

Fitostimoline® in fibro-endoscopic and trans-nasal trans-speculum septoplasty as a beneficial tool to improve post-surgical outcome: Preliminary results of a case-control study

Pietro De Luca^{a,1}, Ignazio La Mantia^b, Federico Maria Gioacchini^c, Massimo Re^c,
Marco Radici^a, Angelo Camaioni^d, Arianna Di Stadio^{b,*,1}

^a Otolaryngology Department, Fatebenefratelli Isola Tiberina - Gemelli Isola, Rome, Italy

^b GF Ingrassia Department, Otolaryngology Unit, University of Catania, Catania, Italy

^c ENT Unit, Department of Clinical and Molecular Sciences, Polytechnic University of Marche, Ancona, Italy

^d Otolaryngology Department, San Giovanni-Addolorata Hospital, Rome, Italy

ARTICLE INFO

Keywords:

FEES
Septoplasty
Nasal mucosa
Synechia
Surgical outcomes
Gauze
Ointment
Nasal breathing

ABSTRACT

Objectives: Topic treatment can be useful to improve short and long-term nasal outcomes after nasal surgery, reducing discomfort and risk of synechia. This study aimed at evaluating the effect on clinical outcomes of nasal packaging using Fitostimoline® gauze in FESS and septoplasty.

Methods: A case-control study on hospitalized patients was performed in a tertiary referral center. The control group included 20 patients treated with the standard surgical protocol for septoplasty and standard nasal packaging; treatment group included 21 patients underwent same surgical procedure but in whom the nasal tampon was wrapped with a gauze containing Fitostimoline® before being placed into the nose.

Results: Patients in treatment group had better outcomes than control; nasal mucosa showed better healing - recovery of normal color- in those patients in whom we applied the Fitostimoline® gauze around tampons. Moreover, 100 % patients in the treatment group did not refer discomfort during at tampon removal versus 60 % subjects in the control group who referred pain, tension or tearing during the same action.

Conclusion: Our results, although preliminary because of the small cohort of subjects included, suggest that the apposition of a gauze with Fitostimoline® after nasal surgery might improve the mucosal healing with consequent reduction of patients discomfort during the post-surgical period.

1. Introduction

Functional nasal surgery comprises a vast range of nasal approaches and procedures that are proposed based on individually pathological condition. Conventional trans-nasal trans-speculum. (TNTS) septoplasty and fibro-endoscopic (FE) septoplasty are both valid solutions to improve the respiratory function in patients affected by anatomical obstruction of nasal choana [1]. Traditional septoplasty allows the removing of septal defects and remodeling of irregular cartilage and bone portions and can be associated to rhinoplasty, when necessary, to improve both functional and aesthetic functions [2]. The use of an endoscopy to perform septoplasty allows directs vision of the tissue and to carefully explore the nasal cavities to identify and remove polyps or

hypertrophic tissue (chronic sinusitis) and tumors. As additional can be used for closure of nasal fistula and removal of pituitary tumors [3].

Overall TNTS septoplasty and fibro-endoscopic septoplasty have strength -they improve the anatomy and the physiology of nose, nasal choana and paranasal sinus- and weakness-risks of hypertrophic scare and re-obstruction of the ostiomeatal complex [2]. In fact, despite the complications related to the nasal mucosa manipulation and inflammation seems less in endoscope-assisted septoplasty compared to the traditional one [4], bad outcomes like formation of synechiae between the middle turbinate and lateral nasal wall can be observed. The presence of synechia can reduce the respiratory flow and create unsatisfactory results for the patient; to reduce the risk of this unpleasant problem the surgeons are used to do nasal packing after septoplasty so to prevent

* Corresponding author at: GF Ingrassia Department, University of Catania, Italy.

E-mail address: arianna.distadio@unict.it (A. Di Stadio).

¹ Equal contribution as first author.

synechiae, hemorrhage and septal hematoma [5]; anyway, nasal packing procedures may cause a mucosal trauma from which local infections can arise [6].

