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TITLE Postoperative Pain Management in Rhinoplasty: A Double Blind Randomized Controlled Trial

YEAR 2026

DOI https://doi.org/10.1177/26893614261429310

VERSION Final Draft

CITATION Kandathil CK, Spataro EA, Saltychev M, et al. Postoperative Pain Management in Rhinoplasty: A Double Blind Randomized Controlled Trial. *Facial Plastic Surgery & Aesthetic Medicine*. 2026.

Postoperative Pain Management in Rhinoplasty: A Double Blind Randomized Controlled Trial

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FUNDING: None to declare

CONFLICT OF INTEREST: None to declare

KEYWORDS: Rhinoplasty, Postoperative pain, Nasal surgery, Opioid medication, Non-opioid medication, Hydrocodone, HC, Acetaminophen, APAP, Ibuprofen, IBU, SCHNOS, VAS, Pain VAS scale.

Word Count: 3250

Key Points

Question: Do non-opioid pain medications offer adequate pain control compared to opioids, following rhinoplasty?

Findings: This study demonstrates no difference in postoperative pain control with non-opioid medications compared to opioids.

Meaning: Adequate postoperative pain control in rhinoplasty can be achieved with non-opioid pain medications.

Abstract

Background: There is inadequate evidence for the utilization of non-narcotic pain medications for postoperative pain management following rhinoplasty.

Objective: To compare the effectiveness of opioid and non-opioid medications for postoperative pain control in rhinoplasty as measured by a visual analog scale (VAS) on postoperative days 0-5.

Methods: In this double blind randomized controlled clinical trial, adult patients who underwent primary rhinoplasty at a tertiary center were enrolled from August 2019 to October 2024. Patients were randomized to receive either a combination of acetaminophen (325 mg) and hydrocodone (5 mg) or acetaminophen (325 mg) and ibuprofen (200mg), 1-2 tablets every 4 hours for five postoperative days. Tramadol (50mg) was prescribed for breakthrough pain.

Results: 130 patients (65 per group) completed the study. The average age (SD) was 32 (10.7) years. The majority were women (77%), white (68%), and underwent combined functional and aesthetic rhinoplasty (52%). There was no difference detected in mean postoperative pain (VAS) scores recorded on postoperative days 0-5, between treatment groups (p=0.156). Among side effects, only itchiness was significantly higher (*p*=0.001) in the hydrocodone-acetaminophen group.
Conclusion: This trial demonstrates a lack of difference between opioid and non-opioid pain medications in postoperative pain control after rhinoplasty.

Introduction

Rhinoplasty is the fifth most commonly performed aesthetic surgical procedure worldwide[1] and is among the top ten in the United States[1, 2]. A comparative increase (21.6% worldwide[1] and 6% in the United States[2]) in rhinoplasties performed in 2023 has been reported from previous years. Although postoperative pain in rhinoplasty has been described as "negligible to moderate and seldom severe"[3], pain thresholds can be relative and tend to vary between patients. Typically, postoperative pain management strategies in rhinoplasty include opioid and/or non-opioid pain medications such as oxycodone, hydrocodone, tramadol, or a combination of oxycodone-acetaminophen, hydrocodone-acetaminophen, and acetaminophen-codeine, and anti-inflammatory medications.

In 2017, published rhinoplasty clinical practice guidelines (RCPG) acknowledged a lack of randomized controlled trials, related to postoperative pain management in rhinoplasty.[3] The recommendations for postoperative pain management in rhinoplasty using non-opioid medications were based on evidence of 'medium' confidence derived from non-rhinoplasty or low-quality studies. The RCPG concluded that further investigation was warranted to encourage the use of non-opioid pain medications as the primary modality of postoperative pain management.[3]

The RCPG were formulated at a time when United States was in a public health crisis with the opioid epidemic.[4] Over-prescription of opioid medications, the initial driver of this epidemic, lead to its increased misuse, dependance, opioid use disorder (OUD) and related overdose deaths.[5, 6] Since 2016, stricter policies and strategies were instituted both at the federal and state level in an attempt to reduce over prescriptions of opioid pain medications.[7, 8] Despite, significant reductions in opioid overdose deaths due to opioid prescription from these policies, the overall numbers to date are still high, partly due to inadequate and often inaccessible pain management strategies and a shift to illicit opioids.[9]Patients undergoing rhinoplasty have a higher incidence of filling perioperative opioid prescriptions than those undergoing other plastic and reconstructive surgeries. They also have the second-highest odds of filling their opioid prescription 90-180 days postoperatively, after breast surgery.
[10]

Prior studies have demonstrated a substantially high variability within and between facial plastic and reconstructive surgery (FPRS) centers in prescription patterns of opioid pain medications following rhinoplasty.[11, 12] A multicenter study reported patient utilization rate of less than 50 % of the prescribed postoperative opioid pain medications in rhinoplasty and interestingly, providers being cognizant of the ongoing opioid crisis significantly reduced the number of prescribed postoperative opioid medications.[12] There is evidence indicating that nonsteroidal anti-inflammatory drugs (NSAID) are a reasonable alternative for postoperative pain management without a significant increase in postoperative bleeding risk in various plastic and reconstructive procedures.[13, 14] Studies have also demonstrated that postoperative use of NSAIDs in rhinoplasty does not cause any increase in postoperative complication rates.[15]

This study was conceptualized based on the recommendation put forth by the 2017 RCPG[3], coupled with the evidence from the above-mentioned studies[10-12]. This double-blind, randomized controlled trial was designed in to address a specific literature gap in postoperative pain management in rhinoplasty and to assist rhinoplasty surgeons in making informed decisions about implementing non-opioid pain control protocols. The primary objective of this study was to compare the effectiveness of opioid and non-opioid medications for postoperative pain control following rhinoplasty, as measured by a VAS on postoperative days 0-5, with a secondary objective to compare perioperative complication rates related to medication use amongst groups.

