorders, focusing instead on those with NAO amenable to septoplasty and/or ITRF. Trigeminal sensitivity was evaluated using a multimodal framework incorporating menthol lateralisation detection thresholds, mucosal expression of TRPV1 and TRPM8, and the BAST-24 trigeminal subtest, enabling assessment of both peripheral receptor-level activity and behavioural responses.

At baseline, trigeminal sensitivity did not significantly differ between NAO patients scheduled for surgery and healthy controls across the three assessment modalities. This suggests that in anatomically confirmed NAO, trigeminal dysfunction is unlikely to reflect primary sensorineural impairment. Instead, a conductive mechanism related to mechanical airflow limitation remains plausible, consistent with previous reports linking nasal obstruction to altered trigeminal activation through reduced mucosal cooling rather than nasal resistance [1–3,14–17]. Our findings fit with the notion that perception of nasal patency depends largely on trigeminally mediated mucosal cooling, as sup-

Table 4. Correlations between Postoperative Outcome Evaluation and Baseline Chemosensory Assessment and Patient Reported Outcome Measures (PROMs).

Correlations (rho value, p-value)		Improvement in VAS ON (score reduction)	Improvement in NOSE-e (score reduction)	Overall satisfaction with the procedure (score)
Baseline PROMs on NAO and Olfaction	NOSE-e questionnaire	-0,32 (p 0,09)	0,21 (p 0,29)	**0,36 (p 0,05)**
	VAS on NAO	0,12 (p 0,52)	0,01 (p 0,96)	**0,35 (p 0,05)**
	VAS on Olfactory Loss	-0,21 (p 0,28)	-0,12 (p 0,53)	0,17 (p 0,36)
Baseline Chemosensory Assessment	Menthol LDT	0,04 (p 0,84)	-0,13 (p 0,49)	0,04 (0,84)
	TS: BAST-24	-0,21 (p 0,27)	**-0,38 (p 0,04)**	**0,4 (p 0,03)**
	TRPV1 Gene Expression Levels	-0,01 (p 0,95)	-0,17 (p 0,38)	-0,05 (p 0,81)
	Olfaction: BAST-24	0,16 (p 0,4)	0,05 (p 0,8)	0,018 (p 0,92)
	Taste: BAST-24	0,14 (p 0,47)	0,2 (p 0,29)	-0,23 (p 0,21)

Statistically significant results ($p < 0.05$) are indicated in bold for clarity. Abbreviations: PROMs, Patient-Reported Outcome Measures; NAO, Nasal Airway Obstruction; NOSE-e, Nasal Obstruction Symptom Evaluation (Spanish version); VAS, Visual Analog Scale; LDT, Lateralization Detection Threshold; BAST-24, Barcelona Smell Test, 24-item version; PCR, Polymerase Chain Reaction; TRPM8, Transient Receptor Potential Melastatin 8; TRPV1: Transient Receptor Potential Vanilloid 1.

ported by CFD and physiological studies showing that increased heat transfer after surgery correlates with symptom improvement [1,2,6]. This broader context supports our interpretation that NAO-related symptom perception is predominantly conductive rather than sensorineural in origin, in line with recent reviews emphasizing the contribution of intranasal trigeminal function to sinonasal disease burden [9,27–29].

The absence of group differences in menthol LDT sensitivity may be attributed to the use of a passive delivery method in our protocol. Unlike active sniffing, which more closely replicates natural nasal airflow and enhances detection of airflow-related (conductive) changes, our approach used hand-squeezed bottles for menthol delivery. This passive method may have reduced test sensitivity for detecting conductive impairments. These findings align with prior studies in non-neuropathic populations [23], suggesting that active inhalation paradigms may be better suited to uncover trigeminal dysfunction in such contexts.

Interestingly, we observed a positive correlation between LDT and BAST-24 performance. To our knowledge, this is a novel finding, indicating that although related, the tests capture different aspects of trigeminal function: LDT reflects a peripheral detection threshold, whereas BAST-24 involves stimulus identification, engaging central cognitive processes. These results support the use of multimodal assessment for a comprehensive evaluation of trigeminal function. By contrast, TRPV1 expression did not correlate with either behavioural measure, consistent with prior reports indicating that receptor expression and perceptual thresholds may represent different facets of trigeminal function [24]. Thus, TRPV1 expression levels may not directly reflect functional trigeminal capacity in vivo. Moreover, TRPM8 expression was undetectable in most cases, likely due to sampling limitations or inherently low mucosal expression, as previously reported [25,26]. These findings underscore the difficulty of quantifying peripheral receptor expression and support the value of integrating molecular and psychophysical measures in assessing nasal trigeminal function. Baseline olfactory function, assessed by BAST-24, was significantly poorer in NAO patients than in controls, confirming prior evidence of olfactory impairment in nasal obstruction [27]. Notably, olfactory scores showed no correlation with trigeminal sensitivity, supporting the distinct yet interacting roles of olfactory and trigeminal pathways in NAO symptomatology [28,29].