The macroscopic good appearance of the nasal mucosa could not correspond to its microscopic integrity; the latter modifying the nasal clearance might be responsible of the unsatisfactory nasal breathing sensations (persistent obstruction) reported by some patients. This phenomenon is probably related to post traumatic dysregulation occurring in the nasal wall mucosa that determines loss of nasal ability of heating and humidifying the air flow into the nasal cavities [7]. In addition, the nasal immunological capacity could be compromised in case of bad mucosal healing [8].

Cho et al. in 2020 in their multicenter randomized study showed that using Rhino-protect was possible to improve the outcomes of FESS. The authors concluded that the application of the ointment reduced the formation of edema and crusts, leading to improving the patients' discomfort for pain, dryness, and crust [9]. Various substances with different administration methods were proposed as adjuvants to favor a rapid wound healing after nasal surgery [1,8–10].

Our study aimed at evaluating the effectiveness of Fitostimoline® gauzes, based on patented triticum vulgare extract and Phenossietanol, as pharmacological option to ameliorate nasal mucosal healing and relieve nasal discomfort in patients who performed TNTS septoplasty and FE septoplasty.

2. Material and methods

This case-control study was conducted from August 2022 to December 2022 in a tertiary referral center in Italy (San Giovanni-Addolorata Hospital, Rome). All enrolled patients signed a written consent before the inclusion in the study to declare their interest in participating. The study was approved by the Internal Review Board (IRB) of the hospital with number RM23XX. Our research was conducted in respect of the Helsinki rule for human rights.

Patients were sequentially numbered; even numbers were assigned to control, while odd numbers to the treatment group at the moment of the first consultation. Then they were allocated 2:1 to TNTS or FE septoplasty to obtain a homogeneous distribution of the subjects among the two groups. The first consultation was done by a physician not involved in the surgery, who also did the evaluation (including tampon removal) at T1 and T2 and was blinded about patient belonging group.

Patients assigned to the control group performed the standard surgical protocol for traditional septoplasty or fibro-endoscopic septoplasty and at the end of the surgery were medicated by standard nasal tampon wrapped with Surgicel (Ethicon); the same surgical procedures were performed in the treatment group but, in these cases, the nasal tampon were wrapped with Fitostimoline® gauze based on patented triticum vulgare extract (Damor Pharmaceutical, Naples, Italy) before being placed. To maintain the blinding of the first operator, the nurse prepared the tampon to place after surgery.

We applied inclusion and exclusion criteria. *The inclusion criteria* were age between 18 and 69 years, diagnosis of septal deviation, hypertrophy of inferior turbinate, presence of subjective nasal breath deficit, no previous nasal surgery. *The exclusion criteria* were patients with autoimmune disease, cystic fibrosis, coagulation disorders, pregnancy, diabetes, sinonasal malignancy, severe cognitive impairment, previous chemotherapy, or radiotherapy treatment or declining/withdrawn participation.

All patients were evaluated as following: before surgery (T0) by Sino-Nasal Outcome test (SNOT)-22 questionnaire, nasal endoscopy with 0° or 30° endoscopes, Lund Kennedy (LK) endoscopy score. 15 days after surgery (T1) all patients were re-evaluated by nasal endoscopy with 0° or 30°, LK score and SNOT-22. Then 45 days after surgery (T2) the subjects were checked by nasal endoscopy with 0° or 30°, LK score and SNOT-22. As additional we asked to all the patients (control and treatment) if they had discomfort (pain, tension or tearing) at the moment of

tampon removal. The conditions of nasal mucosa were evaluated using Kim e al. assessment [11]. In case of hyperemia “1” was assigned, in presence of normal color “0”.

Surgical Techniques Septoplasty was performed as described by Watters et al. in 2022 [12]; fibro-endoscopic septoplasty as previously describe by Na’ara et al. [4].

All patients (treatment and control) performed nasal washes with physiologic tamponade solution two times a day until follow-up at 30 days; after this follow-up all patients suspended nasal wash.