Methods

This study was a double-blind, two-arm, randomized controlled trial conducted at a single site. The study was approved by the institutional review board (protocol ID 46945). The trial was registered on the United States national clinical trials registry on 6/27/2018 (NCT 03584152; https://clinicaltrials.gov/study/NCT03584152) . No external funding was received for the trial. All the authors had no financial or other conflicts of interest to declare. The trial included adult patients who underwent rhinoplasty for functional, cosmetic, or combined reasons. All surgeries were performed by the senior author (S.P.M.) at a tertiary hospital from August 2019 to October 2025. Patients were excluded from the trial if they were <18 years of age, undergoing revision rhinoplasty, requiring autologous rib cartilage graft or ear cartilage graft, had a history of allergies to any medications utilized in the trial, or had current use of selective serotonin reuptake inhibitors (SSRI) or monoamine oxidase inhibitors (MAOI).

Intervention

The trial consisted of two treatment arms. Treatment arm ‘A’ included 5mg hydrocodone (HC) and 325mg acetaminophen (APAP) compounded pills, and treatment arm ‘B’ included 200mg ibuprofen (IBU) and 325 mg acetaminophen (APAP) compounded pills. To avoid any bias, the combinations of treatment medications for each arm were compounded as a single pill to appear identical and packaged in sequentially numbered containers. Mariner Advanced Pharmacy (Redwood City, CA, USA) was solely responsible for generating the randomization sequence for the study medication allocation, compounding, and delivering the study drugs to the study site. Patients were randomized to treatment arm ‘A’ (APAC-HC) or treatment arm ‘B’ (APAC-IBU) utilizing block randomization with a block size of 10 by the pharmacist (H.T.) based on a randomization schedule generated using SAS software, version 9.4 (SAS Institute Inc Cary, NC, USA). Every trial participant received a total of 30 tablets of the study medications. The recommended daily dosage for both treatment groups was one or two tablets every four hours for a total duration of five postoperative days. The request for these double-blinded medications was made directly on the pharmacy order-entry portal, based on participant recruitment. The study site personnel did not have access to the randomization sequence. In addition to the randomized treatment medications, to account for breakthrough pain, all enrolled

patients were also prescribed 10 tablets of tramadol 50 mg with instructions to take one tablet every 6 hours. Patients were also explicitly advised to stop the assigned treatment medications before starting on tramadol tablets. After achieving adequate control of their breakthrough pain or after exhausting their quantity of tramadol tablets, patients were requested to continue on their assigned treatment medications, if required. The trial ended for each participant when they returned to the FPRS clinic for their first postoperative visit, typically within seven days after surgery. Participants were advised on safe disposal practices for remaining treatment medications at home, via the "MED-project USA" with an option to return the remaining treatment medications to the FPRS clinic for proper disposal. Unblinding of the study participants was carried out only after the required number of patients for the trial were enrolled and completed their related study process.

Outcome Measures

Each trial participant was provided with a booklet to record the following particulars at every dosage interval: the number of treatment medication taken, their intensity of pain experienced, any side effects experienced, whether the pain was adequately controlled or not, and the number of tramadol tablets taken, if any. (Supplemental File 1) The intensity of pain was assessed utilizing a pain visual analogue scale (VAS) scale of 0-100 points (with '0' indicating no pain and '100' indicating worst possible pain)[16]. The postoperative periorbital sequelae of eyelid edema, ecchymosis, and subconjunctival hemorrhage was assessed by the senior author (S.P.M.) at their first postoperative visit.[17] (Supplemental File 2) Patients' nasal obstructive symptoms and nasal aesthetic problems was assessed using the Standardized Cosmesis and Health Nasal Outcomes Survey (SCHNOS) questionnaire.[18, 19]. Patients also graded their perceived severity of nasal obstruction and satisfaction with their nasal aesthetics using a visual analogue scale.[20] (Supplemental File 3) Both SCHNOS and VAS scores were recorded at two postoperative time periods, <6 months and >/= 6 months.

Statistical analysis

Study power was calculated using G*Power 3.1.9.6 software based on independent samples t-test based on difference between two means. This was a non-inferiority trial to demonstrate that APAP-IBU is

not 'inferior' to APAP-HC. In other words, the combination of APAP-IBU is 'not unacceptably worse' than the combination of APAP-HC. Thus, the null hypothesis stated that the combination of APAP-IBU is worse than the combination of APAP-HC by more than -Δ, where -Δ is the 'non-inferiority margin'. In this study, the 'non-inferiority margin' of -20 was based on the difference between treatment groups in change in pain severity based on a 0-100 pain VAS scale. The minimal clinically significant difference for pain numeric rating scale has usually been established at around two points on a zero to 10 scale (20 points for a visual analogue scale from zero to 100).[21, 22] The standard deviation (SD) of change in pain severity of four points resulted in effect size 'd' (Cohen's d) of 0.5. Due to non-inferiority design, a one-tailed *p*-value was used resulting in the following estimates: α err prob = 0.05; power (1-β err prob) = 0.80; allocation ratio N2/N1 = 1; non centrality parameter δ = 2.52; critical t =1.66; df =100; sample size per group = 51; and total sample size = 102.

Descriptive statistics were reported as mean (SD), and as absolute numbers and percentage where appropriate. Treatment groups were compared using the Pearson Chi-squared test or Fisher's exact (if n<5) for categorical variables and the t-test for continuous variables. To assess the severity of postoperative pain experienced by patients over time in both the groups, a univariate linear regression was utilized to examine differences in mean pain VAS scores at various dosage intervals, between groups. A multivariable linear regression was utilized to analyze the effect of number of inferior turbinate reduction (ITR) or osteotomies performed, number of study medications consumed, the number of additional tramadol tablets taken by the study participants, or their postoperative periorbital sequelae of eyelid edema, ecchymosis, and hemorrhage on differences in mean postoperative pain VAS scores between treatment groups. For analyses of the SCHNOS (O and C) and the VAS (F and A) scores, since all 130 patients did not have a postoperative score at both time intervals, a mean postoperative score (SD) was calculated for each treatment group and compared to their mean preoperative scores utilizing a paired t-test. The calculated mean changes in score (□) was compared between the two treatment groups utilizing an unpaired t-test. Two-tailed *p*-values were reported, when appropriate. The level of significance of *p*-value was set at <0.05. All analyses were carried out using Stata/BE Statistical Software: Release 19 College Station (Stata Corp LP, TX, USA).

Results

A total of 159 eligible patients were enrolled during a period from August 2019 to October 2024. (Figure 1) 130 patients successfully completed the trial with 65 patients each assigned to APAP-HC and APAP-IBU arms of the trial. Patients were excluded if their surgery was cancelled and /or postponed (n=6), for non-adherence to pain control protocol (n=11), and dropouts (n= 12). No serious adverse event (SAE) occurred for the duration of the trial.