Taste sensitivity did not differ significantly between NAO patients and controls. Although nasal airflow may centrally influence taste perception [30], our findings do not support this association. Preserved taste despite olfactory impairment suggests either differential chemosensory vulnerability or methodological limitations. Given the known correlations between olfactory and gustatory dysfunctions [31], further studies using more sensitive gustatory assessments are warranted.

Age and smoking status showed expected associations with chemosensory function. Age correlated negatively with olfactory performance, consistent with known age-related decline [28]. Smoking reduced olfactory sensitivity but had no significant effect on trigeminal or taste measures. These findings highlight the need to consider demographic and lifestyle factors when interpreting sensory data in NAO.

Surgical intervention resulted in significant subjective improvement in NAO symptoms, as shown by reduced VAS and NOSE-e scores, confirming the effectiveness of septoplasty and ITRF. In contrast, olfactory function remained largely unchanged, suggesting that airflow correction alone may not address sensori-

neural or central deficits.

Identifying predictors of surgical benefit is key in NAO management. In this study, lower baseline trigeminal sensitivity—measured with the BAST-24—was significantly associated with greater improvement in NOSE-e scores and higher patient satisfaction. Patients with a reduction >6 points on the NOSE-e had lower baseline BAST-24 scores, suggesting that reduced trigeminal input may heighten symptom perception preoperatively and enhance the sense of postoperative relief.

Menthol LDT and TRPV1 expression showed no significant associations with outcomes, possibly reflecting limited sensitivity to airflow-related (conductive) deficits. Overall, although global trigeminal function appeared preserved in NAO patients relative to controls, lower BAST-24 scores within the surgical group were linked to greater benefit. This suggests that the BAST-24 may capture subtle, clinically relevant differences not detected by molecular or threshold-based measures, meriting further validation as a prognostic tool. These findings support the hypothesis that, in NAO patients requiring surgery, trigeminal-related symptom perception may be influenced more by conductive airflow limitation than by primary sensorineural dysfunction [27].

The lack of olfactory recovery after surgery emphasizes the need for adjunctive therapies targeting sensorineural or central dysfunctions in NAO-related olfactory impairment. Preserved taste function suggests differential chemosensory resilience, meriting further investigation. Future studies should integrate standardised multimodal sensory testing, longitudinal follow-up, and mechanistic analysis in large, phenotypically diverse cohorts, incorporating objective airflow metrics to refine patient stratification and elucidate NAO-related neural pathways.

This study has several limitations. The modest sample size (n=43) limits statistical power and subgroup analyses, making our findings preliminary and in need of validation in larger, multi-centre cohorts. The surgical group was heterogeneous, and the absence of a formal allergy work-up represents a relevant confounder, as allergic rhinitis may alter trigeminal sensitivity. Methodologically, the lack of objective airflow measures (e.g., rhinomanometry) restricted correlations with chemosensory and PROM outcomes, while LDT testing with passive stimulation may underestimate dysfunction. TRPM8 expression was undetectable in most samples—likely for technical reasons—and superficial epithelial sampling may not fully reflect receptor function or central processing. In addition, gustatory testing excluded umami and used a shortened protocol, potentially reducing sensitivity. Finally, PROMs such as NOSEe and VAS, though clinically relevant, remain subjective. Future studies should address these shortcomings with larger, more homogeneous cohorts, objective airflow and allergy testing, and extended follow-up.This study shows that NAO patients requiring surgery exhibit preserved baseline trigeminal sensitivity compared to controls. Notably, lower BAST-24 trigeminal scores were significantly associated with greater symptom improvement and overall satisfaction following surgery.

Conclusion

These findings highlight the potential role of multidimensional trigeminal assessment, particularly BAST-24, as a complementary tool for preoperative evaluation and outcome prediction in nasal obstruction surgery.

Conflict of interest

The authors declare no conflict of interest.

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Authors' contributions

MSB: conceptualization, investigation, project administration, writing – original draft. MM: methodology, investigation, funding acquisition – review & editing. AGP: methodology, conceptualization, supervision – review & editing. LM: methodology, investigation – review & editing. PSU: formal analysis, methodology – review & editing. MAC: funding acquisition, resources, supervision – review & editing.

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SUPPLEMENTARY MATERIAL

Table S1. Correlations between age and baseline chemosensory assessment.