2.1. Statistical analysis

One-way ANOVA was used for comparing the score of the SNOT questionnaire within and between the group at the different follow-ups (T0, T1 and T2). The same test was performed to evaluate the variations of the LK scores. One-way ANOVA was used to analyze the variations at the different follow-ups of the condition of mucosa within and between the groups. Finally, because rhinorrhea was considered as nominal data (presence or absence) this outcome was analyzed by using Chi-square (χ). The same analysis was done to evaluate the discomfort at the moment of tampon removal. *p* was considered significant <0.05. All tests were performed by Stata®.

3. Results

3.1. General

A total of 41 patients (25 men and 16 women) age 36.6 + 13.2 were collected. 21 subjects (13 men and 8 women) age 36.8 ± 13.5 were in the treatment (nasal tampon + Fitostimoline® gauze)) group and 20 (12 men and 8 women) age 36.5 + 13.2 in the control (standard treatment with nasal tampon only). All patients included in the study were affected by nasal septal deviation and subjective respiratory nasal concerns. Considering the entire number of patients 56.1 % of the sample presented a right nasal septum deviation (23 subjects) and 43.9 % a left sided septal deviation (18 people). 12 patients with right sided deviation were in the treatment group and 11 in the control; the remaining patients presented left septal deviation, 8 in the treatment and 10 in control. 4 patients in the treatment group and 5 in the control suffered from nasal allergies (different allergens) (Table 1).

3.2. SNOT (Fig. 1A)

Patients both in the treatment group and in the control improved the score of the SNOT comparing the changes between T0, T1 and T2 with statistically significant value (ANOVA: *p* < 0.0001). In detail, treatment group showed statistically significant improvement of the SNOT comparing T0 and T1 (BH: *p* < 0.01) and T0 and T2 (BH: *p* < 0.01);

Table 1
Characteristic of patients included in the study.

Variable	Group 1 (n = 21)	Group 2 (n = 20)	P
Mean age ± SD (range), yr	36.8 ± 13.22 (18–61)	36.5 ± 12.88 (18–58)	>0.05
Gender - no (%)			n/a
Female	8 (38 %)	8 (40 %)	
Male	13 (62 %)	12 (60 %)	
Type of surgery - no. (%)			n/a
Traditional septoplasty	13 (62 %)	14 (70 %)	
Fibro-endoscopic septoplasty	8 (38 %)	6 (30 %)	
Pre-operative (T0) SNOT-22 results, mean ± SD (range)	41.9 ± 11.51 (29–60)	42.8 ± 11.46 (22–60)	>0.05
Post-operative -month (T1) SNOT-22 results, mean ± SD (range)	19.9 ± 8.86 (8–37)	18.2 ± 8.62 (4–38)	>0.05
Post-operative -month (T2) SNOT-22 results, mean ± SD (range)	4.7 ± 5.75 (0–18)	3.68 ± 4.43 (0–12)	>0.05