The trial participants had a mean age (SD) of 32.1 (10.7) years. The majority were women, 100 (77%), white, 89 (68%), and underwent combined functional and aesthetic surgery, 68 (52%). No difference in mean preoperative SCHNOS-O (p=0.818), SCHNOS-C (p=0.975), VAS- F (p=0.632), and VAS-A (p=0.971) scores were observed between the two treatment groups. No mean differences were observed between the two groups in the dosages of intra operative drugs that were administered. The majority of patients (59%) did not undergo ITR as part of their rhinoplasty, but there was no significant difference between treatment groups (p=0.592). In trial patients who underwent osteotomies (76%), no significant differences were observed between treatment groups(p=0.846). The majority of osteotomies were performed using a Piezotome. (Table 1)

While a higher trend of number of study tablet utilized was observed in the APAP-IBU group (treatment ‘B’) =19 (9.9) compared to the APAP-HC group (treatment ‘A’) =16 (9.5), no significant difference (p=0.112) was observed. There was no difference in mean postoperative pain VAS scores between the two groups, [44.4 (14.1) for APAP-HC group (treatment ‘A’) vs. 40.6 (16.3) for APAP-IBU group (treatment ‘B’), p=0.156].(Table 2) The 95% confidence intervals (CI) (-1.47 – 9.12) for the difference in mean postoperative pain VAS scores between groups (3.82) do not include the pre-specified non-inferiority margin of -20. The linear regression model did not demonstrate a significant difference between mean pain VAS scores between groups (p=0.156 , R-squared=0.0157). Predicted estimates from linear regression demonstrated a slightly lower trajectory of mean pain VAS scores at various dosage intervals for APAP-IBU group (treatment ‘B’) compared to APAP-HC group (treatment ‘A’) but based on overlapping 95% confidence intervals between the two treatment groups, there were no significant differences at any dosage

interval. (Figure 2) For the response to the query, “adequate pain control or not” at each dosage interval, there was no significant difference between 61 (94%) patients of APAP-HC group (treatment ‘A’) and 63 (97%) of APAP-IBU group (treatment ‘B’) who indicated “yes” to the query (p=0.403).

For break through pain, 19 (29%) patients from APAP-HC group (treatment ‘A’) consumed a total of 95 tramadol tablets compared to 15 (23%) from APAP-IBU group (treatment ‘B’) who consumed a total of 104 tablets (p=0.425). When comparing mean differences in the number of tramadol tablets consumed between groups, no significant difference was observed (*p*=0.803). Analyzing the difference in various side effects reported between treatment groups, besides itchiness being greater in the APAP-HC group (treatment ‘A’) (*p*=0.001), no other side effects (nausea, constipation, dizziness, bleeding, headache or other) demonstrated any significant difference between the two groups. (Table 2)

For the reported patient outcomes, there were no differences in the mean change in score (□) when compared between the two groups for SCHNOS-O (*p*=0.732) and C (*p*=0.527), and VAS-F (*p*=0.916) and VAS-A (*p*=0.535) (Table 3). The median periorbital sequelae grading for eyelid edema, (range 0-2) periorbital ecchymosis extension (range 0-4) and subconjunctival hemorrhage (range 0-2) was 0, respectively. Comparison of periorbital sequelae grading between groups utilizing a Wilcoxon rank-sum test did not demonstrate differences for eyelid edema (p=0.378), periorbital ecchymosis extension (*p*=0.195) and subconjunctival hemorrhage (*p*=0.682).

A multivariable linear regression did not demonstrate any significant difference between mean postoperative pain VAS scores between treatment groups based on the number of study medications consumed, the number of additional tramadol tablets taken by the study participants, their postoperative periorbital sequelae of eyelid edema, ecchymosis, and hemorrhage experienced by the patients, or when inferior turbinate reductions/ or osteotomies were performed (*p*=0.207, R-squared=0.176).

Discussion

In this study, the effectiveness of postoperative pain control in patients undergoing primary rhinoplasty utilizing either a combination of compounded pills containing APAP-HC or APAP-IBU were compared. This study represents one of the earliest double-blind randomized evaluations of opioid versus

non-opioid regimens in rhinoplasty, finding equivalent pain control and supporting non-opioid first-line care.

Based on mean postoperative VAS pain scores, there was no significant difference between the two both opioid and non-opioid but these regimens achieved adequate postoperative pain control which is supported by two additional findings. First, the lack of significant difference in participants' responses to the query, "adequate pain control or not", where it was observed that the majority in both the treatment groups achieved adequate postoperative pain control. Secondly, the average number of tablets of study medications consumed by the patients in the two treatment groups did not differ significantly either.

Across all dosage intervals, there were no significant differences in the postoperative pain severity between treatment groups. Although the trajectory of the postoperative pain severity, as indicated by the average postoperative pain VAS scores, in APAP-IBU treatment group appears slightly lower than the trajectory for the APAP-HC treatment group at all recorded dosage intervals, the overlap of the confidence intervals indicates there is no meaningful difference in the pain control between the two treatment groups. It should be noted that none of the trial participants received nasal hemostatic packing after surgery as the senior author (S.P.M.) commonly uses only silastic nasal splints, nasal taping, and external splinting as standard practice. All patients in this trial, following surgery, were prescribed a five-day course of antibiotics and advised to use icepacks on the nose/ face to reduce swelling and pressure in addition to the assigned pain medications. We also demonstrate that concurrent ITR and/or osteotomies performed during rhinoplasty do not influence the severity of patients' postoperative pain or their breakthrough pain, as evidenced by the lack of significant difference in the number of study medications taken or the count of tramadol tablets taken. These procedures also do not seem to worsen postoperative periorbital eyelid edema, ecchymosis, or hemorrhage experienced by patients in either of the treatment groups. Except for a higher incidence of itchiness in APAP-HC group, there were no differences in other side effects between the treatment groups. The results of this trial provide good evidence that a combination of APAP-IBU could be considered an alternative for postoperative pain management in rhinoplasty.