Variable	Correlation with Age (rho value)	p-value
Menthol LDT (dilution step number, mean ± SD)	-0,06	0,73
Trigeminal Sensitivity: BAST-24 (correct forced-choice answers, %)	0,02	0,91
TRPV1 Gene Expression Levels (comparative ΔΔCt method ± SD)	0,1	0,54
Olfaction: BAST-24 (correct forced-choice answers, %)	0,08	0,6
Gustometry: BAST-24 (correct forced-choice answers, %)	-0,48	0,002

Table S2. Comparison of baseline chemosensory assessments between smokers and non-smokers.

Variable	Smokers (n=14)	Non-smokers (n=29)	p-value
Menthol LDT (dilution step number, mean ± SD)	9,75 ± 1,81	9,96 ± 2,31	0,76
Trigeminal Sensitivity: BAST-24 (correct forced-choice answers, %)	51,56 ± 19,3	68,27 ± 27,89	0,042
TRPV1 Gene Expression Levels (comparative ΔΔCt method ± SD)	8,94 ± 2,18	9,26 ± 2,43	0,68
TRPM8 gene Expression Levels (comparative ΔΔCt method ± SD)	Non detectable	Non detectable	
Olfaction: BAST-24 (correct forced-choice answers, %)	73,75 ± 16,18	78,65 ± 12,45	0,28
Gustometry: BAST-24 (correct forced-choice answers, %)	85,94 ± 28,82	95,19 ± 12,29	0,16

Abbreviations: LDT, Lateralization Detection Threshold; BAST-24, Barcelona Smell Test, 24-item version; PCR, Polymerase Chain Reaction; TRPM8, Transient Receptor Potential Melastatin 8; TRPV1: Transient Receptor Potential Vanilloid 1.

Table S3. Comparison of baseline Patient Reported Outcome Measures (PROMs) and chemosensory assessments among patient subgroups defined by postoperative Visual Analogue Scale (VAS) and Nasal Obstruction Symptom Evaluation – Spanish version (NOSE-e) questionnaire score improvements.

		Improvement in VAS ON (score reduction)			Improvement in NOSE-e (score reduction)		
		> 3 points	≤ 3 points		> 6 points	≤ 6 points	
Baseline PROMs on NAO and Olfaction	NOSE-e	11.43 ± 2,85	16.06 ± 3,62	0,0005	14,05 ± 3.75	13.25 ± 4,45	0,4
	VAS on NAO	6,5 ± 1,39	6,56 ± 1,95	0,93	6,28 ± 1,76	6,96 ± 1,57	0,28
	VAS on Olfaction	2,75 ± 2,23	3,08 ± 2,28	0,68	2,9 ± 2,23	3 ± 2,33	0,9
Baseline Chemosensory Assessment	Menthol LDT	10,14 ± 2,48	9,82 ± 2,07	0,7	9,55 ± 2,16	10,73 ± 2,24	0,16
	Trigeminal Sensitivity: BAST-24	55,36 ± 22,31	60,29 ± 28,03	0,6	51,25 ± 24,97	70,45 ± 21,85	0,04
	TRPV1 Gene Expression Levels	9,0 ± 2,19	8,96 ± 2,4	0,94	8,7 ± 2,57	9,56 ± 1,42	0,33
	TRPM8 Gene Expression Levels	Non detectable	Non detectable		Non detectable	Non detectable	-
	Olfaction: BAST-24	76,43 ± 14,73	71,76 ± 14,02	0,38	74,25 ± 14,53	73,18 ± 14,54	0,85
	Gustometry: BAST-24	92,86 ± 18,16	86,76 ± 26,69	0,47	91,25 ± 18,63	86,36 ± 30,34	0,58

NOSE-e, VAS on NAO and VAS on olfaction results are given as mean ± SD; p-value. Menthol LDT results are given as dilution step number, mean ± SD; p-value. Trigeminal Sensitivity: BAST-24, Olfaction: BAST-24 and Gustometry: BAST-24 results are given as correct forced-choice answers, %; p-value. TRPV1/TRPM8 results are given as comparative ΔΔCt method with GAPDH. Abbreviations: PROMs, Patient-Reported Outcome Measures; NAO, Nasal Airway Obstruction; NOSE-e, Nasal Obstruction Symptom Evaluation (Spanish version); VAS, Visual Analog Scale; LDT, Lateralization Detection Threshold; BAST-24, Barcelona Smell Test, 24-item version; PCR, Polymerase Chain Reaction; TRPM8, Transient Receptor Potential Melastatin 8; TRPV1: Transient Receptor Potential Vanilloid 1.