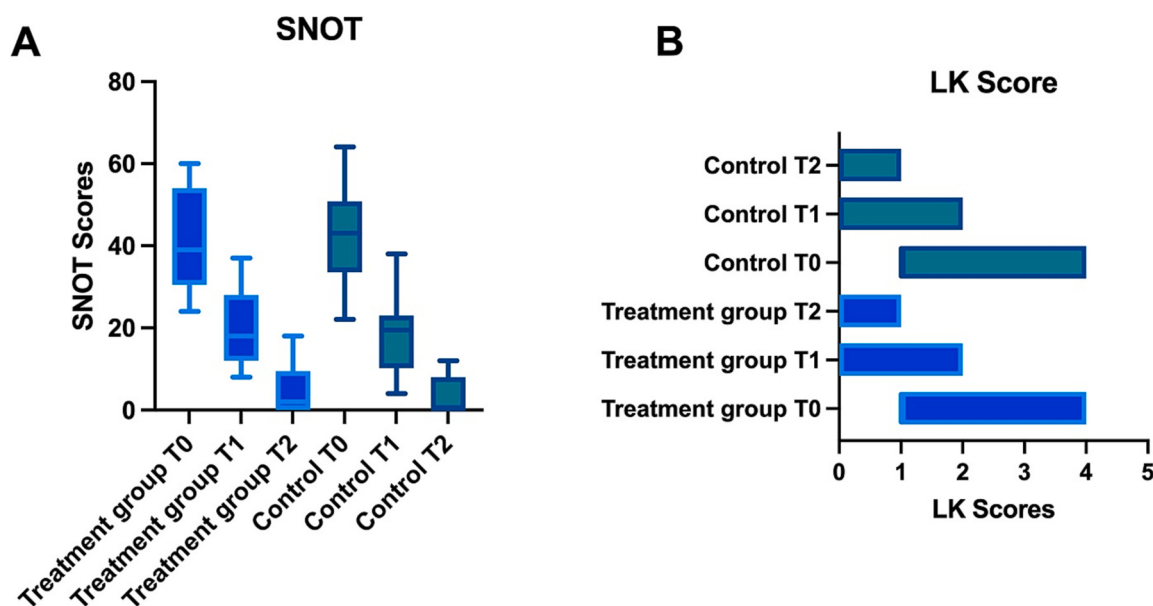


Fig. 1. Comparison of SNOA and LK score changes among control and treatment group of patients. A) Comparison of SNOT score changes between T0, T1 and T2. B) Comparison of LK score changes between T0, T1 and T2.

statistically significant improvements were observed in this group comparing T1 and T2 (BH: $p < 0.01$).

Control group showed statistically significant improvement of the SNOT comparing T0 and T1 (BH: $p < 0.01$) and T0 and T2 (BH: $p < 0.01$); statistically significant improvements were observed in this group comparing T1 and T2 (BH: $p < 0.01$).

No statistically significant differences were observed between groups comparing the SNOT score at T0 (HB: $p > 0.05$), T1 (HB: $p > 0.05$) and T2 (HB: $p > 0.05$).

3.3. LK (Fig. 1B)

Patients both in the treatment group and in the control improved the LK score comparing the changes between T0, T1 and T2 with statistically significant value (ANOVA: $p < 0.0001$). In detail, treatment group showed statistically significant improvement of the LK comparing T0 and T1 (BH: $p < 0.01$) and T0 and T2 (BH: $p < 0.01$); without statistically significant differences between T1 and T2 (BH: $p > 0.05$). Control group

showed statistically significant improvement of the LK comparing T0 and T1 (BH: $p < 0.01$) and T0 and T2 (BH: $p < 0.01$); without statistically significant differences between T1 and T2 (BH: $p > 0.05$).

No statistically significant differences were observed between groups comparing the LK score at T0 (HB: $p > 0.05$), T1 (HB: $p > 0.05$) and T2 (HB: $p > 0.05$).

3.4. Mucosa aspect (Fig. 2A)

Statistically significant improvements (reduction of nasal mucosa hyperemia) (ANOVA: $p < 0.001$) were observed comparing T0 and T1 ($p < 0.05$) and T0 and T2 ($p = 0.01$) only in the treatment group.

No statistically significant changes were instead observed in the control ($p < 0.05$). The differences between the two groups for this finding were statistically significant ($p = 0.01$).