Tramadol with its lower potential for dependance and safer risk profile for short-term use, was chosen for the management of breakthrough pain due to its effectiveness in moderate pain control. Tramadol

is known to lower seizure threshold and cause serotonin syndrome. Owing to this reason, this trial excluded those patients' undergoing rhinoplasty with history of current intake of serotonergic drugs such as selective serotonin reuptake inhibitors (SSRI), serotonin-norepinephrine reuptake inhibitors (SNRI), or monoamine oxidase inhibitors (MAOI). The dosage of hydrocodone (5 mg) utilized in the trial and the average number of tablets consumed by patients in the study was in line with the recommended the dosage of "5mg" for opioid medications and a quantity of "8-21" pills put forth by the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) clinical practice guideline for opioid prescription in postoperative pain control in intermediately painful procedures including rhinoplasty.[23] This recommendation by the AAO-HNS was based on two randomized trials on pain prophylaxis in rhinoplasty, a single blinded trial[24], an unblinded one[25], and a trio of observational studies[12, 26, 27]. However, the average number of opioid tablets taken ithe current study was higher than in the earlier trials[24, 25], which can be attributed to differences in dosage protocols between the trials. Moreover, the mean pain VAS score of 44.0 (14.1) for the opioid treatment group in this trial was comparable with two prior trials, which also reported no difference in postoperative pain control based on pain VAS score between opioid and non-opioid treatment arms of the study.[24, 25] In both trials, there were marked variations in the types of patients undergoing rhinoplasty, and specific details of the type of rhinoplasty were also not forthcoming. [24, 25] . Although the side effects of opioid medications are well documented, unlike the current study, one of the earlier trials did not report any related side effects[24], and the other trial reported no side effects in their treatment groups[25]. Our larger, double-blind trial complements the trial by Frants et al. [25], with symmetric rescue and prespecified, clinically meaningful endpoints supported by a prospective power analysis. Compared with these two prior trials[24, 25], the current trial is a more robust, comprehensively designed clinical trial assessing postoperative pain control in rhinoplasty.

This trial was conceptualized at a time when rhinoplasty surgeons were beginning to be aware of their unwitting contribution to the national opioid crisis. During the period of this trial, the American Academy of Facial Plastic Surgeons (AAFPRS) has actively recognized the role of its members to help alleviate the national opioid crisis, and there is growing evidence suggesting a considerable improvement in

general awareness among rhinoplasty surgeons regarding the unmet need to reduce opioid prescriptions drastically.[11, 28]. Level II evidence from this trial now provides a framework for rhinoplasty surgeons to tailor a multimodal postoperative pain management regimen. Also, it helps patients make informed decisions regarding reduced reliance on opioid pain medications for their postoperative pain control. The main limitation of this trial is that it is a single-center study that includes patients undergoing rhinoplasty by a single surgeon. The majority of participants in this current trial were white, female, and underwent cosmetic rhinoplasty, which can be attributed to the study's geographic location and the tertiary center's target population. An inherent limitation of trials of this type across settings is selection bias, since patients with higher anxiety or perceived low pain tolerance were less likely to consent to randomization. Exclusion of primary rhinoplasty candidates requiring auricular or costal cartilage grafts, although carried out to avoid secondary donor site morbidity, limits the generalizability of results of the trial to a certain extent. Another limitation of the study is the inherent bias in the senior author's assessment of the patient's postoperative periorbital sequelae of eyelid edema, ecchymosis (bruising), and subconjunctival hemorrhage. It is also worth highlighting that only 77% patients of the non-opioid arm of the study was truly opioid free with 23% requiring an opioid break through pain medication. Future research directions include conducting a multicenter clinical trial on the topic from different regions of the country to provide a more accurate representation of the country's demographics and include both primary and secondary rhinoplasty cases to understand differences in postoperative pain and pain control.

Conclusion

This double-blind, adequately powered randomized trial definitively demonstrates that non-opioid multimodal analgesia (acetaminophen–ibuprofen) provides postoperative pain control comparable to acetaminophen–hydrocodone after primary rhinoplasty. These results support adopting non-opioid therapy as the preferred first-line regimen, reserving opioids for rescue.

Figure Legend

Figure 1.The CONSORT Flow Diagram Demonstrating Phases of The Double Blind Randomized Controlled

Trial.

Figure 2. Differences In Mean Pain VAS Scores at Various Dosage Intervals Between Treatment Groups Based on Predicted Estimates from Univariate Linear Regression Model. The Error Bars Signify the Lower Bound of the 95% Confidence Interval.

Supplemental File 1. Details of Pain VAS Scale and Particulars Completed by Patients at Each Dosage Interval in the Study Booklet.

Supplemental File 2. Grading Scale Utilized for Periorbital Grading of Eyelid Edema, Periorbital Ecchymosis Extension, and Subconjunctival Hemorrhage.

Supplemental File 3. Standardized Cosmesis and Health Nasal Outcomes Survey (SCHNOS) – (O) & (C) and Visual Analog Scale (VAS) – (Functional) & (Aesthetic)

References

1) ISAPS. 2024 ISAPS INTERNATIONAL SURVEY ON AESTHETIC/COSMETIC PROCEDURES PERFORMED IN 2023. (International Society of Aesthetic Plastic Surgery). 2024.

2) ASPS. 2023 American Society of Plastic Surgeons (ASPS) Procedural Statistics. 2024.

3) Ishii LE, Tollefson TT, Basura GJ et al. Clinical Practice Guideline: Improving Nasal Form and Function after Rhinoplasty Executive Summary. Otolaryngol Head Neck Surg 2017;156:205-219 PubMed .

4) HHS. HHS Acting Secretary Declares Public Health Emergency to Address National Opioid Crisis. media@hhs.gov, ed. (United States Department of Health and Human Services (HHS)). 2017.

5) NIDA. Drug Overdose Deaths: Facts and Figures. 2024.

6) CDC. Understanding the Opioid Overdose Epidemic. 2025.

7) CDC. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. 2016.

8) CDC. CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022. 2022.

9) NIH. The Opioid Crisis. 2024.

10) Olds C, Spataro E, Li K et al. Assessment of Persistent and Prolonged Postoperative Opioid Use Among Patients Undergoing Plastic and Reconstructive Surgery. JAMA Facial Plast Surg 2019;21:286-291.

11) Sethi RKV, Lee LN, Quatela OE et al. Opioid Prescription Patterns After Rhinoplasty. JAMA Facial Plast Surg 2019;21:76-77 PubMed .