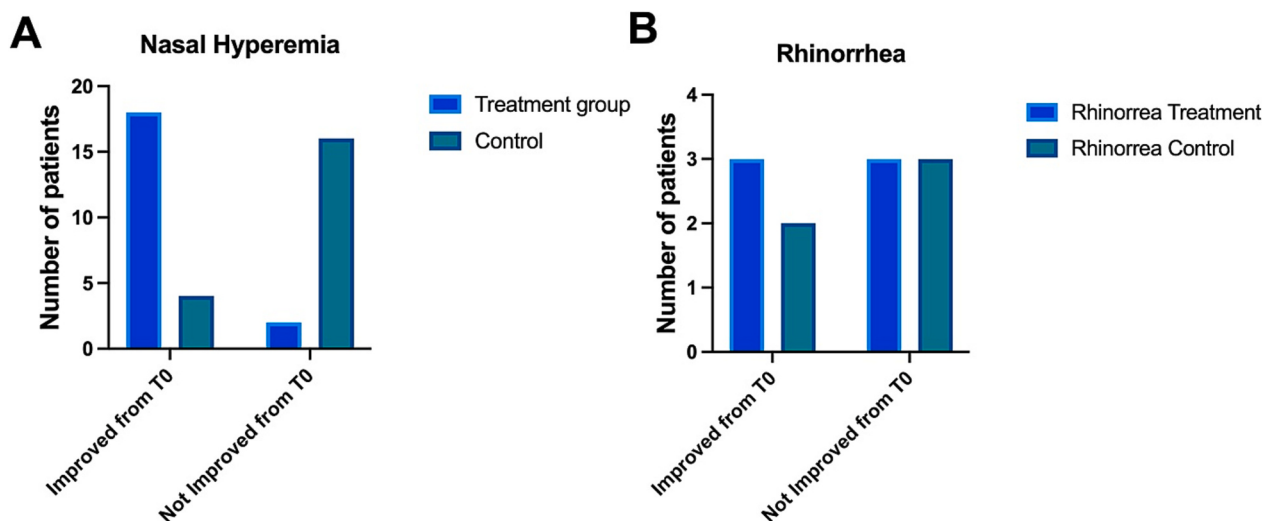


Fig. 2. Comparison of nasal hyperemia and rhinorrhea score changes among control and treatment group of patients. A) Comparison of nasal hyperemia score changes between T0, T1 and T2. B) Comparison of rhinorrhea score changes between T0, T1 and T2.

3.5. Rhinorrhea (Fig. 2B)

7 patients (33 %) in the treatment group suffered from rhinorrhea and 5 (25 %) had the same symptom in the control at the baseline (T0). No statistically significant differences were observed among groups ($p > 0.05$).

4 (57.1 %) of the 7 in the treatment group improved this symptom at T2, 2 (40 %) of the 5 in the control noted a reduction of the phenomenon at T2.

No statistically significant differences were observed within ($p > 0.05$) and between ($p > 0.05$) groups looking at the improvement of rhinorrhea.

3.6. Discomfort during tampon removal

None of the patients in the treatment group referred discomfort during the removal of tampon, while 60 % (12 on 20) patients in the control suffered from pain (4), sensation of tension (6) and tearing sensation (2). The difference between treatment and control groups was statistically significant ($p = 0.0016$) (Fig. 3).

4. Discussion

Our results confirmed the efficacy of TNTS and FE septoplasty as valid tools to solve nasal obstruction related to nasal septal deviation mechanical problem, as showed by the improvement of the SNOT and LK scores comparing baseline and the other observation points [1,4].

Although FE has been described as less aggressive and invasive of TNTS [1,4], the nasal mucosa through sub-perichondral detachment undergoes micro-trauma despite not clearly visible [13]. The improvement of the septal anatomy ameliorates the nasal clearance, but the micro-trauma on the mucosa prolongs the time of micro-wound healing explaining the reason why patients need months to fully appreciate their improved respiratory functions [13].

The susceptibility to the trauma, as well as the inflammatory response, are individual characteristics, so it is hard to predict the effect of the surgery on the nasal mucosa. Anyway, it is possible to indirectly evaluate the inflammation after surgery by analyzing the color of the mucosa and the presence of some symptoms as rhinorrhea [11].

In this study, we observed that, independently from the surgical technique used (TNTS or FE septoplasty), only the patients in the treatment groups presented a statistically significant improvement of

their nasal findings at T2; in fact, the comparison of the mucosa aspects between treatment and control group only showed the patients in treatment group recovered of normal color after 30 (T1) and 45 (T2) days after surgery (Fig. 2A).

Rhinorrhea, which is the sign of hyperactivity of the nasal mucosa [14], although was reduced more in the treatment than in control, did not reach statistically significant results. These data could be justified by the small sample analyzed, and by the fact that only few patients presented this symptom at the baseline (Fig. 2B).

The use of Fitostimoline® gauze was able to totally delete the nasal discomfort generally perceived by the patients at the moment of tampon removal; in fact, 100 % of patients in treatment group versus 40 % in the control did not refer pain, tension or tearing during the removal of tampon. We speculate that this benefit was related to the hydration guaranteed by the cream and anti-inflammatory proprieties of the component of the Fitostimoline® [15]. This drug could ameliorate wound healing because stimulates fibroblast and reduce the local inflammatory process [16]. Analyses of mucociliar transport on animal should be performed to explain the exact effect that Fitostimoline has on nasal mucosa.

This treatment in form of soaked gauzes and cream was widely employed from some decades in the management of dermatological alterations in which a stimulation of repairing processes (e.g., ulcerative-dystrophic damages, burns, delay in healing) is required [15]; the aqueous extract of *Triticum vulgare* which is the active ingredient of Fitostimoline®-based treatments can rapidly activate the tissues repairing stages by stimulating chemotaxis and the fibroblastic maturation [16]; these phenomena significantly increase the fibroblastic index, which is an essential element in wound repairing processes [16].

To date gauzes are rarely used for the treatment of skin lesions because cream are preferred; however, these tools are largely used in nasal surgery to avoid adhesion of nasal tampon on the mucosa. As additional, gauzes with cream are largely used in aesthetic rhinoplasty to substitute nasal tampon, to guarantee blood coagulation and avoid patient's discomfort.

The wound healing in the nasal mucosa has different phases; as first there is the coagulation process 5–10min after trauma, followed by inflammation during 24–48 h after surgery. During the following days, average 4 days, the phase of tissue re-growth starts. The last phase of healing is represented by the tissue remodeling that could continue approximately until 6 months after surgery. During these processes the extracellular matrix provides nutrients, support and adhesion for structural cells participating in the repair process [17]; growth factor and cytokines play an important role in this healing process. In fact, pro-inflammatory cytokines can extend and worsening the healing process due to an uncontrolled inflammation [17]. Several molecules, as for example topical N-acetyl-cysteine (NAC), have been used with good results [18,19]. However, because NAC has anti-coagulant proprieties could not be the best option after septoplasty because could increase the post-operative bleeding risk. Other substances like Silver sucrose octasulfate have been tries [20] to improve surgical outcomes after nasal surgery; this molecule has anti-microbial proprieties and indirectly improves the nasal healing reducing the risk of post-surgical infection, and improving nasal flora. The latter concurs to reduce nasal inflammation [8]. Several studies [21,22] have been performed by using hyaluronic acid (HA) to prevent bad outcome after septoplasty, but the most consistent results have been extracted by a recent meta-analysis. This recent study showed that the main effect of HA is reducing the adhesion rate after sinus surgery [23].

Despite preliminary, our results seem very promising. In fact, the application of the gauze with Fitostimoline on the nasal tampon presents a series of practical advantages, in addition to the improvement of mucosa healing. As first it maintains the nasal environment hydrated, and this could potentially reduce the formation of crust [16,17]; then it allows simple removal of the tampons because facilitates the slip and reduces the pain and discomfort for patients.

Discomfort during tampon removal

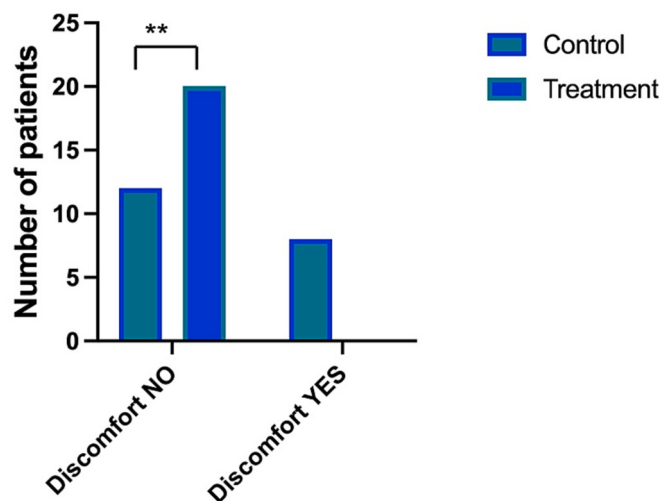


Fig. 3. Comparison of discomfort during tampon removal. “***” indicates $p < 0.001$.