12) Patel S, Sturm A, Bobian M et al. Opioid Use by Patients After Rhinoplasty. JAMA Facial Plast Surg 2018;20:24-30.

13) Stephens DM, Richards BG, Schleicher WF et al. Is ketorolac safe to use in plastic surgery? A critical review. Aesthet Surg J 2015;35:462-466 PubMed .

14) Kelley BP, Bennett KG, Chung KC et al. Ibuprofen May Not Increase Bleeding Risk in Plastic Surgery: A Systematic Review and Meta-Analysis. Plast Reconstr Surg 2016;137:1309-1316 PubMed .

15) Olds C, Spataro EA, Li K et al. Nonsteroidal Antiinflammatory Drug Use after Nasal Surgery Is Not Associated with Increased Postoperative Complications. Plast Reconstr Surg 2019;144:1130e-1132e.

16) Breivik H, Borchgrevink PC, Allen SM et al. Assessment of pain. Br J Anaesth 2008;101:17-24 PubMed .

17) Kara CO, Gokalan I. Effects of single-dose steroid usage on edema, ecchymosis, and intraoperative bleeding in rhinoplasty. Plast Reconstr Surg 1999;104:2213-2218 PubMed .

18) Moubayed SP, Ioannidis JPA, Saltychev M et al. The 10-Item Standardized Cosmesis and Health Nasal Outcomes Survey (SCHNOS) for Functional and Cosmetic Rhinoplasty. JAMA Facial Plast Surg 2018;20:37-42.

19) Kandathil CK, Saltychev M, Abdelwahab M et al. Minimal Clinically Important Difference of the Standardized Cosmesis and Health Nasal Outcomes Survey. Aesthet Surg J 2019;39:837-840 PubMed .

20) Kandathil CK, Patel PN, Spataro EA et al. Examining Preoperative Expectations and Postoperative Satisfaction in Rhinoplasty Patients: A Single-Center Study. Facial Plast Surg Aesthet Med 2021;23:375-382.

21) Hawker GA, Mian S, Kendzerska T et al. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). Arthritis Care Res (Hoboken) 2011;63 Suppl 11:S240-252.

22) Olsen MF, Bjerre E, Hansen MD et al. Pain relief that matters to patients: systematic review of empirical studies assessing the minimum clinically important difference in acute pain. BMC Med 2017;15:35.

23) Anne S, Mims JW, Tunkel DE et al. Clinical Practice Guideline: Opioid Prescribing for Analgesia After Common Otolaryngology Operations. Otolaryngol Head Neck Surg 2021;164:S1-S42.

24) Nguyen KK, Liu YF, Chang C et al. A Randomized Single-Blinded Trial of Ibuprofen- versus Opioid-Based Primary Analgesic Therapy in Outpatient Otolaryngology Surgery. Otolaryngol Head Neck Surg 2019;160:839-846.

25) Frants A, Garber D, Lafer MP et al. Prospective Randomized Trial Comparing Opioids versus Nonsteroidal Antiinflammatory Drugs for Postoperative Analgesia in Outpatient Rhinoplasty. Plast Reconstr

Surg 2021;147:56-62 PubMed .

26) Sclafani AP, Kim M, Kjaer K et al. Postoperative pain and analgesic requirements after septoplasty and rhinoplasty. Laryngoscope 2019;129:2020-2025 PubMed .

27) Rock AN, Akakpo K, Cheresnick C et al. Postoperative Prescriptions and Corresponding Opioid Consumption After Septoplasty or Rhinoplasty. Ear Nose Throat J 2021;100:462S-466S.

28) Barbarite E, Occhiogrosso J, McCarty JC et al. Opioid Prescribing Patterns Among Facial Plastic and Reconstructive Surgeons in the Medicare Population. Facial Plast Surg Aesthet Med 2021;23:401-404.

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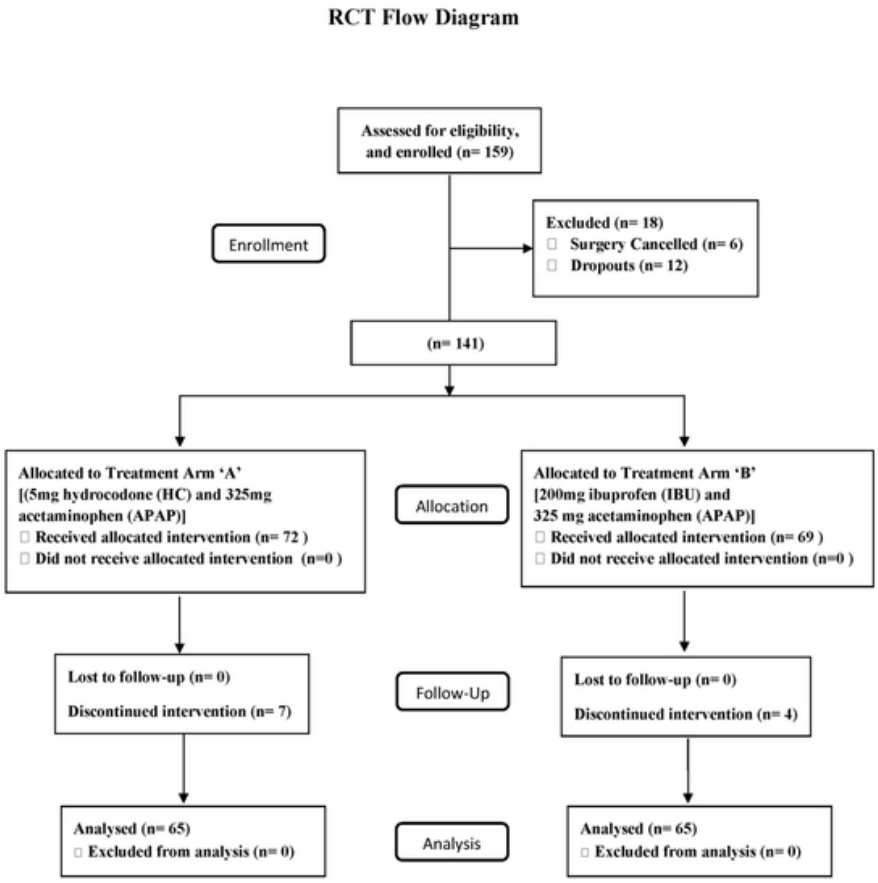
Supplemental File 3. Standardized Cosmesis and Health Nasal Outcomes Survey (SCHNOS) – (O) & (C) and Visual Analog Scale (VAS) – (Functional) & (Aesthetic)



The CONSORT Flow Diagram Demonstrating Phases of The Double Blind Randomized Controlled Trial.