4.1. Study limitations

This study presents some limitations. As first the small sample size; larger sample are necessary to confirm our results. Secondly, the patients did not have performed specific analyses of mucociliary transport that could explain how the drug acts on nasal mucosa. As third, the method used to evaluate both rhinorrhea and color of nasal mucosa is quite subjective (despite to limit the inter-operator bias the controls have been made by the same physician).

5. Conclusion

Despite preliminary, the statistically significant reduction of mucosa hyperemia in those patients, in whom we applied Fitostimolone gauze, after TNTS or FE septoplasty, seems suggesting that these gauze might improve mucosal wound healing. Both surgeries are notable resolute to treat septal nasal deviation; however, in some cases, despite the excellent surgical results, the presence of bad nasal mucosa healing, ie crust or synechiae, are perceived as a fail by the patients. The use of Fitostimoline® gauze reducing the inflammation in the nasal mucosa might improve wound healing, reducing bad outcomes. Moreover, these particular gauzes facilitates the removal of tampon improving the comfort in these patients.

Ethical approval

This prospect research was approved by the Ethic Committee of San Giovanni-Addolorata Hospital (10/06/2022/4563-22).

Funding

No funding to declare.

Declaration of competing interest

The authors declare no conflicts of interest.

Data availability

This study has no supplementary available data.