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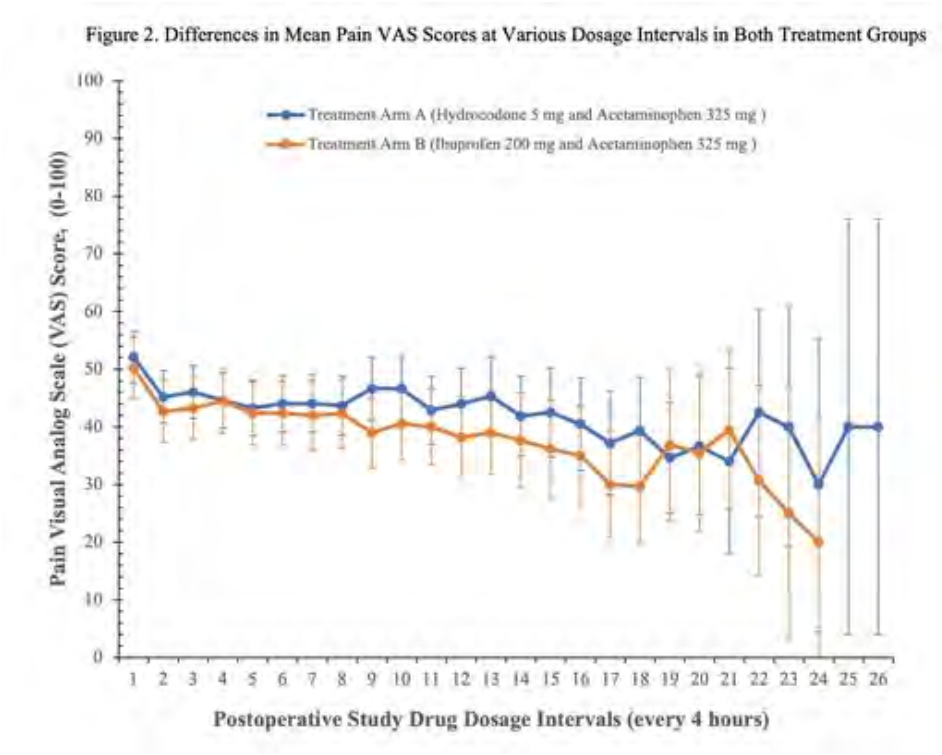

Differences In Mean Pain VAS Scores at Various Dosage Intervals Between Treatment Groups Based on Predicted Estimates from Univariate Linear Regression Model. The Error Bars Signify the Lower Bound of the 95% Confidence Interval.

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Table 1: Characteristics of Participants Who Completed the Clinical Trial

	Hydrocodone 5 mg and Acetaminophen 325 mg (Treatment A)	Ibuprofen 200mg and Acetaminophen 325 mg (Treatment B)	Total	*p* value*
Sample Size, n (%)	n=65 (50.0%)	n=65 (50.0%)	n=130 (100.0%)	
Age , Mean (SD), years	30.7 (8.6)	33.5 (12.4)	32.1 (10.7)	0.125
Sex, n (%)				
Male	17 (26%)	13 (20%)	30 (23%)	0.405
Female	48 (74%)	52 (80%)	100 (77%)	
Race, n (%)				
White	44 (68%)	45 (69%)	89 (68%)	0.366
Asian	15 (23%)	10 (15%)	25 (19%)	
Latino/Hispanic	6 (9%)	10 (15%)	16 (12%)	
Type of Surgery, n (%)				
Functional	15 (23%)	15 (23%)	30 (23%)	1
Cosmetic	34 (52%)	34 (52%)	68 (52%)	
Combined	16 (25%)	16 (25%)	32 (25%)	
Preoperative SCHNOS-O, Mean score (SD)	40.0 (33.2)	41.0 (36.1)	41.0 (34.5)	0.818
Preoperative SCHNOS-C, Mean score (SD)	54.0 (29.0)	54.0 (26.4)	54.0 (27.6)	0.975
Preoperative VAS-F, Mean score (SD)	4.0 (3.1)	4.0 (3.1)	4.0 (3.1)	0.632
Preoperative VAS-A, Mean score (SD)	3.0 (2.3)	3.0 (2.5)	3.0 (2.4)	0.971
Postoperative Time period-1(<6 months), Mean (SD), months	2.8 (1.5)	2.6 (1.6)	2.7 (1.5)	0.562
Postoperative Time period-2 (>/=6 months), Mean (SD), months	13.8 (8.3)	11.1 (5.7)	12.2 (6.9)	0.136
Intraoperative Medications Administered, Mean dosage (SD)				
APAP (mg)	612.2 (487.5)	560.5 (490.6)	586.0 (485.5)	0.649
Midazolam (mg)	2.0 (0.6)	2.0 (0.6)	2.0 (0.6)	0.676
Fentanyl (mcg)	126.0 (81.1)	121.0 (66.1)	124.0 (73.8)	0.721
Lidocaine 2% (mg)	77.0 (213.1)	41.0 (42.5)	59.0 (152.8)	0.3
Lidocaine-Epinephrine 1% (1:100000) (ml)	12.0 (9.5)	29.0 (147.4)	20.0 (104.0)	0.349
Propofol (mg)	998.0 (776.9)	897.0 (660.4)	947.0 (719.5)	0.426
Rocuronium (mg)	27.0 (31.4)	30.0 (39.0)	28.0 (35.5)	0.725
Succinyl Choline	3.0 (16.2)	7.0 (24.7)	5.0 (21.1)	0.376
Clindamycin (mg)	39.0 (173.3)	49.0 (206.3)	44.0 (189.1)	0.835

Cefazolin (mg)	1953.0 (415.2)	1938.0 (530.8)	1945.0 (474.7)	0.853
Vancomycin	. (.)	1000 (.)	1000 (.)	
Celecoxib (mg)	5.0 (32.9)	0 (0.0)	3.0 (23.1)	0.314
Dexamethasone (mg)	8.0 (1.6)	8.0 (1.4)	8.0 (1.5)	0.241
Ondansetron (mg)	5.0 (2.0)	5.0 (1.7)	5.0 (1.8)	1
Promethazine (mg)	8.0 (2.3)	7.0 (2.0)	7.0 (2.2)	0.813
Metoclopramide (mg)	13.0 (5.2)	10.0 (1.6)	12.0 (4.3)	0.223
Suggammadex (mg)	59.0 (92.7)	71.0 (106.3)	65.0 (99.3)	0.617
Remifentanil (mcg)	1749.0 (846.6)	1485.0 (855.9)	1615.0 (856.0)	0.183
Normosol (ml)	641.0 (466.8)	649.0 (408.8)	645.0 (435.4)	0.936
Ephedrine (mg)	7.0 (8.8)	5.0 (8.8)	6.0 (8.8)	0.269
Phenylephrine (mcg)	389.0 (1500.6)	480.0 (1019.8)	434.0 (1275.2)	0.758
Glycopyrrolate (mg)	0 (0.1)	0 (0.2)	0 (0.2)	0.437
Gabapentin (mg)	8.0 (49.3)	21.0 (81.1)	15.0 (67.2)	0.408
Ketamine (mg)	3.0 (10.8)	1.0 (6.5)	2.0 (8.9)	0.351
Meperidine (mg)	6.0 (9.3)	6.0 (9.8)	6.0 (9.5)	0.773
Hydromorphone (mg)	0 (0.3)	0 (0.3)	0 (0.3)	0.756
Oxycodone (mg)	3.0 (4.3)	2.0 (3.4)	3.0 (3.9)	0.375
Morphine (mg)	3.0 (1.2)	. (.)	3.0 (1.2)	.-
Labetalol (mg)	3.0 (8.4)	5.0 (13.9)	4.0 (11.6)	0.267
Hydralazine (mg)	5.0 (0.0)	8.0 (2.9)	6.0 (2.3)	0.134
Esmolol (mg)	3.0 (16.7)	3.0 (16.2)	3.0 (16.3)	0.97
Tranexamic acid (mg)	325.0 (334.4)	354.0 (379.9)	341.0 (353.1)	0.851
Inferior Turbinate Reduction, n (%)				
Not Performed	37 (57%)	40 (62%)	77 (59%)	0.592
Performed	28 (43%)	25 (38%)	53 (41%)	
Osteotomies (0=None,1=piezo,2=traditional)				
Not Performed	16 (25%)	16 (25%)	32 (25%)	0.846
Performed with Piezotome	41 (63%)	43 (66%)	84 (65%)	
Performed with Traditional Osteotome	8 (12%)	6 (9%)	14 (11%)	

* *p*-values from t-test for Mean (SD=Standard deviation) and from Pearson Chi2-test or Fisher's exact (if n<5) for n=Frequency (Percentage); Age was defined in years at the time of surgery. Biological sex was dichotomized as male and female. Race was defined as White, Asian, Latino/Hispanic, or Black. The type of surgery was defined as functional for patients who underwent rhinoplasty for functional reasons only, cosmetic for patients who underwent rhinoplasty for cosmetic reasons only and combined for those who underwent rhinoplasty for both functional and combined reasons. "Postoperative time periods 1 and 2" were defined as follow up time period of <6 months and >/= 6 months, respectively, after surgery. "Perioperative medications administered" were defined as any medications administered to the patients before, during, immediately following surgery, or at the postoperative

recovery care unit. The amount of perioperative medications was reported as milligram (mg), microgram (mcg) or milliliter (ml), when appropriate. “Number of study drugs” was defined as the total number of study drug tablets used by a participant. “Number of tramadol tablets” was defined as the total number of tramadol tablets used by a patient for breakthrough pain. The “side effects experienced from study drugs”, were defined as ‘yes’ or ‘no’ for symptoms of nausea, itchiness, constipation, dizziness, bleeding, headache, and other. “Adequacy of pain control” was assessed by a questionnaire and defined as ‘yes’ or ‘no’. Standardized Cosmesis and Health Nasal Outcomes Survey (SCHNOS-O and SCHNOS-C), Visual Analog Scale (VAS), Aesthetic (A), Functional (F), APAP=N-acetyl-para-aminophenol/acetaminophen.

Table 2: Details of Postoperative Pain Control and Side Effects Experienced in Trial Participants

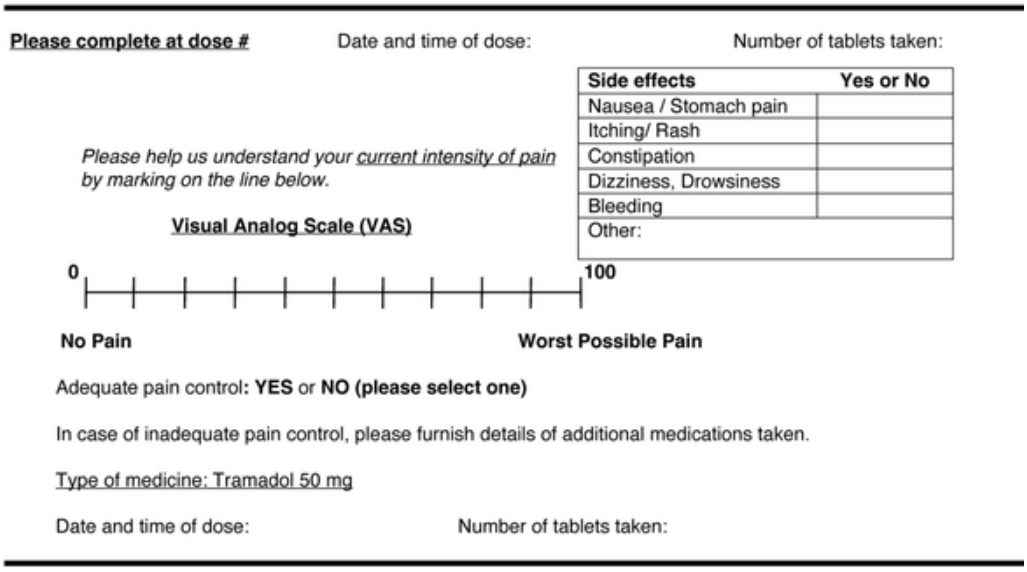
	Hydrocodone 5 mg and Acetaminophen 325 mg (Treatment A) n=65	Ibuprofen 200mg and Acetaminophen 325 mg (Treatment B) n=65	Total	*p* value*
Pain VAS (0-100) Score, Mean (SD)	44 (14.1)	41.0 (16.3)	43.0 (15.3)	0.156
# of Study Drugs Utilized, Mean (SD)	16.0 (9.5)	19.0 (9.9)	18.0 (9.8)	0.112
# of Tramadol Tablets Utilized, Mean (SD)	1.0 (2.5)	2.0 (3.7)	2.0 (3.1)	0.803
Number of Patients who Utilized Tramadol for Breakthrough Pain, n (%)	19 (29%)	15 (23%)	34 (26.1%)	0.425
Side Effects Experienced from Study Drugs, n (%)				
Nausea	17 (26%)	13 (20%)	30 (23%)	0.405
Itchiness	14 (22%)	2 (3%)	16 (12%)	0.001
Constipation	22 (34%)	19 (29%)	41 (32%)	0.571
Dizziness	41 (63%)	31 (48%)	72 (55%)	0.078
Bleeding	30 (46%)	28 (43%)	58 (45%)	0.724
Headache	9 (14%)	8 (12%)	17 (13%)	0.795
Other	7 (11%)	3 (5%)	10 (8%)	0.188
Response to Query – Adequate Pain Control or Not, n (%)				
No	4 (6%)	2 (3%)	6 (5%)	0.403
Yes	61 (94%)	63 (97%)	124 (95%)	