References

- [1] Paradis J, Rotenberg BW. Open versus endoscopic septoplasty: a single-blinded, randomized, controlled trial. *J Otolaryngol Head Neck Surg* Feb 2011;40(Suppl. 1): S28–33 [PMID: 21453658].
- [2] Balaguer García R, Mompó Romero L, Carrasco Llatas M, Cuesta González MT, Dalmau Galofre J. Septorhinoplastias, un estudio descriptivo [Septoplasty and rhinoplasty, a descriptive study]. *Acta Otorrinolaringol Esp* Nov-Dec 2009;60(6): 383–9 [Spanish], <https://doi.org/10.1016/j.otorri.2009.06.004>.
- [3] Yildirim U, Kemal O, Aksoy A, Karaca E, Terzi O, Atmaca S. Effects of submucosal PRP injection on wound healing in endonasal surgeries: an experimental study. *Eur Arch Otorhinolaryngol* Jun 2020;277(6):1681–9. <https://doi.org/10.1007/s00405-020-05884-1>.
- [4] Na'ara S, Kaptzan B, Gil Z, Ostrovsky D. Endoscopic septoplasty versus traditional septoplasty for treating deviated nasal septum: a prospective, randomized controlled trial. *Ear Nose Throat J* Nov 2021;100(9):673–8. <https://doi.org/10.1177/0145561320918982>.
- [5] Berlucchi M, Castelnovo P, Vincenzi A, Morra B, Pasquini E. Endoscopic outcomes of resorbable nasal packing after functional endoscopic sinus surgery: a multicenter prospective randomized controlled study. *Eur Arch Otorhinolaryngol* Jun 2009; 266(6):839–45. <https://doi.org/10.1007/s00405-008-0841-3>.
- [6] Gioacchini FM, Alicandri-Ciuffelli M, Kaleci S, Magliulo G, Re M. The role of antibiotic therapy and nasal packing in septoplasty. *Eur Arch Otorhinolaryngol* May 2014;271(5):879–86. <https://doi.org/10.1007/s00405-013-2578-x>.
- [7] Kayahan B, Ozer S, Suslu AE, Ogretmenoglu O, Onerci M. The comparison of the quality of life and intranasal edema between the patients with or without nasal packing after septoplasty. *Eur Arch Otorhinolaryngol* Mar 2017;274(3):1551–5. <https://doi.org/10.1007/s00405-016-4403-9>.
- [8] Di Stadio A, Costantini C, Renga G, Pariano M, Ricci G, Romani L. The microbiota/host immune system interaction in the nose to protect from COVID-19. *Life (Basel)* Dec 11, 2020;10(12):345.
- [9] Di Stadio A, Della Volpe A, Ralli M, Ricci G. Gender differences in COVID-19 infection. The estrogen effect on upper and lower airways. Can it help to figure out a treatment? *Eur Rev Med Pharmacol Sci* May 2020;24(10):5195–6.
- [10] Cho KS, Kim SW, Kim JK, Kim CH. Efficacy of rhino-protect ointment after endoscopic sinus surgery: a prospective, randomized, multicenter study. *Eur Arch Otorhinolaryngol* Jan 2021;278(1):109–15.
- [11] Kim K, Yun Y, Nam HJ, et al. Inter- and intra-rater reliability of a nasal endoscopy index for pattern identification in patients with allergic rhinitis. *Orient Pharm Exp Med* 2015;15:167–71.
- [12] Watters C, Brar S, Yapa S. Septoplasty. (2022) Nov 8. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; Jan 2022. 33620795.
- [13] Sakallıoğlu O, Düzer S, Kapusuz Z, Soylu E. The evaluation of nasal mucociliary activity after septoplasty and external septorhinoplasty. *Indian J Otolaryngol Head Neck Surg* Aug 2013;65(Suppl. 2):360–5. <https://doi.org/10.1007/s12070-012-0532-7>.
- [14] Baraniuk JN, Kim D. Nasonasal reflexes, the nasal cycle, and sneeze. *Curr Allergy Asthma Rep* May 2007;7(2):105–11. <https://doi.org/10.1007/s11882-007-0007-1> [PMID: 17437680].
- [15] Martini P, Mazzatenta C, Saponati G. Efficacy and tolerability of fitostimoline in two different forms (soaked gauzes and cream) and citrizen gel in the topical treatment of second-degree superficial cutaneous burns. *Dermatol Res Pract* 2011; 2011:978291. <https://doi.org/10.1155/2011/978291>.
- [16] Fiore, Scapagnini U, Riccio S R, Canonico PL. Differential activities of *Triticum vulgare* extract and its fractions in mouse fibroblasts. *Acta Therapeutica* 1993;19 (2):151–62.
- [17] Watelet JB, Bachert C, Gevaert P, Van Cauwenberge P. Wound healing of the nasal and paranasal mucosa: a review. *Am J Rhinol* 2002;16(2):77–84.
- [18] Yılmaz B, Türkçü G, Şengül E, Gül A, Özkurt FE, Akdağ M. Efficacy of N-acetylcysteine on wound healing of nasal mucosa. *J Craniofac Surg* Jul 2015;26(5): e422–6. <https://doi.org/10.1097/SCS.0000000000001880>.
- [19] Gomez-Aparicio LS, Bernáldez-Sarabia J, Camacho-Villegas TA, Lugo-Fabres PH, Díaz-Martínez NE, Padilla-Camberos E, et al. Improvement of the wound healing properties of hydrogels with N-acetylcysteine through their modification with methacrylate-containing polymers. *Biomater Sci* Feb 9, 2021;9(3):726–44. <https://doi.org/10.1039/d0bm01479f>.
- [20] Ottaviano G, Blandamura S, Fasanaro E, Favaretto N, Andrea L, Giacomelli L, et al. Silver sucrose octasulfate nasal applications and wound healing after endoscopic sinus surgery: a prospective, randomized, double-blind, placebo-controlled study. *Am J Otolaryngol* Sep-Oct 2015;36(5):625–31. <https://doi.org/10.1016/j.amjoto.2015.02.014>.
- [21] Kimmelman CP, Edelstein DR, Cheng HJ. Sepragel sinus (hylan B) as a postsurgical dressing for endoscopic sinus surgery. *Otolaryngol Head Neck Surg* 2001;125: 603–8. <https://doi.org/10.1067/mhn.2001.120229>.
- [22] Shi R, Zhou J, Wang B, Wu Q, Shen Y, Wang P, et al. The clinical outcomes of new hyaluronan nasal dressing: a prospective, randomized, controlled study. *Am J Rhinol Allergy* 2013;27:71–6. <https://doi.org/10.2500/ajra.2013.27.3833> [PMID: 23406605].
- [23] Fong E, Garcia M, Woods CM, Ooi E. Hyaluronic acid for post sinus surgery care: systematic review and meta-analysis. *J Laryngol Otol* Jan 2017;131(S1):S2–11. <https://doi.org/10.1017/S0022215116009269>.