* *p*-values from t-test for Mean (SD=Standard deviation) and from Pearson Chi2-test or Fisher's exact (if n<5) for n=Frequency (Percentage); Visual Analog Scale (VAS)

Table 3: Mean Change in Patient Reported Outcome Score (Δ)

Variable	N	Mean	SD	95% CI		*p*-value
SCHNOS-O						
Treatment A	65	-25.7	35.0	-34.4	-17.0	
Treatment B	65	-23.4	41.9	-33.8	-12.9	
Total	130	-24.5	38.4	-31.2	-17.8	
Difference		-2.3		-15.8	11.1	0.7318
SCHNOS-C						
Treatment A	65	-39.6	30.7	-47.2	-32.0	
Treatment B	65	-36.0	34.2	-44.5	-27.5	
Total	130	-37.8	32.4	-43.4	-32.2	
Difference		-3.6		-14.9	7.7	0.5267
VAS-F						
Treatment A	52	-1.8	3.0	-2.7	-1.0	
Treatment B	54	-1.8	3.5	-2.7	-0.8	
Total	106	-1.8	3.3	-2.4	-1.2	
Difference		-0.1		-1.3	1.2	0.9158
VAS:A						
Treatment A	52	-1.5	2.7	-2.3	-0.8	
Treatment B	54	-1.2	3.1	-2.0	-0.3	
Total	106	-1.3	2.9	-1.9	-0.8	
Difference		-0.4		-1.5	0.8	0.5351

* *p*-value from two sample t-test; SD=Standard deviation, Standardized Cosmesis and Health Nasal Outcomes Survey (SCHNOS), Visual Analog Scale (VAS), Aesthetic (A), Functional (F), Hydrocodone-5 mg and Acetaminophen-325 mg group (Treatment A), Ibuprofen-200mg and Acetaminophen-325 mg (Treatment B). For the analyses of the SCHNOS (O and C) and the VAS (F and A) scores, since all 130 patients did not have a postoperative score at both time intervals, a mean postoperative score (SD) was calculated for each treatment group compared to their mean preoperative scores utilizing a paired t-test. The calculated mean changes in score (Δ) was compared between the two treatment groups utilizing an unpaired t-test.



Please complete at dose # Date and time of dose: Number of tablets taken:

Side effects	Yes or No
Nausea / Stomach pain	
Itching/ Rash	
Constipation	
Dizziness, Drowsiness	
Bleeding	
Other:	

Please help us understand your current intensity of pain by marking on the line below.

Visual Analog Scale (VAS)

0 100

No Pain **Worst Possible Pain**

Adequate pain control: **YES** or **NO (please select one)**

In case of inadequate pain control, please furnish details of additional medications taken.

Type of medicine: Tramadol 50 mg

Date and time of dose: Number of tablets taken:

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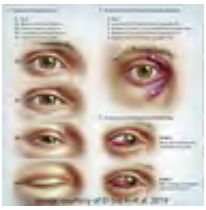

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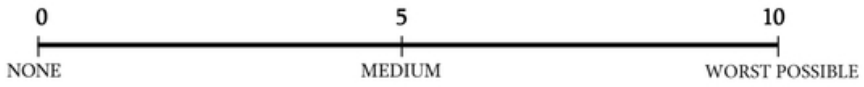
STANDARDIZED COSMESIS AND HEALTH NASAL OUTCOME SURVEY (SCHNOS)

Over the past **month**, how much of a **problem** was the following:

	No problem					Extreme problem
1. Having a blocked or obstructed nose	0	1	2	3	4	5
2. Getting air through my nose during exercise	0	1	2	3	4	5
3. Having a congested nose	0	1	2	3	4	5
4. Breathing through my nose during sleep	0	1	2	3	4	5
5. Decreased mood and self-esteem due to my nose	0	1	2	3	4	5
6. The shape of my nasal tip	0	1	2	3	4	5
7. The straightness of my nose	0	1	2	3	4	5
8. The shape of my nose from the side	0	1	2	3	4	5
9. How well my nose suits my face	0	1	2	3	4	5
10. The overall symmetry of my nose	0	1	2	3	4	5

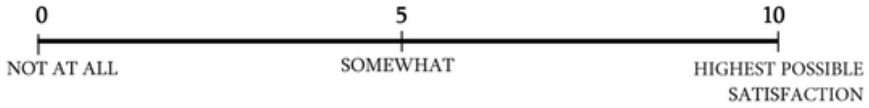
Visual Analog Scale- Functional (VAS-F)

11. Please mark on this line how troublesome is your difficulty in breathing through your nose



Visual Analog Scale- Aesthetic (VAS-A)

12. Please mark on this line how satisfied you are with the appearance of your nose



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